



“Being Human”: A Grounded Theory of Complexity and Serendipity in Cancer Clinical Trials

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“Being Human”: A Grounded Theory of Complexity and Serendipity in Cancer Clinical Trials

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Declaration of Authorship

I declare that this thesis and the work presented herein is the result of my own original research.

Signed: Helene Markham Jones

Date:

Abstract

Background

Cancer presents a complex and intractable disease resulting in millions of deaths worldwide each year. As a metastatic disease bearing metamorphic characteristics, cancer's emergent properties continue to challenge science, medicine, and society. Cancer research is a specialist field crucial to the advancement of patient treatment and care, yet it faces growing challenges due to the complex nature of an evolving disease, stratified treatments, and intensive trial protocols, compounded by increasing global disease burdens. Human ingenuity and resiliency are central to overcoming the greatest challenges facing contemporary populations, achieved through research innovation and knowledge exchange across ranging disciplines. Improving population health and patient-centred outcomes stands at the fore of global challenges facing society in the twenty first century, requiring novel and dynamic responses to increasing chronic disease burdens and exposure risks to emergent viral pathogens.

Aims

The aim of this thesis was to understand the nature of cancer clinical trial operational delivery, evaluating challenges and burdens of professionals and patients participating in cancer research studies. The nature of multi-agency working and transdisciplinarity across health sciences is as complex as the biological and societal challenges that their research seeks to address. Establishing sustainable, cohesive, and collaborative relationships across the medical continuum is pivotal to solving persistent challenges of complex diseases and societal burdens. The study sought to develop a contextualised grounded theory elucidating situated challenges and complexity experienced at NHS sites in the UK. The purpose of the grounded theory would be to support the development of enhanced, person-centred models of clinical research operational delivery, which could respond to emergent and dynamically adaptive healthcare and epidemiological population needs.

Methods

Evaluating Follow-up and Complexity in cancer Clinical Trials (EFACCT), the study presented in this thesis, was conducted at ranging NHS secondary care sites in England and Scotland. Drawing on constructivist grounded theory (Charmaz, 2006), the multi-faceted realities of cancer clinical trial delivery are unveiled, using a mixed methods—grounded theory (MM-GT) design. The comprehensive, contextual evaluation combines

evidence from quantitative and qualitative paradigms, using inductive and deductive methods. The study drew together multifaceted perspectives and values of 165 participants from six studies; Delphi, questionnaire, and interview studies, separated into patient and professional cohorts.

Results

The research provides original insights into the nature of cancer research delivery, its challenges and complexities, highlighting the importance of coherency in healthcare systems. The Constructivist Grounded Theory presented in this thesis, provides an organising framework and practical model for managing and embracing transformative learning and practice in response to dynamically evolving challenges that exist within complex healthcare delivery systems and networks. The original data generated provides new knowledge on the human aspects of clinical research and the contexts for its practice. The situated experiences led to the development of a grounded theory of human perceptions of complexity and serendipity in clinical research and the conception of a Prismatic Coherence Model (PCM) for the evaluation and designing of patient care and follow-up and the effective operational management of complex relationships, practices and processes existing within adaptive clinical research and healthcare delivery systems. PCM is an inclusive and responsive strategic design approach, sensitive to variable contexts and system complexities, and promotes transdisciplinarity in order to advance opportunities, knowledge and resources to advance population health through clinical research.

Publications

Conference Abstracts

Markham-Jones, H., Bridle C., and Ahmed T. (2017) A protocol for evaluation Study of Patient Follow-Up and Cancer Clinical Trial Complexity: the EFACCT study, 2017 The NCRI Cancer Conference, November 5-8, Liverpool

Poster Presentations

Markham-Jones, H., Curtis F., G., Law., Bridle C. and Ahmed T. (2019) Mapping the Cancer Clinical Research Landscape to develop a Trial Rating and Complexity Tool: TRACAT and the EFACCT Study. Conference stand and poster presentation at: Connected, EDGE Annual Conference; 2019 Apr 03-04; Birmingham.

Journal Articles

Jones HM, Curtis F, Law G, et al. Evaluating follow- up and complexity in cancer clinical trials (EFACCT): an eDelphi study of research professionals' perspectives. *BMJ Open* 2020;0: e034269. doi:10.1136/ bmjopen-2019-034269

Dedication

In Piam Memoriam:

This work is lovingly dedicated to the memory of my mother, Ruth Mary Markham Jones.

Epigraph:

In Memoriam [Ring out, wild bells]

Ring out the grief that saps the mind

For those that here we see no more;

Ring out the feud of rich and poor,

Ring in redress to all mankind.

Ring out slowly a dying cause,

And ancient forms of party strife;

Ring in the nobler modes of life,

With sweet manners, purer laws.

In Memoriam. Alfred Lord Tennyson (1850).

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The expedition to possibilities undertaken in conducting this research and in writing this doctoral thesis has been made possible and memorable by the many special people with whom I collaborated and engaged with along the route.

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Finally, I would like to dedicate this research to the memory of my mother, Ruth Mary Markham, who worked for the NHS for her entire career. She bravely battled cancer for over ten years. To her and all other cancer patients who have fought or continue the fight against cancer, and to all the researchers around the world who are dedicated to beating this indiscriminate and destructive disease, I devote this study. This research was supported through cancer charitable funds provided in the memory of Roman Kopyt, to whose family I extend my untold thanks.

Abbreviations

CCT	Cancer Clinical Trial
CPMS	Central Portfolio Management System
CRN	Clinical Research Network
eCRF	Electronic Case Report Form
EFACCT	Evaluating Follow-up and Complexity in Cancer Clinical Trials
GCP	Good Clinical Practice
GTM	Grounded Theory Method
HSP	Highly Sensitive People
IQR	Interquartile Range
IS	Inquiring System
LCRN	Local Clinical Research Network
LPMS	Local Portfolio Management System
NIHR	National Institute for Health Research
NCRI	National Cancer Research Institute
TRACAT	Trial Rating and Complexity Assessment Tool
REC	Research Ethics Committee
R&I	Research and Innovation

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Chapter One: Introduction

“I was actually told it was secondary cancer, told obviously by the surgeon and the oncologist, ‘You’re the captain of the ship’, he said, ‘and I’m your second in command, so it’s for you to make this decision, and the decision will be yours and I will go along with whatever you decide, but I will guide you down that road.’” Participant ID: 005006.

1.1 Introduction

The complex realms of medical science, disease mechanisms and human health require dynamically evolving research innovation systems and frameworks to advance knowledge and support approaches to delivering sustainable and equitable healthcare solutions. Clinical research is a trans-disciplinary field of healthcare science, with a global purpose of translating empirical medical knowledge and scientific advancements into human health benefits. From studying the causes and mechanisms of disease, developing pharmaceutical and technological solutions, through to delivering effective medical practices and public health strategies, clinical research is a diverse and constantly evolving operational field. Such a dynamic interactional field is reliant upon effective, mutually dependent relationships between scientists, clinicians, research professionals and patients. Medical science and ethical standards have gradually evolved through methodological eras and paradigms of clinical research, progressing knowledge, and contributing to a continual advancement of clinical care (Nelhaus and Davies, 2017). Ranging professions, scientific disciplines and organisational networks collaborate in endeavours to innovative and progress medical treatments, regimens, devices, diagnostics, technologies, clinical epidemiology, and patient care. This thesis describes the complex realm of healthcare and cancer clinical research delivery, providing an illuminating, contextualised grounded theory, informed and developed by the situated experiences and perspectives of NHS research professionals and patients.

This chapter introduces the journey undertaken in studying cancer clinical trial operations within the UK’s national health service, the NHS. The study, entitled Evaluating Follow-Up and Complexity in Cancer Clinical Trials (EFACCT), was conducted at NHS clinical research hospital sites across Scotland and England. Research professionals and cancer trial participants engaged in a collaborative and detailed examination of the interacting systems, processes and complexities present within clinical trial delivery, and the treatment, management, and follow-up of patients. The voices and faceted perspectives of those patients and research professionals, who generously committed their time to the EFACCT study, provide unique insights into the complex mechanisms, relationships and dynamic

systems influencing cancer clinical trial delivery and patient care across ranging UK hospital trusts and geographical locations.

A guiding synopsis of the study stages and its inquiring framework are presented, alongside motivations for conducting an evaluation of the operational delivery of cancer clinical research trials and patient follow-up at NHS secondary care hospital sites. This opening chapter commences with a summary background to the research problem and a brief introduction to the history and development of clinical research. An orientation of relevant contextual settings and healthcare systems leads into a discussion of key thematic areas, and an overview of the study's aims, design, and researcher's positionality. The study's contribution to knowledge is introduced alongside its significance and limitations, followed by an outline structure of the thesis and the chapter's summary.

1.2 Background and Rationale

In a new era of personalised medicine and a century characterised by exponential growth in technological and societal complexity (Kodish, 2014), evaluation of the capacities and capabilities of healthcare organisations and systems is needed, to support equitable and sustainable models of health. Population growth and disease burdens pose complex societal challenges requiring innovation in clinical and epidemiological research, and the realisation of enhanced systems of medical practice, patient care and health promotion. Health and disease are compound concepts which are inherently complex morphological entities where physical, biological, and psychological states are in constant flux, featuring dynamically interacting and shape-shifting components within a '*complex jigsaw puzzle of biopsychosocial aetiology*' (Bolton & Gillett, 2019). Healthcare scientists and medical practitioners advance their fields in response to human needs, informed by the research of antecedents over generations (Doll, 1998), facing new ethical, regulatory, and organisational challenges, which emerge in tandem with scientific discoveries and medical innovation (Bhatt, 2010). Science, medicine, and healthcare are thus evolutionary practices exploring and responding to the emergent nature of human disease, chronic illness, and population behaviours; professional disciplines adapting to epidemiological, demographic, and societal change (Figueroa et al, 2019).

This thesis describes an exploratory study whose aims were to understand the nature of cancer clinical research delivery in a national health service, and develop a grounded theoretical framework accounting for the complex networks, relationships and phenomena influencing the experiences and circumstances of healthcare professionals and cancer patients engaged in clinical research at NHS hospitals in England and Scotland. Previous

evaluation of clinical trial delivery has predominantly focused upon challenges faced in participant recruitment and retention, but there is limited study into the nature of complexity within its systems, processes and research environments, and the potential operational and human impact upon clinical trial delivery (Lawton et al, 2011). To develop sustainable, equitable healthcare solutions, at the same time as pushing the boundaries of science and medicine, it is vital that the human aspects of trial involvement, either from the research professionals' or participants' perspectives are understood and acknowledged. To maximise opportunities for science and technology to effectively address contemporary healthcare challenges, the strategies for clinical research operations and medical progress need to engage with and respond to human capacities, capabilities and comprehensibility for such change and innovation, and be responsive to the inherently complex nature of health and disease. Implications for cancer research sites in managing effective and sustainable patient-centred models of trial delivery are manifestly challenging, faced with; growing patient populations, disease and system complexities, the NHS's plans for precision medicine and the UK government's ambition to be the world's most advanced genomic healthcare ecosystem (Genome UK, 2021).

With a growing and ageing population, the burden of cancer for society is accelerating (Smittenaar et al, 2016). Global incidence and mortality rates, influenced by changes in the prevalence and distribution of the main risk factors for cancer, have resulted in close to ten million deaths worldwide in 2020, and 19.3 million new cancer cases (Sung et al, 2021). The International Agency for Research on Cancer (IARC) have predicted a doubling of the incidence of all combined cancer types by 2070 (Soerjomataram and Bray, 2021), highlighting the urgency for nations to respond with public health strategies for cancer control and prevention. In 2018 the National Cancer Advisory Group in the UK published the following joint statement on the NHS ten year plan:

“Over the next decade emerging technology, genomics, artificial intelligence, new types of diagnostic test, and better ways of working will shape the healthcare landscape and how care is provided. Cancer care will become more personalised, and an ageing population means more patients will be diagnosed with cancer, many with multiple conditions and complex care needs”.

Healthcare systems and professions operate in a continually evolving and increasingly complex interactional environment, with growing demands on resources and capabilities. Expectations for delivering innovation and development in cancer treatments and care, within continuous quality improvement frameworks, places significant demands upon NHS healthcare providers and professionals working across ranging disciplines and institutions.

Evaluation of the human impact of growing operational and clinical complexity, and associated workloads and intensity is a neglected area, which needs to be understood through the lived experiences of patients and professionals. Systematic, structured evaluation of research delivery is limited with minimal, current empirical study of trial acuity, follow-up challenges and the impact of institutional dynamics, geographical location, or operational processes across complex NHS healthcare systems and interacting organisations. In-depth human-centred review is a paramount priority for the healthcare industry, to comprehend heterogeneous and dynamic variables contributing to service pressures, identify changing stakeholder needs and facilitate evidence-based commissioning of services through appropriately aligned funding and support models (Jones et al, 2020). This thesis presents the research stages, processes, and outcomes of an in-depth evaluation study into the practices, environments and experiences relating to cancer clinical trials in the NHS, with an orienting focus on the concepts of complexity and patient follow-up in their operational delivery.

1.2.1 History and Development of Clinical Research and Trial Methodology

The advancement of healthcare and medicine arises out of a historical legacy of scientific study and experimentation over millennia. The clinical sciences have systematically evolved through innovation and the development of evidence-based trial methodologies, including participant selection, randomisation, allocation, blinding and statistical analyses, as well as ethical approaches to research. One of the earliest recorded medical studies influencing public health decision-making, which dates back to around 500 BC, was a reported experiment in population diet attributed to King Nebuchadnezzar, described in the Book of Daniel in the Old Testament (Collier, 2009). This study is one of the earliest recorded examples of the use of a control group to determine the efficacy of a public health intervention, by studying the outcome on health between two groups. In the described study one group consumed a diet of meat and wine, whilst another followed a regimen of legumes and water. After ten days the vegetarian and alcohol-free arm appeared better nourished than the group following a meat and wine diet (Bhatt, 2010). Whilst this early research was not a planned, controlled clinical trial, the basic concept of establishing comparison groups in human studies to evaluate the outcomes of health interventions has endured to the present day, albeit with advancing sophistication, precision, and complexity in methodologies (Nelhaus and Davies, 2017).

Clinical trials can be summarily defined as multiphase studies ‘conducted by researchers on human subjects to test a medical treatment or prevention strategy’ (Collier, 2009). International Clinical Trials Day, an event held annually on the 20th of May, highlights the

importance and achievements of clinical researchers and patient contributions to healthcare sciences and exponential advances in medicine. The designated date of the event marks the start of James Lind's celebrated scurvy trial of 1747. In his role as a ship's surgeon on HMS Salisbury he conducted a comparative trial, studying a cure for scurvy using citrus fruits, which he later published as a 'Treatise on Scurvy' in 1753. James Lind is widely recognised as the first physician of the modern era to have conducted a controlled clinical trial; a planned, comparative treatment study, which he published with a systematic review of existing literature on scurvy (Bhatt, 2010).

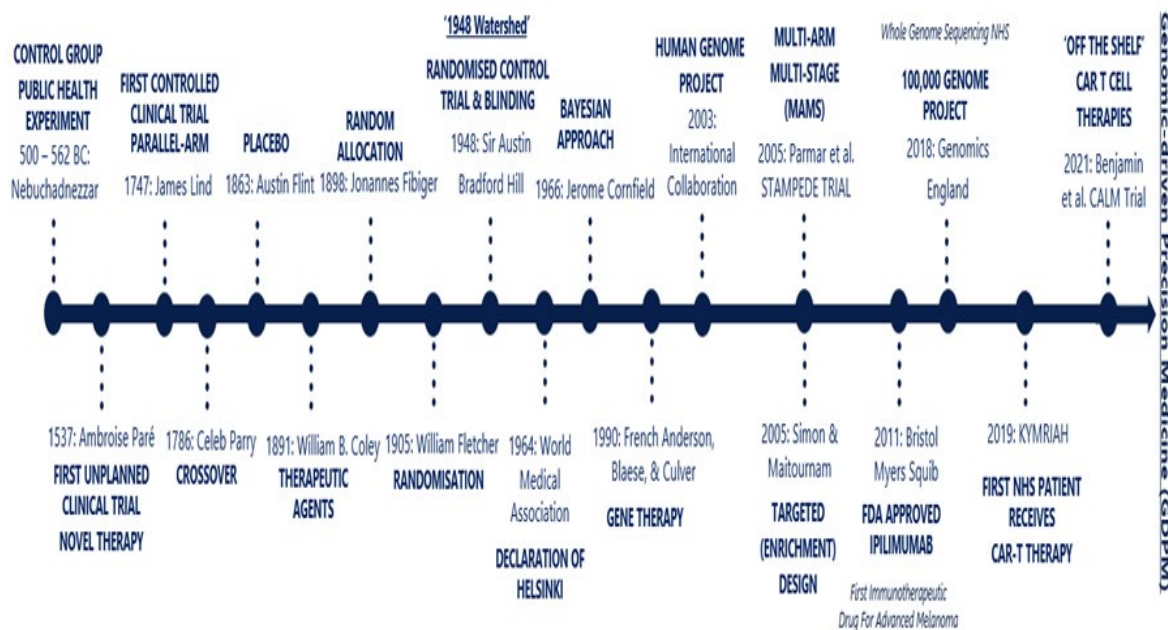


Fig 1.1 Clinical Research Development Milestones

In Figure 1.1 key landmark dates in the development of medicine and associated advances in trial methodologies are highlighted; a timeline tracking a trajectory towards increased complexity and intensity in medical science and healthcare. The development of clinical research methodologies and the environments for their implementation have witnessed incremental growth in complexity, moving from simplified cohorts, comparison groups and basic randomisation techniques to the highly intricate, networked, convergent processes and transdisciplinary innovation in an evolving Precision Medicine Ecosystem of the 21st century, a new paradigm in healthcare (Ginsburg and Philips, 2018). Rapid acceleration in the development of laboratory sciences, medical technologies, and therapeutics, calls for matched innovation in the design and governance of healthcare operations.

Clinical research in the present era is required to address and solve progressively challenging, dynamically emergent, and complex problems, relating to clinical practice (Bird & Strachan, 2020). The move to personalised medicine, and the adoption of advanced participant stratification methods, based on their genetic profile rather than by tumour site

(such as breast, prostate, or lung cancer), brings greater challenges to NHS sites in the delivery of cancer clinical trials. Translational research, adopting the use of biomarkers in patient selection, along with new protocol designs involving pharmacodynamic assessments, surrogate endpoints and patient classification based on gene expression, present further challenges to sustainable delivery models and equitable access to research participation across cancer patient populations. The pace of change in cancer clinical research, and the integration of personalised and precision medicine (PPM) into cancer clinical pathways is challenging for organisations (Horgan et al, 2015). The translational research disciplines of cancer therapeutics, immunology and drug development are amongst some of the most complex and challenging fields in biomedical sciences (Hernandez-Lemus and Martinez-Garcia, 2021). Further adding to contemporary complexities in clinical trial delivery and patient care is the nature of cancer as a heterogenous and evolving disease. Also embedded within the framework for evaluation is the care and treatment of ‘the complex patient’ (Manning and Gagnon, 2017), which pre-empt the need in clinical trial delivery to consider the application of precepts relating to complex adaptive systems (CASs), as well as understanding the interacting properties and relationships in healthcare research between, people, disease and situated environments; a biopsychosocial analysis of cancer clinical research.

1.2.2 Evolution of Cancer, Disease Responses and Complex Systems

Cancer is not a singular disease but a multiplex of evolving pathologies, which continues to present a major healthcare burden across the globe. The WHO fact sheets on cancer summarise the term as follows;

“Cancer is a generic term for a large group of diseases that can affect any part of the body. Other terms used are malignant tumours and neoplasms. One defining feature of cancer is the rapid creation of abnormal cells that grow beyond their usual boundaries, and which can then invade adjoining parts of the body and spread to other organs; the latter process is referred to as metastasis. Metastases are the primary cause of death from cancer” (WHO, 2021).

Mukherjee (2011) introduced his biography of cancer, *The Emperor of Maladies* with the following literary definition;

‘an ancient disease - once a clandestine, “whispered-about” illness – that has metamorphosed into a lethal shape-shifting entity imbued with such penetrating metaphorical, medical, scientific, and political potency that cancer is often described as the defining plague of our generation’

The clinical and epidemiological complexity of cancer, and its multifaceted nature is challenging, with its complex factors determining not only its occurrence and development but also significantly impacting upon the capacities and resources of patients to respond to treatment (Gnjatic et al, 2017). Human responses to the multiplicity of illness-wellness states are highly sensitive to environmental conditions and imbued with contextual meaning. From the point of receiving a cancer diagnosis, and through the differing stages of treatment, patient follow-up, remission, progression, survival or beyond, individual patients vary in their biological and psychological responses. Genes, diseases, humans, and societies are all examples of complex adaptive systems, existing at different levels yet sharing similar properties, such as emergence and uncertainty, and formed from networks of intricate, relating components, which cannot be easily reduced to simple determinate elements. The capacities and capabilities of individuals and organisations to respond and adapt to such emergent phenomena need to be evaluated through interdisciplinary, humanist, and digital systems perspectives. The complex challenges faced by society in the 21st century, in responding to growing cancer burdens and chronic diseases, cannot be managed through traditional medical models and generalist approaches to healthcare delivery.

Traditional methods in treating cancer have looked for commonalities, with clinical trials developing new surgical, radiological and chemotherapy regimens, and combinations of these, to eradicate cancerous growths and lesions. Interdisciplinarity in science and medicine is changing the landscape of clinical oncology research and drug development, yet imports its own complexities, especially in relation to coherence and communication. Analogies of terrains and horizons are often used to describe the nature of cancer, and the response of patients and professionals to their experiences and interactions with its plethora of states and forms. Scientific advances in mapping the human genome have fundamentally changed future treatment paradigms for cancer, revealing its mutational spectrum (Trent and Touchman, 2007), with commonly mutated genes in “the mountains” and heterogeneity seen in “the hills”. Wood et al (2007) stated, *“Historically, the focus of cancer research has been on the gene mountains, in part because they were the only alterations that could be identified with available technologies...It is the “hills” and not the “mountains” that dominate the cancer genome landscape”*. Recognising the evolutionary and metastatic nature of cancer and unlocking its changing features through interdisciplinary practice and sustainable, translational research can reveal new horizons for patient-centred healthcare. Improved clinical insights, patient care and health outcomes for cancer patients, can be realised through the integration of genomic medicine into clinical practice (Quigley, 2015). However, the full implications of pharmacogenomics in cancer clinical trial delivery, and clinical practice within the NHS, need to be understood across ranging contexts,

professional fields, and perceptual aspects of healthcare. Pharmacogenomics is a relatively new field which studies how a person's genes affect their response to drugs. With paradigmatic shifts into macro-level, genomic landscapes for cancer research the specialisms of medical imaging and histopathology have become increasingly important. The anatomical watercolour shown in Fig 2.1, was published in 1898 by Professor Robert Carswell, and is one of the earliest known colour illustrations of the morbid anatomy of Hodgkin's disease (Rosenfeld, 1989). This illustration was displayed by Thomas Hodgkin at the reading of his classic paper on the disease in 1832 (Hollman, 1995). Hodgkin suggested a relationship between the spleen and lymph nodes, recognising the pathological presentation as a disease in an era before histopathology, a hypothesis supported by the case example provided by Carswell, entitled "Cancer Cerebriformis of the Lymphatic Glands, and of the Spleen" (Dawson, 1999). Physicians' illustrations of pathological conditions served to advance the knowledge of human disease and presentations before the field of morbid pathology was revolutionised by the microscope. The malady described by Hodgkin in 1832, is now recognised as a cancer of the lymphatic system, a disease which demonstrates biological intricacies (Ferry, 2014), complex molecular pathways, micro-environments, and T-cell subpopulations, the nature of which remain to be fully understood nearly two hundred years later (Villasboas et al, 2017).



Fig 1.2 "Hodgkin's Malady" Dissection of cervical and axillary lymph glands.
Sir Robert Carswell. (Source: Rosenfield, L, 1989).

1.2.3 Clinical Research Environment and Healthcare Systems

The environments and nature of healthcare systems, and the level of cohesion and cooperation between parts of universal networks, from localised entities to global operations, are all sensitive to fluctuating conditions. Increasingly complex clinical trial designs and rapidly changing treatment paradigms, involving strict eligibility criteria, molecular profiling, and targeted therapies, have significant procedural complexity and workload intensity implications for cancer clinical trial operational delivery (Malik and Lu, 2019), impacting patient treatment, care and follow-up as well as the research capacity and capability of clinical trial sites. The challenges of managing dynamic and emergent properties in complex adaptive systems (CAS) in clinical research, bring into focus the importance of adopting multi-modal systematic approaches in conducting process evaluation into healthcare delivery and its research policies and practices. Dynamic and reflexive evaluation is needed to understand present challenges in order to develop effective and sustainable solutions with the requisite cohesive structures and adaptive capabilities to manage the intrinsic complexities of clinical research, and its pace of change.

Complex organisations like the NHS, need to strategically evolve in response to the dynamic influences and demands of their larger, external connected networks (or supra-systems), capturing the disturbances to its sub-systems and identifying the resources necessary to facilitate their sustainable functioning and development (Terra & Passador, 2016). Symbiotic relationships exist between emergent scientific discovery and interacting operational fields of clinical research and healthcare delivery. As scientific research advances the knowledge, application and implications of novel therapeutic agents, medical devices, and clinical practice, there is a symbiotic evolution in the systems, professional fields, and social environments to which they relate. Increasing collaboration and symbiosis between stakeholders across the clinical research delivery continuum supports the development of innovative, coherent, and sustainable healthcare models and strategies. West et al (2019) highlight that the implementation process is a critical element required in ensuring strategic plans are 'converted into practical operational plans,' and 'allow for risk analysis, evaluation techniques and accountability'. Dynamic strategic vision engages with empirical and operational symbiotic relationships, recognising their critical roles in research implementation and health system resilience (Biddle et al, 2020; West et al. 2019). The ability of individuals to manage the capacities and limitations of systems, whether they be healthcare professionals or patients, and to navigate the complexities of inter-relating components, networks, and relational interfaces, influences the determinants and outcomes of population health. Within the realm of healthcare and clinical research delivery, the effectiveness and sustainability of an organising system is reliant on its ability to respond to

emergent needs of the people and purposes that it is instituted to serve, and through the implementation of creative, adaptive, and coherent systems and operational solutions. With such a breadth of interacting phenomena, the realm of healthcare and clinical research delivery is inherently complex, and witnessing rapid evolution in a new era, described as *The Information Age and a VUCA World* (Watkins, 2014). VUCA is an acronym representing the characteristics of the age which are *volatility, uncertainty, complexity, and ambiguity*.

There is a need for greater conceptual clarity regarding the nature of complexity of patient care and follow-up in cancer clinical trial delivery, as well as the interactions between professionals and organisations within the translational healthcare field. The concept of coherence within the field of healthcare is a growing area of study, which facilitates the examination of complex adaptive systems (CAS) and an evaluation of the interfaces between paradigmatic perspectives in the health sciences. Sociologist Aaron Antonovsky brings a human sensibility to understanding health and his following statement is a maxim which should be central to the design and delivery of all healthcare.

'We are coming to understand health not as the absence of disease, but rather as a process by which individuals maintain their sense of coherence (i.e. sense that life is comprehensible, manageable and meaningful) and ability to function in the face of changes in themselves and their relationships with their environment.' (Antonovsky, 1987).

The concept of coherence and an engagement with multiple perspectives, are used throughout the thesis as sensitising constructs to comprehend, manage, and provide a meaningful presentation of the diverse, complex, and advancing field of clinical research and healthcare delivery.

1.2.4 Research Participant Perspectives

Clinical research is an operational environment involving a high level of social interaction requiring interpersonal skills and empathy in the complex management of ranging values and perspectives. The way in which we act, interpret, and understand current and evolving realities requires tolerance and respect for the multiple perspectives, values and situated knowledge of our fellow humans (Barrett et al, 2018). The importance of understanding human perspectives within the context of healthcare systems and organisations introduces the concept of ergonomics, which is a discipline aligned with operational evaluation. The International Ergonomics Association provides the following definition:

‘Ergonomics (or human factors) is the scientific discipline concerned with the understanding of interactions among humans and other elements of a system, and the profession that applies theory, principles, data, and methods to design in order to optimize human well-being and overall system performance’ (IEA, 2016, Shorrock & Williams, 2017).

To understand the true nature of cancer research delivery within the NHS it is essential to understand the experiences of those professionals and patients directly involved in the realities of delivering and receiving clinical trial treatments and interventions. The situated, contextual knowledge and experiences of clinical research professionals and cancer patients needs to be acknowledged and considered in the design and delivery of clinical trials, which should also be sensitive to varying circumstances, environments, and workplaces. Hanson (2007, p144) emphasises that in health promotion work the situated, experiential knowledge of the workforce deserves attention and should be incorporated into analysis, planning, and operational management processes. This study illuminates ranging views and circumstances of participants and presents how these are influenced and understood through localised experiences of social, physical, and perceptual environments of care (EOC) and their interactions within them. Ergonomics in relation to cancer clinical trial delivery offers a potential framework for interdisciplinary coherence and resilience in complex healthcare systems, which will be discussed further in Chapter Two. Throughout the thesis ‘slices of data’ (Glaser and Strauss, 1967) and participant quotations, drawn from the in-depth, multi-faceted inquiry, will be used to emphasise, illustrate, and explain differing views and perspectives from the study: ***Evaluating Follow-up and Complexity in Cancer Clinical Trials (EFACCT)***.

1.2.5 Research Rationale

Clinical research delivery exists within a complex adaptive system which is facing growing challenges in an era of personalised medicine and growing numbers of patients with chronic, long-term healthcare needs. In order to meet global challenges posed by cancer, healthcare organisations need to adopt transdisciplinary research strategies which embrace design-thinking and resiliency approaches, increasing the capacity and capability of medical research to deliver health benefits to patients worldwide (Kozlakidis et al, 2020). The rationale in undertaking the EFACCT study was manifold. The national, multi-centre evaluation of follow-up and complexity in cancer clinical trials arose from localised interests at a district general hospital in studying the implications of growing patient volumes in clinical trial follow-up. In presenting a proposal for a PhD studentship, to investigate the nature of follow-up and its implications for clinical trial delivery at NHS, broader implications of

growing complexity in clinical trial delivery, were incorporated into the mixed-methods study design. The nature of the type and frequency of trial interventions, whether they are part of active treatment stages of a study or defined as follow-up interventions, are intrinsically linked to workload burdens and study intensity, and significantly impact the research delivery capacity and capability of hospital sites, professionals, and patients. To develop detailed understanding of the nature and impact of trial procedures, and their operational and human impact, a systems approach was required which acknowledges complexity.

The increasing complexity of clinical research and the NHS's ambitious moves toward personalised medicine approaches, particularly in relation to gene therapy and immunotherapy in treating cancer, has significant implications for the delivery of clinical trials. Stratified and personalised medicine import operational complexities into the healthcare and clinical research model, which need to be evaluated in relation to their scientific, technical, financial, and logistical impacts but also need to be understood from the perspectives of professionals working within the field and from the viewpoint of patients and clinical trial participants. Capacity to manage research designs supporting scientific advancements in cancer research will require new approaches, acknowledging increasing study complexities and the logistical implications of delivering bespoke therapies specific to smaller populations. The phases of clinical trials, research protocols and study designs also substantially impact the effectiveness and resources of clinical trial sites, and have a significant influence on treatment delivery, as well as the capacities and resilience of patients and professionals. Human factors and ergonomics as a process of evaluation within cancer clinical research delivery, design and strategic management is a neglected field, which could provide important insights leading to improved system performance and patient care. Five core interfacing domains require critical analysis to support NHS ambitions:

1. *Human Patients and Human Professionals Needs and Capacities*
2. *Cancer, Disease and Healthcare System Complexities*
3. *Cancer Clinical Research and Healthcare Operational Delivery Models*
4. *Communication Interfaces and Coherence in Healthcare and Clinical Research*
5. *Sustainable Strategies for Healthcare and Clinical Research in CAS Systems*

Contextual, structured evaluation of cancer clinical research delivery in secondary care settings is limited with minimal empirical study into trial complexity, institutional dynamics, or the organisational realities of operational processes in large complex healthcare institutions, such as the NHS. Studying system complexity, problem definition and causation analysis within healthcare organisations and adaptive environments is challenging

(Catchpole and Jeffcott, 2017). Operational evaluation and human factors ergonomics (HFE) researchers can experience difficulties gaining buy-in from governing and commissioning bodies, who seek 'value for money' and 'measurable outcomes' in the performance of healthcare organisations, trusts and professionals. The NHS and medical sciences, traditionally characterised by mechanistic, deterministic, top-down hierarchical approaches to strategic planning and policy development have sought simplicity where there is none, an approach which is ethically and strategically short-sighted. Evaluation of NHS cancer care and research delivery is a moral imperative, requiring systematic and cyclical review of organisational capabilities as well as epidemiological analysis, as diseases, treatments and the social, technical, and economic environments evolve and mutate.

The results of both the research professional and patient studies, which are presented in Chapters Six and Seven, have highlighted the importance of interpersonal relationships and their impact in practical, operational terms and on human physicality and emotional sensibilities. The Prismatic Coherence Model (PCM) presented in this thesis offers a framework for understanding and responding to the complex interfaces between the medical reductionist and mechanistic worlds of quantifiable properties and the sensory, emotive, and nuanced interacting properties and agents of uncertain, complex, emergent, and dynamic organic biological and human systems. Cristancho and Helmich, (2017) state:

“Rich pictures are pictorial representations that attempt to capture a person’s perspective of a complex situation with all its interacting elements: things, ideas, people, character, feelings, beliefs and conflicts...”

The importance of analogies, language and graphical visualisation are recognised within this study as important methods of communication and analysis, and are used throughout the thesis to illustrate ranging perspectives of clinical trial patients and professionals. Methods of representative analysis include the use of insightful patient pathologies. The combining of graphic and literary tools within qualitative inquiry and their facilitating role in theory construction, provides novel perspectives and approaches to unravelling the complexities of healthcare and disease, as well as offering up potential new salutogenic strategies for healthcare and clinical research through holistic insights.

1.3 Research Aims and Objectives

The study was entitled 'Evaluating Follow-Up and Complexity in Cancer Clinical Trials (EFACCT)'. By incorporating the term 'evaluating' within the title, the nature of the research approach was clear, along with the orienting focus and field of the study, but it is useful to

consider the concept of evaluation as a research strategy and its relative importance as a sensitising perspective. Evaluation is an approach to understanding a situation, context, or social environment in which meaning of terms, concepts, and individual perspectives about these is significant in both the conduct and the outcomes of research. From the outset of the study, being sensitive to situated knowledge, perspectives and meaning meant recognising the importance of language, communication, meaning and context in achieving comprehension of both research professionals and trial participant's realities in real world settings. Comprehension of ranging perspectives, experiences and contexts, requires a research stance which accepts the nature of complexity in healthcare and organisational systems, one which is open to the concept of cohesion. In order to develop sustainable and person-centred models of clinical research and medical practice, organisations and individuals need to identify challenges and limitations with systems and process, in order to optimise scientific advancements for societal benefit. Through conducting an in-depth mixed-methods grounded theory study using a sequential design the key research objectives were to:

- define, describe, and evaluate the nature of patient follow-up in cancer clinical trials
- examine complexity and its related properties contributing to service pressures
- identify challenges to capacities and capabilities for research delivery
- illuminate the situated and personal perceptions of research professionals and patients and their experiences of participation in cancer clinical trials
- understand barriers to efficiency within the operational delivery of clinical trials
- identify best practices in evidence at different sites
- develop a situated grounded theory and theoretical model sensitive to contextual complexity and capable of providing enhanced strategies for clinical research and healthcare delivery

Within the UK, contextual, operational evaluation of cancer clinical research delivery in secondary care settings is lacking, which studies the nature of trial complexity, patient follow-up, as well as protocol and procedural burden from the situated perspectives of cancer patients and research professionals, alongside an analysis of NHS research strategies and infrastructure. Within this study the implementation of cancer clinical trials was studied within the context of interacting institutional, political, and social environments in which clinical research is conducted. Through the integration and analysis of qualitative and quantitative data on cancer clinical trial protocols, interventions, patient follow-up, and study management alongside the complex nature of the disease the research aims were to develop a grounded theory explicating cancer clinical trial delivery, and to identify effective,

sustainable operational models and person-centred theoretical frameworks which can be applied within appropriate clinical and organisational contexts, enhancing governance, resiliency and NHS research delivery.

1.4 Themes of Inquiry and Research Design

The substantive area of focus is in determining the nature of cancer research follow-up and complexity in an operational context and the impact on sites and patients. To enhance our ability to comprehend, manage and respond to complex environments and constantly changing, emergent phenomena, we need to embrace multi-faceted approaches which place mutual respect and shared values at their core. Strübing (2019) suggests that Straussian grounded theory is a radical solution resolving dualism into a “continuum of perspectival processing differences with interactive problem-solving as its *modus operandi*”. This approach requires an evaluation of medical paradigms which have traditionally evolved with a pathogenic approach, as well as the social and holistic aspects of patient and professional staff health and well-being, requiring a salutogenic perspective. In this study these concepts are evaluated using a mixed methods grounded theory design. The focus areas of inquiry central to the study's multi-site process evaluation, and leading to its developed grounded theory and Prismatic Coherence Model (PCM), are summarised under the following themes:

- *Conditions and Features Defining Complexity in Healthcare and Research*
- *Capacities and Challenges of Patient Management and Follow-up in Cancer*
- *Perspectives and Nature of Participants and Organisations in the Field of Study*
- *Systems and Processes in Clinical Research Operational Delivery in the NHS*
- *Healthcare Environments and their Structural and Functional Characteristics*
- *The Clinical Research Landscape and Sustainable Futures*

1.4.1 Research Approach and Design

The thesis investigates the nature of patient treatment delivery, interventions, and follow-up as part of their healthcare and clinical trial journey delivered by clinical trial professionals in the NHS, and discusses the implications of these from multiple levels using grounded theory. A choice was made to select a complexity lens in the study of cancer clinical trials, in order to gain a deeper understanding of the nature of cancer clinical trial delivery within the context of healthcare settings in the NHS, and the related characteristics, properties and behaviours of actors within its realms of reality. It is important to understand the perspectives of professionals delivering trials to analyse the diversity or commonality of

experience, relative to respective scales of operation, patient populations and nature of their supporting Local Clinical Research Network (LCRN).

In developing a research design sensitive to context and multiple perspectives, which adopts a communal, collaborative approach in synthesising findings to understand the complexities of phenomena with the aim of developing practical solutions, the influences of John Dewey's form pragmatism are recognised. Dewey defined inquiry as 'the controlled or directed transformation of an indeterminate situation into one that is so determinate in its constituent distinctions and relations as to convert the elements of the original situation into a unified whole' (Dewey, 1938). To paraphrase this definition, inquiry translates into a purposive act of transforming uncertain contexts or problems, through a systematic synthesis of its discernible characteristics and the inherent inter-relations of those elements, to form a conceptual interpretation, effectively an interpretive synthesis of particular contextual problems, developing new knowledge or theory. This view of inquiry is commensurate with a mixed grounded theory (MGT) approach. Using an MGT approach supports the development of new knowledge at system-wide as well as sub-system levels, which assist in the formation of practical, workable theoretical models, sensitive to contextual challenges and nuanced local levels of reality. The approach has been applied and recognised as a practical and beneficial methodology within the social sciences, and across ranging research applications and contexts (Howell Smith et al, 2020).

Evaluating Follow-Up & Complexity in Cancer Clinical Trials (EFACCT) Theoretical Dimensions and System Models

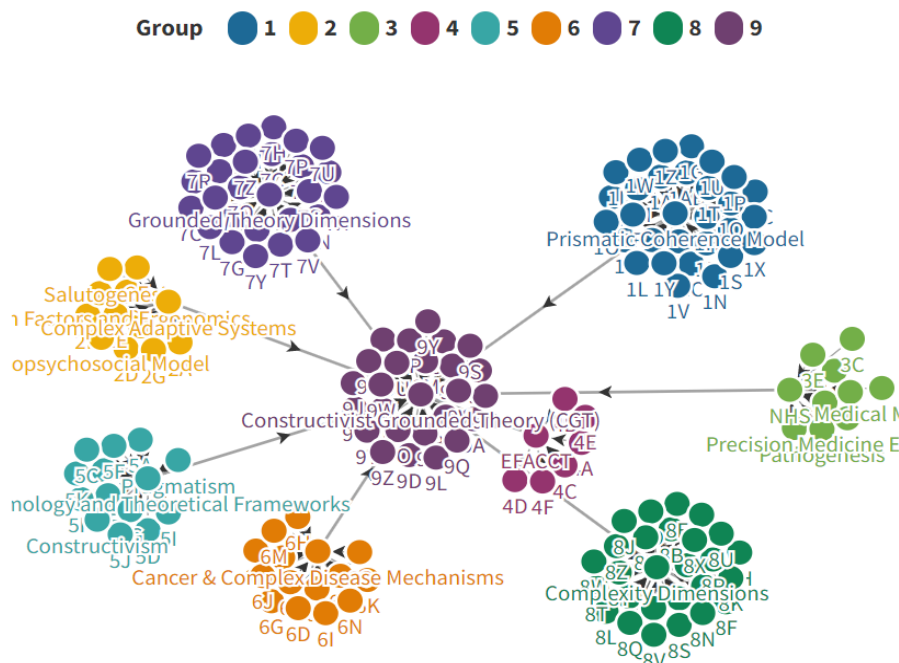


Fig. 1.3 Theoretical Dimensions and System Model Network Visualisation

In studying the nature of complexity within research operational delivery and healthcare systems, an open and pragmatic framework supporting theoretical sensitivity and the integration of methods, was perceived as an approach sympathetic and responsive to the nature of the problem. Figure 1.3 provides a visualisation of a reflexive tool used to consider multiple theoretical dimensions and system models, supporting the analysis of constructs relating to cancer clinical trial complexity. This approach of linking nodes and expanding dimensions within the data demonstrates a Constructivist Grounded Theory (CGT) as well as a Mixed Methods Research (MMR) approach. MMR has been described as the third major research paradigm (Burke Johnson et al, 2012), a philosophical movement or 'metaparadigm' suited to research and analysis at micro, meso, macro and meta-levels. The collation, analysis, and synthesis of qualitative and quantitative data and purposive combining of methodologies is respected by MMR practitioners, illustrating an approach to inquiry which assumes a wider meta-theoretical stance, that is concerned with "epistemological and empirical divergence and obtaining knowledge of different perspectives of the social and natural world" (Burke Johnson & Walsh, 2019). To provide a comprehensive, contextual evaluation of cancer clinical research delivery it was necessary to combine evidence from quantitative and qualitative paradigms, using inductive and deductive methods, forming a prismatic model.

1.5 Researcher's Lens and Positionality

An expedition to possibilities was the embarkation point for my doctoral journey, with no a priori theory proposed in an evaluation of cancer clinical trial delivery, but a strong desire to discover its nature through a synthesis of prismatic perspectives. With a background in business management, process evaluation and systems implementation my professional experience is grounded within a field of interpretive evaluation focused on socio-technical systems. The theoretical framework recognises the interactive nature of both humans and technical systems. My epistemological influences have been drawn from the historical development of paradigms, which have arrived at a confluence of methodologies, justified in their meta-theoretical foundations and subsequent and substantial application within the social sciences, descended from the work and sociological contributions of John Dewey (pragmatism) and Arthur Singer, (systems thinking). My approach to conducting the study of clinical research delivery incorporated interpretive, critical, and humanist perspectives, which share a synergy with dialogical analysis (Gillespie et al, 2010) and was considered in the formation of the adopted research framework. The influences of American Pragmatism (Peirce), Symbolic Interactionism (Dewey & Mead), Interpretive Interactionism (Denzin), and Constructivist Grounded Theory (Charmaz), form the basis for my theoretical stance informing the research strategy.

A predominantly naturalistic approach underpins the study design, noting the importance and relevance of the researcher as human instrument, and the relation and interdependence of belief systems in contextual inquiry. One element seldom referenced in the researcher's positionality is a physiological dimension as an influence on their approach to inquiry. In recognition of the role of reflection and cognitive influences the study is approached from a neurologically diverse perspective, valuing prismatic and refractive thought processes. The positionality of the researcher is an integral part of the research process with influences on both theoretical perspectives and selection of methods. In seeking to provide a voice to research delivery professionals and cancer clinical trial participants the research approach is dialectical and through studying context, experience and seeking multiple perspectives the epistemological stance is pluralistic. In adopting a dialectical pluralist approach, as defined by Johnson et al (2012), potential researcher bias, which may impose a limiting view on reality, is mitigated through the consideration of multiple ontologies and engagement with multiple stakeholders in the process of evaluation. The journey taken has changed my perceptions and knowledge of the world on multiple levels, gaining learning from the realities of clinical trial professionals and patients, and up through system and theoretical levels of understanding, the differentials and aspects that combine at points in time and in specific contexts to provide a sense of coherence which define our individual realities through comprehensibility, manageability, and meaningfulness. This 'adaptive dispositional orientation' is significant from a personal perspective and is an enabling coping strategy in adverse circumstances central to Antonovsky's Sense of Coherence (SOC) theoretical construct (Hammond and Niederman, 2010), which will be discussed further in Chapter Two.

1.6 Contribution and Significance

This thesis provides an analysis of the nature and complexity of cancer clinical research, and the influence of environment and localised interactions in relation to its operational delivery across ranging secondary healthcare sites in the NHS. Through the situated perspectives and experiences of participants who are involved in the delivery of clinical trials, whether they be clinical professionals or patients, the study elucidates the nature of complex systems in healthcare and provides many illustrations of the challenges that it needs to address. The study addresses the lack of qualitative and quantitative research into operational processes, system capacities and efficiencies through a human factors analysis evaluation process. The EFACCT study engaged with key stakeholders, research professionals and patients with experience of involvement in clinical trials conducted at NHS secondary care sites across the UK, in a collective dialogic learning process to understand their experiences and perceptions of cancer research delivery. Properties of uncertainty

and complexity which have operational and resource implications for clinical trial sites and impact upon patients' environments of care are identified, highlighting the importance of salutogenic relationships in their cancer journey.

Harnessing principles of patient and staff engagement the study has developed unique data sets and insights into cancer clinical research, presenting a contemporary reality of the NHS operational delivery model through the eyes of those who are intimately experienced and involved. The original data generated and developed led to the conception of a Prismatic Coherence Model (PCM), a model which provides a launch point for developing strategic dialogue between healthcare providers, patients, and professionals, as well as the clinical research industries, governance and funding bodies which form part of a complex network in healthcare and clinical research delivery. The research findings contribute to important conclusions about the nature of interdisciplinarity, its challenges and complexities and highlights the importance of coherency in healthcare systems. The future sustainability, strategic development and advancement of clinical research and healthcare delivery, needs to recognise the nature of complexity and the situated realities of individuals in order to meet the future demands and healthcare burdens.

1.7 Structure of the Thesis

Chapter One: Introduction. In this preliminary chapter, the field of study and situated context is introduced. A high-level overview of the research problem is presented, and the objectives, approach, significance, contribution, and limitations of the study discussed. The thesis structure, researcher's positionality and key terminology are also clarified.

Chapter Two: Literature Review. This chapter discusses relevant conceptual, procedural, and contextual literature relating to clinical research delivery within complex healthcare systems, alongside emergent phenomena arising from the research data during the course of the study. In a grounded theory study, the data that is generated is constantly compared against theoretical and contextual literature, so the review ran concurrently with data collection and analysis throughout the lifecycle of the study. Following an initial discussion of the role of the literature in Grounded Theory, the chapter is thereafter structured into three stepped stages involving foundational, emergent, and situated critical analysis and synthesis of literary evidence. Key challenges for cancer clinical research within the NHS are highlighted, as well as the nature of complex systems, networks and phenomena and their implications for sustainable models. Perspectives are introduced outlining a need for new strategic approaches capable of supporting scientific advances and equitable healthcare and responsive clinical research models in an era of personalised medicine.

Chapter Three: Research Methodology and Framework. Chapter Three provides an in-depth discussion on the ontological and epistemological perspectives and theoretical underpinnings for the study, and the conceptual reasoning involved in the adoption of a mixed methods grounded theory approach. The history, relevance, and importance of grounded theory methodologies in studying the nature of complexity and follow-up in cancer clinical trial operational delivery and healthcare systems are presented. The defining features of constructivist grounded theory and mixed methods frameworks are discussed, and how these contributed to shaping the selected research design and methods to evaluate complex, dynamic, and interacting phenomena.

Chapter Four: Research Design and Methods. Chapter Four details the rationale in developing a mixed methods grounded theory research design, and discusses how the selected methods were applied in the study entitled Evaluating Follow-Up and Complexity in Cancer Clinical Trials: EFACCT. The protocol design and implementation stages of the study are illuminated and details of the practical application of methods in the process of research site and participant selection, recruitment, consent, and management. Additional elements of the research strategy are discussed, covering ethical considerations and approval, risk management, data processing and software applications.

Chapter Five: Data Analysis and Integration. Chapter Five reviews the data analysis and integration stages of the study, and explains the relevant processes in the context of grounded theory methodology. The constant comparison approach to data and coding techniques in Grounded Theory are detailed, alongside a discussion on the role of *memoing*, *reflexivity* and *theoretical saturation* in the development of the study's core conceptual categories. The chapter also details how visual models and CADQAS software were used to identify core constructs and their properties during the analytic stages of the study, highlighting their central role in synthesising conceptual data from research outcomes across multiple study stages.

Chapter Six: Research Professional Perspectives. Chapter Six presents the outcomes of three participant studies involving research professionals whose role involves the operational delivery of cancer clinical trials within the NHS. The perspectives of research professionals relating to concepts of patient follow-up, complexity, and clinical trial delivery workloads were comprehensively explored through the use of three studies designs; an e-Delphi, a semi-structured questionnaire study and in-depth participant interviews, which were conducted at NHS clinical research sites in England and Scotland. The responses of participants and their situated perspectives in relation to emergent constructs, are discussed, and their contribution to the study's developed grounded theory.

Chapter Seven: Clinical Trial Patient Perspectives. Chapter Seven presents the results of three studies involving cancer patients, who were currently or had recently participated in a clinical trial at an NHS site in England or Scotland. Drawn from three study designs; a Delphi study, semi-structured questionnaires and in-person qualitative interviews, the findings present the human voices and perspectives of cancer patients, highlighting their values, emotions, journeys, and meaningful experiences as NHS cancer clinical trial participants. The concepts and dimensions developed using grounded theory methods contribute to the overall core categories discussed in Chapter Eight.

Chapter Eight: The Grounded Theory. In this chapter the synthesised results are presented as an integrated constructivist grounded theory. The multiple realities of cancer patients and research professionals who have situated, contextualised experiences of participating in cancer clinical trials are presented, with substantive conceptual categories and properties developed from integrated participant perspectives to develop a contextually-situated grounded theory and theoretical model, sensitive to the highly complex and emergent nature of cancer clinical research at NHS secondary care hospital sites.

Chapter Nine: Conclusion. Chapter Nine critically evaluates the study's developed Prismatic Coherence Model (PCM), presenting it as an original, constructivist grounded theory and pragmatic model recognising the complexity and the importance of embracing its Complex Adaptive Systems (CAS) and Quantum Perspectival theories, models, and approaches in order to provide sustainable, equitable solutions and practices within networked healthcare and research delivery systems and their dynamic, emergent contexts.

1.8 Chapter Summary

As research processes and the needs of society and medicine evolve the mechanisms, systems and ecology of clinical research have become increasingly complex, dynamic, and interpolated phenomena. Research in the present era has evolved into a complex socio-technical and bio-technical field of medicine and healthcare development. This chapter has provided a high-level overview of the background to the research into complexity and follow-up within the context of cancer clinical trial delivery in the NHS. The thesis's aims, purpose and research objectives were introduced. The strategies used in investigating the operational delivery of cancer clinical trials and the nature and the environments in which the nature of complex adaptive systems impact clinical trial professionals and participants were outlined. Following an explanation of the thesis's contribution to operational process and management evaluation incorporating complexity science, and the implications for healthcare and research delivery, this chapter concluded with a summarised structure of

the individual thesis chapters. An introductory quotation to each thesis chapter will provide a theoretical perspective or guiding insight into the content and themes to be discussed, some of which are participant quotations which directly illuminate the nature of human voices in the context of the study.

Chapter Two - Literature Review

“One reason for the openness of inquiry is that, when obtaining data on different groups, the sociologist works under the diverse structural conditions of each group: schedules, restricted areas, work tempos, the different perspectives of people in different positions, and the availability of documents of different kinds. Clearly to succeed he must be flexible in his methods and in his means for collecting data from group to group.” (Glaser and Strauss, 1967, p65)

2.1 Introduction

Within this chapter, literature relevant to the study’s design, implementation, research foci and emergent conceptual themes are discussed. In order to provide a structured evaluation of the core literature relating to clinical research, healthcare delivery, complex systems, and the study’s developed grounded theory, this chapter is divided into three distinct review stages; the foundational, the emergent and the situated analysis of the theoretical and empirical evidence. The introduction leads into an initial discussion on the approach to the literature review in grounded theory research, followed by three review stages. The foundational review (section 2.3) presents the initial engagement with the literature, relevant to the field of study, which was conducted prior to the commencement of data collection. The emergent review (section 2.4) discusses literature relating to the study’s emergent concepts which forms part of the constant comparison and theoretical sampling of research data. The situated review (section 2.5) evaluates the study’s empirical findings, its constructivist grounded theory and developed Prismatic Coherence Model (PCM) in relation to pertinent theoretical literature covering clinical research, patient management and complexity in healthcare systems. The chapter summary highlights the study’s particular focus on complex adaptive systems, coherence, and the importance of strategic engagement with the prismatic perspectives of cancer patients and healthcare professionals, in order to facilitate human-centred models for healthcare and research.

2.2 The Literature Review in Grounded Theory Research

Grounded theory studies are empirically directed and the approach to conducting a literature review, and its timing within the research process, is a problematic area where there is considerable debate between methodologists (McGhee et al 2007, Dunne 2011). A traditional approach to commencing research and investigation of phenomena is through a review of key literature and existing theories relevant to the subject area (Locke, 2001). However, in a grounded theory study, reflexivity is an essential part of ensuring rigour

throughout all research stages (Engward & Davis, 2015), and therefore the literature review is a reflexive element within the research process commencing at the design stages and incorporating data collection, analysis, and integration. Undertaking a literature review prior to commencing data collection and analysis in a grounded theory study risks assuming a theoretical position, potentially leading to bias or the impedance of the natural emergence of theory (Simmons, 2011). Glaser and Strauss, founders of the methodology, initially held the view that a review of the literature within the substantive area prior to commencing data collection could lead to a contamination of the data, thereby imposing a theory rather than allowing one to generate naturally from the grounded, situational experiences and contextual data. In their 1967 foundational book on grounded theory methodology, *The Discovery of Grounded Theory*, they suggest that the 'theory should fit the data' (1967, p261) and that a focus on emergence of theoretical categories maintains their richness and relevance, stating that:

"An effective strategy is, at first, literally to ignore the literature of theory and fact on the area under study, in order to assure that the emergence of categories will not be contaminated by concepts more suited to different areas. Similarities and convergences with the literature can be established after the analytic core of categories has emerged." (Glaser and Strauss, 1967, p.37).

Their views subsequently diversified with Strauss recommending an early review but Glaser maintaining that this process should come at the end, to prevent pre-existing theories being imposed upon the data (Thornberg and Dunne, 2019). Dunne (2011), critiques the suggestion that researchers may be unduly influenced, stating such an argument 'appears to give little credit to the ability of researchers to be mindful of how extant ideas may be informing their research'. There are risks attached to engaging too deeply and too early with the theoretical literature and the researcher needs to remain open to pertinent and relevant emerging concepts whilst reviewing literature, acting as a reflexive instrument within the data collection and analysis stages, and as constructor of theory, ensure the relevance of conceptual categories and sensitivity of related properties within studied contexts.

In an approach which accepts the properties for extant theories, a researcher would be viewing data through the existing lenses of other researcher's as a 'received theory' (Charmaz, 2014, p306). An example might be that it would be a plausible approach to adopt the three sources of uncertainty (scientific, practical, and personal), defined by Han et al (2011) in relation to breast cancer treatment, and apply these to the concept of complexity within cancer research as accepted taxonomies. To do so would be to apply a fine filter prior to conducting the field research, which may lead to core concepts being

missed in data collection, synthesis and coding and therefore represents a confirmation bias. These categories do however lend structure to a data collection approach and provide possible categories to which emerging themes can be compared alongside related literature. A grounded theorist who embeds reflexive practice within their methodology is therefore capable of undertaking an initial orientating literature review to critically analyse existing theoretical and subject literature, which may inform thinking without letting it dominate or influence any innovative or novel constructs that may emerge through the data collection and analysis stages of the study. An approach recommended by Charmaz is to *'consider treating extant concepts as problematic and then look for the extent to which their characteristics are lived and understood, not as given in textbooks'*. She further suggests that a researcher may allow their existing knowledge of other key studies in the field and extant theories to 'lay fallow' until the study's grounded theory, analytic categories and relationships are developed, but that they should nonetheless *'remain alert as to whether, when, and to what extent earlier ideas and findings enter your research and, if so, subject them to rigorous scrutiny.'* (Charmaz, 2014, p307).

It is useful to conduct a foundational review of literature within the field of interest to ensure that the study does not replicate existing work, and at the same time support the theoretical sensitising of the researcher. A grounded theorist who substantially engages with the literature at an early stage may develop enhanced theoretical sensitivity allowing them to realise the relevance of the emergent concepts within the field of study (Goulding, 2005, p71). These emergent concepts can be developed or incorporated into their substantive theory at a later stage. Thornberg and Dunne (2019, p210) suggest that reviewing the literature enhances and encourages critical analysis of emergent concepts and that early reading in the field, 'does not eliminate a need to return to the literature both during and at the end of the analysis'. In analysing different approaches to the literature in grounded theory studies, Bryant (2019) presents Thornburg and Dunne's three phase format: initial, ongoing, and final review. The initial review forms the understanding and basis for future work, the second (or ongoing phase) is guided by the initial review as well as the data collection and analysis stages, where existing empirical studies may be relevant to emergent data, and the later review (or final phase) where the constructed grounded theory is compared, contrasted, and contextualised in relation to existing research and established theories (Bryant, 2019, pp108-111). Bryant suggests that the latter stages of theoretical coding should be referenced as a 'return to' or 'engagement with' the literature. It is therefore useful to be engaged and familiar with a wide range of relevant literature and research appropriate the field of study, and to revisit, analyse and incorporate published material at multiple stages throughout the research process.

2.3 Foundational Literature Review: Pre-data Collection

The foundational literature review was conducted as part of the study's reflexive strategy, to engage with the contextual realities and challenges of conducting translational cancer research within healthcare systems. This review, undertaken in the design stages of the study purposefully did not develop a priori theory in relation to cancer clinical trial delivery. McGhee et al (2007) emphasise the importance of not forming an *a priori* framework and that the study focus should be related to, but not grounded in the initial literature review. The importance of the role of reflexivity is highlighted as a necessity in preventing 'prior knowledge distorting the researcher's perceptions of the data' (McGhee et al, 2007, p340). The constructivist approach to conducting the literature review pre-data collection is recommended by Charmaz (2006, p166) as a method of 'outlining the path'. This aligns with the first phase of Charmaz's social constructionist version of developing grounded theory, "(1). Creating and refining the research and data collection questions" (Charmaz, 1990).

The initial review of existing, situated knowledge and theoretical frameworks within the literature provided a pragmatic orientation for conducting research into organisational processes. It further supported the contextual sensitising of the researcher in developing an understanding of the nature of complex behaviours and interacting phenomena present within social and technical systems which form part of the implementation of translational cancer research within national healthcare systems, such as the NHS. Nunes et al (2010) proposed that grounded theory researchers develop contextualised insight and understanding from the outset of the "complex contextual characteristics of the human-activity system being studied." Developing an understanding of key thinking and awareness of contextual challenges relating to a particular field in order to initiate inquiry is an approach supported by Charmaz (2006). An orienting literature review can also be useful in gaining a broader conceptual understanding of the field of study and be effective in identifying any important theory-practice gaps worthy of further research. This foundational literature review was undertaken prior to engagement with research participants to provide a sensitising orientation of the field of cancer, clinical epidemiology and advances in therapeutic advances and treatments, developed through translational science and medical research. Broad searches of literature were conducted relating to translational research covering such terms as: cancer research, clinical trial delivery, disease epidemiology, patient management and follow-up, as well healthcare systems and governance, which remained open and sensitive to complex and detailed subject areas. This initial review therefore served to; develop contextual sensitivity, determine key priority research areas, provide a framework for investigation, and ensure that the proposed study did not duplicate existing work on clinical trial delivery, and met institutional and regulatory requirements for

researchers to examine and cite relevant literature and existing research with the field of study at the proposal and development stages (El Hussein et al, 2017).

2.3.1 The Research Problem – Interfacing with Cancer

The human condition is emergent, complex, and dynamic. Health and disease states across global populations evolve in response to multiple interacting agents operating within ranging systems and networks, from cultural, social, economic, and political arenas to genetic, biological, and physical environments (Henly et al, 2011). The result of such agents of change on human evolution is genetic diversity, which in turn introduces biological risk factors and genetic preconditioning for disease susceptibility within populations. Donaldson et al (2015, p367) highlight the importance of studying human genetic variation in order to better understand complex diseases. Significant advances in genomic science have heralded in a new era of medicine, revealing new layers of complexity, and introducing ethical, financial, and practical challenges for clinical research and healthcare delivery. Where medical science meets clinical practice there needs to be a matched capacity to evolve, a premise put forward by Erichsen and Chanock (2004) who stated:

“If the promise of the genomic era is to be realised, we must integrate this information into new strategies for implementation in both public health measures and, most importantly, provision of individual cancer-related care”.

The challenge and promise of the era is highlighted by Sledge (2012) who stated:

“The pace of clinical cancer research is threatened even as scientific knowledge continues to explode. These are largely self-inflicted wounds, human in cause and therefore amenable to human solution, given sufficient resources and political will.”

The promise of a genomic era presents a **capacity and capability paradox** in translational science. The identification of this concept within the foundational literature provided an important emergent conceptual category which was recorded as a memo and carried forward to later stages of coding and comparison (see section 6.4.2).

2.3.2 Cancer Incidence and Epidemiology

Cancer is a leading cause of death globally posing a major healthcare challenge for populations around the world, who are witnessing increases in both incidence and mortality rates (Sung et al, 2021). GLOBCON 2020 estimated that there were 19.3 million new cancer cancers and 10 million deaths worldwide in 2019 (Sung et al, 2021). These figures

show an upward trend based on WHO reported figures of 14 million new cancer cases each year and 8.8 million deaths around the globe (Montagnana and Lippi, 2017). With the global cancer burden expected to grow to 28.4 million cases in 2040 (Sung et al, 2021), cancer malignancies are set to be one of the leading healthcare issues which will impose major clinical, societal, and economic burdens locally and globally (Mattiuzzi and Lippi, 2019). Projected figures anticipate that 4 million people are expected to be living in the UK with the disease by 2030, with a further growth of over 1 million over the following decade to reach 5.3 million by 2040 (Maddams et al, 2012). Whilst the disease population is growing, similarly short term and long term survival rates are increasing, with overall net survival rates of 50% of people diagnosed with cancer surviving for ten years or more (Quaresma et al, 2015). For the NHS this translates into substantial escalation of costs each decade, with accumulating economic and patient logistical burdens for treatment and management of long-term complex diseases. This highlights the requirement to accelerate translational cancer research but also review the infrastructure enabling clinical study implementation, to realise operational efficiencies and deliver benefits to the growing cancer population. The dilemma and paradox here is one of facilitating the capabilities of science to develop effective new treatments for cancer, whilst developing sustainable solutions to enhance the capacity of healthcare organisations to deliver translational medicine and long-term patient management and follow-up. Clinical Epidemiology (CE) is a core scientific field contributing to the provision of evidence-based medicine informing clinical medicine and healthcare provision. This scientific field's key principles are succinctly described in the following quotation:

“The purpose of clinical epidemiology is to foster methods of clinical observation and interpretation that lead to valid conclusions and better patient care...observations should address questions facing patients and clinicians and results should include patient-centred health outcomes (the 5 Ds).” (Fletcher, 2021)

Cancer epidemiology is pivotal to understanding the multifactorial drivers of such growth in order to develop adequate responses to slow and reverse the growth trajectory (Mattiuzzi and Lippi, 2019). Cancer research is a specialist field within clinical epidemiology which is crucial to the advancement of patient treatment and care, yet it faces augmenting challenges due to the complex nature of the disease itself, stratified treatments, and intensive trial protocols, compounded by increasing global disease burdens. The interrelation between genetic and environmental risk factors in the development of cancer, in combination with an ageing population make cancer one of the most complex diseases for society to manage.

2.3.3 The Capacity of the System in Clinical Research and Healthcare

The increase in cancer incidence combined with improving survival rates, follow-up demands, and funding pressures necessitates operational review of trial designs and implementation frameworks to articulate impacts on sites, patients, and professionals. The unique nature of the NHS warrants in-depth study to comprehend variables and phenomena contributing to service pressures in trial delivery and identify the changing needs of patients and research professionals. Capacity to manage research designs supporting scientific advancements in cancer research will require new approaches acknowledging increasing study complexities and bespoke therapies specific to smaller populations, which are likely to test existing NHS strategies. Amendments and complex designs place significant burden on participating sites and cancer, as a multi-factored disease, adds to the intensity.

Research is a critical element within the provision of healthcare enabling patients to benefit from the latest drugs and treatments, yet within the NHS and internationally there are augmenting challenges in the management of clinical trials, with cancer studies featuring amongst the most complex incorporating prolonged follow-up and intricate protocols. Substantial growth in protocol procedures, frequent amendments and complex designs place significant burdens on the individuals and sites delivering cancer clinical trials (Getz & Campo, 2018). Studies delivered in NHS settings experience further complexity factors of which financial, cultural, and organisational systems are elements. The evidence in relation to clinical research operational delivery issues focused predominantly on procedures, interventions and protocol design and their impact upon operational efficiency. Core themes emerging from the literature indicated that complexity in protocols is increasing with augmentation in number of procedures, inclusion criteria, data collection elements and subject questionnaires, in addition to extended trial duration and follow-up requirements. These elements have resulted in a growing burden for participating sites, increased the number of adverse events, impacted subject enrolment and placed pressure on site capacity and capabilities to deliver studies. There is a significant gap in the literature however which explains the impact of operational demands and procedures on the key patient and research professional stakeholders central to their delivery.

2.3.4 Clinical Research in the National Health Service (NHS)

The initial orienting focus areas of the study was an investigation into the nature of cancer research implementation within the NHS, with an aim to develop detailed knowledge of the key determinants influencing future growth and sustainability. The study sought to develop in-depth contextualised knowledge of the resources and opportunities within the NHS, and

identify the barriers or facilitators present in the delivery of cancer clinical trials. These elements were investigated through an engagement with NHS patients and research professionals taking part in a clinical trials to understand their perceptions of phenomena the meaning they applied to concepts, and any implications for practice. At the outset of the project the model shown below (Fig. 2.1) was developed, and included in the study protocol, to structure the initial approach to the research. This outlines areas of research interest which were pertinent to an investigation into the barriers and facilitators influencing the capacity of the NHS system to delivery cancer clinical research, and guide the first literature searches.

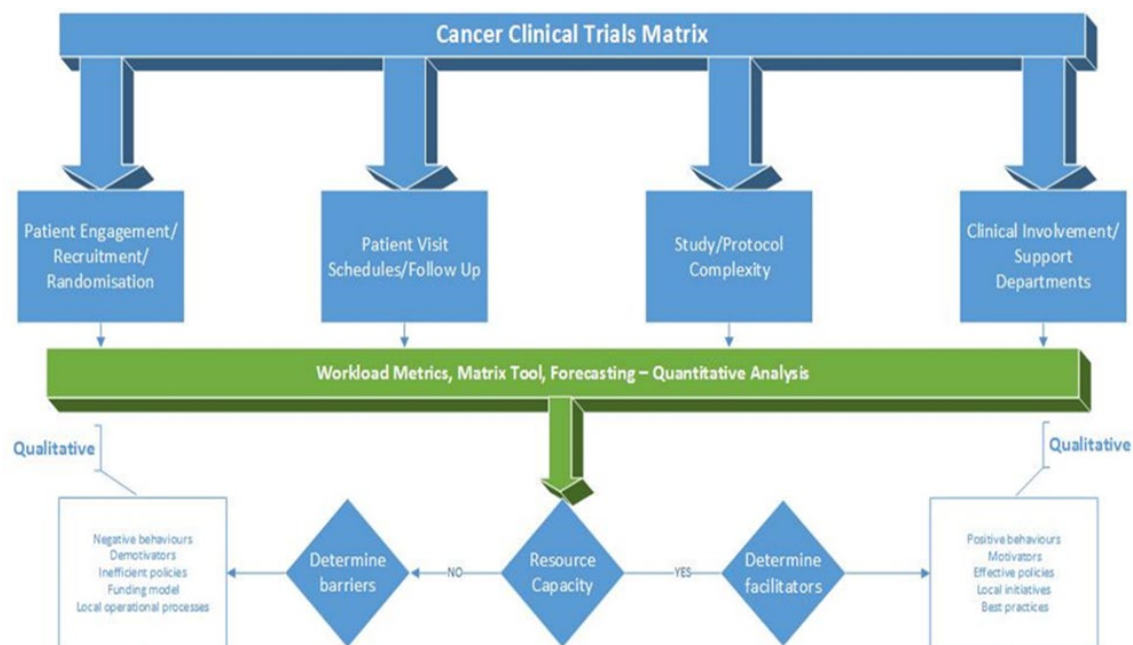


Fig 2.1 Cancer Clinical Trials Matrix.

Clinical Research is a transdisciplinary science and a clinical practice which draws on innovation, endeavour and critical analysis of professionals working across the health sciences and is often described as a translational science, which is part of a continuum of intra-relational bench to bedside study and practices from research laboratories to clinics. A report in response to the House of Lords inquiry into genomic medicine stated:

“We need to ensure that the NHS is ready for future developments and that new technologies are properly introduced, without hindrance, from laboratory bench to bedside.”

The commissioners within their recommendations made the following statements:

“We recommend that the Government should reconsider how they will prepare NHS commissioners and providers for the uptake of genomic medicine in the NHS. We also

recommend that the National Institute for Health Research, as part of its remit, regularly monitors developments in genomic medicine and their implications for the NHS now and in the future (Paragraph 8.14)...we do not believe that the NIHR is best placed to prepare commissioners and providers for the uptake of genomic medicine in the NHS". (House of Lords, 2009).

2.3.5 Patient Management and Follow-Up

Patient management and follow-up in cancer clinical trials is a significant element of the workload of trial sites in delivering research studies, yet one which receives limited acknowledgement in terms of its impact and long-term sustainability. The definition of these terms is also indeterminate and fluid (indicative of complex adaptive systems). Challenges were also identified that length of follow-up and clinical trial designs were demonstrating sustained, incremental growth, and that the burden in delivering cancer research at trial sites was a significant problem for healthcare organisations and research staff. Evidence also showed that the growing procedural demands and complex trial interventions were impacting patients and their capacity to participate in clinical trials.

Follow-up within clinical trials is a term which can have different interpretations dependent upon the role of the researcher. A search of NIHR, INVOLVE, NCRI and related industry websites and documents provides a range of nuanced definitions, some incorporating interventions and others indicating a more observational stance. In practice clinical research nurses refer to 'study visits' interchangeably with the term 'follow-up'. The description shown on the NIHR Involve website defines follow-up as "a process of periodic contact with participants enrolled in the trial for the purpose of administering the assigned intervention(s), modifying the course of intervention(s), observing the effects of the intervention(s), or for data collection" (INVOLVE, 2017). Alternative NIHR documents have identified follow-up as a study phase which starts when a participant stops receiving the study intervention. Confusion in terminology, whether occurring through procedural and documentation disparity or common parlance makes it difficult to determine the scale of the potential UK-wide associated workload. This study seeks to create a standardised terminology for use across trusts and networks so that all review and quantifying of 'follow-up' work and resource allocated is undertaken on a like-for-like basis. Clarity will be sought through researching usage of the term and undertaking consensus methods to achieve a working definition. In addition to terminology confusion, the burden of follow-up is intrinsically linked to the complexity of studies and so a review without determining their inter-related nature would be incomplete.

Follow-Up: The term follow-up used in relation to patient care is defined in the National Cancer Institute (NCI) dictionary of cancer terms as “Monitoring a person's health over time after treatment. This includes keeping track of the health of people who participate in a clinical study or clinical trial for a period of time, both during the study and after the study ends.” (NCI, 2021). The definition for follow-up however is not universally agreed upon between healthcare organisations and professionals, and these ranging interpretations are discussed in later chapters with research professional participant’s definitions presented in Chapter Six (Section 6.2).

2.4 Emergent Literature Review: The Research Data Collection Stages

The emergent literature review was an unfolding evaluation of concepts relating to operational complexity and patient follow-up in cancer research, revealing core issues and concerns from the perspectives of research practitioners and trial patients. This fluid and responsive approach allowed for a reflexive and contextualised review of the research data, allowing key concepts to emerge from through participants’ experiences and perspectives, who are the conductors or receivers of clinical research interventions and operations. My concern has been to remain as unbiased as possible in relation to the subject area and to identify the core issues facing research practitioners. From a practical stance it is a valid approach to conduct literature review concurrently with the emerging data and critically analyse the themes against it. This stage is conducive with Glaser and Strauss’s original concept that ‘all is data’. You can then review again as the data analysis draws to a close. To that extent, the literature review in this study is mindful of a Straussian and Constructivist approach, whereby the researcher maintains a relationship with the extant literature throughout the research process (Thornberg and Dunne, 2019, p211).

An initial review was conducted to identify existing work and perspective relevant to clinical research operational delivery and the focus areas of complexity and patient follow-up. However, as the research progressed there was a continual engagement with literature, and emergent phenomena which was directed by the data collection, theoretical sampling, and the process of constant comparative analysis. The critical analysis of key theoretical literature and context-related publications therefore ran concurrently with data collection throughout the life of the study. The data generated was constantly referenced against the existing theoretical and contextual literature. It is important to develop theoretical sensitivity and to this end extensive literature sampling was undertaken throughout the course of the data collection, in order to understand how existing theory may have relevance to the themes emerging and how these may be either accepted, developed, or rejected.

2.4.1 Emergent Perspectives

As the focus of the research was to understand the unique characteristics and nature of operational and clinical aspects of delivering cancer clinical trials in the NHS, the investigation needed to open to emergent themes and perceptions. All emergent data therefore had the potential to develop, as the research progressed, into core conceptual categories with the potential to form explanatory frameworks and viable interpretations of organising structures, behaviours and outcomes present within the clinical research and healthcare delivery systems under study. The potential for emergent phenomena to reveal unique properties of systems and their transactional behaviours therefore requires that an openness and dialogue is maintained throughout the study, with the multifarious and faceted data, ensuing from interactions with research participants, and being cognisant of the potential value of their testimony and situated experiences. A sensitised grounded theory approach which remains open and sensitive to wide-ranging phenomena has greater potential and power to illuminate and account for evolving cultural nuances relevant to the field of study (McCall and Edwards, 2021). The initial challenge for the grounded theorist therefore lies in making sense of the proliferation of conceptual data and interactions between niche and nuanced sub-categories. The next step for the researcher is to compare and contrast the kaleidoscopic data segments to extant theories within the core organising environments of cancer, healthcare, and operations research. The complexity and scale of the challenge then expands, leading to asking questions about the nature of knowledge extraction from complex organisational networked systems with stakeholders approaching and understanding and reality from different perspectives. Scale and relationship and the levels of analysis in understanding problematic and emergent phenomena require asking questions at different levels. Waring and Skoumpopoulou (2011) raise the issue of levels of organisational analysis, asking the question:

“Should researchers only explore the culture at the holistic, corporate level or should they consider the sub-groups and individuals who constitute the organisation?”

Where specialists and practitioners interact in the delivery of translational medicine, guided by ambitions and aspirations for genomic and personalised medicine, yet delivered within a complex, varied and challenged national healthcare system the capacity and capability paradox, which inevitably arises, needs to develop comprehensive, perspectival, and responsive analysis at all system levels. The point of transition in systems is where properties and values of one realm interact and communicate or share with the properties and values of another. The interactional and relational interfaces across all system levels is therefore the point at which tension, conflict and paradox emerge. A conceptual framework

to analyse phenomena occurring within and across human, system and organisational levels needs be receptive to all sensitising and complex properties at play. Environment, initial and fluidity of elements within systems along with their values, behaviours, scale and stability are organising constructs to understand concepts of meaning, enablement and resistance across multiple levels of reality, from macro to micro system levels.

The framework for comparison of the emergent data therefore required an understand of the nature of complexity in cancer clinical research operational delivery and interacting levels of phenomena influencing clinical research and patient outcomes. This brings into scope the study of phenomena within Complex Adaptive Systems (CAS), quantum mechanics the analysis of linear and non-linear systems, broadening the explanatory power of the study's emergent data and the relevance of variety and diversity in advancing healthcare sciences and the capacity and capability of organisations to keep pace with cancer and its dynamically evolving research paradigm.

2.4.1.1 Complexity in Cancer Clinical Research and Healthcare Delivery

Healthcare is a complex domain. Health services research and operations are recognised as dynamic and rapidly evolving systems, yet remain neglected fields of research and methodological evaluation, “desperately seeking an overdue paradigm shift” (Greenhalgh and Papoutsis, 2018). The scientific community has heralded advances in cancer research and targeted medicine as paradigmatic shifts (Xue & Wilcox, 2016; Emens et al, 2016) yet in the context of operational delivery there has been limited action and dialogue of the relational shift in healthcare operational delivery. It is an adaptive system which cannot be measured or analysed, in terms of its operational effectiveness and interacting behaviours, by applying simplistic performance measurement tools. Neither can it be understood by simply knowing about individual components of the system (Braithwaite, 2018, p1). This is problematic for developing sustainable and goal orientated models for healthcare delivery and management when its systems and processes are non-linear, unpredictable and indeterministic. Braithwaite (2018) argues that no other operational industry's system is more complex and its “future cannot be predicted by extrapolating from the past”. He goes on to recommend that effective change within healthcare systems needs to factor in systemic knowledge recognising complexity as opposed to applying the methods of the current ‘improvement paradigm, which applies linear thinking in blunt ways. (Braithwaite, 2018). Enabling research growth necessitates structured workforce planning yet there is poor application of this crucial management function across the NHS (Alderwick & Dixon, 2019). To build capacity, manage increasingly complex trials and support patient-centred care, research organisations, funders and policy makers need to evaluate current delivery

and performance management models, seek interdisciplinary stakeholder feedback, and consider adopting creative, design-thinking approaches with reflective and critical capabilities (Paquet & Ragan, 2012).

Clinical research is a field of healthcare which is by nature complex, it is emergent, exploratory and its purpose is to advance knowledge of biological responses to therapeutic agents or healthcare interventions. It is an enterprise carrying many complex characteristics, one which demonstrates a complex order composed of continual development and change, states of flux and evolution. The complexity of the humans who are at the core of the healthcare system and their exposure to complex phenomena is an area where there is little research being undertaken and limited strategies to address complexities from the human perspective. The growth in complexity of clinical research delivery, and augmenting challenges of personalised medicine, increasing cancer rates and the long-term management and follow-up of patients with chronic, long-term healthcare needs “requires us to think, work and collaborate in different ways” (Britnell, 2019). Understanding complexity in clinical research and healthcare is a priority. Chu et al (2003) present a strategy for identifying sources and ‘generators’ of complexity in a specific system under study, and conclude that to gain a general understanding of the system and its complexity phenomena, such generators must be considered. Failing to recognise the complexity of an operational system or the challenges of complexity at different levels and types of systems, such as healthcare systems can have significant consequences, including technical, financial, and human impacts. Healthcare organisations, professionals and governance bodies need to develop and promote wider understanding of its complexity, in order to provide safe, effective, and equitable healthcare, which promote health and reduce system errors and failures, for example preventing staff burnout, patient harm, critical clinical incidents or serious adverse events. In a patient safety and learning system paper published by WHO (2020) the following statements are made:

“Understanding why and how an incident happens involves establishing why and how errors occur within the context of complex systems and what part human behaviour plays in this process...Health care is a complex system, and all the general and specialist services that make up the whole are also complex subsystems. Within such complex systems the propensity for error is high, and in some cases its consequences will be serious or even catastrophic”.

Phillips et al (2017) address the nature of complexity and uncertainty within the emergent areas of Precision Medicine and Digital Health, which they suggest are ‘underpinned by convergent or cross-industry innovation’, which in consequence challenges traditional

organisational and methodological processes, knowledge and belief systems, roles and specialisms. In cancer clinical trials which are investigating the effects of novel, combined or repurposed therapeutics for use in humans, there are multiple layers of complexity and systems, involving risk, emergence, adaption, and uncertainty. In the manufacture, testing and delivery of new therapies and the necessary interaction between clinical research organisations, governance and political bodies, and the networks of healthcare providers, professionals, and clinical trial participants there are ranging processes, systems, and perceptions in continual states of evolution, interaction, and negotiation. Healthcare and clinical research involving biological and social systems, and the multiple interacting levels and agents, are therefore by nature inherently complex (Wilson and Holt, 2001). The extant literature underlines a need for broad, cyclical, and continual analysis of research advancements and disease burdens to anticipate future demands for resources, as well as facilitating sustainable growth, productivity, and improvements in patient care.

2.4.1.2 Cancer as a Complex Disease

The nature of cancer and its multiplicity of forms, combined with its astounding ability to transform and evolve, has made it one of the greatest challenges for medical science over millennia. The extant literature on cancer presents it as a complex set of diseases which historically and contemporaneously continues to be problematic for public health globally. Mukherjee (2011) in his book “The Emperor of All Maladies” refers to the inherent heterogeneity of cancer, describing it as an expansive disease which demonstrates a “spectrum of behavior”. Cancers are complex, dynamic and continuously evolving heterogeneous cell masses (Bleijs et al, 2019, McGranahan & Swanton, 2017). The appellation of cancer as a single disease is a confounding misnomer which fails to express its complexity and plethora of states and variant forms of diseases. Fymat (2021) eloquently describes cancer as *‘the pernicious clonally evolving disease braided in our genome’*. In describing the condition he states:

“Many diseases are lumped together under the denomination “cancer” because they share a fundamental biological feature, namely abnormal cell growth. However, cancer is not a single disease. It is a multiplicity of diseases caused by the uncontrolled growth of a single cell unleashed by mutations. Cancer cells can grow faster, flourish more profusely, adapt better, recover more rapidly, and repair faster...than normal cells. They are in effect more perfect versions of normal cells...and can even become immortal! We naively thought that cancer could be defeated by either preventing mutations from occurring in normal cells or else finding the means to eliminate the mutated cells without

compromising normal growth. Unfortunately, this view did not take into account the pernicious genetic intertwining of normal and cancerous growths” (Fymat, 2021, p10).

Cancer demonstrates complex properties such as emergence and variability, and one that continues to evade control or cure, and in its treatment and management is an “intricate multi-dimensional economic, social, anthropological and political issues with considerable consequences “ (Miramontes & Alvarez-Buylla, 2019, p2). Caldu-Primo et al (2019, p5) state, *“A systemic approach to cancer must consider it as an emergent process from the interrelationship of genetic, environmental, and developmental processes”*.

Understanding the heterogeneity and emergent properties of cancers is a critical requirement for designing clinical trials and the optimisation of “therapeutic strategies for defeating the complex battle against cancer” (Lopez Castillo et al, 2019, pp63). Interfacing with cancer requires an analysis of complexity at different systems levels and their interfaces; an analysis across and between macro, micro and meso systems, and biological, technical and social systems. However, results from this study demonstrate that strategic approaches to healthcare and clinical trial delivery demonstrate a disconnect with the substantive thinking by failing to recognise that cancer as a complex, systemic disease. Greaves (2015, p816) in discussing the evolutionary characteristics of cancer suggests that “Cancer is replete with evolutionary legacies. It might well yield to an evolutionary fix.” Matching the dynamic, evolving and complex nature of the disease requires systems approaches across the disciplines involved in translational cancer research implementation.

2.4.1.3 Clinical Research Populations

Traditionally cancer has been categorised and treated based upon the location in the body of the primary tumour (Cunanan et al, 2017). With a move to personalised medicine the provision of clinical trials based on incidence of cancers by primary location is not suited to the modelling and provision of care relative to patient populations and geographical location. With the specialist requirements for complex treatments which may only be suitable for delivery at larger, specialist cancer centres there is a risk of building in population inequalities into the access to the latest treatments provided through clinical trials. This study highlighted both patient and research professional participant’s concerns relating to locale and access to clinical research treatments. Other issues exist with implications for the future of clinical research delivery, and these include issues around the fair representation of populations and the ethical basis of inclusion and exclusion criteria. Jones (2010, p394) raises the issue of chronic diseases and the representation of elderly and complex patients within clinical trials, stating:

“Clinical trials of new drugs are invariably conducted according to trial protocols with explicit inclusion and exclusion criteria. These exclusion criteria are likely to exclude from study the very patients whose complex medical problems we need to address — the very old, the demented, frail patients with serious co-existing disease, abnormal liver and renal function, and taking multiple drug treatments — they are too difficult for inclusion in drug trials in search of a ‘clean’ study population and a clear result.”

Ford et al. (2008) state: *“The lack of diversity in randomised study populations reduces opportunities for discovering effects that may be particularly relevant to underrepresented populations and contributes to inequitable distribution of benefits and risks of trial participation.”*

The development of healthcare models of personalised and precision medicine (PPM) development and the delivery of clinical research have expanded to include specialist services and expertise which are located in metropolitan areas. This has an impact on the ability to deliver more complex, specialist trials involving personalised medicine across the NHS estates with implications for rural and remote populations.

2.4.2 Complex Adaptive Systems (CAS) or Complexity Science

A complex adaptive system can be defined as ‘a collection of individual agents with freedom to act in ways that are not always totally predictable, and whose actions are interconnected so that one agent’s actions changes the context for the other agents’ (Plsek and Greenhalgh, 2001). Complexity Science, also known as complex adaptive systems, is a broad field of systems science which can be applied to many different professional fields and contexts, for example healthcare delivery, information technology, operational research. Complexity as a science, an approach, a perspective and as a property of multiple systems, is studied in depth throughout this thesis. Mossman (2014, p212) defined complexity as a “Property of certain systems characterised by components acting interdependently such that the behaviour of the entire system cannot be accounted for or predicted by the properties of individual components”. The interactions and behaviours between local agents give rise to emergence in complex systems (Vasileiadou, 2012). In Chapters Six and Seven the perspectives of EFACCT participants in relation to the nature of complexity, and its situated meaning and localised impact are presented. Braithwaite et al, (2018) argue that complexity sciences is useful as a conceptual framework for change, and as a ‘theoretical approach to understanding interconnections among agents and how they give rise to emergent, dynamic, systems-level behaviours’.

Coherence: The concept of coherence is applied in different academic fields and its definitions are relative to context. Generalised dictionary definitions refer to coherence as a property or state of logical or natural interconnections and consistencies between parts which form an aesthetic whole. It is a property of complex adaptive systems, present in biological, organisational, and global level systems, which is in a relationship with the property of emergence. Lissack and Letiche (2002) state, “Due to emergent events and behaviour, boundaries shift. Coherence and identity act as countervailing forces to the short-term aspects of emergence”. Braithwaite et al (2017) delineate CASs as having four constituent features: individual agents, interconnections, dynamic behaviours and rules and governance. Johnson (2002, p128) suggests that ‘an adaptive information network capable of complex pattern recognition could prove to be one of the most important inventions in all of human history’.

The challenges of negotiation complex pathways, process and relationships in clinical research delivery was revealed by many of the study participants. Braithwaite et al (2017) state ‘the diversity of agents and the multiplicity of interactions in a CAS means that relationships are always shifting, mutating and modifying, because, for example, participants interact idiosyncratically, process information in different ways and respond to their environment and each other distinctively’. A human systems framework is needed in healthcare to develop effective feedback loops, improve communication, facilitate shared knowledge and raise awareness of the complex challenges in interfacing and interacting between different contexts and levels within cancer clinical research operational delivery. Substantial improvements are required in communication between different groups and levels in the system (macro to micro level) - from the ‘coal-face to the interfaces with CRNs, decision-makers, sponsors and funders. Wilson and Holt (2001) argue that:

“Complexity science suggests an alternative model— that illness (and health) result from complex, dynamic, and unique interactions between different components of the overall system. Effective clinical decision making requires a holistic approach that accepts unpredictability and builds on subtle emergent forces within the overall system”.

Complex Behaviour, Complexity Theory and Complex Systems

Complexity as a phenomenon will be investigated as a core theme and its place within clinical trial operations and cancer as a ‘complex disease’. One element contributing to complexity at multiple levels is uncertainty which requires a mixed-methods approach to address, due to its subjective and objective nature. Complexity and uncertainty straddle both the realms of social interaction involved with disease management and trial delivery

and the nature of cancer itself. Han et al (2011) describe three taxonomies in relation to uncertainty in healthcare; 1) sources of uncertainty, 2) substantive issues of uncertainty and 3) locus of uncertainty. They progress to form the subcategories of scientific (disease-centred), practical (system-centred), and personal (patient-centred) areas of uncertainty (Han et al, 2011), classifications well suited to studying clinical, organisational, technological and social challenges faced within cancer clinical research delivery. Context influences complexity but the knowledge and understanding of participants acting within that field influences its scale. Complexity can be transitory or pervasive, influenced by time, circumstance, and human interaction. Interaction with technology and how it confounds or supports efficiency forms part of the complex model within clinical research and healthcare, forming a sociotechnical system (Randhawa et al, 2016). The study will inductively query complexity through a review of perceived complex interventions, compare interpretations and approaches to scenarios and issues, measure and quantify occurrences and analyse patterns to bring clarity, interpretation, and possible solutions. An elemental form of complex behaviour is described by Johnson as “a system with multiple agents dynamically interacting in multiple ways, following local rules and oblivious to any higher-level instructions’ (Johnson, 2001, p19).

2.4.2.1 Comparing and Situating Complexity

The foundational literature highlighted the rise in complexity within cancer clinical trials and was therefore included as a central element of the study. The initial stages of the study demonstrated that the notion of complexity was broader than the initial orientation had suggested, with emergent themes around complexity encompassing broader social, systems and theoretical aspects of complexity. The nature of protocol complexity and its associated challenges for clinical trial delivery, is a field of research predominantly led by Ken Getz and the Centre for the Study of Drug Development (CSDD). Getz et al. (2016, p441) has reported on the continued growth in the technical aspects of trial protocols over the last decade, but also highlighted the challenges that frequent protocol amendments are posing for trial delivery sites internationally, and calls for further granular analysis into the impact of protocol amendments at sites. The research findings in this thesis provide in-depth qualitative analysis on the nature of complexity in operational and social terms, including the impact of protocol amendments and the resultant follow-up and workload burdens. The granularity of the data within this grounded theory study, as well as its breadth, allows for the range and depth of complex factors in clinical research to be understood at many levels.

The emergent property of complexity (in this example relating to protocol amendments) emerged as key theme in the study. Significant difficulties are faced by NHS clinical trials sites in managing resources in the face of uncertainty and moveable end points in trials emerged as a major challenge, and was consistently reported by research professional participants at sites across England and Scotland. The notion of changing parameters is an important element to consider in operational contexts, but it also serves to highlight the multi-faceted nature of complexity and its influence on ranging environments and interactions within clinical research and healthcare systems. Such phenomena therefore needed to be compared and interpreted in relation to the wider literature on complexity, its levels and its properties. Burns and Gentry (1980, p19) reference the challenges of managing complexity stating, “*Complexity mounts as the results of input decisions become more vague, and as the scope of the problem broadens.*”

2.4.2.2 Defining Complexity

Braithwaite et al (2017) provide the following guiding explanation of complexity: “Complexity refers to the density of interactions between different components (agents, parts, elements, artefacts) in a system or a model representing a system and produce roles and behaviours that emerge from those interactions.” This definition describes the nature of delivering clinical trials within a large networked system where relationships, regulations and requirements are constantly evolving and entangles. Cohn et al. (2013) describe complexity as “*a dynamic and constantly emerging set of processes and objects that not only interact with each other, but come to be defined by those interactions.*” In this study we examine the nature of experiential complexity and its implications for cancer patients and clinical research professionals.

2.4.2.2 Properties of Complexity

The key properties of complexity identified within the substantive literature encompass the following characteristics present within environments and systems:

1. Emergence
2. Variability
3. Uncertainty
4. Sensitivity to conditions
5. Instability

Emergence is a property of complex systems. Mitleton-Kelly (2003) states, “Emergent properties, qualities, patterns or structures, arise from the interaction of individual elements:

they are greater than the sum of the parts and cannot be predicted by studying the elements. Emergence is the process, which creates those properties or qualities or new structures.” Clinical research is an evolving and emergent field, elements which are properties of complexity. Its function is to ‘trial’ and ‘test’ new medicines and interventions, which logically places the work of researchers in the exploratory realms of uncertainty and unpredictable outcomes. Research and experimentation within humans and within healthcare systems involves emergent properties and behaviours, from biological to organisational systems and from individuals to operational networks, all contributing to complexity and uncertainty on the research journeys to discovery – expeditions to possibilities. Johnson (2001) describes emergence as ‘the movement from low-level rules to higher-level sophistication’ and the beginnings of emergence as ‘a higher-level pattern arising out of parallel complex interactions between local agents’ (Johnson, 2001, p19).

Cancer, through its transiency and burdensome characteristics, whether these are biological, psychological, or societal, means that its course of development and behaviour are unpredictable, which means that any approaches to its treatment and management need to recognise its conceptual properties of complexity, uncertainty, and emergence. These associated concepts have a significant impact on how clinical research and treatments are developed and delivered, which in turn impact operational and organisational models and strategies, as well as bringing associated complexities around prediction, resourcing, and sustainability of healthcare provision. Uncertainties linked to cancer’s transcendental nature are the complexities of the human genome, immune system and psychological response to disease and treatments.

2.4.2.3 Clinical Research and Healthcare as a Complex Adaptive Systems

The interacting systems across fields of medicine are by nature complex, yet theoretical and empirical study into the nature of complexity and its systemic implications for clinical research delivery, and more generally in healthcare provision, lacks substantial engagement. Greenhalgh and Papoutsis (2018, p16) argue that in “*open systems characterised by dynamically changing inter-relationships and tensions, conventional research designs predicated on linearity and unpredictability must be augmented by the study of how we can best deal with uncertainty, unpredictability and emergent causality.*” Our research has demonstrated that there is limited understanding or engagement with the complex nature of healthcare, and more specifically the emergent nature of cancer clinical trial designs and a move to personalised medicine, has not been matched by an effective

design and evaluation of the systems for their implementation. One research professional described the operating model for clinical research as “*barely sustainable*” stating, “There needs to be a complete overhaul of the funding of them, just the overall management.” The research professional studies exposed a disconnect between the clinical staff engaging with patients face to face in delivering cancer trials and the management and executive levels of staff who are involved in the strategic development of research implementation models or the commissioning and funding of services. **Professionals lacking understanding** and **lacking understanding** were dominant codes across all the research packages involving professionals, which is discussed further in Chapter Six (Section 6.4). The lack of understanding of complexity in trial delivery was also linked to themes of **Disengagement in Leadership** and the concept of a **Communication Vortex** (see section 6.4.1.1). The concept of a vortex was compared to the literature on Complex Adaptive Systems (CAS) theory which returned related literature on understanding healthcare systems, its reforms, and its key stakeholders. The metaphor of the **healthcare system as a vortex** is employed by Sturmberg et al (2010, p475; 2012, p206) who argue:

“Despite a health system not actually being a vortex, the vortex metaphor provides many insights to inform health system redesign.... [and visualise] the healthcare vortex as a metaphorical representation of a complex adaptive people-centred health system ...highlighting the patterns of its organisation, its structures and processes. At its centre is the patient’s experience of health — the system’s core attractor — all agents and interactions align and constantly realign around this....The health care vortex is a useful way to illustrate the cascading physical configuration of the agents within the health system, and to highlight the interactional behaviour between its agents concordant with the system’s shared vision (attractor). As a metaphor, the health care vortex embodies the self-organizing power inherent in a complex adaptive system around its attractor”.

Clinical research is a complex science of innovation and implementation, an evolving field of experimentation, adaption and solution development for clinical advancement, epidemiological study, and human health promotion. To advance scientific knowledge and therapeutic innovation, there needs to be a parallel model of operational and organisational development, which is capable of facilitating the environments, resources, and capabilities of research. Transdisciplinarity and incremental complexities in clinical research need to be understood and studied in order to develop sustainable solutions for effective delivery.

In creating the supportive environments and capacities for sustainable development it is necessary to manage the increasing complexities of problems and situations, and the ‘growing connectivity among processes and phenomena at different levels’ (Briceno, 2006).

To manage such complex adaptive systems and networked interfaces, it is necessary to provide mechanisms and frameworks which have the ability to enhance communication and levels of understanding between multiple disciplines, interacting organisations, and stakeholders. Sustainable development, complexity and transdisciplinarity in relation to the delivery of cancer clinical trials, and clinical research models in general, are neglected, under-researched fields of study. Understanding their connected properties and dimensions, is a critical area where new knowledge can make a significant contribution, in supporting the future growth, effective management, and sustainability of clinical research delivery within the NHS, and wider healthcare organisations.

Recognising clinical research as a complex adaptive system provides a framework for understanding the nature of its properties and challenges, and interacting behaviours from the macro to the micro levels of its scientific, organisational, and social environments. Its systems and professionals can develop transdisciplinarity behaviours to develop global understanding and new unified forms of knowledge, offering new models of developmental support, operational effectiveness and sustainable solutions for clinical research and healthcare delivery. Transdisciplinarity is an approach which can develop cohesion between, across and beyond the different disciplines (Nicolescu, 2014). Nicolescu argues that 'from a transdisciplinary point of view, complexity is a modern form of the very ancient principle of universal interdependence'. Within the realms of healthcare and research transdisciplinarity approaches seek to engage with the multiple perspectives and situated knowledge of stakeholders to develop effective, holistic and sustainable healthcare solutions, to solve and manage complex and intractable healthcare challenges. Pineo et al (2021, p489) theorise that transdisciplinarity 'responds to the demands of complex societal problems by recognising that academic knowledge and single discipline approaches will not be sufficient to understand causes and solutions for these issues'. They suggest that there are three core challenges in transdisciplinary research, which are: (i) participation, (ii) knowledge integration and (iii) moving from knowledge to action. The challenges of inclusion, cohesion, integration, and praxis in clinical research are discussed by Flinterman et al (2001) who suggest that 'patients are rarely partners in biomedical research; their influence on priority setting, research design, the undertaking of research, and interpretation or dissemination of results is thus marginal.' In recent years there have been moves to involve patients in the clinical research process; an area of patient engagement within the UK, named as Patient and Public Involvement and Engagement (PPIE). NICE guidelines were introduced in 1999 to promote the involvement of patients and the public in developing quality healthcare services and standards. NICE's patient and public involvement policy (NICE, 2013) is based on two key principles:

- “that lay people, and organisations representing their interests, have opportunities to contribute to developing NICE guidance, advice and quality standards, and support their implementation, and
- that, because of this contribution, our guidance and other products have a greater focus and relevance for the people most directly affected by our recommendations”.

Clinical Research Operational Capacities and Challenges

Clinical research is delivered within a complicated procedural, legislative and governance matrix environment, essential to protect the rights of participants and professionals, but this inevitably adds the complexity. A review of the hierarchical legislation and procedures that impact the delivery of research was required to understand the challenges faced by individuals and organisations in their endeavours to delivering efficient, timely and compliant studies. The addendum to the EMA 2016 E6(R2) guidelines for good clinical practice (GCP) acknowledged the growing complexity of clinical trials since the initial publication stating, ‘Since the development of the ICH GCP Guideline, the scale, complexity, and cost of clinical trials have increased.’ In the revised guidelines it was stated that these had been amended, “to encourage implementation of improved and more efficient approaches to clinical trial design, conduct, oversight, recording and reporting while continuing to ensure human subject protection and reliability of trial results” .

2.4.2.4 Clinical Research and Sustainable, Equitable Healthcare

Clinical research is by nature progressive and exploratory, developing new therapeutic approaches for chronic and emergent diseases in an era of growing technological and societal complexity. Steven Hawkins hypothesised that the twenty-first century would be ‘the century of complexity’, one which has implications healthcare and clinical research capacity and sustainability. In an era of novel precision medicine scientists, researchers and clinical research professionals need to engage with complexity and multi-disciplinarity, collaborating with their surrounding research fields and environments ‘to show future scientific impact’ (Wang & Wang, 2020). As targeted and personalised cancer treatments develop, research is required to understand clinical trial methodology, evolving protocol designs and operational implications for sites and patients to interpret the paradigm in the present era. Immunotherapy is a rapidly advancing field in clinical research, involving the study and targeting of immune checkpoint inhibitors (ICIs), yet clinical knowledge of the risks, incidence and duration of late onset, immune related toxicities from ICI trials is limited (Ghisoni et al, 2021). Long-term patient follow-up and the complexity of trials in the era of personalised medicine needs to be supported with a concurrently adaptive, creative, and responsive paradigm for delivery which can keep pace with the scientific advances of

clinical research. Presently the bench to bedside concept for cancer clinical trials is in an incoherent system, where comprehensibility, manageability, and meaningfulness between fields of operations and professions are lacking.

Rapid advances in cancer clinical research call for in-depth study into the existing NHS research infrastructure to comprehend stress points and factors affecting the capacity to support future demands. Without the evidence to understand existing operational effectiveness appropriate strategic decisions cannot be made with confidence. An adaptive NHS research implementation framework is needed to define operational models, ensuring resource and support structures align to changing research landscapes. With the advancements in personalised medicine and stratified biomarker studies, the models supporting clinical trial recruitment, management and follow-up need to be substantially re-designed and evaluated, as patient cohorts stratified by multiple biomarkers get smaller (Baumann et al, 2016). The impact and long-term effects on operational delivery of growing complexity and evolving trial designs needs to be understood across all stages of implementation and fields of systemic interventions; medical, organisational, and social.

The accumulation of scientific and medical knowledge across the centuries, have systematically advanced the frameworks and models for healthcare, fostering increasing scientific rigour and clinical observation (Sessler and Imrey, 2015), progressing to translational genomics and precision research approaches. Genomically driven research and precision medicine are important and necessary paradigm-shifting approaches to the management of complex, mutating and heterogenous diseases, such as cancer. In Chapter Two the importance and implications of such approaches to advancing cancer treatment are discussed in greater details, along with the need for a comprehensive evaluation of NHS capabilities to ethically provide an effective, fully-costed, model of precision cancer clinical trials is a key priority. At the forefront of research methodologies is the highly complex field of genetic medicine and gene therapy, a next generation approach, described in the following quotation by Martin Schulz, senior medical director for the gene therapy platform at Pfizer Rare Diseases (The Irish Times, 2021).

“Gene therapy is probably the most high-concept form of so-called “personalised” or “precision” medicine. As we learn more about the underlying genetic mechanisms of disease, we can deliver increasingly targeted treatments, tailored to the individual patient. It is the “next generation of medicine...In the beginning of the last century we had medicines that focused on treating symptoms, then towards the end of the 20th century we had disease modifying agents. But what truly excites me is that now we are focusing on developing medicines that target the underlying cause of a genetic disease at a cellular level.”

The changing nature of the political climate, the research landscape and cancer as an evolving and systemic disease means that the subject is convoluted, involved and complex. In developing a sustainable solution to support the future development of clinical research in ways which are innovative, make use of technological and therapeutic advances, and also sensitive to conditions and public health demands, clinical researchers, epidemiologists, and strategists need engage with the complexities of human biological and social systems. Understanding cancer as a complex disease and acknowledging the complexities of healthcare systems, has implications and benefits for research professionals involved in managing patient care and delivering clinical trials. The study's investigation of the social dimensions of clinical research and related properties of complexity brings into focus interfacing systems and the disease-health paradigms of pathogenesis and salutogenesis.

“Research and evaluation approaches need to provide a holistic and systemic view on the problem and/or solution. This is the challenge of scope” (Marchal et al, 2014).

Forming part of an evidential systemic relationship, efforts in overcoming persistent complexities of chronic disease and cancer complexities require the scientific, medical and operational healthcare professions to be strategically aligned maximising the opportunities for interdisciplinarity, knowledge exchange and the resourcefulness of societies to succeed in the face of intractable issues which confound the efforts of society and healthcare providers to improve public health in wide-ranging contexts, communities and disparate environments.

2.4.3 Social Dimensions of Clinical Research and Healthcare

In reviewing the literature of complexity in clinical trials, the focus of research is predominantly centred around the technical aspects of clinical trials and protocol designs, with limited study on the social and human dimensions of complexity from both the perspectives of patients and professionals and their experiences as key participants within the field. Hawkins (1999) suggests that medical schools should enhance the education of students in the humanistic dimensions of medicine, recognising the patient and their persona as ethically and intrinsically central to the medical situation and patient care.

The research data across all three research professional studies provided narrative and testimony on the importance of developing positive professional relationships within clinical research practice to promote effective working and enhanced outcomes for patients and professionals alike. ***Interprofessional working*** emerged as a sub-category of ***Complexity Interfaces***.

Developing programmes and policies which mandate the adoption of integrated and democratic approaches to interprofessional working and decision-making in healthcare organisations is not sufficient to ensure that their implementation is effective or understood by all stakeholders. There needs to be a significant step-change within large healthcare providers (such as the NHS) and their interacting partner organisations in how they advance and develop integrative cultures and transdisciplinary practice to meet the needs of patients and professionals alike. Brown (2021) argues that policies and statements which pronounce the requirement for collaborative working can be counterproductive.

“Simply putting structures in place without a contextually and professionally sensitive consideration of the needs and working practices of those who must enact joint working on a daily basis, is essentially, flawed” (Brown, 2021, p258).

Brown makes a good point, in that assumptive strategies are naïve where organisations believe that through issuing policy mandates for the implementation of collaborative practices and interdisciplinary engagement is sufficient to ensure their effective adoption across complex networks of interacting professionals, with their own localised challenges.

The development of person-centred philosophies for medicine and care are a priority, and these need to align with dynamic progression in societal medicine and scientific advancements but place social engagement and embed ongoing professional education of

The traditional medical model is based on a linear, mechanistic paradigm and pathogenic orientation which can limit progression within the healthcare system. Golembiewski (2017, p275) states, “The pathogenic model of health is dominant in the healthcare sector, and that has enormous inertia, which will not reorient towards health promotion easily.’ The challenges of implementing innovative solutions and effective change within large public healthcare organisations such as the NHS frequently encounter resistance which can take many forms, but typically involves bureaucratic and top-down behaviours and entrenched cultures. Braithwaite (2018,p1-3) argues that in order to implement change and effective improvements in healthcare systems there needs to be a movement away from linear thinking but instead embraces complexity and learning systems thinking with stronger feedback. He puts forward six principles on which to base a new approach to change in the healthcare sector:

1. *Pay more attention to how care is delivered at the coalface*
2. *Meaningful improvement is local, centred on natural networks of clinicians and patients*
3. *Appreciate how clinicians handle dynamic situations daily, constantly adapting, and getting so much right, and identify the factors underpinning that success*

4. *Identifying achievements across healthcare delivery and understanding their common factors (commonly reflecting complexity thinking)*
5. *Humble aspirations - recognition that small initiatives can yield unanticipated outcomes*
6. *Adopt a new mental model that appreciates the complexity of care systems and understands that change is always unpredictable*

These six recommendations align closely to the findings of this study and recommendations to addressing key challenges in clinical research delivery within the NHS reinforce these principles. Antonovsky (1979, p193) stated,

“In this era of chronic diseases (and not much less applicable to infectious diseases in such an era) the single-bullet approach can no longer be seen as viable in and of itself or even as the dominant weapon. In this context the sense of coherence becomes important”.

2.4.4 Salutogenic and Sustainable Models for Cancer Clinical Trial Delivery

Clinical research, in particular cancer clinical trial delivery, has not previously been studied from a salutogenic perspective. The research data and perspectives of study participants suggest that there is a need to develop new models for sustainable, equitable and health promotion through clinical trial models which acknowledge complexity of healthcare systems and also look to salutogenic resources for the benefit of patients, professionals and the environments for healthcare provision in the NHS, or other support networks and organisations for clinical research. Holistic, patient-centred models of health are guided by a salutogenic orientation, and humanistic, relationship-centred environments which Miller and Crabtree (2005) describe as healing landscapes offering “*an ecology of hope.*”

Antonovsky (1979) proposed the concept of the sense of coherence as a “*critical variable in explaining movement on the health ease/dis-ease continuum*” and defined it as a “*global orientation that expresses the extent to which one has a pervasive, enduring though dynamic feeling of confidence that one’s internal and external environments are predictable and that there is a high probability that things will work out as well as can reasonably be expected*” (Antonovsky, 1979, p123). In Antonovsky’s model (see Chapter Eight, Fig. 8.6) the stressors and resources, which are dynamically interacting during our lives and influencing our position and movement along the health ease/dis-ease continuum, contribute to our sense of coherence. Antonovsky argues that these life experiences, shaping our sense of coherence, are characterised by; consistency, participation in shaping outcomes, and balance (underload-overload balance). The resources at our disposal, which Antonovsky classes as Generalised Resistance Resources (GRRs) and Specific

Resistance Resources (SRRs), are mobilised in response to the stressors that we encounter in life, and in turn, ‘a strong sense of coherence, mobilising GRRs and SRRs, avoids stressors’ (Antonovsky, 1979, p184-185). Mittelmark et al (2017) offer a clarification of the nature of these different classifications of resources:

- Generalised Resistance Resources (GRRs), *“arise from the cultural, social and environmental conditions of living and early childhood and socialisations experiences, in addition to idiosyncratic factors and chance”*.
- Specific Resistance Resources (SRRs), *“are optimised by societal action in which health promotion has a contributing role, for example the provision of supportive social and physical environments”*.

In the context of the study of clinical research delivery, there is a gap in the knowledge relating to the understanding and application of GRRs and SRRs, both from the patient’s and research professionals perspectives, which influences their sense of coherence. In Chapter Four, the research design is explicated, and illustrates how the multi-dimensional design systematically analyses these different types of resources and stressors (aka barriers and facilitators) which influenced the life experiences of participants in the EFACCT study, their sense of coherence and strategies for managing and coping in their personal, situated contexts. This highlights the constructivist nature of human responses to health and disease experiences, where comprehensibility, manageability and meaning fullness (the core constructs of a sense of coherence) have a significant impact upon our reality and perceptions. Understanding the generalised and specific resources as well as the common or particular stressors interacting across the different healthcare networks, organisations, and patient environments, is the central purpose of this thesis. The particular and the general phenomena and sources of knowledge influencing health equity and sustainable delivery, calls for multiple viewpoints and methodologies to develop coherency in healthcare. To develop resources which are generalised as well as context-specific utility is through Antonovsky’s explanation of the role of GRRs and SRRs, and cited by Mittelmark et al (2017) as being:

“...imperative to focus on developing a fuller understanding of those generalised resistance resources that can be applied to meet all demands.” (Antonovsky, 1972, p.541).

2.4.5 Governance and Funding Models for Clinical Research

Governance is moral social act, which requires the governors and managers of organisations and enterprises to develop in-depth knowledge and understanding within their

professional field. They also have a moral obligation to ensure the health and well-being of all who are involved and interact within their areas of responsibility for governance. The ethical and moral principles for conducting either research or any operational endeavour within healthcare, requires inclusive and compassionate leadership. Research is needed to develop greater understanding of the nature of complexity within the delivery of cancer clinical research but also more widely across the social sciences and in healthcare organisations and systems. The Academy for Social Sciences (AcSS, 2022) state that:

“Social science is the study of people: as individuals, communities and societies; their behaviours and interactions with each other and with their built, technological and natural environments. Social science seeks to understand the evolving human systems across our increasingly complex world and how our planet can be more sustainably managed. It’s vital to our shared future”.

Findings from this study highlighted significant areas of discord and disengagement between leaders within organisations or networked governance bodies and commissioning services. This led to the development of the focused (intermediate) codes of **Strategic Misalignment**, **Acknowledging Complexity**, and **Moral Vacancy**, concepts which are discussed further in Chapter Six (section 6.6). Clinical research is delivered within a complicated procedural, legislative and governance matrix environment, essential to protect the rights of participants and professionals, but this inevitably adds the complexity. A review of the hierarchical legislation and procedures that impact the delivery of research was required to understand the challenges faced by individuals and organisations in their endeavours to delivering efficient, timely and compliant studies. The addendum to the EMA 2016 E6(R2) guidelines for good clinical practice (GCP) acknowledged the growing complexity of clinical trials since the initial publication stating, ‘Since the development of the ICH GCP Guideline, the scale, complexity, and cost of clinical trials have increased’ and included the following recommendations:

Quality Management: The sponsor should ensure that all aspects of the trial are operationally feasible and should avoid unnecessary complexity, procedures, and data collection.

Extent and nature of monitoring: The sponsor should determine the appropriate extent and nature of monitoring. The determination of the extent and nature of monitoring should be based on considerations such as the objective, purpose, design, complexity, blinding, size, and endpoints of the trial.

Auditing procedures: The sponsor's audit plan and procedures for a trial audit should be guided by the importance of the trial to submissions to regulatory authorities, the number of subjects in the trial, the type and complexity of the trial, the level of risks to the trial subjects, and any identified problem(s).

2.5 Situated Literature Review: Engaging Theoretical Constructs

Within this situated review the socially constructed grounded theory of *being human*, involving inductive examination of clinical research and abductive reasoning and theorising about the multiple social realities of participants, is now examined and discussed through an engagement with the broader theoretical literature. This is commensurate with a constructivist theory reasoning which is:

“A type of reasoning that begins with the researcher examining inductive data and observing a surprising or puzzling finding that cannot be explained with conventional theoretical accounts. After scrutinizing these data, the researcher entertains all possible theoretical explanations for the observed data, and then forms hypotheses and tests them to confirm or disconfirm each explanation until he or she arrives at the most plausible theoretical interpretation of the observed data.” Charmaz (2014, p341).

Comparing and situating the theory with established thinking and practice highlights the study's contribution to the field, sensitising its novel perspectives and conceptualising its future utility for broader applications (Trowler, 2012, p280). This builds upon the process of theoretical sampling and sufficiency, which is discussed in further detail in Chapter Five. Revisiting the literature as the data analysis draws to a close positions the emergent concepts and theory within the wider theoretical and empirical data. It also seeks to situate, compare, and critique the theory and its properties, in relation to conceptual models, frameworks and perspectives, pertinent to the field of healthcare and complexity research.

2.5 Clinical Research as a Wicked Problem

Clinical research is a 'wicked problem', and as an evolutionary, translational field, is placed at the forefront of complex fields of healthcare. Mertens (2015, p3-6) classified healthcare as a 'wicked problem,' borrowing the term from Rittel and Webber, whilst discussing the utility of applying diverse approaches and Mixed Methods to develop greater understanding of inherent complexities. The conceptualisation of 'wicked problems' arose from operational and management research, and describes problems which are challenging to manage or develop solutions for due to their incomplete, contradictory, changing and indeterminate

properties (Kuipers et al, 2011). Rittel and Webber (1973, p155) argue that science has developed to deal with “tame problems”, not the “wicked problems” of planning and delivering social strategies, solutions and policies. Bainbridge et al, (2019) argue that “complex problems require complex solutions and must be context-dependent” which provides justification for the adoption of pluralistic approaches in their evaluation. Within healthcare contexts Fleck (2012, p757) considers the nature of ‘wicked problems’ posing ethical questions relating to equitable allocation of resource and provision of personalised medicine. Fleck highlights the dilemmas of genomic medicine and personalised, which offers the hope of extended life expectancy (and possible cure) in the strongest patient responders whilst faced with the uncertainties caused by different genotypes and the variability of genetic responses to targeted therapies in some populations. This leads to a wicked moral dilemma of whether to limit the use of expensive personalised medicine relative to genotype and where to draw the line in offering extended life relative to overall survival by genotype subgroup which Fleck refers to as “ragged edges and ethical precipices”. There is also a moral dilemma in the selection of participants and their potential survivability in the timeline of delivery of delivering precision medicine and immunotherapies such as Car-T therapy. The following extract from the study results describes the challenges:

“So there's a huge challenge...the first challenge there is patient expectations, because it's been all over the media as a cure...it can be extremely effective, but firstly the slots for manufacturing the cells are very limited, so the wait time potentially, if you get to the point where you can have your leukapheresis, and have your cells sent off for manufacture, if you can get to there, there's still a sizeable wait...and the labs have limited manufacturing ability so there is a sense of keeping the patient alive until they're ready... I think we've probably done about, close to fifteen cell infusions this year but yeah, there have been patients who just, you know, haven't, their disease burden is too much before we get the cells back... And then of course, they're admitted for a significant amount of time. The risk of CRS and their neurotoxicity is high. So there's a lot of, I think we were all hoping in the beginning, as time went on, we would be able to cut down the admission time, but a lot of the side effects present reasonably late, so actually we need to keep them here and keep an eye on them.” (Participant ID:029114).

In Operational Research (OR) sustainability, leadership, appropriate use of resources, as well as fair and equitable treatment of employees all form part of a moral contract. This study has identified that there is limited engagement by healthcare leaders, responsible for the planning, commissioning and implementation of research, with the inherent complexities and challenges of its “wicked problems”. Churchman, in discussing the ‘framing of

problems, states that the “the moral principle is this: whoever attempts to tame a part of a wicked problem, but not the whole is morally wrong.” (Churchman, 1967, p141). A failure to respond to perspectival and contextualised complexity leads to tension, mistrust, misrepresentation, insufficiency and inequality within research delivery and its outcomes. The results of the study raise concerns that the NHS and its partners are failing to acknowledge the challenges and burdens of clinical trial sites and the complexities faced by research professionals in implementing cancer research studies, as revealed in the following interview extract:

“The burden on pharmacy gets bigger but of course it's the same patient numbers, and I have said to the [organisation name] on so many occasions about complexity... and I mean I've actually been told by [name of senior research leader] in a meeting, 'we're not going to look at complexity because it's too complicated'. (Participant ID:029114).

Interests in optimising equitable patient care and maximising research capacity underpins the study’s aim of understanding and responding to the nature of complexity and follow-up burdens in cancer clinical trials. Capacity management and governance within clinical research delivery involve the problematic and “wicked problems” of planning problems described by Rittel and detailed in their paper on “Dilemmas in a General Theory of Planning”. Table 2.1 below. The categories were compared to the coding framework used to develop grounded theory within this study to identify shared features and properties.

Wicked Problem Properties
There is no definitive formulation of a wicked problem
Wicked problems have no stopping rule
Solutions to wicked problems are not true-or-false, but good-or-bad
There is no immediate and no ultimate test of a solution to a wicked problem
Every solution to a wicked problem is a “one-shot operation”; because there is no opportunity to learn by trial and error, every attempt counts significantly
Wicked problems do not have an enumerable (or exhaustively describable) set of potential solutions, nor is there a well-described set of permissible operations that may be incorporated into the plan.
Every wicked problem is essentially unique.
Every wicked problem can be considered to be a symptom of another problem.
The existence of a discrepancy representing a wicked problem can be explained in numerous ways. The choice of explanation determines the nature of the problem's resolution.
The planner has no right to be wrong.

Table 2.1. “Wicked Problems in General Theory of Planning” (Rittel & Webber, 1973)

Wicked problems and poly-contextual complexity needs to be acknowledged and continually evaluated in the development of healthcare operations and clinical research.

Alrøe and Noe (2011) argue that rapidly increasing complexities in science and society are system problems, characterised by functional and perspectival differentiation, stating that:

“Scientific intervention in a complex problem field should not strive for consensus on problems and goals. In such a situation there will be many different stakeholders, and the heterogeneity of stakeholder perspectives and their relation to different scientific perspectives should be exposed and coordinated through a separate second order research process. A process that involves polyocular, contextual communication based on second order observations of scientific and stakeholder perspectives, and which can maintain a dynamic, multidimensional space of understanding as a basis for research and stakeholder cooperation throughout the intervention process.”

2.5.1 Embedding Resiliency and Sustainability in Clinical Research

Developing resiliency in the delivery of cancer clinical research trials enhances healthcare organisation’s ability to meet population needs and challenges in alignment with the 17 sustainable development goals (SDGs), shown in Fig. 2.2. The SDG framework below provides a coherent model for tackling some of the greatest challenges facing society globally, which highlights effective responses to emergent phenomena. The United Nations (UN, 2021) reported on the important role that resilience, adaptability and innovation have played in responding the global challenges of the Covid 19 pandemic, and called for transformational change to tackle deeply rooted societal problems and health inequalities. The report highlights the inadequacy of public healthcare provision, which is systemically and structurally weak, and state that ‘Tackling inequality will be crucial for reducing vulnerability to health and other emergencies and for enhancing the resilience of societies’ (UN, 2021). This phrase demonstrates the inter-twined relational properties of conceptual constructs as well as the complexity of the effect of emergent phenomena on different sectors of society. All of the 17 SDGs are conceptual constructs with sub-domains of inter-related properties, which you need to understand at a macro level within the framework of the inter-dependence of the overall goals. Understanding the localised challenges within each of the domains is necessary to develop resilient and equitable solutions, requiring a ‘bottom-up’ approach to governance, creating partnerships for achieving goals. To develop coherent and resilient partnerships to respond to the emergent complexities of clinical research, and healthcare provision more generally, necessitates the creation of coherent models and solutions that embrace complexity through collaboration, communication, and contextual sensitivity. Chandler (2014) states that:

“Resilience policies seek to work with existing capabilities and practices and to enable them to operate more efficiently and effectively” (Chandler, 2014).



Fig. 2.2. The 17 Sustainable Development Goals (United Nations, 2021)

Developing resilient and sustainable models of clinical research delivery requires engagement across disciplines and healthcare networks to understand the localised and wicked nature of complex delivery of cancer clinical trials and the capacity and capabilities of healthcare patients, professionals and systems. Delivering research in a new era of precision and personalised medicine therefore requires new models of research praxis encompassing;

- Evidence-based research into contextualised realities of translational medicine and operational delivery
- Responsive and evolving workforce development and supportive, collaborative management frameworks
- Development of mutual coherence, engagement cultures and interdisciplinarity
- Recognition of the creative potential of individuals, shared knowledge and understanding supported by personalised training and education
- Encouragement of creative dialogue & conceptualisation of research trajectories supporting meta-methodologies and inquiring systems approaches
- Embracement of complexity for strategic development and management of solutions to cope with emergent challenges in population health and disease

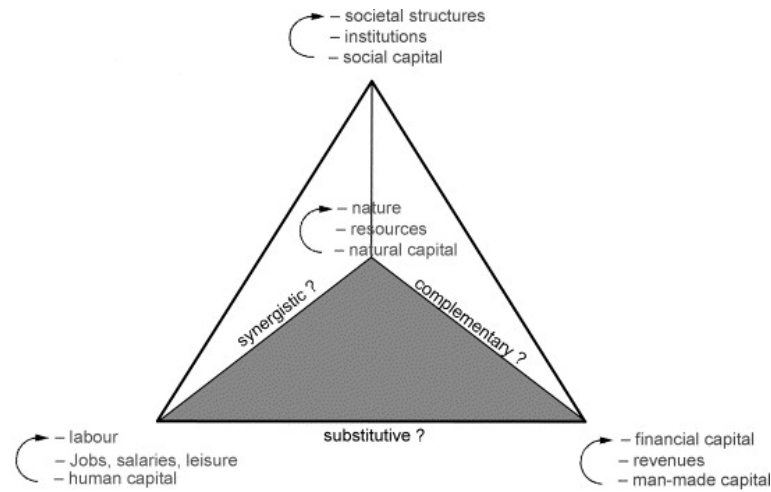
2.5.2 The Prismatic Paradigm

This prismatic paradigm places contextual, negotiated, and synthesised knowledge at its core, in researching social systems and complex phenomena, with the aim of creating better systems within organisations and society, based on shared values, a “transdisciplinary axiology.” McGregor (2011) argues that “within transdisciplinary problem solving of complex, emergent issues, thinking (valuing) and action are intricately bound.” Critical awareness and reflection on values is integral within communication and decision-making, requiring transdisciplinary axiology to understand and resolve complex problems through collaborative interaction. Desbois (2012), in discussing the nature of complexity and risk in human interactions, describes the relationship as an intimate construct linked to our person, our revealed behaviours and is dependent upon context. The nature of relationships within variable and situated contexts emerged as a dominant theme across all of the study phases.

2.5.2.1 Prismatic Concepts

The notion of a prismatic construction as a model for viewing and analysing the world appears within the literature across a number of scientific fields, including the social sciences, healthcare, management and organisational studies. Guba and Lincoln (2005, p181), discuss examining crystalline geometry metaphorically and suggest that the crystal as a central imagery, “*combines symmetry and substance with an infinite variety of shapes, substances, transmutations, multidimensionalities and angles of approach.*” As an analytical model and a framework for viewing, understanding, translating and articulating the nature of reality, and its multidimensional and prismatic nature, the crystal offers a new, and constructive approach to research. Prisms are crystalline and may take different forms, such as trigonal and hexagonal prisms. Whilst the discussion of geometric form as a way to analyse systems may seem to digress from the problems of cancer clinical trial delivery and healthcare provision, it does provide a new dimension of analysis, which moves away from the traditional linearity and top-down perspectives which have informed the design and analysis of the provision and delivery of medical practice and clinical science.

The notional concept of the prism has also been adopted within the analysis of society and administration. Fred Riggs developed the concept of “prismatic societies”, which are characterised by **formalism**, **heterogeneity** and **functional overlapping** (Peng, 2008, p213). Spangenberg (1998, p. 303) adopts the visual construct of a prism of sustainability, describing its utility in visualising the interlinkages between environment and society.



Source: Spangenberg 1998

Fig. 2. 3 The prism of sustainability (Spangenberg, 1998).

Spangenberg and Bonniot's (1998) work on sustainability indicators and the importance of interlinkages fits closely with the results of this study, which have led to the proposal of the Prismatic Coherence Model (PCM), informed by the concept of **Quantum Perspectives** in clinical research and its wider application to healthcare and operational management. Spangenberg and Bonniot (1998, p23-24) argues that social sustainability and social and human capital are interlinked, stating:

“social capital refers to the institutional interaction between individuals on all levels of a company, a process which constitutes the social system “firm” and its coherence”.

They suggest that enhancing human and social capital in an organisation is part of the capacity building process and requires the following elements to be present:

- (1) *“maintenance of human capital by education and training in order to keep the knowledge updated and available, promoting the active use of competencies by management systems and flat and flexible hierarchical structures in the firm”.*
- (2) *“income levels which permit to lead a dignified life in the respective societies, well above the minimum income set by legislation or negotiation. For this behalf, not only the level, but the distribution if income between genders, top and bottom income groups etc. is of crucial importance”.*
- (3) *“satisfaction of human needs (social security, identity, satisfaction...) not only by high levels of workplace safety and by paying adequate salaries, but by organisational structures which support independent decision making, competence and responsibility in each job, and promote active participation and co-decision on all levels of the company”.*

The results of this study identified significant challenges in the abilities of NHS Trust sites and network partners in being able to support social sustainability. Research professionals involved in the delivery of cancer clinical trials at the “**coalface**” and who were patient facing reported issues with staff retention, lack of education, poor career opportunities and a wide-range of other weaknesses and limitations in social and human capital investment. A lack of coherence was also a dominant theme in the study within the context of human resources and staff development, as well as in a research delivery context. The concept of coherence then links into the role of **salutogenesis**, both within the workplace and in the context of health and well-being, which is discussed in Chapter Eight (section 8.5). **Interlinkages** between themes and concepts, within both the research data and the substantive literature informed the development of the thesis of quantum perspectives in healthcare research, the development of a grounded theory of complexity and serendipity in cancer clinical trials and the forming of a Prismatic Coherence Model (PCM). The concept of coherence is an important feature within legal systems, appearing within the literature for that professional field, in which it is reviewed as a property of an entire system of law (Levenbook, 1984, p356). Berteau (2005, p389) states that the “argument for coherence is a complex form of coordinative argument structured on various argumentative levels” and one “that connects with a dynamic idea of system.” The idea of prismatic coherence as a structure for a systemic tool was informed by the study of prismatic systems and models as well as quantum properties and behaviours. The PCM tool provides an analytical framework for human systems evaluation which can identify tensions and gaps within operational management and facilitate the designing of positive discursive enterprises with effective interacting agents underpinned by transdisciplinary philosophy and collaborative approaches.

2.5.3 Prismatic Perspectives

Prismatic perspectival approaches recognise the value of personal experience, influenced by exposure to specific barriers and facilitators at points in time and space; spatial, environmental, social and temporal factors determining outcomes, whether these relate to health outcomes, or the outcomes of operational processes, applications or policies. Prismatic perspectives in practice allows the situated perspectives and values of interacting parties and individuals to engage in productive and interdisciplinary dialogue, to synthesise knowledge and experiences between varied, complex, or multi-dimensional interfaces. In drawing upon such resources, a response can be developed which is sensitive to the diversity of phenomena and interests of the relating parties. Quantum systems are ethical and democratic which are adaptable and sensitive to contexts, as well as spatial and temporal phenomena across different layers and levels within the system.



Fig. 2.4. Quantum Systems & Ethics. H.M.Jones

2.5.4 Transdisciplinary Theory and Practice

“We live in an age of model building for decision making, and we can make this age the most significant of all time if we work on the problem together” C. West. Churchman.

Interdisciplinary coherence and resilience in complex healthcare systems offers new ways of cross-disciplinary working and communal research practice. Etherington et al (2021) suggest that optimal team-working in healthcare contexts (such as operating theatres) may require ‘multi-level interventions that address individual, team and systems-level factors’ and also ‘pay particular attention to complex social and professional hierarchies’.

Transdisciplinary research processes and their role in relation to the incremental of complexities in clinical research operations need to be understood and studied in order to develop sustainable solutions for effective delivery. Briceno (2006) proposed a new knowledge production model of *transdisciplinarity* to address the challenges of complexity, and provided the following definition for sustainable development:

“Sustainable development is the name given to the quest for such a solution, in which development is understood to be the genesis and unfolding of qualitative potential – not just the pursuit of quantitative growth – and sustainability covers the ecological, economic and social dimensions”.

Arnold (2021) argues that 'in transdisciplinary contexts knowledge needs to be generated meeting the complexity of today's problems and includes socially distributed knowledge beyond scientific boundaries'. Developing new knowledge in interdisciplinary contexts however can be challenging, with communication and collaboration impacted by hierarchies and imbalances of power between professionals and organisations, specialist disciplines approaching problem-solving and research practice with different perspectives and priorities. To enhance the delivery of research, all participants in joint enterprises need to establish a mutually coherent framework of practice, where joint problem framing, reflexivity and communication are iterative and democratic processes. In advancing scientific and praxiological knowledge supporting sustainable healthcare and clinical research delivery the challenges of dimensional differences and domain dictates need to be examined and responded to. Arnold (2021) recommends that transdisciplinary groups need to define the terms and conditions for collaborative research and its outcomes, stating:

'The task of knowledge production, processes, evaluation bases and design options have to meet both, the scientific requirements (de-contextualisation) and the culture, interests and needs of local actors (contextualization). Local contexts versus global conditions and interdependences should be met as well....The simplification of complexity leads to the misunderstanding of insights and results and might end up in a kind of misuse of results.'

2.5.5 Quantum Perspectives in Healthcare Research

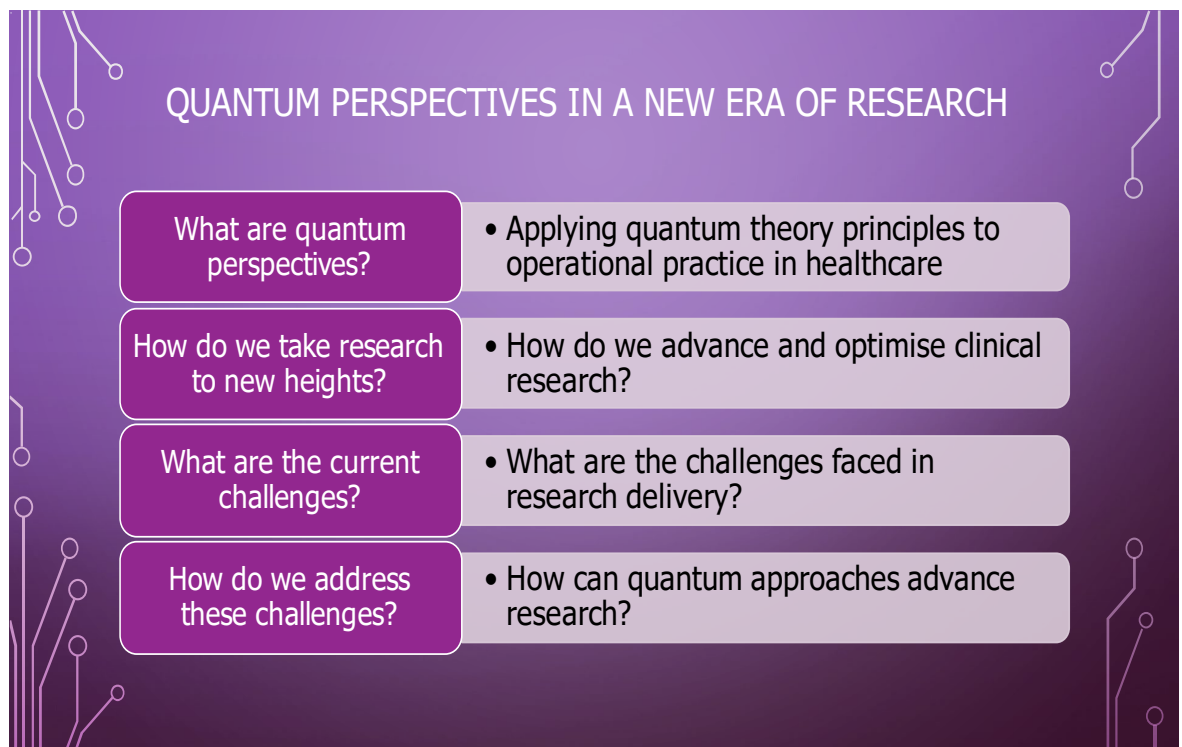


Fig. 2.5. Quantum Perspectives in a New Era of Research. H.M.Jones

In reviewing the nature of complexity within healthcare Cohn et al (2013) pick up the quantum aspect of complexity, recognising that “alteration in one part provokes change throughout the system, and that the system can never be isolated from its environment”. Quantum perspectives accept that illness is both predictable yet dynamic, “evolution demonstrates that viruses and bacteria continue to develop and thrive, and environments and our interactions with them are in flux” (Goldie, 2017). A new vision for research from a quantum perspective allows us to develop a new vision of reality, making the unseen visible and the unheard audible. A quantum systems approach is holistic, in the sense that it recognises the inter-related nature of elements (or particles in a quantum sense). Multiple perspectives and well-informed dialogue are essential criteria in understanding a whole system. Quantum particles once linked remain connected across the universe. If you prod a particle, it has an instant effect on a connected particle across the universe. In the same way that we work within networks and systems, if we change an element and perceive it as an improvement, we need to accept responsibility for the effect that change may have on other elements across the entire system. This emphasises the role of ethics in decision-making. Within healthcare especially, the strategist, researcher or decision-maker needs to be cognisant of their ethical role in promoting change. Collaborative and prismatic inquiry must consider the morality and humanity, which is integrated and connected within systems. C. West Churchman (1967), who promoted philosophical and epistemological study within operations and management research, stated “There is no such thing as improving part of a system without taking into account what happens to the whole”, a concept that recognises quantum entanglement.

2.5.5.1 Quantum Emergence and Properties

The literature of quantum systems, which shares similar properties was therefore compared to research and textual data. The comparative data slices offer new insights into clinical research systems and processes, and have informed the development of the study’s grounded theory. The concept of the Prismatic Coherence Model (PCM) developed in this PhD recognises the quantum nature of biology, medicine and the social sciences and is suitable for educating professions on the nature of quantum properties and the emergence of the quantum social sciences. The shared values approach and attention to the contextual properties and phenomena of serendipity and synchronistic behaviours are compatible with holism and the promotion of creative, inquiring organisations with respect for instinct and the ethics of the whole system, which are qualities promoted by Churchman. Operations research “looks at the whole system” or organisation – “justification of optimality and the stability of its subsystems” (Churchman, 1967).

2.5.6 Prismatic Coherence Models and Design Thinking

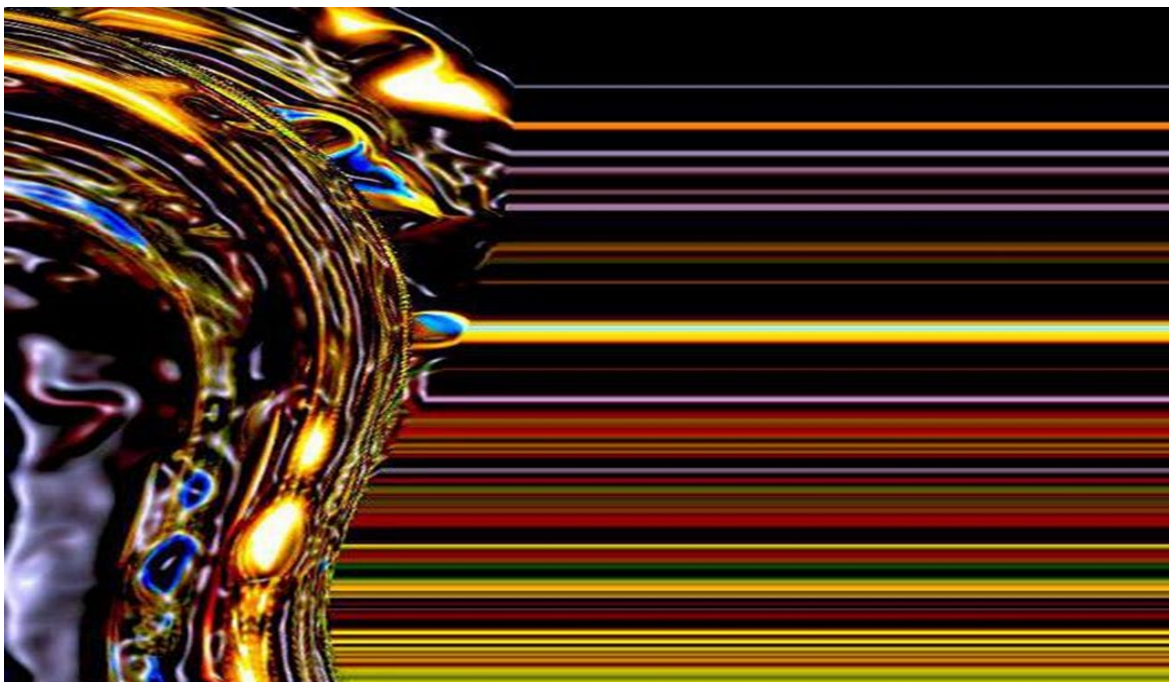


Fig. 2.6. Prismatic Coherence, Visual by H.M.Jones

In a constantly evolving complex adaptive system, like the NHS, priorities, challenges and needs of participants within its networks of environments, contexts and relational events, there needs to be a system of attenable models and theories to create coherence and actionable solutions based on evidence of situated perspectives and contextual complexities. Antonovsky (1979, p193) stated, *“In this era of chronic diseases (and not much less applicable to infectious diseases in such an era) the single-bullet approach can no longer be seen as viable in and of itself or even as the dominant weapon. In this context the sense of coherence becomes important.”*

The concept of the Prismatic Coherence Model (PCM) was formed through the comparison of the multiplicity of patient and professional experiences of delivering or participating in cancer clinical trials in the NHS, with data from the research surveys, questionnaires, and interviews and with empirical and theoretical literature. Due to the ranging properties and coded segments that drew in wide-ranging publications over broad fields it was necessary to compare literature which began to form its own complex networked reference of theoretical constructs. Many themes linked elements of data which seemed relevant and highly important in understanding the challenges of clinical research in a complex healthcare system. A problem began to emerge as the iterative process of continual comparison of the data continued. This was a question of bias in selecting by quantitative summation and linking of concepts which at a point in time was relevant to some, but all. In an equitable system which is complex and emergent, these data points were fluid and

transient. The more data that was compared the more it was apparent that the nature of healthcare operations, and the nature of being a patient with cancer, or trying to deliver clinical trials at differing sites with localised operational and political challenges, meant that a grounded theory sensitive to nonlinearity needed to look to the literature on complex, adaptive and dynamic systems including theoretical and particle physics.

Scale, position and **context** emerge as important variables which may significantly impact health outcomes of specific populations which are dependent upon **coherency** of their properties to **maintain stability**. These terms introduce terminology and phenomena which are key constructs within **chaos theory** and **theoretical physics**.

A Prismatic Coherence Model (PCM) is an aspirational model of associations, a taxonomy of taxonomies, a theory of theories and an interface for interdisciplinary connections. It highlights the values of disciplines, the properties of disciplines and promotes the synergies of disciplines in responding to the challenges and complexities within society, medicine and across multi-faceted contextual worlds within Complex Adaptive Systems (CAS). As a synthesising philosophy it serves to link theoretical domains of knowledge to praxiological outcomes and actions and is a transformative, trans disciplinary and trans theoretical paradigm for salutogenesis, serendipity and sustainability.

2.5.6.1 Prismatic Perspectives & Thinking

The prismatic paradigm adopted in this thesis investigates multi-dimensional realities, and the relations, interpretations, and perceptions at play between patients and professionals and within complex interacting phenomena. The prismatic paradigm incorporating SCIS and MGT provides an adaptive framework and meta-method approach towards generating actionable knowledge, capable of addressing wicked problems and 'sense-making in complex, multifaceted, subjective' contexts (Van Gigch et al, 2006). Delivering cancer clinical trials and patient care is a social act, dealing with complex interactions between patient and healthcare providers, influenced by subjectivity in specific contexts. Hanson (2007, p2) states:

“Every workplace has its own people, preconditions, problems and possibilities which must be considered when we set out to create conditions for a healthy and sustainable workplace”.

Holistic inquiry and metagovernance approaches which adopt quantum thinking and prismatic perspectives can address complex paradoxes and challenges in healthcare.

Prismatic Perspectives	Inquiring Systems	Metagovernance
Rural/urban contextual challenges & implications	TRACAT – Trial rating and complexity tools	Governance principles & meta-governance strategies
Objective/subjective	Workload forecasting & capacity planning	Stewardship
Synthesis/analysis	Knowledge Management & Exchange	Capacity-building frameworks
Conflicting/shared values	Organisational learning	The Detox Prism
Multiple perspectives methods	Creative, innovative environments	Research agendas & design-thinking approaches
Dialectical & informed decision-making	Exponential technology & AI	Communal approaches
		Sustainability

Table 2.2 Prismatic Inquiring Systems

A new approach is needed to manage the growing complexities within healthcare and society, which is prismatic, holistic, responsive, and ethical. As such it needs to embrace existing theories supporting cultural diversity as well as be open to previously hidden agendas and precepts, such as neurodiversity. The potential for the discovery of new insights, knowledge, and solutions in response to the challenges faced in an evolving, fragmented yet inter-related society requires new approaches. In essence, in the new quantum era there is a need to advance approaches to inquiry where enlightened attitudes and behaviours, which are cross-cultural, interdisciplinary, and receptive to diversity, creativity and innovation lead to enhanced knowledge, collaborative working and problem-solving. Traditional operational models, governance approaches and hierarchical systems in healthcare are potential constraints to creativity and progress, which Zohar and Marshal (1994) argue could be released through the loosening of structures and sensitive to emergence and spontaneous, a quantum holism approach. Holism and ethics are central concerns within healthcare delivery, which are fluid and emergent, constantly transforming in response to governance, societal conditions, and disease populations. Zohar and Marshall (1994) discuss quantum systems and aspects of holism as emergent reality and group identity, where a shared repository of skills, knowledge and potential, distributed across organisations are ‘preserved and enhanced within a collective identity’ (Zohar and Marshall, 1994). Feyerabend (1975) similarly argued the benefits of holistic knowing stating, “variety of opinion is necessary for objective knowledge. And a method that encourages variety is also the only method that is comparable with a humanitarian outlook.” The world in which we live is uncertain and indeterminate, in constant flux and in a biological sense, metastatic. From a moral and ethical stance our approach to knowledge advancement,

problem solving and solution finding for the challenges of the present should be multi-dimensional and inclusive, to support the needs across society through recognition of diverse, multiple perspectives. Engagement with research delivery professionals to understand evolving contexts and the impact of scientific and therapeutic emergence is an epistemological priority for healthcare. The study of theoretical perspectives and frameworks for clinical research delivery is limited but a field rich in its transformative potential for practical application of knowledge, supporting effective implementation of scientific advances and novel therapies to meet the challenges of epidemiological and demographic disease burdens.

2.5.7 Capacity of the System in Clinical Research and Healthcare

The sustainability of cancer clinical research deliver in the NHS requires an embedded understanding of the situated realities and localised capacities across its entire domain. The capacity of any system is its overall cumulative ability to achieve and sustain its purposeful functions for which it is instituted and designed to enact. These generally are described as operational, technical, managerial and financial capacities and compliance with the strategic plans and policies for governing these. However in the realms of healthcare and medicine there is a human capacity which is often neglected as part of the design, planning and regulation of systems. Results from this study have identified areas relating to human capacity, which are a central concern requiring development and investment within clinical research and healthcare operations. The human-centred aspects of clinical research are a neglected area within the strategic planning and design of systems, particularly with regard to the capacity of systems. The development of critical systems thinking across professions is a pre-requisite for enhancing sustainable models for clinical research and healthcare delivery. The human aspect of a system is a moral, aesthetic and intellectual concept which is crucial to future sustainability of healthcare delivery and is also a key factor in the determinants of health of individuals and organisations who are embedded and interacting within it.

2.5.8 Serendipity in Research

Serendipity as a term and a concept was first coined by Horace Walpole in 1754, which he explained as “making discoveries, by accidents and sagacity, of things which they were not in the quest for” (Merton, 2004, p2). Serendipity as a concept only made its leap from its literary beginnings into the world of science in the 1930s, when it was taken up by Walter B. Cannon, a professor of physiology at the Harvard Medical School. Merton and Barber (2004, pp.61-64). Cannon used serendipity as an expression for the philosophy of science and in relation to the accidental discovery of phenomena in science. The term has since been adopted across the fields of arts and science, and has evolved as broad unifying explanatory conception. Serendipity shares an affinity with the characteristics and purpose of Grounded Theory research, in their shared endeavour for discovery.

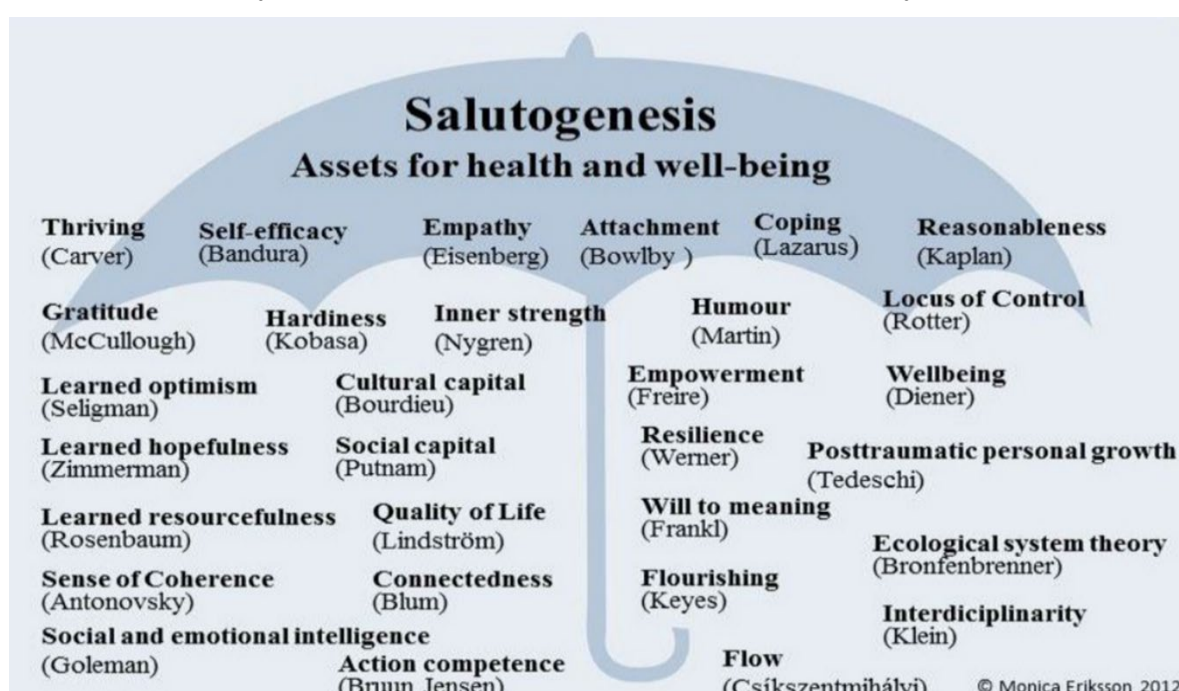


Fig. 2.7 Salutogenesis Assets for Health and Well-being (Eriksson, 2012)

The conceptual category of serendipity emerging from this study's data was compared with appearances within the literature pertaining to the science of discovery, research and innovation, health, disease and their management, and its use as theory in the delivery of cancer clinical research in healthcare. The theory of serendipity as applied in this study is presented as a substantive theory capable of explicating phenomena existing within the operational systems and social networks relating to clinical research delivery in the NHS.

The research findings in this study identified **serendipity** as a central explanatory theme which is used to conceptualise the human experience of clinical research, clinical practice and healthcare. The substantive literature references the utility of **serendipity** as an important component within research and innovation, and the concept is linked to major

discoveries in science and medicine, with references to the happy accident and the magic bullet in clinical research (Gaynes, 2017, p849). In situating **serendipity** within the context of health, disease, and the management of these states along the health-disease continuum, the concept can be useful as a sense-making device which can act as a psychological mechanism for resiliency or viewed as a pendulum may swing towards negative emotional states. Serendipity in relation to human conditions of health and disease states links the construct to the literature on Pathogenesis and Salutogenesis and developed as a transtheoretical construct that drew together many of the complex phenomena that emerged from the research under a taxological umbrella. The visualisation of taxonomies using the umbrella as a device for categorising theories and properties as well as an operational mechanism for organising complexity is a concept adopted for defining health assets. The concept of **serendipity** supports Antonovsky's **Sense of Coherence** model (1987, p19), by providing another perspective and mechanism for comprehending and managing different emotional and physical states and attributing meaning. Sartorius (2006, p662) in discussing the meanings of health states that:

“ Health is a state of balance, an equilibrium that an individual has established within himself and between himself and his social and physical environment.”

The results from the clinical trial patient interviews within this study revealed many different approaches to making sense of their physical and psychological status and their situated experiences of participating in cancer research trials. The notion of **luck** and **being lucky** as a cancer patient on a clinical trial was theme present across many patient narratives, and is discussed further in Chapter Seven (see section 7.3). A cancer patient during an interview reflected on their experience as a clinical trial participant stated:

*“I put that story down to there's being **lucky** and unlucky because I was unlucky to get the cancer but **lucky** that [Consultant name] and a clinical trial was there for me at that time” (Participant ID 005006).*

Another participant stated:

*“I think I've been so **lucky** because I felt like I'd had a whole **holistic approach**” (Participant ID 034001).*

Holism and serendipity are linked within this patient's psychology for managing their care. The same participant also referenced their luck as being able to have a say in their treatment and thereby retain a **locus of control** which is another construct linked to salutogenesis.

The complexities of health, disease their management are discussed within an ontological framework by Broom and Kenny (2021, pp.1-16) who argue that living with cancer is a paradox, where the moral cosmology and ontological construction reveals critical facets and consequences for survivorship and well-being. Through a sociological examination of cancer paradoxes they introduce **serendipity** as a being central to this “moral cosmology of cancer” stating:

“Luck, as illustrated throughout participants, is central to the meaning-making of cancer...our analysis suggests that luck is central to the ethic of survivorship-in-practice, albeit in an inherently paradoxical way.” Broom & Kenny (2021, p.13).

The findings from this study’s research interviews with cancer clinical trial participants reinforces the positioning of **serendipity** as an important concept within the clinical and sociological literature examining cancer survivorship, salutogenesis and the meaning of health. The role of luck and chance in relation to health and disease states, as well as the situated experiences, conditions and social relationships experienced by cancer clinical trial patients was conceptualised positively and negatively. The negative aspects of the role of chance and luck within healthcare contexts, as described by one cancer patient in the study was discussed by Broom and Kenny (2021, p.7) who stated:

“ ...the deployment of luck could fall flat if it jarred with people’s experiences (including the inevitability of terminality)...or more perniciously, where it functioned as an overt injunction towards compliance.”

This highlights the very complex, individualised human experiences of living with cancer as well as the challenging and paradoxical consequences for healthcare professionals in delivering personalised medicine within a national healthcare system.

2.5.8.1 Serendipity in Cancer Clinical Research

The role of serendipity in medicine is articulated within the extant literature and many popularly cited examples such as Alexander Fleming’s discovery of penicillin, Wilhelm Conrad Rontgen’s discovery of X rays, and Louis Daguerre’s discovery of photography and the ‘Daguerreotype’ (Roberts, 1989). Serendipity is recognised as a contributing element within the advancement of clinical research, particularly in the field of pharmacological sciences. Prasad et al (2016, pp435-450) discuss the role of serendipity in cancer drug discovery and highlight that the process of developing new drugs is lengthy and prone to high rates of failure, especially in oncology trials. They suggest that “targeted therapies have minimal roles in drug discovery” but in contrast “serendipity has played a major role in

their discovery” (Prasad et al, 2016, pp436). Flexner (2009, p390) discusses the challenges of drug development stating:

“Molecules drop out for a variety of reasons, but this 90% failure rate is axiomatic, and has not changed in the last 50 years. One possible explanation is that we have been unable to identify unifying theories about drug development that would allow us to improve our success rate. Another possibility is that clinical drug failures result from factors that are largely beyond our control including the inherent unpredictability of human biology.”

In this statement Flexner is highlighting the central challenges of translational science in that it is a field that is unpredictable and the absence of a unified theory (or grand theory). Clinical research resides within a complex adaptive system and demonstrates properties which are emergent, unpredictable and dynamic. The literature of quantum systems, which shares similar properties was therefore compared to research and textual data. The comparative data slices offer new insights into clinical research systems and processes, and have informed the development of the study’s grounded theory. The concept of **serendipity** is proffered as an ontological model for the profession, and also as an applicable unified theory for the medical sciences and healthcare implementation.

The serendipitous element in the drug development process often relates to the re-purposing of drugs which arises from the discovery that a particular agent or medicine can be beneficial for another purpose or condition from that which it is being tested or developed for. One such example is the drug sildenafil (Viagra) which was initially developed as an anti-angina medication by Pfizer (Prasad et al, 2016, pp436), but has since been used in the treatment of erectile dysfunction (AHFS, 2019) and as an anticancer agent in the treatment of lung cancer (Keats et al, 2018). In following up long-term pharmacological effects of drugs, the potential to discover new knowledge about their safety and efficacy is maximised, as well potential value and application to other conditions and applications. The length of follow-up and monitoring of drug efficacy does add to the workloads for sites in delivering clinical trials. Research professionals in this study discussed the implications of delivering novel agents and therapeutic interventions, highlighting that offering novel treatments to patients also added additional layers of complexity (see section 6.6.3).

The requirements for serendipitous discovery are; intuition, knowledge, experience and critical thinking (Prasad et al, 2016), as well as an ability to make connections between different fields of research and innovation. McBirnie (2008, p614) suggests that serendipity provides significant potential for Knowledge Exchange (KE) but that practioners need to

embrace the “opportunity to act in the unpredictable dynamic environment that informs the reality of information seeking”. Critical thinking is a pre-requisite for serendipitous discovery, and an important skill for researchers, a perspective which is supported by a comment from a clinician participating in this study. In discussing the limitations of the medical training in the UK he highlights the importance of critical thinking stating:

*“...one of the things that I am concerned about is that young doctors aren't participating as much in research now. Their careers are written out for them and there are a series of milestone exams they have to take... But they are not necessarily able to have any research experience, they haven't even had a reason to even think about it. They move through the system so smoothly and quickly they don't develop a **relationship with a problem** which might be a question that they'd like to ask, or be a question that might have an answer that might be important. And that's my anxiety is that you're designing doctors but a doctor with all that brainpower [who] hasn't got the potential to have original thoughts and couldn't do good clinical research, even if it isn't in full time clinical practice. You're not developing **critical thinking** and you're not really encouraging, kind of, it's encouragement in **asking questions**.”* (024004, Pos. 139).

This extract was coded as **designing doctors**, but in comparing this slice of data to the literature on **serendipity**, a link is highlighted between education of medical professionals and clinical researchers, and points to a gap in developing skills and opportunities in the NHS for creating critical thinkers with the capacity and capability to advance medical practice through research and innovation. Educating students in the sciences about the importance of serendipity as a phenomena is highlighted by Lenox (1985, p285) who states:

“Serendipitous or chance discovery is one of the important avenues for discovery in the sciences. As such, it is important to recognise it and to educate students of science in such a way so as to maximise their chances of benefitting from such discoveries during their years as functioning scientists... The truly successful scientist will no doubt benefit from all modes of discovery. It is the task of the science educator to ensure that his students are prepared in the best possible manner for discovery”.

Lenox's call for serendipity to be adopted within the science curriculum to develop student's as independent researchers with the critical analytical skills for observation and discovery is supported by the research findings of this study. The substantive literature supports the perspective that serendipity is a critical element in the fields of science and medical research as stated by Stoskopf (2005, p332):

“It should be recognized that serendipitous discoveries are of significant value in the advancement of science and often present the foundation for important intellectual leaps of understanding”.

2.5.8.2 Grounded Theory and Serendipity

Serendipity shares an affinity with the characteristics and purpose of Grounded Theory research, in their shared endeavour for discovery. The conceptual category of serendipity emerging from this study’s data was compared with appearances within the literature pertaining to the science of discovery, research and innovation, health, disease and their management, and its use as theory in the delivery of cancer clinical research in healthcare. The theory of serendipity as applied in this study is presented as a substantive theory capable of explicating phenomena existing within the operational systems and social networks relating to clinical research delivery in the NHS.

2.5.9 Being Human

The concept of “**Being Human**” was grounded in the personalised experiences, perceptions, knowledge and situated realities of patients and professionals participating in this study. One quotation from a patient interview stood out as a human motif for clinical research:

*“ I think **the human bit** of it **is important**, about going into a new trial.” (Participant ID: 024004).*

Human-centred themes arising from this study are discussed in Chapter Eight, alongside the complexities and implications of delivering personalised medicine and cancer clinical trials in the NHS. Two striking quotations emerged as metaphorical keystones upon which to design a blueprint for future clinical research and healthcare strategies, building upon the situated experiences and perspectives of patients and professionals, simply stated as:

*“**I was complex**” (Participant ID:005009) and “**I’m a human**” (Participant ID: 033103)*

The discovery of the human DNA structure, and subsequent human genome sequencing and research have revolutionised the biomedical sciences (Miga & Wang, 2021, p81). Johannes Friedrich Miescher made the serendipitous discovery of the nuclein (DNA), or the “molecule of life” whilst analysing cell proteins and their structures. Our DNA is our most personalised and elemental human properties, the element of life that makes us the unique, complex individuals that we are. The rapid advances in genomics have created a new

paradigm in medical research and healthcare, transforming the human clinical experience. Hood and Rowen (2013) state that The Human Genome Project (HGP), a global project sequencing the entire genetic blueprint of the human being, has “*profoundly changed biology and is rapidly catalysing a transformation of medicine.*”

2.6 Chapter Summary

Within this chapter the approach and methods for conducting a review of empirical literature in a grounded theory study have been discussed. In this study acknowledging the perspectives of key participants and relevant experiential data were central to the design of the study, and as such the literature review critically engages with multiple data sources to understand complex emergent phenomena. A practical approach has been undertaken in conducting an orienting review of the area under study to inform the study design, identify gaps and ensure that work being undertaken is relevant and original. The reflexive approach allowed for the limitation of researcher bias in relation to the subject area and the development of constructivist grounded theory which is sensitised to the conditions and realities of cancer research in the NHS. The initial foundational literature review highlighted the key challenges already identified as challenges and features of cancer research and trial implementation in secondary healthcare environments. It was identified that there was limited empirical study into institutional dynamics and critical analysis of the effect of organisational realities of both research and healthcare delivery within large complex institutions, particularly from the situated experiences of patients and research professionals. The gap in the literature highlighted the need for in-depth, contextual evaluation of clinical trial operational management and delivery, involving key participants with relevant, contextual knowledge and understanding. This identified the need to adopt a pluralist approach and a study design involving critical analysis of clinical research strategies, processes, technologies, and stakeholder perceptions. In the following chapter the research methodology and framework applied in gaining an in-depth analysis of the nature of cancer clinical trial delivery are discussed. The initial review was undertaken to determine the priority areas and develop the overall approach and methodology to evaluating operational delivery of cancer clinical research implementation in the NHS and to identify the core issues facing key stakeholders. The literature studied prior to the data collection stages presaged for change to meet future challenges in clinical trial management and patient care, addressing augmenting uncertainty and intensity of clinical trials and healthcare operations. The review identified gaps in the empirical study and critical analysis of relationships and institutional dynamics impacting cancer research implementation within the UK, and internationally, particularly in relation to the situated and qualitative realities of cancer patients and research professionals within complex healthcare organisations and

networked institutions. An effective evaluation of clinical trial research delivery in secondary care settings therefore required a pluralist research design and approach to understand the complex interacting networks and wide-ranging phenomena encompassing NHS and partner infrastructures, strategies, processes, technologies, behaviours, and stakeholder perceptions.

The literature identified that most operational research has focussed on investigating challenges around patient recruitment and retention, alongside research into technical aspects of protocol design and related workload implications for trial sites. There is however limited study into the human aspects of clinical trial participation, either from patient or research professionals' perspectives. Also absent in the literature is the growing demand for involvement of specialist professionals and support departments professions in supporting the implementation of cancer clinical trials in an era of exponential change in cancer research. This knowledge gap in the understanding of clinical research and healthcare delivery from a human and complex systems perspective, has been addressed through this study. The knowledge gap centred around the disconnect between scientific advancements and aspirations for clinical research and the operational challenges and capacity management aspects in delivering advanced trial designs and personalised medicine within a national health service highlighted that the voices, experiences, complexities and human emotions of cancer patients and clinical research professionals participating in trials was absent within the literature.

Chapter Three: Research Methodology

“Prismatic inquiry methodology utilises the convergence, divergence and juxtaposition of data in the exploration of hidden or unexpected relationships, opening the paths to other ways of knowing while maintaining a criterion of quality and definition of success.” (Fisher, 2013).

3.1 Introduction

This chapter articulates the methodology and philosophical perspectives which have informed the research strategy, providing clarity and supporting the assessment of the “credibility of the theoretical framework” presented in this thesis (Glaser & Strauss, 1967, p232). The realms of healthcare and cancer clinical research are kaleidoscopic enterprises involving multiple actors, scenarios, and stages, which implicitly infer the need for theoretical sensitivity to explain the varieties of occurring phenomena. This chapter opens with a reflection on relevant ontological, epistemological and theoretical perspectives, reviewing their foundations and appropriateness to the research topic and researcher positionality.

The research concerns investigated within this study span complex interactional fields of social and operational systems and medical research, calling for an emergent and prismatic approach to inquiry. Through an examination of research methodologies and their contribution to social science inquiry, this chapter examines the development of a framework for investigation. After laying out the foundations of the methodological framework, the chapter discusses interpretive methodologies and how the adoption of Mixed Methods (MM) and Constructivist Grounded Theory (CGT) supports and evaluation cancer clinical trial operational delivery within a national healthcare system.

3.2 Ontology, Epistemology and Theoretical Perspectives

The way in which we understand reality and our existence within the world defines our ontological position. The representation or meaning attributed to a phenomenon is determined by our belief systems based on ontological posits, with objective and subjective views at opposite ends of the spectrum. Epistemology involves the researcher’s theoretical conceptualisation of knowledge, through their consideration of the nature of objects, elements, and problems within society relative to the polarities of inquiry, which are positivist (objective) or antipositivist (interpretivist, subjective). Degrees of philosophical interpretations form along a metaphorical ontological scale, relative to the nature of

concerns and perceptions of the inquiring individuals or societies. The process of knowledge creation however is not a binary, linear concept and the selection of any research framework reflects the nature, diversity, and complexity of the subject of inquiry and the context within which it is situated. The complex and multi-faceted nature of the research problems introduced in Chapter One, necessitated a critical analysis of ranging ontologies and paradigms.

In the process of conducting research we seek to establish knowledge and understanding of the object of inquiry through justification of our approach, theories and methods into its investigation, and in drawing conclusions that the results are realistic, without bias, factual or representative of the problem. The theoretical lens that we apply is relevant to whether we deem 'reality' to be universal and external to social and human cognition (realism) or whether it is integral to its context and interpretation through human experience and perception (idealism). Knowledge formation is achieved through an examination of the nature of 'objects' and 'elements' in the realm of inquiry where the researcher may selectively arrive at 'objective', 'subjective' or 'constructive' views of reality. An objective, subjective or constructivist ontological stance determines our epistemological position and applied theoretical perspectives.

3.2.1 Relativist Ontology

A relativist ontology is interpretive and recognises that knowledge is relative to the multiple realities of people, their interactions and their experiences. Levers (2013, p1) states, "The purpose of science from a relativist ontology is to understand the subjective experience of reality and multiple truths". In the study of the interactions and situated realities of cancer clinical trial patients and research professionals a relativist ontology is adopted. A relativist approach perceives the realities of our existence as being intersubjective, where understanding and meaning relate to social and experiential levels. The formation of knowledge within the field of the researcher's interest is a synthesising process, where reality is formed through the perceptions of societal groups and diverse individuals, and places particular emphasis on axiology and the value of perspectives. The ontological framework facilitates the development of new knowledge and theory to support decision-making within organisations, drawn from contextually grounded and synthesised data.

3.2.2 Constructivist Epistemology

A constructionist paradigm of inquiry combines postpositivist and interpretivist critical realism ontologies with epistemological subjectivism, where meaning and understanding is

a subjective epistemology co-created between the interaction of interpreter and the interpreted (Crotty, 1998). Critical realist and constructivist approaches place emphasis on dialogue and the use of data triangulation in the validation of theory, fitting a grounded theory methodology and “sharing a focus on abduction and commitment to fallibilism and the inter-connectedness of practice and theory” (Oliver, 2011).

In designing a paradigm for inquiry, the researcher accepts an ethical responsibility to build in epistemological consistency to ensure that their findings and version of reality are verifiable and defensible. Theoretical perspectives of individuals or societal groups form over time, influenced by their epistemological stance (how they consider knowledge) and determine how they arrive at understanding (their methodologies). Context, culture, historical traditions, and personal exposure to experience all contribute to the formation of theory. These theoretical perspectives in turn lead to the application of rules and principles in our approach to knowledge formation and discovery of evidence informing a research paradigm, or meta-theory. The application of these principles and rules is our methodological framework that we then apply to our investigation of the research question or problem, and our selection of appropriate methods to collate, analyse or synthesise data in the pursuit of new knowledge. The following section details key paradigms for inquiry, which can inform a multi-faceted framework for research, conducted within interacting contexts between healthcare, technical and organisational systems, and social fields of inquiry.

3.2.3 Theoretical Paradigm and Philosophical Traditions

As society has progressed, expanded, and diversified, imbibing the knowledge realised through the discoveries of its ancestors, the nature of thinking and inquiry has evolved. Within the realms of science and physics the traditional, mechanistic ‘either’ ‘or’ approach to theory has been challenged by more expansive quantum approaches and multi-paradigmatic perspectives accepting ‘and’ and ‘both’ conceptions of phenomena. As human experience, knowledge and capabilities advance, so should our approach to the philosophy of science and society. Karl Popper (1935) in his treatise on scientific logic stated “theories are nets cast to catch what we call the world: to rationalise, to explain, and to master it. We endeavour to make the mesh even finer and finer.” The formation of knowledge within the field of the researcher’s interest is a synthesising process, where reality is formed through the perceptions of societal groups and diverse individuals, and places particular emphasis on axiology and the value of perspectives.

3.2.3.1 Positivism & Subjectivism

A positivist approach to the empirical study of phenomena (Positivism) is based within the objective domain, involving experimentation and *a priori* hypothesis testing, whilst the social and cognitive sciences are aligned with subjective and conceptual worlds of human perception, reasoning and rationale (Subjectivism), an inductive and interpretive *a posteriori* research process sensitive to context and experience. A traditional conception of the sciences and their study of phenomena to understand reality are based upon a positivist, Newtonian approach to verification. The epistemological stance of Positivism (based on the philosophy of Comte) combines rationalism and empiricism (Bhattacharjee, 2012) in adopting deductive methods for reasoning and data analysis.

An alternative metaphysical view is subjective, where an understanding of what reality is and what it is like, is influenced by human conceptual constructions formed through social interaction between researchers, participants, or other societal groups, using qualitative methodologies. Postmodernism is an era characterised by subjectivism (relativism). Postmodernists believe that reality is a construction rejecting Positivist claims to the objectivity of knowledge, arguing that discourse informs reality, which is therefore relative, subjective, and indeterminate due to multiple perspectives affecting our perception of nature. Personal perceptions, beliefs and values are subject to influences and experiences derived from our exposure to history, culture, education, circumstances, and position in society. The theoretical stance of postmodernism is democratic and discursive, embracing ethics, diversity, and multi-culturalism. With the development of the social sciences an antipositivist approach emerged, reflecting the need to investigate human interaction and pluralistic conceptions of reality, rather than focus solely on the scientific verification of objective phenomena and properties existing within a physical world. This required a change in approach to investigating, interpreting, and comprehending the pluralities of human perception, consciousness, and the nature of existence. Postpositivism argues that reality is a construction of multiple perspectives, a pluralistic conception adopted by critical realists and constructivists, acknowledging that multiplicity and complexity are 'hallmarks of humanity' (Ryan, 2006).

3.2.3.2 Naturalistic Inquiry, Interpretivism and Symbolic Interactionism

A naturalistic approach to inquiry (a post-positivist approach) and the study of phenomena, their behaviours and properties is an interpretive act. As science and society evolve the act of interpretation and evaluation becomes an increasingly complex process, as accumulated human and artificial intelligence extends the corpus of inquiry and methods.

Interpretivism (antipositivism) with roots in hermeneutics and phenomenology, advocates inductive, qualitative methods of inquiry, emphasizing the importance of interpretation and meaning within social action. Qualitative methods, which are interpretive, draw on the antipositivist tradition (Bhattacharjee, 2012) whilst quantitative methods are associated with the positivist tradition.

Symbolic interactionism is a philosophical view which “focuses on dynamic relationships between meaning and actions, it addresses the active processes through which people create and mediate meanings” (Charmaz 2014, 345).

Critical realist and constructivist approaches place emphasis on dialogue and the use of data triangulation in the validation of theory, fitting a grounded theory methodology and “sharing a focus on abduction and commitment to fallibilism and the inter-connectedness of practice and theory” (Oliver, 2011). Tanlaka et al (2019) position postpositivist critical multiplism as a participatory approach to nursing and scientific knowledge development which respects the individuality and uniqueness of patients and other related stakeholders whilst suitably addressing ‘the complexities of human phenomena’.

A naturalistic study (post-positivist approach) to investigate phenomena, their behaviours and properties and subsequent transformation into ‘substantive’ theory or knowledge is an interpretive act. As science and society evolve the act of interpretation and evaluation becomes an increasingly complex process, as accumulated human and artificial intelligence extends the corpus of inquiry and methods. The proliferation and rapid evolution of instruments for observation, increases the opportunities for the study of phenomena from granular through to expansive behaviours, moving through the micro, meso, macro and meta-levels of scientific analysis. Bainbridge et al (2019) argue the case for “methodological innovation and accountability” in response to increasing complexities in a dynamic society. In a post-modern era of rapid scientific and technical advancement and the diversification and globalisation of society, the nature of research and the approach of inquirers needs to reflect the challenges and opportunities of the present, informed by new paradigms, the meta-methodologies and meta-methods of the quantum era.

3.2.3.3 Pragmatism

Pragmatism is a school of philosophy developed in the United States which adopts an interpretivist approach and supports the use of inductive and deductive strategies in defining knowledge. Its key proponents (Charles Sanders Pierce, William James and John Dewey) were concerned with the study of thought and meaning. Dewey argued that reflection and conjecture, involved systematic inference involving induction and deduction, “a fruitful

interaction of observed (or recollected) particular considerations and of inclusive and far-reaching (general) meanings” (Dewey, 1930). This definition suggests that through a systematic process of inquiry to develop new knowledge or theory, the combining of inductive and deductive methods for generating contextual (particular considerations) and (far reaching meanings) is a productive, interactive enterprise. The emphasis on interaction and the importance of meaning, embraces the pragmatist’s concern for hermeneutics, which is allied to the interpretivist paradigm. Language and terminology and the importance of meaning, interpretation and understanding within research and healthcare is a high value concept as the impact of cognitive dissonance or misinterpretation carry significant risks. Instrumentalism was a key element within Dewey’s form of pragmatism, which through his interpretation of metaphysics absorbs interpretivism and hermeneutics. Instrumentalism argues that constructs or hypotheses are tools used in a process of problem identification, interpretation, reflection, action and review of consequences, an emergent and cyclical process.

3.2.3.4 Constructivist-Interpretivist Paradigm

A constructivist-interpretivist paradigm underpins the methodological approach for this study, which assumes a relativist ontology (multiple realities), a subjectivist epistemology (co-construction of understanding) and naturalistic methodologies (non-experimental). Philosophical assumptions and their related paradigms for inquiry are influenced by the historical traditions and social conditions of changing generational epochs. The relevance of the theoretical assumptions and methodologies applied in answering questions is pertinent to each society’s development. Each era of research formulates new knowledge and tools for effective inquiry, which can assist subsequent generations. The contemporary inquirer should be mindful of philosophical traditions and learn from past discoveries, successes and failures, in the process of designing new approaches to challenges faced within present society, and in selecting and applying appropriate methodologies.

3.2.4 Axiology and Praxis

McGregor (2011) states that research methodologies encompass four philosophical categories: metaphysics (including ontology), epistemology, logic, and axiology, but that traditional science has tended to neglect axiology, which she defines as “the science of inquiry into human values.” Axiology relates to the values held by the researcher in combination with their ontological and epistemological stance, formed from their past experiences and personally developed assumptions, which need to be illuminated as an analytic element of their study into a particular field or problem. In an embryonic world where

'big data', 'artificial intelligence' (AI), 'virtual reality' (VR) and human genome sequencing, amongst other technological and scientific advances, are accelerating the possibilities for research, the role of axiology and ethics have increased status, where the risks and opportunities are significant (Schwab, 2017). The way in which we design research and supporting technologies shapes society and how we interact with it, in turn impacting the nature of knowledge acquisition and its subsequent role in decision-making. The character of a social scientist is by nature interactionist and their interpretive and disseminating activities in conducting research bear ethical responsibilities.

In researching phenomena, which is embedded within social structures and where interactions are perpetual and evolving, social scientists are operating within complex and non-linear environments. Where different axiomatic belief systems are meeting and transacting, the researcher needs to develop theoretical sensitivity to engage with and comprehend the multiple interacting perspectives. The social science researcher's methodology therefore needs to involve the study of theories (metatheorising) as part of their investigation. Axiological beliefs direct the actions of individuals, organisations and society based on their ethical principles and what they deem to be of value. From the perspective of the researcher, their axiomatic beliefs should be articulated as this illuminates their ethical approach and values in conducting and designing their study. In relation to organisational research, axiology also involves studying the strategic values held by organisations and their professional staff to understand their approach in transforming their aims and objectives into reality, which links with pragmatism and its concern for praxis. Biddle and Schafft (2015) suggest that pragmatic mixed methods researchers should "engage with axiology" in the "repositioning of the transformative paradigm." To progress pragmatism's transformative paradigm, which accepts the utility of combining qualitative and quantitative approaches to inquiry, there is an opportunity to integrate a quantum axiological approach using MGT and Singerian Inquiry, under an umbrella methodology.

Praxis refers to the practical application of theory and a "grounded praxis approach," as argued by Cho et al (2013), reveals the multi-layered structures and forces influencing knowledge production, interpretation, and dissemination, through contextual engagement. Praxis involves the generation and application of knowledge in order to effect change. Within Operations Research (OR) praxis is a key criterion for evaluation of phenomena and is one of the binding agents between theorising and process improvement within organisations and at a wider aspect, society as a whole. The role of praxis is pivotal in transforming contextual knowledge developed through evaluation into a design model, process or practical solution, and is one of the key elements within Action Research (AR). Praxis is linked to the Aristotelian concept of gnoseology, which is "multi-dimensional, non-

reductionist and relational” and “allows for reintegrating ways of knowing- traditional, practical, tacit, emotional, experiential, intuitive” (Eikeland, 2015). Eikeland states, “praxis should be explored as a gnoseological paradigm for a different organisational science, based on reflective practitioner research where knowers-practitioners study, articulate, and develop their own practice and common standards as collegial principles; i.e. as practitioner action research” (Eikeland, 2015). The concept of praxism is closely linked to the aims, belief systems and conduct of the research. It forms the basis for the design, quality, and dissemination of a study. Evidence-based research is a pre-requisite for determining effective operational models, which involves the process of praxis, the transition from theoretical knowledge to the application of practical solutions to contextual problems. In relation to clinical trials, praxis relates to translational and operational research which lead to; effective and ethical practice, healthcare interventions for patient benefit, and the advancement of scientific, clinical, and professional knowledge.

3.3 Mixed Methods Grounded Theory (MMGT)

The proliferation and rapid evolution of instruments for observation, increases the opportunities for the study of phenomena from granular through to expansive behaviours, moving through the micro, meso, macro and meta-levels of scientific analysis. Bainbridge et al (2019) argue the case for “methodological innovation and accountability” in response to increasing complexities in a dynamic society. In a post-modern era of rapid scientific and technical advancement and the diversification and globalisation of society, the nature of research and the approach of inquirers needs to reflect the challenges and opportunities of the present, informed by new paradigms, the meta-methodologies and meta-methods of the quantum era. Mixed methodology in healthcare research facilitates the adoption of a holistic approach and supports evidence-based policy formation. This ‘third research paradigm’ is necessary in a research world, which is “interdisciplinary, complex and dynamic” (Johnson and Onwuegbuzie, 2004). Through a combination of objective and subjective methods in examining follow-up and complexity in cancer clinical trials, the resultant data provides a deep level of understanding of the multi-dimensional phenomena. The world in which we live is uncertain and indeterminate, in constant flux and in a biological sense, metastatic. From a moral and ethical stance our approach to knowledge advancement, problem solving and solution finding for the challenges of the present should be multi-dimensional and inclusive, to support the needs across society through recognition of diverse, multiple perspectives. Research approaches may draw upon monism, dualism or pluralism, in the process of making their claims to knowledge, and choice of values, perspectives, strategies and methods from within their selected paradigm.

Mixed Grounded Theory (MGT) is appropriate as a methodology in conducting operational evaluation to investigate complex phenomena through a prismatic lens, acknowledging multiple and diverse perspectives. As the study aimed to undertake a comprehensive and systematic investigation into the nature and complexity of cancer research delivery, mixed grounded theory (MGT) offered a dialectical and prismatic design solution, using “both-and logic” to synthesise multiple perspectives through prismatic lenses. Multiple ways of viewing and comprehending research objects are achieved using MGT and dialectical pluralism, a process using constant comparison to understand divergent perspectives, forming “new syntheses of interpretations, results and wider practical applications” (Johnson and Walsh, 2019, p523). The following section details the rationale for the research linking into the selection of appropriate methods, which are discussed in Chapter Four.

3.3.1 Rationale for Mixed Methods Grounded Theory (MMGT)

A mixed methods approach to developing grounded theory is a systematic meta-synthesis that compares and integrates the findings of multiple studies to develop a conceptual or theoretical holistic interpretation of the evidence (Pope et al, 2007). It is both a method for conducting inquiry and an outcome of that process, the study’s developed conceptual framework or ‘grounded theory’ (Johnson and Walsh, 2019, p 518). In mixed methods research (MMR) or multimethod research the process of mixing can occur at multiple levels, from paradigmatic to practical levels. Through the use of mixed grounded theory (MGT) this study uses within-method mixing and between-method mixing. The Delphi studies use within-method mixing, starting with open-ended questions in the initial round and moving to quantitative scales in later rounds. Between-method mixing in the study involves the synthesis of results from all the work packages in the study, for example integration of semi-structured questionnaire data with in-depth qualitative interview data.

Rapid progress in science and technology needs a supporting framework for operational research within healthcare, capable of evolving with and responding to its changing reality. An approach to understanding such contexts therefore needs to draw upon multiple paradigms and their respective tools of inquiry, to study phenomena using qualitative and quantitative approaches, and be cognisant of the roots of relevant informing philosophical traditions and paradigmatic perspectives. Cancer clinical research delivery forms part of a complex system, which is in perpetual flux and ill-suited to linear, determinate operational models and processes. An interactionist approach and multiple perspectives are suited to studying contextual and operational elements of clinical trial delivery and the potential for “organisational heterogeneity” (Lounsbury, 2008). Until accounts of participants are collated and interpreted, applying a pre-defined theoretical model would apply a narrow field of

vision. Through the development of theory that is "grounded in data" (Strauss & Corbin, 1994), multiple sources and perspectives can be analysed to illustrate diversity and complexity of the realities of cancer clinical research operations. The methodological rationale for the research ascribes the nature of the tools and methods for inquiry, which in this investigation illustrated the need for a pragmatic, mixed methods approach to analyse the complex area of cancer research delivery and to combine large volumes of data, practices, interdisciplinary teams, and human experiences. Naturalistic inquiry with its emphasis on context is highly relevant to the study of operational practice, requiring qualitative analysis whereas empirical study supports quantitative analysis of measurable data and metrics. Both naturalistic and empirical inquiry, and application of their associated methods, contributes to the understanding of research data, systems, contexts, and cultures.

3.3.2 Mixed Methods Research, Grounded Theory & Pragmatism

Grounded theory developed from the collaborative working of Glaser and Strauss, whose underlying philosophical perspectives were divergent, namely post-positivism (Glaser) and symbolic interactionism (Strauss). As both a methodology and a method grounded theory has evolved over forty years and been adopted by social researchers across a range of philosophical perspectives, Charmaz (Constructivist Grounded Theory). Grounded Theory is descended from the Chicago School of Symbolic Interactionism, with its heritage and philosophical stance based on the work of American Pragmatists Pierce, Dewey, and Mead. The first proponents of the methodology were Glaser, Strauss, and Quint Benoliel who launched this influential methodology through their study of terminal illness, leading to the key text 'Awareness of Dying', in which they positioned grounded theory as an approach to developing substantive sociological theory with practical applications (Glaser & Strauss, 1965). Their interest in context and applied theory follows an epistemological lineage from American Pragmatism and Symbolic Interactionism. The diagrammatic model in Fig. 3.1 details some of the epistemological influences leading to the development of grounded theory.

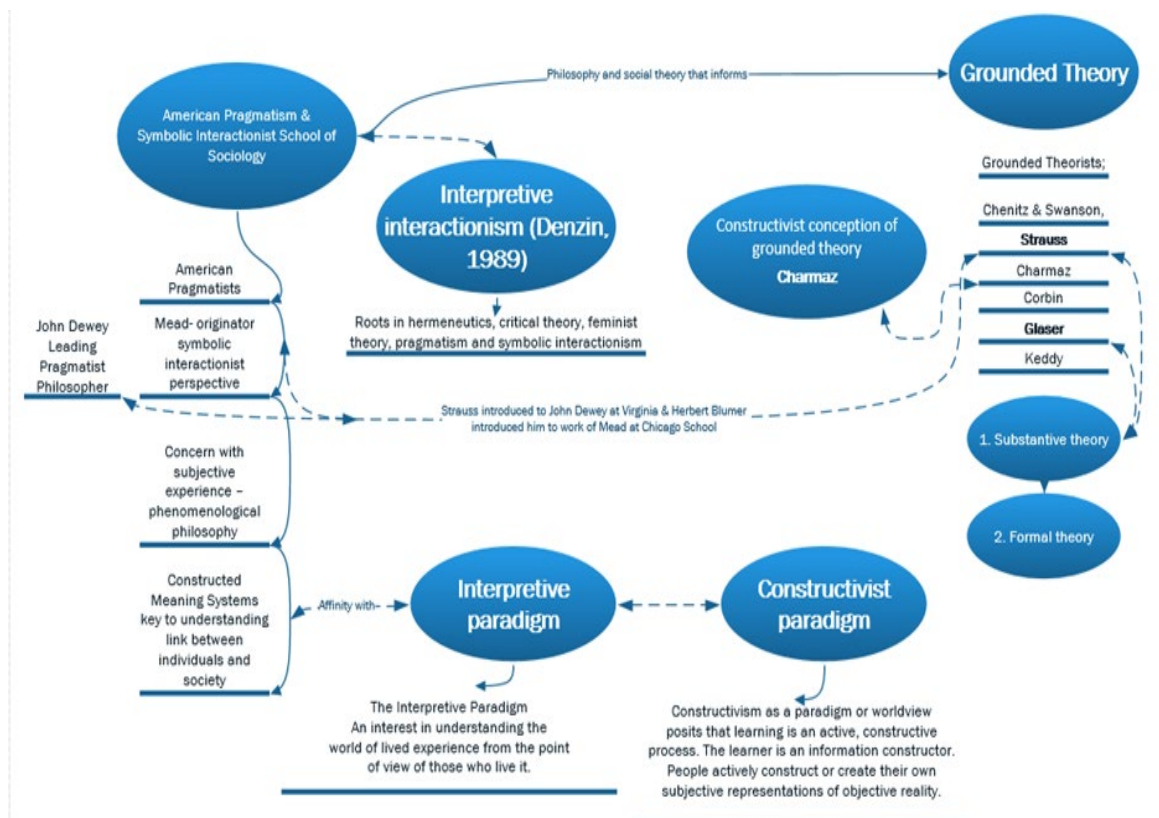


Fig. 3.1 Epistemological associations of Grounded Theory

The application of the grounded theory method (GTM) as a process for inquiry has continued to evolve and diversify since its initial development in the 1960s, with the nature of its multiple incarnations attracting some criticism. Bryant (2019) in discussing the evolution, development and varieties of application of its methods, a phenomenon which he highlights is not unique to GTM, suggests that this is a healthy progression, stating “researchers should never forget that the ultimate significance of a method is how it facilitates developing new and critical insights; something that often involves departing from the well-trodden paths of specific disciplines and common procedures. This proviso should come as no surprise to those involved in GTM, since the method itself grew from precisely these motivations.” To counter criticisms relating to the varieties of methods adopted in GTM, Bryant states, “it is important to respect alternative methodological positions, and to encourage and foster methodological sensitivity as part of research practice” (Bryant, 2019).

Burke Johnson and Walsh (2019), define MGT as “a research approach that includes the development of a grounded theory using qualitative and/or quantitative data and it uses elements, logics, and strategies from both GT and mixed research traditions” and “a methodological approach that keeps evolving and being enriched as it is applied in specific research projects.” A systems approach using grounded theory “can connect domains and explain the situations under study” (Bainbridge et al 2019). MGT within a prismatic

framework is appropriate as a methodology in conducting operational evaluation to investigate complex phenomena through a prismatic lens, acknowledging multiple and diverse perspectives. The study is an exploratory investigation undertaken to evaluate current practices and perceptions in relation to operational delivery of clinical trials drawing on methods from different paradigms.

3.3.3 Systems and Meta-Systems Approaches

The key challenges in determining the nature of reality are the quantification or qualification of an entity's existence or definition of its characteristics and behaviours. Essentially an entity can be classified based on its characteristics or taxonomy, whose qualities may be transient, amorphous, unstable, or subjective in nature or by contrast may possess quantifiable and measurable elements. In determining the characteristics or existence of phenomena, the research framework adopted should therefore allow for the application of suitable qualitative or quantitative methods to perceive reality or multiple realities, based on the context and nature of the problem being investigated. Reality within Inquiring Organisations is revealed through perspectival synthesis, a collective thought process. Haynes argues that perspectivalism involves the application of self-awareness to an object and the process of applying "subjectivity-as-objectivity" or perspectival thinking, a self-referential construct with the 'capacity to bring together a possibility with a reality. The reality is the object of study, and the possibility is the subjective interpretation of that object' (Haynes, 2007). A systems science approach using grounded theory 'can connect domains and explain the situation under study' (Bainbridge et al, 2019).

A metasystems approach to research within organisation is developed from Churchman's concepts of meta-systemic inquiry (Yu, 2017) which engage with multiple levels of reality within systems: social, scientific and philosophical and is purposefully orientated to understand context through interaction and values grounded knowledge in designing better systems. In conducting social inquiry, a researcher needs to reflect upon personal meta-theoretical concepts as well as engaging in a process of interpreting and synthesising multiple participant perspectives and belief systems. A meta-systemic approach is a quantum concept, facilitating the synthesis of multiple perspectives and pragmatic development of grounded theory, useful in informing policy and practice. Meta-systemic management adopts a whole systems approach to designing systems and governance based on complexity management (Espinosa & Walker, 2017).

3.3.3.1 Singerian Inquiry Systems Approach

Singerian Inquiring Systems approaches are allied with pragmatism and support mixed methods and grounded theory approaches, adding rigour to a pragmatist's transdisciplinary approach to axiology and praxis. The term and concept of transdisciplinarity was developed by Jean Piaget and progressed by the Basarab Nicolescu, a theoretical and particle physicist. Nicolescu (2010) draws on quantum theory in describing the nature of reality and suggests that the interaction between 'subject' and 'object' forms different transdisciplinary levels of reality, described as the 'Hidden Third.' Nicolescu argues that 'scientism' transformed the subject into an object, with negative consequences for knowledge and reality, but that the quantum revolution has substantially changed the status quo by introducing new scientific and philosophical concepts, discussed in section 3.2.3.

Research into Singerian organisational models has shown that holistic and dialectic approaches to understanding context-related challenges supports process improvement and knowledge generation. Organisations cultivating positive communication with well-integrated systems are associated with improved performance and healthcare outcomes (Vaughn et al, 2019). Mitroff and Turoff (2002) describe Singerian Inquiring Systems as the "epitome of synthetic multimodal, interdisciplinary systems...in effect meta-inquiring systems. In effect Singerian-IS are meta-IS, i.e., they constitute a theory about all other IS (Leibnizian, Lockean, Kantian, Hegelian)." Singerian Inquiry offers a meta-systems approach to conducting collaborative and reflective evaluation within healthcare organisations, and was adopted as a consensus method in the research in the form of a Singerian-Delphi, a method concerned with "raising and building explicitly into the design of the technique the self-reflective question; How do I learn about myself in the act of studying others and the world?" (Mitroff and Turoff, 2002).

3.3.3.2 Holistic Approaches

A holistic approach in healthcare, as well as the researchers approach to operational evaluation, should be at the core of any model operating within a social domain. As discussed in Chapter One, this study sought to determine the nature of barriers and facilitators experienced by clinical research professionals in delivering effective patient care and implementing clinical trials. This is an area which is highly influenced by individual and group perceptions relative to context, experience and roles, and the effectiveness of their interactions with colleagues within their organisation and across networks, and with wider external bodies. The nature of their relations is therefore indeterminate, emergent, uncertain and subjective. This necessitates detailed qualitative study to understand this moveable,

unfixed and contextual realm. Within healthcare contexts, relationships are multi-dimensional, involving patients and professionals and the nature of their collaborations and inter-relations, as well as the interprofessional, interdisciplinary relationships between and across organisations, networks and authorities. The research sought to understand the nature of these relationships and their effect on sustainable growth for clinical research, and the ability to support and enhance patient needs and experiences, as well as the role of governance and management approaches in facilitating patient-centred care and employee health, well-being and personal development. In advancing research practice the social sciences need to consider that the way in which we measure and evaluate entities adjusts our perception of reality, therefore axiology and praxis should be considered as foundational criteria within a prismatic approach to inquiry. A holistic paradigm for inquiry, which is dynamic, evolving and dialectical unites pragmatism, Singerian Inquiry and quantum perspectives provide a whole systems approach to study, valuing ethics and multiple perspectives and recognizing the concept of synthesised reality. Engaging with patients, professionals and key stakeholders in organisations through the adoption of a holistic, consensus-based designs elicits expert views and grounded knowledge.

3.3.3.3 Critical Systems Thinking and Transdisciplinarity

Traditional authoritarian and hierarchical systems within healthcare organisations can therefore have a limiting effect on the capacity and capability of both individuals and organisations to evolve, respond, adapt and innovate to provide optimal care and operational solutions. By contrast, organisations adopting critical systems thinking or systemic governance are embracing, holistic and open to creative and innovative dialogue which foster collaborative environments for problem solving. “Critical systems thinking, and practice or critical systems praxis (CSP) stresses the links between transcultural thinking and practice. It is applied to a particular case in order to develop grounded theory and practice to address social and environmental justice pertaining to sustainable health, education and employment, irrespective of age, gender or culture” (McIntyre-Mills, J. 2003, p7).

3.3.3.4 Quantum Sociology & Meta-Systemic Approaches

Metatheoretical considerations and quantum perspectives are of increasing relevance in a digitised and global society, where the social sciences can benefit from applying the concepts of quantum theory to understand multiple and fluid realities in an era of rapid advancements in science and technology. Postmodern and postpositivist approaches have witnessed seismic shifts in the perception of reality, with key philosophical contributions

ranging from Kuhn's conception of the paradigm shift in 'The Structure of Scientific Revolutions', Popper's 'The Logic of Scientific Discovery' and Feyerabend's 'Against Method', and the major upheaval to metaphysics with the shift from Newtonian approaches to Quantum perspective (Fris & Lazaridou, 2006). Debate in respect of methodologies within the field of the social sciences still pervades discourse within published papers, with authors frequently calling for a paradigm shift within a particular field of inquiry. Semantics and siloing of perspectives within specialisms perpetuate a state of flux in defining acceptable methodologies within the social sciences. As Newton's physics defined the 'scientific approach' in the 17th century, quantum mechanics theoretical constructs and associated principles of uncertainty and relativity, may offer a metatheoretical methodology for the social sciences, a quantum paradigm of inquiry. Nicolescu (2010) introduces the concept of 'beyond disciplines', derived from quantum superposition and indeterminism, in the formulation of 'transdisciplinarity' (TD). He situates TD as an approach that has "an exclusive concentration on joint problem-solving of problems pertaining to the science-technology-society triad" (Nicolescu, 2010).

A meta-systemic approach supports the emergent paradigm of quantum sociology, which moves from mechanistic and deterministic frameworks to creative approaches adopting multiple perspectives. Based upon discoveries within quantum physics, our perception of reality needs to shift from polarities of beliefs to pluralistic '*both/and*' thought processes, which can cope with 'quantum contextualism.' Pluralistic paradigms are necessary to study complex phenomena within interactional fields of social inquiry and healthcare. A metasystems approach to research within organisation is developed from Churchman's concepts of meta-systemic inquiry (Yu, 2017) which engage with multiple levels of reality within systems: social, scientific and philosophical and is purposefully orientated to understand context through interaction and values grounded knowledge in designing better systems. In conducting social inquiry, a researcher needs to reflect upon personal meta-theoretical concepts as well as engaging in a process of interpreting and synthesising multiple participant perspectives and belief systems. A meta-systemic approach is a quantum concept, facilitating the synthesis of multiple perspectives and pragmatic development of grounded theory, useful in informing policy and practice. A quantum perspective comes into existence recognising that reality is both observable and interpreted. Measurable phenomena within clinical research operations can be observed through mechanistic processes of measurement to form the basis of prediction, forecasting and strategic modelling through objective instrumentation.

3.3.3.5 Meta-Methodologies & Prismatic Inquiry

In the collation and synthesis of evidence to inform practice and policy, the researcher needs to engage with the different types of knowledge that exist within contexts and their transition across and between boundaries, an analytic approach calling for meta-methodologies. The study of meta-methodologies is a vast and rich field for review, which extends beyond the scope of this thesis and provides avenues for future research, but the concept of meta-theoretical approaches are recognised within this study in the design of a prismatic model for inquiry. Research approaches may draw upon monism, dualism or pluralism, in the process of making their claims to knowledge, and choice of values, perspectives, strategies and methods from within their selected paradigm. Meta-methods, meta-aggregation and meta-governance are methodological approaches, which value whole systems approaches with respect for local context. Other meta-methods include meta-aggregation, a data synthesis method which is an inductive process capable of consolidating complex data sets, predominantly qualitative in nature, with the intention of developing actionable knowledge, providing strategic or practice guidance (Coulter, 1989). Meta-aggregative methods are underpinned by pragmatism (Hannes & Lockwood, 2011) and are synonymous with a praxis approach.

3.4 Chapter Summary

This chapter has defined the philosophical traditions and theoretical perspectives informing the adopted research framework, providing a detailed critique of their underlying principles. The methodological rationale presented provides a justification for their selection and details how these logically link to the selection of methods. An adaptive theoretical framework was needed to comprehensively evaluate the research problem. The social, interactive, and holistic elements of healthcare delivery are subjective and value-laden, requiring interpretivist approaches to inquiry in defining prismatic and quantum realities. A prismatic or meta-theoretical approach has underpinned the approach to investigating the nature of cancer clinical trial delivery, and its sub-domains of patient follow-up and complexity. The developed research framework is sensitive to theoretical perspectives and concerns relevant to socio-operational contexts, forming a prismatic inquiry model critical in understanding the complexities of disease and healthcare delivery. The study design and methods applied in conducting the research are described in the following chapter.

Chapter Four – Research Design and Methods Rationale

“In a dynamic, pluralist, complex world, the challenge is not to discover a solution to a fixed problem but to elicit and imagine a process capable of generating effective design responses to evolving situations.” (Paquet, 2013).

4.1 Introduction

Discussed within this chapter is the adopted design framework, its development, reasoning and procedural methods of application in studying clinical trial operational delivery, along with related considerations around approaches to research ethics and data management. Underpinning the research approach is a desire to facilitate progress in healthcare design through adoption of empathetic and discursive methods, forming the basis of ethical principles guiding collective operational decision-making in emergent, dynamic systems: a prismatic perspective model.

This study is an exploratory investigation undertaken to evaluate current practices and perceptions in relation to operational delivery of clinical trials. The design of the participant study and selection of methods followed an initial literature review into subject, policy, theoretical and methodological literature. This initial orientating review, alongside preliminary consultations with NHS and NIHR professionals, identified key challenges for cancer research delivery. The development of the research protocol drew upon a detailed review of qualitative and quantitative methodological approaches, leading to a mixed-methods study design employing grounded theory. In adopting a mixed grounded theory approach, the study design supports theoretical emergence, allowing participants to reveal core conceptual categories through their lived experiences. The following sections detail the approach, rationale, and implementation of the selected methods. Qualitative research in healthcare is integral to evidence-based practice and valuable in improving the quality and relevance of health service delivery (Lockwood et al, 2015). Qualitative aspects of the research provide in-depth context-specific evidence through the ‘voices’ of patient-facing professionals, articulating human and social aspects of research.

The design reflects the Singerian-Churchmanian model of Inquiring systems (SCIS) valuing ethics and community knowledge in complexity evaluation and decision-making (Haynes, 2012). A democratic approach was needed recognising multiple perspectives combined with individual knowledge and experience, to form a comprehensive understanding of the complexities of the systems and networks in which they operate, through a dialectical group consensus process, fitting a Singerian philosophy. In this study, crossing multiple

disciplines, organisations and societal groups, the nature of the research problem called for a broad yet contextually sensitive approach, which was inductive and emergent, aligned with both grounded theory and Singerian inquiry criteria.

4.2 Ethical Considerations and Approval

The study design, methods and implementation of the research respected professional, academic and legislative standards, alongside continued reflection throughout all study stages, ensuring ethical practice, moral conduct and protection of participants. The research protocol and participant documentation were developed with due consideration to patients and research professionals, providing accessible information to allow them to make an informed decision prior to agreeing to participate in the research. For cancer patients any potential emotional aspects of describing their experiences of participation in clinical research were considered in advance. Effective support for participants was identified in advance, for all stages and settings in which the research was conducted and outlined in participant information sheets. Ethical considerations also apply to the development of a tool upon which operational decisions may be undertaken. This means that the design of the tool and the inclusion criteria for its evaluative and quantitative judgements should be based upon the input of 'experts' in the field (patients and professionals), the users and benefactors of 'human-centred automation' (Randhawa et al, 2016). For this reason, the research commences with a Delphi consensus study. Throughout the research journey the guiding principles of the Social Research Organisation (SRA) were observed to ensure compliance with good ethical practice, respecting the concerns and interests of participants and maintaining professional standards in social research methods. SRA (2021, p29) highlight the following foundational ethical principles of the Academy for Social Sciences (AcSS), which have been tailored to the needs of the social sciences:

4.2.1 Ethical Approval

Prior to applying for ethics approval, the study had been reviewed by the Lincolnshire Research Patient and Public Research Forum, with recommendations from the group incorporated into the study's design. Their principal recommendations related to amending participant documentation to make the vocabulary more accessible to a lay person. The research proposal was subsequently submitted for ethical and peer review, initially receiving approval from the University of Lincoln School of Health and Social Care ethics committee. The East Midlands regional ethics committee was then attended by the Chief Investigator, where the review panel requested minor amendments to documents and additional confirmation that travel payments would be provided to participants attending interviews,

where required. Following the amendments, the research received approval in October 2017 from the NHS Health Research Authority (HRA) and East Midlands – Derby Research Ethics Committee (REC ref: 17/EM/0292).

4.2.2 Ethical Practice and Protection of Participants

Ethical and moral responsibilities of researchers encompass concepts of autonomy, non-maleficence, beneficence and justice (Wiles et al, 2005). Participants' freedom to choose to participate in research should be protected, and the researcher must consider the vulnerability of potential participants within particular social contexts, who may feel obligated to join a study. There were different ethical considerations in relation to autonomy and capacity to provide informed consent for cancer clinical trial patients and clinical research professionals, such as the potential for participants to feel an obligation to undertake the research, either as an employee or a patient receiving care at a participating organisation.

4.2.2.1 Informed Consent and Right to Withdraw

The participant information sheets provided clear and detailed information relating to the different participant types, the nature of their involvement, and rights. The research did not involve participants lacking the capacity to consent for themselves and did not include vulnerable groups such as children, prisoners, or young offenders. The consent process was relative to the study phase and participant type. A proportionate approach to consent was adopted ensuring participants had sufficient and clear information to allow them to make an informed and voluntary decision as to whether they wished to participate. For the Delphi and interview studies written consent was obtained and for the questionnaire study, participants provided their consent by completing the survey online or returning by post. Voluntary participation for all study phases was made explicit in participant documents. Participants taking part in any of the study stages were informed of their right to withdraw at any time and that there was no obligation to offer a reason for withdrawal if they no longer wished to participate. Prior to commencing interviews participants were advised that they could stop the interview at any point and were not obliged to continue, if they did not wish.

4.2.2.2 Confidentiality and Anonymity

A central concern in the conduct of social research is the protection of participants, their data and identity. Great care was taken throughout the study to observe all legal and moral responsibilities in respecting confidentiality and anonymity of participants. Participants were advised how their identity would be protected and personal data would be managed, prior to their consent to participate. All participant research data was stored in linked anonymised

form and all digital files encrypted. Participants were advised that where it was deemed appropriate to use direct quotations from the research data, the identity of the participant would be protected. In the Delphi rounds some participants referenced their role in their textual responses. In the analysis between rounds the reference to any roles was removed to protect the identity of participants. Only the Chief Investigator had access to the linked participant code and the study data. Principal Investigators at sites were involved in the recruitment of participants but did not have access to any of the participant research data, once an individual had been recruited.

4.2.3 Data Security and Risk Management

Prior to the commencement of research activities, a comprehensive risk management review was undertaken, and the prospective approach documented in risk assessment and data management plans. Participants rights were protected, and a risk register developed as part of the study's quality management system, in accordance with ICH E6 (R2) guidelines. The risk assessment tool (as used by NHS R&I departments) rated the risk to participants as low, as the study did not involve any medical interventions.

Participants lacking the capacity to consent or communicate in English were not included in the study, to minimise risk of misinterpretation of comprehension of the study's documentation or interventions. Whilst this did limit the potential recruitment for non-English speaking citizens to participate, it was recognised that the capacity of the research team did not extend to providing translation services for study documentation or communications. Further risk mitigation in the study design considered the health and capacity of cancer patients to participate in the study. To minimise the burden and risk on patients the clinical research team at participating sites undertook the role of participant screening, including undertaking appropriate death checks on patient records. Patient participants were also provided with contact details for their local research and PALS team, to ensure that they had relevant support available should they find that their reflection on their cancer journey and prior participation in clinical research became distressing.

4.2.4 Data Management Plan

A data management plan (DMP) was developed prior to the commencement of the research to ensure the secure and ethical handling of all research and participant data, and to mitigate any risk or loss to confidential information. Study documentation detailed all procedural and ethical management of research data. Data management complied with DPA and GDPR legislation, NHS and University of Lincoln policies. During the course of

the research GDPR regulations were introduced and all sites and participants were provided with information regarding their rights. A study amendment was approved in accordance with NIHR and HRA requirements, and updated study documentation issued to sites and participants to comply with the introduction of new GDPR legislation, with information made available at each participating site and on the EFACCT study website.

4.3 Research Design Overview

The study was an exploratory qualitative and quantitative design where constant comparative analysis and theoretical sampling were conducted throughout the research process, a “hybrid design” remaining open to emerging concepts involving multiple dimensions and methods (Johnson and Walsh, 2019). Multiple work packages were incorporated into the study design to form a systematic approach capable of capturing the organisational realities of NHS sites participating in the delivery of clinical trials to cancer patients, and to determine the core dimensions and constructs defining complexities and characteristics witnessed within research operations. Quantitative components captured volumes and frequencies of interventions, whilst qualitative elements explored perceptions and experiences of patients and professionals involved in clinical trial participation or delivery, in order to elicit the contextual factors and experiential themes.

Through constant comparison and analysis of data drawn from the four work packages, shown in Figure 4.1, the study formed insights into cancer research operational delivery. Through the combining of evidence, synthesised from multiple approaches, materials and participants, a strategy is created that adds “richness and depth to any inquiry” (Denzin, 2012, p82). The methods applied in comprehending the complexities of the current UK cancer clinical research delivery landscape facilitated a knowledge synthesis of multiple perspectives, seeking out the differentials and shared experiences across ranging sites, to form a holistic view which remains sensitive to the concerns of individual patients and professionals, in turn detailing operational practice. Evidence was collated across three navigating data collecting categories; realms used to facilitate a pragmatic, mixed-methodology approach but not selected to predicate the conceptual categories of the grounded theory, which is discussed in Chapter Five. Richardson et al (2001) developed a decision-making model of inquiry (TOPEA), to synthesise data from “technical (T), organisational (O) and personal (P) perspectives with ethical (E) and aesthetic (A) considerations and synthesizes them into an integrated whole”. The prismatic model of inquiry used within this study, draws upon the TOPEA approach, to understand complex and interacting phenomena through a comparative synthesis of data situated within the following domains:

- Object-oriented (objective, scientific, technical, structured and quantifiable data)
- Systems-oriented (evolving complex systems, policies, infrastructure and operational data)
- Person-oriented (beliefs, perspectives, values, dialectical and subjective data)

4.4 The Research Process and Strategy

Within a grounded theory study ‘all is data’, (Glaser and Strauss, 1967) with data collection guided by emerging concepts and the use of theoretical sampling. The research process evolves from the researcher’s sociological interest or problem concerns within the area of study, not from a priori stance designed to test a hypothesis. Theory is emergent therefore the initial data collection is orientating in nature with the overall sampling strategy remaining open and responsive to evolving themes and concepts. The participant sample is purposively ‘chosen according to theoretical criteria’ (Glaser and Strauss, 1967). Data collection is cyclical and iterative, commencing with initial purposive and snowball sampling techniques. Analysis starts early in the research process with emergent concepts in the initial data collection being compared to new incidents, through use of the constant comparative method (Mathison, 2005), in combination with memoing and theoretical sampling, which further guides data collection until theoretical saturation of concepts is achieved. The analytic procedures describing the development of grounded theory in this study are discussed in greater detail in section 5.4 of the following chapter. Chun Tie et al (2019) describe the inquiry process as one which is ‘iterative and dynamic and is not one directional’, a framework which mirrors the complex, emergent nature of healthcare operational contexts. A Constructivist Grounded Theory (CGT) informed the research strategy, with concept generation and theoretical framework development supported through Charmaz’s four-phased approach (Charmaz, 1990):

- (1) creating and refining the research and data collection questions*
- (2) raising terms of concepts*
- (3) asking more conceptual questions on a generic level*
- (4) making further discoveries and clarifying concepts through writing and rewriting*

4.4.1 Research Design Rationale

Within management and organisational research grounded theory is a long-established qualitative approach, well adapted to studying concepts involving operational change and decision-making (Locke, 2001). The combined application of mixed-methods with grounded

theory that is now described, linking the practicalities of data collection and analytic processes to the generation of theory grounded in its social-contextual realities.

4.4.2 Protocol Design and Research Phases

To investigate the research focus areas described in Chapter One (see section 1.4), the study design needed to facilitate the collation of multi-faceted data, ranging from structured quantitative data to complex contextual, qualitative data, required to interpret clinical trial operational delivery in depth. To access such a diversity of data necessitated a multi-phased, national study employing purposive and theoretical sampling strategies, authentic to mixed methods grounded theory designs, in combination with systems and operational research methodologies. The data collection commenced with the participant phases of the study, recruiting cancer clinical trial professionals and patients involved in cancer clinical trials at NHS research sites. As key stakeholders within translational science they represent the human voices of cancer research, providing vital perspectives into the nature of cancer clinical trial delivery in the UK. The research professionals and cancer patients formed separate research arms within each of the study stages, but the conceptual themes collected through the Delphi, questionnaire and interview studies have been analysed and synthesised to form the overall theoretical model, as described in Chapter Five.

The research protocol and associated participant documents were developed with input from lay, clinical, and academic reviewers, prior to submission for study approval. The protocol provided a detailed manual for the core research team and participating sites to follow. In addition, lay protocols, principal investigator guides, site files and site initiation training were provided to sites, to ensure that the research progressed in accordance with ethics and HRA version-controlled approvals. Study amendments were limited to the addition of new sites during study set up and a later amendment during data collection stages, to update sites on the introduction and requirements relating to new data protection legislation, namely the General Data Protection Regulation (GDPR).

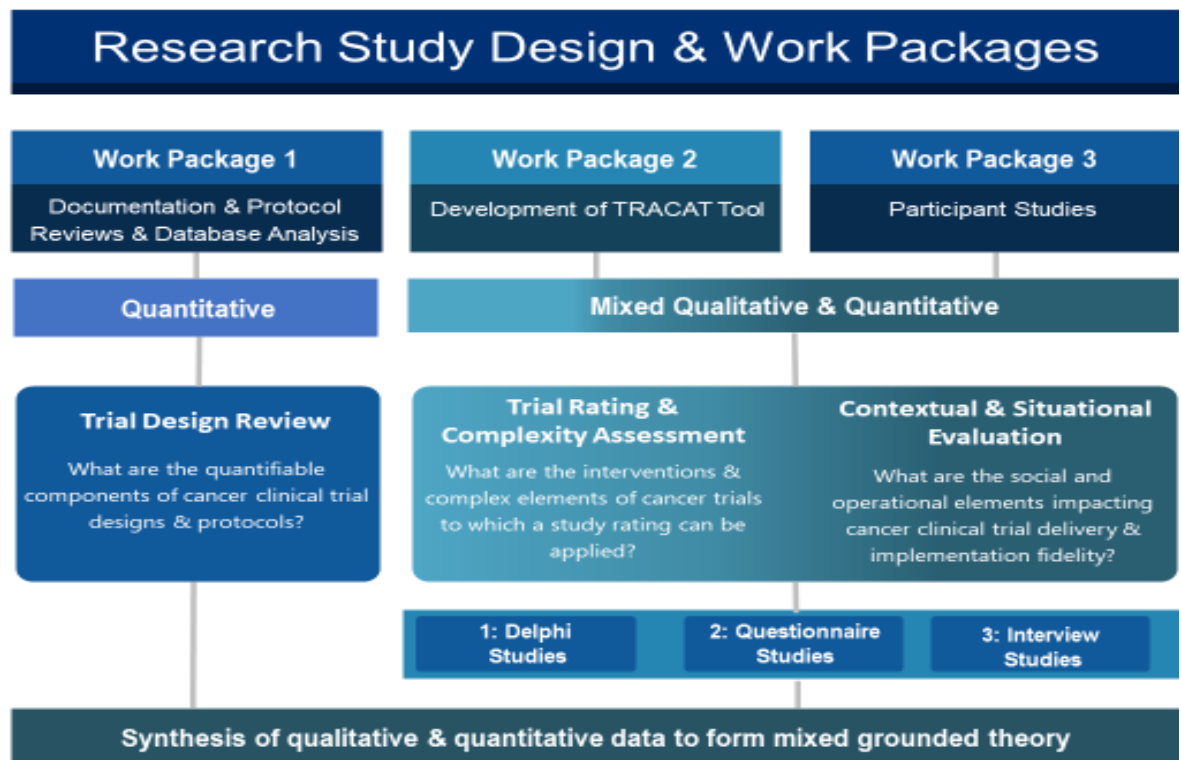


Figure 4.1 Research Work Packages

4.4.3 Research Setting

Data in this study were collected and constantly compared across the multiple work packages shown in Figure 4.1. Whilst the work packages below are numbered from 1 to 4, this does not denote the order in which the research was conducted. Following an initial guiding literature review, which informed the design of the research, the initial data collection commenced with Work Package 3 and the Phase 1 Delphi studies. The nature of the Work Packages evolved during the study.

Research settings included multiple secondary care hospital sites across the UK, as well as cancer patient homes, close to participants' regional NHS clinical trial sites. Remote research elements were also incorporated into the study design, comprising of the e-Delphi and questionnaire studies conducted online or by post. All participant interviews were conducted by the Chief Investigator, at appropriate hospital locations or patient homes, which were agreed in advance with Principal Investigators based at participating sites. The collaborative, multi-centre study design engaged clinical trial professionals and patients, closest to cancer research delivery in the UK, in a democratic project defining areas of importance to stakeholders, who possess contextual, practical knowledge to inform strategic decision-making and design responses. Inquiry capable of evaluating contextual problems and developing effective solutions for operational delivery needs to engage with

those participants who reside within the setting and the types of knowledge and perceptions they hold relating to it, to synthesise the “diverse modes of human thought” in interdisciplinary systems (Mitroff et al, 1973). NHS sites delivering cancer clinical trials were purposively selected to allow for comparisons between differing scales of operation and location, to understand best practices in evidence supporting patient-centricity, and to evaluate follow-up and complexity in operational practice. By researching organisational delivery of cancer clinical trials in the NHS it was necessary to understand varying cultural environments and the diverse experiences and multiple perspectives of patients and professionals. The study sought to build a comprehensive dataset capturing the phenomenon of cancer research operational delivery across the UK. It was therefore important to have a national distribution of hospital sites and participants to avoid potential regional effects on the research results, which may have occurred had sites been selected from only a single, local Clinical Research Network (CRN). A mix of teaching, acute and district general hospitals were approached to participate in the study, varied by regional network, scale and type of NHS site, and covering both rural and metropolitan patient populations. The participant recruitment plan shown in figure 4.2 guided the initial recruitment, which employed both purposive and snowball sampling techniques, described further in section 4.3.4).

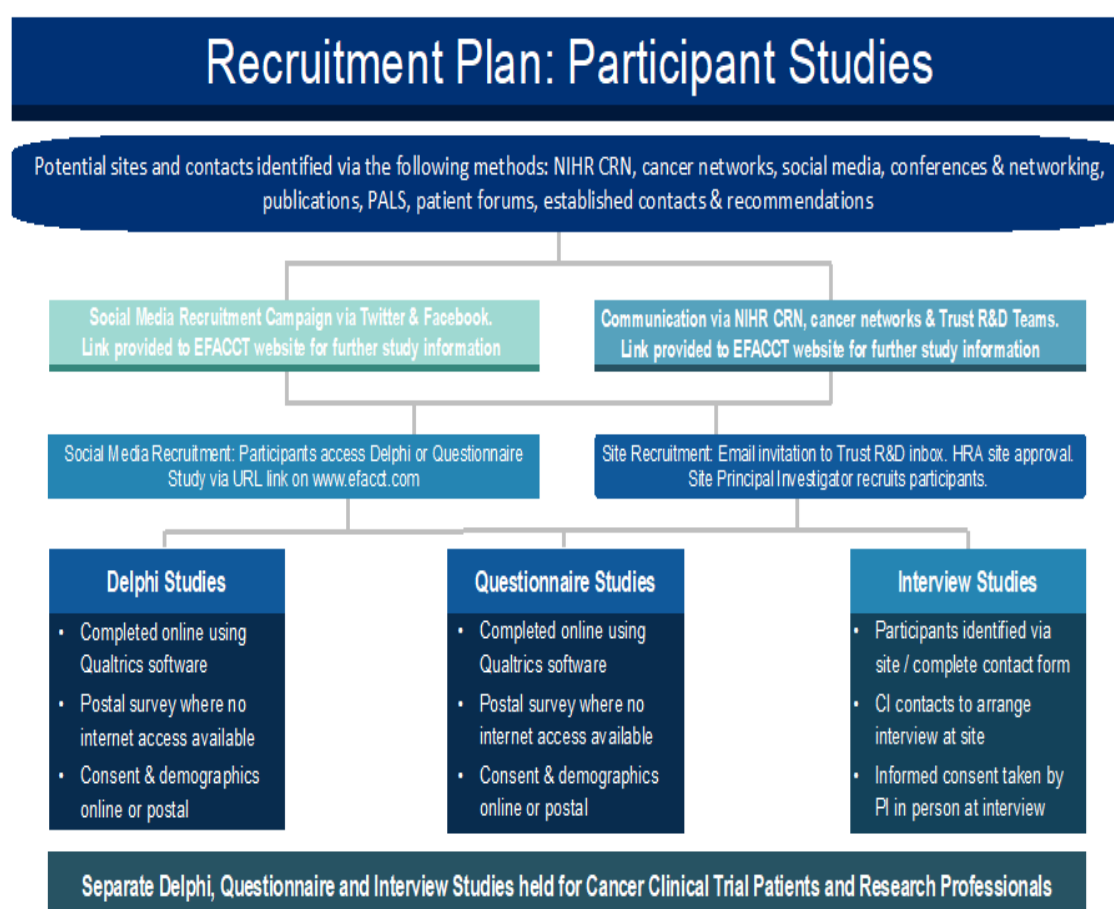


Figure 4.2 Participant Recruitment Plan

4.4.4 Site Recruitment and Management

NHS secondary care sites delivering cancer clinical trials within the UK were eligible to participate in EFACCT, a multi-centre, and mixed methods study. The EFACCT study was promoted via social media, conference attendance (see section 9.4.2) and through communications and presentations to the NIHR National Co-ordinating Centre, regional CRN's, and related professional contacts within the clinical research industry and the NHS. Following full study approval in October 2017, invitations to participate were issued to NHS sites who had already expressed an interest in the study, across the UK. Further site invitations were sent to Research & Development/Innovation departments which were purposively selected based on region, hospital type and scale, and the nature of the population they served. Interested sites reviewed their capacity and capability to take part in the research. Additional direct approaches were made to Chief Operating Officers of local CRN's, to request support in identifying potential sites where difficulties were experienced in recruiting to a particular geographic region.

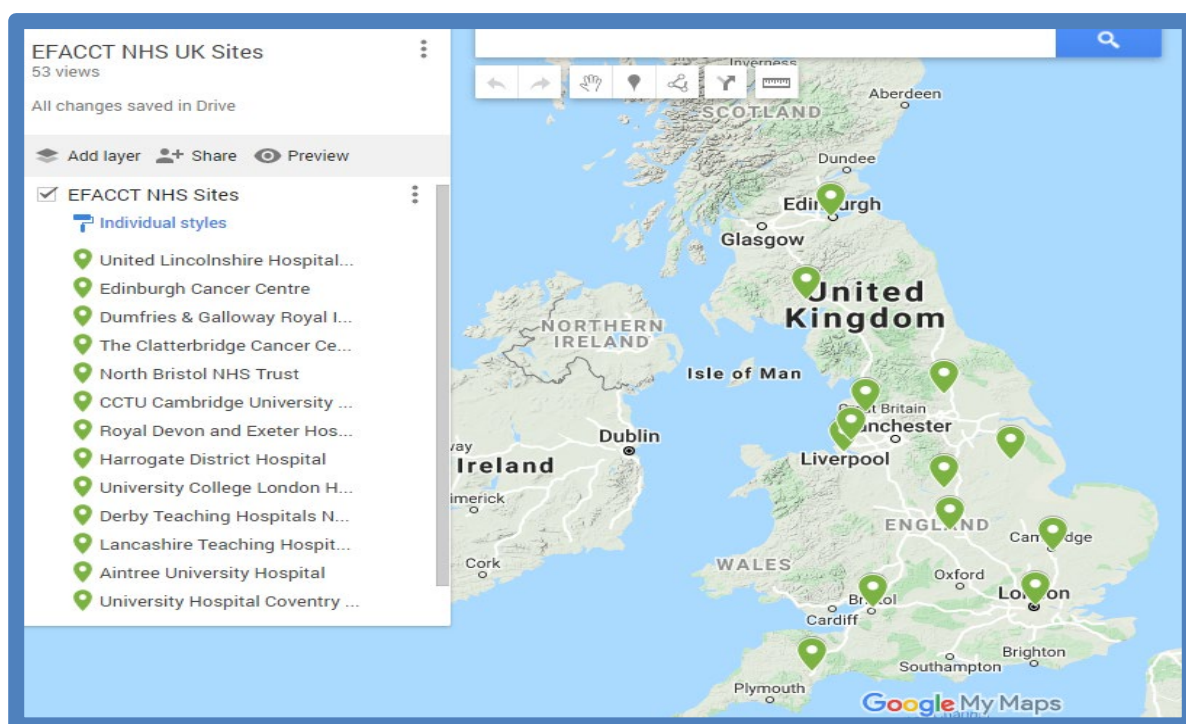


Fig. 4.3 Site Recruitment Map

A monthly study management report was maintained to track recruitment progress, site set-up and communication with sites. Investigator Meetings (IM) and Site Initiation Visits (SIV) were held on sites, with the exception of one, where these meetings were conducted remotely due to Principal Investigators' limited availability. Communication updates on the study's progress and achieved milestones were issued to Principal Investigators at all sites. As part of the purposive selection of study sites, a review of the type and nature of cancer

studies they were hosting was undertaken. This information was accessed via 'Performance in Initiating' and 'Performance in Delivering' NIHR reports published on trust websites and via study data in EDGE.

4.5. The Participant Studies

The mixed methods study design explored human perceptions and experiences of participating in cancer clinical research, from the perspectives of healthcare professionals and patients. The purpose of including patient and professional voices in research is to gain rich insight to comprehend the multiple realities of complex interacting relationships and contexts. Research involving participants took place in Work Package 3 with data collected conducted in three stages with each element (type of study) conducted with both cancer clinical trial patients and research professionals. Trial sites were involved in identifying, approaching and recruiting potential participants to the varying stages of the research. The initial exploratory participant stages commenced with the Delphi consensus studies, with separate arms for research professionals and cancer clinical trial patients. Following completion of these the questionnaire and interview studies were progressed (stages 2 and 3), with each study designed relative to the needs of each group and based on the findings of the Delphi studies (stage 1). Principal Investigators at sites approached potential participants who were offered the option of participating in either the questionnaire or interview studies, or both should they wish. Delphi participants did not take part in the questionnaire studies but were able to opt to take part in the more in-depth interview studies. By allowing Delphi or questionnaire participants to take part in the later interview stage, they had further time and opportunity to consider aspects of cancer clinical trial delivery and discuss their experiences and perceptions in greater detail.

- Stage 1 - Delphi studies with research professionals and cancer trial patients.
- Stage 2 – Semi-structured questionnaires involving research professionals and cancer trial patients.
- Stage 3 - Semi-structured interviews involving research professionals and cancer trial patients.

This participant studies focussed on the collation of the person-oriented, experiential evidence aimed at evaluating the facilitators, barriers and variables impacting efficiency such as; internal and external structures, resource and capacity, morale, design methods, cultural values and multi-disciplinary communication. Research professionals and patients offered the potential to impart deep insight into the phenomena of cancer clinical trial delivery and follow-up from the perspective of the key stakeholders. Their contextual and

expert knowledge as stakeholders was also vital in informing the development of an operational workforce management tool to monitor and evaluate follow-up, complexity, and workload in cancer research delivery. The participant studies sought to obtain rich descriptive participant content, collate subjective experiences and study social interactions within the field, gaining qualitative insight to contextualise research delivery and formulate theory. The social values of professionals and patients, their perspectives, knowledge, experiences, and interactions are complex, multi-faceted elements to be evaluated in understanding the complexities and social aspects of clinical trial delivery. The mixed methods used in this study were designed to draw out the broad nature of themes within complex social systems and to understand the facilitators, barriers and variables impacting the efficiency and quality of trial delivery, such as; internal and external networks and structures, resource capabilities and capacities, morale, system and governance designs, cultural values and multi-disciplinary communication.

4.5.1 Research Participant Selection and Sampling

An initial project sampling strategy was developed within the study protocol, detailing the purposive samples for site selection and recruitment, and participant inclusion and exclusion criteria, for research professionals and cancer trial patients. Initial purposive and snowball sampling guided the site and participant sampling, in line with grounded theory methodology. For the Delphi study participants, it was specified that they would need access to the internet. During the course of the research however, allowance was made for some elderly participants who had been approached by Principal Investigators at site who wished to take part but were not at ease with internet use. For these participants the Delphi questionnaires were sent by post with return envelopes provided. In the conduct of the Delphi study there were no other adaptations required to accommodate participant requests, other than the Chief Investigator entered the returned postal surveys into the Qualtrics portal for data analysis and reporting purposes. The sampling frame is shown in the Appendix 10.

4.5.2 The Delphi Studies and Consensus Methods

The Delphi technique is widely used within the healthcare setting and was selected for its suitability as a consensus method in to elicit the opinions of 'experts' on the importance and priority of trial delivery variables and as an effective process for the analysis of complex problems by a group (Linstone & Turroff, 1975). Experts in Delphi studies are individuals knowledgeable within a specific field of personal knowledge or professional experience, selected within a field of interest to the researcher to gauge levels of agreement on specific 'problem' or research subjects, with a view to defining priorities for operational and

forecasting applications. The freedom of expression of participants was important and therefore it was appropriate to select the Delphi method in place of a focus group, where the lack of anonymity and potential for over-dominance by hierarchical individuals or bodies may compromise open expression. Two separate Delphi studies were conducted online, using a classic approach and involved research professionals experienced in cancer clinical trial delivery and cancer clinical trial patients (the experts), in developing and rating themes for review in the subsequent questionnaire and interview stages of the research.

The Delphi studies sought to develop grounded, context-specific knowledge capable of supporting organisational analysis and reflecting the Churchman-Singerian model of Inquiring systems, valuing ethics and exoteric knowledge in complexity evaluation and decision-making (Jones et al, 2020; Haynes, 2012). The initial intention in conducting the study was to define an optimal research delivery framework to enhance patient access to the latest treatment options and services. In the creation of knowledge through an evaluative instrument, designed using consensus methods and intended to support researchers in identifying and solving shared operational problems, the concepts of instrumentalism and theories of John Dewey were considered, along with the Churchman-Singer philosophies of Inquiring Systems.

The selection of participants aimed for balance between group homogeneity and heterogeneity in order to ensure that a wide range of perspectives was considered but consensus was achievable. It was therefore decided not to combine both sets of participants into a single study as this would have made the group too heterogeneous and achieving consensus would have been challenging and required a much larger sample size. As professional and patient perspectives are vital a separate arm was deemed necessary.

The Delphi study with research professionals sought to gain consensus on trial rating and complexity attributes for cancer trials and a definition of follow-up, whilst the patient Delphi study elicited themes on participation in trials, considering elements which might be burdensome or supportive from a patient's perspective. It is important to remove uncertainty in terminology usage and comprehension of issues, so consensus was sought in the universal application of terms and approaches by the NIHR and researchers, ensuring consistency in reporting and resolution. The outcome informed the design of the subsequent questionnaires and interview content, contributing to the developing grounded theory and a democratic synthesised review of cancer trial delivery. Using the e-Delphi technique also allowed participants from across the UK to provide expert input into the design and creation of a trial rating tool to support sites in delivering cancer trials.

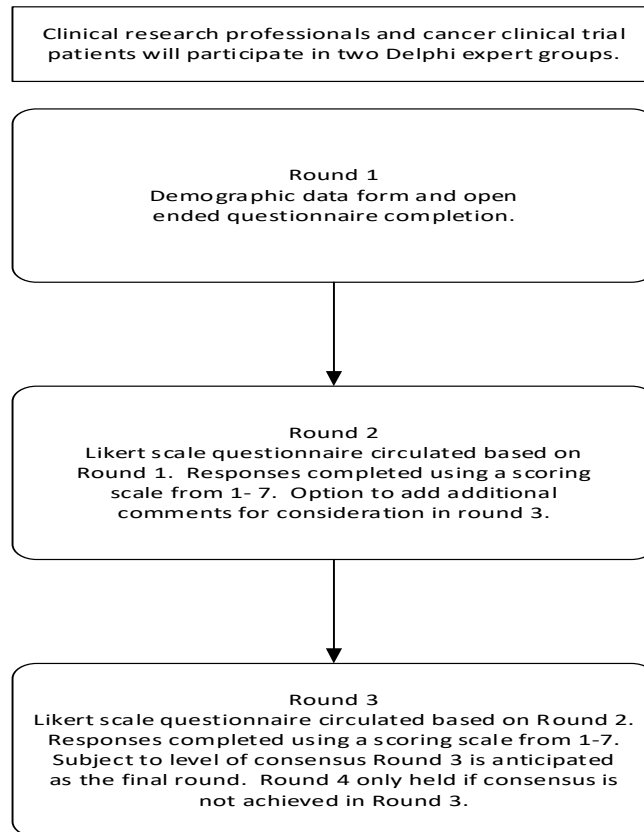


Fig. 4.4 Delphi summary.

Both Delphi studies were conducted in 3 successive questionnaire rounds, commencing with open questions in round 1 (analysed qualitatively) and then moving to quantitative analysis in subsequent rounds, using a 7-point Likert scale. All responses were collated, analysed and fed back as a statistical measure of group responses with individual responses remaining anonymous. Consensus achieved based on 70% of experts agreeing on item ratings. All items achieving consensus were put forward for review in phase 2 and 3 of the study and considered as TRACAT tool rateable values. The data analysis processes are discussed in Chapter Five.

4.5.2.1 Delphi Sampling and Participant Recruitment

The EFACCT Delphi studies used a purposive sampling approach and selection criteria based on participants' knowledge and experience of clinical trials, either as a patient or professional, an important selection criterion within Delphi studies. To achieve a sample of 15-20 panelists the aim was to recruit between 22-30 participants to each study arm. Whilst this is a relatively small sample size, if the participants are similarly knowledgeable and expert in the field of study a small sample size can be deemed effective (Atkins et al, 2005). Principal Investigators at each study site identified and approached potential clinical research and cancer patients to join the Delphi studies as panellists, based on the inclusion

criteria set out in the protocol. Within the research professional group (Delphi Arm 1), the study sought to recruit a multi-disciplinary panel to include research professionals who were sufficiently heterogeneous not to produce bias, and in engaging a range of knowledge and skill sets within a democratic project defining areas of importance to stakeholders, and the creation of a mechanism to monitor and improve operational delivery. The research professional Delphi study was run in tandem with a cancer patient study (Delphi Arm 2), both producing both qualitative and quantitative data outputs. Within the patient group the study recruited from a range of patients involved in cancer studies across the UK, study phases and cancer types. For professionals their role, site, gender, age group and years of experience in clinical trial delivery were recorded. For patients their gender, age group, disease category, type of study and the length of participation on a clinical trial were captured. Core participant characteristics and demographics are detailed in Chapter Seven.

4.5.2.2 Delphi Survey Design and Process

The Delphi studies were fully anonymised designs, conducted in 3 successive questionnaire rounds, commencing with open questions in round 1 (analysed qualitatively) and then moving to quantitative analysis in subsequent rounds, using a 7-point Likert scale. All responses were collated, analysed and fed back as statistical measures of group responses with individual responses remaining anonymous. The level of consensus was defined as 70% of experts agreeing on item ratings. All items achieving consensus were put forward as themes for review and constant comparison in subsequent study phases, and for consideration as rateable attributes within the TRACAT tool. The data analysis processes are discussed in Chapter Five. The e-Delphi studies were conducted using the Qualtrics electronic online survey platform.

Participants were able to provide open feedback and freely express their experiences and perspectives on subjects, as participants did not know the identity of the other panel members. A key benefit of the Delphi technique is that it provides anonymity to respondents without domination from individuals, such as senior influential colleagues, which may lead to bias as participants submit to peer pressure within an open group. References to roles within individual textual responses were omitted, protecting both the participants' anonymity and preventing the influence of role seniority on consensus development. Participants consenting to the study received an invite and link to the online questionnaire, hosted in Qualtrics. In addition to guidance provided in participant information sheets, panellists received specific instructions on the Delphi process and the completion of each survey round. The questions and results for all the Delphi rounds are published on the EFACCT study website: www.efacct.com. Panel participant feedback was encouraged throughout

the study, which supported the concept of the Delphi as both a self-reflective technique and a collective decision-making process, whereby there is a move towards consensus or a conscious informed choice by participants to revise their opinion or personal philosophy, based on a wider perspective of peer group experiences. The Delphi design was developed in keeping with a Singerian inquiry approach where a Delphi study serves as a process for adding to 'substantive knowledge' but also adds to "participants' knowledge of themselves" in a group reflective process (Linstone & Turoff, 2002). The design supports reflection and retains the full sentiments and nuances of meaning of participants in sharing the broad and descriptive statements with the Delphi panel in multiple rounds. All panel members received individual feedback between rounds and had the option of giving additional free-text comments throughout the study.

4.5.3 The Questionnaire Studies

The purpose of the structured questionnaires (with free text addition) is to take the findings from the Delphi study and test this with a wider group of professionals and patients. The target sample size for the questionnaires ($n = 100$) was divided equally between professionals and patients. Questionnaire responses in turn led to the development of themes for discussion in the interview study. The results of the questionnaire round also provided additional data to inform the trial-rating tool.

4.5.4 Interview Studies

Interviews were conducted with cancer clinical research professionals and trial patients at a range of geographical locations across Scotland and England. Interviews were semi-structured but conducted in an informal, conversational style to build rapport with the participants in order to encourage revealment of lived, personal experiences and the contextualised perceptions and challenges in which they are situated. Time was spent at the initial greeting before commencing the interviews to place participants at their ease, ensure that they were familiar with the environment, the interviewer, and the purpose of the study, to reduce any potential stress or apprehension they may have.

4.5.4.1 Interview Design and Conduct

The design of the interviews was semi-structured with interview guides developed from the themes arising in the Delphi studies for each respective study arm, the research professionals or the cancer trial patient consensus studies (discussed in section 4.5.2). As the research progressed the interview conversations were further guided by emerging conceptual categories from questionnaire and earlier interview findings, and therefore

employing theoretical sampling, which is discussed in greater detail in Chapter Five. The interviewer took notes during the interview, which formed research memos for later reflection, but was concerned to ensure this activity did not interfere with the natural discussion and social interaction, maintaining eye contact throughout the interview. Edwards and Holland (2013, p.69) suggest that audio recording of interviews allows the qualitative researcher to 'focus on listening, probing and following up.' These are important interview techniques enabling the participant's voice to emerge through a more open and responsive researcher-participant engagement. Although there were a large number of interviews conducted during the research, all transcription was undertaken by the researcher conducting the interviews, as the combined knowledge of the participant, the interview interaction and the perceptual information in the form of transcribed data, all contribute to contextual understanding and form essential elements in the development of grounded theory. Participants were informed that interviews would be recorded but recordings would only be accessed by the interviewer for the purposes of transcription. Prior to commencing the recorded interview, time was taken to make participants feel comfortable, build a friendly rapport and put them at ease. The use of a discrete audio-recording device facilitated more natural conversations with participants, as it was possible to maintain face to face discussions, which can be inhibited if the interviewer is focussed on notetaking during the interview. Only one participant felt initially inhibited by the recording at the start. The interview was stopped, and further time taken to discuss the interview process, and ensure the participant was comfortable before proceeding. Time was taken to allow the participant time to relax. The reason for the presence of the recorder was discussed and highlighted that the recording would only be used by the researcher to help transcribe the discussion, and the option of not recording the session was offered. The interviewee was happy to proceed with the session being recorded, and after a few minutes they became fully relaxed and appeared to be no longer aware of the recording device. A confounding factor in this particular interview was that the participant and interviewer were known to each other, which may have meant that existing familiarity led to a certain sense of unease in relating personal experiences and perceptions. On reflection after the interview, thought was given to how best to approach conducting interviews with participants where there is an existing professional or personal relationship. Pre-existing associations should be considered in advance by the researcher, who should discuss this with the participant prior to commencing the interview, allowing both parties to be prepared and acknowledge their existing personal or professional relationship in relation to the process and content of the planned interview. The benefits of taking extra time to understand the characteristics and personality of the interviewee allowed the researcher to develop a deeper relationship with the participant and respond better to cues in their

discourse, which can elaborate their needs and concerns relative to the substantive area of inquiry. Maintaining a visual engagement with the participant during the interview also allows the researcher to better engage with visual expressions, enhancing the understanding of dialogue. A concern for establishing rapport and empathy with participants is aligned with a qualitatively focussed research approach. Showing respect for participants through attentive listening helps gain the trust of interview participants, which is an important element in achieving a reflexive and 'constructive research encounter' (Raheim et al, 2016, p5-6).

The semi-structured interviews were each approximately one hour in length and held in either a private room at a participating hospital site or at a cancer patient's home if this was more convenient and comfortable for the patient. Only one interview with a research professional was conducted in a public area, which was at their preference. All interviewees were provided with detailed participant information sheets prior to their agreement to take part. The aims of the study and their rights as participants were again discussed in person at the time of the interview and before signing written consent forms. They were also advised that they could stop the interview or not answer specific questions, if at any point they felt uncomfortable. The interview topic guides are shown in Appendix 2 and 3.

4.6 Data Processing and Software

The following sections detail the data types collated in conducting the research and how these were processed and managed either via software applications or analogue processes relative to their nature, study stage and characteristics.

4.6.1 Data Types, Recording and Transcription

Research data during the study included analogue reflexive journal notes, interview notes, card coding and participant consent forms, whilst digital data was collated in the form of audio recordings, surveys, questionnaires, interview transcriptions, memos, NVIVO and SPSS coded data, participant demographics and consents. Research portfolio trial performance and metrics as well as trial protocols and their recorded attributes were stored within the EDGE research management system. In accordance with the study's DMP, NHS and University policies and GDPR all source and metadata were stored in secure password protected databases or in locked cabinets, accessible only by the Chief Investigator. Principal Investigators managed site data in line with the DMP, DPA, GDPR and NHS policies and GCP guidance.

4.6.2 Software Used in Study

During the course of the research a wide range of software packages were utilised supporting data collection and management for both qualitative and quantitative data. The use of Computer Assisted Qualitative Data Analysis (CAQDAS) offers significant benefits in review, sorting, interrogation and integration of large in-depth sets of qualitative data. Through experimentation and optimisation of emerging technologies social researchers have the opportunity to build analytics strategies capable of handling large sets of data. Reflection and transparency in the use of software adds to a researcher's methodological armamentarium, providing further tools to justify, conduct, analyse and report their research (Silver and Lewins, 2014). Whilst Table 4.6 below is not a definitive list of software packages used during the course of the study, it shows the most commonly used and their role in different stages of the research. Standard Microsoft packages were also used throughout the study. Due to the large volume of interview transcripts some experimentation with Google Docs voice-to-text software was attempted, with varying degrees of success relative to the quality of the audio recording. The software struggled to manage colloquialisms and regional accents, so after a trial period of having to correct a high number of transcriptions, due to voice-to-text audio interpretation errors and limitations with managing punctuation and emphasis in interview transcription, a standard manual audio transcription was resumed using SO and MS Word.

Software Application / Platform	Study Stage	Description / Role
EDGE	All work packages: WP1 – Protocol/Database Reviews WP2 - TRACAT WP3 - Participant Studies WP4 - Meta-Aggregative Review	WP1 – Recording and reporting of protocol attributes WP2 - TRACAT – development of attribute tool to support trial management WP3 – Site data collection, reporting and management WP4 – Study searching for Meta-Aggregative Review
NVivo 12	WP3 – Participant Studies	Qualitative data management & analysis
SPSS	WP3 – Participant Studies	Quantitative Data management & analysis
Qualtrics	WP3 – Delphi & Questionnaire Studies	Design, hosting and management of online questionnaire study data
MAXQDA 2020 (VERBI Software 2019)	Data Analysis and Integration	Used for memoing, reflexive journal and integrating coding from multiple work packages
Microsoft Power BI	Delphi, questionnaire, and interview studies	Visualisation of data for reporting and interpretation

WordPress	All stages	Hosting of website www.efacct.com , promotion of study, repository for essential participant documents, data compliance statement and dissemination of research outcomes
ConceptDraw	Intermediate data collection stages	Used for concept illustration Presentation of research complexity Study dissemination at national conference
SoundOrganizer (Sony)	Interview studies	Audio file management and transcription software
Electronic portals	Literature Reviews	Data searching and collection via electronic journals and internet search engines
Bibliographic software	Literature Reviews & Thesis Write-Up	Literature data management
Social Media: Twitter, Facebook, LinkedIn	Study set up, interim and closure	Promotion and communication of research progress

Table 4.6 Software Packages

4.7 Chapter Summary

This chapter has detailed the rationale for the selection and application of mixed methods used within the study to address the research problems detailed in Chapter One, and the data collection procedures applied supporting the development of grounded theory. Further elements discussed are the approaches taken in the management of risk, data handling and ethical concerns, along with any challenges experienced en-route during study's substantial data generation phases. In respecting the principles of a mixed grounded theory methodology, the data collection, using initial purposive samples of research professionals and cancer patients, commenced with two classic e-Delphi. The outcome and emergent themes from these generative consensus studies then informed the design of semi-structured questionnaires and interviews and guided the nature of further data collection. The nation-wide studies involved a wide range of geographical locations, networks, scales of operations and trust sites in order to understand the common and unique factors determining operational efficiency within the NHS. The initial study design and methods were defined within the study protocol, but in progressing through the research stages the study evolved in response to emerging themes, data and researcher interaction with participants, context and operationalism (including practical elements of time and capacity). In Chapter Five, the data analysis, constant comparison, and integration procedures applied in developing the theoretical framework explicating cancer clinical research operational delivery, are discussed in detail.

Chapter Five: Data Analysis and Integration

“Different kinds of data give the analyst different views or vantage points from which to understand a category and to develop its properties; these different views we have called slices of data.” (Glaser and Strauss, 1967, p65).

5.1 Introduction

In the two preceding chapters the theoretical and methodological rationale for the research and selected methods were discussed. This chapter provides a detailed review of how the research data were managed and analysed throughout the study stages, leading to the development of the grounded theoretical framework interpreting cancer clinical trial delivery in the NHS. Commencing with an overview of approaches to data analysis in both grounded theory and mixed methods studies, the chapter then moves on to discuss how data from the different work packages were analysed, coded, and integrated. The data analysis and coding techniques relevant to the three data collection methods are initially discussed, before moving on to provide an in-depth explanation of the grounded theory stages of coding, constant comparison analysis and the subsequent development of the theoretical concepts. A discussion on the study’s approach to quality, rigour and credibility then leads into the chapter’s conclusion, which provides a summary of how the large volumes of data generated during the study, using mixed methods and mixed grounded theory, were systematically integrated to form a cohesive theoretical framework relevant to the nature and complexity of cancer clinical trial delivery and participation, from the perspectives of both clinical research professionals delivering them and the patients participating in them.

5.2 Analytic Processes and Study Stages

A key characteristic of grounded theory is its utility to inductively generate theoretical concepts that are ‘grounded’ within the collected research data. The process of conducting grounded theory is iterative, moving through cyclical stages of sampling and coding before reaching theoretical saturation and the authoring of a substantive theory or analytic model which is born out of the data and sensitive to the situation under study. Throughout the analytic process the data were evaluated with consideration for the values and meaning expressed by participants and the relationship of perspectives and concerns with respect to their contextual origin. In constructing the theory, the socio-cultural interactions within healthcare contexts and the complexities of relationships, conditions and their consequences were central to the process, with communication and collaboration emerging as core constructs. Adopting the analytic device of the conditional, consequential matrix

shown in Fig. 5.1, a diagrammatic tool offered by Corbin and Strauss (2015, p163), the nature and layers of complexities, relationships and interactions across the multiple contexts involved in cancer research delivery were analysed in detail. The modelling of these conditions and relationships and their consequences are discussed in the results chapters, with visual models representing the relational concepts and theoretical constructs for both cancer trial participants and research professionals, and further levels of theoretical construction described and visualised in Chapter Eight.

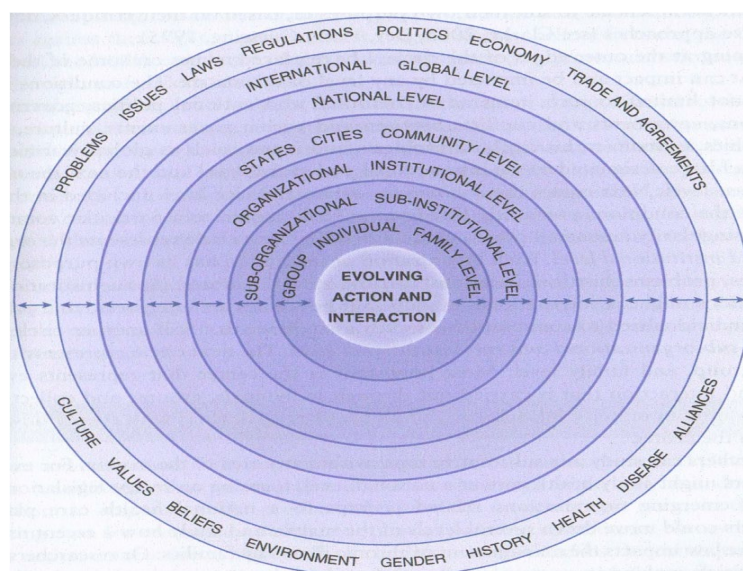


Fig 5.1. The Conditional/Consequential Matrix (Corbin & Strauss, 2015)

Table 25.1 illustrations of basic designs of mixed grounded theory studies found in the literature*

<i>Data collection</i>	<i>MMR basic designs</i>	<i>MGT basic designs</i>	<i>Description</i>	<i>Stance</i>	<i>Qualitative and quantitative data analyzed...</i>	<i>Constant comparative analysis performed...</i>	<i>Illustrations</i>
Concurrent/ Parallel	QUAL + QUAN	QUAL GT + QUAN	Qualitative GT study and quantitative non-GT study conducted in parallel	Exploratory QUAL and confirmatory QUAN	Separately	Only during QUAL phase with QUAL data	Kaplan & Duchon (1988)
		(QUAL + QUAN) GT	GT study involving qualitative and quantitative data and methods	Exploratory QUAL and QUAN	Together	All through the research process	Walsh (2014)
Sequential	QUAL → QUAN Exploratory sequential	QUAL GT → QUAN GT	Qualitative GT study followed by a quantitative GT study	Exploratory QUAL followed by exploratory QUAN	Together	All through the research process	Ågerfalk & Fitzgerald (2008)
		QUAL GT → QUAN	Qualitative GT study followed by a non-GT quantitative study	Exploratory QUAL followed by confirmatory QUAN	Separately	Only during QUAL phase with QUAL data	Spears & Barki (2010)
	QUAN → QUAL Explanatory sequential	QUAN GT → QUAL GT	Quantitative GT study followed by a qualitative GT study	Exploratory QUAN followed by exploratory QUAL	Together	All through the research process	Renaud et al., 2016
		QUAN → QUAL GT	Non-GT quantitative study followed by a qualitative GT study	Descriptive QUAN followed by exploratory QUAL	Separately	Only during QUAL phase	Forrest et al. (2013)

*Notation: QUAL denotes qualitative data collection/analysis, and QUAN denotes quantitative data collection/analysis. An arrow (→) denotes a sequential design, and a plus sign (+) denotes a concurrent/parallel design. The components of the concurrent/parallel design are often placed in parentheses, e.g., (QUAL+QUAN). Note that you can construct more complex designs through the joint use of parentheses and arrows, e.g., (QUAL+QUAN)→QUAN.

Fig 5.2 Mixed Grounded Theory Designs from Johnson and Walsh (2019).

Within this study a concurrent qualitative and quantitative exploratory approach was adopted with data triangulated and compared as part of the analytic process, as illustrated in Fig. 5.2. This approach has synergy with a concurrent transformative strategy (Terrel, 2012), allowing perspectives from multiple workstreams to be compared and integrated into theoretical concepts.

The data collection for the research involved three studies involving two participant types:

1. *Research Professionals* – NHS healthcare professionals currently working in the delivery of cancer clinical trials at participating sites, or within a Local Clinical Research Network (LCRN).
2. *Cancer Clinical Trial Participants* – NHS patients who had previously taken part or are currently enrolled on a clinical trial at a participating site.

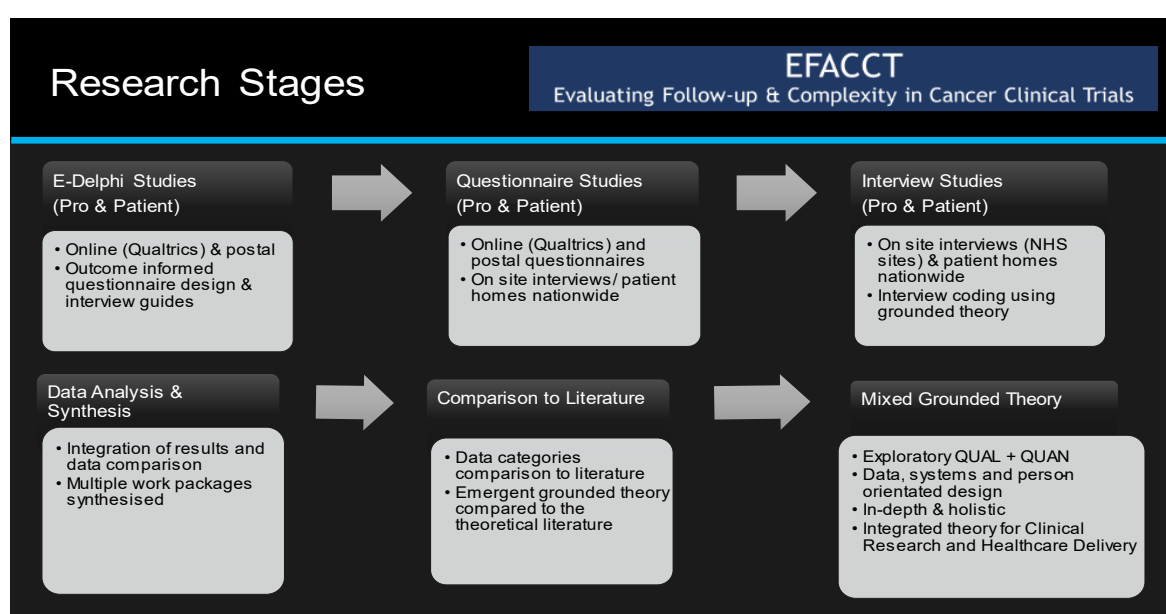


Fig 5.3 EFACCT Research Stages

Each stage of the data collection involved representatives from each of these groups, commencing initially with the Research Professional Delphi study and followed shortly by the Cancer Clinical Trial Patient Delphi study, once the initial open round with the professionals had been analysed. The results from the each of the respective Delphi studies then informed the content and nature of the subsequent questionnaire and interview stages, as shown in Fig 5.3. Outcomes from the initial Delphi and questionnaire studies later provided confirmatory data for the grounded theory developed during the interview analytic stages. All data were compared and contrasted as part of the overall integration process, supporting a systematic and rigorous formation of the core conceptual categories and their related conditions relating to all work streams. Data analysis included descriptive statistics,

thematic content analysis, constant comparison methods and the use of data visualisation for coding, comparison, and theory development.

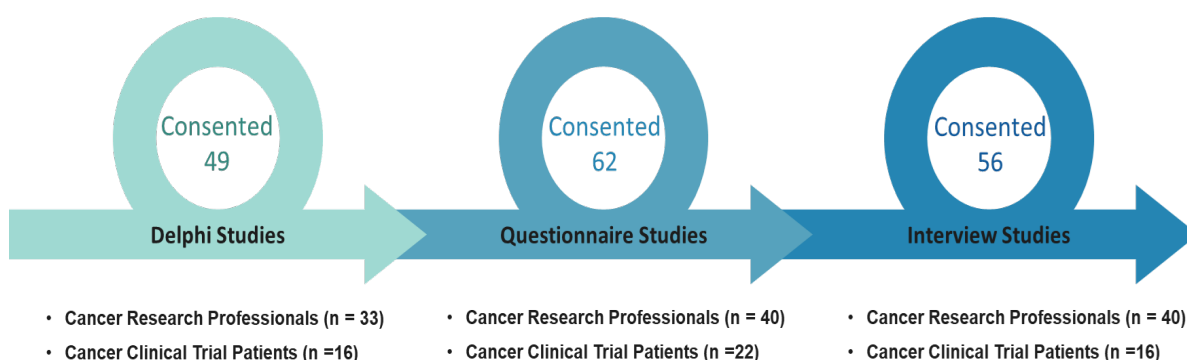


Fig. 5.4 Consents by Stage and Participant Type

Consents for each stage are shown in Appendix 7 (cancer patients) and Appendix 8 (research professionals). Data analysis was a cyclical process with emerging data from each study stage informing further data collection and prompting new or adapted questions in the interviews, both in relation to the responses of participants from the Delphi and questionnaire studies but also in relation to the developing theories and concepts across and between participants and sites. Emerging theoretical ideas were captured in field memos during the on-site data collection and also in further data analysis stages, with theoretical memos recorded and analysed in MAXQDA 2020 (VERBI Software 2019). The role of memoing, field notes and reflexivity are discussed in section 5.3.7.

5.2.1 Delphi Studies Analysis

The Delphi studies involved both qualitative and quantitative data analysis methods. Analysis methods included content analysis, descriptive statistics, and statistical summaries. Qualitative content analysis applied to the opening round, where statements were coded and organised into themes. Subsequent rounds used qualitative analysis and provided group responses alongside respondents' original scores. Descriptive statistics and statistical summaries used the median response as a measure of central tendency and the Inter-Quartile Range (IQR) for each topic. The IQR showed the clustering or scattering of the responses. Analysis of Likert scale responses performed in SPSS V.22.0. In the Research Professional Delphi study, a framework approach was used to analyse responses and create the initial complexity categories, later used to develop an additional category in the second round (question 7 – see Appendix 9). A second stage of hand coding to validate the initial analysis was performed. Quantitative analysis of the second and third round Likert-type scale responses was performed using SPSS V.22.0. Summary statistics,

reported to panellists, described frequency of responses to statements (percentage level) and the median (measure of central tendency). In addition, the IQR was used as a measure of dispersion in analysing stability of responses and move towards consensus in order to decide on the final survey iteration. Data collection and analysis from the Research Professional Delphi were used to inform trial ratings and create attributes for the development of a planned trial rating and complexity assessment tool (TRACAT).

5.2.2 Questionnaire Studies Analysis

The questionnaire studies were analysed using the Qualtrics system analytics software, SPSS and then qualitative coding was conducted using NVivo (version 12). Qualitative content analysis was conducted and then further hand coding, mind-mapping and modelling using the MAXQDA Creative Coding functionality.

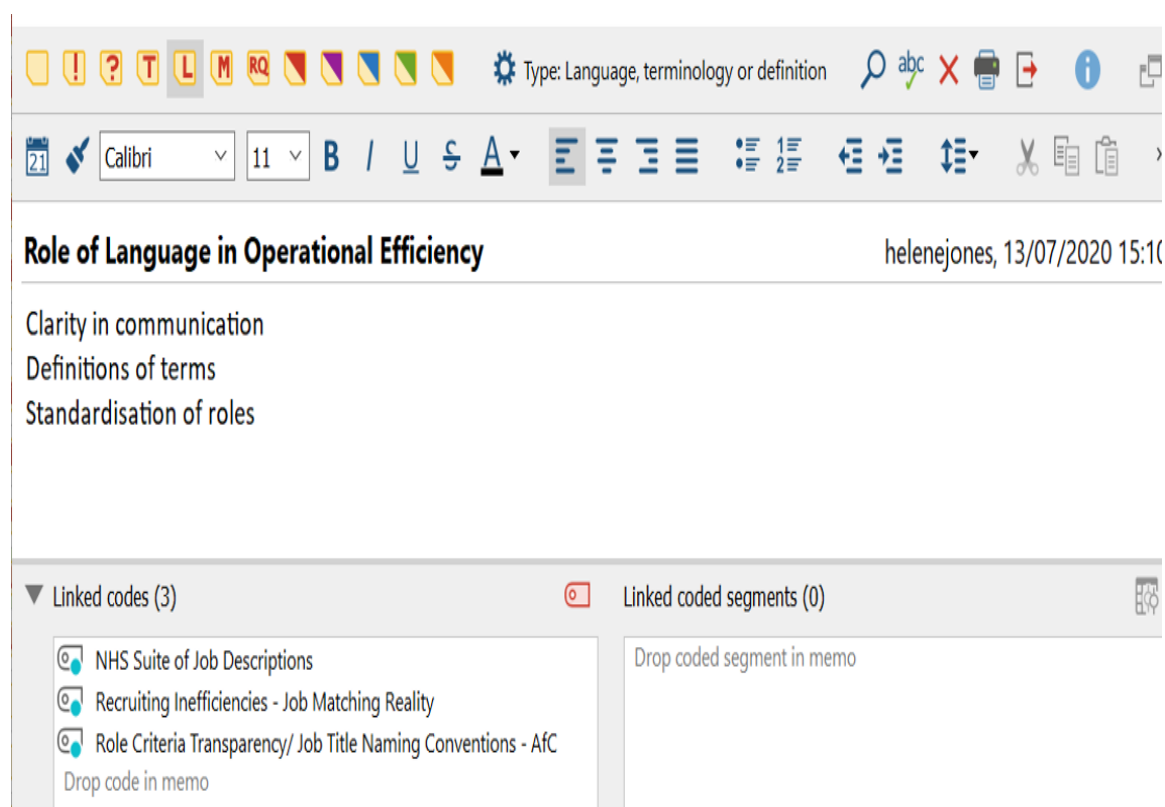


Fig 5.5 In-document memo example

5.2.3 Interview Studies Analysis

Interviews were conducted in the later stages of the data collection and formed the most intensive and in-depth stages of both the data collection and the analysis. Grounded Theory data analysis techniques were applied to the interview data, following completion of data collection at all sites. Due to the nature of accessing sites and participant availability it was

not possible to conduct coding of initial data and then direct sampling based on initial data sets. Further discussion relating to the constraints and approach to the collection of data at sites is discussed in Chapter Nine (section 9.3). Interview guides were provided to participants, the design of which is described in Chapter Four, but the use of theoretical sampling in the study led to evolving themes being discussed with participants as the research interviews progressed. See Appendix 3 for an examples of the interview guides for the research professional participants. The use of memoing and reflexive notes, captured during data collection at different sites, informed further theoretical sampling. Memos created immediately following participant interviews captured the immediacy of analytic thoughts as they arose, which were compared and developed during the detailed line by line coding of transcripts.

Interviews were recorded using a digital recording device and the resultant data transcribed in Sony SoundOrganiser. Initial interview coding commenced using NVivo (version 12) but later transferred to MAXQDA 2020 (VERBI Software 2019) as the software felt more intuitive for qualitative analysis and fitted well with the cyclical nature of grounded theory and constant comparison, as well as supporting data integration (Kuckart & Rädiker, 2019). The software facilitated the process of capturing theoretical memos and the recording of properties and category dimensions as they emerged during the coding process. This allowed analytic coding and data comparison activity to flow without interruption, speeding up the management, analysis and coding of a large set of qualitative data. The transcribed interview data were closely reviewed and analysed via the following steps:

- initial open codes developed
- initial codes analysed and developed into a coding system
- categories established using the MAXQDA Creative Coding function
- theory construction utilised the MAXMaps functionality
- emergent concepts and relationships were compared to wider empirical and theoretical data
- joint display models created of integrated qualitative and quantitative data

The coding process, which is discussed in detail in section 5.3. included the use of line-by-line coding, in-vivo codes, and gerunds. Forty research professionals from eleven NHS research organisations participated in the semi-structured interviews. The initial open coding generated 12,567 initial open codes and 760 memos. Sixteen cancer clinical trial participant interviews created 3122 initial open codes and 1146 memos.

5.3 Grounded Theory and Constant Comparative Analysis

Data analysis in a grounded theory study involves the use of the constant comparison method developed by Glaser and Strauss in their 1967 study examining patients' awareness of their terminal illness. The constant comparative method is an analytic process used within grounded theory studies, which commences at the initial coding stage and then continues throughout the study, with the continual comparison and contrasting of the emerging data, in and between codes, categories and themes. Glaser and Strauss (1967) stated, "using the constant comparative method makes probable the achievement of a complex theory that corresponds closely to the data, since the constant comparisons force the analyst to consider much diversity in the data." They further elaborate on the method in defining four key stages summarised as follows:

- 1) **Comparison of incidents within the data applicable to categories** – This initial stage is an emergent process whereby the analyst begins by coding their data, with incidents forming as many categories as possible, or data is coded according to existing categories. Coding of incidents involves the comparison of previously coded incidents, and the comparison of groups and the properties, dimensions, and characteristics of categories. The process of memoing and use of field notes in developing categories contributes to the developing of theory.
- 2) **Integration of categories and their inherent properties** – The next stage sees the start of a synthesising process whereby the units of comparison move from incident with incident to properties of coded categories. This stage sees the development of the theoretical categories as different categories and properties start to integrate and relationships between these begin to appear. The emergence of themes within the data guides theoretical sampling to further develop conceptual themes.
- 3) **Delimiting of the theory** – At this stage, the analyst begins to refine the developing theory through the modification or reduction of categories, moving towards the core categories relevant to the research field and collated field data. Theory therefore moves to an advanced stage of theoretical coding, which delimits the terminology and further integrates categories, refines the scope and formal level of the theoretical concepts and moves towards theoretical saturation.
- 4) **Writing of the theory** – The final stage in the process is bringing together all data and developed concepts into a theoretical, analytic framework forming a systematically developed, substantive theory for the research. Memos perform a key role in integrating and articulating the theory, forming narrative signposts throughout the research journey.

The application of these four stages of the constant comparative analysis method is illustrated in Fig. 5. 6 and further discussed in section 5.5, which elaborated on the detailed coding stages that progressed towards the emergence of the grounded theory in this research.



Fig 5.6 Constant Comparative Analysis Process

The constant comparison analytic process of the study data involved; analysis of incidents from the Delphi, questionnaire and interview studies, and the continual evaluation of incidents in the literature data, the integration of categories emerging from these incidents, followed by delimiting and writing of the theory, with the inclusion of extensive reflection, memo-writing and theoretical diagramming.

5.3.1 The Grounded Theory Coding Process

In a study using grounded theory the coding process is a multi-phased analytic activity. Codes are developed from data generated from qualitative, quantitative or mixed data, following the iterative framework, as described in Chapter Four. The grounded theory analytic process for this study used coding terms adopted by Birks and Mills (2015), and involved *initial* (first cycle), *intermediate* (second cycle) and *advanced* coding stages (theoretical, conceptual). In the following section these coding stages, which are illustrated in Fig 5.7. are discussed in detail and the systematic study of empirical data, its conditions and linkages described along with the conceptualisation of these to form the study's integrated grounded theory.

Grounded Theory Coding Stages

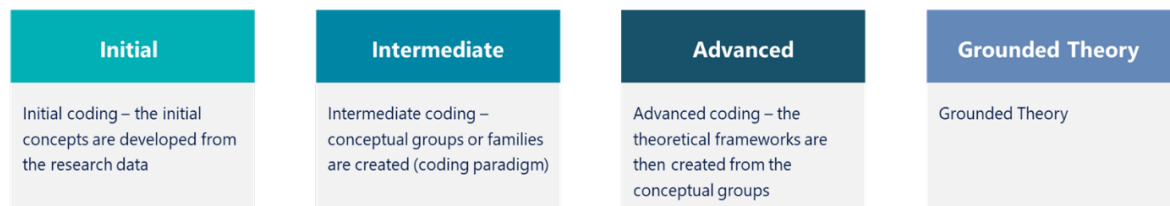


Fig 5.7. Grounded Theory Coding Stages

5.3.2 Initial Coding (Open Coding)

The first coding stage, known as initial or open coding, is where the first collected data sets are examined to identify the inherent characteristics or phenomena. In this initial coding stage the data is closely analysed, with codes (or labels) assigned to specific segments or lines of data, forming an analytic DNA for the study. Coding in grounded theory allows the researcher to move from data collection to the development of an emergent theory reflective of participants meanings, voices, and experiences. Grounded theory codes are described by Charmaz (2014, p113) as ‘transitional objects’ which ‘connect fragments of data with the analytic abstraction we accord to them’. The following coding techniques were applied to the interview transcripts: line-by-line coding, in vivo codes, and gerunds. The coding examples shown in Tables 5.1 and 5.2 highlight examples of the application of these initial coding techniques to the EFACCT study interview participant data.

Line by line coding from the in-depth interviews supported verification and relevance of the emerging concepts. Adopting a detailed process of line-by-line coding is an interactive analytic process, which directly engages with the concerns and realities of participants’ everyday experiences, the nuances and ‘compelling and consequential scenes and actions’ as described by Charmaz (2014, p125).

In Vivo codes capture the voices and experiences of participants, remaining close to the very essence and nature of the research context, by using the exact words or phrases found within the data’s texts and transcripts. The use of participants’ own vernacular in evaluation research helps retain the grounded nature of the study, a method which attunes the researcher to the participant’s language, perspectives, and world views (Saldaña, 2016, p73).

Gerund coding, also known as process or action coding is an analytic method suited to capturing the nature of processes and actions relating to the research field and collected data. Grounded theory is concerned with examining the nature of phenomena and relational processes, interactions, conditions, and consequences. Three core elements of

'conditions', 'actions-interactions', and 'consequences or outcomes' were central to the coding paradigm promoted by Corbin and Strauss (2015). As the interview transcripts were analysed any sense of action within the data is captured by using gerunds, a noun formed from a verb using the suffix 'ing' to form an action code. In conducting operational evaluation, the use of gerund coding is key to understanding social interactions, networks, activities and procedures and consequences, which in turn is relevant in the development of a grounded theory from empirical data.

Coding Techniques: Patient Study Examples		
Coding Technique	EFACCT CODE	EFACCT Interview Extract
Line-by-line	'Lacking Awareness of Terminality'	"She didn't know that she was terminally ill. She didn't know what the consequences could be if she went into standard care, because again she had the same rare type that I did. She didn't know any of this, so she would of, I think she would have benefited hugely from a patient support group, because it was a bombshell when she found out obviously because she found out in the worst possible way". (Participant 002002)
In Vivo	"SCANXIETY"	"It actually makes me ill scanxiety. That's what I call it my scanxiety." (Participant 002002) "when you've got scanxiety, you think what's going on." (Participant 034002)
Gerund	'Struggling to breathe' 'Preparing for the worst'	"And I was starting to struggle to breathe." (Participant 005002) "well we have to prepare erm for the worst" (Participant 024004)

Table 5.1 Initial Patient Coding Examples

Coding Techniques: Professionals Study Examples		
Coding Technique	EFACCT CODE	EFACCT Interview Extract
Line-by-line	'Approaching the limits of capability'	'I personally think that we're getting close to the edge of what we can do. Err sometimes the resource is time. Sometimes the resource is the number of staff erm. It comes and goes but yes, I do think there's days that you're thinking 'Oh, we're kind of, we're close to the edge of what we can do.' (Participant 002110)
In Vivo	"Holding your nerve"	'There's a wee bit more work to do because, erm if with some of the immunotherapies erm there is this issue with immune flair. Especially early on you may see a slight increase in the tumour size, not with everybody but with some folk, you recognise that, say their immune complex is perhaps causing a degree of swelling so you need to hold your nerve.' (Participant 002110)
	"Sexy specialities"	'whereas in a speciality like mine cardiac, because it's like an ever advancing speciality, it's quite a sexy speciality if you think, there's always something new happening, always new techniques, lot of technological advances...' (Participant 050102)
Gerund	'Linking professionals'	'I'm going to link you up to that nurse, I'm going to link you up, that person needs to talk to you.' (Participant 024101)

Table 5.2 Initial Research Professional Coding Examples

5.3.3 Developing Categories and Theoretical Sampling

In the initial interview stages the questions were guided by the interview guides, developed as an outcome of the Delphi studies, but were responsive to participants' dialogue of broader subjects, and as the study progressed the interview questions included emergent themes identified in previous interviews, thereby providing direction in the research, a feature of theoretical sampling. As participants imparted their experiences, perceptions and

issues relating to cancer clinical trials, these phenomena were identified, through initial coding, which were assigned conceptual codes. As more research data is collected and analysed the coding becomes more focused where the initial coding and concepts are compared with new data. This intermediate phase develops a higher level of conceptual categories, where broader slices of data are compared and contrasted. Theoretical sampling follows on from the initial data analysis and assists the researcher in determining where to steer their further data collection, in response to developing categories. As the properties and dimensions of the emerging categories develop, the researcher moves to the theoretical level of conceptualisation, forming hypotheses and integration of data into the theoretical framework for the study. The sampling frame for the study and theoretical underpinning are described in Chapters Three and Four. Theoretical sampling supports the development of theory by the researcher through their identification of nascent themes within their data and their subsequent actions in data collection and analysis using constant comparison of initial coded incidents and categories. The process of theoretical sampling was supported by the use of field notes and analytic memos.

5.3.4 Intermediate Coding (Focused Coding)

The intermediate stage of coding, also known as selective, axial or focused coding, is where the conceptual groups or constructs are developed. The focus here was on emergent themes and selective sorting and categorisation of the data into concepts. The data sorting process moves the data from its detailed, descriptive status further along the coding paradigm to an intermediate level of conceptualisation.

As this selective coding stage progresses and new data are compared and contrasted the conceptual groups move towards the advanced coding stages to develop theoretical frameworks from the grounded data. The process of intermediate coding refines the developed categories, analysing data to determine shared or varying properties across concepts. The central concerns evidenced within the data begin to emerge as core categories. Further data collection and coding, guided by theoretical sampling and constant comparison, will verify developed core concepts and their sub-categories. Where new data analysis does not generate any new themes or concepts, and the identified concepts sufficient fit and explain the data, theoretical saturation is reached.

5.3.5 Advanced Coding (Theoretical Coding)

The advanced or theoretical coding stage involves the researcher is a synthesising process, requiring theoretical sensitivity, where they reform the coded data extracts and categories, to form an explanatory conceptualised whole, a grounded theoretical framework.

5.3.6 Theoretical Sufficiency

In order to support the ability to theorise, the research strategy involved wide reading across multiple disciplines and the social science literature. As part of the research approach and to develop theoretical sensitivity, a feature of Grounded Theory, a meta-theory database was developed, which was maintained throughout the data collection and analysis, forming part of the memoing process.

5.3.6.1 Theoretical Sensitivity

To avoid drawing early conclusions about the data theoretical conceptualisation needs to be an extended, reflexive process, with sense-checking of developing thoughts by returning to the source data over a period of time, re-visiting the theoretical literature and where necessary re-cutting the 'slices of data'. The development of a grounded theory is a time-consuming and intensive endeavour, which can at moments during the analytical journey seem overwhelming. Over time and through extensive emersion in the process of coding, memoing and comparison of datum to datum, theoretical sensitivity develops. In this study, the connections within the empirical data emerged at a late stage, following comprehensive analysis and comparison of coded extracts and theoretical memos, collected, analysed, and reviewed over an extended period of time.

5.3.6.2 Theoretical Saturation

Glaser and Strauss (1967, p62) detailed the criteria for theoretical saturation as 'a combination of the empirical limits of the data, the integration and density of the theory, and the analyst's theoretical sensitivity'. Due to the nature of study approval processes within healthcare research, a truly emergent theoretical sampling approach was not entirely practical, as the study data collection plan and research site approvals have to be approved in advance, by university and NHS ethics committees and the Health Research Authority (HRA). However, the study design and site recruitment approach described in Chapter Four, allowed for the opportunity to apply the principles of theoretical sampling, albeit from participating sites which had been pre-approved.

The nature of gaining ethics and HRA approval for the conduct of research at NHS sites poses a challenge for the use of theoretical sampling in grounded theory, as sites and timeframes for carrying out the research require pre-approval according to a scheduled plan and set timeframe for data collection. This limited my ability to adhere in totality to Glaser and Strauss's (1967) criteria for the generation of theory through joint data collection, coding and analysis and the use of constant comparison through selection of new comparative groups in response to the emerging theory. In this study the breadth and diversity allowed by the multiple work packages permitted the application of the constant comparative method from all collected data, and the depth of the data collected. Glaser and Strauss (1967) acknowledge the challenges faced in submitting proposals for grounded theory studies to review boards, offering the suggestion that, 'theoretical sampling can be done with previously collected research data, as in secondary analysis, but this effort requires a large mass of data to draw on in order to develop a theory of some density of categories and properties.' Revising an initial plan to conduct a systematic review, and alternatively conducting the three stage literature review supported by literature mind-mapping models, in the later stages of the study, was considered a further solution supporting theoretical sampling.

5.3.7 Memoing, Field Notes and Reflexivity

Memoing, field notes and reflexivity are core features of the grounded theory process, and are activities performing key analytical roles in the development of the theoretical categories and in defining the overall conceptual framework. The memoing process is also a tool that can be used to record your personal impressions in relation to elements or themes arising throughout the data collection and analysis stages.

5.3.7.1 Memoing and Memo Sorting

Memoing provides a fluid process for capturing conceptual thoughts whilst in the interactive stages of coding, without interrupting the flow of moving through the data. During the data collection stages memos were captured within field notebooks, which were then later recorded within MAXQDA and NVivo, during data coding sessions. By using memos within the coding software your emergent thoughts can be captured in-flight which you can then return to later, for comparison with other incidents within the current or previous data sets. As the research progressed earlier memos were reviewed and compared in light of the more recent data collected, to understand their similarities, differences, or degrees of relationship. Theoretical memos were captured as the coding developed, recording the evolving conceptualisation of the research data.

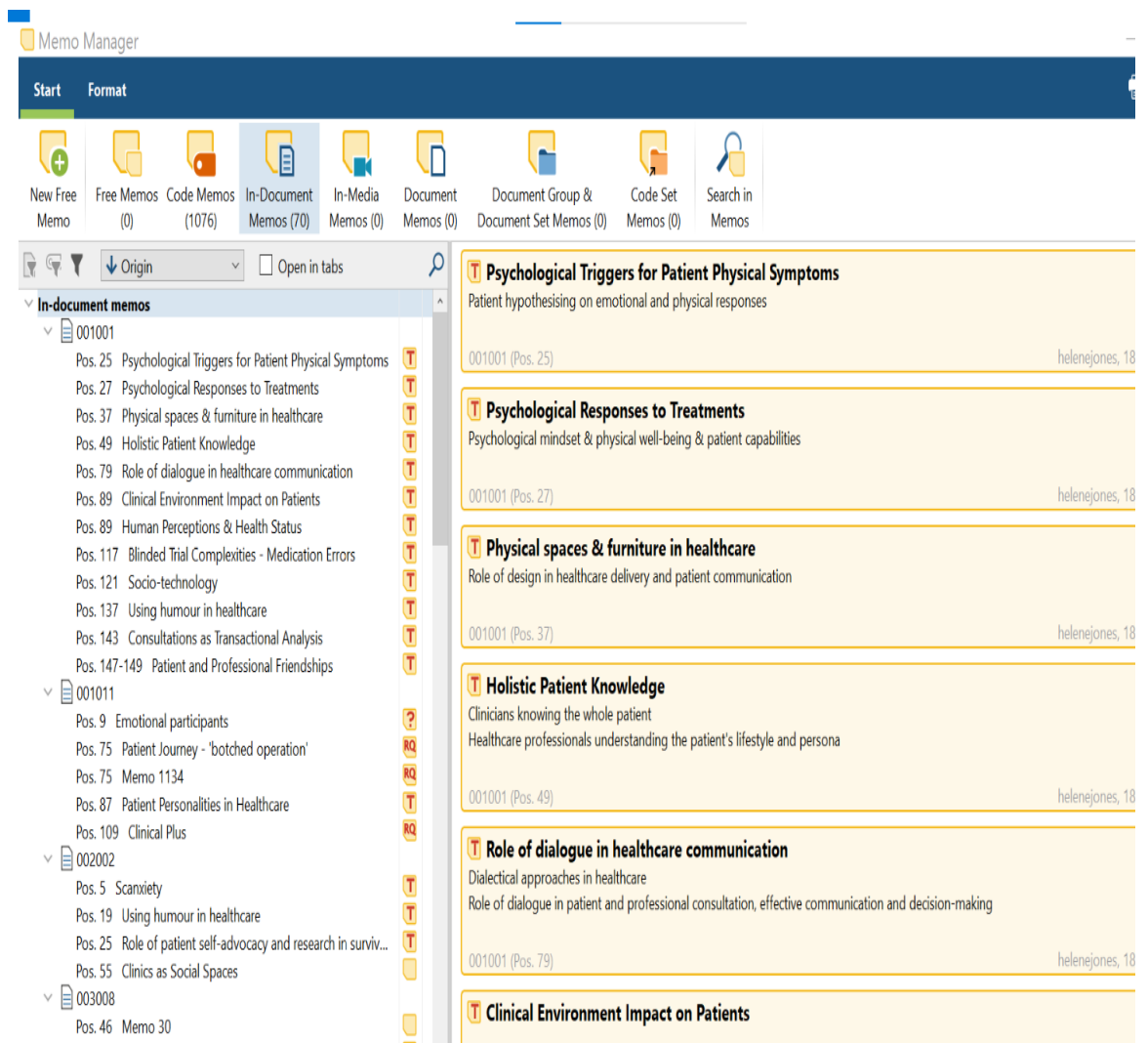


Fig 5.8 MAXQDA In-Document Memos (Patient Interviews)

The sorting of memos generated in the initial coding stages supported integration of the data and its emerging categories into more abstract theoretical concepts, as well as identifying the relationships between properties. A number of methods were used to sort categories and theoretical memos, which were adopted to optimise the potential for the realisation and development of themes and their properties. Such methods included card coding, blackboard and whiteboard modelling, diagramming and visual modelling, and the use of a range of CADQAS tools, which are discussed in greater depth in the following sections. Memos captured within MAXQDA provide both an audit trail of the development of thoughts and concepts as the analysis proceeds, and provides the functionality to sort, visualise and integrate concepts and their categories. For the sorting and categorising of memos, labels can be attached such as T for a theory or concept, RQ for a research quote, M for methodology or as per the example below (Fig. 5.8) L was assigned as a label in relation to the role of language, which later linked with the concept of the sense of coherence and its sub-domains of comprehensibility, manageability, and meaningfulness.

5.3.7.2 Field Notes

Field notes were recorded following site visits and during participant interviews. Whilst the researcher did take notes during the interviews, these were minimised in order to engage more fully with participants and to keep the conversation and interaction more fluid and natural. Notebooks were kept for each study site and following completion of interviews at the site any conceptual thoughts or key concerns that arose on the day were captured, retaining the immediacy of thoughts and ideas. The notebooks were revisited throughout the data analysis and coding stages, with interview transcripts compared to interview notes and spontaneous memos recorded soon after the meetings with the participants. In Fig 5.9 an example of field notes taken immediately following a site visit is shown, with concepts captured relating to **workplace cultures** and bracketed ideas relating to **fear in the workplace** and consideration of a link between **fear and lack of confidence**. The field notes and the initial conceptual memoing in the example capture observations from the field, raise questions about these field observations and begin to form early conceptual categories which are specific to the recent data collection activity, and theorise about connections and consequences. Within this example the constructs of tension and understanding (associated with a sense of cohesion) are captured within the data. The importance of these early field memos, and their value in validating theory is discussed by Glaser and Strauss (1967, p108) who state:

'The generation of theory requires that the analyst take apart the story within his data. Therefore, when he rearranges his memos and field notes for writing up his theory, he sufficiently "fractures" his story at the same time that he saves apt illustrations for each idea.'

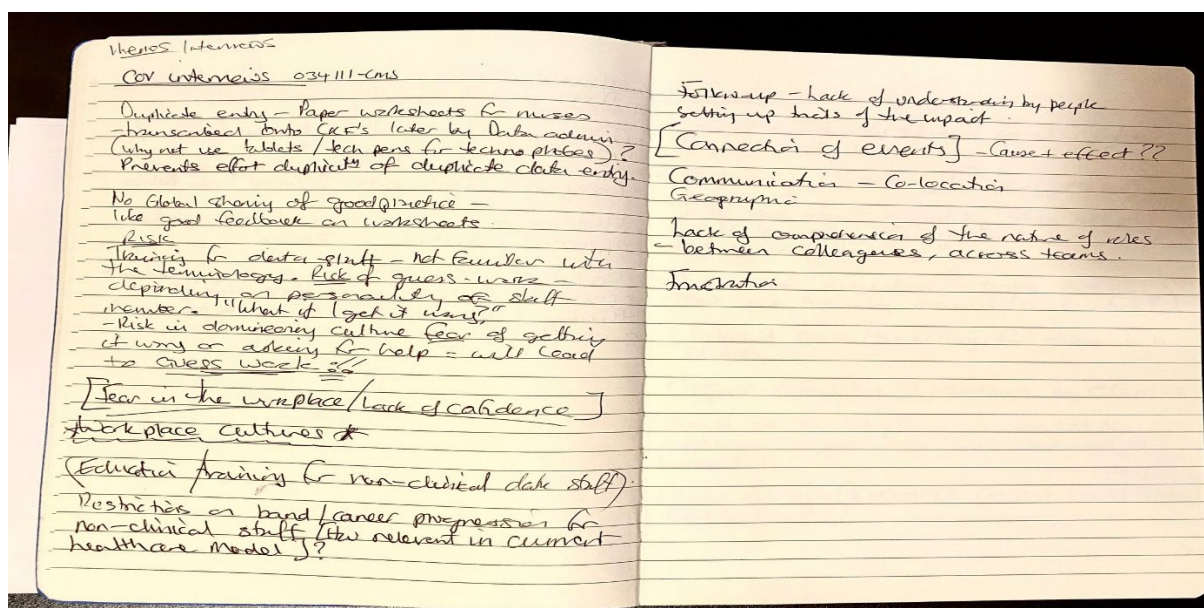


Fig. 5.9 Field notes with early memos

5.3.7.3 Reflexivity

Memoing and taking field notes form part of the researcher's reflexivity. Reflexive memos and notes were collated throughout the research, recording any personal observations and perspectives relating to the emergent data and conceptual themes. Interview notes and reflexive memos (captured within MAXQDA) formed part of the research evaluation.

Gobbledygook Board

As part of the reflexive process during the study a large chalkboard was installed for reflection at home on core concepts that emerged throughout the research. This board parochially named the Gobbledygook Board allowed ideas to be considered over a lengthy period of time, and to be considered in a non-study environment, allowing a longer and deeper reflection on the relationships between concepts and their value in remaining on the board, as retaining their worthiness as contributing to the whole picture.

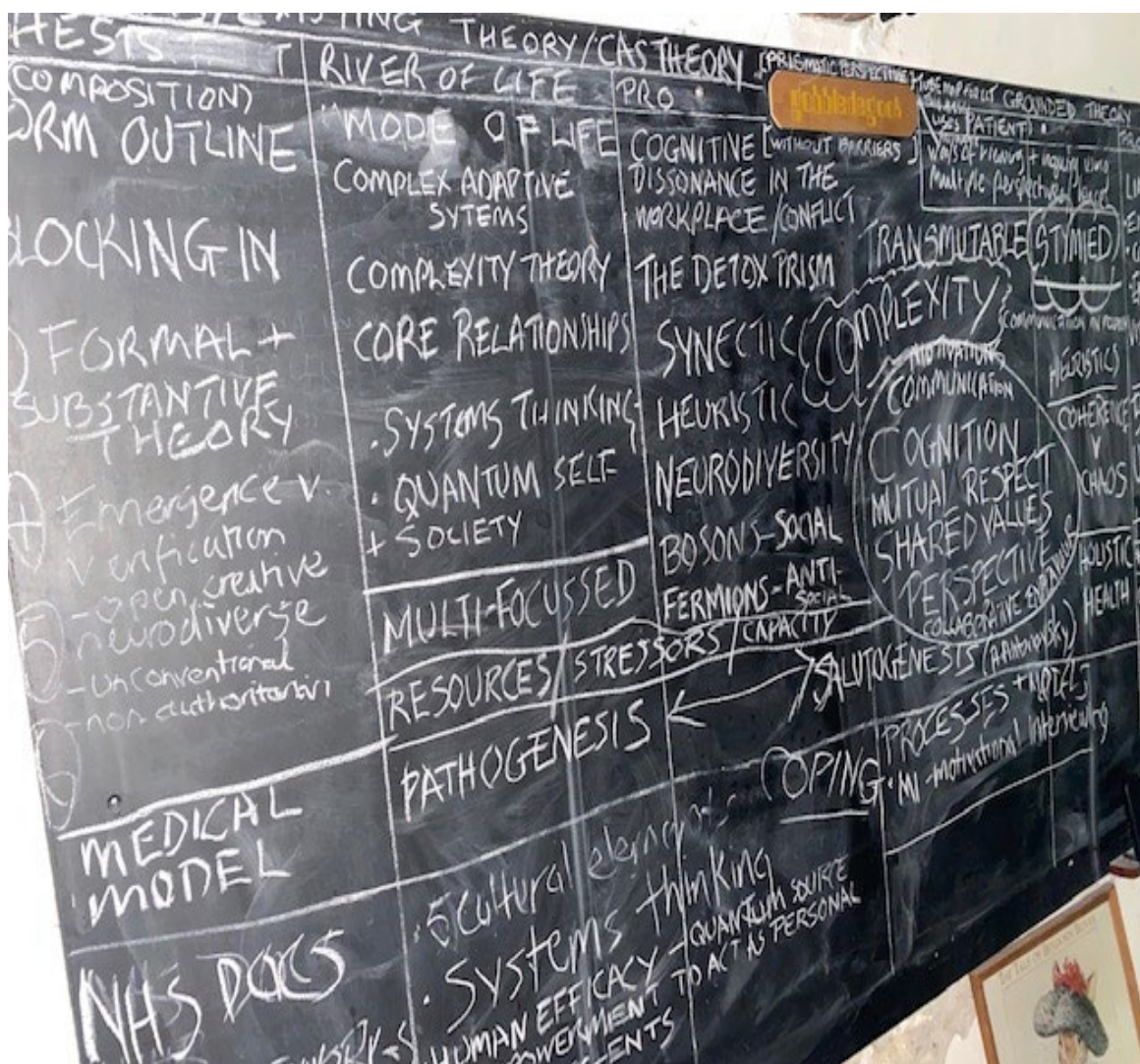


Fig. 5.10 Gobbledygook Reflexive Blackboard (View 1)

The Gobbledygook blackboard was used as a heuristic device as part of the analytic process to assist in the development of theory, by reviewing conceptual themes and the relationships between them. Kelle (2007), suggests that heuristic categories ‘play the role of a theoretical axis or a skeleton to which the flesh of empirically contentful information from the research domain is added’.

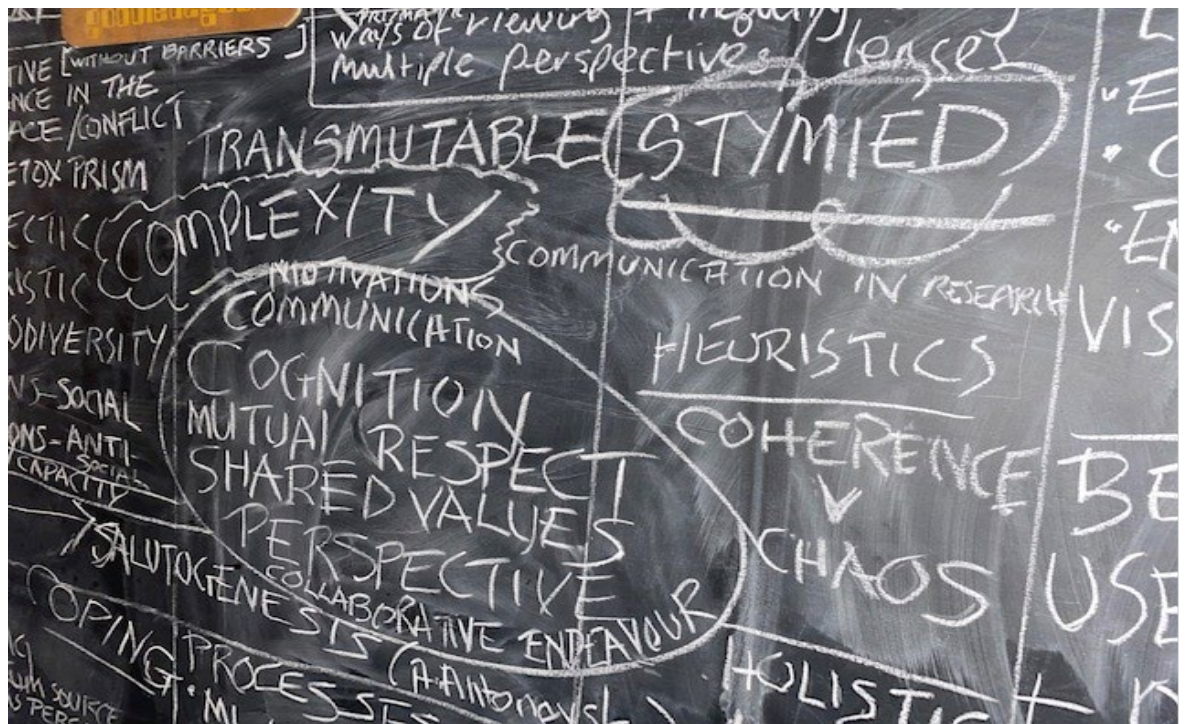


Fig. 5.11 Gobbledygook Reflexive Blackboard (View 2)

Mind Mapping and Visual Modelling

As the volume of data and conceptual categories grew the process of reflexive thinking and theorising was expanded to involve mind mapping and visual modelling (via software and note booking methods), allowing reflection during desk work and also extemporaneously. Engagement with the conceptual data becomes a very personal and all-encompassing process, with theoretical insights occurring at any point of the day. Carrying mind mapping workbooks at all times, allowed for the capturing of these serendipitous ideas as they occurred. This supports the constant comparison method, reflexive thinking, deep-thought and more personally is aligned with my analytical thought processes as a ‘visual thinker’. Mind mapping and visual modelling support the linking of concepts and making connections between data slices, incidents and theoretical constructs. Kachel and Jennings (2020) state that visualisation representations of emergent themes and concepts enables them to ‘see’ their theory. As a way of keeping track of relevant concepts from the literature the use of visual modelling and mind mapping was extended to the analysis of research papers and substantive texts, which were then compared to other coding models. The literature visual modelling and mapping was by hand and using computer assisted software.

5.4 Use of CADQAS software in Data Analysis

The use of computer assisted qualitative data software (CADQAS) in data analysis supports the research process, especially where data is voluminous (and drawn from multiple work streams and data types). A range of software packages were used throughout the study, with NVIVO and SPSS supporting the Delphi and Questionnaire study analytic processes, with MAXQDA adopted in the interview data analysis, and subsequent grounded theory development. Silver and Lewins (2014) suggest that the use of software supports transparency in the analytic process. Within this study the ability to draw upon the benefits of technology supported the process of developing higher levels of abstraction and conceptual analysis, whilst retaining the ability to drill down into the underlying source data, providing an audit trail of the process. During the course of the study, a number of experiments were conducted in the process of data coding, from manual card coding processes to the testing of different software packages. Ultimately, for the stages of grounded theory development MAXQDA emerged as the most responsive, creative, and intuitive tool to purposefully interact with the data, particularly through the use of diagramming and creative coding. Timmermans and Tavory (2012) describe theory construction as a pragmatic process of “puzzling out” and problem solving, a process facilitated by creating concept maps and through using software to identify complex connections and relationships within the data.

5.4.1 Creative Coding and Theory Construction in MAXQDA

Following completion of all interview transcription a number of initial coding tests were carried out to find the most responsive and emergent method, capable of handling the large volume of interview data. An initial test using MS Word to code data within the existing transcription documents proved to be unsuited to category sorting and in vivo theoretical memoing. NVivo had been initially used to code the Delphi surveys, but this was also felt to be less suited to conceptual visualisation and grounded theorising to analyse the in-depth qualitative interview data. This led to the researcher to seek alternative qualitative data analysis software and the experimentation and final selection of MAXQDA to conduct emergent analysis, creative coding, and theory construction, in keeping with grounded theory methodology. The MAXQDA 2020 software (VERBI Software 2019) facilitated the coding process through the adoption of its four core steps:

- Coding the data
- Customising the Code System
- Category building with Creative Coding
- Constructing theories with MAXMaps

Using the mapping features of the software allowed concepts to be categorised and then compared to coded data in other categories. This allowed the connections between concepts to be easily studied and the linking of the utility of categories as facilitators, influencers or barriers to be considered within developing theoretical frameworks. The nature of the properties of concept category being either a **stressor or a resource** within a framework, is allied to Antonovsky's salutogenic model and the processes and mechanisms linking the Sense of Coherence (SOC) and health (Mittelmark et al, 2017, p10).

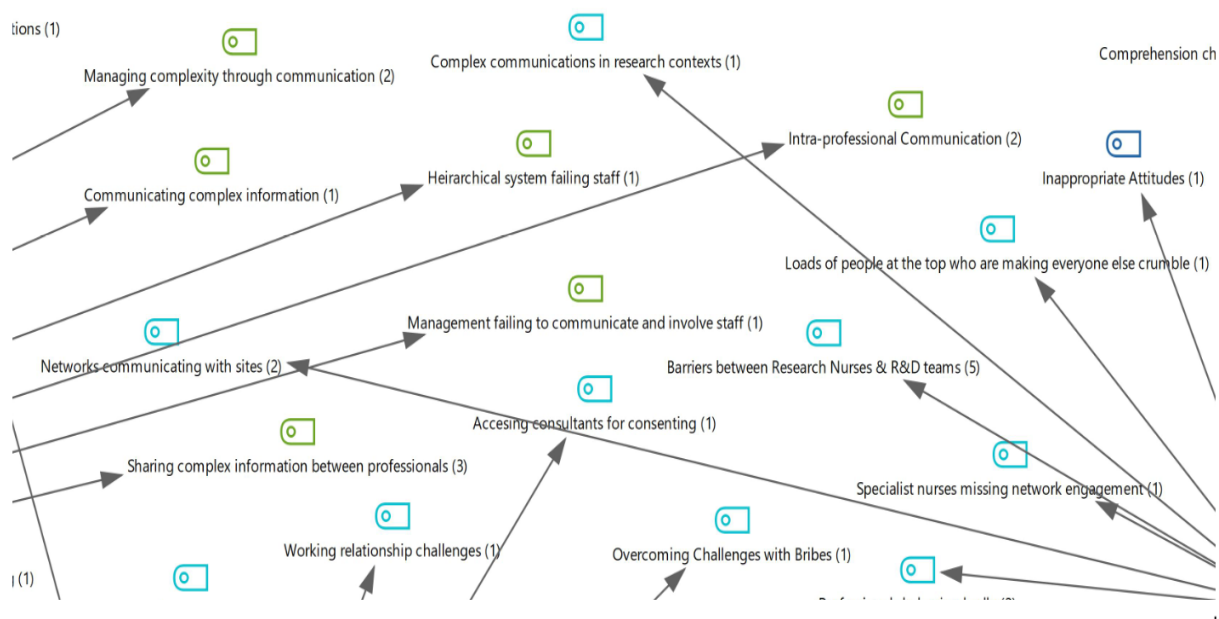


Fig. 5.12 MAXQDA relationship mapping

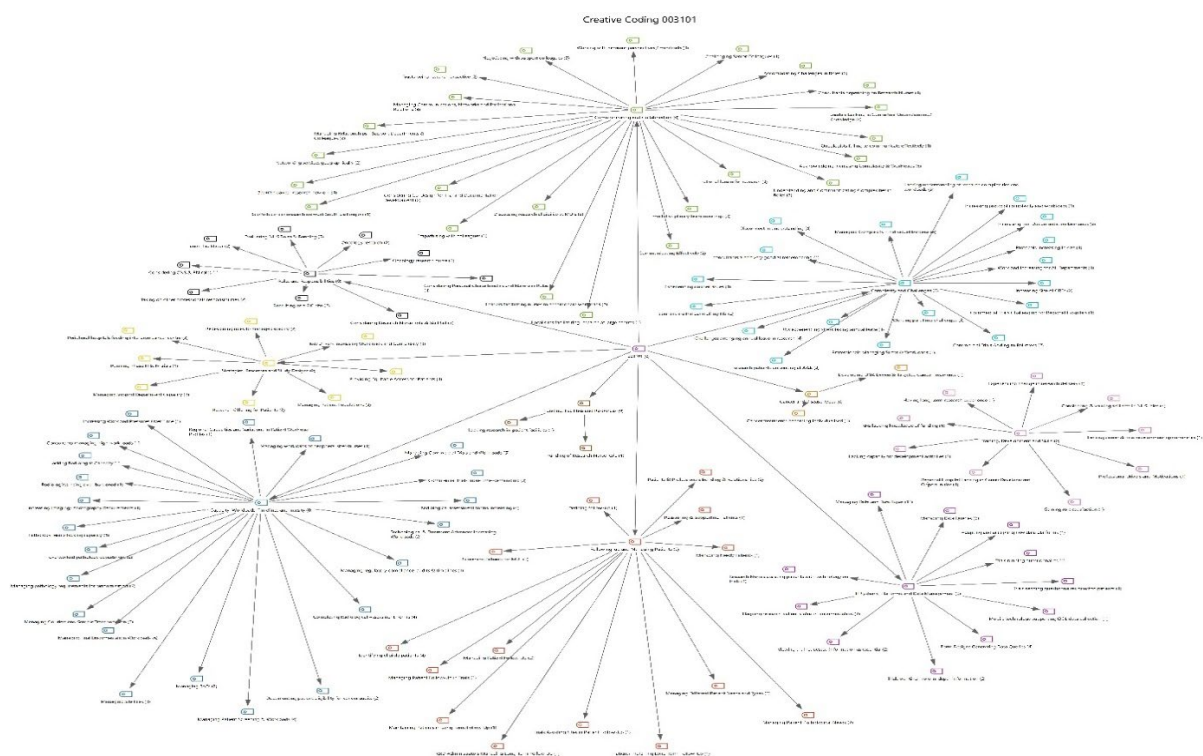


Fig. 5.13 MAXQDA Creative Coding

5.5 Development of the Grounded Theory

The development of the core categories and the relationships between them form the basis of the grounded theory through the use of the constant comparative method. The four stages described by Glaser and Strauss (1967) are now discussed in relation to the data analysis and development of the grounded theory within the context of this study. In addition to the four work packages, evidence was also gathered from the literature review, which formed part of the conceptual data collection process as relevant data were sampled and integrated with the emergent theory.

5.5.1 Comparison incidents of relevant categories

A number of methods were used to compare incidents of relevant categories, which supported the ordering and recording of these within theoretical memos. Such methods included comparison of incidents from card coding, blackboard and whiteboard modelling, diagramming and matrix modelling, and exploration of a wide range of tools available within CADQAS application, such as MAXMAPs functionality. Adopting an exploratory approach to data comparison opened up opportunities for the optimisation and realisation of the development of themes and their properties to emerge from the data. Glaser and Strauss (1967) argued that to develop theory which retains its sensitising nature yet is capable of application to multiple and evolving situations, requires the collation of “a vast number of diverse qualitative ‘facts’.” As a consequence of collating such a diversity of data, the use of a range of supporting techniques and approaches is required to analyse and compare the incidents contained within the situational evidence, sourced from multiple contexts and participants.

5.5.2 Integration of the categories

As comparison of the emerging categories across the source data and theoretical data, patterns and relationships emerged which led to the refinement of categories and their labels. The concept of Salutogenesis and its relationship to healthcare and clinical research delivery emerged as an over-arching metatheory to form an integrated theory which could reveal, illustrate, and explicate the complex and detailed data and then inherent knowledge and concepts situated within. Principle concerns and their categorical components and relationships, which included ***Cancer and Disease Types, Communicating, Collaborating and Relating, Strategies, Processes and Study Designs, Training, Development and Skills*** had both qualitative and quantitative elements and synergies that could be understood from the integration of Pathogenic and Salutogenic Prismatic

Perspective, which could draw on Antonovsky's (1987, p19), Sense of Coherence (SOC) model. The three dimensions of SOC supported the integration of the EFACCT categories into the following elements:

1. Comprehensibility
2. Manageability
3. Meaningfulness

5.5.3 Delimiting the theory

Bryant (2019) argues that grounded theory can be viewed as a leading method for enacting "abstraction and abduction".

- Density
- Scope
- Level of conceptualisation

The grounded theory developed in this thesis is informed by an interpretivist perspective and aligns with the assumptions that such theoretical constructs are emergent, indeterminate and that reality is an interpretation of situated interactionist perspectives and social constructions (Charmaz, 2014, p231). The developed Prismatic Coherence Model (PCM) is a constructivist grounded theory which coheres to the statement by Charmaz (2014) that 'knowledge and theories are situated and located in particular positions, perspectives and experiences' and that the theorists ' build from specifics and move to general statements while situating them in the context of their construction.'

5.5.4 Writing and visualising the theory - Telling and illustrating the story

'The substance of sciences comprises more than the discovery and recording of data: it extends crucially to include the act of interpretation' (Gopen and Swan, 1990).

The writing strategy within a constructivist grounded theory thesis needs to be evocative of the experiences of the participants (Charmaz, 2001; Mills & Francis 2006). The notional constructs revealed through practice-focused research and situational analysis, allows the extracted empirical data to be compared and contrasted across the multiple participant extracts, dialogue, and testimonies, and their contextually sensitive realities and meanings be interpreted and constructed to provide novel theoretical and actionable insights.

5.5.4.1 Writing the theory

In the process of writing the theory the source data and transcripts were frequently revisited in order to ensure that emergent concepts and developed conceptual themes remained grounded in the circumstances, experiences and situated knowledge of study participants, providing a true representation of their voices and perspectives. Participant quotations are used in Chapters Six and Seven to evidence the origin of conceptual categories, their properties, conditions, and contextual relevance, supporting the development of a coherent and meaningful grounded theory. Locke (2001) describes this as an alternating ‘show and tell’ authorial process which moves between the developed theoretical concepts and the contextual data from which it emerged.

5.5.4.2 Visualising the data

The use of creative coding and MAXMaps supported the creating of categories and theory construction, allowing data visualisation methods to support theoretical conceptualisation. Theoretical data visualisation methods or graphical representation of data support comprehension and analysis of the properties and relationships between codes, concepts and their properties.

5.5.4.3 Data visualisation for complexity comprehension

Data visualisation techniques have been used to support the comprehension of complex information. During the later stages of the data collection the study progress was presented at the EDGE Conference 2019, with a visual model (See Fig. 5.14 and 5.15) was developed using ConceptDraw (Cloud Computing Architecture Diagrams, 2017) to express clinical trial delivery complexity which was based upon the London Underground design model developed by Harry Beck in 1933. Conference delegates were invited to discuss the framework and identify gaps, using the theme of ‘Mind the Gap’ as part of the work in developing a Trial Rating and Complexity Assessment Tool (TRACAT). A copy of the map is displayed in the Cancer Clinical Trials unit in Edinburgh.



Figure 5.14 Mapping Complexity- EFACCT Mind the Gap Model

In the later stages of the grounded theory development the emergent theory was reviewed in relation to earlier models developed relating to complexity, with a focus on the nature of clinical trial study designs and protocol complexity.

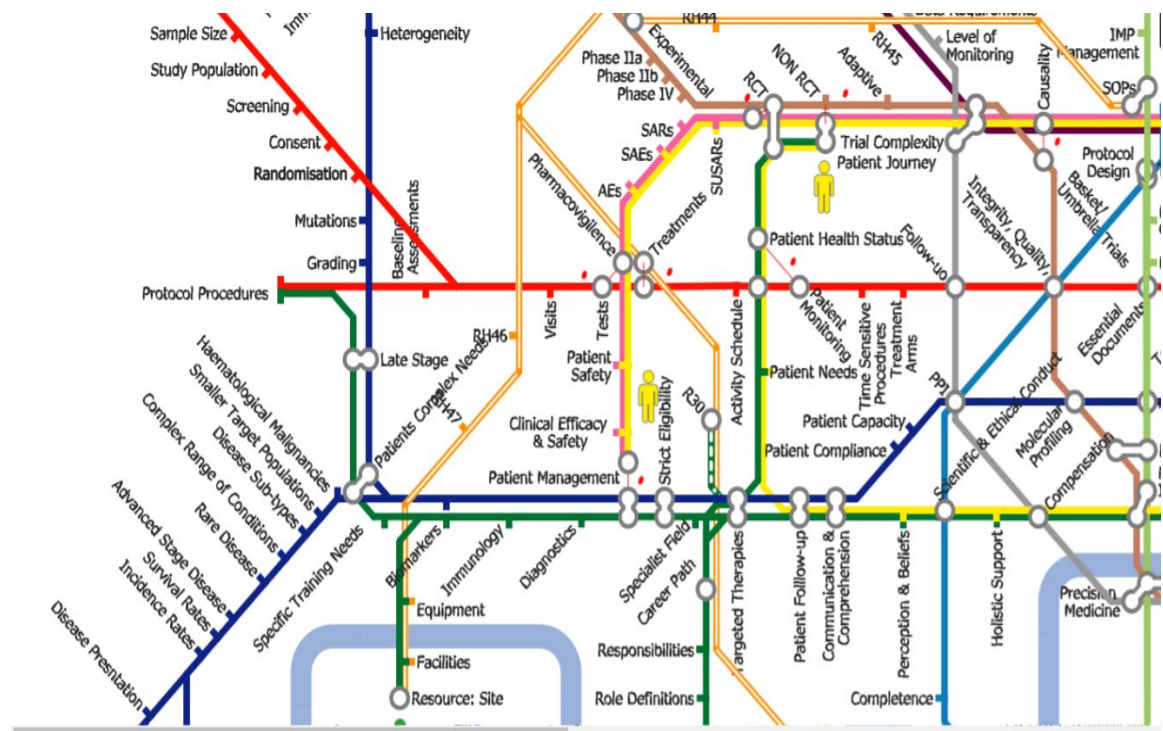


Figure 5.15 Mapping Complexity- EFACCT Mind the Gap Model (Enlarged Section)

5.6.1 Emergence of the Core Category and Theoretical Model

The core category that emerged from the research linked directly to the initial orientating theme and title of the study, which was evaluating follow-up and complexity in cancer clinical trial delivery and paradoxically the in-depth contextual and volumatic nature of the research data collected and analysed revealed the emergent and non-linear nature of conducting and delivering research in healthcare. The core category remained elusive, as analysis continued to reveal multiple layers of complexity, detail and interacting phenomena, in turn posing a challenge in moving from open to focused and conceptual levels, until progressive modelling of participant responses through visual modelling techniques illustrated that the very nature of detail, specificity, non-linearity or reductionist processes of moving to focused categories revealed the concepts and challenges in motion and at play. The core category and sub-categories are discussed further in Chapter Eight.

5.6.2 Emergent Grounded Theory and Literature Review

The coding frameworks (shown in Fig. 5.17) and the developing categories from the in-depth interviews and their sub-themes, which had been substantially compared and contrasted throughout the data collection using theoretical sampling from the patient and professional studies, were synthesised, and further compared and reviewed in relation to the literature.

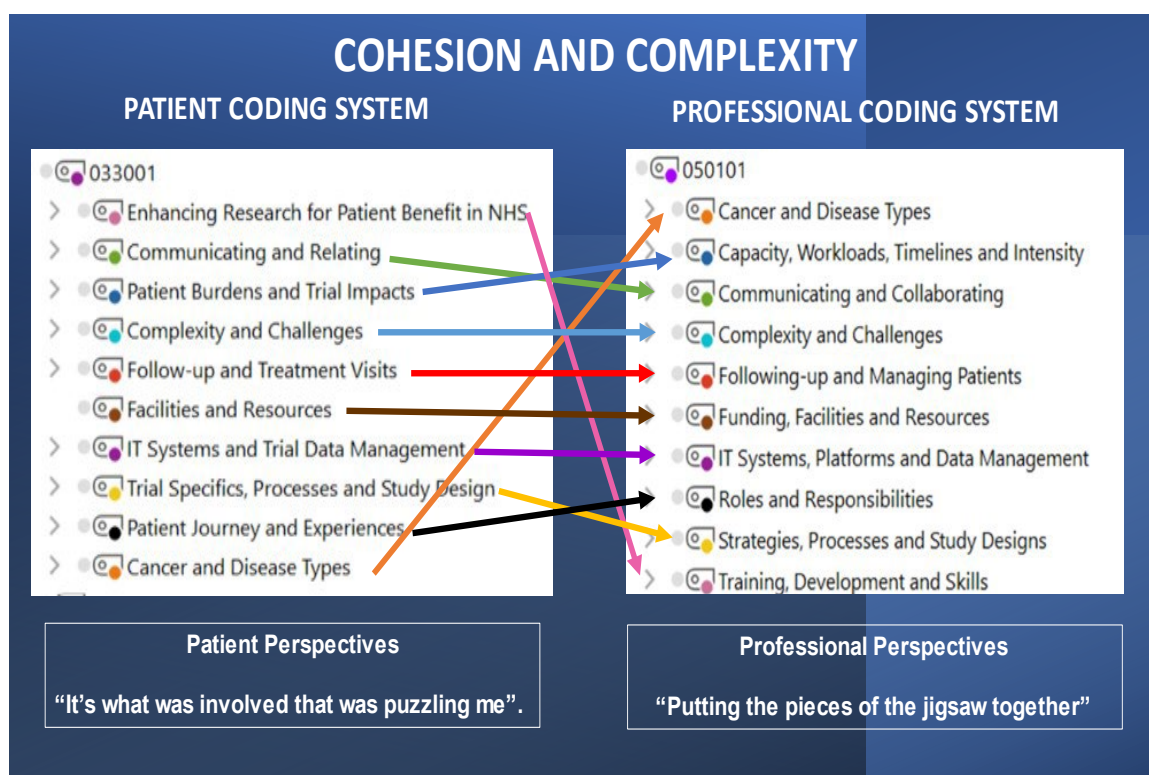


Figure 5.17 Coding System Synthesis

In revisiting the literature and comparing the study's empirical data relating to cancer clinical trial delivery in the NHS, which was both voluminous and contextually detailed, it was important to discover a theoretical framework capable of explaining and illustrating the challenges and opportunities of complex adaptive healthcare systems and their socio-cultural characteristics. To understand the underlying mechanisms involved in healthcare setting, from macro levels and both patient and professional perspectives relating to the nature of ill-health, disease and coping strategies, up to wider organisational, network and operational levels, a systems approach is needed, but one that can incorporate both the concepts of pathogenesis (the origins of ill health) and salutogenesis (and the origins of health and well-being), which brought into consideration the importance of the sense of coherence (SOC) developed by Aaron Antonovsky, who stated, "A Salutogenic orientation, I wrote, provides the basis, the springboard, for the development of a theory which can be exploited by the field of health promotion [...] which brings us to the sense of coherence" (Antonovsky, 1996). A grounded theory for cancer clinical trial delivery guided by a salutogenic framework, provided the canvas to illustrate the intricacies, niche narratives and the depth of perspective witnessed during the research journey, and which can provide a model for managing and shaping health policies and environments that enhance the health, well-being and experiences of patients and healthcare professionals alike. The core conceptual categories and emergent grounded theory for this study and the comparison of these to the theoretical literature, incorporating pathogenic and salutogenic orientation are discussed in further detail in chapters six, seven and eight.

The patient and professional coding systems were colour coded into symbiotic relating categories. These were then further analysed, and their sub-categories compared to investigate relationships and dependencies, using visual models to compare constructs for the theoretical literature, as in the example shown in Fig 5.18, where the coding frame is overlaid onto Antonovsky's Sense of Coherence construct. The nine categories of the coding model and their sub-codes are discussed in relation to patients, their perceptions and experiences in Chapter Six, for the research professionals and their roles and circumstances in Chapter Seven and then considered at a higher conceptual level, through considering the synthesised results to provide a comprehensive analysis of the phenomenon complex clinical research and healthcare delivery, and the development of a cohesive model to improve operational performance and enhance research for patient benefit, health and well-being.

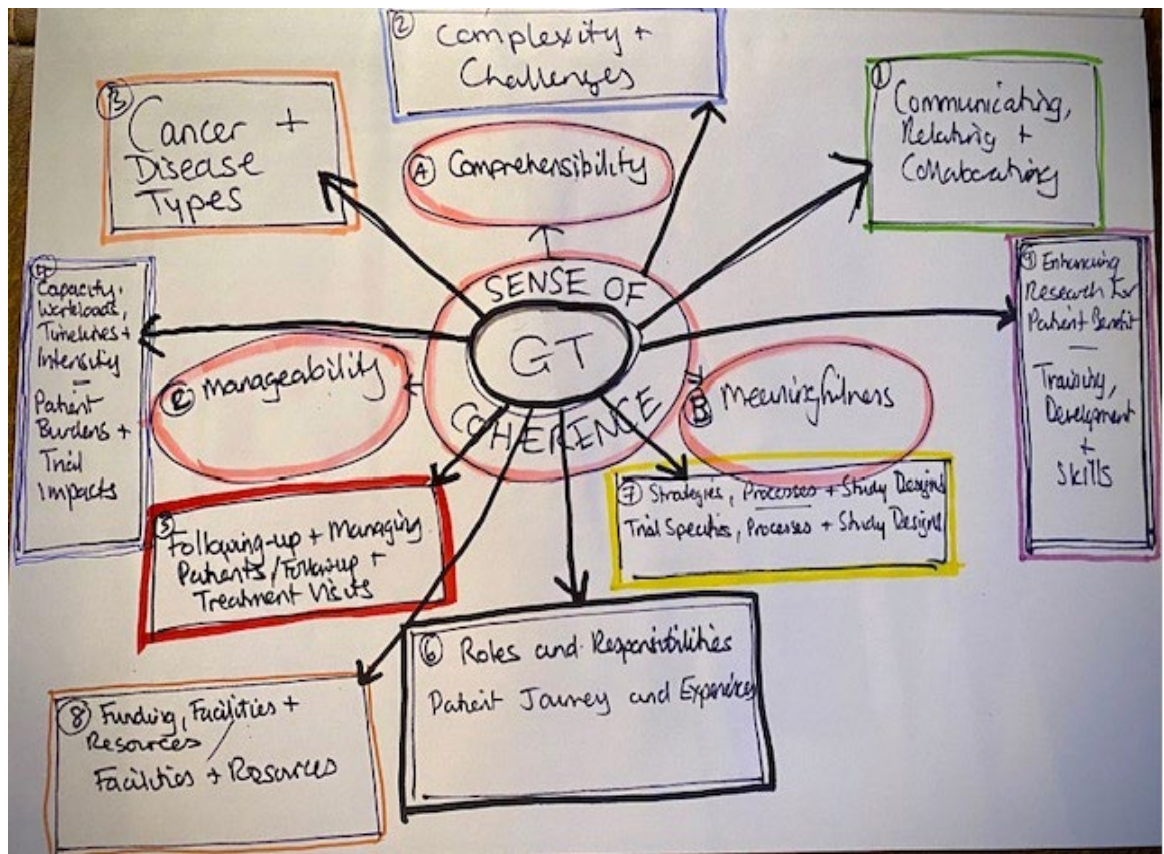


Figure 5.18 Coding Model Comparison to the Salutogenic Sense of Coherence Model

5.6.3 Evaluation Criteria for the Grounded Theory

The criteria applied in the evaluation of a developed grounded theory should be sensitive to the nature of the phenomenon being studied, the overall methodological approach of the research design and the situated experiences of participants. Corbin and Strauss (2015, p341) suggest that the quality of research findings or the developed theory should reflect both the scientific and creative components involved in the process. The research, through an evaluation of follow-up and complexity in cancer clinical trials developed a constructivist grounded theory which proposes a salutogenic framework as a model to support and enhance the delivery of cancer clinical trials, and more widely as a process suited to a new approach to healthcare operations with the patients' and professionals' health and wellbeing forming its core orientation and purpose. The criteria put forward by Charmaz (2006, Pp182-183) as appropriate evaluation criteria for a constructivist grounded theory and are sensitive to the scientific and creative nature of a sensitised theoretical framework have been recognised in the development of this study's grounded theory construction. These four criteria of credibility, originality, resonance, and usefulness are discussed in relation to specific findings in the ensuing results chapter, with their relevance further explicated in Chapter Nine, the concluding discussion of the thesis and the overall contribution of the research.

5.7 Chapter Summary

Within this chapter the analytic processes and use of the constant comparative method and grounded theory coding procedures have been described. The systematic synthesis of data collated across the study's work packages are explained in chronological order and in relation to their analytic methods and subsequent integration into the overall theoretical framework. A detailed description of the specific coding stages is provided along with the approach taken in achieving theoretical sensitivity and saturation, supported by memoing and reflexivity. The chapter concludes with a review of the processes adopted in delimiting and writing the grounded theory, as well as defining the criteria for ensuring quality, rigour and credibility in the conduct and subsequent outcomes of the research. This chapter's narrative elaborates upon the analytical steps undertaken in the process of developing an integrated theory capable of interpreting the nature of cancer clinical trial delivery, its challenges, and complexities within the NHS. In Chapter Six the results of the studies involving cancer clinical research professionals are discussed, followed by the patient study results in Chapter Seven. The outcomes of the research, incorporating the perspectives of both participant groups and the resultant integrated grounded theory are discussed in Chapter Eight.

Chapter Six: Presenting Research Professional Perspectives

" Like people with cancer, physicians often feel isolated from others by the nature of their experiences. They are also isolated from each other by the codes of professionalism." (Remen, 2006, p56).

6.1 Introduction

This chapter presents the main findings of the three participant studies involving research professionals commencing with the Research Professional Delphi study, whose results then informed the content and direction of the subsequent questionnaire and interview stages of the research. As described in Chapters Four and Five, the Delphi study informed later data collection stages, leading to the development of the substantive grounded theory, in combination with the results of the patient studies, which are discussed in Chapter Seven. Complexity and follow-up in cancer clinical trials formed the guiding interest in the initial orientation of the research in relation to operational delivery of cancer clinical trials, but in response to the focus of research professionals, and in keeping with grounded theory methodology, the findings also developed new themes. The empirical findings were compared to the literature which is reviewed and discussed in Chapter Two. As we move through the different stages of the research, involving the voices of ranging NHS professionals across the UK, the multiple concerns, perspectives and experiences of professional stakeholders are revealed. The chapter concludes with a summary of the key findings and core categories contributing to the overall grounded theory illuminating the nature of cancer clinical trial operational delivery, from the stance of those professionals closest to the practical situated realities.

6.2 Research Professional Perspectives and Study Results

The performance for the accrual and completion of the research professional participants to the EFACCT study is summarised in Table 6.1. Participant demographics and the outcome of the respective study elements and the integration of the results is discussed in the following sections. The names of the professionals taking part in the studies, as well as the NHS sites where they are employed, have been removed and an anonymised participant ID is used where their direct quotations and extracts from research data have been used. The first three digits of the participant ID represents the participating site ID.

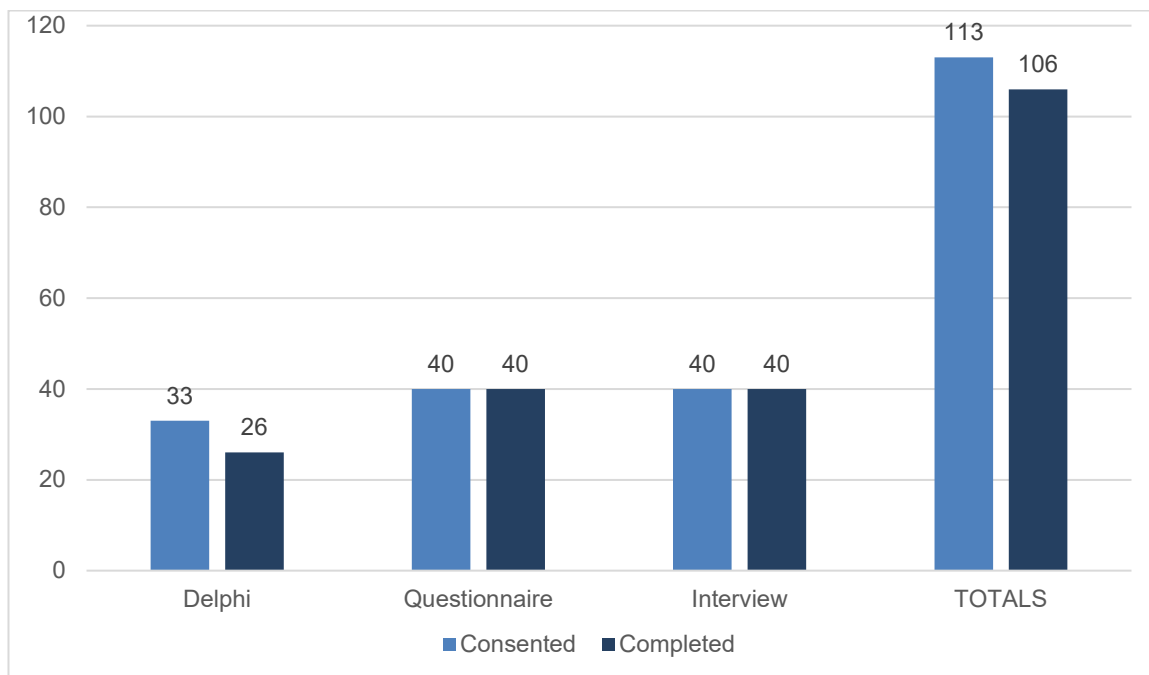


Figure. 6.1 Research Professional Participant Accrual to Completion by Study Type

6.2.1 The Research Professional Delphi Study

The initial launch activity for the EFACCT study was a three-round online Delphi consensus study, which recruited thirty-three clinical research professionals from a wide demographic of thirteen NHS sites, across nine clinical research networks in England and Scotland. Twenty-six professionals completing all three survey rounds. The e-Delphi study results were published in an article online in the BMJ Open in February 2020. The results can be accessed via these links: <https://bmjopen.bmj.com/content/bmjopen/10/2/e034269.full.pdf> and : www.efacct.com.

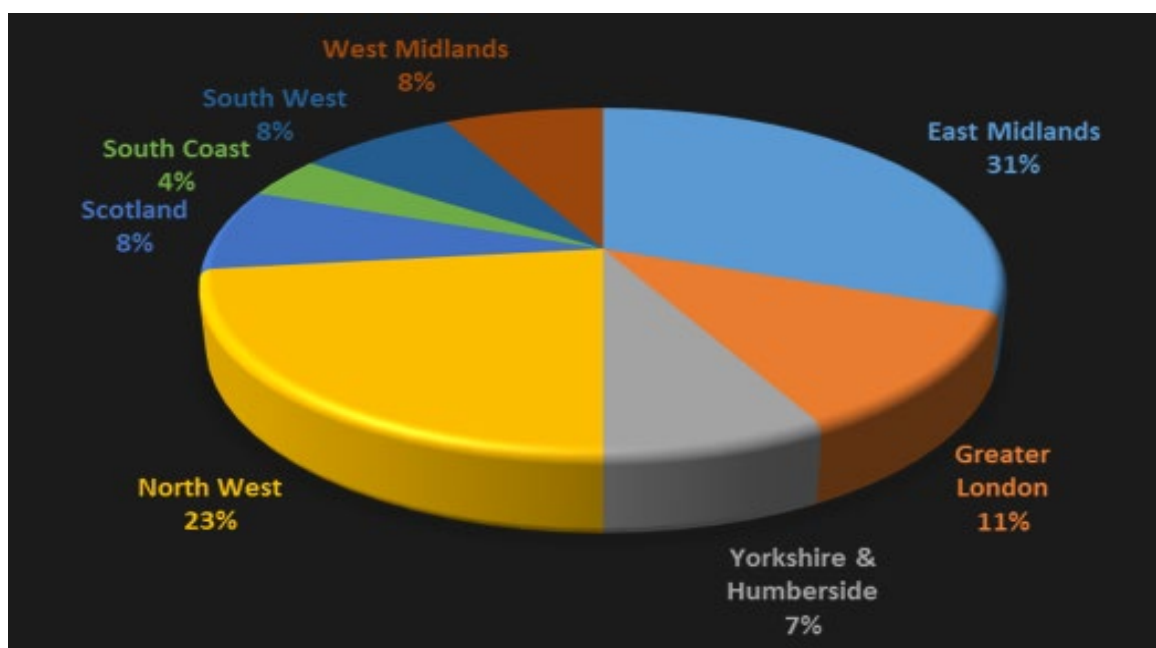


Figure. 6.2 Delphi Pro Panellists by Region

Characteristic	Round 1		Round 2		Round 3	
	n	%	n	%	n	%
Gender						
Male	4	14.81	4	14.81	3	12.00
Female	22	81.48	22	81.48	21	84.00
Other	1	3.70	1	3.70	1	4.00
Age						
25–34	3	11.11	3	11.11	2	8.00
35–44	9	33.33	9	33.33	9	36.00
45–54	10	37.04	10	37.04	9	36.00
55–64	5	18.52	5	18.52	5	20.00
Years in clinical research						
Between 2 and 5 years	8	29.63	9*	33.33	9	36.00
Between 5 and 10 years	11	40.74	11	40.74	9	36.00
More than 10 years	8	29.63	7	25.93	7	28.00
Role						
Research and development manager	4	14.81	3	11.11	3	12.00
Research nurse	8	29.63	9	33.33	8	32.00
Research nurse manager	2	7.41	2	7.41	2	8.00
CI, PI or co-investigator	3	11.11	3	11.11	3	12.00
Data manager	2	7.41	2	7.41	2	8.00
Clinical/senior clinical trials practitioner	3	11.11	3	11.11	2	8.00
Finance business partner	1	3.70	1	3.70	1	4.00
Research nurse and PI	1	3.70	1	3.70	1	4.00
Research support officer	1	3.70	1	3.70	1	4.00
Research radiographer	1	3.70	1	3.70	1	4.00
Research pharmacy technician	1	3.70	1	3.70	1	4.00
Total participants	27		27		25	

*One participant joined the study in round 2.

CI, chief investigator; PI, principal investigator.

Table 6.1 Research Professional Panellist Demographics

One of the initial aims was to seek input from clinical research professionals on attributes they felt should be included in a trial rating and complexity assessment tool (TRACAT). The aim of the planned tool was to support sites in developing rateable attributes for reporting on the complexity and intensity of their clinical trial portfolio of studies, which could be mapped into Local Portfolio Management Systems (LPMS) used across sites nationally, and potentially adopted internationally. Ranked attributes developed by the EFACCT Delphi panel are shown in the right hand panel of Fig 6. 3 and Appendix 5.

TRACAT: Trial Rating & Complexity Assessment Tool

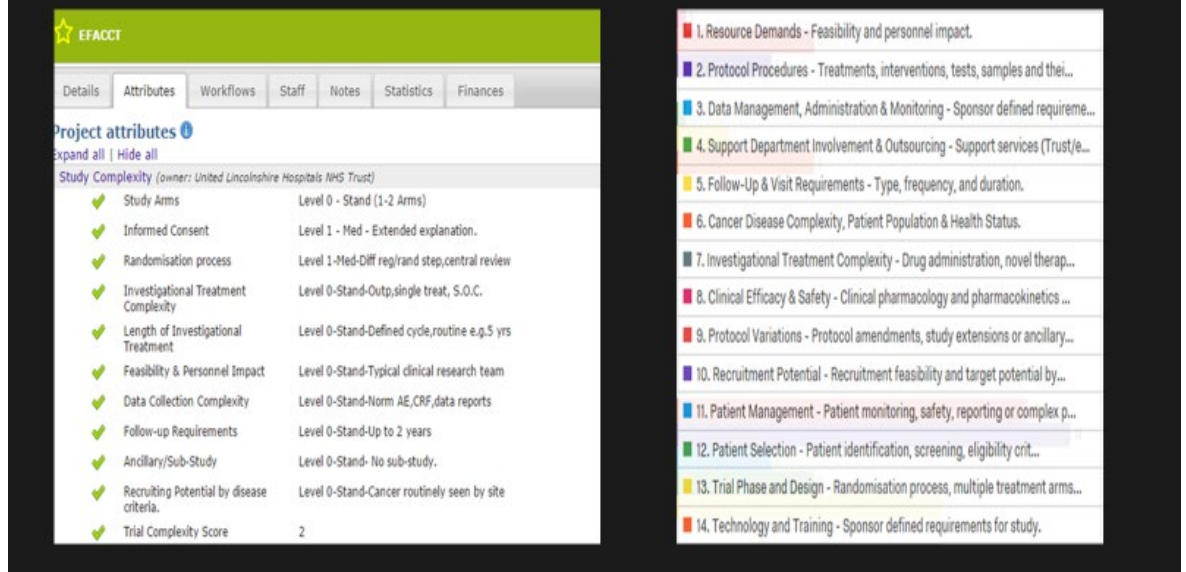


Figure. 6.3 TRACAT: Trial Rating and Complexity Assessment Tool

The consensus statements developed by the panel, as well as the TRI categories, were used to inform the design of the subsequent quantitative Questionnaire study and the qualitative interviews.

6.2.1.1 Participant Definitions of Follow-up

The definition and nature of patient follow-up has significant implications for providing sustainable and patient-centred care in cancer clinical trials. The definitions provided by the professionals, who were all ostensibly involved in the patient-facing side of cancer clinical trial delivery at sites, were varied and demonstrated early on in the data collection that context and meaning in healthcare and clinical research operational contexts were complex constructs. The ranging perceptions and lack of consensus or shared comprehension of the term *follow-up*, between professionals operating at just one level within the NHS organisational strata (the clinical trial site), highlights the multi-faceted nature of clinical trial and healthcare operational delivery. Further complexity is added when different networks, whether they be external or internal to the NHS, interact with agents within a system that already lacks coherence, or shared values and mutual understanding and recognition of core concepts of their professional field. Divergent interpretation of clinical trial *follow-up* is just one concept which can be studied in order to understand the challenges of designing sustainable operational delivery models within complex systems and networks, especially those lacking coherence or synergistic values between agents (patients or professionals).

Whilst the panel did not reach a consensus definition for the term ‘follow-up’ they did reach consensus level of 92% on the following statement:

‘A nationally agreed definition of the term ‘follow-up’ and/or types of ‘follow-up’ in relation to research delivery in the NHS should be published by the NIHR so that all clinical research professionals, allied professions and associated bodies conform to a standard terminology and parameters’. (Jones et al, 2020).

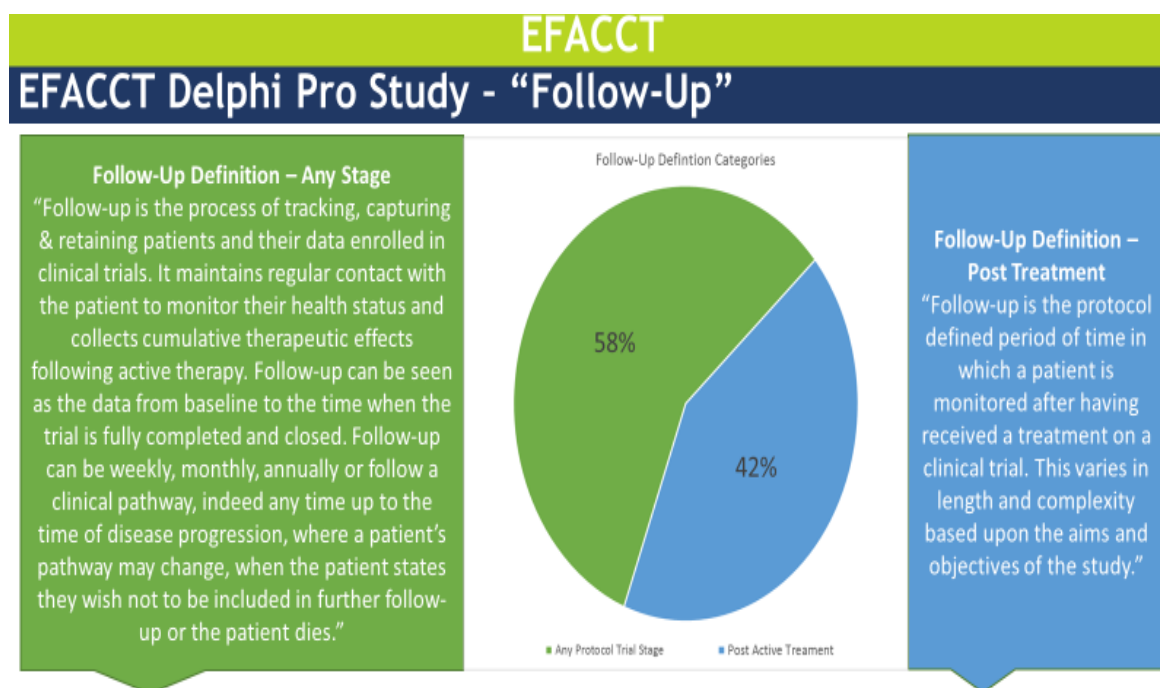


Figure. 6.4 Delphi Panel Follow-Up Definitions

Figure 6.4 provides two differing perspectives and definitions of follow-up, developed by the panellists, and shows that 58% of the research professionals use the term follow-up to define activities from base-line to completion or trial closure (any protocol stage). This disparity in coherent interpretation has implications for resources and capacities to manage clinical trial delivery, as well as leading to inter-operability complexities and challenges. This finding highlights the importance of shared comprehension and meaning of constructs in healthcare and wider interdisciplinary fields. This initial finding from the Delphi formed an early memo, and data category which was explored in the interview studies, and also compared with wider literature. McAlearney et al (2013) suggest that coherence within healthcare organisations is a critical quality improvement element which has three key components: people, processes, and perspectives.

6.2.2 The Research Professional Questionnaire Study

The qualitative questionnaire study was conducted online and recruited forty research professionals. The procedures used in developing the patient questionnaires were mirrored in the research professional questionnaires, as these were designed after the completion of the Delphi study. The questionnaire responses also informed the nature of questions in the Research Professional interview studies.

6.2.3 The Research Professional Interview Study

The research professional interviews were conducted in person at eleven hospital sites across England and Scotland, with forty research professionals consenting to the in-depth interviews. The professional interviews were organised into a ten-category coding system, shown in Fig. 6.5.

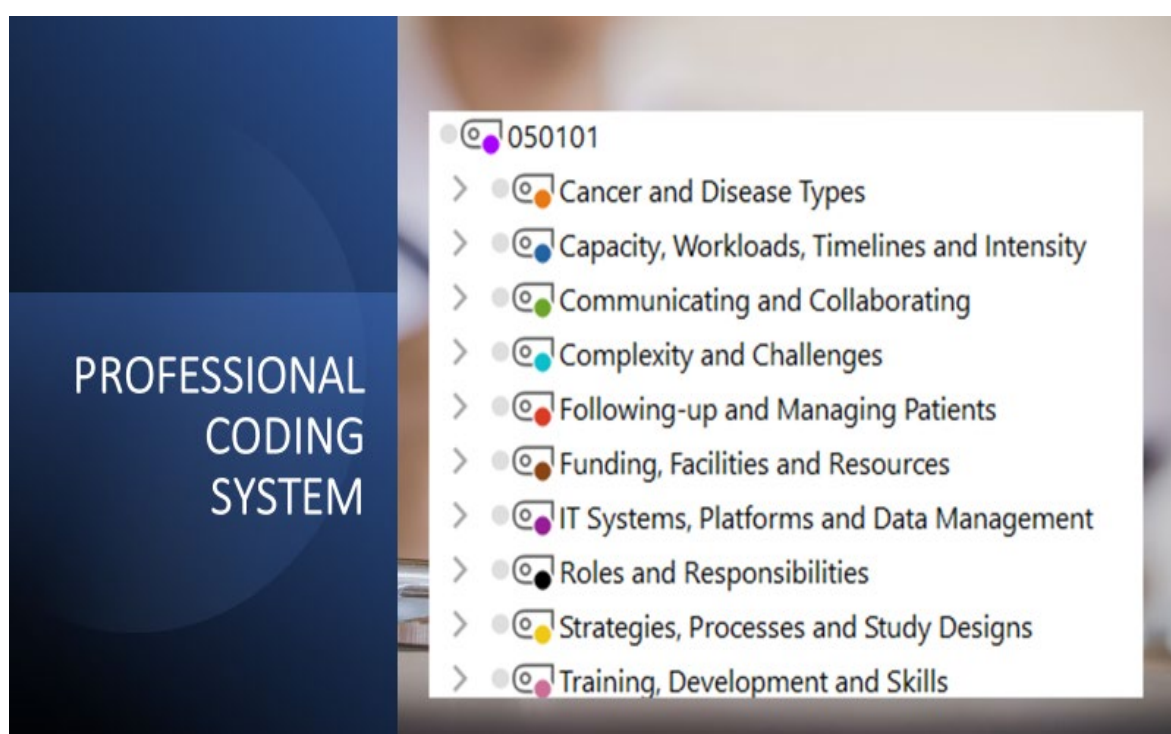


Fig. 6.5 Research Professional Coding Structure

The conceptual categories were further developed into the theoretical concept explaining the phenomenon of cancer clinical trial delivery, developed from Antonovsky's Salutogenesis concept and the Sense of **Coherence** model (Antonovsky, 1987). Using the concept of a sense of coherence (SOC) as a guiding framework for the narration of the experiences and perspectives of clinical research and healthcare professionals, supports a systematic translation of voluminous and diverse data gathered throughout the study.

6.2.4 The Human Professional

The coding methods revealed the nature of being human as a clinical research professional and their experiences of delivering cancer clinical trials within a national healthcare system. The narratives were expressive, emotional and revealing. These dialogues provide unique insights into the situated, complex realities of NHS clinical research professionals.

6.3 Professional Perspectives and Prismatic Thinking: Putting the pieces of the jigsaw together.

Coding Themes:

1. Cancer and Disease Types
2. Capacity, Workloads, Timelines, and Intensity
3. Communicating and Collaborating
4. Complexity and Challenges
5. Following-up and Managing Patients
6. Funding, Facilities and Resources
7. IT Systems, Platforms and Data Management
8. Roles and Responsibilities
9. Strategies, Processes and Study Designs
10. Training, Development and Skills

6.3.1 Complexity in Cancer Clinical Trial Delivery

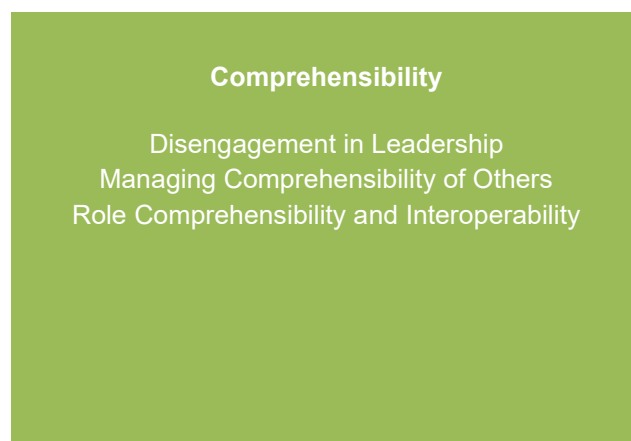
*“We're not going to look at complexity because it's too complicated”.
(Participant ID: 029114).*

The results of the data collection and analysis led to the emergence of communication as a significant conceptual component embedded within the conceptual category of complexity, not only in cancer clinical trial delivery but more broadly in relation to health and wellbeing, from both the perspective of cancer patients, research professionals and wider systems and networks. As the research progressed the inter-related and confounding nature of complexity and the challenges faced by professionals in responding, managing, and coping in their everyday roles and in their unique environments, has thrown a spotlight on the urgent need for a salutogenic approach to cancer clinical research and healthcare delivery.

6.4 The Core Category – Being Human

The properties of being human as expressed through the research professionals' experiences and perspectives were extensive and varied but the essential core element was the nature of being human, whilst working within the field of clinical research. Supporting categories are discussed below, with further examples elaborated on the website.

6.4.1 Comprehensibility – Strategies, Processes, Designs, Knowledge



Analytic Quote Memo - Comprehensibility for CCT Research Professionals

Comprehensibility or the ability to comprehend, understand and make sense of one's own (or other people's) circumstances, environment, condition, or status from a **research professional's** perspective.

Disengagement in Leadership: "I don't know why **they're not listening** [the CRN] to sites. I think there needs to be a real shift, I think, because they're not, they're **not recognising** that, how the work is. **They're not recognising** how the research, like Cancer Research UK...how it's changing, what they're finding. And clinical treatments have changed hugely since I started, and the **changes are immense**. And so many of the chemos that are given, they're not chemos anymore, you know, they're biological agents, immunotherapy...they're not day cases." (Participant ID. 001106)

Managing Comprehensibility of Others (Patient Comprehensibility): "...they don't, for instance, at the beginning they say, 'Oh YES, I would want the research treatment', and then you realise they haven't understood the whole concept of randomisation". (Participant ID: 001119)

"Patients' expectations have changed over time, that they're, you know we are in an area, we have a **population that are very clued up**, are very savvy...there are a lot of educated people

within the population. And they come, you know they've got a whole different, it's a bit different because they've got a bit **more insight** and **they've got different questions**. And so, you know, **you can't always answer all of their questions** all the time...so it's complicated, so there is that and patients' questions can be quite detailed I suppose. So, knowing the studies inside out, you can't all the time, you know you just can't, **you can't know everything inside out all the time.**" (Participant ID: 024104)

Understanding implications and consequences: "As a research nurse, if you don't understand the **implications of multiple follow-up visits**, you can't really explain the study to the patient and what they are, what you're asking them to agree to. You're not just asking them to agree to sign a piece of paper, you could be asking them to agree to come and see you once a month for ten years or whatever the follow-up is. So, **if you don't understand that, you can't really be discussing the study with anybody**". (Participant ID: 024105)

Role Comprehensibility and Interoperability: "So, in terms of people's misconceptions about kind of what we do in our role is, I think that could be training. So, I think research isn't just medicines and curing cancers and what people might seem to think comes into the bubble of cancer clinical research. I think there's a lot of different trials...you get the interventional and the non-interventional and I think that people need to understand and respect what other people are doing, and all of their, you know, positions and the studies they manage. So, I think that's an element that needs some sort of re-education". (Participant ID: 005111)

Shared Understanding, and Interpretation: "So the radiotherapy studies at the moment, that's quite a challenge, in POSNOC for example. And radiotherapy is complicated or it's not. It's not complicated but people don't understand it, so they tend to shy away, and that's not just, that's not just necessarily patients even. That's my colleagues, so even the research nurses don't really understand radiotherapy, and the surgeons don't understand radiotherapy. So, they're the ones that are seeing the patients first. So, I still, for POSNOC, I'm still seeing letters from the surgeons who are criticising us for not entering patients into POSNOC, but they're saying in their letter, which goes to the patient, err, 'and patient requires axillary radiotherapy'. So, if the patient reads that reads that then they're not going to, say then, listen to me say. 'No, you probably don't, you may not need it,' therefore [laughs], so that's, that's a difficulty. So, they're coming to me expecting to get this treatment anyway, because the people that have seen them previously, don't really understand what it's about. They don't understand. They understand the question, but they don't really understand how, how you, how the radiotherapy works to answer that question, if you see what I mean. " (Participant ID: 005120)

Information/Data Management and Clarity: "...what's very important in cancer studies, obviously is pericyclic reviews and then does modification, so we try to take out key information from the protocol about when you might need to modify doses, based on say blood results and toxicity, and summarise that and make it nice and clear. And sometimes, in the actual protocol, it's ambiguous. You find information which contradicts itself, it's not clear. So, we translate that

onto a local protocol which should be clear to all our staff.” (Participant ID: 002101)

Governance and Procedural Awareness: Q: Do you have internal Standard Operating Procedures (SOPs) for every procedure within the department? P: “As far as I know we should do. I mean I’ve been here what, over a year now, and I wouldn’t know where to find them, what they necessarily are, so if we have them, they’re probably, I wouldn’t say they are readily available or used that often. [laughs]”. (Participant ID: 005113)

Knowledge and Progress: “We are at delivering monoclonal drugs, so that’s been really good because we’re expanding our research boundaries.” (Participant ID: 034102)

Patient Choice, Involvement and Feedback: “I was taught a lesson a few years ago when a, in fact I heard someone use it in GCP the other day when one of the managers used it as an example, we had a four arm chemotherapy study and there was a patient who was really, at the time she was extremely emotional about everything, and she was really struggling to take it in. She wasn’t giving a lot of eye contact. The consultant wasn’t there, it was one of the registrars and I was on holiday, so it was the breast care nurse, and they both decided it wasn’t suitable, that the lady wasn’t in the right place. And then about four weeks later that patient was sitting in the waiting room for her first treatment, and she was talking to a lady who was waiting for treatment, and then the lady says, ‘Oh, I, in a trial’. She says, ‘Oh, are you? What did you, did you say you had breast cancer?’. She said, ‘Well no-one offered me a trial.’ So she called me down and I said, ‘I’m really sorry, you know it might have been at the time.’ She said, ‘I completely understand that at the time they probably thought that, but no-one had the right to make that choice for me.’” (Participant ID: 034110)

Table 6.2 Analytic Quote Memo - Comprehensibility

Managing comprehensibility of others has an impact on the capacity of research professionals to manage their knowledge and professional skills. The complexity of studies and the portfolio workload has an impact of clinical staff’s ability to attend and engage in professional development as well as trial specific training. Managing the knowledge of a burdensome or complex study portfolio can lead to staff stress, burnout or de-skilling where their specialist skills are neglected in situations where they are required to work in a more generalist role.

Disengagement in Leadership: Failing to listen, recognise or keep pace with changes in the system. Comprehensibility includes the ability to understand the situations of others in professional healthcare contexts and keep pace with the operational realities and challenges that they face in managing their roles, responsibilities and the care and treatment of patients. Recognising the experiences and situated knowledge of colleagues and stakeholders, as well as demonstrating active listening and facilitating feedback

between groups are essential skill sets of engaged leaders in complex systems. Multiple participants in the EFACCT study highlighted that leaders in the CRN, NIHR and NHS were failing to listen to or recognised the challenges faced by research professionals and patients, who are actively involved in clinical trial delivery in the NHS. Engagement with complexity is a property of comprehensibility. A failure to engage with and comprehend the realities of others leads to system failures, communication challenges and unsustainable organisations and healthcare solutions which lack clarity and cohesion.

"You know so, I think gosh, once you get us onto complexities, I think there's just a whole load of things that we can say about it, but I think the main things are that people don't understand what it is," (Participant ID: 005111)

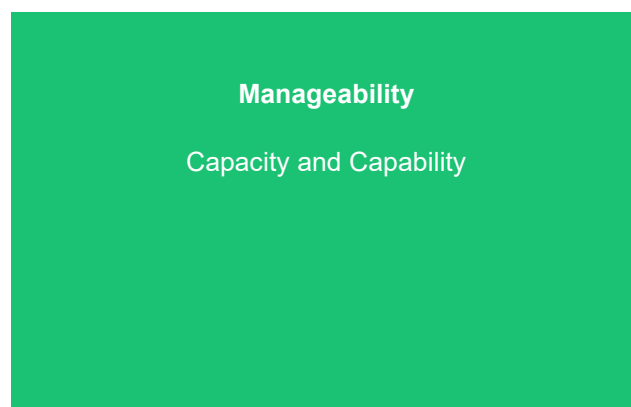
6.4.1.1 Communication Vortex

An illuminating quotation from a research professional described the nature of communication and its effectiveness within their organisation as a '*communication vortex*' stating:

"It's the way it goes in, and it goes down into a system or a vortex and then it comes out and often the wrong people are being informed". (Participant ID: 002114).

This was a surprising yet elaborative and creative use of language to denote the nature of communication within healthcare, which highlighted the usefulness of semantic expression as part of every-day theorising and the metaphorical use of language, as well as the colloquial use of the language of systems within organisations. This is a useful connection to the concept of clinical research and healthcare as a complex adaptive system, as well as a using quantum systems as an alternative model for healthcare and the social sciences.

6.4.2 Manageability – Capacity and Capability



Manageability as the ability to respond to emergent conditions and complexities within healthcare systems and the contextual challenges specific to **research professionals**, clinical trial sites or healthcare organisations managing patient care and clinical trials, and the fluctuation or stability of localised **stressors and resources**. **Capacity and Capability** is a process and terminology adopted by the NIHR/NHS to **strategically manage** the implementation of clinical trials.

Capacity and Capability: *“the research team are not huge numbers. Our capacity is limited because our capacity is already busy dealing with studies in follow-up...The resources are limited and especially with the CRN funding, they are cutting, **we are going down**. So, we need to review how we do things and how we are going to run in the future.” (Participant ID: 001118)*

Supportive Environment: *“The environment has to have experience. That’s right. It’s not that every person within that department has to have it but there has to be experience to, to feed in, you know, to feed off really, to link with, to be supported by.” (Participant ID: 024104)*

Supportive Networks: Q: What are the main themes and changes [in research] P: *“ One of the biggies was the change of networks...When we were [Name of network] they were very hands on...Monthly meetings with network leads and you felt really part of the wider network, because the other sites used to come to [Name of town] every month. We knew everybody and it made good liaison between different hospitals, which helped the sharing of ideas, helping with patient information. Lots of good things. And then the networks changed, and to be perfectly honest you don’t feel part of any network at the moment. You never see the people who are based at [Name of City] who run the network. They are just figures that you never see but feel involved with, so you do feel quite out on a limb. You don’t know whose working at other sites anymore, so yeah, it seems to have taken a backwards step in the way of, you know, being part of a wider team and working well with other people, other networks, hospitals.” (Participant ID: 046102)*

Workloads, Stress and Coping: *“Three or four years ago things were so bad that I couldn’t bear even looking at a blank wall, and it took me three months of having to have time off to get my head straight, because the workload was so huge...and continuing on medication that I was put on at the time. I continue on that [laughs], and you know, but actually half the NHS staff are taking stuff to make them less anxious, just to get through the day. Unfortunately, I sort of, I don’t have any pressures outside of work that stop me working late, so that’s a bad thing really”. (Participant ID: 024101)*

Q: What’s the thing that is the biggest driver for that stress?

P: *“ I think not having enough time to do everything that I’ve got to do and never being able to fully complete everything that needs doing. So there’s always, I know in research there’s always going to be something because the data’s ongoing, the follow-ups are ongoing and everything, but you don’t, I always have in my diary that site file checklists, because every year I want to update my*

site file, make sure my CVs and GCPs are all in there correct. And for, in my electronic diary, I'm forever having to move it to another week, and then another week and it just gets moved and moved." (Participant ID: 033103)

Sustainable Funding and Support Models:

Q: Do you think that follow-up is sufficiently funded by the CRN?

P: "No. **It's not funded at all.** It's not factored in whatsoever, to impact, erm drainage of resources, really. I think networks primarily look at how many people you can get in trials, and they don't look at the other flip side of it, as to how often we need to see these patients, in order to collect back data, because I think historically that has always been an issue. **They have never looked at the follow-up burden.**" (Participant ID: 005108)

Q: Given the pace that science is moving and the current research delivery model we have, how sustainable is it, that it will be able to keep pace or meet the needs of patients?

P: "Barely sustainable, I think. I think we are **teetering on the brink**. There needs to be a complete overhaul of the funding of them, just the overall management". (Participant ID: 029114)

Sufficient Staff Resources: "It's difficult. The nurses, there's **too many patients**, they [Trust] want you to do too many trials...so it's difficult. It's very difficult and I see the **nurses just get stressed out**, but it's the **patients that end up losing out** because we can't like, you know some visits might get missed due to the fact that the nurse is on their own for that day because, I don't know, one nurse is off sick and you know there's only two of them on that trial, or there's one nurse that works on that trial and they're on annual leave. So, the patients, as much as we try and monitor and we try and see them, see the other staff's patients, it's not always possible to do that." (Participant ID: 034111)

Workloads and Morale: "I think people are struggling with their, the volume of work in their day jobs and adding research into that. I think some people struggle to manage all the bits, and think in research as well, I think the nurses, the morale is low because of the pressures they get and I think that people are frustrated as well, I think. " (Participant ID:046105)

Managing Complexity and Disease Burdens: "I think the difficulty is with cancer is that, well cancer has been, up until very recently, the biggest killer in the world, you know, **health burden** problem. So, we obviously need to research cures in lots of ways, and as we've got more knowledge about how cancer manifests itself, although we're still a way of knowing everything, aren't we? I think we then have got to look at so **many different multi-faceted tumours** if you like. So, saying I've got prostate cancer, or I've got breast cancer does not mean the same for the next individual, and I think we're moving toward that prescriptive drug now, and when I mean prescriptive, I mean for that individual. So, it becomes more and more complex in that finding the right person that will fit that criteria of that drug in the early stages...But I think just the **emotional**

complexity of cancer, despite it not being the biggest killer anymore, people don't know that they don't hear it and there's a lot to deal with. You're diagnosed with cancer; your immediate thought generally is that you are going to die. And I think there's a lot to deal with that there, so I think that actually adds in a layer of complexity. The trial itself might be quite simple but you're dealing with an emotional person, so that does make it difficult. But I do think that one size not fitting all is a big issue in cancer complexity. And you know we talk about cancer as a disease, don't we, but actually **it's a million different diseases and that makes it complex**. You can't say, 'Oh, I'm a cancer nurse', in lots of ways because actually what is your specialism?" (Participant ID: 050102)

Networks Responses to Complexity: "I would suggest that the complexity, the increasing complexity of cancer trials is not something that we are lobbying on, because it is a given for our peer group, is that the way that cancer trials in general are going is more complex, more targeted, more around kind of personalised medicine which brings inherently a complexity and a smaller number of potential participants, so I cannot say hand on heart that we are lobbying against that...Everybody is in agreement that this is a fact, this is something that is happening. **We don't think that we as a collective see that there is anything that we can do about it at this time. We are not reacting to it.**" (Participant ID: 050101)

Acknowledging Complexity and Follow-Up Burdens: "...the CRN are basically a defunct organisation and they do not understand the needs of research anymore...follow-up's a huge, huge burden...follow-up is going on for longer. Cancer studies, one of the primary or secondary outcomes is normally disease progression or both, probably. So, the whole point of these studies is that you have to follow-up these patients until they die and then studies will want to extend their, often they are ten years or death, and if they are only ten years they'll want from now on to extend. And then you've got your CRN and manager-type people saying, 'Well, you want to cut follow-up, not do more, don't accept the amendments'...but actually how valuable is that for the study? You've done all that work and you're defeating the object, and then you get people saying to you...'well can't you just tell them [the sponsor/trial centre] that you're not going to do the follow-up?' What? That's the primary outcome of the study. How can you not do the follow-up?". (Participant ID: 0010106)

Table 6.3 Analytic Quote Memo - Manageability

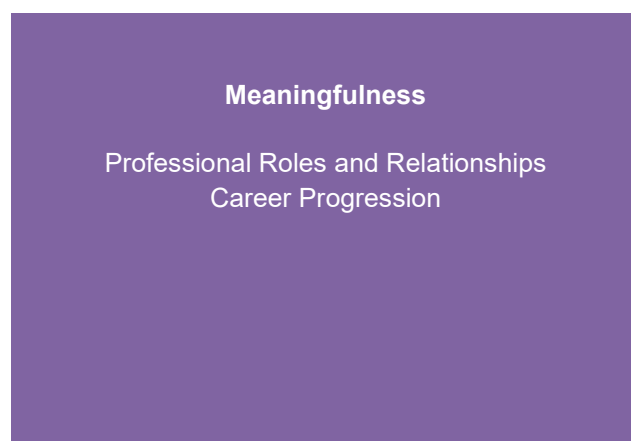
The capacity and capability paradox was identified as an early theme and potential conceptual category in the foundational literature review (see section 2.3.1).

Work-related Pressure and Stress.

Interviewer: "Do you feel under pressure at times or stressed?"

Participant: "Oh, yes. Without a doubt. We all do at times." (Participant ID: 001102)

6.4.3 Meaningfulness – Roles and Goals



Analytic Quote Memo - Meaningfulness for CCT Research Professionals

Meaningfulness - What are shared perceptions of meaning, meaningful activities, or value concepts?

Professional Roles and Relationships: "...governance is around the staff and their needs, and our responsibility is to support our staff as we go through the process as well. So again, part of that is around the processes and procedures in place but the rest is around emotional support for staff. So, they know if there's a governance concern, or the consultants have gone to fast with recruitment, or there are other issues that we've got around transparency, supporting and issues that we will have will be around information, training, understanding. And so that's where I see really, I've tried to make a difference in the role." (Participant ID: 005106)

Career Progression: "I don't think there is a career progression for research nurses at all. Once you're a research nurse what do you do? There's nowhere to go afterwards." (Participant ID: 001102)

Autonomy and influence: "In medical, well in nursing professions especially, they're sort of told to do something and they will do it without any questions...and nobody's ever asking any questions why, until somebody comes from above and says 'No, we have to do it this way', and then we change." (Participant ID: 001103)

Organisational Culture and Coherent Relationships: We've been told recently that we're not allowed to pass comment about this SOP. That's it. 'Please don't share your ideas, minutes won't be taken from this meeting'. So, for example, if we have a meeting, they won't take minutes. So, it's like, 'Well why are we having this meeting because it didn't happen if we don't have minutes?' So, it's things like that. With the new managers that have come in, they're

making their own little rules now, so I'm just ignoring it, hoping it will go away. But it's made me angry, and I'm not listened to really...loads of people at the top who are making everyone else crumble". (Participant ID: 024101)

Meaningless Activities/Concepts: *"The biggest problems for us I think is queries from the sponsor, which are meaningless and stupid and they're getting worse and worse...it does seem to be extremely pedantic now...you know the disease, sorry the toxicity that you've put in, for example, Cold Sore. They go 'it's not in the CTC grading'...and you go, 'well it's a cold sore, mate'...and you have to try and find something else, which funnily enough in the CTC grading, doesn't actually fit what a cold sore is. So, it'll be a lip infection others. You think that's less information that I'm giving you know. You've actually got me to give you less information. "* (Participant ID: 002102)

Ethically Meaningful and Equitable Practice: *"...the level of complexity of studies coming in is enormous...with the personalised slash stratified, whatever you want to call it, programme going forward. There will be a whole group of patients that we're not going to be able to give treatment to, and it's because their molecular make-up won't, they're not right. They haven't got the right DNA or whatever it is. We know that our treatment won't benefit them, so we know that it would be better not to give them treatment, but culturally people will expect treatment."* (Participant ID 010101)

Professional Values and Motivations: *"We all work for the NHS, so we run a ship and the obligations of our roles to assist our colleagues is very important, to keep the wheels turning and to set up studies in a timely manner, particularly for cancer sufferers where there is a time factor for care."* (Participant ID: 005121)

Patient-Professional Relationships: *"You get to know them, don't you? You're part of their journey from the beginning to, whether it be that they come off the trial or whatever the end is, you're there."* (Participant ID: 034109)

Relation to Management: *" It can be difficult when you don't have the support from your manager to support you trying to help them change and develop into a better service and a more efficient service ."* (Participant ID: 033105)

Variation in work: *"I like to have my own workload. I like to have my own caseload of patients. It's very similar to looking after a clinic of patients on the chemotherapy suite. I suppose it's a little bit like having, it's your own speciality, so it's almost like a Clinical Nurse Specialist's role on a smaller scale, if you like. And there are different facets and assets to the job, so it's very varied."* (Participant ID: 033110)

Strategic Direction: *"So my role is part of the leadership team of the network, so I work with our COO and set strategic direction for the work that we do. It's driven very much by our performance operational framework, which is a contractual document...Part of that is a*

*speciality level objective and the idea from my perspective is that the Research Delivery Manager is **doing a very similar thing**, regardless of what division they look after, **regardless of what speciality we** look after. We are there to try and ensure the deliveries of the studies that has been given that management label. That means that we work with our **systems and processes** within the Network to make sure that things are coming into the system, identified into the system, **disseminated**, making sure that the studies are set up. We're keeping an eye on performance in terms of recruitment, erm and any issues in either of those stages, erm that we **interrogate** those issues to make sure that any appropriate steps are taken. If necessary, acting as a **point of escalation**. We, as RDM, in this region, **we are removed from the clinical coalface of delivering the research**. We oversee using a number of **mechanisms**."*

(Participant ID: 050101)

Table 6.4 Analytic Quote Memo - Meaningfulness

6.4.4 Resiliency in Practice

To enable resiliency in organisations and in the practical delivery of healthcare interventions and solutions, leaders and policy developers need to be inclusive of their global population who are the life representatives, and the 'means and the ends of governance' (Chandler, 2014). Chandler (2014) situates resilience in relation to complex life and governance and postulates that it facilitates individuals to overcome barriers and further states that:

"Resiliency-thinking enables power to rule as the governance of life: enabling, empowering, facilitating and capacity-building....Life is the means and ends of governance with practice-based policy-making, self-reflexivity, feedback-loops, reflexive law-making and the inculcation of community capacities and resilience."

The research data demonstrated that NHS is not designed as a reflexive organisation with multiple instances cited of hierarchical governance approaches which were blind to the needs and capacities of patients and professionals, which inevitably restricts its ability to provide person-centred policies at the same time as developing sustainable, capacity-building healthcare delivery solutions. Clinical research delivery, which is conducting experimental studies with ranging complexities, phase-stages and end points is highly sensitive to context (from both human and environmental contexts), with greater degrees of variability and emergence in its operations and relationships, compared with standard care, yet is governed by an external NHS partner who lacks the necessary insight and policies to respond to the context-dependent realities of patients and research professionals. This results in incoherence in the management of its processes and practices leading to barriers to efficient practice and care as well as negative perceptions and experiences.

6.4.4.1 Consistency and Supporting Relationships

Patient Follow-up, Consistency and Linked Concepts of Salutogenic Environments

In the following interview extract the importance of adopting a salutogenic approach within healthcare delivery and clinical research teams is highlighted and shows the relationship of the properties of a sense of coherence, and the linked concepts of sub-properties of consistency, coping strategies, clarity, and communication. The participant also introduces an abstract notion of 'benign humour' as an emotional coping mechanism, which aligns to a "humorous cognitive reappraisal of adverse circumstances" (Perchtold et al, 2019).

Analytic Quote Memo: Consistency and Supporting Relationships

Q: **Follow-up** as well from a **patient and nurse perspective**...a lot of patients want to see the same nurses right from when they are recruited...right throughout their journey, and a lot of nurses want to see those patients...but if we're trying to think of better ways of doing follow-up...should it be the same nurse or perhaps a team?

P: "Patients always love to see the same nurse because you get to know each other. It's like anything that you, the more familiar you are, the more comfortable you are, but having been a midwife for a short time I can see the team approach model. And I think if we're honest with our patients at the beginning, that we won't always, that you won't always see them but there is a team...I think we have to be really realistic and pragmatic. Yes, I would love to see the same patient, week in week out and then follow them up and then when they drop dead have a big emotional upheaval. Sorry, rather inappropriate." (Participant ID: 010001)

Q: It's part of the role though, isn't it?

P: "Oh, absolutely. You know, especially on some of our pancreatic trials and erm, you get quite poorly melanoma patients, well we can get poorly anybody. But yeah. I think that's something that we need to look at, support for." (Participant ID: 010001)

Q: Now the role of the research nurses is quite a specialist role, you've got to have a lot of skills. Do you, in terms of retaining nurses, do you have a fairly stable staff at the moment?

P: We went through a period where we lost a few and then we had a little look at what we were doing...that's helped us make some changes. We have a very strong flexible working policy...we also have a buddy system...we want to encourage cross fertilisation...in a friendly way...we have a coffee club so that they're all mixed in. When people first start, we have a welcome morning...they have an overview of what's what...they have input from the lead professor, our director, myself, so they have a good understanding of where we're going, what our views are. We have quizzes. I make them do some craft, you know, a whole

range of things...The team leads are very well supported...I and other people have worked really hard on putting these things in place...I don't think you can underestimate, when you are asking your staff to work above and beyond, all this has to be right." (Participant ID: 010001)

Table 6.5 Analytic Quote Memo – Consistency and supporting relationships

6.4.4.2 Interprofessional Relationships: Tension and Tension Management

Tension and tension management arose as key themes in the study. Effective and sustainable interprofessional relationships and collaboration in clinical research and healthcare work environments rely on the successful navigation of conflicts and diverse perspectives. One participant described the concept of tension:

“And tension sometimes. People constantly think that somebody should be doing something else and somebody else doesn't know, they constantly frustrate each other or eventually just cut each other out of each other's processes”. Participant 050101.

In the following memo the concept of **empathy** for the situated challenges of other professionals is described by a research professional interview participant, and an unconventional approach adopted in overcoming workload and capacity challenges. This pragmatic tension management technique demonstrates the unique and creative strategies adopted by site professionals to achieve positive outcomes for patients participating in clinical trials, where local resources are stretched, and support department colleagues lack sufficient capacity.

Professional Empathy and Tension Management Memo
<p>Understanding Peers: ‘Radiologists love chocolate’</p> <p>‘There are certain pockets of attitudes, however, what we do is overcome that by actually spending more time with those people and making life a bit easier for them, providing chocolate. Radiologists love chocolate.... So, when we need films doing, and they're tearing their hair out, and you say, “I know. It's horrendous what you're going through. We understand, but look, here's a Twirl” [laughs]. (Participant ID:024101)</p>
<p>Analysis: The above extract includes the concepts of ‘bribing colleagues’, ‘collaborating’ and ‘empathising’ in the process of overcoming challenges and barriers relating to localised context. This is a characteristic of resiliency in practice. The stressful workload of the radiologist is inferred.</p>

Table 6.6 Analytic Quote Memo – Professional Empathy & Tension Management

6.5 The Healthcare Environment: Professional and Clinical Spaces

The environment in which we live and work has a profound impact upon our psychological and physiological capabilities as well as influencing our professional and practical capacities to manage our duties and routine activities in our daily lives. Environment, and its role in healthcare, both from a patient's and professional's perspective is a neglected area of public health and policy. The environments in which research professionals conducted their profession, and the associated access to appropriate facilities and resources formed a significant element in all stages of the research. These important components of real work healthcare impacts were explored in detail with research professionals in the later interview stages of the study. Themes emerged which highlighted complex relationships between the healthcare environment in which cancer clinical trials are conducted, and associated domains impacting patients and professionals and their ability to cope and manage in particular circumstances. The results of our study highlight a need to develop a strategic programme of improvement to address the existing challenges within the NHS as both a workplace and a healthcare space for patient treatment and care. Hanson (2007, p229) in highlighting the importance of the workplace as a setting for health promotion quoted the WHO declaration (1967) which states, "Comprehensive workplace approaches are essential which take into consideration physical, emotional, psychosocial, organisational and economic factors both within work settings and all other settings, in which people fulfil their multiple life roles...This approach is based upon the following four complementary principles: 1. Health promotion, 2. Occupational health and safety, 3. Human resource management, and 4. Sustainable (social and environmental development)".

6.6 Clinical Research and Healthcare Delivery

Augmenting complexity and increasing demands on resources were revealed in the study with personalised medicine and immunotherapy approaches proving challenging.

"Immunotherapy definitely means that we are looking at a lot more body systems..."
(Participant: 029114)

Contextual Challenges, Uniqueness and Complexity: *"If you really want to improve research in the country you can't always, you know, benchmark with big teaching hospitals or simple settings, where it's on one site in a big city, and it's easy to get the patients there. So, you need to look into where actually the population is. And you need to look at, within rural places such as Lincolnshire or other areas, but you also need to appreciate there is a rural factor but there is a very good response on how we are actually dealing with, and now*

we are very good at doing what we do in a very difficult environment. That needs to be part of the, you know, the funding. Patients in [Name of Rural County City] are not the same as patients in Central London or Cambridge (Participant ID: 001118)

Clinical Research Policy and Strategies in the NHS.

In undertaking an evaluation of operational delivery of cancer clinical trials within the NHS, the research has focused on the local circumstances of clinical trial sites and the teams involved in the direct delivery of clinical care and trials to patients, or closely linked to the delivery of local research practices and policies. The research professional perspectives and narratives presented in this thesis, whilst spread across differing sites across England and Scotland, and involving many differing clinical research roles and professions, do reflect a cohort of professionals working in close proximity with patients. The broader relationships and their interaction with external networks and organisations represent faceted views of the complexities and challenges of the operational delivery of clinical trials. This provides a contextualised understanding of local circumstances and the concerns of professionals within those clinical and patient-orientated operational roles, as well as their issues and problems in socio-strategic relations. **Strategic misalignment** of values and goals between professions and organisations was highlighted in the testimonies of research professionals delivery clinical trials across the UK. In the following statement the coherence between the clinical professionals who are delivering research at sites and the Clinical Research Network (CRN) who are there to facilitate and support research delivery in the NHS is critiqued, with reference to the growth of targeted treatments.

“ That’s something the CRN don’t get. They are behind the times, and they need to catch up. The treatments are not big trials, even AML trials are changing, they are becoming really targeted. It’s different mutations, different genetics, you know, that sort of thing. You see, you’ll have within maybe AML...well actually within breast, you haven’t got breast cancer, you’ve got maybe 20 different breast cancers. Each one will be treated differently with a targeted drug. And that’s a huge problem for clinical trials, because it means we’ve got to, instead of opening one big trial to enter all our patients in, that could be good numbers, that could be good money, you’re now going to have to open 20 trials. Massive amount of people, time input from R&I staff and delivery staff, and you’ve got to maintain those trials, amendments, all the stuff that goes with them. Not to mention knowing the protocols, what you’re doing, screening the right patients, and you’re going to get small numbers in them. So, you are going to have 20 trials with maybe 5 in each, instead of one trial with 50 in. And the CRN don’t like that.” (Participant ID: 001106)

The failure of NHS and NIHR leadership teams to engage with complexity or recognise the challenges faced by sites in delivering clinical research was a source of tension that was highlighted by many of the teams involved with the practical realities of delivering clinical trials at sites. One senior research professional related the difficulties faced in trying to open up negotiations with leaders around the challenges sites faced in the following quotation:

"I have said to the network on so many occasions about complexity...I mean I've actually been told by [Network leader name] in a meeting 'We're not going to look at complexity because it's too complicated'. I think it serves them not to recognise it."
(Participant ID 029114)

Another participant described the nature of disconnected and remote leadership and the impact of neglected communication and understanding of the contextual realities of both workloads and environments in trial delivery and follow-up. Responding to a question on how research nurses manage complex studies, patient follow-up and the opening of new studies the research delivery professional stated:

"It's very difficult, it's very difficult, because we're being pressurised into recruiting and the follow-up work isn't being acknowledged, and never has been...There isn't the training there and we should be training our staff because people are getting despondent, and they are leaving...They know [the NIHR]. They know there's a problem with follow-up. They've always known there's a problem with follow-up...I don't know. I mean sometimes I wonder whether people [leaders], they may have done the job in the past, but people soon forget what it's like on the ground...it's like the decisions that are being made about services and everything. People need to be on the ground...come out with me, come to clinic, get an understanding for what we do. I don't think they understand, and you can tell someone until you're blue in the face, but it's like me saying, 'Oh, it's been horrendous in clinic', but unless you come to clinic and actually see what we are dealing with, you don't grasp how bad it is. Most people don't know where actually here in [site name] ...like facilities, the buildings falling down at this end. There's buckets in the corridor. When it rains, sometimes it comes through. Should we really be working in this, really? The toilets are disgusting. Should we? Does this do anything for staff morale? I mean my health's never been worse than it has since I came to work here." (Participant ID 001117)

In the above extract there are a number of important concepts and provide examples of interacting phenomena which relate to the complexity of systems and useful in using as analytic data extracts to evaluate the utility of a **Sense of Coherence** model, as a tool for

bringing together key focus areas of the research from three short interview data extracts. In Figure 6.6 below the inter-related nature of these concepts are highlighted, with references to conceptual memos. The quotation on '**Acknowledging Complexity**' was captured as a Memo in MAXQDA and is useful as a short extract from the research professional interviews, to illustrate an example of a 'slice of data' which is used for the purpose of analytic comparison and theoretical sampling. It also illustrates the challenges of inter-related properties in complex adaptive systems, and the value of acknowledging complexity as drawing attention to the diversity and plurality of experiences and challenges in healthcare operational delivery. The value and approach in recognising the infinite variety of circumstance and the role of prismatic perspectives is discussed further in Chapter Eight.

Analytic Process Memos : Slices of Data and Theoretical Sampling	
Networks Acknowledging Complexity 029114\Communicating and Collaborating\'we're not going to look at complexity because it's too complicated'. (Participant ID: 029114)	
Theoretical Sampling: The above data extract was coded under the category of Communicating and Collaborating in the Research Professional coding framework, but could also be re-evaluated when analysing and comparing data involving the concept of Moral Vacancy . The extract also links the notion of Acknowledging Complexity to a Sense of Coherence and its sub-property of Comprehensibility .	

Table 6.7. Analytic Process Memo

6.6.1 Acknowledging Complexity or Moral Vacancy?

The consequences of moral vacancy in leadership have significant impacts for the future sustainability of operations and the retention of skilled and experienced staff and where there is a neglect of the needs of patients and professionals the outcome may result in cases of moral injury. Shale (2020) states, "potentially morally injurious circumstances arise whenever patients are harmed; when staff are poorly treated for raising concerns; when patients or staff suffer discriminatory behaviour; when inadequate resources put staff and patients at risk; when there is avoidance of accountability at the highest level of public institutions and so on." Developing moral awareness and empathy amongst healthcare leaders, strategists and governing bodies, and the importance of engaging with grounded experiences, complexity, and multiple perspectives, is an urgent imperative. A salutogenic approach to healthcare and its environments, offers the potential to co-design clinical, research and care models which are ethically and operationally sustainable. The multiple examples of professional disconnect and discord between research professionals was incorporated into the concept of **prismatic perspectives** and captured in an early memo

on **collaborative endeavour** and properties of *mutual respect* and *shared values* between healthcare and clinical research professionals which links to **professional empathy and tension management**. What funders, leaders and strategists choose to focus on as priorities, and which realities, professional resources and capacities are either neglected or misunderstood, can have significant implications for the health and wellbeing of patients, professionals working in those systems (and fields) as well as the ‘health and efficacy’ of those systems. Kline (2019) states that inclusive approaches in healthcare delivery will facilitate recognition of valuable sources of information: “the reports and voices of patients, carers and staff” and that NHS leaders need to act upon that understanding, and suggested that such ‘enabling inclusion is an essential pre-requisite for success, not an optional extra.” (Kline, 2019).

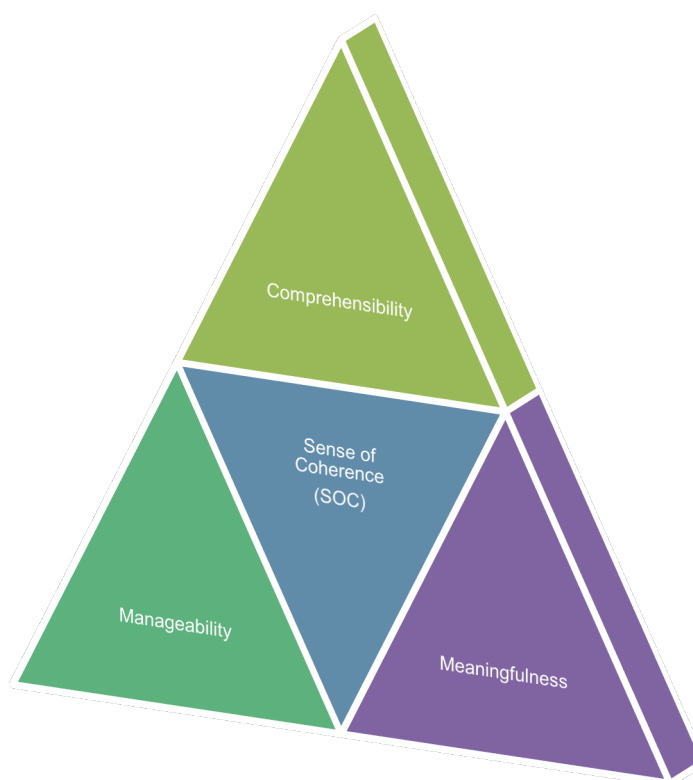


Fig. 6.6 Sense of Coherence in Clinical Research

6.6.2 Coherence and Interoperability

For meaningful and effective collaboration and engagement between differing social, cultural, organisational, or political entities it is necessary to achieve coherence in strategic goals, visions, and values. Coherence and interoperability are capacity and capability enabling conceptual properties within complex systems, which facilitate communication, understanding and information exchange between different groups, organisations, or networks, where there is either an interface or interaction or exchange between varied components. Berteau (2005) describes coherence as a type of ‘internal interconnectedness’

and ‘plausible connection’ that is non-linear, circular and symmetrical. Whilst there may be differences in the perspectives and foci of interacting parties or interfacing elements within the linked systems, there needs to be **comprehensible**, **manageable**, and **meaningful** relationships (all properties of a **sense of coherence**) in order to achieve operational effectiveness or a convergence of understanding. This requires the acceptance of **prismatic perspectives** relating to contextual knowledge and experiences but a shared ambition to converge and synthesise situated understanding to form a higher level of knowledge using a **Prismatic Coherence Model (PCM)**, a conceptual construct which offers mutually supportive systems and processes to manage complex operations. The concepts and properties of prismatic coherence are further discussed in Chapter Eight.

6.6.3 Follow-up and Complexity in Cancer Clinical Trials: Professional Perspectives

Follow-up Quotes - Research Professional Perspectives on Follow-up in CCTs

Research Professionals and Patient Follow-up – Research professionals experiences and responses to delivering or supporting patient follow-up and interventions in cancer clinical trials.

Table 6.7. Quote Memo – Follow-up

Complexity Quotes - Research Professional Perspectives on Complexity in CCTs

Research Professionals and Cancer Clinical Trial Complexity – Research Professionals’ perceptions and perspectives on the nature of complexity in cancer clinical trials.

Offering novel treatments: "...offered the opportunity to take part in research which could be a novel treatment, it could be about, you know, long term effects, those sorts of things so I think that is an **added layer of complexity**." (Participant ID: 050102)

Table 6.8. Quote Memo – Complexity

6.7 Chapter Summary

The results of the research professional studies have highlighted the need to develop responsive, supportive, and integrated models for healthcare promotion and delivery. Failure of leadership teams to engage with the challenges and complexities faced by sites in delivering clinical trials was a common theme across participating sites.

Chapter Seven: Patient Perspectives - “It’s what was involved that was puzzling me”.

“February 11th Day 6: I am on my own again, my sole companion being Parrot. We both despair at my present (hopefully only present) inability to whistle. This is our means of communication which - as an unusual (presumably) side effect - has been taken away from us. Parrot is very bewildered, and I am depressed. My consultant says it is nerves which are drug-affected...Poor Parrot, poor me” (anonymous participant, 2019).

7.1 Introduction

This chapter presents the synthesised results of the patient participant Delphi, questionnaire, and interview studies, providing unique insights which are representative of the voices of NHS cancer patients who were currently or had previously participated in a clinical trial. The core categories and their properties which emerged from the data, are the result of the applied theoretical sampling and use of constant comparison, and investigate themes of complexity, health, and clinical trial participation from patients’ situated experiences. Whilst some of the categories and properties discussed are linked to existing research and theories, the application and further development of these ideas is unique in the construction of a grounded theory for clinical operational research delivery. The creation of a *Prismatic Coherence Model (PCM)* provides novel explanatory evaluation tool, and an approach to designing and planning sustainable operational models for complex environments, be they in a clinical research and healthcare operational delivery context or wider fields involving complex socio-cultural and technical phenomena.

The core category of ***being human***, with its related sub-categories and properties, are elaborated and discussed in relation to the conditions and circumstances to which they are relevant and in the field of cancer research operational delivery in the NHS. The emergent concepts are illustrated through the use of direct participant quotations from the source data, which were compared to wider findings from literature pertinent to the emergent theory. The findings from the patient studies are compared to perceptions and experiences of research professionals to form the integrated grounded theory, which is discussed in Chapter Eight. These concepts are discussed in relation to their situated, contextual relevance and value from participants’ viewpoints, but are then further compared to wider healthcare and operational contexts and reviewed at different conceptual levels.

7.2 Patient Perspectives and Study Results

The overall participant accrual for the EFACCT patient studies is summarised in Figure 7.1. The nature of each of the studies and their contribution to the overall thesis is discussed in the following sections. The names of patients and the sites where they were recruited have been removed to protect patient confidentiality. Where quotations and extracts from the research data are used, in order to illustrate theory development and key concepts, the participant's unique ID number is shown. The first three digits of the participant ID represent the recruiting site and the location of where the patients were treated and took part in a cancer clinical trial.

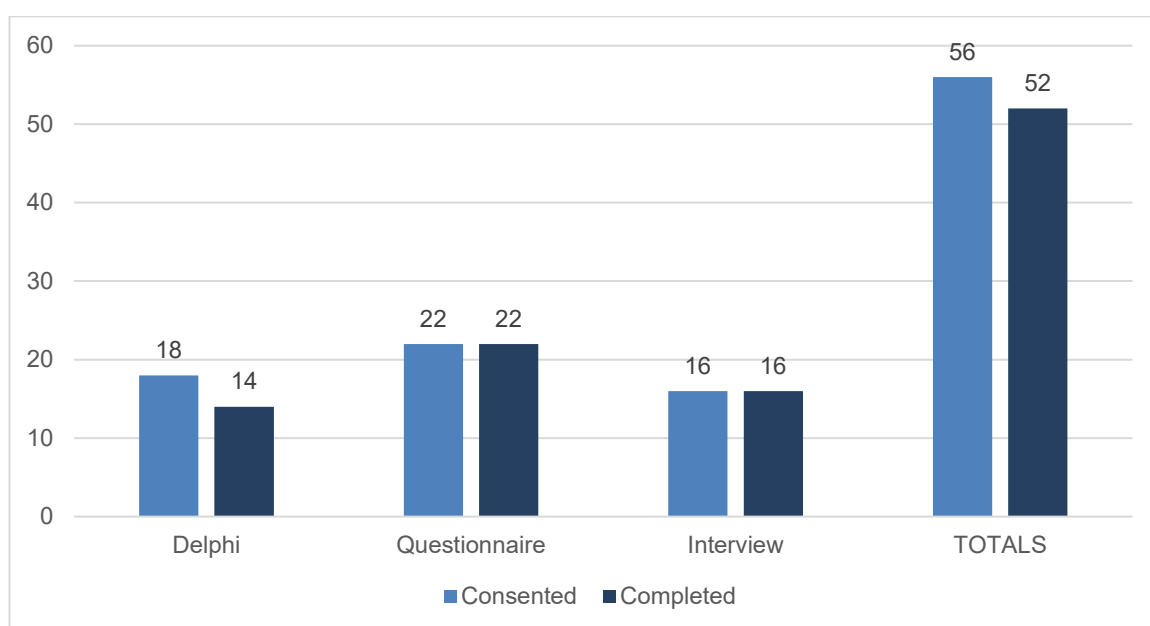


Figure. 7.1 Patient Participant Accrual to Completion by Study Type

7.2.1 The Patient Delphi Study

The Delphi study, which was the initial participant data collection element for the research, recruited and consented eighteen participants from NHS sites who had agreed to take part in the EFACCT study. The Delphi panel constituted research participants who had previously taken part in a cancer clinical trial and were recruited from a wide geographic base of NHS secondary care sites across the United Kingdom. The distribution of panellists is shown in Figure 7.2 below. The Delphi patient panelists provided their responses online or via post, to a three-part Delphi, commencing with an initial open round questionnaire, and the option to add free text comments in subsequent rounds. Fifteen cancer trial patients completed the Delphi study, with one patient withdrawing due to declining health, one site not returning the consent form and one postal participant failing to respond to the initial first round survey.

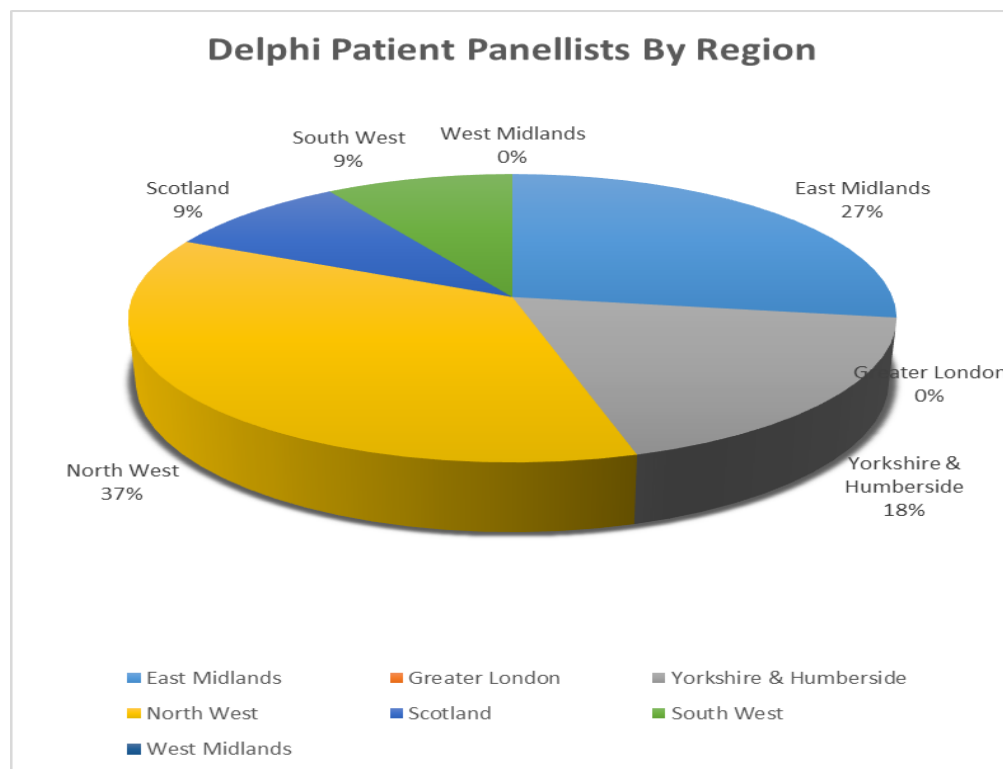


Fig. 7.2 Delphi Panellists by Region

7.2.1.1 Consensus and Levels of Agreement

Consensus was considered as being reached where 70% of the expert panel selected the same agreement option for an item on the 7 point Likert-type scale (level of agreement). All items achieving frequency consensus and median strength of agreement in the final round (round 3) were put forward as items for review in the questionnaire and interview studies. The items achieving consensus are reported under the summary question headings, shown below. The original questions asked in the opening Delphi survey are detailed in Chapter Four in Table 4.3.

Consensus statements by question section	Qty
Total Statements Achieving Consensus	44
Q1. Experiences of participating in a clinical trial	10
Q2. Patient benefit, support & efficient practice in clinical trials	12
Q3. Support, treatment, care services & processes in clinical trials	5
Q4. Key priorities to enhance patient research experience	14
Q5. Additional patient Delphi comments	3

Table 7.1 Patient Delphi Consensus Statements

7.2.1.2 Every patient is unique

The outcome of the Delphi study developed understanding of patient experiences which contributed to the design of the subsequent questionnaire study and interview questions. Panel participants received a final report of the outcome of the Delphi study, which highlighted that the statements which did not reach consensus were also considered important in understanding patient experiences across the UK. Themes raised which were not experienced by the majority of participants were as important to understand and review in later research stages, as well as the items which achieved a high level of consensus. The patient Delphi study highlighted common themes of importance to research participants, even though panel members may have had varied experiences in relation to these. The individual and emotional content of patient responses highlighted the complexity of managing patients, whether they be participants on a trial or receiving standard of care treatments.

Using consensus methods to ascertain key areas of importance to patients is a useful starting point in a grounded theory mixed-methods study design, but items achieving high levels of consensus are only one faceted perspective of patient experiences. The outliers and unique personal realities of patients are just as important as the general 'experience consensus'. Individual responses carry significant weight, value, and importance, even if they are situated outside of the general experience of others. The complexity and skill in the management and care of patients, and one which brings workload and intensity into the delivery of patient treatments, interventions and follow-up care, is the importance of ensuring that patients feel valued and that their thoughts, sensitivities and personal circumstances are recognised and responded to. An early reflexive diary notation from the patient Delphi study captured initial personal thoughts on the sensitive nature of participant responses to the open questions posed in the first qualitative round.

Patient Responses: As a researcher I was unprepared for the emotional content of patient responses and comments around the nature and knowledge of dying.

Subject Matter Sensitivity: I found the sensitivity of the subject a challenge in considering what would be appropriate to include as statements in a second round.

Sensitive Statements: The researcher has a role in determining whether a statement should be included or excluded due to the sensitivity of the statement and concern about the effect that the statements may have on other members of the panel.

Issues of Patients: As a researcher I was not prepared/sure how to deal with a patient's statements which raised issues of care and patient handling at a specific trial site.

The following extracts from the patient Delphi highlight the complexities of patient management, and the important role in the management of a patient's psychology and emotional responses to clinical treatments, environments, and relationships. The first extract demonstrates that the patient does not have the sufficient psychological capacity and resources to manage his diagnosis and the rapid events unfolding around this, as well as consenting to participate in a clinical trial. The patient felt that not participating may jeopardise his treatment. This experience contrasts with the second extract, where the patient feels central to the process, involved and informed. These responses were provided in answer to the following question:

Q1. Please describe your experience of participating in a cancer clinical trial detailing any elements which you felt were complicated or difficult for you, took up a lot of time or where you would have benefited from additional support. Please feel free to list as may issues or concepts as you wish.

Patient Delphi Free Text Comments	Q. No.	Pat. ID
'When I was first diagnosed it was a shock , and during that first contact I was enrolled onto the trial with my consent, but without really understanding the nature of my illness and without understanding what being on a trial entailed for me. I did not have the time or facility to process what was happening, I was eager to be seen as cooperative so as not to jeopardise my treatment , this was due to shock, confusion and being scared . Within a very short time of being given my diagnosis I had a bone marrow biopsy, a list of appointments for Chemotherapy, a large bag of medications and bloods taken. I also signed up for the [STUDY NAME] trial, all within one hour. All of this was difficult to comprehend , and I really didn't know what the trial would do, except that it was for the benefit of others in the future. '	Round 1, Q1.	012001
'My experience of participating was quite an interesting one. At no time did I feel uniformed or worried. The team that supported the trial were very inclusive of the patient and at all times I felt that I was an integral part and was always kept informed. '	Round 1, Q1.	001001

Table. 7.2 Delphi Panellists Free Text Comments Round 1.

The contrasting experiences of patients as part of their experience, highlighted in the initial opening Delphi round, contributed to the formation of early concepts around **prismatic**

perspectives, patient-clinician relationships, and comprehensibility, which were captured in handwritten memos in a reflexive journal.

The role of the Delphi study as a mechanism for patient reflection over time and in relationship with the experiences of other participants, had a significant effect on one particular panellist. With the intervention of time for reflection and comparing their personal responses to those of other panellists answering the same question, the patient provided a very analytical and self-critical review of their initial responses in the opening Delphi round. The following comments from the second and third rounds illustrate that the patient is clearly concerned that his perception wasn't the same as others and attributed initial responses to a lack of comprehension of the context situation. The patient changed his initial scores given to the statements in the second round survey, followed by a detailed breakdown of reasons for the change in his scores and altered perceptions. The language used also reflects the sensitive nature of the patient, which is an element adding to the complexity in the management of patients on clinical trials.

Patient Delphi Free Text Comments	Q. No.	Pat. ID
'It took me a while, a couple of weeks probably, to comprehend that there is a distinct difference between the functionality of the trial team and the ward clinical staff . I gradually became aware that there were different roles between the two and that the trials team had their own specific office. This distinction was never made clear to me. It would have been helpful to understand because initially I would ask the ward staff questions regarding the trial which they could not answer '.	Round 2, Q1.	012001
1) A change of response due to my acknowledging that I may have been more included than I was able to process at the time . 2) A change of response due to, upon reflection , although what was happening was not always fully explained to me , my questions, when asked, were answered by trials nurses. 20) A change of response due to my now reflecting that my original answer was unfair and not as accurate as I would wish . This latest response is more indicative of the liaison I received .	Round 3, Q1.	012001
I do appear to be at odds with other panellists , and my responses tend to be in a minority , or, maybe, I've been unlucky , but I'd like to point out that I haven't got an axe to grind , I am genuinely grateful to competent and approachable clinicians , in whose care I felt safe.	Round 3, Q5.	012001

Table. 7.3 Delphi Panellists Free Text Comments Rounds 2 and 3.

Research professionals and clinicians need to be able to comprehend and respond to the individual patient's sense of coherence and sensibilities, and be able to adapt to psychological and physical capacities and resources of patients when recruiting them to a clinical trial, and throughout their treatment and follow-up stages of the trial, or when they potentially transfer to standard of care, or a different trial or clinical/patient pathway. The temporal nature of patient capacities to manage situations and relational complexities are highlighted in the patient's narrative. In Chapter 6 the ideation of a Singerian Delphi was discussed and highlighted as a unique Delphi design that was adopted in this thesis. The potential to develop the Singerian Delphi further as a salutogenic methodology for patient experiential research, including its application as a process for developing a *Sense of Coherence* model for clinical research and patient healthcare delivery, should be explored in future research. The opportunities for patient qualitative and salutogenic research models will be reviewed in Chapter Eight. The Delphi survey final report is available on the study website www.efacct.com.

7.2.2 The Patient Questionnaire Study

The questionnaire study recruited twenty-two clinical trial patients from six clinical research networks across England and Scotland. All participants consenting to the questionnaire completed the study either online, via post, or whilst attending a patient clinic at a participating site. Statements developed by the patient Delphi panel formed the content of the questionnaire. Participants were also given the opportunity to provide written comments in the final section of the questionnaire, with a significant space provided to allow patients to relate their experiences of participating in a cancer clinical trial from a patient's perspective. Contrasting perspectives are shown in Table 7.3. These written narratives were later compared to the emergent grounded theory arising from the patient interview study coding.

Reflection by the researcher on participant comments from the questionnaire study also informed themes discussed with the interview study participants. Patient perspectives on the nature of relationships and circumstance in clinical trials and healthcare contexts were explored further, in order to understand their impact on the patient's ability to manage, comprehend and respond to their situated reality. It was important to compare patients experiences of care and their perceptions of relationships across different sites and research networks around the country but also to understand the localised differences of patient experiences and relationships taking part in clinical trials at the same site.

Questionnaire Section 4 - Patient Comments	Pat. ID
I am still on trial but not having treatment and feel sometimes I am just left to get on with it no-one checking I am alright and how everything is going.	005007
1) After consenting to the trial, I felt totally 'abandoned' by the research team with no contact from the research nurse or consultant that signed me up for it. 2) All follow up has been done by my oncologist with little input from the research team 3) During what I considered a critical part of the trial - finding out what arm I had been randomised to - I had to chase up the information over several days - from the allocated research nurse - causing me immense stress/anxiety which I didn't need. 4) The research nurse's attitude was anything but caring or professional when she finally gave me the result 5) The research nurse allocated was extremely difficult to contact and was poor at returning calls. 6) Participating patients should have regular updates from the research team about how the trial is progressing and access /information re results on completion. 7) Patients should be advised whether they would be eligible to be recalled into the trial for the most successful outcome .	005009
I was very apprehensive when I was first offered this trial, but I was fortunate enough to be able to confide in a friend who was very knowledgeable in cancer treatments and guided me in my final decision, this was the best decision I could have made . There are people who do not have this support , so it is vital that the support is given at first hand from the dedicated teams within the hospital.	005006
The staff have kept me fully informed of any issues and will contact a doctor immediately if I am showing any adverse symptoms. They are dedicated professionals, put you at ease and it is a very friendly atmosphere . After experiencing chemotherapy in a much larger unit, I am extremely grateful that I am able to participate in a clinical trial as you have one to one support .	034001
For me personally being part of the trial and having a team of experts on hand has helped me so much and it felt like a holistic approach to beating cancer which I felt is needed.	034002

Table. 7.4 Patient Questionnaire Free Text Comments

The importance of environment and relationships in the patient clinical trial experience and their cancer journey emerged as central concerns for participants. In both the Delphi and the Questionnaire study the socio-cultural aspects of healthcare and clinical trial delivery were dominant, with limited reference to the nature of the clinical trial in which they participated and the type and intensity of its procedures and interventions. The additional focus on patients, including extended follow-up of patients on a trial was predominantly seen as a patient benefit, with participants feeling that clinical trial participation was an enhanced form of care and treatment. The last patient comment in Table 7.4 demonstrates

a salutogenic perspective, in a sense that they see trial participation as a holistic approach which supported them in beating cancer, a salutary benefit of clinical research studies.

7.2.3 The Patient Interview Study

The themes explored in the patient interviews were emergent in response to earlier analysis of the Delphi and Questionnaire studies. The interview study recruited sixteen patients from seven of the participating sites. As detailed in section 4.5, interview participants were provided with topic guides (see Appendix 2), but the direction and format of the interview was responsive to the patient's individual experiences, with concepts emerging from earlier study elements introduced if relevant to the participant's circumstances, disease, trial and environment of care. The interview transcripts were coded using the grounded theory methodology as described in Chapter Five. As the coding progressed the themes were organised into a coding framework of ten categories (shown in Figure 7.3) which mapped closely to the categories developed from the research professional interviews (see Figure 6.5) and discussed in detail in Chapter Six.

In the same way that a sense of coherence offered a guiding framework to understand the perspectives of research professionals in relation to their role in cancer clinical trial delivering, the concept of a sense of coherence (SOC) serves the same pragmatic role in providing a guiding framework for the narration of the experiences and perspectives of cancer patients and their journey, with regards to their experiences as individuals, patients and participants within a clinical trial in the UK.

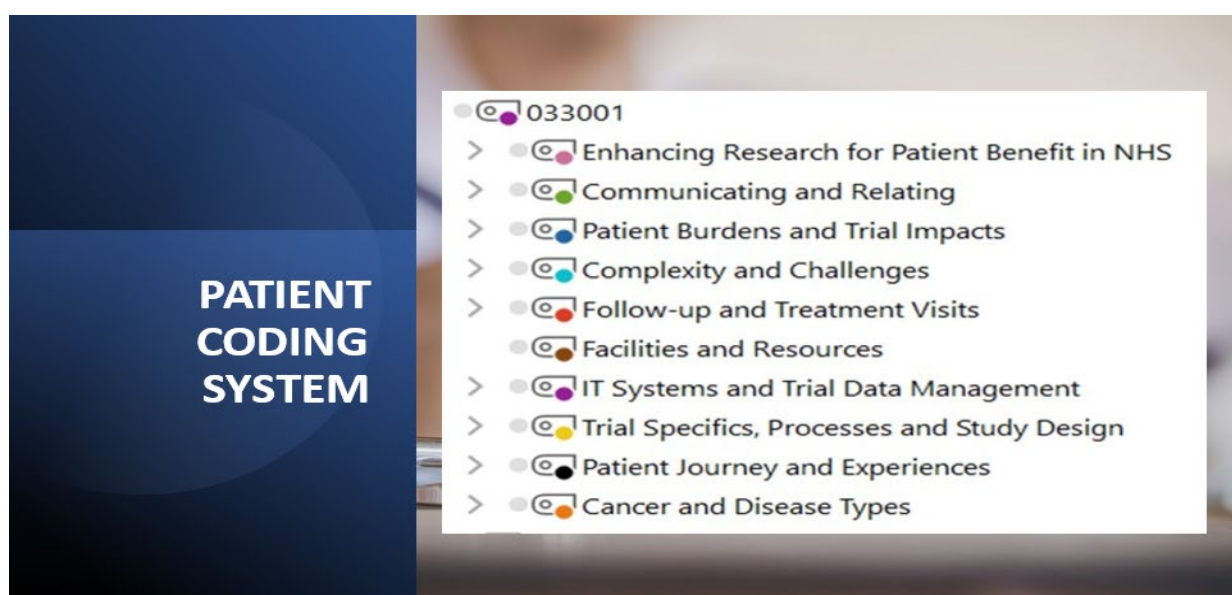


Fig. 7.3 The Patient Coding System

The patient's perspectives revealed detailed and highly personal journeys, and these are best understood through the interrelated sense of coherence constructs which all have complex associations across and between them, with sub-categories discussed in the following pages in this chapter. Key areas which link together the core concepts of comprehensibility, manageability and meaningfulness from patient stances include:

- Pathogenesis and Salutogenesis (the disease-health continuum)
- Relationships and Trust
- Communication and Comprehension
- Coping Mechanisms and Strategies
- Environment and Settings
- Health, Circumstance and Complexity

7.2.4 The Human Patient

The following extract details the nature of being human with terminal cancer and experiences of participation in a cancer clinical trial. The patient's narrative is inspirational, articulate, expressive and emotional, and it is enlightening how complexity and serendipity are important bio-psycho-social concepts embedded in our personal realities.

Being Human: A Cancer Clinical Trial Patient's Narrative (Participant ID: 002002)

Being Human Quotations

Genetic characteristics:

"I was classed as a **super responder** I had amazing results in the body. Fortunately everything had gone,"

Humour and hilarity: *"The particular team that I had at that time was brilliant in fact to the point where we was all getting into trouble for too much hilarity. You know, it's good because it actually brings you up as a patient."*

[raising up or bolstering is a resilience and coping attribute]

[humour is a coping mechanism but also a property of serendipity]

[self-advocacy]

"I've taken a lot of responsibility for my own treatment. I mean I was actually given my prognosis two and a half years ago, potentially 6 months, and I'm now two and a half years later still here still bouncing".

"You know you've got to be an advocate for your own health".

"And I'm now actually in a better position than I was at the point of that diagnosis, do you know, erm and I think had I not been my own advocate and done a lot of research, I possibly wouldn't be sitting here in these trials, possibly wouldn't be sitting here at all, you know".

[lucky - property of serendipity]

"Prior to that I was living up in [place name] in the middle of nowhere. Had my diagnosis been given then I'm pretty certain I wouldn't be sitting here talking to you at all, you know, because it would have been a mission for me to get anywhere. Especially now that I've lost my driving licence as well, I'm relying on other people to get me here, erm so yeah, I think that will be very, very difficult for some patients. I think I've just landed lucky because of exactly where I am".

Table 7.5 Quote Memo – Being Human

7.3 Patient Perspectives - Voices of Complexity and Individuality

Patients are individuals with complex emotions and differing responses to their environments and the people that they encounter during their journey as a patient. These interactions, environments, relationships, and unique factors may have a profound impact on both the physical and psychological responses of patients participating in clinical trials, and their wider journey as a cancer patient, from diagnosis, to treatment, to follow-up and beyond. The study of patient responses to their healthcare journey and the emerging nature of their differing stances and experiences are important concepts to be viewed from a prismatic perspective, to enable the development of contextualised and holistic responses to enhance both the experiences of patients and the optimisation of their healthcare and management, whether that be as a patient on a clinical trial, or as a patient receiving treatment and care in alternative healthcare settings.

The patient narratives are studied in relation to both the individual perspectives and perceptions of 'the patient's journey' and in relation to the concept of a **Sense of Coherence** (Antonovsky, 1979, p123) and its sub-domains of '**Comprehensibility**', '**Manageability**' and '**Meaningfulness**'. Generalised resistance resources (GRRs) which are enabled in the process of health promotion activities (Antonovsky, 1979), were studied in relation to the complexity of health and well-being from the human to the system levels, in order to develop sustainable and appropriate models of healthcare, whether this be in the field of clinical research trials, standard care, palliative care, or in any other bespoke medical and societal health care models, which seek to develop health promoting approaches which are human-centred and holistic.

7.3.1. Cancer Clinical Trials and Patient Comprehensibility

Golembiewski (2017, p272) states ‘the most important aspect of comprehensibility in healthcare settings revolve around the normalities of a patient’s sequential experience while negotiating ‘the patient journey’. Patients are individuals, with complex emotions and differing responses to their environments and individuals that they encounter during their journey as a patient. These interactions, environments, relationships, and unique factors may have a profound impact on both the physical and psychological responses of patients participating in clinical trials, and their wider journey as a cancer patient, from diagnosis, to treatment, to follow-up and beyond. The environment and stimuli in healthcare contexts affects patients differently, with some patients experiencing heightened responses with physical effects. Aron (2017, p233) states **Highly Sensitive People (HSPs)** ‘augment stimulation’ and ‘in a medical context they may appear more anxious or even “neurotic”. The study of patient responses to their healthcare environment and the nature of their differing stances and experiences are important concepts to be viewed from a prismatic perspective, to enable the development of contextualised and holistic responses to enhance both the experiences of patients and the optimisation of their healthcare and management, whether that be as a patient on a clinical trial, or as a patient receiving treatment and care in alternative healthcare settings.

The concept of comprehensibility that emerged as an explanatory concept for patients’ contextualised experiences and perceptions of their cancer or clinical trial journeys are captured in the following analytic quote memos.

Analytic Quote Memo - Comprehensibility for CCT Participants

Comprehensibility or the ability to comprehend, understand and make sense of one’s own circumstances, environment and condition or status from a patient perspective.

Understanding illness: “Patients... will look at their own illness and they will try and understand their illness.” (Participant 001001)

Layperson’s capacity for understanding: “Being a layman you don’t understand everything, you can’t, it’s impossible...although you try and take it all in you can’t, I don’t think the human brain, just doesn’t compute, or mine doesn’t.” (Participant 001002)

Lacking awareness of terminality/own condition: “I had one patient friend who sadly passed away last year, but she came onto the [name of trial] which is for terminally ill patients with stage 4 cancer. She didn’t know that she was terminally ill. She didn’t actually realise that this was as far as it could go, you know...she genuinely had no clue until I brought it up in conversation one

day and then we were all looking at her face and we were like, ‘Oh my god, did you not know?’ because she wasn’t the type of person to ask questions, do any research...she genuinely didn’t understand what the trial was about...she didn’t know that she was terminally ill”. (Participant 002002)

Table. 7.6 Analytic Quote Memo Comprehensibility

7.3.1.1 Pathographic and Salutographic Perspectives

“Pathography (noun) - The study of the life of an individual or the history of a community with regard to the influence of a particular disease or psychological disorder”.

<https://www.lexico.com/en/definition/pathography>

Hawkins (1999) suggests research into patient pathographies highlights a need for patient individuality to be recognised in theory and in practice, and that present-day pathographies are ‘a reaction to our contemporary medical model, one so dominated by a biophysical understanding of illness that its experiential aspects are virtually ignored.’ Written pathographies, or illness narratives, may enhance knowledge and understanding of the patient experience, with opportunities for the salutary benefits needing greater study in the field of cancer clinical trial delivery. Alongside the written word opportunities for other methods, including visual and graphical tools should be exploited to gain greater understanding of the patient experiences along the pathogenesis and salutogenesis continuum. Graphic pathographies are an emerging field which are useful in enhancing patient comprehensibility and meaning of their condition and experiences but also provide doctors with greater understanding of patients’ illness experiences and nuanced perceptions which may provide useful insights into their disease, treatment, compliance and prognosis (Green and Myers, 2010).

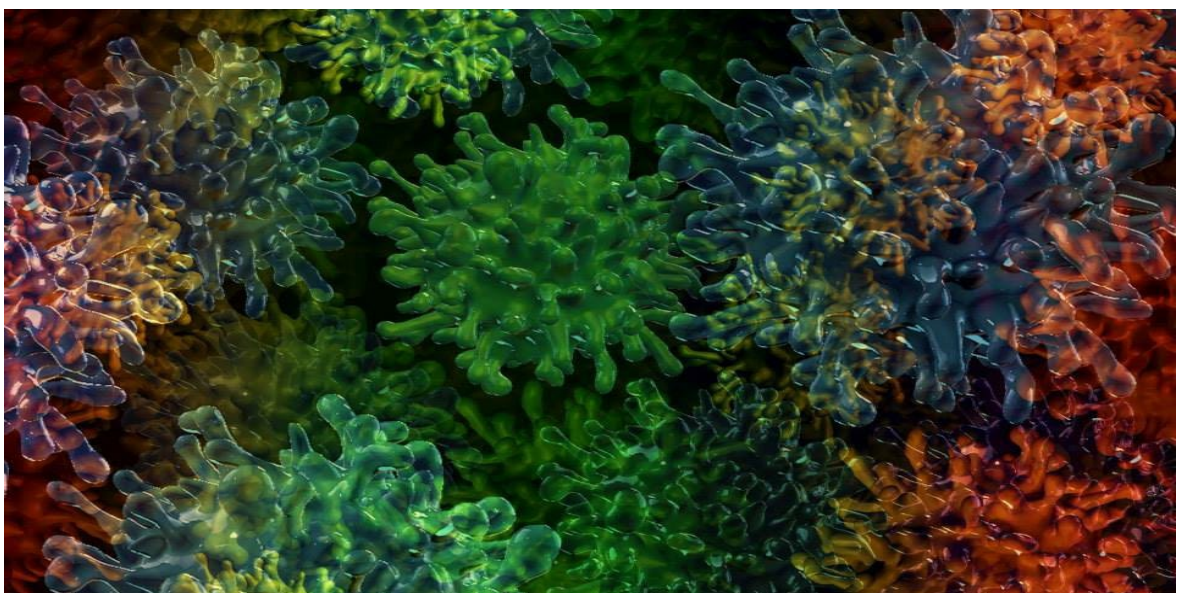


Fig 7. 4 Pathogenesis (Graphic by H M Jones)

Whilst the term '**salutographic**' has not yet been utilised as an alternative to a pathographic perspective, from the narratives of participants in the study, this is a useful perspective from which to understand patients coping mechanisms and management of their experiences of illness and positive, meaningful aspects of the patient journey, which can be positively termed as '**salutography**'. In keeping with the health continuum poles of pathogenesis and salutogenesis, '**salutography**' as a methodology would embrace the health promoting and healing influences (generalised resistance resources) present in the lives of individuals or communities in relation to disease and ill-health. The following tables provide examples of narratives from patients taking part in the EFACCT, which illustrate both pathographic and salutographic perspectives in relation to their cancer journey and clinical trial experiences.

Patient Narrative - Pathogenic Perspectives	Study	Participant ID
"Now begins the slow drip of the poisons which will reduce my present energy into apathy, inaction, and sickness. Can I endure this until treatment ends in mid-February?"	Patient Diary	024006
"And like his parting words to me were, "Right, well as far as I'm concerned, yes, you are suitable for the surgery, erm but as you know it's a flip of the coin... therefore it'll depend whether it lands on the right side as to whether you get the surgery". And his parting words were "good luck", and you know, I thought, God, that's not the right thing to say to somebody. You already know you've got a terminal illness. I knew how bad mesothelioma was and for somebody to just turn round and say, "good luck" you think that is not, I think, do you know what I mean?...And like I say I didn't appreciate the "good luck" after it because I felt that was like adding to the death sentence hanging over my head".	Interview	005009

Table 7.7 Clinical Trial Participant: Pathogenic Perspectives

In the above patient pathographies a negative perspective is expressed by the clinical trial participants. In the following **salutographies** a positive perspective is related with the patient providing praxiological insights which can be purposefully built into future research strategies and healthcare models.

Patient Narrative – Salutogenic Perspectives	Source Study	Participant ID
“The trial lead was the main factor to the success in my opinion. If the lead is totally patient focused and inclusive the outcome is enhanced because of the total trust by the patient”.	Delphi, Round 2. Q. 2 – Patient Benefit, Support & Efficient Practice in Clinical Trials	001001
“For me personally being part of a clinical trial and having a team of experts on hand has helped me so much and felt like a holistic approach to beating cancer which I felt is needed”.	Questionnaire	034002
“I think I had such a strong belief in the fact that it was going to cure me that, you know, I didn’t, I didn’t feel sorry for myself or anything like that because I was ill. You know, when I was ill, OK, yea, I’ll go and sit and deal with that myself”.	Interview	024005

Table 7.8 Clinical Trial Participant: Salutogenic Perspectives

7.3.2 Cancer Clinical Trials and Patient Manageability

The ability of patients to manage their condition and varying stages of their journey from initial diagnosis and prognosis, to navigating patient pathways and treatment options, as well as interventional elements of receiving treatments and subsequent follow-up processes, are all unique, contextualised, and emergent processes. Every patient is different and their ability to manage their circumstances cannot be predicted or pre-determined by healthcare processes. Patient manageability is influenced by individual relationships to concepts of comprehension and meaningfulness, which in turn is impacted by localised systems and networks.

Analytic Memo - Manageability for CCT Participants

Manageability as a patient’s sense that they have the resources, facilities, mechanisms, and support networks available to them to meet the challenges of their illness, healthcare, and life.

Mental capacity and psychological resources: “They did ask me to take part in an Aspirin trial after radiotherapy, but at the time I wasn’t in a good place mentally, so I didn’t agree to anything because I didn’t think it was worth agreeing when I wasn’t quite there. “(Participant ID: 034001)

Coping strategies: “...my way of coping with it [cancer trial journey] was to do a journal. It’s not a diary, it’s a journal, my experiences....the first three months was tolerable but the second was

appallingly bad from the point of view of the patient....you see I think from a patient point, if you're a different sort of patient, and I think it's recognised in psychology, if you are in a difficult situation, write a diary." (Participant ID: 024006)

Patient resources for support: "I actually felt as if I wasn't important. I wasn't part of the, I just wasn't part of it...I just felt as though nobody was actually sitting down with me, with all this turmoil going on, and actually saying 'this is what it is, this is your prognosis, this is the expectation for your...I had to do all of that research myself. And I was, yeah, that was quite hard to start with.'" (Participant ID: 024006)

Managing patient stress and holistic care: "I think maybe it was the way that the consultant was very different. I can't explain how important that was, but I didn't ever feel he was hiding anything from me...it was a different type of care, it was much more involving...I was an integral part...that breaks down a lot of barriers and you're able to talk about your fears and things that might well affect the research, because they need to know your lifestyle. I actually feel that it's really important that you need to know what problems, and I know that's difficult because you don't want to know all the baggage that a patient has got, but you, it's important you know a certain amount of what's going on in their life because the stress that they actually have is important for you to be able to deal with along with the stress of the research." (Participant ID: 001001)

Patients witnessing staff pressures: "Sometimes you can see it in the professor, you know. I mean he explained to me they're supposed to see 16 people in a day and sometimes it will be up to 30. You know, I mean that's double the workload, so you know, everything is doubled, and sometimes you can go in there and, not when he sees you, but when you can see him through the door you think, 'Yeah, you've had a bit of a hard morning'." (Participant ID: 001011)

Competence and coherence of specialisms/services: "I was unsure when I started radio. So after I'd finished chemo I had surgery and then I was due to go onto radiotherapy, erm but because that wasn't part of the clinical trial as such, I had a, the treatment was very different and it seemed very, like getting all that set up, was like very wishy washy, nobody seemed to be coherent about anything." (Participant ID: 034001)

Table. 7.9 Analytic Quote Memo Manageability

7.3.2.1 Coping

Coping mechanisms are an important patient response to disease, treatment and potential recovery and prospective positive health outcomes. Whilst many coping mechanisms can be highly individual, it is important to understand the characteristics and processes involved in the development of such health promoting assets within the context of clinical trial participation, and their potential for developing supportive systems to optimise better responses to treatment and healthcare interventions for other clinical trial patients, as well

as in more generalised healthcare environments. Humour emerged as an important coping strategy, and potential salutogenic health promoting approach which should be studied in greater depth and across wider medical landscapes.

7.3.2.2 Humour in Healthcare

The concept of humour in healthcare is complex due to its highly personal, sensitive, and contextualised nature. The role of humour held significant meaning in terms of both the clinician-patient relationship and also the ability to cope with the challenges of their disease, its treatment, and their maintenance of 'life as normal'. One patient placed humour as a highly valued health promoting asset during their cancer journey. The highly personalised nature of humour adds to the complexity of patient management and the fostering of salutogenic relationships, where research professionals need to be skilled in assessing the patient's persona and psychological status for utilising the therapeutic benefits of humour. McCreddie and Payne (2014) argue that humour is an evolving element of the patient's healthcare experience and identity stating, *'the contextual elements of humour as ambience and support ostensibly operate in a vacuum of the initial flux of diagnosis, prognosis, initial treatment and on-going treatment'*. McCreddie (2010) suggests that *'humour per se can be used to therapeutically enhance healthcare interactions particularly with disenfranchised groups'* but that the use of humour in healthcare involves risk, positing that *'nurses' approaches to risk are a contributory factor in 'an apparent reluctance to initiate humour'* McCreddie (2010, p333).

The complexity and prismatic perspectives of patients' and professionals' approaches to humour, as an element of the salutogenic approach to clinical trial delivery and patient coping, was demonstrated in the dialogues of interview participants, noted in the following analytic quotation memo (Table. 7.10). The concept of humour in healthcare as an approach to delivery is one element that has been extracted from the diverse participant data, relating to participation in a clinical trial which illustrates the dichotomous nature and presentation of complex levels of social interactions as problematic aspects of healthcare, involving individual patient's subjective experiences and their situated sense of well-being or coherence.

Analytic Quotation Memo - Role of Humour for CCT Participants

The role of humour and its importance as a salutogenic coping mechanism was an early finding from the Delphi study and was explored in greater depth with interview participants. Humour emerged as an important element of the patient-professional relationship as well as a social aspect of patient-patient social experience in clinics and support networks. Humour is also a very problematic and highly personalised construct, which cannot be easily used or replicated as a process in health promotion. The recognition of its role is however something that can be communicated to encourage the conditions for allowing the salutary benefits to be explored and optimised for patient benefit, and to reduce anxiety and break down barriers in the clinical environment.

Hilarity: “hilarity, you know it’s good because it actually **brings you up as a patient**...I like a bit of banter. I like a bit of a crack and it **makes you feel better**. It gets people laughing and not just myself but other patients, where they can start laughing and then **they can join in**, and instead of having these patients sitting there miserable, you end up with a whole room laughing and joking...and I think that’s great, and I think that’s great when you’ve got the **nursing staff that are capable of actually orchestrating that**, you know....you’re treated differently by every different nurse...and the trial I am on just now...the humour’s not there. There’s no crack, there’s no barracks, very serious, you know. It’s like ‘this is my job’ and it doesn’t matter how much I try and sort of like pull the humour out, it’s just not happening.” (002001)

The above extract introduces the concept of **humour as a salutogenic property** and an approach to improving the patient experience in the clinical environment and also proposes that nursing staff can play a positive role in **orchestrating humour**.

As humour is socially constructed and is a complex phenomenon, which is dynamic and highly sensitive to context and to individuals it is therefore not easily replicated for patient benefit and brings with it risks. It is reliant upon the **comprehensibility** of multiple parties, but is nonetheless a property of the therapeutic relationship which is valued by some patients.

Role of Humour in Patient-Professional Relationship: Humour - “It **broke down so many barriers**, particularly when you are frightened, particularly, and you have got to remember that these people all know each other, and you are coming into their area. And I’m from an age where we were taught to be quite respectful of people that have got that level of knowledge and expertise. So, you know, there is automatically that barrier we put up, not necessarily that the healthcare people put up, but it’s there. I mean the **humour** between Professor [Consultant name] and [Research nurse name] used to have me in fits but it used to **put you at ease**, because they would always be having little jibes at each other, but **involving you in that humour**, you know definitely **diffused lots of situations**.” (001001)

Sense of Humour as a coping strategy: “ I think if you can’t have a **sense of humour** and if you can’t laugh about things, especially when you’re going through all this with, either with the patients, the medical staff or anybody, then I think that’s really sad. Like Dr [Consultant name], she thinks I’m hilarious [laughs]...like she says, ‘**having a sense of humour** is important’. I think you have to have that. You have to have a **positive frame of mind** and you **have to have a sense of humour going through any of this**, or I don’t think you’ll get very far unfortunately”. (034001)

Gauging humour and patient personalities: Q: How much do you think the personality of the people delivering the research trial impacts the patient? P: “I think you talk about humour and trust; I would put friendliness and trust. I mean I don’t want a stand-up comedian talk to me about, ‘Did you hear the one about the guy who came...?’ I don’t want, you know. I mean, I like it to be light-hearted but often you’re, you might be dealing with something that is really serious, but then you want to have somebody that’s, that’s why continuity is important because you develop a relationship. If you’re somebody who doesn’t get on with people, then you ought to be doing something else.” (024004)

Table. 7.10 Analytic Quote Memo - Humour

Dean and Major (2008) in their paper which explores the sustaining value of humour in healthcare state that humour, when combined with scientific skill and compassion ‘offers a humanising dimension too valuable to be overlooked’ and highlight its importance in ‘enabling communication, fostering relationships, easing tension and managing emotions’.

7.3.2.3 Patient Narratives and Serendipity

Being lucky as a cancer patient on a clinical trial was a key concept that was highlighted across participant interviews. Use of luck and chance as a semantic expression was viewed from prismatic perspectives by study participants. For some **serendipity and luck** were positive notional therapeutic constructs whilst others objected to its role in their relationship with disease management and healthcare, as described by a patient with a progressive form of cancer, who stated:

Patient Narrative – Serendipity and Luck	Participant ID
“And his parting words to me were, ‘Right, well as far as I’m concerned, yes, you are suitable for the surgery, but as you know it’s a flip of the coin , erm and therefore,’ what do you call it? ‘it’ll depend whether it lands on the right side as to whether you get the surgery” [cough]. And his parting words were ‘ good luck ’, and I thought, God, that’s not the right thing to say to somebody. You already know you’ve got a terminal illness . I knew how bad mesothelioma was and for somebody to just turn round and say ‘ good luck ’	005009

<p>you think, that is not, I think, do you know what I mean? ...And like I say, I didn't appreciate the 'good luck', after it, because <i>I felt that was like adding to the death sentence hanging over my head</i> [cough]".</p>	
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Table. 7.11. Patient Narrative – Serendipity and Luck

7.3.3 Cancer Clinical Trials and Patient Meaningfulness

Meaningfulness for patients is again a very personal and unique concept, involving different perceptions of life and society, where personal behaviours, values, goals, and cultures carry complex meanings, associations, and implications. Clinical trial participants' narratives, contributed during the study, highlighted these personalised aspects of meaningfulness through the value that individuals attributed to social aspects of their patient journeys, and the importance of relationships and encounters within complex healthcare and research contexts. The concept of meaningfulness is a complex, temporal and highly personal construct. In the context of healthcare, and more specifically the rehabilitation of patients with chronic pain, the following definition is proposed: '*Patient-identified meaningfulness describes that which patients themselves select as being of value, and contributes to their personal sense of identity*' (Liddiard et al, 2019).

Analytic Memo - Meaningfulness for CCT Participants

Meaningfulness as a patient's reasoning and motivations for behaving, responding, and acting in certain ways to their conditions, environments and existence and involves perceptions of their own identity and personal values.

Patient self-advocacy: "You've got to be an advocate for your own health. And I've taken a lot of responsibility for my own treatment...I think had I not been my own advocate and done a lot of research, I possibly wouldn't be sitting here in these trials, possibly wouldn't be sitting here at all". (002001)

Altruism and beneficence: "The only route for me was to go on a clinical trial. Even if it didn't help me it could maybe help someone in the future, so it was worth giving it a go." (034003)

Salutary benefits and positive psychology: "I had total belief in this trial that it would make be better, which it has done. And I think that the things that they are trying to say on the forms is that people have to believe, and I think they will recover quicker. The mindset is very important. I mean you can't force people to be better [laughs] but if they are more willing to be better, the quicker it happens". (024005)

Being human: "...proper concern was shown for the patient and understanding for the bigger

person...I think the human bit of it is important, about going into a new trial..." (024004)

Compassionate/Just Treatment: "I'm still a patient and I want them to give me that compassion and that care that I'm a patient, and I'm a patient with a terminal illness that's not going away. And I don't feel as though you get that from the research, well I've not got it from the research, you know, at all." (Participant ID: 005009)

Consistent relationships: "I do like to see the same person because I think you can build rapport...I mean there was a case in point where I had to see a locum twice, and I had to have a bone marrow and the consultant couldn't do the bone marrow, so when I saw Professor [Consultant Name] I said, 'Now look. When we started on this journey it was me and you. Now I've seen three people. I have no idea who they are, and I've got a botched operation, and believe me it was shocking.' And he said, right...from now on I will see you through this'. And as I say, it's the rapport. He knows me and he knows how I think and feel and am, and all the rest of it. "(001011)

Patient autonomy and identity: "I actually felt as if I wasn't important. I wasn't part of the, I just wasn't part of it...I just felt as though nobody was actually sitting down with me, with all this turmoil going on, and actually saying, this is what it is, this is your prognosis, this is the expectation for you...I had to do all the research myself. "(001001)

Table. 7.12 Analytic Quote Memo - Meaningfulness

7.3.3.1 Relationships, Communication & Trust

Clinical practices and encounters are complex phenomena and relational processes, which are 'nonlinear, iterative, reciprocal, self-organising patterns of relating (the webs of relationships) and patterns of meaning (stories of change and continuity) that are enacted in the everyday living present of each practice and clinical encounter' (Miller and Crabtree, 2006).

In answer to an interview question about what was most important to a patient one participant answered, "Probably the relationship with the staff is the most important thing, because I think once you've established a good relationship everything else comes behind it" (Participant ID: 002002).

7.3.3.2 Emotional Intelligence, Psycho-Oncology and Humanistic Approaches

In discussing the nature of patient-professional transactions in clinical trials, one cancer patient highlighted the importance of continuity in such relationships and the necessary healthcare professional skills, stating:

“I think that people who execute research protocols need to be as engaged with that person as with the science of what they are trying to study. I think that’s important. I think that comes across...They need to be emotionally intelligent.” (Participant ID: 024004 – Patient Interview).

This perspective was reflected in a discussion with a senior clinical research nurse, whose role involved the recruitment of clinical research delivery staff, and highlighted the skill-set needed for research professionals who are likely to develop intensive relationships with long-term clinical trial patients.

“There’s something called emotional intelligence that you really have to develop...it is really, it makes people, it either makes you stay in clinical research or makes you go.” (Participant ID: 002104 – Research Professional Interview).

This requirement infers the need for skilled, trained and specialist staff, with implications for resources, capabilities and training and development within clinical research.

Emotional intelligence (EI) has been defined as the “set of abilities (verbal and nonverbal) that enable a person to generate, recognise, express, understand, and evaluate their own, and others, emotions in order to guide thinking and action that successfully cope with environmental demands and pressures” (Van Rooy & Viswesvaran, 2004, p.72).

7.4 Collaborative Therapeutic Relationship and Salutogenic Environments

The environment and conditions in which clinical trials are delivered are key factors influencing the experiences and relationships of both clinical research professionals and cancer clinical trial participants. Hanson (2007, p257) refers to perspectives and conditions governing participation and highlights the importance of empowering individuals and their knowledge in relation to their own situation, positioning this as a salutogenic approach which is ‘perhaps the most important prerequisite in promoting health’. The therapeutic relationship is a vital component in the patient journey, and their experiences of trial participation and treatments. The relationships of clinical trial participants to both the healthcare environment in which they were involved during the course of their treatment and care, as well as the relationships, whether patient-to-patient, or patient-to-professional, and the values and significance that they attributed to these social interactions emerged as key themes within the research. The complexities of social and environmental influences are discussed in the following sections, with relevant perspectives of the EFACCT study participants evidencing personal experiences from their patient journeys as cancer clinical trial patients.

7.4.1 Needing a Human Being

The relationship between patients and professionals can positively or negatively impact meaningfulness for patients, and affect both their comprehensibility and manageability of their clinical trial or cancer journey. In the context of a patient-professional relationship where communication and cohesion was limited, the patient's self-esteem and morale were negatively affected, becoming a source of tension in the relationship. In this case the patient was not randomised to the treatment arm, and was disappointed by this. They also did not seem to comprehend the nature of trial randomisation. The lack of shared communication and comprehensibility is a stressor for the patient, leading to a state of tension. The consultation and communication between patient and clinician or healthcare professional in healthcare settings is a value-laden process from the perspective of patients, which one participant's reflection in an interview revealed.

'I never thought I was being stupid with the questions because I never felt as though they looked down on me. It actually felt as though we were on a level, the same level. You know it was very much transactional analysis. It was very much on an adult to adult basis, that's how we were communicating'. (Participant 001001)

This participant had moved to a new consultant, due to poor experiences with another clinician at a different location. The above statement is in contrast to another reflection the same participants had offered about her earlier experiences of the patient-professional communication process.

'I went to see the haematologist...he was old school. I don't mean that unkindly, but he didn't really understand that nowadays patients will go away and do their own research, and they will look at their own illness and they will try to understand the illness. And so, he didn't discuss it with me, he just told me...and he was actually quite condescending because I felt that he, when I was asking questions, he was almost, you know 'why are you asking me these questions? I've just told you what I'm going to do'. (Participant 001001)

The phrase of '**transactional analysis**' as part of the patient-clinician relationship and communication process was a striking participant perspective and potential construct for comparison with other participant data and wider theoretical literature. Transactional Analysis Theory (TA) proposed by Eric Berne (1961) was compared to participant data and related use of the construct within the context of the patient-healthcare professional relationship.

“...you feel like you’ve signed your life away. You’re a number and you don’t matter to them. That’s personally how I feel. Do you know, I go to an asbestos support group and mentioned this, you know, at one of the chats after and other patients said, ‘that’s exactly how I felt.’ I’ve had not contact with anybody, nobody’s been in touch, nobody’s said how the trial’s doing, where they’re up to, you know...A surgeon came to speak to us at one of the meetings...and he was on about the [name of trial], he said ‘their showings so far are in favour of the surgery. Surgery seems to be giving a longer, a better prognosis than just chemo’. I said, ‘right, well my next question to you is, the people that didn’t get the surgery, didn’t get randomised to the surgery, partake, you know, participated in the trial, will they get the chance of surgery?’ And he just stuttered and said, ‘well, that’s something that you’d have to take up with your consultant.’ So I’ve had nothing...you feel like you’re a number, you know, which I can understand now why people say, No, not going on any trial’. Because you just feel like you’ve been abandoned...it’s not been a good experience at all.” (Participant ID: 005009)

Facilitating patient to patient relationships and communication can provide an additional support mechanism and network for clinical trial participants, if they are open to and able to engage in such interactions. This creates a sense of coherence at an individual and a group level between patients as part of their cancer journey and treatment. One interview participant related the following narrative:

“...my sister is going through chemo at the moment and it’s funny because when we went...there was three ladies there, well two ladies and my sister. And they’ve all been in hospital at the same time and had the same procedure...and they were talking across the room to each other, and other people were saying, ‘did you have this, did you have this, and did you have that?’ and it was funny listening to them because my sister’s been worried about all these side effects, all these things that are sort of happening to her, but obviously hadn’t voiced it. The other lady had the same effects and had the same problems, and in the end, I actually turned around and said, ‘you three need to sit down together and discuss and then you’ll all reassure each other.” (Participant ID: 005006).

Bonino (2021, p88) postulates that continuity is an essential requirement of the ‘collaborative therapeutic relationship’.

7.4.2 The Serendipitous Patient

Holism and serendipity are linked within this patient’s psychology for managing their care. One cancer patient comment on the notion of luck in the clinical team they worked with, as these professionals included the patient in a partnership in their care, which allowed them

to be able to have a say in their treatment and thereby retain a **locus of control** which is another construct linked to **salutogenesis**. They also stated that *“I think I’ve been so lucky because I felt like I’d had a whole holistic approach”* (Participant ID 034001). Another participant stated, *“I put that story down to there’s being lucky and unlucky because I was unlucky to get the cancer but lucky that [Consultant name] and a clinical trial was there for me at that time”* (Participant ID 005006).

7.4.3 Healthcare Environments and Clinical Settings

Environment is a significant factor in health and wellbeing. Golembiewski (2017, p267) states *“Substantial evidence shows aesthetic design changes in healthcare settings can improve health outcomes for patients”*. This also has implications for the negative impact of certain environments on the psychological as well as physical health and wellbeing and is one that is often overlooked in healthcare and clinical environments. The environments that the study’s research participants experienced during the course of their clinical trial and healthcare treatments emerged as a category, but with varying connotations specific to contextual settings, scenarios, and individuals. These unique experiences, perceptions and responses all contribute to the complexity of clinical research and healthcare delivery.

Miller and Crabtree (2005) discuss the concept of the healing landscape, which they define as ‘the potential emergent life space, the terrain and particular places and living beings wherein and with whom a patient coevolves, journeys, experiences, and particular relationships and medical care from which healing emerges’. In the following extract one cancer trial participant describes the challenges of the clinical environment and the psychological and physiological responses that these invoked at treatment visits.

“...but the venesection, it was I think at [hospital name] and again this is definitely mind over matter, is that I had to go to the cancer ward for my venesection, and sitting in the waiting room there, 7c is actually quite a hard ward actually. I don’t know whether you’ve ever been on the ward, the cancer ward at [hospital name], but I remember going on one particular occasion where this lady was in the middle of the corridor saying, ‘Can somebody come and help my husband?’, and you think, oh dear, this is not good, this is really not good.’

Erm and yeah, I just kept passing out there, now whether that was just the white coat syndrome, whether it was because of my illness...I was having these problems with fainting afterwards. And it seems to sort of have, like the day was a bit of a haze after that...I mean I would often go home after venesection, wouldn’t go back to work, I’d just go home and go to bed because I felt poorly...

Erm, it's quite a hard ward is 7c, in that, obviously it's a very busy ward, you're in the waiting room...often you'll find people in there that are obviously undergoing cancer treatment because they are very thin, they are poorly or there might be even patients that are actually sat in there, you know, who have lost their hair. They might be on a drip. It's sort of, the environment is, is a ward environment and so you are going to be seeing all sorts of, I think, trauma. I suppose trauma in a way, how I feel, suffering in a way. I don't know. I don't know. I'm absolutely sure it might have been something to do with it, or it was either that or I, she [registrar] kept me sat up...But I used to be quite frightened about going...because I used to think, am I going to pass out again? It's not a nice feeling. It's just, it was just not a nice feeling of passing out. Almost like I could smell the blood, I don't know. It was strange. I can't explain it. It just used to have all of these things that it used to trigger. It could all have been psychosomatic, I don't know".
(Participant ID: 001001)

The above narrative highlights another element of complexity, relating to the individual nature of patient responses to environments and treatment scenarios, which healthcare professionals need to have the time and capacity to manage. At a newly developed clinical trial site, which had been specifically designed and created for cancer care, a patient participant (and former clinician) stated'

"I was very lucky to be here in [name of hospital] where they've got the time and the space and the ease to look after people properly...I was a consultant in [name of city], again it was very professional but the number of people there, it was as if this whole building was like a, some tessellate affair, hundreds of people there...It's always said that you don't need a good building to do good medicine. You can do medicine in a tent. People did incredible things in the war, medically and surgically, in appalling circumstances but they'd got no option. And if you come into a nice building, architecture, I love this. I think it's a really nice little building. It's designed with patients in mind. I think it's been really thought through, no-one can see anybody, you know, it's quite private and I think of course, it feels like Rolls Royce...but it does make it a nice experience, good experience and it wins your trust, and it won my cooperation as the patient. Places like this also don't get recognised for the good work they do...because they are small. You can do good work in a small hospital. It doesn't have to be a great sodding hospital." (Participant ID: 024004)

Another patient at the same site provided a comparison to the former environment prior to the opening of the new building.

“I mean compared to what we had...I don’t know how they managed...it was hard for the nursing staff and doctors to get round the beds and the chairs...we all laughed together about the dreadful conditions, it was awful...not enough space and trying to cram in beds and chairs and things, and the people that needed to lie down, those who couldn’t sit in chairs, and the equipment, having to go to, trying to go to the loo taking your contraption with you. And the loos were pretty awful too...Environment, environment, mass of space. Space matters and I suspect some people like to be private. You can be private over here, but you couldn’t over there.” (Participant ID: 024006)

The above testimonies link to the research professional data extracts evidencing the resource and logistical challenges in delivering clinical trials in hospitals as well as the negative impact on staff health where they are working in poor environmental conditions, or lack sufficient resources. Creating and designing such environments also has cultural, political, financial, and logistical implications.

7.4.3.1 Salutogenic Environments for Research

The clinical environment featured significantly as an important influential factor influencing participants’ perspectives on participation in a cancer clinical trial. The following patient narrative from the questionnaire study highlighted the value they attached to healthcare surroundings within clinical settings, which supports the theoretical concept of salutogenic environments as an approach to promoting patient health and well-being within hospital settings, which is relevant to clinical trial patients as well as those receiving standard of care treatments.

“The patient needs to believe a cure is possible and that a clinical trial is a positive step towards that cure. Undergoing treatment for cancer is a traumatic experience regardless of the patient guidance and information provided. Attendance at the clinic needs to be as positive as it can be – not just in the assurances given, but the whole experience of the surroundings. Treatment areas need to combine both a social or private capability depending on the condition of the patient. Waiting areas should have a social feel about them which encourages conversation with other patients – not lines of uncomfortable chairs, but comfortable chairs and tables with tea and coffee facilities available, a more pleasurable experience whilst waiting for treatment or consultations. The more positive a patient’s experience is, the more open to treatment and advice being given by the professional team.” (Participant 024005 – Questionnaire Study)

Environments have physical, psychological, and operational implications for clinical research and healthcare delivery with patient orientation forming a critical component of a salutogenic model for clinical research. Patient orientation is an interdisciplinary collaboration process between all relevant parties involved in a patient's care, which aims to understand and deliver the needs and expectations of patients "within the framework of therapeutically correct medical care" (Kirch, 2008). One patient in the study perceived a particular consultation as having a negative impact on their health. In the same way that a sense of coherence offered a guiding framework to understand the perspectives of research professionals in relation to their role in cancer clinical trial delivering, the concept of a sense of coherence (SOC) serves the same pragmatic role in providing a guiding framework for the narration of the experiences and perspectives of cancer patients and their journey, with regards to their experiences as individuals, patients and participants within a clinical trial in the UK.

7.5 Health Determinants, Complexity and Coherence

Health is a notional construct whose definition is subjective, and its achievement is illusive and complex. Miller and Crabtree (2005), whose research examining practice and clinical encounters as complex adaptive systems, suggest that healing is influenced by circumstances and the important doctor-patient encounter, which can be experienced as either an emergent process where an engaged clinician identifies critical health determinants which may lead to a change in treatment, and ultimately better health outcomes. The converse scenario is where a clinical encounter is dis-engaged and fails to identify important symptoms or health determinants, one which can be viewed as a clinical relationship blocking the healing or health promotion of a patient. Such scenarios highlight the nature of health, including the patient's interaction with treatment interventions and clinical encounters, as an uncertain domain, where circumstance, chance and subjective relationships add to the complexity of the patient's journey and health trajectory. The challenge for healthcare providers is posed in being able to meet both patient expectations and needs and continue to evolve and improve the services and environments that they provide, due to financial and logistical constraints, as well as a lack of awareness of theoretical models which can enhance the health and wellbeing of patients (and professionals working withing such environments).

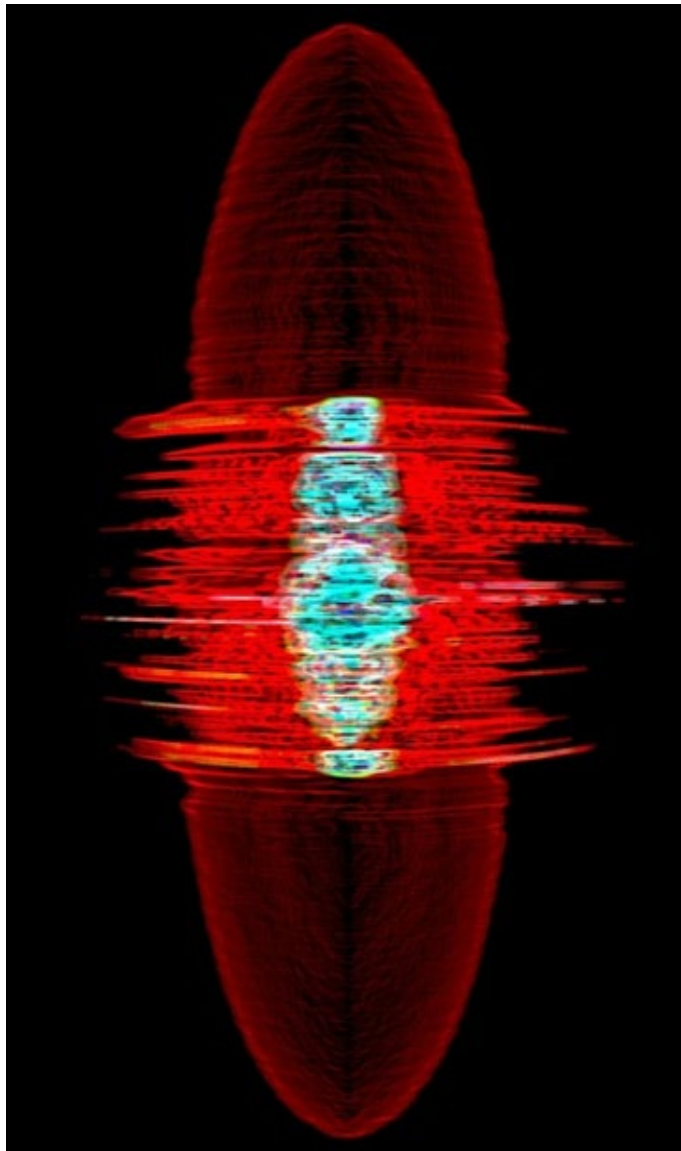


Fig 7. 5 Salutogenesis (Graphic by H M Jones)

7.6 Chapter Summary

This chapter has presented the views of cancer clinical trial patients who participated in the Delphi, questionnaire and interview studies and highlighted the importance of patient orientation and salutogenic approaches to clinical research and healthcare delivery. The factors which influence their experiences and realities of being a cancer patient participating in clinical research are described. These are related to the theoretical concepts which define their individualism and situated, personal experiences. In the following chapter the study's grounded theory is discussed along with how the combined experiences and perceptions of clinical research professionals and cancer clinical trial patients were integrated within the grounded theory and the development of the study's conceptual tool for human systems evaluation and design, the Prismatic Coherence Model (PCM).

Chapter Eight: The Grounded Theory

“My purpose in these pages is not to strain metaphor, or to deal figuratively with important social subjects, but rather to describe truthfully and fearlessly the figure or shape of humanity which each turn of the Social Kaleidoscope offers for observation. Nay, more than this. It will be an endeavour to trace it from the moment when the component parts are hurrying together, and to follow it down to the period when the figure is destroyed.” - George Sims (The Social Kaleidoscope, 1881).

8.1 Introduction

In the two preceding chapters the perspectives of research professionals and patients participating in cancer clinical trials were presented, and the challenges in delivering care and coping with cancer are illustrated from ranging viewpoints. This chapter presents the substantive grounded theory of ***being human***. The substantive theory developed categories and their linked properties are discussed alongside the constructivist grounded theory and developed Prismatic Coherence Model (PCM). The theoretical constructs and model are illustrated using source data extracts and their role and relevance explained, both within the context of cancer clinical trials and research delivery, as well as the implications and utility of the model for translation and application in broader fields of healthcare and operational delivery contexts.

Providing unique insights into the nature of complexity within healthcare systems, the research provides the situated and interpretative perceptions of patients and professionals involved in health services research and clinical care. In the adoption of Grounded Theory as a methodological approach there is a recognition of the multi-faceted identity of clinical research delivery which is driven to adapt and respond to the mutable identities of the organisations and diseases which it serves. To understand the social, dynamic, and complex interactions existing within healthcare and research environments, it is necessary to adopt a sensitising conceptual lens: a theoretical and pragmatic framework which can provide a sense of coherence within such challenging contexts, from which to build enabling, inclusive and sustainable models of care.

8.2 Overview of the Grounded Theory

The process of developing an explanatory theoretical framework to describe the multifaceted and highly networked social environments of clinical research delivery in the NHS was an expedition to discovery. The theorising went through many incarnations, and through the cyclical and extensive process of constant comparison of very detailed, sensitive and comprehensive data, the substantive theory of **being human** emerged. The conceptualisation of the grounded theory of **being human** within the context of clinical research and healthcare delivery arrived late on in the analytical stages, which led to the frequent declaration to colleagues that 'you have to kiss a lot of frogs before you find your grounded theory.' The reflexive diagramming mind map memo below was one of many conceptualisations of the properties and relationships intrinsic to the nature of being human within a clinical research and healthcare context.



Fig. 8.1. Being Human Diagrammatic Memo

8.2.1 The Core Category - Being Human

The core category of being human was developed from the comparison of all conceptual codes and theoretical memos, collected throughout the study and included the Delphi, questionnaire and interview studies, involving both the patient and the professional participant cohorts. The reflexive diagramming mind map memo below was one of many conceptualisations of the properties and relationships intrinsic to the nature of being human within a clinical research and healthcare context. The comparison and integration of incidents within the evidential data from multiple realms using multiple methods, materials, and participants appropriate to answering the research questions adds to the “richness and depth to any inquiry” (Denzin, 2012, p82). The use of Mixed Methods and Constructivist Grounded Theory (CGT) helped to understand, explain and conceptualise the highly heterogeneous and contextualised experiential complexities of being part of cancer clinical trials, either as a patient or as a research professional working in the NHS. At the start of the journey the study sought to evaluate follow-up and complexity in cancer clinical trials, giving rise to the study title EFACCT. An initial interest in studying the more technical aspects of operational delivery, such as trial protocol evaluation and complexity management, with a view to developing a Trial Rating and Complexity Evaluation Tool (TRACAT), evolved into a concern for understanding the far more nuanced and human aspects of the realities of delivering cancer clinical trial in secondary care hospitals across England and Scotland.

The articulate, emotional and sensitive participants who contributed to the study are the ***sentient beings*** at the core of the cancer clinical trial paradigm. The elements of being human within the context of healthcare are multifarious and trying to encapsulate the wealth of personal experiences and expressions became an enormous challenge. Making connections and associations across the spectrum required extensive reflection and modelling. The core category was the outcome of the many manifestations of theorising and visualisation of concepts and the use of theoretical memoing during the course of the data collection and throughout the analytic stages. The following visualisation reflects just a few of the existential properties and concepts offered by participants and their experiences of ***being a human cancer clinical trial participant*** or ***being a human cancer clinical research professional***.

Being Human in Cancer Clinical Research Trials

Being a Human Patient

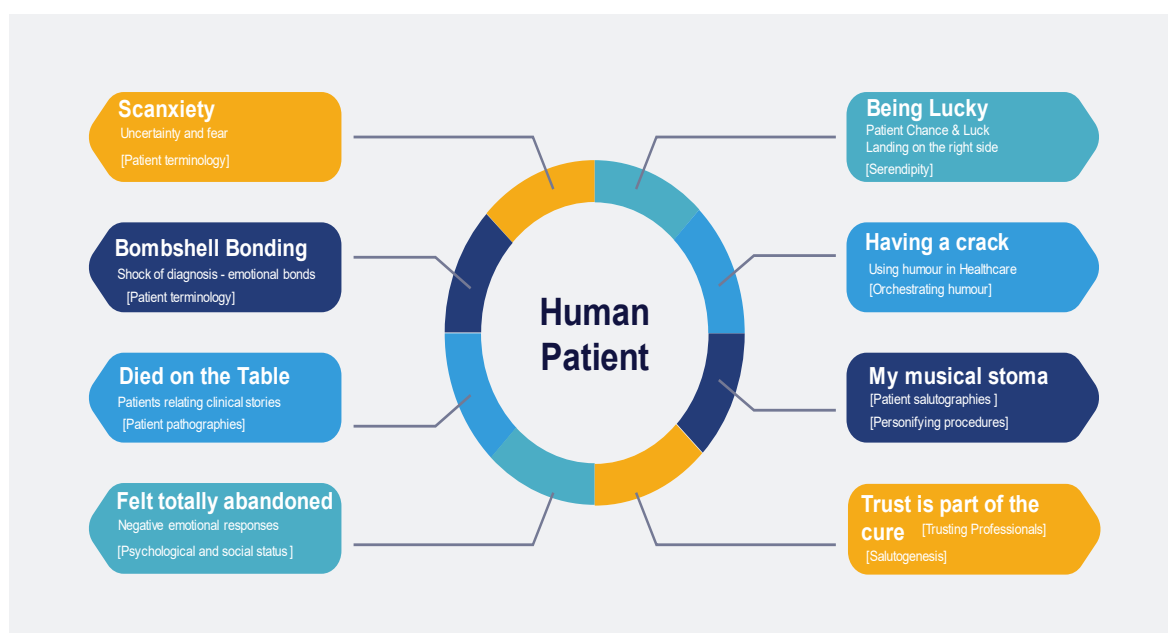


Fig. 8.2. Being Human in Cancer Clinical Trials: The Human Patient

In the model above the headings for each category are the focussed codes which emerged directly from the research data and use the actual dialogue of participants. The table below details the coding stages and how these move from incidents to a theoretical category. The data bank of concepts accumulated in the study will facilitate further theoretical comparisons in future research.

Focussed Code	Potential Categories	Grounded Theory
Scanxiety	Uncertainty and fear [Patient terminology]	Being Human
Bombshell bonding	Shock of diagnosis – emotional bonds [Patient terminology]	
Died on the table	Patients relating clinical stories [Patient pathographies]	
Felt totally abandoned	Negative emotional responses [Serendipity]	
Being lucky	Patient chance and luck – landing on the right side [Orchestrating humour]	
Having a crack	Using humour in healthcare [Patient terminology]	
My musical stoma	[Patient salutographies] [Personifying procedures]	
Trust is part of the cure	[Trusting professionals] [Salutogenesis]	

Table 8.1. Being Human in Cancer Clinical Trials: The Human Patient

8.2.2 The Grounded Theory Sub-Categories

The sub-categories of serendipity and complexity in relation to the substantive theory of being human in cancer clinical trials arose from the frequency within the data slices and their inter-relations with the wider contexts of healthcare, human capacity and innovation as well as their associations and fit with the substantive and theoretical literature involving complex adaptive systems and sustainable systems for advancing science, health and education for human benefit.

8.2.2.1 Serendipity

The **concept of serendipity** as applied in this study is presented as a substantive theory capable of explicating phenomena existing within the operational systems and social networks relating to clinical research delivery in the NHS. Serendipity appeared in wide-ranging literature including social science literature and emerged as an intrinsic property of human endeavour, experience and potential. The construct can be applied as a more formal theory in the conceptualisation of innovation and progress for sustainable society. There is a substantial gap in the application of serendipity as a human asset in healthcare, in a biological sense and the realisation of its utility as a salutogenic resource, as well as the application of serendipity in the advancement of opportunities in clinical research and wider healthcare and management operational professions. Further comparative analysis across wider fields of science and industry can assist in the development of the **theory of serendipity for beneficence**. Glaser and Strauss (1999) stated:

“When advancing a substantive theory to a formal one, the comparative analysis of groups is the most powerful method for generating core categories and their properties and formulating a theory that fits and works.”

In comparing the research findings to the substantive literature on **serendipity**, the utility of its core categories and properties emerged, not only in its application to clinical research and healthcare contexts, but its relevance as a formal theory for innovation and praxis globally. The conceptual category of **serendipity** emerging from this study's data was compared with appearances within the literature pertaining to the science of discovery, research and innovation, health, disease and their management, and its use as theory in the delivery of cancer clinical research in healthcare. **Serendipity** is a phenomenon which is present across many domains and its nature and properties are a central feature of complex adaptive systems (CASs). This links to the sub-category of **complexity**.

Complexity in Healthcare

Cancer Clinical Research Delivery

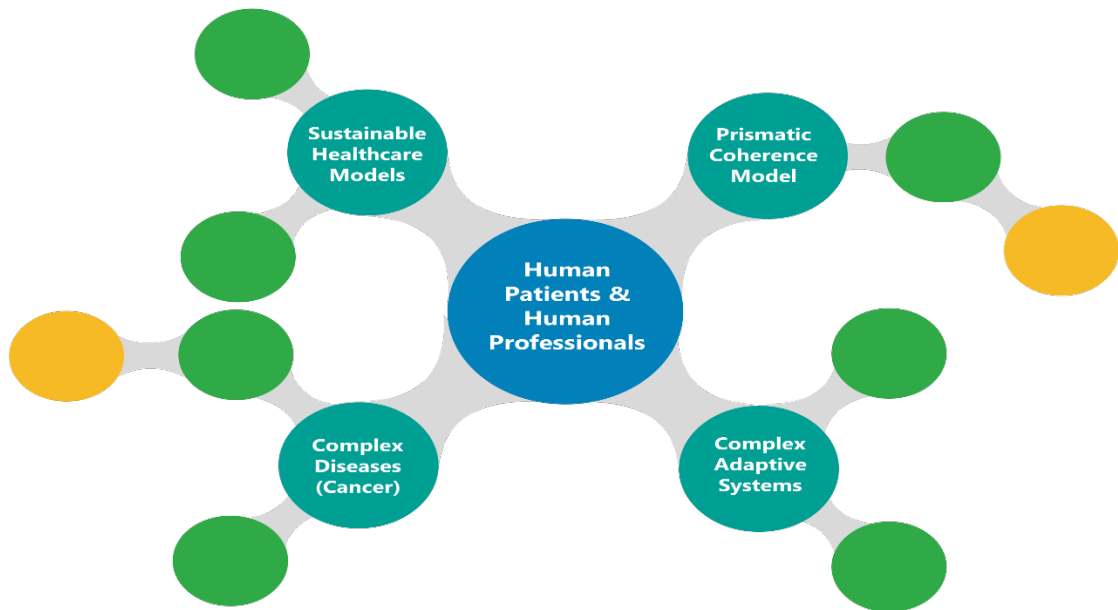


Fig. 8.3 Clinical Research as a Complex Adaptive System

8.2.2.2 Experiential Complexity

The development of person-centred philosophies of medicine and care must be aligned with the dynamic progression of scientific advancements in medicine, and ensure that social engagement and education is embedded within medical practice and healthcare provision. This study's illumination of prismatic perspectives that exist within the NHS and influence or reflect on the nature of cancer clinical research delivery in the NHS provide an original contribution to knowledge and contextualise **experiential complexity**.

A different perspective is that the very nature of complexity of diverse interacting phenomena is that we can apprehend elements of nature and reality at certain points in time and location. This reinforces the need to adopt more holistic approaches in the delivery of healthcare, clinical research, and patient management, if we are to understand reality and experience in a more coherent and humanistic way. This requires healthcare strategists, leaders, organisations, and professionals to understand the limitations of linear, mechanistic approaches, Newtonian science and the traditional medical models based on pathogenesis, and to embrace health promoting, ethical and equitable, dynamic and salutogenic models in healthcare and operational contexts.

8.2.2.3 Quantum Perspectives

The **process of interfacing** with phenomena is a transactional and participatory process, whether that interaction takes place within a biological, psychological or social context: a bio-psycho-social realm existing within systems which are complex and adaptive. The actions and interactions between agents within such fields of reality lead to predictable as well as unexpected outcomes, with notional and physical properties carrying variable meanings, values and consequences. The nature of reality is therefore complex, emergent and subjective, as interacting agents and phenomena behave, react and respond in relation to their position, conditions and context. The process of **interfacing with cancer** was examined within the context of the complex adaptive systems and interacting fields of clinical and organisation research and the social worlds and human aspects of disease and healthcare management.

8.2.2.4 Prismatic Coherence Model

Interdisciplinarity and salutogenesis are complementary fusions of philosophies for the biomedical sciences which should be promoted to bring a sense of coherence to the advancement of healthcare knowledge and management. The ten coding categories presented in Figures 6.5 and 7.2 allowed slices of data and emergent concepts to be analysed within nominal categories, however when the coded segments were modelled within MAXQDA the inter-related, complex and dynamic properties became apparent and it was recognised that concepts could be cross-referenced and incorporated into multiple areas. The visual coding tool allowed for more relationships to be considered providing a tool for not only highlighting the nature of complexity in conceptual terms but for envisaging the realities of managing these mutations and their constantly evolving interactions within the real world of clinical trial operational delivery. Visual mapping methods therefore have the potential for enhancing comprehensibility of the realities and complex nature of clinical trials, and to serve as a conceptual planning and operational analysis tool, with wide applications across healthcare.

8.3 Prismatic Coherence Model (PCM) for Healthcare and Research Delivery

Strategies for delivering healthcare, including research delivery, and coping with illness and disease as a patient are inherently complex. Managing the socio-medical nature of cancer research delivery and patient care poses challenges in reconciling prismatic perspectives and processes across the continuum between medical and social models of healthcare. The perspective from which we approach a subject or situation, influences our response and behaviours, based upon our pre-formed knowledge, situated experiences and cultural

influences. Before even considering the duplicitous and Machiavellian nature of cancer and its many forms, research delivery is increasingly complicated by ambitious personalised approaches, and fragmented due to organisational disparity and patient pathways within independent NHS trusts. A grounded theory interpretation of cancer clinical trial operational delivery cannot be approached from a priori stance and requires a systematic, inductive approach to understand the nature of concerns and challenges, which is open to new discoveries through prismatic vision. Wu and Beaunae (2014) describe their respective doctoral journeys as a 'long, rocky walk through the dark forest of the research process using the GT method'. In a study which sought to evaluate the nature of follow-up pathways as well as complexity and the multiplicity of interactions, states and networks within a large healthcare system, the process of developing a grounded theory was an extensive and challenging expedition, opening rewarding theoretical vistas, and presenting confounding routes and branches of study and cornucopia of conceptual categories. This proliferation and emergence of concepts and multiple realities are representative of entities within complex systems, properties of coevolution. Coevolution is a process within life sciences where 'closely interacting organisms respond to reciprocal selective pressures' (Raguso, 2020). The developed grounded theory presented in this thesis, builds upon the narrative and experiences of this study's participants, and recognises that within complex adaptive healthcare systems there is a coevolution of closely interacting actors, entities and properties. The developed concept of a Prismatic Coherence Model (PCM) encourages the systematic engagement with situated complexity and the embracement of convergent and divergent concepts within healthcare ecosystems. Such a metapragmatic model represents a multidisciplinary framework offering opportunities for innovation, adaption and sustainability of healthcare delivery within complex systems, as well as application in wider operational and organisational contexts.

Human health and disease are challenging constructs which have traditionally been viewed as dichotomous entities, but in reality they are more quantum in nature, perhaps better envisioned as super-positions, which can be better understood by acknowledging inherent tensions and through the adoption of complex adaptive systems thinking approaches. In responding and treating patients who have been diagnosed with cancer (or any other acute or chronic disease or medical condition), healthcare professionals have been traditionally associated with and trained using the medical pathogenesis model. Cohn et al (2013) argue that in acknowledging complexity in relation to health issues, it is necessary to 'find a way of engaging with its dynamic variability'. Through the theoretical framework of a Prismatic Coherence Model (PCM), this thesis presents an adaptive approach to both the study of complexity within clinical research and broader healthcare contexts, and a model for developing agendas and strategies for designing research, health and clinical strategies to

tackle some of the most complex medical and social challenges facing health services, both in the UK and globally.

In the following sections the concept of a Prismatic Coherence Model (PCM) is discussed in relation to the present EFACCT study and key contextual themes which arose out of a systematic evaluation of patient follow-up and complexity and the stressors and resources impacting the operational delivery of cancer clinical trials and the management of patients participating in research studies. The developed grounded theory draws on the concepts of pathogenesis and salutogenesis, and develops Antonovsky's Sense of Coherence (SOC) model, with its dimensions of comprehensibility, manageability and meaningfulness, as intrinsic properties which need to be present in any model aimed at evaluating and responding to complex healthcare phenomena and environments. It is a model which is sufficiently abstracted to be applicable and useful in multiple contexts, and one which is responsive to emergence, adaptability, and uncertainty. With the rapid pace and scale of research and innovation, a flexible yet responsive model is needed which can focus in on the most critical, time-sensitive, and environmentally sensitive issues, if sustainable approaches to healthcare are to be effectively managed and understood. In Chapter Six (see section 6.6.2) coherence was described as a type of 'internal interconnectedness' and 'plausible connection' that is non-linear, circular (Bertea, 2005, p372), yet many of the visual models that are used to illustrate concepts and processes within systems or operational models are linear and geometric, which oversimplify the complexity of interactions. In healthcare delivery, it is useful to build upon the biological concepts and models to illustrate and explicate the notion of complex interactions and coherence.

PCM provides an analytic lens for coherently synthesising complexity, acts as a prism capable of illuminating faceted social perspectives and ranging circumstances, and a responsive open-ended systematic approach to defining the stressors and resources impacting the strategies, processes and capabilities in the operational situation of interest, which in this study is cancer clinical research operational delivery in the NHS. Flax (1990) posits that "contemporary conditions call for a way of philosophising more akin to an analytic search for understanding". PCM is an inclusive and responsive strategic approach, sensitive to context which embraces system complexity and transdisciplinarity, in order to advance opportunities for maximising population health, and develop creative design responses improving system and human resiliency and sustainable healthcare.

8.3.1 Research Delivery Awareness Contexts, Supportive Environments and Cultures

‘Emergence isn’t some mystical force that comes into being when agents collaborate.... there are environments that facilitate higher-level intelligence and environments that suppress it’ (Johnson, 2001, p117).

As the research progressed the initial proposal to develop a Trial Rating and Complexity Assessment Tool (TRACAT) was deemed to not sufficiently solve the nature of complexity experienced within healthcare contexts. Whilst providing benefit at specific points in time and having varying degrees of benefits for differing sites, the substantive theory was developing as a far more nuanced and sensitising construct. To provide a substantive theory which was sensitive and more closely attenuated to local conditions and challenges it was necessary to understand and translate the qualitative and more abstract properties. This in turn led to the adaption of the initial concept of a quantitative assessment tool into a proposal of a theoretical programme for healthcare governance and education development, renamed as Translational Approaches to Complexity and Adaptive Training for Healthcare Systems and Processes . This proposal more closely supports an ongoing and emergent solution to solve existing gaps in the lack of understanding of the nature of complexity in clinical research, healthcare, and wider governance systems.

8.3.1.1 Coherence and understanding

Murphy and Medin (1985) studied the role of theories in conceptual coherence, and asked the question, what makes a concept coherent? They offered an explanation stating, ‘people’s theories of the world embody conceptual knowledge’ (Murphy and Medin, 1985, p289). In a complex system like the NHS, the contextual knowledge of patients and professionals experiencing multiple realities, has wide-ranging implications for strategic capacities, capabilities of people and processes. Greenhalgh and Papoutsi (2018) call for the study of complexity in research to develop ‘context-dependent exemplars’ and ‘ethnographic narratives’ to develop understanding of how systems form through a synthesis of different perspectives. The process of developing coherent knowledge or in-depth understanding of an area of study has been central to the development of the grounded theory in this study. In essence the study has developed a coherent theory for comprehending complexity and using coherence as a strategy for collaborative coping in clinical research and healthcare operational delivery. The importance of theory as praxis is crucial to develop situated knowledge of the challenges and opportunities relevant to contemporary medical practice, research and innovation, which implies the need for

theoretical models to analyse and synthesise paradigms of experience in and across the pathogenic and salutogenic continuum.

8.3.1.2 Mutual Relationships and Emergence

Emergent systems involve mutual relationships, where agents influence each other and through their reciprocal interaction and feedback a higher-level learning emerges (Johnson, 2001, p120). For healthcare organisations to evolve it is necessary to foster collaborative environments where mutual respect and collaborative practice can thrive. Evidence from our research highlighted significant areas of weakness within the NHS with regard to the fostering of such positive connected mutually supportive relationships, or the environments in which they could be fostered. The resourcefulness and resilience of individuals and societies to overcome pernicious diseases such as cancer, rests on the creative and innovative coming together of minds and embracement of Interdisciplinarity Research in Healthcare Sciences (IRIHS) in emergent conditions and environments. This can be viewed as participants in states of flux in systems, which Braithwaite et al (2017) describe as participants “flexing and adjusting to each other, and circumstances, over time.”

8.3.1.3 Coherence, Communication and Complexity

Glaser and Strauss (1965) recommended that research involving interactional analysis should include “consideration of awareness as a strategic general variable”. The data analysis did not commence with a consideration of awareness contexts, but this later emerged directly from the data itself, leading to ‘**awareness of complexity**’ and its related conscious and interacting variable of ‘**recognition of complexity**’. In moving to a higher conceptual level to retain the voice and grounded nature of the study the quotations of interview participants are used to illustrate perspectives of key stakeholders embedded and interacting within complex situations and managing complex relations and interactions.

The operational delivery model for research, evidenced by the testimony of both research professionals and clinical trial patients who took part in the EFACCT study, can be viewed as a fragmented model with loose connections for feedback, and is in essence a disenfranchised system. The results in the study identified themes of **Cognitive Dissonance, Moral Vacancy and Wicked Problems**. Situations, problems, and phenomena involving significant complexity or those which are emergent, indeterminate and evolving, often defined as wicked problems (Rittel, 1972; Rittel & Weber, 1974), may result in cognitive dissonance or analysis paralysis (Nelson, 2004; Kurien et al, 2014) in operational contexts. The lack of cohesion in the complex processes and systems and the poor communication

and feedback channels created friction and tension within operational and social contexts in clinical trial delivery. Johnson (2001, p145) states that “one-way and hierarchical” channels lack “the connections to generate true feedback” and have “too few agents interacting to create any higher-order level”. The NHS structures retain hierarchical structures and the results of the study exposed significant gaps within process of effective communication and collaboration which impacts the coherency and cohesiveness of the systems involving cancer clinical trial delivery and healthcare delivery.

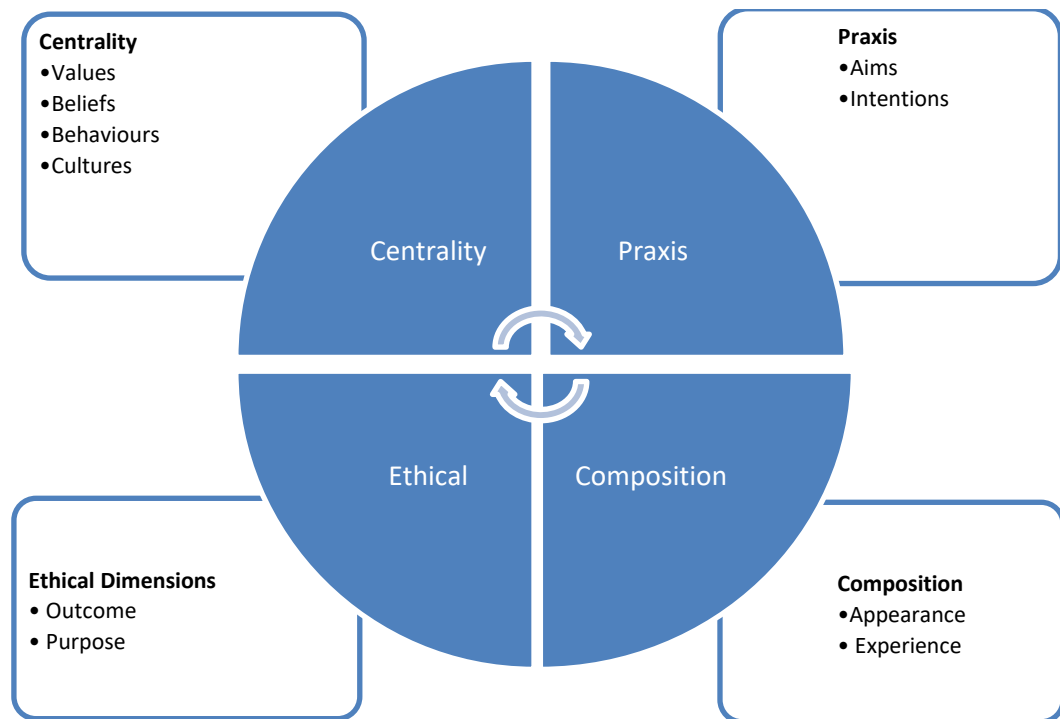


Figure 8.4 Holistic/Humanistic System Design – Integration of Four Conceptual Levels (Based on Nelson, 2004)

8.3.1.4 Fragmentation and Discord

Fragmentation of services and technology was described by participants in the study. The fragmentation of the IT infrastructure reflects the failures in general inter-operability and shared values and understanding between the system users and the NHS commissioners. There was significant evidence of the lack of integration across wide areas of operational processes, where the leadership and managers failed to identify the needs of staff and patients. Education and professional development was an area of particular concern raised by participants. In organisations and complex environments where fragmentation and discord exist there needs to be an analytic process capable of understanding the sources and factors contributing to disorder and conflict. Psychoanalytic approaches which address the subjective and intersubjective aspects of fragmentation and discord, are needed in order

to develop the necessary conceptual understanding and meaningful analysis in complex and problematic contexts (Flax, 1990). Such an approach introduces an ***Intersubjective-Systems Theory***; a psychoanalytic thinking and approach adopting phenomenological contextualism with a central focus on dynamic intersubjective systems (Stolorow, 2013).

8.3.2 Communication, Collaboration and Complexity

Delivering clinical research predominantly encompasses social interactions yet it is governed through mechanistic laws and principles in measuring performance. These contrasting phenomena hold the potential for tension, where their balance or combination is in conflict with the needs, aims and beliefs of participating professionals and the patients they support. Professionals, patients, and healthcare organisations exist in a socio-technical domain where reality is multi-dimensional. To communicate effectively organisations and professionals must develop values recognising diversity and variety in experience, knowledge, and needs.

“Side by side, patient and physician focus on the disease, the symptoms, the treatments, never seeing or knowing each other. The problem gets in the way, and we are each alone.”
– Rachel Naomi Remen, M.D. (2006, p158)

Dialogue and interaction between diverse participants (or agents) are core components to developing effective human-centred design and systems-thinking solutions for complex healthcare environments, including cancer clinical trial delivery and patient care. In addition to focussing on accurate transfer of information, we also need to understand the inherent subjectivity and social construction underlying communication (Miller and Crabtree, 2005; Suchman, 2006). The relational and personal narratives of the social dimensions of clinical research and healthcare are best understood from those individuals and groups embedded and knowledgeable of lived-realities: the ***Social Dimensions of Clinical Research and Healthcare***.

8.3.3 Patient Perspectives

In Chapter Seven the perspectives of patients were presented providing a situated and personalised view of their cancer journey and experiences of participating in a clinical trial. Hawkins (1999) states that pathographic narratives offer a patient perspective on life in the ‘absence of order and coherence.’ Each individual patient’s illness trajectory, environments and perceptions are unique to them, a socially formed view of the world. In describing their experiences, positive and negative emotional responses were related, which can be termed as ***pathographic*** and ***salutographic*** narratives.

8.3.4 Professional Perspectives

In terms of validation of a concept the use of participant narratives as examples of negative and positive cases, the use of pathographies and salutographies can be useful as a conceptual approach to complexity, in acknowledging that circumstances, psychological states and conditions impact upon the analysis of an operational or professional situation. In the study of cancer clinical trial delivery in the UK environment and relationships were significant factors determining the response to context-specific perspectives of clinical research professionals. This outlines the importance of understanding the situated and multi-faceted experiences of professionals through a complexity lens. In seeking to develop coherence within the working and clinical environments of research professionals, the concept of salutogenesis offers a mechanism to support teams and individuals, which the evidence from this study has highlighted is lacking within the NHS. The study acknowledges the importance in obtaining patient perspectives in the design and delivery of research as defined in “the values and principles framework” (INVOLVE, 2015). Similarly, the involvement of research professionals in the analysis and reflection on service delivery is critical from ethical, evaluative and research design perspectives as well as the important role that staff engagement plays in development of a committed and motivated workforce.

8.4 Clinical Research Realities

The development of person-centred philosophies of medicine and care must be aligned with the dynamic progression of scientific advancements in medicine, and ensure that social engagement and education is embedded within medical practice and healthcare provision. In the context of medical, clinical research and healthcare delivery the social and human elements of knowledge involve a cornucopia of positions, perspectives, and possibilities and the interface where these prismatic forms of knowledge come together in the process of solving complex problems and making strategic or meaningful decisions for the promotion of health and wellbeing of society and individuals requires a theoretical model and guiding framework. Key forms of knowledge in the realm include:

- Socio-technical knowledge
- Psychological knowledge
- Biological and physiological knowledge
- Professional and personal knowledge

8.4.1 Patient Management and Follow-Up Models

Follow-up models need to be evaluated across the clinical research professional networks to understand the impact of in-person follow-up, patient consultations and the subtleties of patient assessment. There was a significant variation in the understanding of follow-up across the profession and a lack of recognition by research networks and management in regard to the growing demands of follow-up and patient management in relation to complex and emergent clinical trial designs as well as patient burdens.

8.4.2 Collaboration in Problem Solving

New approaches to collaborative understanding and problem solving in clinical trial delivery are an imperative, a change in thinking and approach was a requirement highlighted by the participants in this study. Hanson (2007, p145) describes the roles and importance of collaboration in problem solving stating:

“Team co-operation in problem solving covers everything from the development of a new technique to the rehabilitation of the long term ill...Specialists manage rather well on their own when it is a question of carrying out further research and deepening their knowledge. It is in the application to complex situations that the specialist must co-operate with others”

8.4.2.1 Visualising and Communication Complex Data and Studies

Visualising complex information, such as clinical trial protocol designs can support enhanced understanding, for example the use of three dimensional (3D) and network visualisations for a clinical trial design illustrating interventions in a single ‘snapshot’ view can support the feasibility assessment within a group evaluation meeting, supporting coherence. Fig. 8.5 below is an output from the study’s research data in the form of a visual model for enhanced perception and cognition of concepts existing within the data.

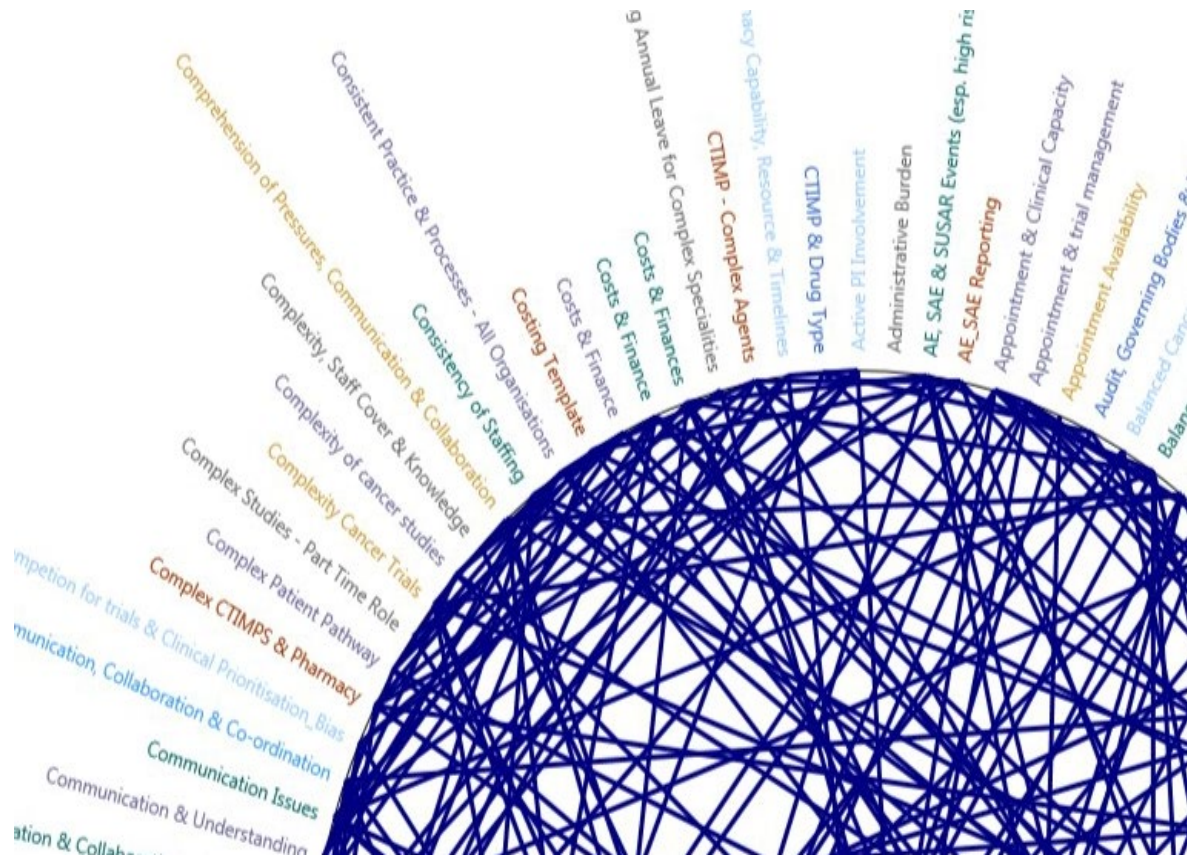


Figure 8.5 Visual model of study data.

Antonovsky (1979, p183) draws attention to the limitations of his Sense of Coherence visual representation, which is shown in Fig. 8.6, stating, “A model frozen in a diagram unfortunately has a static character. It takes a leap of imagination to transform both the elements in the model and the arrows and the lines indicating their interrelationships into a dynamic whole in space and particularity in time.” He makes an important point in how our approach to interpreting concepts tends to oversimplify and apprehend concepts in a static and reductionist manner. This then leads to approaches that adopt a ‘one size fits all’ in the strategic design and management of systems and processes. With the advances of technology, we have enhanced capacities to further our understanding of dynamic relationships and emergent complex systems, but this also requires that we re-educate and further adapt our approaches to visualising and interpreting the nature and properties of systems, as well as our operational models, visions, and goals. This requires a more naturalistic, holistic and creative mindset, the ‘leap of imagination, referred to by Antonovsky. There is a further requirement for us to broaden our boundaries, widen our vision and be more reflexive in order to develop our healthcare environments and strategies to be more adaptable, responsive, and ethical. The following participant observations from the research professional interviews provide contextual evidence of the challenges in applying reductionist approaches to the operational delivery of clinical trials.

Analytic Quote Memo - Reductionist Model Limitations

Reductionist Model Limitations – Problems associated with failing to acknowledge or comprehend complexity, emergence, and variability within systems, e.g. healthcare models.

One Size Fits All? : “One size not fitting all - big issue”

“The trial itself might be quite simple but you're **dealing with an emotional person**, so that does make it difficult, but I do think that **one size not fitting all is a big issue in cancer complexity**.”

(Participant ID: 050102)

Table. 8.2 Analytic Quote Memo Reductionist Model Limitations

8.5 Whole Systems Design and Systems Thinking for Healthcare

Miller and Crabtree (2005) suggest a change in vision is required in healthcare organisations in order to create relationship-centred healing places, one that “instead of having a vision that focuses on improved components and improved measurement, have a vision that focuses on increased capacity for learning, improved systems, and richer connections and relationships.” (Miller and Crabtree, 2005). The importance of connections and relationships within healthcare are highlighted by Scott et al (2004), who put forward a model of healing relationships in healthcare.

8.5.1 Coping and Tension Management in Operational Contexts

In discussing the domain of the *interpersonal environment* underpinning the Optimal Health Environments (OHE) model, Jonas et al (2014) elaborate on the role health organisations should play in promoting *healing relationships* in their culture, leadership and strategic models stating:

“Healing organizations create an expectation that staff are knowledgeable, skilled, caring practitioners who demonstrate mutual respect, practice honest communication, refer appropriately, share a commitment to the concept of healing, work as a team, create integrated plans of patient care, and focus on treating the whole person regardless of their individual specialty training”.

Hanson (2007, p137) provides a summary of factors which can be used to analyse, plan, and reinforce a workplace Sense of Coherence (shown in Table. 8.3) as part of a salutogenic approach to workplace health promotion.

Comprehensibility	Manageability	Meaningfulness
Knowledge about:	Resources and support:	Motivation:
Surrounding world	Material and tools	Visions
Branch	People	Goals
Company's history	Clear organisation	Reasonable wage
Company's organisation	Clear guidelines	Privileges/incentives
Work content		
Working environment	Possibilities to influence:	Values:
Own role	Pace of work	Ethics and morality
Changes	Planning work	Core values
	Decisions	Just treatment
Feedback from:		
Boss	Competence:	Positive experiences:
Colleagues at work	Work skills	Relation to colleagues
Customers/clients	Social competence	Relation to management
	Communicate	Pleasant environment
	Coping ability:	Humour
	Physical coping ability	Variation in work
	Mental coping ability	Recreational activities
	"Distancing"	Self-esteem
	[unwinding from work]	
	Breaks for rest	

Table. 8.3 Workplace Sense of Coherence Factors (Hanson, 2007)

8.5.2 The Salutogenic Model for Healthcare and Research Delivery

To provide a salutogenic and holistic model of care in clinical research trials and in wider healthcare contexts there needs to be a sense of coherence (SOC) between the patient and the research professional. The salutogenic model offers a holistic and whole systems approach to providing ethical, sustainable, and responsive approaches to healthcare and research delivery, as well as a theoretical model supporting wider meta-governance approaches.

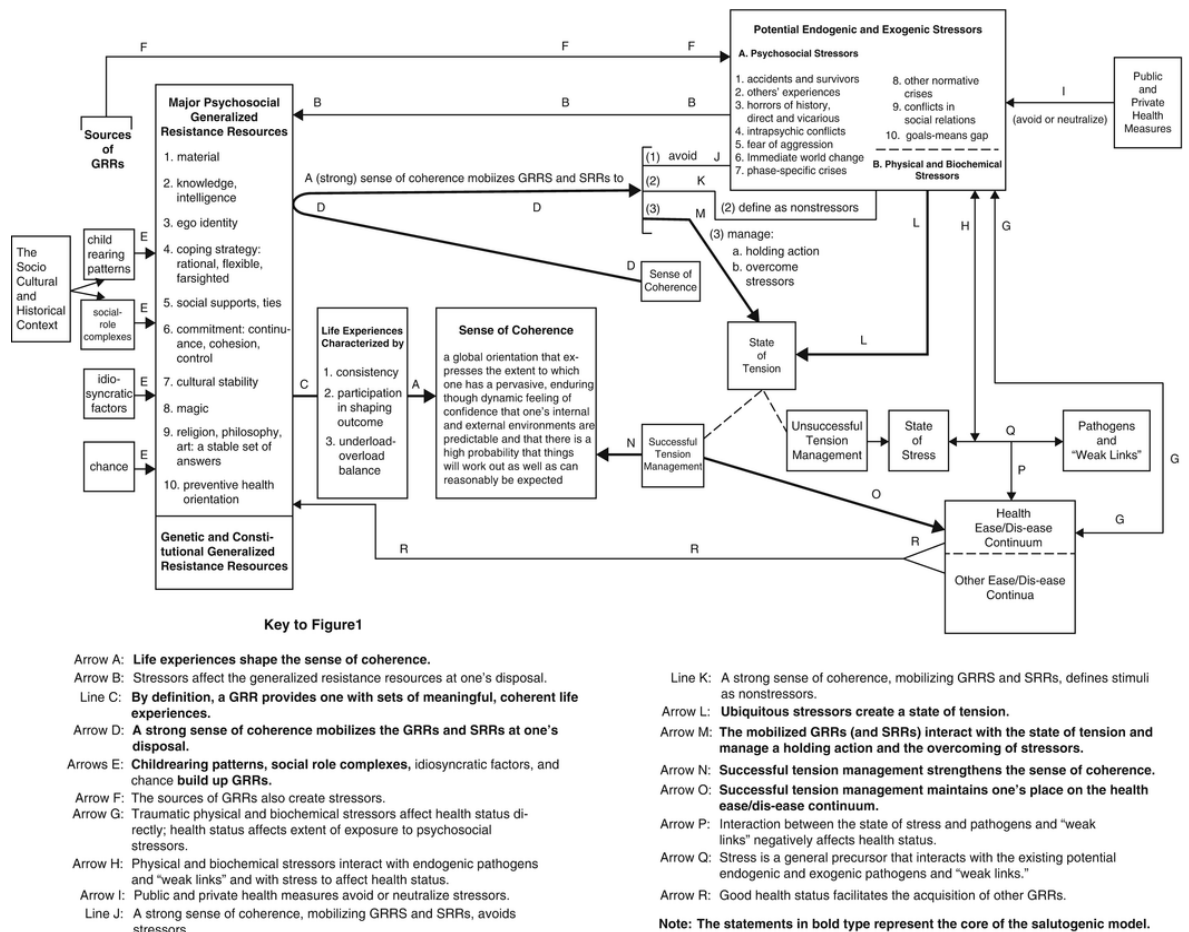


Fig 8.6 The Salutogenic model of health (Antonovsky, 1979)

As this study has reported, cancer clinical research and healthcare delivery is a complex phenomenon, with emergent and evolving properties, which prove challenging in developing sustainable and appropriate models for care, which are appropriate and responsive to all contexts, hospital environments and patient populations. Salutogenic theory, offers a new approach to clinical research delivery (and broader healthcare contexts), which embraces complexity, its evolving nature, and its more elusive and intangible properties. It is therefore a pragmatic solution which 'provides a basis for informed decision making in the absence of specific knowledge, or whenever circumstances are too complex to suggest easy solutions' (Golembiewski, 2017, p267). The ability to adapt, respond and manage ranging elements and inter-related properties requires the application of appropriate and sufficient resources. Antonovsky (1979) proposed the sense of coherence (SOC) which draws on three types of resistance resources; comprehensibility, manageability, and meaningfulness, which he termed Generalised Resistance Resources (GRDs). These are positive resources which can be drawn upon in the promotion of health, from an individual to a system level. Where there is a deficit in such resources, the sense of coherence is lacking, which leads to the breakdown of health. Generalised Resistance

Deficits (GRDs) are 'entropic,' (Golembiewski, 2017) and the lack of a sense of coherence when they are present, and the inability to adapt to circumstances and experiences can lead to a 'breakdown' in physical and mental health. These positive and negative perspectives in relation to forces and resources offer a logical approach to managing the complexities of health and wellbeing from the human and system levels of operating and coping.

8.5.2.1 The Grounded Theory and Relevance of Salutogenesis.

The research journey was a voyage to discovery, which opened a vista of possibilities and new directions, requiring frequent revisiting and reflection on the source data and the nature of health as a complex, emergent, and uncertain domain. To remain grounded throughout the study, during the challenging process of analysing large volumes of qualitative data, and to ensure that the developing theoretical concepts were respectful and representative of the voices of participants, the following question was posed using the method of constant comparison:

What are the stressors and resources in the delivery of cancer clinical trial delivery that influence coping responses?

This question is key to understanding the nature of cancer clinical research delivery and can be more broadly applied to healthcare and operational management. A core theme of relationships in healthcare contexts, with its sub-domains of collaboration and communication were meaningful concepts to both patients and research professionals. Grounded theory is an effective approach to understanding situated processes in organisations and 'capturing complexities of the context in which action unfolds' (Locke, 2001, p95). In the process of theorising and drawing on the grounded evidence provided by study participants, as witnesses to the everyday realities of clinical research practice, different perspectives can be brought into view, which may extend, repurpose or re-interpret established theories, 'enlivening and modifying existing theoretical frameworks' (Locke, 2001, p97). In this study Antonovsky's Salutogenic Model of Health and theory of a Sense of Coherence (SOC) (see Fig 8.6) are applied to new contexts in order to address gaps in knowledge and understanding of the complexity of cancer clinical trial delivery, from the varied and multifaceted perspectives of patients and professionals. The constituent sub-categories of SOC; Comprehensibility, Manageability and Meaningfulness, arose from the study's data as organising and linking concepts which explained the complex nature of clinical research delivery from the perspective of research professionals, and as parallel for understanding, coping and sense-making concepts for clinical patients managing their

cancer journey, life, health and well-being. The conditions and sub-characteristics of the three SOC core categories have been expanded and incorporated into an evolved model for analysing, designing and managing complex adaptive systems, be they in a clinical research delivery context or in wider healthcare, operational or social environments, which are highly dynamic and interactive.

In comparing themes of interpersonal relationships, meaning and perception, multiple perspectives in complex situations and the challenges of human health and disease, as part of the later stages of coding and comparison of emerging concepts to existing literature, a framework began to develop based on the underpinning of the theoretical precepts of pathogenesis and salutogenesis. This allowed the experiences, challenges and complexities of health and disease to be investigated from the medical model paradigm (pathogenesis) and a holistic person-centred paradigm (salutogenesis). Emergent categories in the EFACCT study were compared to the pathogenic-salutogenic literature, leading to the formulation of the conceptual model developed from the grounded theory, as this allowed the research data to be understood from both a patient's and a research professional's perspective.

Salutogenesis and the Patient's Perspective - As a participant in a clinical trial, the patient is not only responding to the challenges and uncertainties of their diagnosis of cancer, but also experiencing and responding to their own personal challenges, including coping with ill-health, treatment side effects and the impact of the condition on their daily life and also the further impact it has on friends, relatives and their social circle.

Salutogenesis and the Professional's Perspective – As a research professional intimately involved in the delivery of clinical trials and the management of patients, their treatment and health outcomes, they are faced with both emotional, logistical, and operational challenges. These include the capacities, capabilities, and complexities around managing, coping, and responding to the inter-relationships with patients, colleagues, managers, NHS Trusts, and wider networks.

8.5.2.2 Salutogenesis Concepts in Cancer Clinical Research

Sense of coherence is a meaningful concept at multiple levels, which allows responses to stressors and resources in ranging contexts to be investigated, understood and managed from the individual, group, organisation and societal level (from the macro to the meso), and how action, responses and strategies can be developed to support and enhance the health and wellbeing of individuals and society in general.

8.6 Developing a Prismatic Approach

In an age of diversity and at the unfolding of the fourth industrial revolution we are witnessing an ontological evolution, which is rapid and unprecedented, where globalisation and fragmentation have proliferated and diversified the nature of knowledge (Schwab, 2017a). The realms in which we communicate and operate have become shifting sands, requiring new research paradigms or meta-theories recognising that “theory is today eclectic” (Seidman, 2008). A prismatic approach to inquiry is based on Singerian meta-systems thinking where reality is multi-dimensional and holistic, and the process of inquiry adopts synthesizing, multimodal and interdisciplinary methods in modelling solutions (Mitroff and Turoff, 1973). In selecting a prismatic paradigm for inquiry, the researcher adopts a stance where there is a construction of reality and possibilities for observable truths, in so far as there exists shared ambitions in the endeavour between parties within an organisation or interactional network context, to understand a particular phenomenon. These realities are accepted as transient or even partially formed entities, where refinement and extended research may adjust or enhance versions of interpretation. This stance brings to the fore paradigms of inquiry from the Multiple Perspectives Approach, Singerian Inquiry, Quantum Perspectives and Grounded Theory, whose historical and epistemological consistency have informed the approach to inquiry adopted in this study, described as the Prismatic Paradigm. Research as a prism and metaphorical device is present across different disciplines. Saukko (2003) argues that prismatic vision of research is ontologically fluid and ‘committed to projects that bring to the fore multiple perspectives on reality, or multiple realities, with the specific aim of challenging the old idea that there is one privileged way of looking at reality, or one reality’. Fisher (2013) places prismatic theory within a surrealist tradition and the philosophy of Breton, which aspired to improve society by resolving ‘diametric oppositions...conscious and the unconscious...the subjective and the objective’ (Klaus, 2016). Fisher identified five core characteristics of prismatic theory: “(1) the call to change, (2) freedom and expression, (3) mapping of the inside/outside, (4) praxis, and (5) convergence and divergence” (Fisher, 2013).

The conceptual framework defines the complex phenomena of trial delivery with the interaction between systems, networks, research professionals, and patients in the act of conducting and participating in cancer research forming the substantive areas of focus. Within operational contexts effective decision-making is dependent upon the co-creation of actionable knowledge formed through collaborative action. The process of moving from localised intelligence or ‘privileged knowledge’ to valid strategic insights is highly dependent upon effective social interaction that facilitates the sharing of values, perceptions, expertise, and contextual evidence. Operational evaluation, capable of defining optimal delivery

models, is therefore a prismatic vision informed by objective, subjective and synthetic knowledge. Within the NHS there is currently no exemplar model to guide NHS organisations and researchers in operational evaluation of effective research delivery, other than the generic principles of Good Clinical Practice, which is more focused on clinical practice. In this thesis, it is argued that clinical trial operational delivery, as experienced by research professionals, participants, and associated partners, requires a prismatic paradigm for inquiry to understand its complexities and challenges. The nature of the prismatic paradigm used in this study is based upon the multiple perspectives and systems approaches of Singer, Churchman and Mitroff, recognising pragmatic knowledge-intensive systems methodologies (Cavaleri, 2005).

8.6.1 Interlinking

Interlinking and transdisciplinarity are enablers within a prismatic approach to the sustainable delivery of cancer clinical trials, a field of healthcare delivery that is witnessing soaring demand for resources and skills but is faced with challenging constraints. A transdisciplinary approach incorporating quantum theory principles, MGT and SIS, offers a framework to study complex problems, either in healthcare or other social contexts, and to design robust, ethical studies optimising, and disseminating validated knowledge within an accelerating society. Healthcare is a transdisciplinary field requiring a theoretical lens capable of range, depth and breadth, a transdisciplinary axiology for conducting study into complex phenomena within context and across transacting interfaces. The developed framework acknowledges the importance of diversity and collaboration (including recognition of neurodiversity) and respects the emergent nature of reality, its challenges and complexities. The paradigm is applicable to multiple fields of social and scientific research, including clinical, operations and management research, as well as meta-governance and an approach supporting operational evaluation of research capacity, capability and feasibility.

8.6.2 Prismatic Coherence

In this thesis an ontological proposition of quantum perspectives in healthcare research is presented which has informed the development of a grounded theory of complexity and serendipity in cancer clinical trials, and an explanatory framework in the form of a Prismatic Coherence Model (PCM).

8.7 Discussion

The ignition for operational change in healthcare research is driven by epidemiological and societal demands, partnered with scientific and medical advancements to address present challenges, factors which delivery professionals and organisations need to consider in designing operational responses. As demands on healthcare organisations and society evolve, and scientific advances change the nature of medical interventions, our supporting operational and governance models need to keep pace. Epidemics and uncertainties in global health may substantially shift the needs, demands and ultimately the approaches to research and healthcare delivery. Kuhn (1962) stated, “Confronted with anomaly or crisis, scientists take a different attitude toward existing paradigms, and the nature of the research changes accordingly.” Britnell (2019) argues that healthcare’s priority is in designing integrated Sociotechnical Systems (STS), enabling technology to undertake the routine tasks freeing up humans to “focus on interpreting and responding to results produced by or with the aid of machines, building relationships with patients and managing their care”.

Complexity can become engulfing and overtake our capacity to manage diversity and networked interventions and integration between systems and their interactions and interfaces. We therefore need to develop new models and mechanisms to manage and comprehend complexity and complex systems. Visual tools are just one of the resources that we can draw upon in creative design systems. The tools we select fit the person and the situation and therefore can be multiple and adaptive. To develop in a VUCA world we need to be as creative and inventive as possible to meet the needs of a new medical era of complexity and one which accepts the concept of complexity is an essential component of healthcare. By engaging with and studying complexity we can adapt and develop an armamentarium for healthcare, one that focuses the facets of knowledge, perspectives and experiences on a Fresnel screen of coherence: a prismatic coherence model.

The role of clinical trials in the NHS and discussion on disconnect between research teams and standard of care professionals. The outcomes of clinical trials influence treatment, practice, benefits, and risks within the NHS/Healthcare delivery organisations and therefore it is important to embed the importance of research and knowledge of the critical role it plays in healthcare delivery as a whole. Clinical research is a field of healthcare which is by nature complex, it is emergent, exploratory and its purpose is to advance knowledge of biological responses to therapeutic agents or healthcare interventions. It is an enterprise carrying many complex characteristics, one which demonstrates a complex order composed of continual development and change, states of flux and evolution. The complexity of the humans who are at the core of the healthcare system and their exposure to complex

phenomena is an area where there is little research being undertaken and limited strategies to address complexities from the human perspective.

The nature of complexity and follow-up in clinical trials is poorly defined and indeterminate. In evaluating their nature, the study design needed to develop an in-depth understanding to adequately describe the nature of the phenomena. In conducting an evaluation of complex properties and characteristics, it is necessary to define and satisfactorily describe the nature of multi-dimensional constructs. In this study we sought to define and evaluate the characteristics of the multi-dimensional constructs of follow-up and complexity in cancer clinical trial delivery with the aim of providing clear operational definitions and insights. The study aimed to develop a conceptual framework to describe complex phenomena in trial delivery, with the interaction between systems, networks, research professionals, and patients, conducting and participating in cancer research, forming the substantive areas of focus. In designing a study to supplement the body of knowledge relating to cancer clinical trials, particular focus was placed on understanding operational aspects of follow-up and complexity from the perspectives of delivery professionals and patients. Multi-disciplinary perspectives were sought by engaging key stakeholders in a democratic, systemic evaluation to identify priorities, understand challenges in context and define priorities for clinical research delivery.

As science and society evolve in response to new challenges, the research methodologies for understanding the complexities of our realities and existence continue to proliferate and fragment. The meanings, values, and priorities we attach to our reality and its properties are not fixed or finite. We cannot solve challenges or create practical and logical solutions for the benefit of mankind if we approach the challenges from a fixed viewpoint. Ackoff (1993), drawing on the work of Singer argues that reality is multi-dimensional and “there are infinite ways to look at it”. A humanist approach to achieving the best possible solutions for society means we must adopt perspectival, prismatic, pluralistic approaches. The benefits and lessons from past paradigms should inform our future actions, where the positives and negatives evidenced in past inquiry are critiqued using aggregative analysis and meta-methodologies. The prismatic paradigm adopted in this thesis investigates multi-dimensional realities, and the relations, interpretations, and perceptions at play between patients and professionals and within complex interacting phenomena. Research within the NHS has shown that involving staff in identifying the issues and challenges that the organisation faces leads to higher levels of engagement, and improved strategic decision making and performance where “initiative has to come from within the NHS” (Ham, 2014).

8.7.1 Being Human in Clinical Research

Being human is a complex notion, carrying a kaleidoscopic array of meaning and consequences, for both patients and healthcare practitioners interacting and relating within the complex, evolving and uncertain worlds of cancer clinical research and healthcare delivery. This study has highlighted the prismatic nature of these interactive worlds, and the importance of recognising the situated complexities of all stakeholders. The capacity and capability of the humans involved in cancer clinical trial delivery needs to be understood in relation to personalised contexts. In the same way that science has advanced through the colossal endeavour of sequencing the human genome, the leaders and commissioners of clinical research and healthcare provision need to recognise the social, cultural, economic and political complexities of clinical practice, and invest in the human factor and ergonomic research to facilitate the detailed analysis and sequencing of the structural properties, compositional elements and behaviours of the complex adaptive human healthcare system.

The proposition of a Prismatic Coherence Model (PCM) is presented as an analytical tool for complex adaptive systems, which supports the development of learning systems within the NHS, and wider organisations. Through the process of interlinking situated knowledge and developing deep insights into the realities of clinical research delivery operational challenges and successes at multiple levels within systems, the development of coherent, synergistic asset-based models of health is made possible.

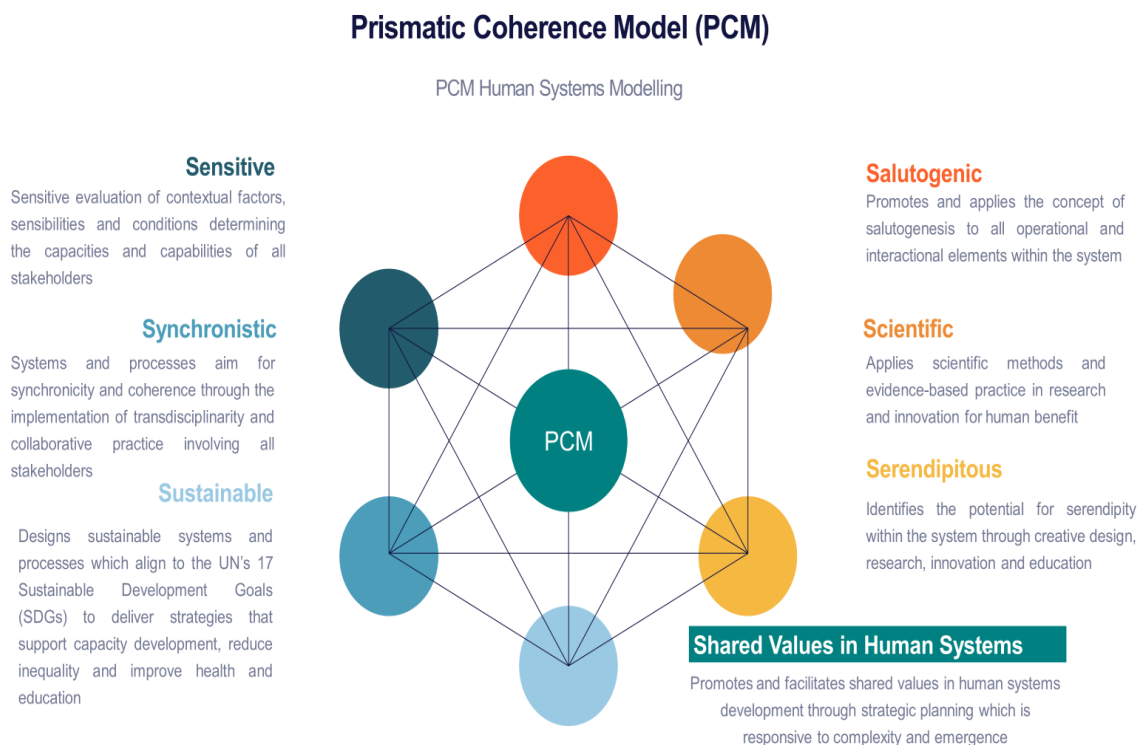


Fig. 8.7 The Prismatic Coherence Model (PCM)

The Prismatic Coherence Model (PCM) is an analytical tool for modelling human systems, which can be applied to healthcare contexts as well as all complex organisational systems and networks. The tool can be used to evaluate existing systems and then applied in their adaption or design of new systems. The shared values in the human systems model incorporates six core conceptual elements, detailed below:

1. Sensitive: Sensitive evaluation of contextual factors, sensibilities and conditions determining the capacities and capabilities of all stakeholders
2. Synchronistic: Systems and processes aim for synchronicity and coherence through the implementation of transdisciplinarity and collaborative practice involving all stakeholders
3. Sustainable: Designs sustainable systems and processes which align to the UN's 17 Sustainable Development Goals (SDGs) to deliver strategies that support capacity development, reduce inequality and improve health and education
4. Salutogenic: Promotes and applies the concept of salutogenesis to all operational and interactional elements within the system
5. Scientific: Applies scientific methods and evidence-based practice in research and innovation for human benefit
6. Serendipitous: Identifies the potential for serendipity within the system through creative design, research, innovation and education

8.8 Conclusion

This chapter has discussed in detail the fully integrated theory mixed grounded theory developed from the multiple studies, and further illustrated its conditions and related concepts. A Prismatic Coherence Model provides an organised analytic framework which is the launch for building inclusive and responsive strategic design approaches, embracing complexity, synthesising structured and unstructured data, drawing together multifaceted perspectives and values and building upon Aaron Antonovsky's Salutogenic and Sense of Coherence concepts, to form a coherent theoretical organising framework and practical model for clinical research delivery. The consequences and implications of the developed core categories are discussed in Chapter Nine. This study contributes unique insights into the conceptualisation and realities of ***being human***, within cancer clinical research and healthcare delivery. The properties of ***being human*** also informs knowledge exchange and future research across the medical and social sciences. The Prismatic Coherence Model (PCM) is an emergent, adaptive conceptual tool which can be employed in multiple domains and complex adaptive systems, supporting and enhancing the design and delivery of sustainable, coherent, human-centred strategies and solutions for **human benefit**.

Chapter Nine: Conclusions and Recommendations

“In the quantum realm, the wave-particle duality and the creative dialogue between quantum potential and experimental circumstances shows us that there is always more to reality than we can experience or express at any one time. Adopted as a wider social paradigm, greater sensitivity to the latent potential of situations might encourage us to think about things not just as they are, but where they are going, what they will become. This could give us a more evolutionary outlook.” (Zohar & Marshall, 1994)

9.1 Introduction

The purpose of this study was to evaluate translational science and clinical research practice through an exploration of the perceptions and experiences of NHS cancer patients and healthcare professionals, and the development of a constructivist grounded theory elucidating and explicating interactional phenomena and their complex relationships. The comprehensive incorporation of qualitative and quantitative evaluation of clinical research operational delivery, from the perspectives of research professionals and trial patients who have situated knowledge and experience, should form part of a national research and innovation coherence operating framework. Such a framework should be capable of understanding the barriers and facilitators for effective practice and ethical care, with systems and methodologies in place tracking and analysing changes to research demands, pressures, practices and designs over time and across the geographical footprint of the NHS.

The chapter opens with an overview and summary of the study and its key findings, and a revisiting of the central constructs informing the development of the grounded theory and its core category of ***Being Human***. The main outcomes of the grounded theory research are related to the existing literature discussed in detail in Chapter Two (Section 2.5). Implications and recommendations for clinical research practice and healthcare operational delivery informed by the ***Being Human*** are addressed alongside the utility of the study’s developed Prismatic Coherence Model. The final chapter of the thesis then concludes with an examination of the study’s contribution to knowledge, which is discussed in relation to clinical research, as well as in the broader context of healthcare research, management operations and population science.

9.2 Overview of the study

The results of the EFACCT study provide unique insights into the nature of cancer clinical trial delivery within a national healthcare system, the NHS. The study offers a multi-faceted analysis and ways of viewing and acting holistically, encouraging design-thinking approaches to expand on an armamentarium of salutogenic resources, which can further build on the capacities and visions of individuals and organisations to support sustainable and equitable health in a complex VUCA world. The EFACCT study explored the nature of complexity relating to cancer clinical research and intervening factors impacting health outcomes and professional experience, situated within the interactional realms of healthcare sciences and evidence-based medicine. The pragmatic approach undertaken in the study is supported by the following core principles proposed by Kelly and Cordeiro (2020) in approaching the research, stating there should be:

- (1) An emphasis on actionable knowledge
- (2) Recognition of the interconnectedness between experience, knowing and acting
- (3) Inquiry as an essential process

This thesis provides an account of the experiences, emotions and perspectives of cancer clinical trial patients and research professionals. Adopting a social constructivist grounded theory approach (Charmaz, 2014), the research respects the situated knowledge, values, perspectives of all participants. The situated and detailed knowledge which led to the development of the grounded theory, provides contextually sensitised evidence and a conceptual framework from which to create and develop new responsive models of care and effective strategies for operational delivery of patient-centred healthcare and clinical research. An adaptive NHS research delivery framework capable of analysing and monitoring research capacity and operational models in real-time and over time is needed to develop the human capital and the in-depth, contextualised understanding supporting sustainable and cohesive clinical research strategies and public healthcare delivery solutions. A systems-based approach to developing effective research capacity planning performs an ethical role in the review of current NHS research delivery and should be adopted to support improved operational performance and enhance patient experiences. The nuances and complexities of cancer clinical research delivery necessitated a study design involving a critical analysis of strategies, processes, and technologies, through a collation and synthesis of prismatic perspectives and experiential data.

9.3 Reflections on the Study

One of the key challenges faced in recruiting NHS sites to participate related to financial provision, as the study did not qualify for inclusion as an NIHR portfolio study. Sites therefore received no incentives in the form of accrual for recruited participants to take part in the research. The responses to the site recruitment campaign formed part of the early data analysis, recorded in the form of research memos. Some of the issues faced in the recruitment of sites and subsequent decline reasons were paradoxical in that reasons cited for not being able to participate in the study, despite many professionals at site supporting the nature of the research, were due to capacity issues, a key area of the study's focus. Those sites facing problems around capacity would likely have been able to provide valuable contextual data, but as the EFACCT study was classed as a non-portfolio study, their decline reasons were understandable. Additional site decline reasons cited included: staff redundancies, budget constraints, high numbers of complex CTIMP studies running, R&D focus on portfolio and commercial studies and a reduction in the number of studies being set up locally.

9.3.1 Methodological reflections

The study sought to develop grounded, context-specific knowledge capable of supporting organisational analysis and reflecting the Churchman-Singerian model of Inquiring systems, valuing ethics and exoteric knowledge in complexity evaluation and decision-making (Jones et al, 2020; Haynes, 2012). The initial intention in conducting the study was to define an optimal research delivery framework to enhance patient access to the latest treatment options and services. In the creation of knowledge through an evaluative instrument, designed using consensus methods and intended to support researchers in identifying and solving shared operational problems, the concepts of instrumentalism and theories of John Dewey were considered, along with the Churchman-Singer philosophies of Inquiring Systems.

The development of the methods and tools were very personal to my own capacity and capabilities of analysis of large, complex, and highly theoretical qualitative data. The developed Singerian Delphi technique was a novel application of the Delphi method, which is widely used in healthcare. The adaption was particularly useful in developing very nuanced knowledge of *being human* within healthcare contexts. The sensitivities and perspectives of all participants formed an *armamentarium of human perceptual data*. An interesting case arose in the cancer patient participant Delphi study, where the patient's responses were significantly different to the consensus statements. The patient became

troubled that his perceptions and experiences were unique and lay outside the field of consensus. On many of the questions where the participant's perspective was significantly different to the consensus, the process of personal reflection on their original thoughts led to a change in response. The Singerian Delphi encouraging the participants to reflect on their thoughts and perceptions over time, revealed the very human perceptual and emotional complexities which are brought to the interactions between patients and health care professionals. As the researcher and a reflexive instrument within the analytic process, this one incident became a prominent datum slice. Long term reflection on this incident, in the process of continual comparison, led to its recycling and re-evaluation with wide-ranging data across all studies, and arose as being central construct, revealing the true nature of the **complexities of human experience**. This was my own personal **serendipitous discovery** that was buried within the panoply of data.

9.4 Contribution of the Study

This thesis has developed a unique insight into the realities of cancer clinical trial delivery within the NHS, developing a grounded theory that acknowledges the complexities and situated perspectives of patients and professionals who are participants in its emergent and diverse systems, processes, and scenarios. This study contributes in-depth qualitative review into operational aspects of clinical trials by engaging key stakeholders in defining variables relating to service pressures as well as highlighting best practices. The Prismatic Coherence Model (PCM) provides a theoretical model for understanding and managing complexity in operational contexts, with particular application to clinical trial delivery and healthcare, thus providing an inclusive, pragmatic, and sustainable approach capable of embracing multiple perspectives and contextualised variability. It offers a framework for developing greater understanding and coherence between interfacing and interacting agents, levels, and structures within complex systems, whether they be individuals, groups, organisations, or networks. The study offers a multi-faceted analysis and ways of viewing and acting holistically, encouraging design-thinking approaches to expand on an armamentarium of salutogenic resources, which can further build on the capacities and visions of individuals and organisations to support sustainable and equitable health in a complex VUCA world. This doctoral study provides an original contribution to knowledge through the collation and interpretation of rich contextual evidence and the systematic analysis of cancer research trial variables and operational data contributing to study intensity, complexity, and follow-up. The following sections summarises the novel contribution to knowledge provided by this thesis, which includes the study's grounded theory and it's sub-categories which led to the Prismatic Coherence Model.

9.4.1 Summary of Contribution to Knowledge

In summary this study contributes new knowledge by:

- Evaluating the nature of follow-up and complexity in cancer clinical trial delivery
- Exploring patient perceptions and experiences of participating in a CCT
- Exploring research professionals' experiences and perspectives of CCT delivery
- Analysing the stressors and capacities within the complex field of CCTs
- Examining complex relationships and values and their relevance in CCTs
- Identifying salutary resources for clinical research and healthcare delivery
- Identifying stressors within systems through situated perspectives
- Providing a theoretical model and framework for managing operational complexity

Study outcomes include:

- Grounded Theory of Being Human in Clinical Research and its sub-categories of complexity and serendipity in Cancer Clinical Trials
- Prismatic Coherence Model (PCM)
- TRACAT: (Trial Rating and Capacity Assessment Tool), which is being reconceptualised as TRACAT: (Transformative Collaboration Tool) for a future funding proposal to support transdisciplinary knowledge exchange platform for the development of actionable theory and sustainable solutions within complex adaptive systems and networks
- Novel adaptive methodologies for qualitative, perspectival research with particular utility in the study of complex, adaptive and emergent systems
- In-depth analysis and development of comprehensive datasets supporting future research collaborations with particular relevance to Bio-Psycho-Social studies

9.4.2 Dissemination

The research has been disseminated through publication of posters, abstracts and articles, with the outcomes of the research professional Delphi study published on BMJ Open (see Appendix 16). In person presentations have included talks with research professionals at hospital sites, oral presentations at conferences and an exhibitor stand at EDGE conferences. Dissemination via talks, posters and stands include the following conferences:

1. National Cancer Research Institute Conference (NCRI) 2017 - BT Convention Centre, Liverpool

2. Life with Cancer Conference 2017 - Harrogate Convention Centre (2017)
3. EDGE Conference 2017 –Grand Harbour Hotel, Southampton
4. EDGE Conference 2018 – Vox Conference Centre, NED, Birmingham
5. EDGE Conference 2019 – Vox Conference Centre, NED, Birmingham
6. EDGE Conference 2020, Farnborough International Exhibition & Conference Centre

An abstract for the research protocol design was accepted for presentation at the 2017 NCRI Conference in Liverpool. Promoted research by acting as NCRI conference ambassador help promote the event to contacts within research networks. The EDGE conferences are hosted specifically for research professionals and users of EDGE, which is the predominant CTMS (Clinical Trials Management System) and LPMS (Local Portfolio Management System) application in the NHS.

9.5 Limitations of the Study

The study was carried out at sites under the administration of The Department of Health (England) and the Scottish Government Health and Social Care Directorates. Due to resource and time limitations the evaluation did not include sites coming under the authorities of the Department of Health (Northern Ireland) and the Department of Health and Social Services (Wales). It is recommended that further research is carried out to encompass all four UK Health Departments to fully understand operational delivery models nationally. Future clinical epidemiological research, that engages with human factors and ergonomics (HF/E) practitioners, is required to expand upon the multi-faceted nature of complexity in cancer clinical trials and human experiences of clinical care across every healthcare organisation.

A limitation of the study is that all the relational properties and multifaceted interfacing concepts could not be conceptualised into a single theoretical model. The participants in the study were limited to those who were closest to the clinical delivery elements of cancer trials in the NHS. To gain a broader understanding of the field of research and innovation and the wider range of stakeholders, sponsors, funders and professionals contributing to the advancement of medical care and drug development through clinical trials, an extended portfolio of operational evaluation studies is needed, using grounded theory to compare and contrast the contextualised experiences and perspectives across the Research and Innovation (R&I) continuum and professions.

9.6 Implications for research and practice

Evidence identified gaps in resource and reimbursement in relation to the work contribution by sites. A national review into existing funding and operational models, including the relevance of current site performance metrics is a critical requirement and should be prioritised by the NIHR and NHS collectively.

Results from this study have identified that the capacity and capability of the system is constrained by many complex and interacting factors. Paradoxes are prevalent in the clinical research delivery model and entangled operational healthcare systems in which they reside. Health care organisations (HCOs) need to evolve in tandem with progress in the medical sciences in order to fulfil ambitions for the delivery of personalised medicine within the NHS. Without a levelling-up of resources and knowledge in the clinical research and operational delivery fields, genomic and personalised medical models are unsustainable. Healthcare factors and ergonomics research and evaluation is needed to answer questions on how clinical research delivery is advanced, optimised and sustained, such as:

- What are the population level criteria for conducting precision medicine trials in the NHS and will they be designed to prevent demographic disparities?
- How are misaligned objectives and system tensions addressed?
- Where are the resource and capacity deficits in the system?
- How can fair and sustainable funding allocations and delivery models be designed to support ambitions for complex clinical trials with intensive procedures and extensive follow-up of patients?
- How do we maximise performance within systems where there are challenging constraints?
- How do we design rational models with the capacity to manage the growing demands of healthcare research?

The implications of the growing demands of clinical research delivery and healthcare systems in general requires a significant shift in the way that the NHS and its network partners interact and operate. To deliver personalised medicine and clinical research in the era of genomic medicine and in a VUCA (Volatility, Uncertainty, Complexity, Ambiguity) world, a human-centred and complex adaptive systems approach is required. A systems approach reflects a holistic concern for the potential of the system as a whole as well as the capacities, capabilities and sensibilities of the humans within it and for who it is created to serve and support. Future governance and funding models need to develop supporting philosophies and cultures alongside designing system responses and mechanisms capable

of responding to emergence and complexity to effectively manage; the workloads, burdens, capacities, capabilities and resources for clinical research delivery and healthcare operations and environments. There is an argument to state that to undertake regular evaluative research of the state and nature of the clinical research delivery industry in the UK should be an ethical requirement of the NHS, NIHR and its partners. There is a moral obligation for researchers to ensure that the work they undertake, and resource allocated to perform these activities provides value, service efficiency and participant benefit. This study performs an ethical role in the review of current NHS research delivery with the intent of improving performance and patient experience through grounded knowledge of current practice. Future research should consider the inclusion of the larger patient and professional ethnic and rural communities in operational and service delivery evaluation research.

9.7 Recommendations

The recommendations arising from the study's grounded theory are based upon the views and experiences of key stakeholders, be they patients or research professionals, and seek to provide praxiological and sustainable solutions for healthcare and clinical research delivery which provide are holistic, inclusive and health promoting, whilst recognising the inherent nature of complexity in systems (human, technical and operational). A systems-based approach to developing effective research capacity planning and performs an ethical role in the review of current NHS research delivery and should be adopted to support improved operational performance and enhance patient experiences. The solutions and models we develop for delivering sustainable and equitable health, which can continue to progress scientific knowledge and design new therapeutic drugs and effective, innovative healthcare interventions, must embrace and accept the complexity and emergent nature of human and social systems to build our knowledge and capacity to manage and promote public health and the provision of salutogenic environments.

An adaptive NHS research delivery framework capable of analysing and monitoring research capacity and operational models in real-time and over time would enhance knowledge and support strategic planning. This study contributes in-depth qualitative review into operational aspects of clinical trials by engaging key stakeholders in defining variables relating to service pressures as well as highlighting best practices. The nuances and complexities of cancer clinical research delivery necessitated a study design involving a critical analysis of strategies, processes, and technologies, through a collation and synthesis of prismatic perspectives and experiential data.

In Chapter Two (section 2.4.3) the 6 principles proposed by Braithwaite (2018, pp.1-3) as an approach to change in healthcare were highlighted, and their fit with the findings from this study in relation to cancer clinical trial delivery. These principles have been incorporated into the following recommendations for the advancement and enhancement of clinical research within the NHS.

Principles for healthcare improvement
Pay more attention to how care is delivered at the coalface
Meaningful improvement is local, centred on natural networks of clinicians and patients
Appreciate how clinicians handle dynamic situations daily, constantly adapting, and getting so much right, and identify the factors underpinning that success
Identifying achievements across healthcare delivery and understanding their common factors (commonly reflecting complexity thinking)
Humble aspirations - recognition that small initiatives can yield unanticipated outcomes
Adopt a new mental model that appreciates the complexity of care systems and understands that change is always unpredictable

Table. 9.1 Principles for healthcare improvement

9.8 Future Research

The concepts discussed and presented through the voices of the EFACCT study participants are abundant and offer a cornucopia of relational properties, which warrant further detailed and directed research. Future research in collaboration with the NIHR, HRA and NHS Digital will facilitate further enhancements to clinical trial delivery based on the research findings. Theoretical models and the TRACAT tool, created as a result of the research should be assessed for the potential for future research in wider contexts such as primary care or in other therapeutic areas. The data bank of concepts accumulated in the study will facilitate further theoretical comparisons in future research.

Future research is needed looking at the nature of transdisciplinary practice and knowledge exchange across the interacting professions and organisations involved in the delivery of translational medicine. The NHS, NIHR and government health bodies need to enhance existing clinical research governance frameworks to develop effective environments, policies, and practices, which align with international conventions that recognise “the right of everyone to the enjoyment of the highest attainable standard of physical and mental health” (United Nations, 1976). To achieve this there needs to be investment in education and development as well as research on the operational aspects of clinical research and healthcare delivery. Future research therefore needs to be conducted within the field of human factors and ergonomics (HFE) and the analysis of systems and the humans within

them to manage the complexities, challenges and emergent phenomena that are present. This requirement is prescient for the field of clinical research delivery, due to the pace of change and demands on resources which the profession is currently experiencing with the move to personalised medicine, limitations on resourcing and increasing patient burdens arising from an ageing population with complex diseases and chronic conditions with comorbidities.

9.9 Concluding Summary

This study contributes unique insights to literature fields linked into the conceptualisation and realities of ***being human***, within the domain of cancer clinical research and healthcare delivery. The properties of ***being human*** also informs knowledge exchange and future research opportunities across the medical and social sciences. The Prismatic Coherence Model (PCM) is an emergent, adaptive conceptual tool which can be employed in multiple domains and complex adaptive systems, supporting and enhancing the design and delivery of sustainable, coherent, human-centred strategies and solutions for **human benefit**. Through engagement with current practices and contexts, the resultant grounded data and testimonies of key stakeholders provided grounded theoretical concepts which can educate and inform healthcare providers, strategists and policy makers in designing optimal and efficient clinical research studies and delivery models, which maximise opportunities for cancer patients to access the latest treatment options, support the health and capacities of research professionals, meeting the human needs and wellbeing of individuals (patients or professionals). The design of clinical trials as well as the operational models supporting their deliver requires the meaningful involvement and engagement of key stakeholders with situated knowledge and experience (including patients and clinical trial delivery professionals) to ensure the sustainable and equitable advancement of human-centred cancer clinical research and personalised medicine.

Respecting the quantum nature of health and the importance of understanding the reality of ***being human within a healthcare system***, either as a patient or as a professional, strategic planning and ongoing operational delivery models should incorporate continuous contextualised evaluation and conceptual modelling with embedded feedback loops. In order to maximise the potential for research and innovation in clinical research and healthcare the implementation and governance frameworks need to ensure that there are processes in place to conduct cyclical qualitative and quantitative evaluation of the capacities and capabilities of the system, adjusting funding and resources in line with evolving and dynamic changes and demands. The human perspectives presented in this thesis, which have informed the development of a grounded theory of complexity and

serendipity in cancer clinical trials, offer an explanatory framework to support future research into strategy planning and operational management, in the application and development of a Prismatic Coherence Model (PCM). The research has established foundations for broadening the field of knowledge into focused operational understanding of cancer research delivery, and highlighted the need for developing better communication and effective feedback and support mechanisms for research professionals, across the ranging interfaces of the NHS and between its professions, organisations and complexes of networked processes and systems continually evolving and interacting in the development of scientific and clinical advancements for sustainable population health promotion. Evidential systemic relationships between scientists, healthcare professionals and policy makers need to be ethically and strategically aligned in order to maximise the opportunities for discovery, knowledge exchange and human capacities. This thesis has presented a detailed, contextual evaluation of cancer clinical trial delivery complexities in the UK, and offers a humanistic perspective and conceptual framework to support dynamic NHS design thinking.

Throughout the study the voices of patients and professionals have been central to understanding the nature of cancer clinical trial delivery in the NHS. It is therefore germane to offer two concluding statements from the study's participants to encapsulate the nature of the study and the realities of clinical research in the NHS from the perspective of the research professionals and the patients closest to its experiential realities:

Research Professional	Cancer Clinical Trial Patient
"I think we live in a complicated world and research is complicated ...complexity is not necessarily appreciated by the rest of the world." (Participant ID: 005120)	"I think I've been so lucky because I felt like I'd had a whole holistic approach whereas speaking to other patients who've just gone through regular treatment, I don't think they have. And I've also been lucky because I've been able to give my input into what I want, what I want to happen" (Participant ID: 034001)

Table 9.2. Concluding Participant Statements

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Appendices

Appendix 1: EFACCT Study Documentation List

EFACCT		
Document List		
Document Name	Document Date	Version
EFACCT - Participant Information Sheet –Delphi Study - Patient – Version 3.0 – 24/08/2017	24/08/2017	3.0
EFACCT - Participant Information Sheet – Delphi - Research Professional - Version 3.0- 24/08/2017	24/08/2017	3.0
EFACCT - Delphi Demographics Form – Patient- Version 3.0 – 06/07/2017	06/07/2017	3.0
EFACCT - Delphi Demographics Form – Research Professional- Version 3.0 – 06/07/2017	06/07/2017	3.0
EFACCT - Delphi Round 1 Questionnaire – Patient- Version 3.0 – 06/07/2017	06/07/2017	3.0
EFACCT - Delphi Round 1 Questionnaire – Research Professional- Version 3.0 – 06/07/2017	06/07/2017	3.0
EFACCT_ Delphi Invitation Letter _ Patient_ V2.0_ 24/08/2017	24/08/2017	2.0
EFACCT_ Delphi Invitation Letter _ Research Professional V2.0 24/08/2017	24/08/2017	2.0
EFACCT - Delphi Participant Consent Sheet - Version 3.0 – 24/08/2017	24/08/2017	3.0
EFACCT - Participant Information Sheet - Questionnaire Study – Patient - Version 3.0 – 24/08/2017	24/08/2017	3.0
EFACCT- Participant Information Sheet Questionnaire Study – Research Professional - Version 3.0 - 24/08/2017	24/08/2017	3.0
EFACCT Questionnaire – Patient- Version 1.0 – 19/06/2017.	19/06/2017	1.0
EFACCT Questionnaire – Research Professional- Version 1.0 – 19/06/2017.	19/06/2017	1.0
EFACCT - Questionnaire Invitation Letter _ Patient _ V1.0_ 20/06/2017	20/06/2017	1.0
EFACCT - Questionnaire Invitation Letter _ Research Professional _ V1.0_ 20/06/2017	20/06/2017	1.0
EFACCT - Participant Information Sheet –Patient Interview - Version 3.0 – 04/09/2017	04/09/2017	3.0
EFACCT - Participant Information Sheet – Interview - Research Professional - Version 3.0 - 24/08/2017.	24/08/2017	3.0
EFACCT Demographics Form– Patient Interview- Version 1.0 – 19/06/2017	19/06/2017	1.0
EFACCT Demographics Form– Research Professional Interview- Version 1.0 – 19/06/2017	19/06/2017	1.0
EFACCT– Interview Invitation Letter _ Patient_ V1.0_ 20/06/2017	20/06/2017	1.0
EFACCT– Interview Invitation Letter _ Research Professional _ V1.0_ 20/06/2017	20/06/2017	1.0
EFACCT - Interview Participant Consent Sheet – Version 3.0 – 24/08/2017.	24/08/2017	3.0
EFACCT Interview Guide _Patient _v1.0_ 22/06/2017	22/06/2017	1.0
EFACCT Interview Guide _Research Professional _v1.0 22.06.17	22/06/2017	1.0
EFACCT - Participant Contact Details Form – Interview Study - Version 1.0 - 19/06/2017.	19/06/2017	1.0
EFACCT Patient Poster Version 1.0 16.06.17	16/06/2017	1.0
EFACCT- Twitter Promotion- Version 1.0 – 16/06/2017	16/06/2017	1.0
EFACCT - Website Landing Page _v1.0_ 30/06/2017	30/06/2017	1.0
EFACCT Lay Protocol Summary Version 1.0 - 19.06.17	19/06/2017	1.0
Evaluating Patient Follow-up And Complexity in Cancer clinical Trials Protocol V3.0 (040917) FINAL	04/09/2017	3.0
EFACCT – Email template to site – v2.0 24/08/2017	24/08/2017	2.0
IRAS Form		
MNCA		
SoA and SoE		
Site File & Supporting Set Up Documents		
REC Letters		
Sponsor Docs inc. Insurance		
CVs GCPs		

Appendix 2: Patient Interview Topic Guide (ethics approved version)

Evaluating Patient Follow-up and Complexity in Cancer Clinical Trials- EFACCT

Take consent and complete demographics form

Interview Guide

The following statements be given at the start and end of each interview.

Interview start

Thank you for agreeing to take part in this interview today.

Before we begin the interview do you have any questions you would like to ask?

If you feel uncomfortable at any point and would like to stop the interview please let me know.

Please feel free to let tell me if you don't want to answer any questions or find anything too distressing to talk about.

Can I just check again that you are happy for me to record the interview and make notes?

The interview will last approximately one hour but we can take a break at any point.

Are you happy to start the interview?

Interview close

Thank you for your giving your time today.

Is there any else you feel you would like to discuss?

Are there any questions you would like to ask me about the study?

How are you feeling after talking to me today? [Prompt to identify if need to involve support from current clinical research professionals, direct to PALS or to GP]

Interview purpose

This research is part of a PhD study supported by the United Lincolnshire Hospitals NHS Trust and the University of Lincoln which is involving patients and research professionals in describing their experiences of participating in clinical trials. The aim is to understand the important elements that the NHS should focus on to develop solutions to support patients and researchers alike. Your insight as a patient is very important in being able to guide future pathways and services that enhance the patient experience and access to the latest treatments and services.

Interview outline topics and example questions [these are initial sample questions which will be developed further following the completion of the Delphi and questionnaire studies]

1. Please describe your experience of participating in a cancer clinical trial?
2. Were there any elements which you felt were complicated or difficult for you understand?
3. Are there any areas that you felt took up a lot of your time which you think could be managed differently?
4. Do you feel you could have benefitted from additional support during the trial?
5. Can you tell me about the follow-up visits you attended and how these impacted your life?
6. Can you tell me about elements of the trial you took part in, the different teams and staff you met?
7. Were there any elements that you found very beneficial or seemed efficient and supportive?

Appendix 3: Research Professional Interview Topic Guide (ethics approved version)

Evaluating Patient Follow-up and Complexity in Cancer Clinical Trials- EFACCT

Take consent and complete demographics form

Interview Guide

The following statements be given at the start and end of each interview.

Interview start

Thank you for agreeing to take part in this interview today.

Before we begin the interview do you have any questions you would like to ask?

If you feel uncomfortable at any point and would like to stop the interview please let me know.

Please feel free to let tell me if you don't want to answer any questions or discuss any particular topics.

Can I just check again that you are happy for me to record the interview and make notes?

The interview will last approximately one hour but we can take a break at any point.

Are you happy to start the interview?

Interview close

Thank you for your giving your time today.

Is there any else you feel you would like to discuss?

Are there any questions you would like to ask me about the study?

Interview purpose

This research is part of a PhD study supported by the United Lincolnshire Hospitals NHS Trust and the University of Lincoln which is involving patients and research professionals in describing their experiences of participating in clinical trials. The aim is to understand the important elements that the NHS should focus on to develop solutions to support patients and researchers alike. Your insight as a research professional is very important in being able to guide future pathways and services that enhance the patient experience and access to the latest treatments and services and support professionals in delivering research.

Interview outline topics and example questions [these are initial sample questions which will be developed further following the completion of the Delphi and questionnaire studies]

1. Please describe your current role in clinical trial delivery?
2. What do you perceive to be elements that contribute to the complexity in the delivery of cancer clinical research in the NHS?
3. Can you describe your views in relation to patient follow-up visits across the trials you have worked on and the capacity for trial sites in managing patient visits?
4. Can you describe to me other activities or processes which can place a significant burden upon operational resources of participating sites?
5. What do you perceive to be barriers in delivering trials in the NHS?
6. What do you believe support sites and researchers in delivering effective cancer research in the UK?

[Additional guide questions will be prepared following the outcome of the Delphi survey and questionnaire study.]

Appendix 4: Research Professional Delphi Consensus Statements

Table 6.1 Summary of Consensus Statements by Category & Highest % Agreement Level			
Q. No. & Category	Consensus Statement	Median Response	% Level Agreement
Q1.4 Follow-up Definition	NIHR/Nationally Agreed Definition of Follow -Up: A nationally agreed definition of the term 'follow-up' and/or types of 'follow-up' in relation to research delivery in the NHS should be published by the NIHR so that all clinical research professionals, allied professions and associated bodies conform to a standard terminology and parameters.	Strongly Agree (7)	92%
Q2.19 Barriers & Burdens	Trial sites are under constant pressure to open trials with expectations to recruit high numbers of trial participants to increasingly complex and higher intensity trials treating patients with rare cancers whilst being faced with reduced resources. Budgetary constraints and outdated payment terms which do not accurately reflect the requirements, time and effort of sites, represent a high risk to NHS organisations where audited and reduce the capacity to maintain effective trial delivery and meet patient needs through inadequate staffing levels. The NIHR needs to acknowledge the increased complexity of cancer trials, the workload impact in co-ordination and management, augmented lab work & data management demands and comprehend the nature of academic and commercial trials and their associated pressures on research delivery sites and staff through the development an effective and consistently validated funding & support model.	Strongly Agree (7)	92%
Q2.13 Barriers & Burdens	Principal Investigator oversight and involvement is lacking at times in certain tumour sites, studies or hospital locations, particularly for multi-site trusts where the PI works from one centre, leaving Research Nurses feeling unsupported. When new studies are set up it is important to ensure there is a clear understanding of roles and responsibilities of the research team so that workloads can be accurately assessed. Principal Investigators should be aware that they can delegate tasks according to GCP but retain overall responsibility for the study beyond the treatment elements and need to maintain involvement in patient follow-up and review.	Strongly Agree (7)	88%
Q2.35 Barriers & Burdens	The management of patient follow-up in cancer studies is a key factor affecting site capacity and ability to implement, recruit to and deliver effective research. Follow-up visits for cancer patients and research studies can continue for many years and often until death. Patients may also transfer from other hospitals for follow-up care, which has an impact of the research staff and capacity at site. Follow-up data is essential to the outcomes of research studies, but the NIHR research delivery model focuses on and supports recruitment but not follow-up activities. With continual pressure to open studies to gain accruals the ability of teams to manage existing numbers of patients in follow-up is compromised leading to missed timelines, patient visits and missing data, which could be extremely detrimental to follow-up studies and invalidate results of the trial. These burdens and issues are not recognised within research delivery.	Strongly Agree (7)	85%
Q2.22 Barriers & Burdens	Clinical Research Organisations tend to outsource a lot of work which adds to a site's administrative burden and complexity in having to deal with multiple supplier IT platforms and electronic data capture systems (e.g. RTSM, EDC, eCRFs, ePRO & eQoL), all with different user logins and interfaces. The complexities of some systems can require significant time to train which is difficult to include into the busy schedules of teams and represents a further burden to sites.	Strongly Agree (7)	84%
Q2.23 Barriers & Burdens	Protocols and study documentation supplied to assess capacity and capability do not show the impact of eCRFs or the full extent of information and demographic data required. High data demands and the management of sponsor data queries are a	Strongly Agree (7)	84%

	significant and time-consuming administrative burden for sites. Difficulties in communication or slow responses can lead to extended or additional work for sites especially where a sponsor's representative does not comprehend the problems in obtaining retrospective information or understand the nature of certain data issues		
Q2.29 Barriers & Burdens	Protocol defined timelines within some trials can be difficult for sites to achieve. Requirements for additional tests at trial entry or specific time points, such as CT scans, ECHOs, ECGs, can be challenging to co-ordinate due to resource issues, limited appointment availability or the length of time taken to receive some results e.g. blood results from pathology or slow reporting of scans from the imaging team.	Strongly Agree (7)	84%
Q3.21 Complexity	Cancer clinical trial protocols have varying degrees of complexity, but the burden of protocol procedures is growing which adds to the complexity of implementing and delivering studies, with incremental levels of training (e.g. 450 training slides on a 5 arm study with strict guidelines) and increased volumes of tests, questionnaires, visits, assessments and more detailed data requirements.	Strongly Agree (7)	96%
Q3.1 Complexity	Cancer is no longer one diagnosis but a complex range of conditions with many sub-groups. Cancer clinical research complexity is growing as trials now study a wide range of cancers, rare tumours, haematological malignancies and molecular sub-types with treatments becoming precise, targeted and having more options at each stage of the cancer journey. Trials may now only be suitable for a subgroup of the cancer population, such as lymphoma, which has more than 70 sub-types. Sites need to have a greater number of trials open to ensure patients have the opportunity to participate, but each trial will recruit a smaller number of patients adding to the complexity of delivering research.	Strongly Agree (7)	92%
Q3.6 Complexity	The clinical trial phase is a key determinant in study complexity with earlier phase studies typically more complex, requiring lots of visits, extra tests or PK analysis. Early phase clinical trials frequently need input from other departments e.g. ophthalmology or dermatology requiring collaboration to arrange time and appointments. Studies involving overnight stays can be hard to organise due to bed and resource capacity. Admitting patients for trial monitoring can be hard to justify and negotiate when beds are full. Later stage studies such as Phase 3 may include standard of care, but complexity is added due to the larger volume of patients required and lengthy follow-up.	Strongly Agree (7)	88%
Q3.17 Complexity	Managing the communication and co-ordination of clinical trial appointments, procedures, and diagnostics, e.g. mammography, ECHO, ECGs, clip insertion, CT scans, bone marrow & surgical/specialist procedures is pressurised and complicated when liaising with multi-disciplinary teams and support services to meet protocol specific timeframes or treatment windows. Aligning a study with the two week wait or fitting it into a surgical pathway isn't always possible due to operational problems and capacity issues.	Strongly Agree (7)	88%
Q3.16 Complexity	Protocol designs that involve short timelines and windows for procedures are more complex and logistically challenging for sites to deliver when trying to schedule registration, randomisation, assessments and treatment around the availability of NHS resources, especially where there is little flexibility from the sponsor. It can be difficult when a patient is excluded from a trial because of scan timings or initial bloods not having been taken by other clinicians who saw the patient first at diagnosis, but not as part of a trial. Additional complexities arise from late diagnostics where a patient comes to the centre late.	Strongly Agree (7)	80%
Q3.33 Complexity	The management of Adverse Events, Serious Adverse Events and SUSARS can be time consuming in high risk trials or trials where there are a lot of these and can become complex if patients become very unwell. The cancer type, the nature of the patient population and how well they are will all significantly affect the complexity of the study and will affect the number of likely	Strongly Agree (7)	80%

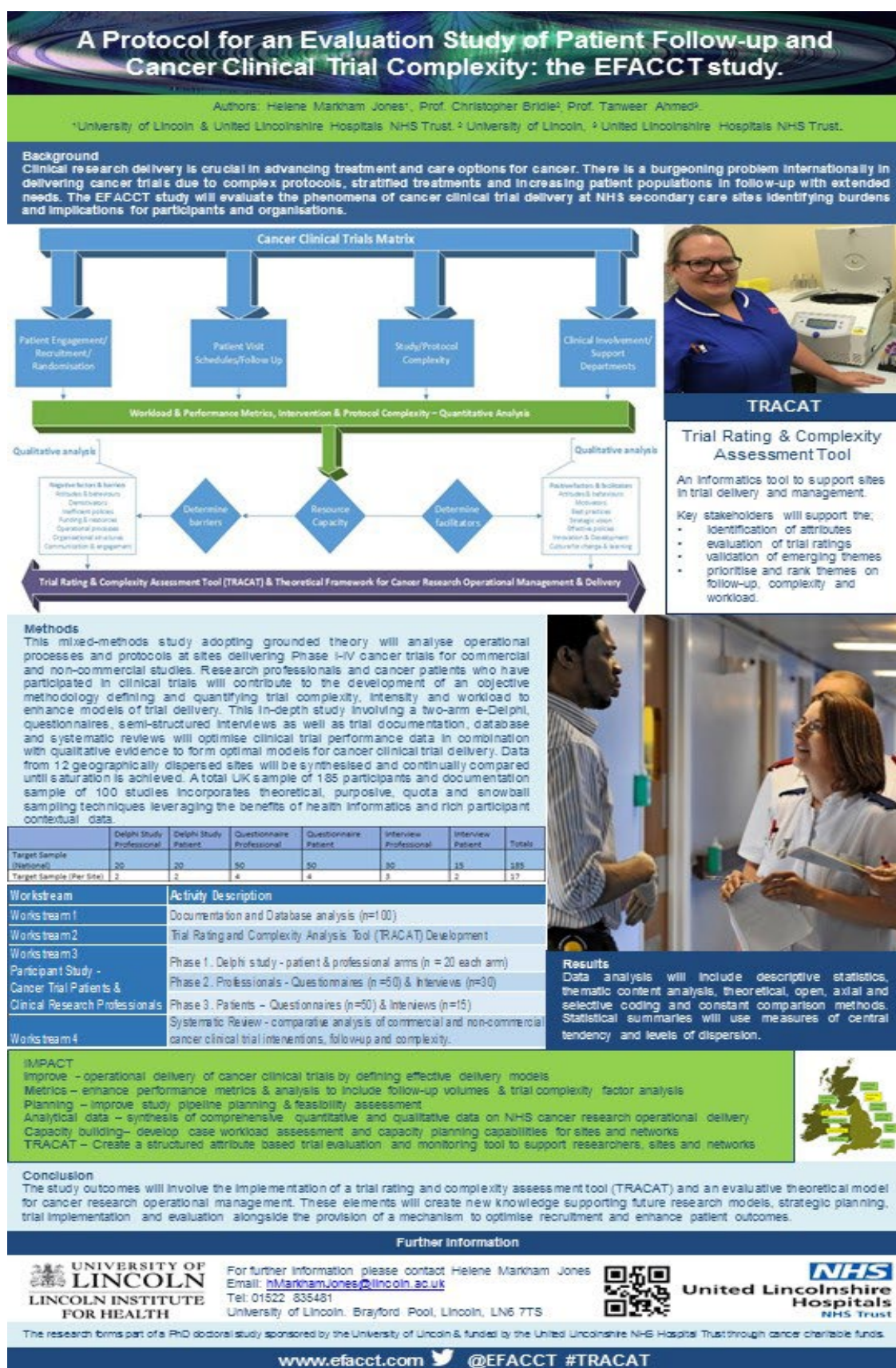
		SAEs and amount of clinical input required.		
Q4.2	Factors Affecting Capacity	Effective communication is the golden thread, which ensures an organisation can work effectively. The lack of integration, communication and collaboration across hospital sites and departments impacts trial delivery.	Strongly Agree (7)	88%
Q4.4	Factors Affecting Capacity	Inadequate resources and facilities affect the capacity of research staff to conduct their jobs to the standards expected.	Strongly Agree (7)	88%
Q4.3	Factors Affecting Capacity	Inadequate staffing levels make it difficult for teams to meet the demands of current trials and to run as efficiently and effectively as possible.	Strongly Agree (7)	84%
Q4.8	Factors Affecting Capacity	Allied professional services and support departments such as radiology and pathology are crucial to the running of cancer clinical trials. It is essential that their involvement in trials is adequately rewarded financially, and that professionals and teams are motivated by recognition of their scientific or academic contribution to research in trial publications.	Strongly Agree (7)	84%
Q4.45	Factors Affecting Capacity	Protocols which are overly complicated, do not realistically work with hospital systems or have been written in such a way that they are hard to interpret impact capacity and efficiency. Studies with well written protocols that consider the practicalities of trial delivery are much easier for sites to run.	Strongly Agree (7)	84%
Q4.46	Factors Affecting Capacity	The increasing complexity of new cancer trials and protocols can be challenging for sites to deliver and therefore detailed feasibility is essential, but the implication of running the study is not always apparent at the outset as frequent or unnecessary amendments can impact the capacity of the team as the study progresses.	Strongly Agree (7)	84%
Q4.6	Factors Affecting Capacity	Research support staff and data managers are essential to effective trial management and in supporting clinical teams through trial administration, laboratory work, quality assessments and data management, all of which are crucial in answering the clinical trial hypothesis. Ensuring there is continued funding in place to maintain their jobs is time consuming and challenging. Capacity is affected by the lack of data management and administrative resource available.	Strongly Agree (7)	80%
Q4.7	Factors Affecting Capacity	Workforce limitations of support departments involved in trial delivery e.g. radiology, pathology, cardiology etc. affects research capacity with some departments limited by resource and their ability to accommodate additional trial work in a timely manner.	Strongly Agree (7)	80%
Q5.2	Top Strategic Priorities	Development of biomarkers for predicting suitability and response to treatment and early diagnosis techniques.	Strongly Agree (7)	88%
Q5.6	Top Strategic Priorities	Improve collaboration and communication between Trusts and organisations (including non-NHS care providers such as hospices) to ensure patient care and choice is prioritised and all are given the opportunity to participate in research, where desired and appropriate.	Strongly Agree (7)	88%
Q5.13	Top Strategic Priorities	Decision makers at national and local levels require a greater level of understanding of the constraints, resource and capacity issues and the priorities for research delivery and funding in the NHS.	Strongly Agree (7)	88%
Q5.20	Top Strategic Priorities	Promote cultural change and education to raise the profile of research and highlight the importance of clinical trials in the provision of cancer care within the NHS.	Strongly Agree (7)	88%
Q5.22	Top Strategic Priorities	Ensure development of strong working relationships and rapport between research teams and supporting departments.	Strongly Agree (7)	88%
Q5.3	Top Strategic Priorities	Investment in technology and the development of a national centralised database to enable access to trial information for researchers and patients with the ability to search by tumour site, patient factors and study eligibility in real time to expand trial opportunities to more patient groups.	Strongly Agree (7)	84%

Q5.4 Strategic Priorities	Top	Increase accessibility, choice and participation in clinical trials to make a difference for patients in the NHS and to advance medicine, care, survival and access to the best evidence based treatments options.	Strongly Agree (7)	84%
Q5.7 Strategic Priorities	Top	Cancer research should be recognised as a speciality area with a core funding model developed to reflect the service and support requirements of research sites and meet the needs of patients within this complex field.	Strongly Agree (7)	84%
Q5.9 Strategic Priorities	Top	Improve data sharing between departments, hospitals and NHS care providers to facilitate accurate and timely data collection.	Strongly Agree (7)	84%
Q5.12 Strategic Priorities	Top	The structure, activity and provision for research across the UK is variable and inconsistent. CRN funding needs to be reviewed to develop a clear equitable banding structure, which is measured and fairly reflects research activity.	Strongly Agree (7)	84%
Q5.19 Strategic Priorities	Top	Facilitate a detailed multi-disciplinary feasibility process to include all relevant staff and services ensuring all parties have capacity and capability to deliver all elements of the trial from the outset and can provide continued and consistent care during the treatment and follow-up stages.	Strongly Agree (7)	84%
Q5.28 Strategic Priorities	Top	Provide research specific induction training for registrars and consultants rotating hospitals to raise awareness of current trials and clinical research activities.	Strongly Agree (7)	84%
Q5.31 Strategic Priorities	Top	Increase the use and uptake of IT systems, software and computer tablets for data capture and storage (e.g. eCRFs and electronic site files), support paper-light research and reduce or remove paper based data forms.	Strongly Agree (7)	84%
Q6.17 Effective Research Practice		Good communication skills and effective patient relationships help participants understand the trials and what participation will mean for them.	Strongly Agree (7)	88%
Q6.26 Effective Research Practice		Well run, established departments and research teams who receive regular training, are efficient, proactive, flexible to change and demonstrate a wealth of knowledge and excellence in clinical trial delivery.	Strongly Agree (7)	84%
Q6.14 Effective Research Practice		Principal Investigators who proactively support and engage with the research team, are available to provide advice when required, maintain oversight on their trials, including follow-up visits and discussion of treatment plans, ensure that trials are run effectively and safely in their research area.	Strongly Agree (7)	80%
Q6.18 Effective Research Practice		Effective practice is demonstrated by dedicated staff who are willing to go above and beyond to recruit and support patients in clinical trials. Caring and skilled research professionals who treat patients as individuals and not just as a recruitment figure are appreciated by patients who value their support, and continue on the trial for follow-up visits and are less likely to withdraw from studies.	Strongly Agree (7)	80%
Q6.21 Effective Research Practice		The provision of dedicated teams and specialists for specific cancer disease areas/sites within trial units enhances research delivery and staff knowledge in their speciality, in contrast to stretching resources across multiple specialisms.	Strongly Agree (7)	80%
Q6.24 Effective Research Practice		The dedication, passion and skill of research staff and putting the patient's best interest first greatly contributes to the effective running of trials in the NHS, despite being understaffed, and strong collaborative teamwork supports staff retention under very tight circumstances.	Strongly Agree (7)	80%
Q6.25 Effective Research Practice		Excellent communication and collaboration between supporting departments, clinics, staff roles and specialisms is demonstrated in effective research practice and will support efficient trial delivery.	Strongly Agree (7)	80%
Q7.3 Additional Delphi Considerations		Supporting the primary end points of clinical trials should be the main goal of the NIHR and follow-up should be appropriately funded to achieve this.	Strongly Agree (7)	72%

Appendix 5: Research Professional Delphi TRI Rankings

Table 6.2 Trial Rating Indicators (TRIs) Priority Rankings				
Rank	Q. No	Trial Rating Indicators (TRIs) Priority Categories	% Ranked 7 (Highest Priority)	Median Response
1	Q8.2	Protocol Procedures - Treatments, interventions, tests, samples and their volumes, frequencies, and timelines.	72.00%	7 - Highest Priority
2	Q8.1	Resource Demands - Feasibility and personnel impact.	72.00%	7 - Highest Priority
3	Q8.7	Investigational Treatment Complexity - Drug administration, novel therapy/drug, toxicity & risk, treatment windows and timelines.	64.00%	7 - Highest Priority
4	Q8.5	Follow-up and Visit Requirements - Type, frequency, and duration.	60.00%	7 - Highest Priority
5	Q8.3	Data Management, Administration & Monitoring - Sponsor defined requirements.	48.00%	6.5 - Ranking Priority
6	Q8.4	Support Department Involvement & Outsourcing - Support services (Trust/external), e.g. RECIST reporting, QA procedures, specialist skills, facilities, equipment, central review, or sub-contracted requirements.	48.00%	6 - Ranking Priority
7	Q8.8	Clinical Efficacy & Safety - Clinical pharmacology and pharmacokinetics requirements.	44.00%	6 - Ranking Priority
8	Q8.11	Patient Management - patient monitoring, safety, reporting or complex patient pathways.	44.00%	6 - Ranking Priority
9	Q8.12	Patient Selection - Patient identification, screening, eligibility criteria and consent process.	36.00%	6 - Ranking Priority
10	Q8.6	Cancer Disease Complexity, Patient Population and Health Status.	32.00%	6 - Ranking Priority
11	Q8.13	Trial Phase and Design - Randomisation process, multiple treatment arms, blinding, study phase.	28.00%	6 - Ranking Priority
12	Q8.10	Recruitment Potential - Recruitment feasibility and target potential by disease and study type.	24.00%	6 - Ranking Priority
13	Q8.14	Technology & Training - Sponsor defined requirements for study.	24.00%	6 - Ranking Priority
14	Q8.9	Protocol Variations - Protocol amendments, study extensions and ancillary/sub studies.	16.00%	6 - Ranking Priority

Appendix 6: Publications and Conference Poster Examples



A Protocol for an Evaluation Study of Patient Follow-Up and Cancer Clinical Trial Complexity: the EFACCT study.

Abstract ID: 922

Year: 2017

Session type: Proffered paper

Theme: Healthcare delivery

Helene Markham-Jones¹, Prof. Christopher Bridle¹, Prof. Tanweer Ahmed²

¹University of Lincoln, ²United Lincolnshire Hospitals Trust

Abstract

Background

Clinical research delivery is crucial in advancing treatment and care options for cancer. There is a burgeoning problem internationally in delivering cancer trials due to complex protocols, stratified treatments and increasing patient populations in follow-up with extended needs. The EFACCT study will evaluate the phenomena of cancer clinical trial delivery at NHS secondary care sites identifying burdens and implications for participants and organisations.

Method

This mixed-methods study adopting grounded theory will analyse operational processes and protocols at sites delivering Phase I-IV cancer trials for commercial and non-commercial studies. Research professionals and cancer patients who have participated in clinical trials will contribute to the development of an objective methodology defining and quantifying trial complexity, intensity and workload to enhance models of trial delivery. This in-depth study involving a two-arm e-Delphi, questionnaires, semi-structured interviews as well as trial documentation, database and systematic reviews will optimise clinical trial performance data in combination with qualitative evidence to form optimal models for cancer clinical trial delivery. Data from 12 geographically dispersed sites will be synthesised and continually compared until saturation is achieved. A total UK sample of 185 participants and documentation sample of 100 studies incorporates theoretical, purposive, quota and snowball sampling techniques leveraging the benefits of health informatics and rich participant contextual data.

Results

Data analysis will include descriptive statistics, thematic content analysis, theoretical, open, axial and selective coding and constant comparison methods. Statistical summaries will use measures of central tendency and levels of dispersion.

Conclusion

The study outcomes will involve the implementation of a trial rating and complexity assessment tool (TRACAT) and an evaluative theoretical model for cancer research operational management. These elements will create new knowledge supporting future research models, strategic planning, trial implementation and evaluation alongside the provision of a mechanism to optimise recruitment and enhance patient outcomes.

<https://abstracts.ncri.org.uk/abstract/a-protocol-for-an-evaluation-study-of-patient-follow-up-and-cancer-clinical-trial-complexity-the-efacct-study/>

NCRI Cancer Conference Abstract, BT Convention Centre, Liverpool 2017


SPECIALIST: TALKS**'Pick & Mix': 12:50 - 13:55****GATE: LLOYD****GROUND FLOOR****Helene Markham-Jones**

PhD Student, University of Lincoln

Helene's session will focus on embracing new ways of cross-disciplinary working and communal research approaches which recognises the creative potential of individuals, shared knowledge and understanding. Her talk will present the results of the 3 year EFACCT study, conducted at NHS research sites across the UK and demonstrate the outcomes, including the TRACAT tool which maps trial complexity and operates as a workforce planning and capacity tool. The key message of the session is that, as individuals and communities of researchers we can create powerful new models and processes to support research in an era of rapid change, but this has to be through a quantum perspective approach.

Quantum perspectives in a new era of research**Talk 4****12:50-13:20****1 hour**

BMJ Open Evaluating follow-up and complexity in cancer clinical trials (EFACCT): an eDelphi study of research professionals' perspectives

Helene Markham Jones ^{1,2}, Ffion Curtis,¹ Graham Law,³ Christopher Bridle,⁴ Dorothy Boyle,⁵ Tanweer Ahmed²

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ABSTRACT

Objectives To evaluate patient follow-up and complexity in cancer clinical trial delivery, using consensus methods to: (1) identify research professionals' priorities, (2) understand localised challenges, (3) define study complexity and workloads supporting the development of a trial rating and complexity assessment tool (TRACAT).

Design A classic eDelphi completed in three rounds, conducted as the launch study to a multiphase national project (evaluating follow-up and complexity in cancer clinical trials).

Setting Multicentre online survey involving professionals at National Health Service secondary care hospital sites in Scotland and England varied in scale, geographical location and patient populations.

Participants Principal investigators at 13 hospitals across nine clinical research networks recruited 33 participants using pre-defined eligibility criteria to form a multidisciplinary panel.

Main outcome measures Statements achieving a consensus level of 70% on a 7-point Likert-type scale and ranked trial rating indicators (TRIs) developed by research professionals.

Results The panel developed 75 consensus statements illustrating factors contributing to complexity, follow-up intensity and operational performance in trial delivery, and specified 14 ranked TRIs. Seven open questions in the first qualitative round generated 531 individual statements. Iterative survey rounds returned rates of 82%, 82% and 93%.

Conclusions Clinical trials operate within a dynamic, complex healthcare and innovation system where rapid scientific advances present opportunities and challenges for delivery organisations and professionals. Panellists highlighted cultural and organisational factors limiting the profession's potential to support growing trial complexity and patient follow-up. Enhanced communication, interoperability, funding and capacity have emerged as key priorities. Future operational models should test dialectic Singerian-based approaches respecting open dialogue and shared values. Research capacity building should prioritise innovative, collaborative approaches embedding validated review and evaluation models to understand changing operational needs and challenges. TRACAT provides a mechanism for continual knowledge assimilation to improve decision-making.

Strengths and limitations of this study

- The multimodal study design developed consensus-defined trial rating and complexity indicators to support objective analysis of cancer research delivery adaptable to operational evaluation in other therapeutic areas and global settings.
- Qualitative aspects provide in-depth contextual evidence through the 'voices' of patient-facing professionals, articulating human and social aspects of research.
- This study is the first, to our knowledge, to present a Delphi methodology adopting a Singerian approach involving research professionals, in a consensus process which is holistic and dialectical.
- The study involved key stakeholders from a wide geographic base reflecting a heterogeneous sample of clinical trial professionals.
- Participants were limited to research professionals delivering studies at National Health Service sites in Scotland and England. Future research is planned involving a wider demographic to include sponsors, funders, networks and policymakers.

INTRODUCTION

Clinical trial delivery in hospital settings is crucial in advancing cancer care and treatment options with evidence indicating sustained commitment to research enhances performance and patient outcomes.¹ Cancer research has evolved rapidly in recent years, with innovations in immunotherapy and precision medicine increasingly prioritised in healthcare policy. The National Health Service (NHS) has published ambitions to accelerate innovation, outlining a framework for rapid adoption of next generation treatments offering personalised, stratified care and follow-up models.^{2,3}

The ability to translate scientific, laboratory advances in cancer research into clinical and patient benefit through clinical trials is a critical requirement for healthcare providers,

Appendix 7: Patient Participant Recruits

Study	Participant ID	Consent Date	Gender	Date Received First Round Survey	Date Received Final Round Survey	Completed	SITE ID	Comments
Patient Delphi	001001	08/05/2018	F	02/06/2018	28/08/2018	Y	001	
Patient Delphi	001002	09/05/2018	M	31/05/2018	24/08/2018	Y	001	
Patient Delphi	002001	04/05/2018	F	03/06/2018	27/08/2018	Y	002	
Patient Delphi	003001	21/05/2018	F	14/06/2018	Not completed	N	003	
Patient Delphi	005001 - D	21/05/2018	M	21/05/2018	24/08/2018	Y	005	
Patient Delphi	005002 - D	01/06/2018	F	01/06/2018	25/08/2018	Y	005	
Patient Delphi	005003 - D	25/05/2018	F	25/06/2018	05/09/2018	Y	005	
Patient Delphi	005004 - D	24/05/2018	M	25/06/2018	31/08/2018	Y	005	
Patient Delphi	012001	03/05/2018	M	01/06/2018	26/08/2018	Y	012	
Patient Delphi	024001	08/05/2018	M	03/06/2018	Not completed	N	024	
Patient Delphi	024002	18/05/2018	F	05/06/2018	29/08/2018	Y	024	
Patient Delphi	033001	27/04/2018	Female	03/06/2018	31/08/2018	Y	033	
Patient Delphi	033002	08/05/2018	Male	13/06/2018	03/09/2018	Y	033	
Patient Delphi	033003	09/05/2018	Male	12/06/2018	28/11/2018	Y	033	
Patient Delphi	042001	09/05/2018	M	Not completed	Not completed	N	042	
Patient Delphi	042002	08/05/2018	M	15/06/2018	08/09/2019	Y	042	
Patient Delphi	046001	01/05/2018	M	31/05/2018	Not completed	N	046	Withdrawn (ill health)
Patient Delphi	046002	01/05/2018	M	Not issued	Not completed	N	001	Consent form received but no contact details - followed up with site
Patient Questionnaire	001003-Q	Printed	M	09/07/2019	08/08/2019	Y	001	
Patient Questionnaire	001011-Q	Printed	M	20/03/2019	21/03/2019	Y	002	
Patient Questionnaire	002002-Q	Printed	F	14/11/2018	16/11/2018	Y	002	
Patient Questionnaire	002004-Q	Printed	M	14/11/2018	16/11/2018	Y	002	
Patient Questionnaire	002006-Q	Printed	F	14/11/2018	14/11/2018	Y	002	
Patient Questionnaire	002008-Q	Printed	M	14/11/2018	29/11/2018	Y	002	
Patient Questionnaire	003002	Printed	F	30/11/2018	12/12/2018	Y	003	
Patient Questionnaire	005005 - Q	Printed	F	Via site	12/12/2018	Y	005	
Patient Questionnaire	005006 - Q	Printed	M	Via site	12/12/2018	Y	005	
Patient Questionnaire	005007 - Q	Printed	F	Via site	05/02/2019	Y	005	
Patient Questionnaire	005008 - Q	Printed	M	Via site	29/01/2019	Y	005	
Patient Questionnaire	005009 - Q	Printed	F	Via site	24/01/2019	Y	005	
Patient Questionnaire	024003-Q	Printed	M	04/12/2019	22/01/2019	Y	024	
Patient Questionnaire	024004-Q	Printed	M	04/12/2019	22/01/2019	Y	024	
Patient Questionnaire	024005-Q	Printed	M	04/12/2019	22/01/2019	Y	024	
Patient Questionnaire	024006-Q	Printed	F	04/12/2019	12/01/2019	Y	024	
Patient Questionnaire	033004	Printed Q	F	14/12/2018	29/01/2019	Y	033	
Patient Questionnaire	033005	Printed Q	F	14/12/2018	29/01/2019	Y	033	
Patient Questionnaire	033006	Printed Q	F	14/12/2018	05/02/2019	Y	033	
Patient Questionnaire	034001-Q	Printed	F	11/12/2018	07/01/2019	Y	034	
Patient Questionnaire	034002-Q	Printed	F	11/12/2018	07/01/2019	Y	034	
Patient Questionnaire	034003-Q	Printed	F	11/12/2018	08/01/2019	Y	034	
Patient Interview	001001-I	Interview	F	22/05/2019	22/05/2019	Y	001	
Patient Interview	001011-I	Interview	M	09/04/2019	09/04/2019	Y	001	
Patient Interview	002002-I	Interview	F	15/11/2018	15/11/2018	Y	002	
Patient Interview	003008-I	Interview	F	10/12/2018	10/12/2018	Y	003	
Patient Interview	005002-I	Interview	F	05/12/2018	05/12/2018	Y	005	
Patient Interview	005006-I	Interview	M	28/01/2019	28/01/2019	Y	005	
Patient Interview	005008-I	Interview	M	28/01/2019	28/01/2019	Y	005	
Patient Interview	005009-I	Interview	F	11/02/2019	11/02/2019	Y	005	
Patient Interview	024004-I	Interview	M	25/01/2019	25/01/2019	Y	024	
Patient Interview	024005-I	Interview	M	25/01/2019	25/01/2019	Y	024	
Patient Interview	024006-I	Interview	F	23/01/2019	23/01/2019	Y	024	
Patient Interview	033001-I	Interview	F	22/02/2019	22/02/2019	Y	033	
Patient Interview	033004-I	Interview	F	22/02/2019	22/02/2019	Y	033	
Patient Interview	034001-I	Interview	F	06/02/2019	06/02/2019	Y	034	
Patient Interview	034002-I	Interview	F	06/02/2019	06/02/2019	Y	034	
Patient Interview	034003-I	Interview	F	06/02/2019	06/02/2019	Y	034	
Totals	56							

Appendix 8: Research Professional Recruits

Study	Participant ID	Consent Date	Gender	Date Received First Round Survey	Date Received Final Round Survey	Completed	SITE ID
Professional Delphi	001101	21/11/2017	F	15/01/2018	29/07/2018	Y	001
Professional Delphi	001102	22/11/2017	F	25/01/2018	16/07/2018	Y	001
Professional Delphi	001103	22/11/2017	F	22/01/2018	13/07/2018	Y	001
Professional Delphi	001104	27/11/2017	F	05/02/2018	02/08/2018	Y	001
Professional Delphi	001105	19/12/2017	F	31/01/2018	02/07/2018	Y	001
Professional Delphi	001106	19/12/2017	F	12/02/2018	19/07/2018	Y	001
Professional Delphi	002103	15/01/2018	F	29/01/2018	19/07/2018	Y	002
Professional Delphi	003101	02/02/2018	F	06/02/2018	03/07/2018	Y	003
Professional Delphi	005106 - D	11/01/2018	F	23/01/2018	28/06/2018	Y	005
Professional Delphi	005104 - D	11/01/2018	F	29/01/2018	02/07/2018	Y	005
Professional Delphi	005101 - D	14/12/2017	F	18/01/2018	19/07/2018	Y	005
Professional Delphi	005105 - D	12/01/2018	F	31/01/2018	22/08/2018	Y	005
Professional Delphi	005102 - D	11/01/2018	F	Not completed	N/A	N	005
Professional Delphi	005103 - D	11/01/2018	F	Not completed	N/A	N	005
Professional Delphi	005107 - D	11/01/2018	F	Not completed	N/A	N	005
Professional Delphi	012101	15/01/2018	F	16/01/2018	02/07/2018	Y	012
Professional Delphi	024101	20/12/2018	F	02/02/2018	09/07/2018	Y	024
Professional Delphi	024102	16/01/2019	F	31/01/2018	25/07/2018	Y	024
Professional Delphi	029101	27/12/2017	M	Not completed	N/A	N	029
Professional Delphi	029102	29/12/2017	M	31/01/2018	Not completed	N	029
Professional Delphi	029103	03/01/2018	F	27/01/2018	01/08/2018	Y	029
Professional Delphi	029104	29/12/2017	M	15/02/2018	02/07/2018	Y	029
Professional Delphi	033101	12/01/2018	F	24/01/2018	17/07/2018	Y	033
Professional Delphi	033102	23/01/2018	F	07/02/2018	18/07/2018	Y	033
Professional Delphi	034101	16/01/2019	M	16/01/2018	24/07/2018	Y	034
Professional Delphi	034102	16/01/2019	F	05/02/2018	Not completed	N	034
Professional Delphi	039101	30/01/2019	F	31/01/2018	30/07/2018	Y	039
Professional Delphi	042101	08/02/2018	F	Not completed	Not completed	N	042
Professional Delphi	045101	16/01/2018	F	Not completed	Not completed	N	046
Professional Delphi	046102	15/01/2018	F	18/01/2018	02/07/2018	Y	046
Professional Delphi	046103	12/01/2018	F	17/01/2018	04/07/2018	Y	046
Professional Questionnaire	001108	Printed	F	17/01/2019	28/02/2019	Y	001
Professional Questionnaire	001117	Online	F	07/03/2019	12/03/2019	Y	001
Professional Questionnaire	001120	Online	F	11/03/2019	24/06/2019	Y	001
Professional Questionnaire	002101-Q	Printed	M	14/11/2018	19/11/2018	Y	002
Professional Questionnaire	002104-Q	Printed	M	14/11/2018	19/11/2018	Y	002
Professional Questionnaire	002105-Q	Printed	F	14/11/2018	07/01/2018	Y	002
Professional Questionnaire	002106-Q	Printed	F	14/11/2018	12/12/2018	Y	002
Professional Questionnaire	002108-Q	Printed	F	14/11/2018	12/12/2018	Y	002
Professional Questionnaire	003102-Q	Printed	F	30/11/2018	12/12/2018	Y	003
Professional Questionnaire	005108 - Q	Online	F	19/11/2018	20/11/2018	Y	005
Professional Questionnaire	005109 - Q	Online	F	19/11/2018		N	005
Professional Questionnaire	005110 - Q	Online	M	19/11/2018	20/11/2018	Y	005
Professional Questionnaire	005111 - Q	Online	F	12/11/2018	19/11/2018	Y	005
Professional Questionnaire	005112 - Q	Online	M	19/11/2018	13/02/2019	Y	005
Professional Questionnaire	005113 - Q	Online	F	19/11/2018	20/11/2018	Y	005
Professional Questionnaire	005114 - Q	Online	F	19/11/2018	30/11/2018	Y	005
Professional Questionnaire	005119 - Q	Online	F	19/11/2018	21/11/2018	Y	005
Professional Questionnaire	005120 - Q	Online	F	19/11/2018		N	005
Professional Questionnaire	005122 - Q	Online	F	13/02/2019	05/03/2019	Y	005
Professional Questionnaire	024103-Q	Printed	F	30/11/2018	15/02/2019	Y	024
Professional Questionnaire	024104-Q	Printed	F	30/11/2018	14/01/2019	Y	024
Professional Questionnaire	024105-Q	Printed	M	30/11/2018	14/01/2019	Y	024
Professional Questionnaire	029108-Q	Printed	F	27/06/2019	06/08/2019	Y	029
Professional Questionnaire	029110-Q	Printed	F	27/06/2019	28/06/2019	Y	029
Professional Questionnaire	029111-Q	Printed	F	27/06/2019	28/06/2019	Y	029
Professional Questionnaire	029112-Q	Printed	F	27/06/2019	28/06/2019	Y	029
Professional Questionnaire	029113-Q	Online	F	27/06/2019	27/06/2019	Y	029
Professional Questionnaire	029115-Q	Online	M	27/06/2019	08/07/2019	Y	029
Professional Questionnaire	029116-Q	Online	F	01/07/2019	03/07/2019	Y	029
Professional Questionnaire	029118-Q	Online	M	27/06/2019	04/07/2019	Y	029
Professional Questionnaire	033103	Printed Q	F	14/12/2018	05/02/2019	Y	033
Professional Questionnaire	033105	Printed Q	M	14/12/2018	05/02/2019	Y	033
Professional Questionnaire	033106	Printed Q	M	14/12/2018	05/02/2019	Y	033
Professional Questionnaire	033107	Printed Q	F	14/12/2018	25/02/2019	Y	033
Professional Questionnaire	033108	Printed Q	F	14/12/2018	05/02/2019	Y	033
Professional Questionnaire	033109	Online	F	06/02/2019	07/02/2019	Y	033
Professional Questionnaire	033110	Online	F	07/02/2019	15/02/2019	Y	033
Professional Questionnaire	034109-Q	Online	F	10/12/2018	11/12/2018	Y	034
Professional Questionnaire	034110-Q	Online	F	10/12/2018	11/12/2018	Y	034
Professional Questionnaire	034111-Q	Online	F	10/12/2018	18/12/2018	Y	034
Professional Questionnaire	034112-Q	Online	F	15/01/2019	15/01/2019	Y	034
Professional Questionnaire	034113-Q	Online	F	15/01/2019	16/01/2019	Y	034
Professional Interview	001101-I	Interview	F	11/03/2019	11/03/2019	Y	001
Professional Interview	001102-I	Interview	F	27/02/2019	27/02/2019	Y	001
Professional Interview	001103-I	Interview	F	25/02/2019	25/02/2019	Y	001
Professional Interview	001106-I	Interview	F	15/03/2019	15/03/2019	Y	001
Professional Interview	001117-I	Interview	F	21/03/2019	21/03/2019	Y	001
Professional Interview	001118-I	Interview	M	08/03/2019	08/03/2019	Y	001
Professional Interview	001119-I	Interview	M	04/06/2019	04/06/2019	Y	001
Professional Interview	002101-I	Interview	M	14/11/2018	14/11/2018	Y	002
Professional Interview	002102-I	Interview	M	15/11/2018	15/11/2018	Y	002
Professional Interview	002104-I	Interview	F	15/11/2018	15/11/2018	Y	002
Professional Interview	002105-I	Interview	F	14/11/2018	14/11/2018	Y	002
Professional Interview	002109-I	Interview	M	24/07/2019	24/07/2019	Y	002
Professional Interview	002110-I	Interview	M	24/07/2019	24/07/2019	Y	002
Professional Interview	002114-I	Interview	F	24/07/2019	24/07/2019	Y	002
Professional Interview	002115-I	Interview	M	24/07/2019	24/07/2019	Y	002
Professional Interview	003104-I	Interview	F	10/12/2018	10/12/2018	Y	003
Professional Interview	005108-I	Interview	F	04/12/2018	04/12/2018	Y	005
Professional Interview	005111-I	Interview	F	04/12/2018	04/12/2018	Y	005
Professional Interview	005113-I	Interview	F	04/12/2018	04/12/2018	Y	005
Professional Interview	005120-I	Interview	F	04/12/2018	04/12/2018	Y	005
Professional Interview	005121-I	Interview	F	04/12/2018	04/12/2018	Y	005
Professional Interview	005106-I	Interview	F	29/05/2019	29/05/2019	Y	005
Professional Interview	010101	Interview	F	12/07/2019	12/07/2019	Y	010
Professional Interview	024104-I	Interview	F	23/01/2019	23/01/2019	Y	024
Professional Interview	024105-I	Interview	M	23/01/2019	23/01/2019	Y	024
Professional Interview	024101-I	Interview	F	31/07/2019	31/07/2019	Y	024
Professional Interview	029114-I	Interview	F	29/07/2019	29/07/2019	Y	029
Professional Interview	033103-I	Interview	F	22/02/2019	22/02/2019	Y	033
Professional Interview	033105-I	Interview	M	22/02/2019	22/02/2019	Y	033
Professional Interview	033110-I	Interview	F	22/02/2019	22/02/2019	Y	033
Professional Interview	034102-I	Interview	F	08/01/2019	08/01/2019	Y	034
Professional Interview	034109-I	Interview	F	08/01/2019	08/01/2019	Y	034
Professional Interview	034110-I	Interview	F	08/01/2019	08/01/2019	Y	034
Professional Interview	034111-I	Interview	F	08/01/2019	08/01/2019	Y	034
Professional Interview	044104-I	Interview	F	10/07/2019	10/07/2019	Y	046
Professional Interview	046101-I	Interview	F	10/07/2019	10/07/2019	Y	046
Professional Interview	046105-I	Interview	F	10/07/2019	10/07/2019	Y	046
Professional Interview	046102-I	Interview	F	10/07/2019	10/07/2019	Y	046
Professional Interview	050101	Interview	F	24/05/2019	24/05/2019	Y	050
Professional Interview	050102	Interview	F	04/07/2019	04/07/2019	Y	050
Totals	113						

Appendix 9: Consensus Statements For Research Professional Delphi Study

Round 2 Performance	Qty	% Total Statements	% Question Group Statements	Number of Statements by Group
Total Statements Achieving Consensus	15	7.46%	-	201
Q1. Follow-Up Definition	1	0.50%	25.00%	4
Q2. Barriers & Burdens	6	2.99%	13.04%	46
Q3. Complexity	1	0.50%	2.86%	35
Q4. Capacity Factors	1	0.50%	2.17%	46
Q5. Top Priorities	2	1.00%	5.88%	34
Q6. Effective Practice	4	1.99%	15.38%	26
Q7. Additional Delphi Considerations	0	0.00%	0.00%	10
Statements within 5% of consensus	9	4.48%		
Statements within 10% of consensus	14	6.97%		
Statements within 15% of consensus	30	14.93%		
Total Proximity Range of Consensus	53	26.37%		
Round 3 Performance	Qty	% Total Statements	% Question Group Statements	Number of Statements by Group
Statements Achieving Consensus	75	35.05%	-	214
Q1. Follow-Up Definition	1	0.47%	25.00%	4
Q2. Barriers & Burdens	21	9.81%	45.65%	46
Q3. Complexity	10	4.67%	28.57%	35
Q4. Capacity Factors	9	4.21%	19.57%	46
Q5. Top Priorities	23	10.75%	67.65%	34
Q6. Effective Practice	10	4.67%	38.46%	26
Q7. Additional Delphi Considerations	1	0.47%	4.35%	23
Statements within 5% of consensus	8	3.74%		
Statements within 10% of consensus	24	11.21%		
Statements within 15% of consensus	18	8.41%		
Total Proximity Range of Consensus	50	23.36%		

Table 1. Consensus Statements For Research Professional Delphi Study

Appendix 10: Sampling Frame

Participant Type	Inclusion Criteria
Cancer Clinical Trial Participants	<ul style="list-style-type: none"> • Aged 18 or over • Willing to participate in the particular type of study they were approached for (Delphi, questionnaire or interview study) • Had a diagnosis of cancer and have previously participated in a clinical trial at an NHS site • Had completed a cancer clinical trial or attended at least one follow-up visit
<p>Cancer Clinical Research Professionals</p> <p>*Clinical/R&D directors, Principal/Co-Investigators, R&D Managers, research nurses, officers and assistants, research pharmacists, research radiographers and associated clinical trial professional on site or externally. External professionals may include sponsors (commercial and non-commercial), governance bodies and network professionals (NIHR, HRA, Study Support Service, Research Design Service)</p>	<ul style="list-style-type: none"> • Aged 18 or over • A clinical research professional with a minimum of 18 month's experience of working within cancer clinical research within an NHS secondary care setting • Willing to participate in the particular type of study they were approached for (Delphi, questionnaire or interview study) • A member of one of the specified professions or groups*