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Uplifting the standard of monitoring in clinical trials – developing evidence and tools

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Declaration

“I, Shiva Taheri, confirm that the work presented in my thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.”

Abstract

Clinical trials are vital for advancing healthcare, improving patient outcomes, and driving economic growth. Effective trial monitoring is critical to ensure participant safety, data integrity, and regulatory compliance. However, monitoring practices across UK Clinical Trial Units (CTUs) are varied, leading to variability in trial quality and efficiency. This PhD aims to enhance clinical trial monitoring by developing and validating a standardised Trial Monitoring Plan (TMP) template, investigating the use of metrics to inform monitoring, and disseminating best practices across the UK monitoring community.

The first objective was to design a TMP template based on input from experienced trialists. The second objective was to pilot and refine the TMP template through feedback from CTUs, ensuring it aligns with practical monitoring needs. This process included qualitative analysis to enhance its usability and effectiveness, followed by dissemination across CTUs. The third objective focused on evaluating the current use of metrics within CTUs to inform monitoring practices. Case studies highlighted the benefits of metrics in identifying risks and enhancing trial oversight, as well as the barriers to their implementation.

Findings from the qualitative part of this research indicate that a standardised TMP template can improve consistency, reduce resource duplication, and streamline monitoring activities across CTUs. Furthermore, interviews with UK CTUs showed integrating metrics into monitoring practices has the potential to enable real-time risk assessment and targeted interventions, enhancing data quality and participant safety. The final chapter of this thesis presents recommendations for UK CTUs on optimising monitoring strategies through standardisation and metric-driven oversight.

This PhD provides a practical tool for CTUs to enhance trial monitoring, ensuring greater consistency, improved risk management, and alignment with regulatory expectations. The findings have implications for future research, aiming to elevate monitoring standards across the clinical trials landscape in the UK.

Impact Statement

This research focuses on uplifting the standards of monitoring in clinical trials through the development of a Trial Monitoring Plan (TMP) template, the testing and validation of this template, and the investigation into the use of metrics in trial monitoring. The findings and tools generated by this work have the potential to impact both academic and non-academic Clinical Trial Units (CTUs), as well as public health policy, with broad effects on clinical trial monitoring and management.

The creation and validation of the TMP template makes a significant contribution to clinical trials monitoring by filling a gap in standardisation across UK Clinical Trial Units (CTUs). By reviewing the monitoring practices of 31 CTUs, this research enhances the methodological understanding of trial monitoring. The Delphi-based development of the TMP template introduces a robust, consensus-driven approach to improving clinical trial monitoring. This research provides CTUs, especially those with less developed practices, with a standardised, evidence-based tool to guide the development of monitoring plans. As a result, monitoring procedures become more efficient and consistent, improving the quality and reliability of clinical trials, which is crucial for the development of safe and effective medical treatments.

This work encourages further research into the wider use of metrics in risk-based monitoring, identifying key barriers to their adoption. By exploring these challenges, the research offers insights into how CTUs can overcome these obstacles. As clinical trials increasingly rely on data-driven decision-making, the findings can inform training programmes and operational guidelines, ensuring trial units are equipped to implement these practices effectively. Ultimately, improved monitoring processes will enhance patient safety, produce more reliable trial outcomes, and reduce resource waste, benefiting both research stakeholders and patients.

This research also has the potential to inform public health policy, particularly in the context of improving the efficiency and accountability of clinical trials. By standardising the monitoring process, this research can contribute to ensuring that trials meet high standards of safety and integrity. The TMP template can be used as a reference for CTUs nationwide, providing a clear framework for monitoring practices that align with regulatory requirements and best practices.

The output of this research has been shared widely, including a publication in *Trials* and presentations at conferences such as the Society of Clinical Trials (Boston 2024), the Operational Research Society (Bangor 2024), and the International Clinical Trials Methodology Conference (ICTMC) (Edinburgh 2024). Engagement with CTUs has continued throughout the PhD, with an invited talk given to North Wales Organisation for Randomised Trials in Healthcare and Social Care (NWORTH) upon completion of the TMP template, and presentation at three UK National Monitoring Meetings, UK Trial Managers Network meeting and UCL Institute of Clinical Trials and Methodology Cancer all staff meeting.

CTUs such as Plymouth, Bristol, Northern Ireland, Exeter, and Cambridge NHS Blood and Transplant CTU have piloted the TMP template, with Northern Ireland and Plymouth CTUs continuing to use and integrate it into their monitoring practices. The ongoing collaboration with CTUs ensures that the findings will reach those who can apply the recommendations directly, encouraging the adoption of best practices and the further improvement of the TMP template.

While the research is focused on UK CTUs, the TMP template has international potential. The principles behind the TMP template could serve as a model for improving monitoring practices across a wide range of healthcare settings. Furthermore, this work has the potential to support broader adoption of evidence-based approaches to trial management, contributing to improvements in trial monitoring globally.

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Shiva Taheri and Sharon Love conducted the classification of trial monitoring plan template items. Shiva Taheri, Sharon Love, and Victoria Yorke-Edwards reviewed the final list of Delphi survey items. Shiva Taheri conducted the Delphi survey and analysis and prepared the first and subsequent drafts of the manuscript. Sharon Love, Victoria Yorke-Edwards, Mathew Sydes and Talia Isaacs contributed to the manuscript.
4. In which chapter(s) of your thesis can this material be found?
Chapters 1 and 2
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Candidate:	Shiva Taheri [redacted]	Date:	01/07/2025
Supervisor:	Sharon Love [redacted]	Date:	08/07/2025

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“Behind every page of this thesis is a quiet moment borrowed from a noisy life, a reminder that even amidst the chaos of school runs, snack requests, bedtime stories, and news around the world something meaningful can take shape.”

This PhD was not completed in silence or solitude, but in the vibrant noise of life, with the laughter, questions, and footsteps of my young children around me, and the quiet resilience required to keep going during difficult times. It is a product of not just personal effort, but of the encouragement, wisdom, and generosity of so many people around me. I would like to offer a massive thank you to a whole host of people without whose help and support I would never have got through my PhD journey.

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'I dedicate this work to my parents, my brother, and my sister. You showed me how to be myself, supported me and believed in me.'

Table of Contents

List of Figures

List of Tables

List of Abbreviations

Abbreviation	Meaning
AE	Adverse Events
CAPA	Corrective And Preventive Actions
CI	Chief Investigator
CRO	Clinical Research Organisation
CONSORT	Consolidated Standards of Reporting Trials
CRF	Case Report Form
CTA	Clinical Trial Authorisation
CRO	Clinical Research Organisation
CTIMP	Clinical Trial of an Investigational Medicinal Product
CTU	Clinical Trial Unit
DMP	Data Monitoring Plan
EudraCT	European Union Drug Regulating Authorities Clinical Trials Database
FDA	Food and Drug Administration
FA	Framework Analysis
GCP	Good Clinical Practice
ICF	Inform Consent Form
ICTM	International Clinical Trials Methodology
IQR	Interquartile Range
ISRCTN	International Standard Randomised Controlled Trial Number
ICH	International Council for Harmonisation
IMP	Investigational Medicinal Product
IRAS	Integrated Research Application System
MRC	Medical Research Council
MHRA	Medicines and Healthcare products Regulatory Agency
NIHR	National Institute for Health and Care Research
NHS R&D	National Health Service Research and Development
NWORTH	North Wales Organisation for Randomised Trials in Healthcare and Social Care
PIS	Participant Information Sheet
REC	Research Ethics Committee
RBM	Risk-Based Monitoring
SAE	Serious Adverse Events
SAP	Statistical Analysis Plan
SCT	Society of Clinical Trials
SOP	Standard Operating Procedure
SPIRIT	Standard Protocol Items: Recommendations for Interventional Trials
TMG	Trial Management Group
TMP	Trial Monitoring Plan
TMRP	Trials Methodology Research Partnership
TSDV	Targeted Source Data Verification
UKCRC	UK Clinical Research Collaboration
UKTMN	UK Trial Managers' Network

Chapter One: Introduction

Research is an important pillar in each leading healthcare system, as it drives improvements in health outcomes, wellbeing, and economic growth. High-quality research in health and social care leads to better population health and wellbeing and promotes economic growth (Kruk et al., 2018). Clinical trials contribute to life-changing treatments being made available to everyone, which leads to a better quality of life and enhances health and care for future generations (Kruk et al., 2018).

In the UK, trial monitoring is a key component of research governance, guided by frameworks such as the UK Policy Framework for Health and Social Care Research (HRA, 2017), Good Clinical Practice (ICH E6 R3) (International Council for Harmonisation (ICH)), and the Medicines for Human Use (Clinical Trials) Regulations 2004 (Medicines for Human Use (Clinical Trials) Regulations 2004). Oversight is provided by bodies such as the Medicines and Healthcare products Regulatory Agency (MHRA) (Medicines and Healthcare products Regulatory Agency), the Health Research Authority (HRA) (HRA, 2017), and the NIHR, each emphasising proportionate monitoring to safeguard participant rights and ensure data integrity (MHRA, 2023). National initiatives, including the MRC/DH/MHRA Joint Project (2011) (MRC/DH/MHRA, 2011), also advocate risk-proportionate approaches to monitoring, recognising the need for efficiency and participant safety.

Together, these documents and bodies do more than recommend good practice, they create the governance architecture within which trial monitoring must operate in the UK. The UK Policy Framework for Health and Social Care Research and the Medicines for Human Use Regulations place legal and ethical duties on sponsors and chief investigators to ensure ongoing oversight and quality assurance, while the MHRA and other regulators perform inspection and compliance functions that translate high-level principles into operational expectations. The MRC/DH/MHRA risk-adapted guidance (MRC/DH/MHRA, 2011) and international standards such as ICH E6 (R3) (International Council for Harmonisation (ICH)) explicitly endorse a risk-proportionate model, that is, monitoring intensity and methods should be scaled to the trial's specific risks and complexity. Framing monitoring in this way highlights two practical implications for CTUs: first, monitoring is simultaneously a regulatory requirement and a tool for protecting participants and data; second, governance documents permit (and

encourage) pragmatic, evidence-based flexibility rather than a one-size-fits-all approach. This regulatory context therefore provides the need for standardised, pragmatic monitoring tools (such as a TMP template) that can be adapted to local trial risk and organisational resources.

The quality of a clinical trial depends on having an effective quality control process in place that ensures participant safety and rights, as well as the integrity of the trial and its data, are always protected (Love et al., 2022). This process is known as monitoring. Monitoring is crucial because it provides quality assurance in the conduct of clinical trial research, mitigates risks, and detects any issues at early stages (Love et al., 2022).

Despite the regulatory importance of monitoring, the empirical evidence base underpinning monitoring practices remains limited. Much of the existing literature focuses on defining monitoring conceptually or describing frameworks such as risk-based monitoring, rather than evaluating how these approaches are implemented in practice (Love et al., 2020; Yorke-Edwards et al., 2022). Research describing monitoring in UK Clinical Trials Units (CTUs) is scarce and heterogeneous, often relying on single-centre case studies or descriptive surveys. While initiatives such as TransCelerate (TransCelerate, 2013) and the FDA (US Food & Drug Administration, 2023) guidance have advanced international understanding of risk-based monitoring, their relevance to non-commercial academic settings remains uncertain. Furthermore, there is little published work exploring how CTUs design, document, and operationalise monitoring plans or use metrics to support decision-making. This gap highlights the absence of shared tools and standards, providing a clear rationale for this PhD's focus on developing and validating a structured, evidence-based Trial Monitoring Plan (TMP) template tailored to UK CTUs.

The aim of this PhD is to improve trial monitoring practices. The first objective is to create a Trial Monitoring Plan (TMP) template, incorporating input from experienced trialists. The second objective is to test and validate the TMP template across UK Clinical Trial Units (CTUs), gathering feedback to refine and enhance its structure, ensuring it aligns with the practical needs of trial monitoring. Upon refinement, the template will be widely disseminated. The third objective is to investigate the use of metrics in monitoring practices within UK CTUs through case studies.

For clarity in this introduction, the term *'trial monitoring plan'* refers to the document currently used by UK CTUs to define their monitoring strategy, while *'trial monitoring plan template'* refers to the document that is the focus of this PhD. The term ‘*'trial monitoring plan'* and what it is referred to as is explained in section 1.4 of the introduction.

This thesis is structured to include a section for each of the three PhD objectives. Each section contains a methods chapter with justification for the chosen methodology, along with results, conclusions, and limitations. The final chapter presents a summary of the overall conclusions and suggests directions for future work.

1.1 PhD Overall Aim and Objectives

Aim

The aim of this PhD is to uplift the standards of clinical trial monitoring through the development of evidence and tools, including a Trial Monitoring Plan template, derived from expert opinions gathered in the UK via a Delphi survey.

The rationale for the creation of this tool, including the identified knowledge gaps and examples of similar tools developed in clinical trials, is discussed in sections *‘1.5-1.7’* of the introduction.

Objectives

1. To create and publish a Trial Monitoring Plan (TMP) template.

2. To actively test and validate the TMP template and encourage CTUs to use it and update it as necessary. To disseminate the final version of the TMP template as the output of this project to the monitoring community to use.

3. To review the use of metrics in informing monitoring practices by UK Clinical Trial Units through case studies.

Figure 1.1 below, illustrates the overall stages of this thesis, outlining the key steps taken in the development and refinement of the TMP template, the evaluation through interviews and piloting, and the exploration of the use of metrics in monitoring clinical trials through interviews with UK Clinical Trials Units.

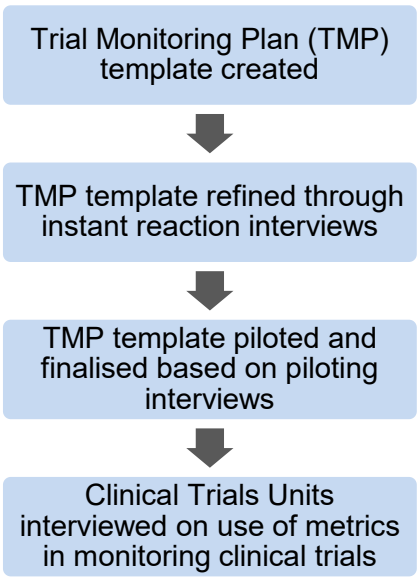

Figure 1.1: The overall stages of this thesis

In summary, this PhD contributes to clinical trial monitoring by developing a tool that has the potential to enhance trial conduct and improve monitoring practices in clinical trials by:

- Maintaining consistency in monitoring standards across all CTUs, resulting in higher monitoring standards and consequently, higher research quality,
- Providing an evidence-based efficient and effective TMP template across all CTUs,
- Providing a simplified and easy to follow TMP template for all CTUs,
- Enabling TMP completion to be more comprehensive and happen earlier in a study,
- Preventing resource waste for funders and CTUs by providing a standardised tool that streamlines monitoring processes, enhances efficiency, and reduces unnecessary expenditure in clinical trials, such as avoiding unnecessary onsite visits that could be conducted centrally,
- Reviewing the current use of metrics in monitoring practices across UK CTUs,
- Producing a summary of recommendations from UK CTUs on how to improve and encourage the more effective and widespread use of metrics in clinical trial monitoring.

In addition to creating the TMP template, this research ensure that the template is fit for purpose through a refinement process, including instant reaction and piloting. This iterative process has played a key role in enhancing the TMP template's quality and

usability, ensuring that the final version is a well-developed, practical tool ready for broader implementation. Further details on this process are provided in Chapter 3 of this thesis.

This research has the potential to make a lasting impact on the clinical trials community, ultimately contributing to improved patient safety, data quality, and the overall success of clinical research. Utilising the TMP template can benefit healthcare systems and patients. It enables the completion of high-quality clinical trials that are evidence-based, efficient, and effective. CTUs can improve their monitoring practices and standardise the way monitoring is performed by implementing the TMP template. Furthermore, research participants can have confidence that their participation is being carefully monitored to ensure that their data or any samples provided are treated with confidentiality, integrity, and respect and that their rights and well-being are protected.

1.2 The importance of monitoring in clinical trial conduct

Monitoring is essential as it ensures that participants' rights, safety, and well-being are always protected. It also ensures that the trials are conducted as per the trial protocol, and that any problems are identified and addressed before they escalate (Love et al., 2022). Effective monitoring maintains the integrity of the trial data while safeguarding the health and rights of participants. Without adequate monitoring, trials may fail to detect issues in real-time, leading to compromised data quality, participant harm, or delays in treatment development.

Attitudes in the clinical trials profession toward monitoring have evolved significantly in recent years, though there remains variability in how monitoring is perceived and prioritised across different institutions (Love et al., 2020; Yorke-Edwards et al., 2022). This variability is explored further in the thesis, with the presentation of results from the qualitative research conducted as part of this PhD. Historically, there has been a focus on regulatory compliance and ensuring participant safety, but less emphasis on the broader aspects of trial conduct that directly impact the efficiency and cost-effectiveness of trials. The increasing complexity of clinical trials, particularly with the rise of multi-centre, multi-country studies, has highlighted the need for more robust and flexible monitoring approaches (Love et al., 2020). However, the discipline has

traditionally placed more attention on the logistics of data collection and patient safety, rather than on refining monitoring processes to improve overall trial conduct (Love et al., 2022). This may be due in part to the perceived cost and time implications of adopting new methods, as well as a lack of consensus on best practices for monitoring (Yorke-Edwards et al., 2022).

Up until now, the clinical trials discipline has paid significant attention to ensuring adherence to regulatory standards and safeguarding participant wellbeing, as well as meeting recruitment targets (Kruk et al., 2018). However, there has often been less focus on optimising the efficiency of trial monitoring. The priority has frequently been compliance-driven, rather than driven by the need to improve the quality of monitoring and reduce inefficiencies. This can be attributed to a historical emphasis on meeting regulatory requirements, with less attention given to proactive, evidence-based strategies for improving monitoring practices (Kruk et al., 2018). The 2025 revision of ICH E6 (R3) ((ICH), International Council for Harmonisation (ICH)) further supports this by stating that trial processes should be operationally feasible and avoid unnecessary complexity, procedures, and data collection, highlighting the importance of streamlining monitoring practices. This underscores the need for research into improving monitoring practices, which forms the motivation behind this PhD.

1.3 How and by whom monitoring is carried out

Qualified and trained members of the research team such as monitors, quality assurance staff and trial managers perform monitoring (Love et al., 2022). They are involved in a research study from study design to final study close-out. This includes their involvement in the development of the study protocol, Participant Information Sheet (PIS), Informed Consent Form (ICF), and Case Report Forms (CRFs), as well as conducting site initiation visits, centralised and on-site monitoring, and close-out visits.

Monitoring may be done centrally, on-site or remote. Centralised monitoring (formerly known as central monitoring) involves reviewing data from each site or identifying any missing data to determine if additional support is required (Fox et al., 2021). For example, monitors check the database system to ensure all adverse events and deviations are reported correctly by the site. If a site has a persistent record of protocol

deviation or missing data, this is an indication that the site may need more training input from the central research team. Additional training is necessary to ensure that the trial site operates in adherence with the trial protocol, protecting participant safety and ensuring the collection of data suitable for analysis (Fox et al., 2021).

On-site monitoring visits are typically scheduled for a day or two, depending on the study and participant population. During these visits, monitors adhere to the study TMP and Standard Operating Procedures (SOPs) to assess the trial process. They check the CRFs to ensure that trial data are accurate, complete, and verifiable, and they also review participant eligibility by checking the inclusion and exclusion criteria in patient notes (Fox et al., 2021). Additionally, consent forms, participant information sheets, and all regulatory approvals are reviewed to confirm that the trial complies with the approved study protocol, Good Clinical Practice (GCP), and other relevant regulatory requirements (Fox et al., 2021).

Remote monitoring involves off-site evaluation of clinical trial data, allowing study coordinators or monitoring personnel to assess data without being physically present at the trial site ((ICH), International Council for Harmonisation (ICH)).

1.4 A Trial Monitoring Plan (TMP)

A Trial Monitoring Plan (TMP) outlines the systematic actions designed to ensure that the research is conducted, documented, and reported in compliance with GCP, in the UK the research governance framework for health and social care (2005) (Department of Health, 2005), and any other applicable regulatory requirements, such as those set by the Medicines and Healthcare products Regulatory Agency (MHRA) or the U.S. Food and Drug Administration (FDA). The TMP *“should describe the monitoring strategy based on the trial risk assessment, the responsibilities of parties involved, the methods to be used, and the rationale for their use"* (Fox et al., 2021).

TMPs are developed based on the research risk level, and participant population and are reviewed as needed to ensure they remain up to date. The purpose of a TMP is to document the monitoring procedures and action plans to be followed before, during and at the end of the research (Fox et al., 2021). These plans typically include information such as centralised, on-site or remote monitoring, as well as the specific research parameters to be monitored (Fox et al., 2021). For example, the timing of the

first monitoring visit and the frequency of subsequent visits are defined in the monitoring plan. These details may change depending on the trial type, associated risks, and the standard procedures at the CTU.

A TMP is specific to each trial and is created during the early stages of trial development to assist in design and planning. Developing this document early on allows for risk assessment and planning mitigation strategies at the early stages of the trial (Love et al., 2022).

1.5 A TMP template and the benefits of having a TMP template

A TMP template is a standardised document which intends to make the monitoring process easier and more efficient as it provides evidence-based guidance to create a fit-for-purpose document that meets the needs of a specific trial. The proposed TMP template will include fields for users to complete based on their trials, along with guidance at the beginning of each section to assist in completing these fields.

A TMP template not only provides structure and guidance but also plays a crucial role in preventing the negative consequences that can arise from inadequate monitoring plans. The consequences of having an inadequate monitoring plan can be significant. For patients, it may mean that safety risks are not properly identified or mitigated, potentially leading to harm. For the CTU, the repercussions can include regulatory non-compliance, which could lead to trial delays, reputational damage, or even suspension of the trial. Inadequate monitoring plans also compromise the reliability of trial data, which can undermine the trial's credibility and validity. This underscores the importance of having a robust, evidence-based monitoring plan that meets both regulatory and safety standards.

A TMP template can improve the quality of research by providing a standardised approach for all CTUs, as well as prevent time and resource waste during a research study (Ahmed et al., 2012; Daniels et al., 2003). The NHS R&D forum published a document to help organisations prepare for the MHRA inspections which includes information on common findings from inspections conducted by the MHRA (NHS R&D Forum, May 2011). These findings covered a variety of areas, including organisational

oversight of clinical trials (e.g., ensuring appropriate approvals and GCP training), pharmacovigilance (reporting of adverse events, Serious Adverse Events (SAEs)), Investigational Medicinal Product (IMP) management, informed consent, data integrity, sample and laboratory management, and pharmacy management (NHS R&D Forum, May 2011).

Additionally, the MHRA published a GCP inspections metrics report in 2021 (Medicines and Healthcare products Regulatory Agency, 2021). A part of this report highlighted monitoring findings for non-commercial sponsors. Four major findings classified as monitoring issues included protocol compliance, pharmacovigilance, IMP management (pharmacy), and CRF data (source data). Having a comprehensive TMP template that ensures all these areas are covered in detail can help CTUs reduce MHRA monitoring findings and maintain trial integrity. It can also expedite the development of a CTU-specific monitoring plan by providing a template that can be adapted to the specific trial's needs.

1.6 The role of risk assessment documents in monitoring clinical trials

Risk in clinical trials is defined by the MRC/DH/MHRA Joint Project as *"the likelihood of a potential hazard occurring and resulting in harm to the participant, the organisation, or the reliability of the results"* (Fox et al., 2021; MRC/DH/MHRA, 2011).

In clinical trials, risk assessment is a process that identifies potential hazards in trial design and methodology (MRC/DH/MHRA, 2011) and prepares a trial risk assessment plan to minimise those risks. *"This document will create a shared understanding amongst all trial stakeholders of the risks involved in the trial, and enable the adoption of a risk-appropriate strategy for conducting trial activities"* (MRC/DH/MHRA, 2011).

Once the trial risk assessment plan is developed, a formal risk assessment should be conducted by or on behalf of the sponsor and documented as early as possible during protocol development. This helps identify potential risks to participants, the organisation, and the reliability of the trial results (Fox et al., 2021; MRC/DH/MHRA, 2011).

The likelihood of occurrence, and if applicable, the critical data needed to monitor those risks throughout the trial, should be identified. The risk assessment typically results in an overall risk classification for the trial, e.g., low, medium, or high (Fox et al., 2021; MRC/DH/MHRA, 2011).

The trial risk assessment process directly informs the TMP. The identified risks, whether related to participant safety, data integrity, or trial compliance, are incorporated into the TMP to determine how those risks will be monitored throughout the study (MRC/DH/MHRA, 2011). It is important to note that not all risks can or should be mitigated solely through monitoring; rather, the TMP should specify the appropriate mitigation strategies for each identified risk, which may include additional actions beyond monitoring.

The TMP outlines the strategies and methodologies for monitoring these risks, based on their likelihood and potential impact on the trial's success. For example, if a trial is classified as high risk due to the nature of the investigational product or the patient population, the TMP will specify more frequent monitoring visits or closer scrutiny of adverse event reporting. Thus, the risk assessment serves as the basis for designing the TMP, ensuring that monitoring efforts are tailored to the specific needs and challenges of the trial.

1.7 Why does the monitoring community need a TMP template and what is the problem with the current practice?

Currently in the UK, each CTU develops its own trial monitoring plan based on the unit's specific regulations and SOPs, GCP guidelines ((ICH), International Council for Harmonisation (ICH)) , and regulations set by regulatory bodies such as MHRA (MRC/DH/MHRA, 2011) or the FDA (US Food & Drug Administration, 2023), and other relevant tools (Fox et al., 2021) . However, there is considerable variation in how CTUs create their monitoring plans, often duplicating efforts every time this process is repeated. Creating a TMP is a time-consuming task that requires expertise and knowledge. Moreover, when monitoring personnel transition between or work across different CTUs, they often must adapt to various formats for presenting the same information. Additionally, while some CTUs benefit from having more experienced staff who can produce well-structured monitoring plans, others may lack similar resources

and expertise. This inconsistency highlights the necessity for a standardised template that can be accessed by all CTUs, ensuring widespread benefits across CTUs.

Research shows the implementation of standardised templates simplifies document creation, saves time and money, improves consistency, and enhances quality and clarity (Ahmed et al., 2012; Daniels et al., 2003). This results in the reduction of workload and stress and increases staff productivity. This can be particularly helpful for less experienced staff, where training and adaptation periods could be significantly reduced (Ahmed et al., 2012; Daniels et al., 2003).

The MHRA is placing increased emphasis on the importance of monitoring clinical trials (MRC/DH/MHRA, 2011). This increased focus indicates a commitment to improving the quality and safety of clinical trials, ultimately benefiting both participants and the overall integrity of trials.

Additionally, there are growing concerns regarding the costs of conducting clinical trials (MRC/DH/MHRA, 2011). These concerns have brought attention to the financial aspects of clinical research, prompting discussions about efficiency, cost-effectiveness, recruitment and retention strategies and the need to ensure clinical trials remain economically viable while maintaining the highest scientific standards (Murphy et al., 2022). Salman et al recommended four strategies to reduce costs in clinical trials (Salman et al., 2014). One of these strategies emphasised improving the efficiency of recruitment, retention, data monitoring, and data sharing in research by using research designs known to reduce inefficiencies. Further research is needed to explore how efficiency can be increased in these areas (Salman et al., 2014).

Gamble et al conducted a Delphi survey to create guidelines for the content for Statistical Analysis Plans (SAPs) in clinical trials (Gamble et al., 2017). In this Delphi survey, 74% (54 of 73) of participants who completed both rounds reached a consensus on 42% (n = 46) of 110 items. Through a consensus meeting of 12 expert members, the paper recommends a minimum set of 55 items to be included in a SAP to ensure appropriate reporting of clinical trials (Gamble et al., 2017). Although the publication is too recent to assess its long-term effectiveness, as of April 2025 it had been viewed 141,243 times and had 278 citations. This high level of engagement indicates the visibility and impact of this content guideline research amongst trialists. It also suggests that the research has made a meaningful contribution to the intended

field and is actively shaping the discussion and understanding within the academic and research community. This underscores the need within the trials community for structured guidance and templates, such as the TMP template developed in this PhD, to improve monitoring practices and ensure greater consistency and efficiency.

SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials), is another good example of how a template in research can enhance quality and therefore provide benefits for everyone. SPIRIT 2013 (Chan et al., 2013) provides a 33-item checklist, while SPIRIT 2025 (Chan et al., 2025) includes a 34-item checklist, both apply to all clinical trial protocols and focus on content. SPIRIT provides evidence-based recommendations for the minimum content of a clinical trial protocol (Chan et al., 2025; Chan et al., 2013). The SPIRIT guidelines have been widely endorsed as an international standard for study protocols by numerous journals, research ethics committees, funders, regulators, and other key stakeholders in the clinical research community (SPIRIT Endorsement). These endorsements include general support, encouragement for adherence, and explicit requirements for following the guidelines when developing clinical trial protocols (SPIRIT Endorsement). SPIRIT states that *"adherence to this guidance would enhance the transparency and completeness of trial protocols for the benefit of investigators, trial participants, patients, sponsors, funders, research ethics committees or institutional review boards, peer reviewers, journals, trial registries, policymakers, regulators, and other key stakeholders"* (Chan et al., 2013). I believe having a TMP template will bring the same benefits for monitoring clinical trials.

The CONSORT (Consolidated Standards of Reporting Trials) is a checklist and flow diagram that standardise the reporting of trial methodologies, participant recruitment, and outcomes in randomised clinical trials. The CONSORT statement includes recommendations on how to report randomisation, blinding, statistical analyses, and the handling of missing data (Schulz et al., 2010). These guidelines provide a framework for the transparent and complete reporting of randomised controlled trials (RCTs). The primary goal of CONSORT is to improve the quality and transparency of RCT reports, helping readers assess the reliability and generalisability of trial findings. The CONSORT statement is widely endorsed by numerous high-impact medical journals and prominent editorial organisations (Shamseer et al., 2016). A 2016 survey

of 168 biomedical journals found that 63% mentioned CONSORT in their *'Instructions to Authors'* with 42% explicitly requiring its use, 38% requesting a completed CONSORT checklist, and 39% asking for a flow diagram to be included with submissions (Shamseer et al., 2016).

Love. et al. (2020) conducted an online survey of monitoring policy which was sent to all 50 UK Clinical Research Collaboration (UKCRC) registered CTUs in November 2018 (Love et al., 2020). The survey showed a wide variation in phase III randomised Clinical Trials of Investigational Medicinal Products (CTIMP) trial monitoring practices by academic clinical trials units within a single research-active country. They called for tools for all CTUs to use (Love et al., 2020). A UK-wide agreed TMP template would be one such tool.

Trial Protocols and Statistical Analysis Plans (SAP) have already been improved by research (Chan et al., 2013; Gamble et al., 2017; Schulz et al., 2010). Improving recruitment and retention also is well emphasised amongst trialists (Chaudhari et al., 2020; Kadam et al., 2016; Murphy et al., 2022; Salman et al., 2014), therefore considering all the rational explained earlier in the thesis it is the right time for monitoring of clinical trials to also be improved. To date, to the best of the author's knowledge, no research has been conducted to develop a TMP template or address this gap. A comprehensive review of the literature has found no studies that directly fill this gap.

Collectively, these established frameworks SPIRIT, CONSORT, and SAP guidance, illustrate how structured methodological tools can improve consistency, transparency, and efficiency in clinical research. The conceptual principles underpinning them, including standardisation, evidence-based content, and adaptability, also inform the development of the TMP template presented in this thesis. In this way, the study extends the wider methodological movement towards structured, consensus-driven tools into the domain of trial monitoring, an area that has not yet benefited from similar standardisation.

1.8 Testing, validating, and disseminating the TMP template within the monitoring community.

Once the TMP template was finalised I piloted it to conduct testing and validation, ensuring it aligned with the intended purpose. During the testing phase, I invited CTUs to pilot the template, with the aim to qualitatively assess their experience during this trial period. The qualitative phase of the thesis aimed to enhance and improve the template based on real-world practice and evidence. The qualitative analysis evaluated the template's efficacy in an evidence-based manner, aiming to influence a change in the way we monitor clinical trials.

As Rubin & Rubin noted, "*qualitative interviews are like night goggles, permitting us to see that which is not ordinarily on view and examine that which is looked at but seldom seen"* (Rubin & Rubin, 2011).This metaphor highlights the distinct value of qualitative interviews in uncovering hidden insights and nuances within clinical trial monitoring practices, which quantitative data alone might not reveal. Myers & Newman (2007) further suggest that qualitative interviews are one of the most common and crucial data-gathering tools in qualitative research (Myers & Newman, 2007). In this thesis, qualitative interviews are particularly valuable because they allow for an in-depth exploration of the challenges faced by CTUs in adopting new monitoring practices, which can be complex and context dependent. By using this method, I am able to capture rich, detailed accounts of practitioners' experiences and perceptions, which form the foundation for the development of a more effective Trial Monitoring Plan template. In contrast to other methods, qualitative interviews provide a deeper understanding of the subjective experiences and institutional dynamics that impact trial monitoring, which is essential for addressing the gaps identified in this research.

After the piloting phase and once all recommended changes had been made, I disseminated the TMP template to the wider monitoring and research community. Dissemination of any research is an important element to ensure findings reach those people who can make use of them (Research, 2019). I have done this by publishing the template (Taheri et al., 2024) and giving talks at conferences such as Society of Clinical Trials (2024), Operational Research Society (2024) and International Clinical Trials Methodology Conference (2024) as well as making the template available for use by trialists at the MRC CTU websites and giving talks at individual CTUs about the

TMP template and how to use it (North Wales Organisation for Randomised Trials in Healthcare and Social Care (NWORTH) , Southampton, Warwick, and Nottingham CTUs).

1.9 Importance of metrics in monitoring practices in clinical trials

In recent years, a shift towards more targeted and resource-efficient monitoring has led to the adoption of Risk-Based Monitoring (RBM). Risk-based monitoring is an approach to clinical trial management that focuses on identifying and mitigating potential risks to trial outcomes, participant safety, and data integrity (Barnes et al., 2021). Integrating quality and risk management approach into the scientific design and conduct of clinical trials enables the mitigation of risks at early stages of the trial (TransCelerate, 2013). In recent years, regulatory agencies such as FDA and collaborations such as TransCelerate and the International Committee for Harmonisation have been advocating a risk-based approach to monitoring clinical trials ((ICH), International Council for Harmonisation (ICH); TransCelerate, 2013; US Food & Drug Administration, 2023). RBM places greater emphasis on critical data and processes and encourages the increased use of centralised monitoring (US Food & Drug Administration, 2023). This approach allocates resources based on the assessed risks associated with each site, study arm, or participant population. However, the best way to do RBM remains unclear, with significant variation in the tools and methodologies used. Challenges, including the non-prescriptive nature of regulatory guidelines, limitations in software technology, difficulties in operationalisation, and the lack of robust evidence demonstrating superior outcomes, have impeded its widespread adoption (Agrafiotis et al., 2018).

A key component of RBM is the use of metrics, which are used to assess trial performance and risk indicators in real time. *“Metrics are numeric measurements, collected and calculated from data held in the trial database, and used to evaluate sites' risk or performance”* (Yorke-Edwards et al., 2022). Metrics can be compared between sites or have set thresholds to highlight trial risks and areas of underperformance (Yorke-Edwards et al., 2022).

Metrics such as those measuring data quality, site performance, and patient adherence are tracked and analysed to detect early signs of issues that may compromise the trial's success (US Food & Drug Administration, 2023). By integrating RBM and metrics, clinical trials can reduce costs, improve data reliability, and enhance participant safety, aligning with modern regulatory expectations for more efficient, data-driven trial monitoring ((ICH), International Council for Harmonisation (ICH)).

Metrics are an important part of central monitoring and are considered when deciding if a site needs more input in the form of interventions such as extra site training and support (TransCelerate, 2013). A metric crossing a set threshold can indicate a problem at a site. For example, a high percentage of missing data on CRFs can indicate if a site needs immediate discussion and a corrective action plan put in place.

Yorke-Edwards et al explain it is essential to regularly assess the sensitivity of metrics, and trialists should take into account the interaction between any intervention such as on-site visits and the metrics they have chosen (Yorke-Edwards et al., 2022). Where metrics do not ever cross a threshold, it could mean that the site has good performance or that the wrong metrics are being used or thresholds are inappropriate i.e., are not sensitive enough. Trial teams need to consider this information when reviewing metrics and their effect on monitoring.

Whitham et al. conducted a Delphi survey to establish a core set of metrics for evaluating site performance in multicentre randomised trials. Researchers can use these metrics to identify and resolve problems before clinical trials are adversely affected. This paper suggests that metrics have not been tested systematically for monitoring effectiveness and future work can evaluate the effectiveness of using the metrics and reporting tool (Whitham et al., 2018).

In this PhD thesis, I examine how UK CTUs use risk-based monitoring and metrics to inform their monitoring practices. This is achieved through interviews with UK CTUs, reviewing their experiences, particularly the challenges they have faced in implementing metrics. Additionally, I have gathered recommendations from CTUs on how to increase the use of metrics in clinical trial monitoring, focusing on tools to be used, training to be offered to staff, and the types of trials considered suitable for the use of metrics.

"Collaboration allows us to know more than we are capable of knowing by ourselves." — Paul Solarz

Chapter Two: Creating a Trial Monitoring Plan (TMP) template

2.1 Chapter Overview and Scope

This chapter outlines the development of a Trial Monitoring Plan (TMP) template, which was created by reviewing monitoring plans and risk assessment documents from 31 UK Clinical Trial Units (CTUs). The data collection process began by gathering monitoring documents (whether monitoring plans or risk assessments) from as many of the 53 UKCRC-registered CTUs as possible. A comprehensive list of potential items for inclusion in the TMP template was generated by reviewing the monitoring plans collected from these CTUs. This list was then reviewed and refined through an iterative process involving myself and my supervisory team. Each item in the list was reviewed and classified into one of three categories: items to be included *'directly in the TMP template'*, items to be included *'in the Delphi'*, or items *'not included at all'*. Details of these categories will be explained later in the chapter. In brief, items that appeared in the majority of CTU monitoring documents were included directly in the template, those that were less commonly seen (and perhaps more specific to individual CTU practices) were excluded from the TMP template, and those for which further consensus was needed were included in the Delphi survey.

The list of items requiring consensus served as the foundation for a Delphi survey, in which monitoring experts from all 53 CTUs and the industry were invited to share their opinions on the necessity of each item for inclusion in the TMP template. Following the creation of a preliminary TMP template based on the Delphi survey results, a consensus meeting was held to review and finalise the template.

For clarity, in this chapter, I will refer to the monitoring plans received from other CTUs as *'CTU templates'* and the template created as part of this PhD as the *'TMP template'*. Additionally, during the review process, the term *'we'* refers to both me and my supervisory team.

This chapter will include sections on the methods, a justification for the choice of methodology, the results, conclusion, and limitations.

Table 2.1 below, illustrates the overall process, from receiving monitoring plans from CTUs to the finalisation of the template, ready for testing.

	Oct 22	Oct-Nov 22	Nov 22-Feb 23	Nov 22-Feb 23	Feb-Apr 23	Apr-Jul 23	Jul-Aug 23	Sep 23	Oct-Nov 23
Email to all UKUCRC CTUs.	x								
Monitoring plan received from 31 CTUs.		x							
Information extracted from 31 plans.			x						
Items and sections categorised.				x					
Classified items through an iterative review process.					x				
Delphi survey						x			
Delphi data reviewed							x		
Consensus meeting								x	
TMP template finalised for testing.									x

Table 2.1: The overall process, from receiving monitoring plans from CTUs to the finalisation of the template.

2.2 Aims and Objectives

Aim

The aim of this chapter is to enhance the conduct of clinical trials through the development of a comprehensive TMP template, with a focus on improving monitoring processes and risk management.

Objectives

To create a Trial Monitoring Plan (TMP) template.

2.3 Methods

Gathering monitoring plan templates from UKCRC registered CTUs

In October 2022, an email was sent to all UK monitoring leads via UKCRC network explaining the PhD project and requesting that they share their monitoring plans with me. As there is considerable variation in the terminology used across the clinical trials community, the email clarified that some CTUs may refer to this document as a risk assessment or quality control plan. Twenty monitoring plans were received after the initial email, and a further eleven were received after a follow-up email was sent, making a total of 31 monitoring plans from 54 UKCRC-registered CTUs. These CTUs had monitoring plans to share and deemed it appropriate to do so, some of which were risk assessment documents. One unit explained they were eager to participate but had recently undergone an inspection by the MHRA, during which their monitoring plan was deemed inadequate. The MHRA is responsible for regulating clinical trials in the UK, ensuring that they comply with the necessary safety and ethical standards. As a result of the inspection, the unit was working on improving their monitoring plan, which they felt was not yet ready for sharing. Another CTU mentioned that they do not have a designated monitoring plan, as they outsource their monitoring activities to a Clinical Research Organisation (CRO). Additional follow-up emails were sent to the remaining 19 unresponsive CTUs, but no replies were received despite these subsequent efforts. It is also important to note that while there were 54 UKCRC-registered CTUs as of October 2022 when this project commenced, the list now contains 53 UKCRC-registered CTUs.

Reviewing the 31 templates and creating a spreadsheet

I began by conducting a textual analysis of each CTU template, systematically extracting each wording item into an Excel spreadsheet (Appendix 1) for comparison and categorisation. Textual analysis is a qualitative research method that involves examining texts to understand their content, structure, and meaning (McKee, 2003).

In this study, I applied textual analysis to review each CTU template, extracting and categorising the wording items into an Excel spreadsheet for further comparison and analysis.

The items were listed individually and grouped under sections such as ‘study details’, ‘introduction to the trial’, and ‘Adverse Events (AE) and Serious Adverse Events SAEs)’, which were found across the CTU monitoring plans and therefore were determined to be necessary for inclusion in a TMP template. These sections of items were similar in many CTU monitoring plans, with some having more sections than others (Taheri et al., 2024). In the Excel spreadsheet, each CTU was represented by a column, and each item extracted from the CTU templates was placed in a row. As I reviewed more CTU templates, the number of items within each section expanded. With every CTU template I opened, I began from the beginning and checked each item against those already in the Excel spreadsheet. If the item’s exact wording was already in the spreadsheet, I entered a code of ‘1’ against it; if the item had different wording, the different wording was entered into the spreadsheet under the similar item and was again coded as ‘1’ for that CTU. Where an item was not found in a CTU’s template, it was coded as ‘0’ for that CTU. New items continued to be extracted and added to the spreadsheet until all the CTU templates were reviewed and completed. The final spreadsheet contained a total of 745 items (including different wordings of the same item) over 38 sections. A list of the sections in order they appeared in the excel spreadsheet can be seen in Table 2.2 overleaf.

Sections of the various CTU templates
Study details
Introduction to the trial: Summary of study design/Trial overview
Study Documentation: key documents in relation to the trial
Introduction to the trial and risks associated
Monitoring
Central Monitoring Activities
Central Quality Checks
On-site Monitoring
On-Site Monitoring activities
Routine Monitoring Visits
Remote Monitoring
Remote monitoring activities
Triggered monitoring visits
Metrics
Thresholds
Central Monitoring Escalation
Site Escalation
Trial Escalation
QA Escalation
Site Initiation Visit
Close out visit
Source Data Verification (SDV)
Pharmacy Monitoring
Medical Device Monitoring
Sample Monitoring
Safety Monitoring
Critical/Safety Data & Processes
Archiving
Annual unit study monitoring exercise
Communication in monitoring
Monitoring reports and escalation
Study Specific Considerations
Trial oversight
CTU Internal Quality Control Procedures
Roles and responsibilities
Training and Set up
Data Management
Data Monitoring

Table 2.2: List of various sections created in the Excel spreadsheet during the CTU templates review.

Examples of different items and sections found in CTU templates received

Many monitoring plans received from CTUs had different wording for the sections and/or items in that section of the plan to express the same meaning. The various wording was also added to the spreadsheet, to allow the best wording to be chosen for the final TMP template.

Table 2.3 below presents the collective count of CTUs that included an item referring to the *'recruitment target'*. Various CTUs used different expressions to represent this item. After reviewing all CTU templates, the phrase *'overall recruitment target'*, the most frequently adopted wording among the CTUs, was selected.

Study details/summary of the trial	Number of CTUs including this item (wording)
Sample size	3
Overall target recruitment	3
Overall recruitment target	6
Number of participants	4

Table 2.3: Example of items found in CTU templates with different wording but same meaning.

There were also instances where the same items were categorised under different sections in the CTU templates. Table 2.4 shows below an example of a series of SAE items categorised under a section titled *'Critical and Safety Data Processes'* by a specific CTU. The TMP template had already included items about SAEs in a section specifically designed for reporting SAEs. Therefore, although the items were included, they were put under the section dedicated to SAE reporting and the wording *'Critical and Safety Data Processes'* was not used in the TMP template.

Critical/Safety Data & Processes
Safety Reporting
Include whether all Adverse Events (AEs) or only Serious Adverse Events (SAEs) or Adverse Events of Special Interest (AESIs) will be reviewed and subject to SDV
Which source documents will be used to identify any unreported safety events
How safety reporting will be followed up by the Monitor and any specific safety arrangements

Table 2.4: Example of SAEs repeating in the spreadsheet under a different section wording.

Furthermore, Table 2.5 overleaf shows trial identifiers that were used across different CTU templates. We decided to choose 3 different trial identifiers instead of including

all of them, considering that the majority of the rest can be found in the trial protocol if needed. We chose 3 different identifiers that were used in the majority of the CTU templates which were '*ClinicalTrials.gov', 'International Standard Randomised Controlled Trial Number (ISRCTN) Number'* and *'European Union Drug Regulating Authorities Clinical Trials Database (EudraCT) Number'.* As seen in the table below, the '*REC reference'* number was used in more CTU templates than '*ClinicalTrials.gov'*, one of the identifiers that we chose for the TMP template. The reason for this choice was that the *'ClinicalTrials.gov'* Identifier (NCT number) is a global identifier assigned to a clinical trial for tracking and referencing purposes on ClinicalTrials.gov (ClinicalTrials.gov), whereas the *'Research Ethics Committee (REC) reference'* number is a local identifier assigned by the Research Ethics Committee for the purpose of tracking and referencing the ethical approval granted for the trial at the local level (Research Ethics Committee review). Therefore, the *'ClinicalTrials.gov'* number was deemed a more suitable choice. Additionally, the Integrated Research Application System (IRAS) ID refers to the identifier assigned to a clinical trial or study application submitted through IRAS in the UK (IRAS). IRAS is used for the submission of applications for regulatory and ethical approval within the UK. We chose not to use the IRAS ID as an identifier for similar reasons to the other identifiers: it is locally recognised within the UK and is primarily used in the context of UK clinical trials for regulatory and ethics approval.

Study Details	**Number of CTUs including this item**
REC Ref	8
IRAS ID	6
ClinicalTrials.gov	1
EudraCT Number	13
ISRCTN number	7
MHRA No. (Devices)	1
Clinical Trial Authorisation (CTA) number	1

Table 2.5: Various trial identifiers used in different templates.

Many CTU templates included sections to guide the user (i.e., trial manager or trial monitor) in completing the monitoring plan. Some of these guidelines were incorporated into the relevant sections of the TMP template to provide guidance and support for those completing the form. Although the exact wording from the CTU

templates was not used in the guideline's sections of the TMP template, the CTU templates served as a guide to format and determine which guidelines to include.

In each CTU template, every detail from all sections of the template was carefully examined and transferred to the Excel spreadsheet. Once I finished reviewing all CTU templates, I had 745 items listed in the spreadsheet. Each of these items belonged to at least one CTU, and in many cases to more than one. The number of items started to reduce when the review process began. The next section explains how I reviewed the items and the decision-making process for their inclusion or exclusion in the TMP template. By the end of the final review, the number of items was reduced to 412 in the TMP template.

Deciding on each item of the spreadsheet

I reviewed every item with my supervisory team, and we classified each item into one of three categories: items to be included '*directly in the TMP template',* items to be included *'in the Delphi'* or items *'not included at all'*. This classification was made by looking at the number of templates that included each item and the importance of the item based on the experience of monitoring and trial management we each have. This includes experience of managing and monitoring various clinical trials as well as developing and implementing trial documents. I reviewed the first two sections of the spreadsheet which were *'study details'* and *'introduction to the trial'* with my primary supervisor. We discussed each item and made mutual agreement on whether to include them directly in the TMP template or Delphi, or not to include them at all. When we encountered an item on which our opinions greatly diverged or we felt it was important to seek the input of other trialists, we included those items in the Delphi list. Furthermore, we each independently reviewed the 'central monitoring' and 'risk assessment' sections and made decisions about the items. We then reviewed our decisions and discussed areas where mutual agreement was not reached. Additionally, we revisited the items where we had mutual agreement to understand the rationale and thought processes behind our decisions. This process helped me critically engage with and refine the categorisation of the items.

After the first four sections were reviewed and discussed in detail with my primary supervisor, I proceeded to review the remaining sections of the spreadsheet independently, applying the same methodology we had used during the joint review.

For these sections, I shared my decisions with my supervisory team. In cases where there was a difference of opinion on a specific item, we engaged in discussions to decide on the appropriate category. Similarly, if there were instances where I couldn't decide how to categorise an item or needed further clarification and guidance, I brought them to the supervisory team discussions.

Those items that were classified to be directly added to the template were those found in the majority of CTU templates. Additionally, FDA (US Food & Drug Administration, 2023) and MHRA (MRC/DH/MHRA, 2011) guidelines were also taken into consideration. For many items, the decision to incorporate them into the template was straightforward. These included items like assessing AEs/SAEs, obtaining consent, monitoring frequency, protocol deviations, Source Data Verification (SDVs), and similar aspects.

Any item that did not appear in more than two CTU templates and seemed less significant, was not included in the TMP template. Careful consideration was given to these items before deciding to not include them. These considerations included whether those items can be found in a trial protocol, and how easily they can be found in the protocol. The goal was to maintain a correlation between the monitor's duty to review the protocol's contents while ensuring that the TMP template contained all necessary information without being overly detailed.

Any remaining items that didn't classify as *'directly in the TMP template'* or *'not included at all'*, were put in the Delphi process. About 10% of the items that we put in the Delphi were items that we did not reach mutual agreement on. The preliminary TMP template and list of items for the Delphi were reviewed extensively over a few months. The final Delphi list for round 1 (Appendix 2) included a comprehensive list of 66 items that could be included in the TMP template.

To enhance transparency, the flow of the Delphi process and the decisions made at each stage are summarised in Appendix 3.

Justification for choice of methodology

Delphi is a technique widely used to establish consensus on group opinion. The advantage of Delphi is that it does not require face to face contact (Trevelyan & Robinson, 2015). The Delphi method seeks consensus through a systematic approach

of repeating rounds, wherein each subsequent set of statements is constructed based on the feedback from previous responses (Holey et al., 2007). The process is stopped when consensus is reached (Holey et al., 2007). Delphi answers are anonymised, which adds the benefit of participants being able to be open and relaxed about their answers, with less pressure from the influence of hierarchy. As Delphi is an online method it is also not constrained by geographical limitations (de Manincor et al., 2015).

Another benefit of using a Delphi survey is that, at each round of the survey, systematic feedback is received from the results of the previous rounds (de Meyrick, 2003). This allows participants to review others' responses to statements from earlier rounds and they can choose to revise their own answers or maintain them unchanged (de Manincor et al., 2015). This results in having a final set of unbiased consensuses which is thoroughly considered and reviewed. The Delphi survey has been used in a number of clinical trial conduct studies (e.g.,Gamble et al., 2017; Whitham et al., 2018).

A number of systematic reviews have identified recurrent methodological weaknesses in Delphi studies and offered practical recommendations for design and reporting. In particular, (Boulkedid et al., 2011) highlight the need to pre-specify consensus criteria, justify the number of rounds, ensure controlled feedback between rounds, define and justify the expert panel, report response/attrition rates at each round, and use transparent, robust agreement statistics (for example medians and interquartile ranges) with sensitivity analyses of stability. The present study was designed with these recommendations in mind, as summarised in Appendix 4, and aligns with contemporary guidance on modified Delphi use in clinical research (Diamond et al., 2014; Trevelyan & Robinson, 2015).

Delphi Survey

Prior to conducting the Delphi survey an ethical approval was received for the study on 6th February 2023 from UCL Research Ethics Services. A Participant Information Sheet (Appendix 5) was designed to explain the study and what the Delphi commitment entailed. Participants confirmed their consent to take part in the Delphi study once they logged in to the software and read all the information about the study.

An online software program called *'Delphi Manager'* that has been used in a number of previous clinical trial methodology research studies (Gamble et al., 2017), was

purchased from the University of Liverpool. The software was handed over with setup instructions, which I followed to configure the survey. The survey was then tested by me and the supervisory team to ensure it functioned correctly. The first page included an introduction to the study, a link to the Participant Information Sheet, information on ethics, contact details for me, and survey instructions. After successful testing, the system went live.

The first round of the Delphi survey started on 27th April 2023 and was initially planned to run for 4 weeks. However, this round was extended by 10 days, concluding on the 31st of May 2023 to allow more participants to take part.

I invited anyone with clinical trial monitoring experience, expertise, or a desire to improve monitoring processes to take part. This was the inclusion criteria that was detailed in the recruitment advert (Appendix 6).

Maintaining active involvement from the monitoring community is crucial for the success of this PhD project overall. Equally important was the effort to maximise participant engagement in all stages of the Delphi survey. During the initial round, the emphasis was on disseminating information widely to ensure that the project and the Delphi survey were well-publicised. To achieve this, I undertook the following initiatives to attract participants to the first round of Delphi:

- I visited various CTUs in the UK to give talks about the project before the Delphi survey started. This activity was funded by the MRC CTU at UCL Training and capacity strengthening grant which I received in January 2023. I contacted CTUs explaining to them that I would like to give a talk about my project and learn about their monitoring practices and use of metrics in their CTU. Five CTUs agreed to see me; these were Nottingham, Southampton, Bristol, Warwick, and Leeds.
- Attended the International Clinical Trials Day organised by UCL Institute of Clinical Trials and Methodology (ICTM) with flyers during round 1.
- Put flyers around the MRC CTU at UCL office while the Delphi survey was live in round 1.
- Made regular weekly tweets by MRC CTU at UCL Twitter (now ‘X’) account.
- Wrote a piece for the MRC CTU at UCL weekly newsletter (send out to all MRC CTU staff).
- Wrote a piece for the UKCRC Exchange newsletter.

- Wrote a piece for the UK Trial Managers' Network (UKTMN) newsletter.
- Wrote a piece for the Trials Methodology Research Partnership (TMRP) Data quality and Monitoring group.
- I also contacted MHRA to encourage them to take part, however, no response was received.
- Lead author of the Statistical Analysis Plan (SAP) Delphi study was contacted; because they had conducted similar work, and I hoped to encourage them to participate in the current study, however, no response was received.
- Individual contacts were made with all the CTUs that shared their monitoring plans or risk assessment documents to encourage them to take part.
- Individual contacts were made with any previous colleagues I had in my role as a trial manager.

In the first round, 47 participants took part. Maintaining a comparable number of participants in the second round was crucial. To address retention and minimise participant loss (Trevelyan & Robinson, 2015), I implemented various strategies. Accordingly, I undertook the following activities in Round 2:

- Presented at the National Monitoring Meeting in June 23 at the beginning of round 2 of the Delphi.
- Made regular weekly tweets by MRC CTU at UCL Twitter (now 'X') account.
- Wrote a piece for the MRC CTU at UCL weekly newsletter.
- Individually contacted participants that took part in round 1 but didn't start round 2 or did not finish their incomplete round 2 survey.

My subsidiary supervisor, Prof. Matt Sydes, also mentioned the Delphi round 2 in the 'Society of Clinical Trials (SCT) Conference' held in May 2023.

Before presenting the findings from the two Delphi rounds, it is important to situate this study within the broader methodological literature. The following section therefore summarises how the design of this Delphi aligns with, and constructively diverges from, established practice, and how it compares with similar studies to highlight its methodological contribution. This Delphi adhered closely to established methodological standards identified in reviews and guidance papers (Boulkedid et al., 2011; Diamond et al., 2014; Trevelyan & Robinson, 2015; von der Gracht, 2012). These sources define good practice as involving a clearly justified expert panel, two

or more structured rounds with controlled feedback, pre-specified consensus criteria, transparent reporting of participation and stability, and measures to preserve anonymity and independence. The present study aligns with these conventions through its defined eligibility criteria for experts, two-round structure with feedback of group medians and distributions, and quantitative thresholds (≥ 70 % rating 7–9; IQR ≤ 2).

It diverges constructively in several ways. First, the initial item set was generated empirically from 31 CTU monitoring templates rather than the published literature, strengthening practical relevance. Second, a structured consensus meeting followed the Delphi to decide unresolved items, reflecting an emerging hybrid model in methodological research (Hasson et al., 2000; Trevelyan & Robinson, 2015). Third, anonymous electronic voting using Mentimeter (*Mentimeter. (2025)*) was employed to combine real-time discussion with anonymity, minimising social conformity effects. These adaptations extend established Delphi practice by integrating pragmatic data-driven item generation with rigorous, transparent consensus methods suited to complex, multi-stakeholder settings.

Although the present study follows established Delphi conventions, it also addresses several limitations noted in earlier studies. Many previous methodological or consensus Delphis have been criticised for limited transparency in item development and reporting of decision criteria (Boulkedid et al., 2011; Diamond et al., 2014). By contrast, this study provides a fully auditable account of item generation, reduction, and retention decisions (see Table 2.B), allowing replication. Other Delphi studies in trials methodology, such as those by Gamble et al. (2017) and Whitham et al. (2018), relied primarily on expert opinion or literature-derived items; here, the item set was empirically drawn from operational CTU templates, providing stronger ecological validity. Furthermore, whereas prior Delphis have occasionally lacked mechanisms to control for dominance or group influence during face-to-face consensus meetings, this study introduced structured facilitation and anonymous electronic voting, which preserved independence while retaining opportunities for clarification. These adaptations reflect a methodological advance rather than a departure from best practice, situating this study as a pragmatic and transparent evolution of Delphi methodology within UK trials research.

2.4 Results

Delphi participants

Demographic data was collected from participants at the time of registration for the Delphi survey. In round 1, 47 participants took part, followed by 43 in round 2. The majority of participants were from 25 UKCRC registered CTUs, but there was also 1 participant from Australia who had previously worked in the UK and 2 participants from the United States, and 1 participant from a CRO in Kenya. The participant from Australia was a former colleague who I knew has extensive monitoring knowledge and I approached directly. The participants from the United States were invited during the SCT conference which Prof. Matt Sydes attended in May 2023. The industry participant from Kenya was a recruitment from the TMRP advertising. Figure 2.1 shows the distribution of participants by CTUs, and Figure 2.2 shows the distribution of participants by role. Participants in both rounds were from a range of different roles in clinical trials, from clinical trial management to trial monitors, Chief and Principal Investigators, Statistics, Research nurses, Methodologists, Quality Assurance, and data management. It is important to note that the participants in round 2 closely resembled those in round 1, except for three new participants: one clinical trial monitor, one quality assurance manager, and one trial manager.

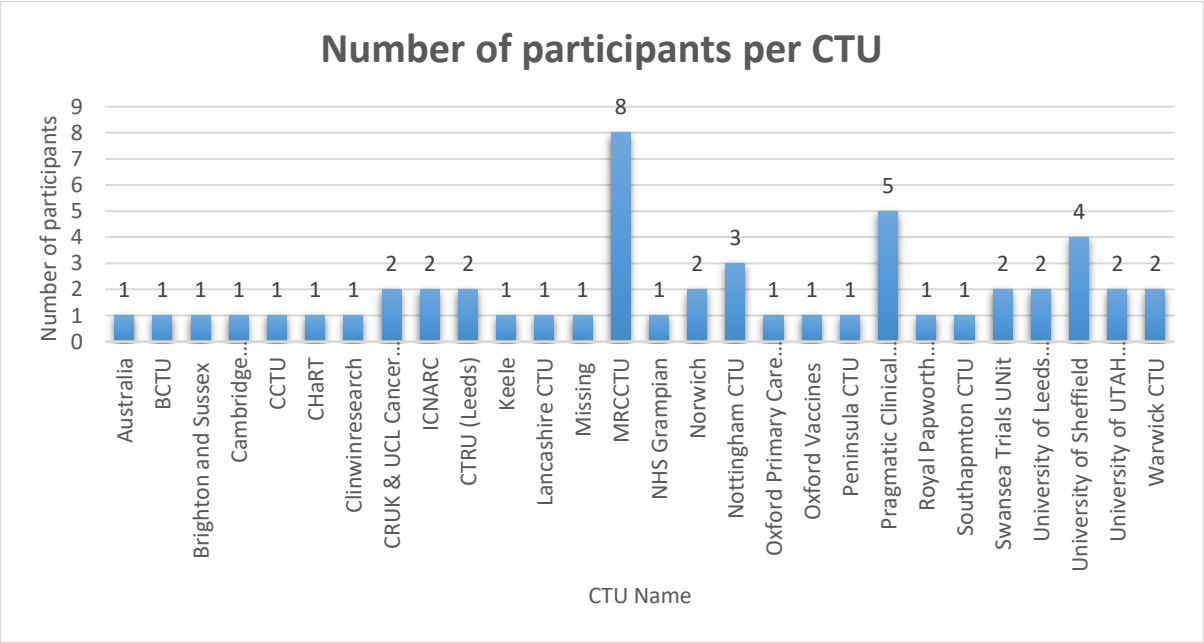

Figure 2.1: Distribution of participants by CTUs

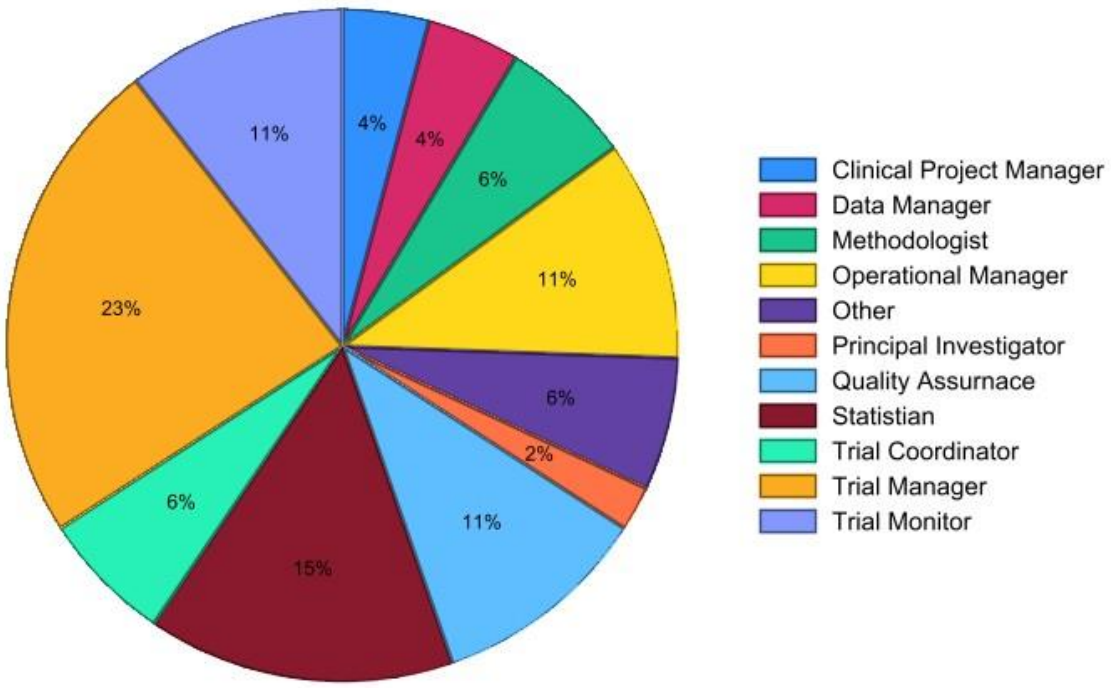

Figure 2.2: Role distribution of all 47 Delphi survey participants.

Of the 47 participants in round 1, 43 (91%) fully completed the survey, while 4 (9%) participants partially completed the survey. The partial completion in round 1 ranged from 1 to 30 questions answered, with participants answering 1, 14, 22 and 30 questions out of 66 in the Delphi survey. In round 2, 37 (79%) participants fully completed the survey, while 3 (6%) partially completed the survey. The partial completion in round 2 ranged from 8 to 48 questions answered, with participants answering 8, 38, and 48 questions out of 72 in the Delphi survey. Seven (15%) of round 1 participants did not engage in round 2. Additionally, round 2 was open to anyone who was interested in taking part in the survey, regardless of whether they participated in round 1. Therefore, in addition to the 37 participants who fully completed round 2, there were 3 new participants, making a total of 40 (93%) participants who fully completed round 2, and 3 (7%) participants who partially completed round 2 (Taheri et al., 2024).

Delphi scoring process

Participants were asked to score each item for importance, to be included in a trial monitoring plan template. The 9-point Likert scale was presented with 1 to 3 labelled as *'not important'*, 4 to 6 labelled as *'important but not critical'*, and 7 to 9 labelled as

'critical' as used by (Gamble et al., 2017). Participants also had the option of *'unable to respond'* if they felt unable or unwilling to answer questions.

The survey items were consistently presented in the same order in each round to maintain standardisation across all responses. This process ensured that each participant responded to the same set of questions, with no variation in the order of presentation. The design of the Delphi survey, including the structure of the items, was developed in multiple stages, as outlined in Section 2 of this chapter (Methods), and will be discussed further in the following sections.

Round 1 included 66 items. In this round, Delphi participants were able to comment on the wording of the items and could suggest additional items to be included in the TMP template. A total of six additional items were suggested by participants in round 1, as shown in Table 2.6 below. The additional items were reviewed for suitability and duplication before including them in round 2. As described by (Trevelyan & Robinson, 2015), I decided to not omit any items from round 1 to be able to have a full analysis therefore, round 2 included all items from round 1 as well as additional items suggested in round 1. Since additional items in round 1 underwent only one Delphi round, we extensively discussed these items during the consensus meeting to reach consensus on their inclusion or exclusion in the TMP template.

TMP template item
On-site monitoring activities
To review consenting process and document completion
Review of consent forms to ensure completed correctly.
Have all SAE been reported by site within the reporting timelines?
Data Checks
Checks for unusual data patterns/Suspected fraud e.g., audit trail end digit review.
Metrics
Space to store thresholds for metrics.
Site initiation visit
Site selection/evaluation plan

Table 2.6: List of additional items suggested in round 1.

We opted for a short time between rounds to maintain participant interest and reduce attrition, and therefore chose to leave only two weeks between rounds 1 and 2 (Becker

& Roberts, 2009). The second round of Delphi commenced on 14th June 2023 and ended on 8th July 2023.

Decisions about how many rounds of Delphi

Trevelyan et al., suggest that three rounds in a Delphi study are optimal (Trevelyan & Robinson, 2015). However, the classic method of Delphi, developed by the RAND Corporation in the 1950s (Linstone, 1975), typically involved four rounds to achieve consensus among experts. In this method, the first round includes open-ended statements generating qualitative data. The subsequent rounds include statements generated from round 1 which participants rank on a Likert scale, generating quantitative data (Trevelyan & Robinson, 2015). Therefore, round 1 in the modified method is round 2 in the classic method. In this study, I used the modified method of doing a Delphi study in which I identified the issue (in this case, not having a standardised TMP template) and used structured statements generated by reviewing 31 CTU templates. Using the classic Delphi method can produce a large number of statements meaning lengthy future rounds and a time burden for participants (Smith et al., 2012). Trevelyan et al., recommends including fewer, well focused open-ended questions or using a modified approach to develop initial statements (Trevelyan & Robinson, 2015). In the case of the TMP template, it would have been impossible to use the classic method due to the number of items that were taken out of the 31 CTU TMPs reviewed (745 items), therefore I used the modified method.

‘’Choosing the number of rounds in a Delphi study depends on whether consensus is being used as a ‘stopping guideline’ or if the number of rounds has been set a priori’’ (Trevelyan & Robinson, 2015). Although the classic Delphi has four rounds (Hasson et al., 2000) many studies set an a priori criterion of three rounds but some only include two (Becker & Roberts, 2009; Ward et al., 2014). Additionally, attrition and participant fatigue are likely to increase with each round. In this study we used consensus as a stopping guideline (von der Gracht, 2012)

Consensus can either be used to determine if an agreement exists or as a stopping guideline (Becker & Roberts, 2009; Holey et al., 2007). Concept of consensus has been used differently across Delphi studies and no agreement exists on which is the best criterion to use (Trevelyan & Robinson, 2015). “Consensus has been determined through the aggregate of judgment, subjective level of central tendency and by

confirming stability'' (Murphy et al., 1998). Consensus within rounds typically measures the agreement of the individual participant with the statement, which then provides group opinion and the extent to which participants agree with each other (Ward et al., 2014). Stability of response can indicate whether consensus was present throughout and whether it developed or changed between rounds (Becker & Roberts, 2009). A systematic review of 80 Delphi studies found five main methods for reaching consensus, with the most common approach being the use of median scores that exceed a set threshold and achieving a high level of agreement among participants. This typically involved setting a specific median score and ensuring a certain percentage of ratings were in the highest or lowest range (Boulkedid et al., 2011). Another systematic review of a random sample of 100 Delphi papers found that percent agreement was most frequently used (Diamond et al., 2014).

Some Delphi studies suggest that stability of response is the more reliable indicator of consensus, however, there is also the suggestion that this measures the internal reliability and not consensus (Trevelyan & Robinson, 2015). Trevelyan et al. explains that reliability, agreement, and consensus are different concepts. Reliability is measuring the proportional consistency of variance among raters, agreement is measuring the extent to which participants agree with the statement under consideration and consensus is measuring the extent to which participants agree with each other (Trevelyan & Robinson, 2015). A study exploring different methods to measure consensus and stability in Delphi studies advised using a combination of statistics to reduce subjectivity and ensure validity of results (Holey et al., 2007).

Median and Interquartile range (IQR) are considered robust measures, with IQR accepted as an objective and rigorous way of determining consensus through measurement of variance in response (von der Gracht, 2012). Medians tend to be preferred over means as they are more robust to the effect of outliers and IQR is considered more robust than standard deviation (Murphy et al., 1998). Some studies additionally provide visual feedback (bar charts) which can help with interpretation (Greatorex & Dexter, 2000). Stability of response could also be reported by providing data on the median and IQR across rounds (Murphy et al., 1998; Ward et al., 2014).

In this PhD, a median of 7-9 was considered to mean agreement and an interquartile range (IQR) ≤2 was considered indicative of consensus as suggested by Gracht et al.,

(von der Gracht, 2012). This paper suggests that consensus is reached if IQR is 2 or less on a 9-point Likert Scale. (von der Gracht, 2012)

For the purpose of this study, consensus was predefined and was used to determine agreement (Gamble et al., 2017). Items that were rated *'critical by 70% or more of the participants and not important by less than 15% of the participants'* were determined to have reached consensus. Items that were rated *'not important by 70% or more of the participants and critical by less than 15% of the participants'* were determined to not have reached consensus, although we did not have any items in this category. This definition has been used in other Delphi surveys conducted for similar research (Gamble et al., 2017; Whitham et al., 2018) and was agreed upon by me and my supervisory team.

Delphi Round Results

On completion of both rounds, the number of items for which more than 70% of the participants responded with a Likert score of 7-9 (critical) increased by 18% from 22/66 (33%) in round 1 to 37/72 (51%) in round 2 (Figure 2.3). This shows participants' agreement with the items being proposed for the TMP template has increased in number. Additionally, median scores were compared to determine if agreement was reached amongst participants on individual items. Comparing the items' median score, in round 1 there were 47/66 (71%) items with a median score of 7-9, and in round 2 there were 51/72 (71%) items with median score of 7-9. There were no items that were rated 'not important' by 70% or more of the participants in either round.

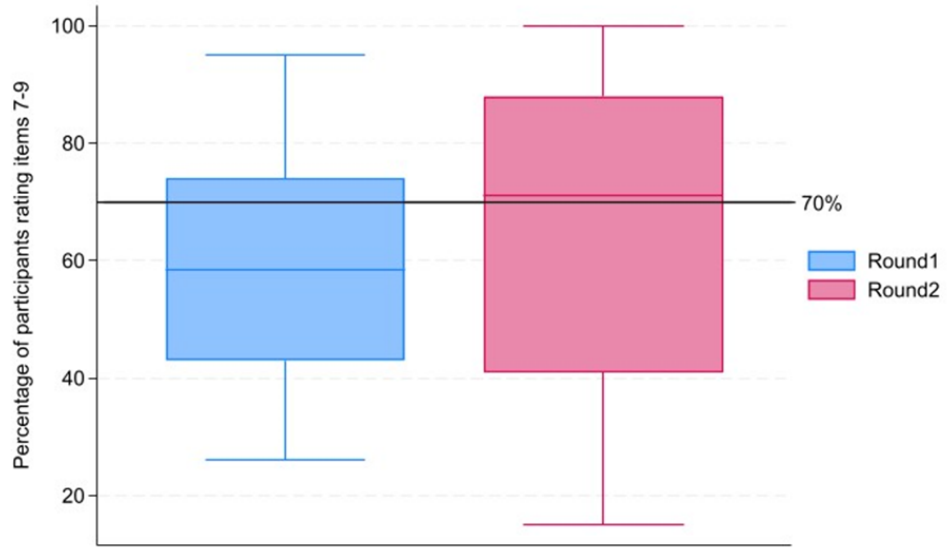

Figure 2.3: Distribution of the percentage of participants rating items with a Likert score of 7-9 (critical) in Round 1 vs. Round 2. The black line represents the threshold where 70% or more of participants rated items as critical. Adapted from (Taheri et al., 2024).

Additionally, considering the Inter Quartile Range IQR≤2 as Gracht et al., suggests (von der Gracht, 2012) as an indication of consensus across all items, the number of items with IQR≤2 in round 1 is 29 and in round 2 is 56 which shows the variance of response is reducing across the group of items therefore indicating consensus (Figure 2.4) (von der Gracht, 2012).

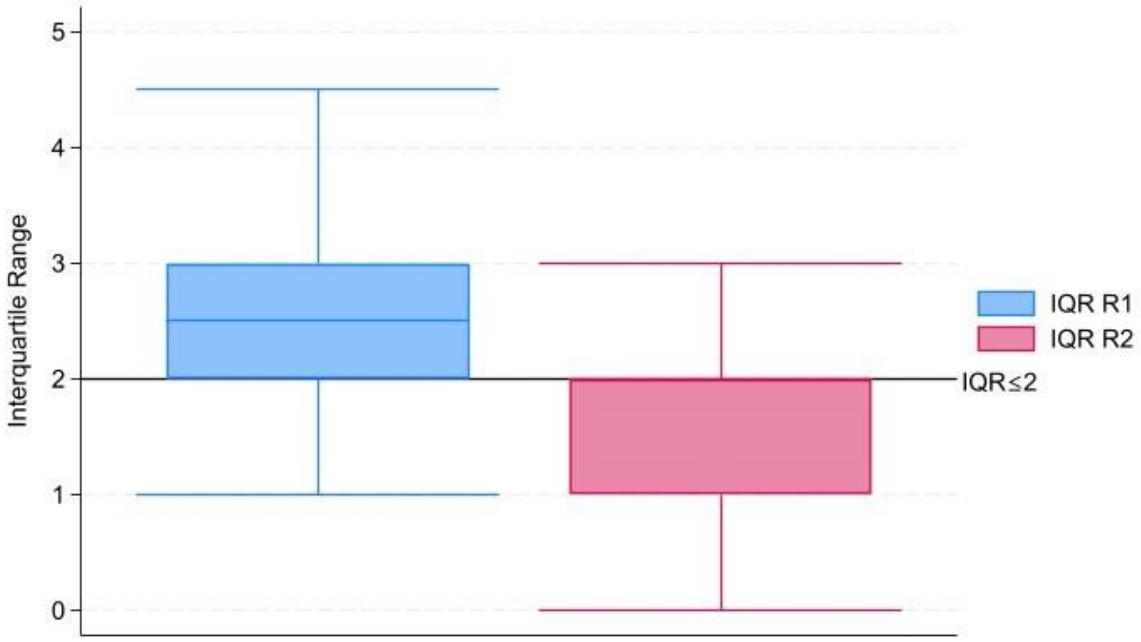

Figure 2.4: Comparing the Interquartile Range in items in Round 1 vs. Round 2. The black line indicates where the Interquartile Range is ≤2. Adapted from (Taheri et al., 2024).

Furthermore, the number of comments in round 2 reduced in comparison to round 1 which is another indication of group opinion moving towards consensus (Holey et al., 2007).

Table 2.7 below shows the total number of items with median score of 7 or more in round 1 vs round 2 as well as total number of items with IQR of 2 or less in round 1 vs round 2.

	Total in R1	**Total in R2**
Median>7	47	51
IQR<2	29	56

Table 2.7: Statistical summary of Median and IQR in round 1 vs round 2.

I further analysed the results of the Delphi study to investigate whether there were any particular items with a high rate of 'unable to respond' answers. I found that this rate was particularly high for the items *'checks for serious adverse events for medical devices'*, *'use of metrics in clinical trials'*, and *'trial oversight of vendor'*. These items were discussed in more details at the consensus meeting. I presented the results and analysis of the Delphi survey to my supervisory team, and we discussed them at length to determine whether a third round of Delphi was necessary. We concluded that with 79% of items (86% of the original list from round 1) likely to remain in their critical categories (i.e., scored 7-9 by more than 70% of participants), I could justify not having another round of the Delphi survey. From the data, it was evident that the group was moving towards consensus. Additionally, I wanted to avoid participant attrition and fatigue, having already seen an 8.5% loss of respondents from rounds 1 to 2. I therefore decided to stop the Delphi survey after 2 rounds and proceed to the consensus meeting, where the results would be discussed, and participants would have a final opportunity to influence the development of the TMP template.

Consensus Meeting

We invited participants who had expressed interest in joining the consensus meeting during their registration for the Delphi survey. While the Delphi rounds preserved anonymity and independent judgement, the consensus meeting reintroduced a group setting where power dynamics can subtly influence discussion. Participants' seniority, reputation, or institutional affiliation may shape how openly others voice disagreement. To minimise such effects, the meeting followed a structured agenda, allocated equal discussion time per item, and used pre-circulated materials showing Delphi results to ground decisions in data rather than authority. The chair explicitly invited quieter participants to contribute before voting. These steps aimed to create an atmosphere of balanced participation and to safeguard the integrity of the consensus process. We decided that with the amount of data to review, a two-day consensus meeting (3 hours each day) seemed sensible. The consensus meeting took place on the 6th of September 2023 with 11 attendees and 8th of September 2023 with 10 attendees. We had 9 voting attendees in day 1, followed by 8 in day 2. The attendees represented 9 different CTUs across the UK, as well as industry, and held various trial roles. Figure 2.5 overleaf shows the role distribution of attendees at the consensus meeting. Voting was conducted through an anonymous electronic platform (*Mentimeter. (2025)*),

allowing participants to submit their decisions anonymously and ensuring that the final outcomes reflected individual views rather than group influence.

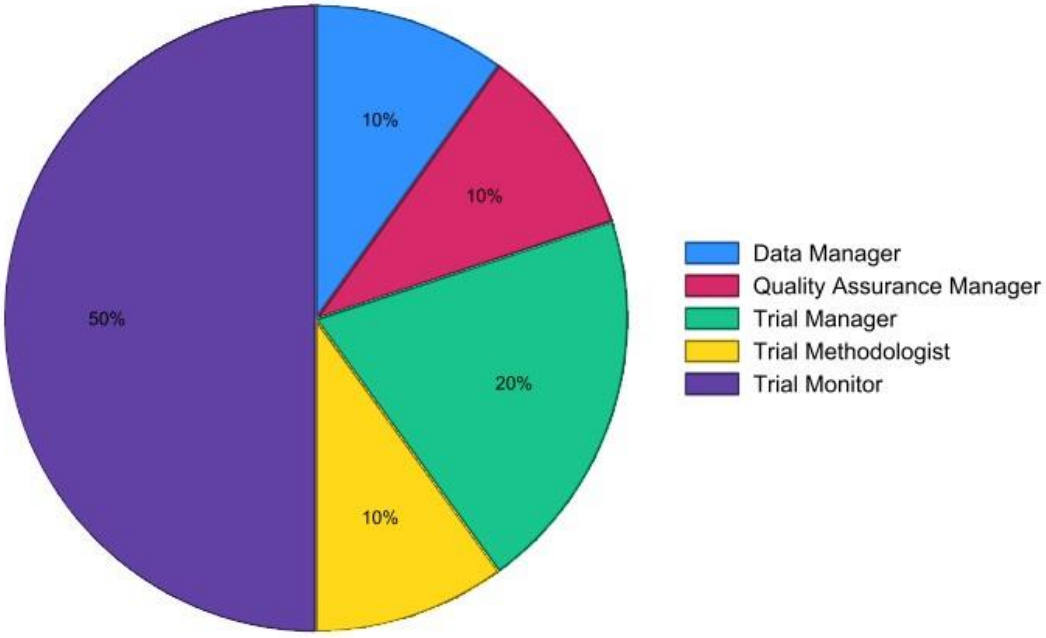

Figure 2.5: Role distribution of consensus meeting participants, consisting of 10 different people across the two sessions. Adapted from (Taheri et al., 2024).

The consensus meeting participants were presented with the template and an instruction about the Delphi results and what they look like in the current template. These were also emailed to them a week prior to the consensus meeting with the aim to provide them with background information before the meeting. Those items that had been rated critical by 70% or more of the participants (and therefore had reached consensus for inclusion in the TMP template) were coloured green within the template and attendees were asked to consider these before the meeting as we would not go through them in detail. Those items that had other ratings, which we needed to discuss and reach consensus on, were coloured orange. At the meeting I presented the 37 items that had reached consensus during the Delphi survey and asked the consensus meeting participants to comment on any issues or concerns including wording of the items or objections about their inclusion in the TMP template. These items can be seen in Appendix 7.

After reviewing all the items, consensus participants made several suggestions regarding the wording of some items, which are discussed below. The first suggestion

was to simplify *'Introduction to the trial: Summary of study design/Trial overview*' which was shortened to *'An overview of the trial design'.* Additionally, it was suggested that the template should not specify values for error rates, as seen in item 9 under *'data checks',* since these rates vary depending on the trial's risk assessment. As a result, the numbers were replaced with *'X'* allowing CTUs and the trial management team to insert trial-specific values. It was also recommended that the item *'Obtaining confirmation that site staff have completed trial-specific training and are aware of the operational requirements'* be removed, as this is already addressed in the *'site initiation'* section of the template.

Following the review of the first 37 items, I presented the 3 additional items that were suggested in Delphi survey round 1 that had reached consensus for inclusion in round 2 of the Delphi. These items are seen in Table 2.8 below. I decided to present these items separately to be able to emphasise the importance of them having been rated only in 1 round (round 2).

TMP template item	**% of participants responding 7-9 (critical)**
On-site monitoring activities	
To review consenting process and document completion	74%
Review of consent forms to ensure completed correctly.	95%
Have all SAE been reported by site within the reporting timelines?	93%

Table 2.8: Three additional suggested items with consensus for inclusion.

Consensus meeting participants discussed these items and concluded that the first two items conveyed the same meaning. As a result, the second item, which had 95% of the Delphi participants rating it as critical, was selected for inclusion in the template. Additionally, it was decided that the third item, concerning the review of SAEs, was already covered in the template, so it was not added.

I then presented the 3 additional items that were suggested in round 1 that we needed to reach consensus on. These items can be seen below in Table 2.9 overleaf.

TMP template item	% of participants responding 7-9 (critical)
Data Checks	
Checks for unusual data patterns/Suspected fraud e.g., audit trail end digit review.	55%
Metrics	
Space to store thresholds for metrics.	15%
Site initiation visit	
Site selection/evaluation plan	33%

Table 2.9: Three additional suggested items without consensus for inclusion/exclusion.

The first two items were discussed in detail and voted for inclusion in the TMP template. The last item, however, was voted for exclusion and is explained further, along with the other items that were excluded from the TMP template.

After discussions, participants in the consensus meeting voted on the 32 further items that had not reached the definition of consensus within the Delphi, regarding each item's inclusion in or exclusion from the TMP template. These items can be found in Appendix 8.

The participants were shown the result of the Delphi for each item. The results were presented in graphs which showed the number of participants that rated the item in round 1 and round 2 and the total number of responses in each category (*'1-3' (not important), '4-6' (important but not critical), '7-9' (critical), '10' (unable to answer)*). An opportunity to discuss the items and ask questions was presented before votes were taken on whether to include each item in the TMP template. Participants discussed each item at length and considered factors such as the significance of each item to trial monitoring, the ease of locating the information within the protocol, and whether these items were better suited for inclusion in the monitoring template or in other trial-related documents such as SOPs, data monitoring plans, or other working instructions.

Figures 2.6 and 2.7 overleaf show an example of the Delphi results presented to the consensus meeting participants and how they voted on this question. In this example, we can see that although Delphi survey participants rated *'Recruitment Target'* as *'important but not critical',* the consensus meeting vote was to exclude this item from the TMP template. This decision was made after a lengthy discussion, during which it

was agreed that the item could be easily found in the trial protocol. To avoid making the TMP template unnecessarily lengthy, it was decided to exclude it. All Delphi graphs and consensus meeting voting to each item can be seen in Appendix 9.

Recruitment Target

Total response in R1	47
Total response in R2	43
Response rate (%) for R2	
Not important (1-3)	7%
Important but not critical (4-6)	49%
Critical (7-9)	42%
Unable to respond	2%

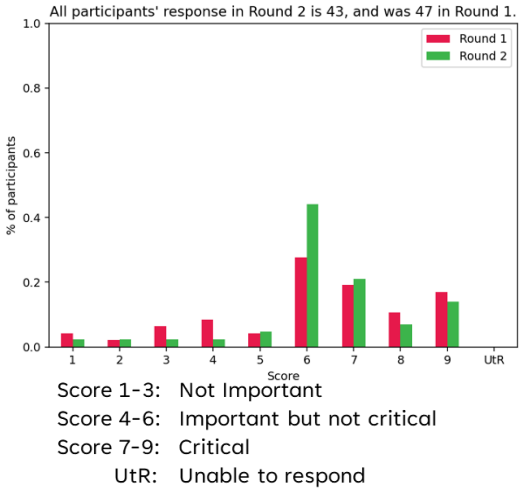

Figure 2.6: Table (left): Responses of Delphi participants on whether to include 'Recruitment Target' in the TMP template. Figure (right): Responses displayed in a bar chart.

Figure 2.7: Consensus meeting voting result to importance of including 'Overall Recruitment Target' in the TMP template.

Consensus meeting voting resulted in 18 items being excluded, leaving 14 items to be included in the TMP template. It is important to highlight that in the Delphi survey; no items were rated as *'not important'* by 70% or more of the participants in either round. However, 18 items were voted for exclusion from the TMP template during the consensus meeting, where items were discussed at length and collective decisions were made about the benefits of excluding them. The list of the 18 items excluded by

vote during the consensus meeting is shown in Table 2.10 below. These items and reasons for their exclusion are discussed below.

1	Site initiation visit: Site selection/evaluation plan
2	Overall recruitment target
3	Secondary outcome measures
4	Duration of patient recruitment
5	Duration of follow up (per patient)
6	Duration of follow up (the trial)
7	Intervention(s)
8	Is the trial placebo or standard of care controlled?
9	On-site monitoring activities: Is the site delegation log the original of the latest copy filed in the site master file?
10	On-site monitoring activities: Has the Site Visit Log been completed at each visit?
11	Site staff discussion: Other- Add any additional checks to be performed during on-site monitoring visits for this trial.
12	Documents and systems to be reviewed: Completion of annual progress and safety reports (as appropriate)
13	Documents and systems to be reviewed: Recruitment rates
14	SDV: Do you want a prompt list of data to SDV on the template?
15	Trial oversight of vendor: Onsite vendor monitoring
16	Trial oversight of vendor: Central monitoring of vendor duties
17	Trial oversight of vendor: Review of vendor related activities (if required)
18	Trial oversight of vendor: Completion of vendor status reports

Table 2.10: The list of the 18 items excluded by vote during the consensus meeting.

The inclusion of '*site selection/evaluation plan'* in the monitoring plan was discussed. This item was proposed by one of the Delphi participants in round 1 and this was highlighted to the consensus meeting participants. Some of the consensus meeting participants felt that while site initiation is a part of monitoring, site selection is more ambiguous. In some units, the trial manager, along with the Chief Investigator (CI), handles site selection, while monitoring teams are not involved in this process. However, it needs to be considered that many trial managers perform monitoring activities too. It was suggested that including site evaluation in the monitoring plan could place unnecessary time pressure on the CTU team, as site selection usually begins early and takes time, whereas the monitoring plan, which takes longer to develop, is often started later in the trial setup process. Several participants agreed

that site selection should remain separate from monitoring activities, with separate Standard Operating Procedures (SOPs). As a result, it was decided not to include site evaluation in the TMP template.

Item 2 to 8 in Table 2.10 were voted for exclusion from the TMP template, as the general consensus was that these items are already covered in the trial protocol. The main focus of the consensus group was to ensure that the TMP template did not become unnecessarily lengthy, as the proposed document was already quite comprehensive.

Item 9 was voted for exclusion from the TMP template after one of the consensus meeting attendees presented a compelling argument regarding the original site delegation log. She explained that at their CTU, there are instances where two sites fall under one trust, with the Principal Investigator (PI) based at one site. The issue arises when delegated staff work across sites, leading to confusion over whether an original document is necessary, as copies and PDFs are often used. While an original document is preferred at the time of monitoring, the definition of an 'original' is unclear, especially when delegation details are signed off by the investigator and shared as PDFs. The main point is to document that staff are trained and delegated, regardless of whether the document is an original or a PDF. As the discussion progressed and other attendees agreed, the group voted to exclude this item but decided to add it as part of a single checkpoint within the TMP template for all documents to be verified, such as delegation logs, training logs (including trial-specific training), CVs, and GCP certificates.

The group discussed item 10 and whether specific details about site visits *'site visit log'* should be included in the monitoring plan template. Some participants felt these details were more appropriate for the site visit report rather than the template. The monitoring plan should ideally focus on general procedures and tasks to be checked, not on detailed documentation of each site visit. One participant suggested that the monitoring plan could serve as a reminder of standard tasks (like checking staff training and delegation) but should not be too prescriptive. Therefore, this item was voted for exclusion from the TMP template.

Item 11 was also discussed at length and voted for exclusion. Consensus meeting participants felt that the document already contained sufficient details, allowing for the

removal of this item from the template. CTUs could add additional information if they wished.

Item 12, completion of annual progress and safety reports, was discussed and voted for exclusion. One of the consensus meeting attendees explained that this particular question is currently included in their monitoring plan template because their unit sometimes monitors investigator-led single-site trials outside of their CTU. This question helps clarify that the monitoring responsibility lies with the investigator, not the CTU. However, they argued that this question may no longer be relevant, as such trials are becoming less common, and most trials are now conducted centrally. Therefore, they suggested that the question could be included for individual trials but should not be a standard feature in the template. Others agreed that it should be assessed on a case-by-case basis rather than included in the template as a default.

For item 13 the discussion centred on the review of recruitment rates in relation to monitoring visits. One of the participants explained that at their CTU recruitment rates are typically reviewed before visiting a site so that the monitoring team is informed about the site's current situation. This information is used to pre-populate the monitoring visit report, ensuring that it reflects the status at a specific point in time. They further explained that any changes between the review and the actual visit would be captured in the consent process, and if a new patient was consented within a short time frame, it would be documented. They emphasised the importance of preparing for the visit in advance, often several days prior, to ensure all relevant information is included in the report. The final vote of the group was the item to be excluded from the TMP template.

For item 14 the participants discussed the idea of having a prompt checklist for Source Data Verification (SDV), and while they acknowledged that it might be a good concept in theory, they raised concerns about its practicality. They pointed out that each trial has its own eligibility checklist, and different trusts have varying practices, therefore, a checklist may not be applicable to quiet a lot of studies because they all have different requirements. One participant pointed out that in their experience focusing on checking key aspects like the primary outcome source data might be more important than getting bogged down in checking a standardised list. The group generally agreed

that the checklist might not be applicable to all studies and voted for the item to be excluded from the template.

The last four items discussed during the meeting related to *'trial oversight of vendor',* which also had a high number of *'unable to respond'* score*,* was discussed at length. In this instance, it was decided that having specific items on vendor oversight could make the template overly complicated as some CTUs may not have the staff with the expertise to monitor external vendors and CTUs might have specific SOPs and working instructions in place for this. This item was therefore modified to a prompt for the trial monitor to refer to the *'vendor oversight SOP'* at the specific CTU.

Items that had a high percentage of '*unable to respond'* were discussed in detail during the consensus meeting. Of these *'checks for serious adverse events for medical devices'* and *'use of metrics in monitoring clinical trials'* were voted to be included in the TMP template by the consensus meeting participants.

We had equal votes of *'Yes'* and *'No'* for the item *'All outstanding payments must be reviewed and invoiced'.* To decide whether to include or exclude the item the participants engaged in further discussion. Some participants argued that financial checks, like outstanding payments, is a trial management activity rather than a monitoring activity. However, there was agreement that, although the finance-related items may not apply to everyone, they could be useful reminders for those who need them. One participant suggested that including them could be helpful, even if it doesn't apply universally, as it might trigger awareness for those who do need to address finances. Others agreed that the template is flexible and allows for customisation based on specific trial needs. The consensus shifted towards including the finance-related items in the template with the understanding that each trial could adapt it as necessary.

An important discussion was raised in the group about the term *'screen failure'* and the group agreed it was a problematic term because it could imply that the patient failed to meet the eligibility criteria, which wasn't always the case. Instead of focusing on the number of failed screenings, it was suggested to shift the wording to *'screening procedures'* to better reflect the broader context of assessing potential participants. The aim was to capture the overall approach and procedures for screening, rather than focusing solely on failed attempts. This revision would emphasise whether the

site is actively screening participants and following proper procedures, ensuring a more inclusive and effective recruitment process. The final decision was to replace *'screen failure'* with *'screening procedures'* in the template, aligning with a more general approach to screening and recruitment. This item referred to reviewing systems and documentation to be reviewed at an onsite visit.

Another important discussion was about the term *'withdrawal'*. The group discussed the use of the term *'withdrawal'* in the monitoring plan and agreed it was a problematic and often misunderstood term. One participant suggested that *'withdrawal'* should be re-worded, as it causes confusion. Instead, they preferred terms like *'early stopping of follow-up'* or *'early stopping of treatment'* to clarify the participant's status. The issue arose because *'withdrawal'* can mean different things in different contexts, such as stopping treatment or simply ceasing to attend follow-up visits. The group decided to revise the terminology to better reflect these distinctions and avoid confusion. It was agreed that the term *'early cessation'* would be more appropriate. The change aimed to clarify trial participation status and improve communication across sites. The new wording was added to the TMP template *'Early cessation of participation in trial (treatments, procedures, and/or data)'*.

I conveyed to participants that this template could be used in its current form when presented to the CTUs, or it could be customised to align with the specific standards and requirements of the CTU. I also clarified that while some CTUs have a comprehensive TMP template, others may not. Consequently, I encouraged participants to consider this when voting for the items.

The template was finalised based on the discussion of the consensus meeting (Appendix 10).

2.6 Chapter Summary and Discussion

This chapter has focused on the importance of standardising trial monitoring processes across UK CTUs through the development of a Trial Monitoring Plan template. It highlights the significant variation currently seen across CTUs in the UK regarding the creation and use of monitoring plans, with many units duplicating efforts and lacking a uniform approach to ensure high-quality, consistent trial monitoring. The research presented in this chapter demonstrates the value of a standardised TMP template, which could potentially streamline processes, improve efficiency, and reduce resource waste across CTUs.

As discussed earlier in the introduction, although regulators like the MHRA emphasise the importance of monitoring and there is a great interest in risk-based monitoring of clinical trials (MRC/DH/MHRA, 2011), there has still been a lack of clear guidance regarding the minimum contents of a trial monitoring plan template. As a result, there has been a wide range of variation in monitoring practices among the UK academic trial units (Love et al., 2020). The research documented in this chapter supports this, showing, in a review of 31 monitoring plans received from UK CTUs, there is wide range of differences between plans in terms of content, length and dept of information.

Through an iterative process, involving the collection of monitoring plans from various CTUs and the development of a Delphi survey, this study has successfully created a comprehensive TMP template, based on input from a wide range of experts in the field. The use of the Delphi method was particularly advantageous, as it allowed for consensus to be reached on the key elements to be included in the TMP, while also allowing room for flexibility and adaptation to suit different CTUs' specific needs. The consensus-building process also revealed the importance of considering the broader context of each trial, as trial-specific risks, design, and patient populations need to be taken into account when implementing monitoring strategies.

The consensus meeting was an important part of the research process, offering trialists the opportunity to discuss and clarify points that may have otherwise been overlooked. This meeting highlighted the value of collective decision-making in refining the TMP template. A key insight emerged from comparing the Delphi survey results with the consensus meeting outcomes. In the Delphi survey, no items were rated as ‘not important’ by 70% or more of the participants in either round. However, in the

consensus meeting, 18 items were voted for exclusion from the TMP template. These items were discussed at length, and collective decisions were made about the benefits of excluding them. This highlighted the advantage of having a consensus meeting in being able to have detailed discussions of participants' varying perspectives.

This shift between the Delphi survey and the consensus meeting is notable. The Delphi process, through iterative rounds, allowed for individual opinions to be anonymously shared, resulting in a broader acceptance of various items. In contrast, the consensus meeting allowed participants to voice differing perspectives, leading to more nuanced discussions and a collective agreement to streamline the TMP template. This reflects a common theme in the literature on consensus processes, while surveys can provide a broad view of group opinions, consensus meetings tend to facilitate deeper, more critical discussions that refine and clarify group decisions (Hasson et al., 2000) (Linstone, 1975).

The findings from this study align with previous research that has shown that consensus meetings, in contrast to Delphi surveys, allow for a more interactive and reflective decision-making process (Jones & Hunter, 1995). The consensus meeting provided an opportunity for participants to reconsider the importance of certain items in light of their practical application in trial monitoring, which might not have been fully captured in the Delphi survey alone. This reinforces the idea that using a combination of methods, such as surveys followed by consensus meetings, can provide a more comprehensive and refined outcome (Hasson et al., 2000).

From a reflexive standpoint, the consensus meeting complemented the anonymous Delphi rounds by enabling clarification and consolidation of overlapping items, yet it also introduced social interaction that could influence judgement. To mitigate this, structured discussion and anonymous electronic voting using Mentimeter were employed, ensuring that decisions reflected individual opinions rather than group pressures. The meeting involved a relatively small group of attendees (11 on day one and 10 on day two, with 8–9 voting), which is typical of consensus panels in modified Delphi studies where smaller groups are recommended for detailed adjudication of borderline items (Hasson et al., 2000; Jones & Hunter, 1995). While some degree of social influence is inherent in any live meeting, these procedures combined with the

transparent presentation of Delphi results helped maintain fairness and methodological rigour.

Ultimately, the discussions at the consensus meeting contributed to the development of a more focused and pragmatic TMP template, ensuring that the final version was both comprehensive and practical for use across a range of UK CTUs. The results of the Delphi survey, supplemented by feedback from the consensus meeting, have provided a clear roadmap for the TMP template's structure, ensuring that it aligns with both regulatory requirements and best practice standards.

There was considerable interest in this study within the UK monitoring community, as shown by the participation of many UKCRC CTUs (31/52) that shared their monitoring plans and the Delphi survey, which involved participants from 25 CTUs across the UK, as well as participants from the US, Australia and industry. Additionally, many CTUs expressed interest in learning more about the study and requested presentations. For me as a researcher, it was both encouraging and promising that trialists are interested in investing time and effort into improving monitoring processes. However, it also highlighted that time is an issue for many trialists, as they have to focus on running the trials. It is only possible to successfully deliver a project like this in a reasonable time frame when there is a dedicated researcher, funding, and time available.

The TMP template was made publicly available via open access publication at *Trials,* thereby extending accessibility within the global clinical trials community. Once the paper and the template were published, I sought to widen dissemination by posting on LinkedIn, X, the MRC CTU website, and by including a link in my email signature. Additionally, Marion Campbell shared a thread on BlueSky and X, discussing the paper as part of her *'Methodology Monday'* series (Campbell).

CTUs can adapt the template to their own unique needs or to make it compliant with their SOPs and other working instructions. The TMP template also includes instructions on how to use it and emphasises that it is not a standalone document; rather, it should be used in conjunction with the CTU's SOPs, trial protocol, or any other documents related to the conduct of the trial or required by the sponsor. The template can be used for both CTIMP and non-CTIMP trials across different trial phases.

Nevertheless, while the TMP template will help streamline the process, there is still the need for continued engagement with CTUs to ensure that it is updated in line with changes in trial designs, regulatory frameworks, and technological advancements. This will be addressed in the subsequent chapter of this PhD, where the TMP template will undergo piloting with UK CTUs. In summary, this chapter has laid the groundwork for improving clinical trial monitoring in the UK through the development of a TMP template, a tool designed to ensure consistency, reduce inefficiencies, and enhance the quality of clinical trials. Future work which is explained in the next chapter focused on testing, validating, and disseminating this template across CTUs, ensuring its effectiveness in improving trial conduct and monitoring practices. The willingness of CTUs to engage with future projects and the recognition of the need for further standardisation suggests that there is a shared interest in improving the monitoring process across the UK.

The TMP template developed in this chapter is based on current practices and opinions, but clinical trial monitoring is an evolving field. New methodologies, tools, and regulations may emerge that could necessitate adjustments to the template. Furthermore, the TMP template is only one part of the wider effort to improve trial monitoring. Future work will be required to assess how the template performs in real-world applications and whether it is adaptable to the changing needs of CTUs.

2.7 Chapter Limitations

While the research conducted in this chapter has concluded in developing a Trial Monitoring Plan (TMP) template and assessing the current landscape of trial monitoring practices across UK Clinical Trial Units (CTUs), there are several limitations that must be acknowledged.

Despite efforts to engage a broad range of CTUs, a subset (31 out of 53) of UKCRC registered CTUs contributed their monitoring plans to the study. Although the response rate was relatively high, this represents less than 60% of the eligible CTUs, which means that the template developed may not fully represent the diversity of practices across all UK CTUs. Among the 19 non-responding CTUs were some larger units with extensive trial portfolios such as King's Clinical Trials Unit at King's Health Partners, Manchester CTU (MCTU), and Cancer Research UK Clinical Trials Unit (CRCTU) Birmingham. However, the 31 UK CTUs that participated also included units with large trial portfolios, covering both CTIMP and non-CTIMP trials. While 31 CTUs may be considered small to represent the monitoring processes of UK clinical trials, it is important to note that the data is limited to UKCRC-registered CTUs, which have met the high standards required for UKCRC accreditation (Love et al., 2020; Taheri et al., 2024).

The quality and consistency of the data extracted from the monitoring plans varied across CTUs. Some CTUs provided well-structured, detailed monitoring plans, while others shared more basic documents or risk assessments that did not align directly with the definition of a trial monitoring plan. This variation presented challenges when attempting to standardise the data for inclusion in the TMP template, as differing formats and levels of detail needed to be reconciled.

Furthermore, the Delphi survey methodology, while useful for achieving consensus, does have inherent limitations. Despite efforts to ensure anonymity and reduce bias, there may have been some degree of subjective influence in the responses. The judgment of participants, which was based on their own experiences and institutional contexts, may not have been fully representative of the wider trial monitoring community. Additionally, although the anonymity of responses in Delphi survey prevents hierarchy bias, it can also restrict the depth of insight into participants' reasoning behind their decisions (Trevelyan & Robinson, 2015). To overcome this, I

held a consensus meeting following the Delphi rounds, which allowed participants to discuss their viewpoints in more detail and address any ambiguities or disagreements. This interaction helped to clarify the reasoning behind certain responses, providing a richer understanding of participants' perspectives. Although, I acknowledge that the final consensus meeting focused on a relatively small group of attendees, which could limit the diversity of perspectives considered in the final decisions.

The Delphi survey rounds were conducted over a relatively short period, which could have led to participant fatigue and reduced engagement, particularly in the second round of the Delphi survey. Retaining participants and maintaining consistent engagement over multiple rounds of data collection can be challenging. However, I tried to overcome this by engaging with trialists at any given opportunity, both before the Delphi survey and in between rounds, i.e., giving an invited talk at the national monitoring meeting, and visiting individual CTUs. I also provided as much information as possible to trialists to encourage participation, such as the estimated time to complete the survey and the option to save and return to it later.

Furthermore, as Trevelyan et al., highlights while Delphi surveys aim to identify group consensus, this does not necessarily equate to the *'best'*, *'expert',* or *'correct'* result (Trevelyan & Robinson, 2015).

There is a potential for groupthink in later rounds of Delphi studies, especially when participants may feel influenced by the responses of others (Hasson et al., 2000). The consensus meeting offered an opportunity for open discussion, which helped mitigate this effect by allowing participants to voice any concerns or alternative views directly, ensuring a more thorough and balanced decision-making process.

While Delphi relies on structured feedback from earlier rounds, this can sometimes limit the scope of participants' responses. The consensus meeting allowed for open discussion, which could further clarify or expand on points raised in the Delphi survey. Nevertheless, the use of the consensus meeting did not entirely remove the risk of groupthink or miscommunication, but it was an important step in providing a more comprehensive understanding of the participants' views.

"Qualitative interviews are like night goggles, permitting us to see that which is not ordinarily on view and examine that which is looked at but seldom seen". (Rubin & Rubin, 2011)

Chapter Three: Introduction to testing and validation of the trial monitoring plan template.

3.1 Chapter Overview and Scope

Objective 2 of this thesis focuses on the active testing and validation of the Trial Monitoring Plan (TMP) template developed under Objective 1. This phase aimed to ensure that the TMP template effectively fulfilled its intended purpose by evaluating its alignment with the goals of standardising and enhancing monitoring practices.

The objectives of this chapter were achieved by conducting two sets of qualitative studies:

- The first part focused on one-on-one semi-structured interviews with participants who had monitoring experience and expertise, capturing their immediate reactions to seeing the TMP template. These interviews will be referred to as 'instant reaction interviews' hereafter.
- The second part focused on semi-structured interviews with trial staff at UK CTUs after participating in piloting the TMP template. These interviews will be referred to as 'pilot interviews' hereafter.

In line with developments across clinical trial methodology, where structured templates and frameworks have become a key mechanism for improving trial design and reporting, the creation and refinement of methodological tools have gained increasing attention. Alongside well-established frameworks such as SPIRIT (Chan et al., 2025) and CONSORT (Schulz et al., 2010), initiatives including the TIDieR checklist for intervention description (Hoffmann et al., 2014), Trial Forge for trial efficiency (Treweek et al., 2015), Quality-by-Design (QbD) for risk-proportionate trial management (CTTI Quality by Design (QbD) toolkit, 2014), the Core Outcome Set a practical guideline (Prinsen et al., 2016), and COMET programme for core outcome development (Williamson et al., 2017) exemplify how consensus-based, iterative development

processes enhance transparency, reproducibility, and usability. These precedents inform the present chapter's approach, situating the TMP template within this lineage of methodological innovation aimed at strengthening trial conduct and oversight.

Building on these methodological precedents, the present study also adopted a mixed-methods approach to integrate quantitative consensus with qualitative insight. The development of the TMP template followed an iterative process in which the Delphi survey and consensus meeting established structured consensus on the importance of individual monitoring items, while the qualitative interviews provided contextual understanding of their feasibility and practical relevance. Integration occurred during analysis and refinement; for example, items rated as highly important in the Delphi but described as resource-intensive during interviews were revised or re-categorised to ensure proportionality. Conversely, areas of uncertainty or lower consensus in the Delphi were clarified through participants' qualitative explanations, which informed clearer definitions and examples within the final template. This iterative comparison between consensus and experiential data reflects recommended principles of mixed-methods integration (Creswell & Plano Clark, 2018; Fetters et al., 2013), and strengthened both the credibility and usability of the final tool.

The combination of consensus-building and qualitative exploration allowed the TMP to evolve as both an evidence-informed and practice-grounded resource. By drawing on multiple forms of evidence, the final version reflects not only expert agreement on key monitoring domains but also the realities of trial delivery across diverse CTUs. This balance between methodological rigour and operational relevance underpins the template's potential for broad adoption and long-term impact on monitoring practice.

Both the instant reaction and pilot interviews used data collected through semi structured interviews. The qualitative analysis was conducted to evaluate the template's suitability, usability, and comprehensiveness in an evidence-based manner, aiming to influence a positive change in the way monitoring clinical trials is conducted within the monitoring community in the UK. The template was updated based on the feedback and suggestions provided by participants during the instant reaction study. It was further refined and enhanced following the piloting phase and the associated interviews.

Although the instant reaction interviews and pilot interviews served distinct purposes, they shared the same overarching study aim. To provide a clearer and more cohesive account of the research process, certain sections will be discussed collectively for both studies. These include the research question, methodology, research design, data analysis methods, reflexivity, and considerations of validity, quality assurance, and study limitations.

Additionally, study-specific aspects such as participant recruitment, sample size, data collection, data processing and results will be discussed separately for each study. These sections will be clearly identified with the respective study name (i.e., Instant Reaction Interviews or Pilot Interviews) in the headings. Figure 3.1 below shows an overview of the sequential steps taken in this chapter to develop, refine, and validate the TMP template through qualitative interviews and piloting across UK CTUs.

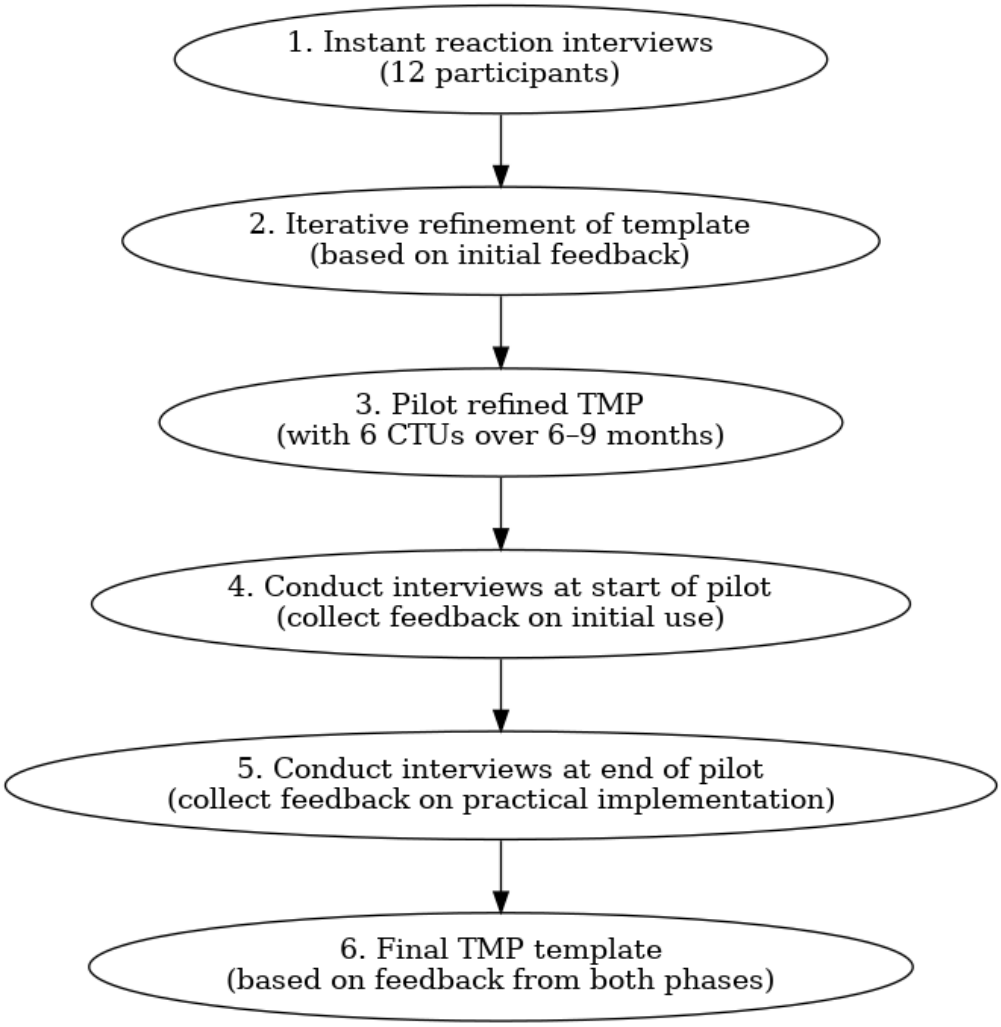

Figure 3.1: An overview of the sequential steps taken in this chapter to develop the TMP template.

3.2 Research aim and objectives

Aim

The aim of the qualitative research part of the thesis is to evaluate the effectiveness of the Trial Monitoring Plan (TMP) template on the monitoring practices across the Clinical Trials Units (CTU)s in the UK. This effectiveness included understanding the template, providing useful monitoring guidance and ease of use for monitors. The overarching aim of the research is to improve the monitoring of clinical trials.

Objective

The objective of this part of the thesis is to actively test and validate the TMP template by engaging CTUs to review, pilot, and refine it as necessary. Furthermore, it aims to disseminate the final version of the template as a key output of this research, making it available for adoption by the wider monitoring community.

3.3 Research Design

Research paradigm and rationale

To choose the correct approach for this part of my thesis I reviewed and considered various paradigms (Creswell, 2018). The interpretivist paradigm seemed well suited to the research because it aligns with the study's aim of understanding how participants construct and interpret their experiences in a particular social and cultural context (Lincoln, 1995). Interpretivism assumes that reality is subjective and socially constructed (Otani, 2020) (Lincoln & Guba, 1985), suggesting that each participant may perceive and respond to their experiences uniquely. This paradigm supports an in-depth exploration of these personal interpretations (Otani, 2020), which are essential for addressing the research questions focused on exploring meaning, perspective, and lived experience (Merriam & Tisdell, 2015).

Through an interpretivist lens, the researcher aims not to identify a single objective truth but rather to uncover the diverse ways participants make sense of their experiences (Merriam & Tisdell, 2015). This approach allows for a flexible, responsive research design that prioritises participants' voices and centres their subjective experiences (Merriam & Tisdell, 2015). Given my research's focus on understanding participants' perspectives in their natural settings, interpretivism seemed a suitable

match as it provides a framework that facilitates rich, contextually grounded insights (Merriam & Tisdell, 2015).

Additionally, the interpretivist paradigm underscores the co-constructed nature of knowledge, recognising that the researcher's values, background, and interactions with participants influence data collection and interpretation (Otani, 2020). This epistemological stance enables the researcher to engage reflexively with the data, ensuring that findings are understood as products of collaborative meaning-making rather than objective observations (Otani, 2020). I will discuss my role as the researcher and interaction with participants in more detail in the result and conclusion of this chapter.

This chapter aimed to understand the participants' immediate and subjective reactions to the new monitoring plan template as well as their subjective experiences and how they perceived the TMP template in practice. Interpretivism is ideal for research that seeks to explore individual perceptions, interpretations, and meaning-making processes (Merriam & Tisdell, 2015). It supports the idea that people's experiences and responses are socially and contextually constructed (Lincoln & Guba, 1985; Otani, 2020). The interpretivist paradigm also supports the goal of generating deep insights rather than seeking to generalise findings to a broader population (Pervin & Mokhtar, 2022). Since I sought to capture detailed feedback and understanding of participants' diverse perspectives on the new TMP template, this paradigm seemed well-aligned with my objectives.

By adopting this approach, the study aimed to generate rich, in-depth insights into how participants perceive and interact with the TMP template, rather than seeking a singular or objective truth. This aligns with the overarching aim of improving trial monitoring practices through a participant-centred evaluation of the TMP template.

Participants' reactions to the new TMP template were likely shaped by their background in monitoring and the specific context of trial monitoring. The interpretivist paradigm enabled me to consider how varying levels of monitoring experience influenced participants' interpretations for instance, whether they had a limited or in-depth understanding of monitoring practices.

Ontology and Epistemology

Ontology concerns the nature of reality and what can be known about it (Creswell, 2018). In this research, an interpretivist paradigm aligns with a relativist ontological stance, which holds that reality is socially constructed and shaped by individual perceptions (Lincoln & Guba, 1985). This stance is particularly relevant to my study, as the effectiveness and applicability of the newly developed TMP template cannot be understood from a singular, objective viewpoint. Rather, it is crucial to recognise that the experiences of participants involved in trial monitoring, which vary based on their roles and professional contexts, form the basis of understanding its success.

By adopting a relativist approach, I acknowledge that each participant's perception of the TMP template is influenced by factors such as their professional background, previous monitoring experiences, and the specific contexts in which they work. These diverse perspectives provide rich, multi-layered insights into the ways in which the TMP template is used and evaluated. Therefore, the study does not seek a ‘one size fits all’ understanding but rather aims to uncover the varying realities participants construct around the template based on their unique experiences and the type of trials their unit mainly host. The research aims to observe patterns among respondents’ accounts of their experiences as this might highlight things that have worked well for them and areas in which things could be improved.

Epistemology, on the other hand, concerns the nature and scope of knowledge, specifically how it is created and understood (Creswell, 2018; Guba & Lincoln, 1994). In this research, the interpretivist paradigm aligns with a subjectivist epistemological stance, which suggests that knowledge is co-constructed through the interactions between the researcher and participants (Schwandt, 1994). This approach emphasises that understanding is not passively received but actively shaped through dialogue.

In the context of this study, I used semi-structured interviews to collect data which serve as a dynamic, collaborative process. Through these interviews, participants not only share their insights but also engage with the researcher, whose interpretations are influenced by the participants' responses. This dialogic process aligns with the interpretivist belief that knowledge is not static or universally generalisable but is

instead socially and contextually situated (Merriam & Tisdell, 2015). The resulting understanding of the TMP template's effectiveness, therefore, is not a fixed truth, but an evolving, context-specific construction that reflects the complexity of trial monitoring practices. Further details about the use of semi-structured interviews are provided in the methods section.

Alternative Paradigms considered and ruled out

In selecting the interpretivist paradigm, I critically reviewed other research paradigms to assess their relevance to the aims of this study. This process reinforced my choice and helped clarify the philosophical stance underpinning my methodological decisions.

Positivism was ruled out as it prioritises objectivity, measurement, and generalisability (Creswell, 2018), which contrasts with my study's aim of exploring participants' subjective experiences with the TMP template. The nature of my research required understanding context-specific perceptions rather than testing hypotheses or identifying universal truths (Lincoln & Guba, 1985).

Post-positivism, while acknowledging some subjectivity, still leans toward structured, often quantitative inquiry and seeks approximate objectivity (Guba & Lincoln, 1994). Its emphasis on generalisable findings made it an imperfect fit for the exploratory and experiential focus of my study.

Constructivism was a closer fit, sharing with interpretivism the belief that knowledge is socially constructed. However, it often places greater emphasis on how individuals build knowledge through social interaction more broadly (Creswell, 2018), whereas my research focused on eliciting participants' immediate interpretations and individual experiences with the template.

Pragmatism, too, was considered, particularly due to its emphasis on usefulness and real-world application (Patton, 1990). However, while my study had practical aims, the core focus was not on outcomes or utility per se, but on the subjective meaning participants ascribed to the TMP template. Interpretivism offered the most appropriate lens for capturing the nuanced, context-rich perspectives needed to inform how the template might be adopted within UK CTUs and beyond.

3.4 Research Methods

To achieve the objective of this chapter, I took the following steps using collaboration from CTUs around the UK:

Instant reaction semi-structured interviews

Conducted one-on-one, informal, instant reaction interviews lasting 30-45 minutes with individuals involved in monitoring in UK CTUs. During these interviews, I presented the participants with the template, gave them time to review it and then I started to ask them a series of qualitative questions (Appendix 11) to capture their immediate impressions and insights of the template. Initially, I had planned to do these interviews in person at the CTU's locations in order to create a rapport with the research participants in an environment they are comfortable in. I also considered face to face conversations to be better for capturing better facial expressions, leading to a better account of the interviewee's reactions. I therefore offered the choice of both, face to face and virtual meetings, to all the participants. However, majority of the participants preferred a virtual meeting, with many trialists now working remotely or attending the office on a day blocked only for essential in person meetings.

Piloting the refined TMP template at various CTUs following instant reaction interviews

After completing the instant reaction interviews and refining the TMP template based on the results, I piloted the template at CTUs that had the capacity to implement it in one or more of their trials over a 6–9-month period. The purpose of this pilot phase was to test the template during a trial, in a real-world setting, collect feedback on its usability and suitability after it was populated for a specific trial, and followed by another feedback collection at the end of the piloting period. A series of qualitative questions (Appendix 12) was asked during piloting interviews.

Sample size for instant reaction interviews

Cohen et al, suggest that there are no specific rules when it comes to sample size in qualitative research as often the sample is constrained by time and available resources (Cohen, 2011). I also learnt this is true by having various discussions with the MRC CTU Qualitative Research group. At the outset of this research, I aimed to conduct 15–21 instant reaction interviews, with the intention of stopping data collection

once no further changes were being suggested. This sample size was chosen based on what I considered achievable within the available timeframe and the anticipated willingness of the monitoring community to participate. Additionally, I reviewed qualitative research literature, which suggests that sample sizes in qualitative studies are often determined based on feasibility and the researcher's judgment of what is manageable (Creswell, 2018; Guest et al., 2006).

However, the process reached data saturation at 12 participants as there were no more significant changes being made to the template. Data saturation refers to the point in qualitative research where no new themes, insights, or information are emerging from the data collected (Guest et al., 2006). It is often used as a marker to determine when data collection can be stopped, as additional data would likely only confirm existing patterns without contributing further understanding (Fusch, 2015). During the interviews and while reviewing the transcripts, I assessed whether new interviews provided additional insights relevant to the research aim and whether the existing data offered sufficient detail to comprehensively address the research objective (Bowen, 2008). Based on this evaluation, I concluded that data saturation was reached after 12 participants and decided to stop conducting further interviews.

I planned to start conducting the instant reaction interviews from Dec 2023 until the end of 2024 or until there were no more changes being suggested to the template by the participants. I carried out these interviews iteratively, which meant I interviewed 3 participants, gathered their feedback and insights, made the necessary changes to the TMP template, and then repeated the interview process with another 3 participants with the refined version of the TMP template. I chose this approach as it enabled me to gradually enhance the template and achieve a refined final product as described by (Morgan & Nica, 2020). This iterative process where data collection and analysis occur in cycles, allowed for continuous refinement of the TMP template. This approach emphasises the importance of revisiting and adjusting research instruments based on participant feedback (Morgan & Nica, 2020).

In addition to sample size, I also ensured that the participants represented a variety of CTUs as well as a variety of roles at CTUs as much as possible. I ensured that I did not interview too many participants from one CTU. I had a maximum of 2 participants per 1 CTU. There were a good variety of CTUs from across the UK involved in the

instant reaction interviews. I ensured a diverse range of participants with varying levels of monitoring experience, interviewing individuals with experience ranging from 18 months to over 20 years. Figure 3.2 below shows the role distribution of participants who took part in the instant reaction interviews.

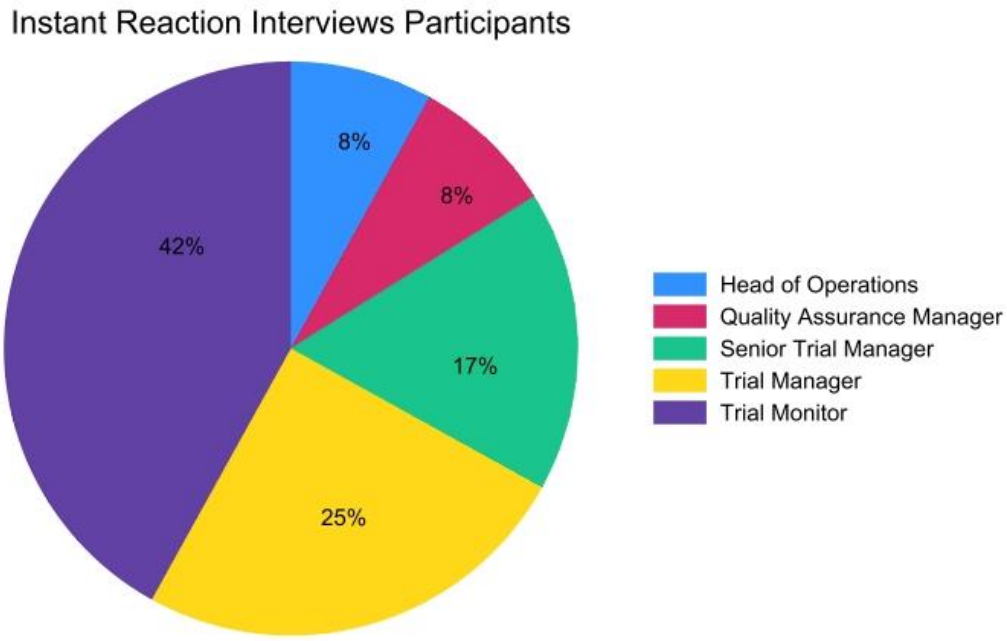

Figure 3.2: One to one instant reaction interviews participants by role.

Sample size for pilot interviews

The sample size for CTUs piloting the template depended on the number of CTUs that were able to complete the endeavour. I decided that I need participation from at least five CTUs across the UK to pilot the template for their next one to two upcoming trials over a period of 6–9 months. I made this decision based on advice from my supervisory team and initial conversations with various CTUs. Since many CTUs were unable to accommodate this, targeting five CTUs seemed achievable given the scope of this research and the number of CTUs available. Additionally, the 6–9-month period was chosen as it provided sufficient time for at least two monitoring visits to take place, allowing for the TMP template to be effectively implemented and assessed during that period.

Although I initially planned for five CTUs; after sending the invitation email, I received interest from six CTUs, all of which I included in the end. I was also interested in including both those CTUs with robust monitoring plans and those that have expressed a need for a more comprehensive monitoring plan. This was to ensure a true reflection

of the use of the template by both CTUs with experience of using a well-designed monitoring plan and those without access to such document or the means to create one (due to lack of time or experienced staff members). The purpose of piloting was to facilitate a meaningful comparison between the TMP template and each CTU's own monitoring plan, derived from interviews with the respective CTUs. I decided to do two sets of interviews with the CTUs. One interview was to take place as soon as the monitoring plan template was populated with information for the specific trial. Another interview was to take place at the end of the piloting period to allow staff from these CTUs to evaluate their experience using the new template. The first interview after completing the monitoring plan for the trial aimed to capture the trial staff's experience of using and populating the TMP template. I conducted this interview early to ensure everything was captured from memory (Merriam & Tisdell, 2015). Many trials may not update their monitoring plan months after start of the trial due to lack of recruitment or other factors affecting the trial. Therefore, I did not want to chance losing that vital information which may have been difficult to remember after months of completing the TMP template.

Recruiting for instant reaction interviews

To promote participation in the instant reaction interviews, I took several steps. I started the process by sending an email on 10th October 2023 via the UKCRC Registered CTU Network to all monitoring leads informing them about the instant reaction interviews and invited interested participants to contact me. This email also included information about piloting the TMP template and asked them to contact me if they wanted to collaborate. Additionally, I requested 'UK Trial Managers' Network (UKTMN)' to provide a project description paragraph for their bulletin, which was approved and published in the November 2023 issue. In addition, I requested the 'MRC CTU Weekly News Team' to advertise the study in their weekly newsletter. I also reached out to every CTU that shared their monitoring plan with me at the beginning of my PhD, extending an invitation to continue collaborating on this project.

Recruiting for CTUs to pilot the TMP template

I started the process by sending an email on 10th October 2023 via the UKCRC Registered CTU Network to all monitoring leads informing them about piloting the TMP template and asking them to contact me if they wanted to collaborate. The email also

included information about the one-on-one instant reaction interviews and invited interested participants to contact me. I also personally followed up with all CTUs who had shared their monitoring plan with me, especially those that did not have a comprehensive template to encourage them to take part in piloting of the template. This allowed me to have a good mix of different CTUs, some from those that have robust monitoring processes in place and some from those that are still developing their monitoring plans and processes.

I received interest in the pilot from Southampton CTU, Cambridge NHS Blood & Transplant CTU, Oxford Clinical Trials Research Unit (OCTRU), Exeter CTU, Northern Ireland CTU (NCTU), Bristol CTU, Edinburgh CTU, Plymouth CTU, and Cardiff Cancer Division CTU. All these CTUs confirmed that they had trials due to start in the required timeframe to pilot the TMP. The final CTUs that were able to pilot the template were Southampton CTU, Plymouth CTU, Bristol CTU, Northern Ireland CTU, Exeter CTU, and Cambridge NHS Blood and Transplant CTU.

I held meetings with monitoring leads from these CTUs to explore the feasibility of piloting the template. During these discussions, I explained the importance for the template to be implemented in a trial for a minimum of 6-9 months and utilised in at least two monitoring visits to enable a meaningful comparison of it with their current monitoring template. All CTUs confirmed the feasibility of this.

3.5 Methods of data collection and analysis

This section describes the methods of data collection, analysis and justification for both instant reaction interviews and pilot interviews.

The Semi-structured interviews

To collect data for this chapter, I used semi-structured interviews (Adams, 2010), a common qualitative method that offers both structure and flexibility. This approach provided a consistent framework across interviews while allowing me to probe areas of interest and follow up with open-ended questions (Swain, 2018). The interview questions (Appendices 11 & 12), reviewed by my supervisory team, was designed to explore the TMP template's usability, credibility, understandability, usefulness, and potential for future use, alongside comparisons with existing monitoring plans.

I conducted all interviews online via Microsoft Teams. They were recorded digitally, transcribed verbatim using the platform's automated transcription function, and manually reviewed for accuracy. All data were pseudonymised and securely stored on UCL drives, with access restricted to authorised personnel to ensure confidentiality.

One key advantage of this method is its alignment with the interpretivist paradigm, which emphasises understanding subjective meaning and context-specific experiences (Otani, 2020). Semi-structured interviews enabled participants to guide the discussion toward issues they found most relevant, reducing researcher influence and supporting a co-constructed understanding of the TMP template in practice (Cohen, 2011). For example, not all participants could directly comment on future use, but they were able to express their attitudes toward potential implementation.

Furthermore, by conducting qualitative interviews, I was able to engage in a form of data collection that is inherently interactive, with meanings being co-constructed through the conversation between me (the researcher) and the participants. Participants were encouraged to elaborate where they had more to contribute, and follow-up prompts were used to deepen understanding where responses were brief. Through this interactive approach, data were shaped collaboratively, consistent with the interpretivist view that knowledge is co-produced between researcher and participant. Interpretivism recognises the researcher's role in shaping and interpreting the data, which aligns with my methodological approach. I will elaborate on my role as the researcher and how I think this shaped my research in the summary of this chapter.

The interview questions (also referred to as interview guide) were developed in line with the objectives of the research, which was about the usability and usefulness of the TMP template. Interview questions provided the grounds for theoretical or inductive coding. Deductive coding also took place to ensure any themes not accounted for by the interview questions but suggested by participants were captured.

While the interview guide included questions focused on usability, usefulness, and future use of the TMP template, participants were encouraged to raise any reflections they felt were relevant. Some themes, including challenges in customisation or preferences for layout, were prompted by specific questions. Others, such as perceived benefits of standardisation, often emerged unprompted. This balance

between structured questions and open-ended discussion allowed for both targeted insights and spontaneous reflections, aligned with best practices in semi-structured interviewing (Adams et al., 2015).

The interview guide was developed with reference to qualitative methodological sources, particularly (Adams et al., 2015)'s guidance on semi-structured interviewing and the frameworks proposed by (Kallio et al., 2016) and (Fereday & Muir-Cochrane, 2006) for designing and analysing qualitative interview data. Questions were sequenced from general impressions to specific usability aspects, and care was taken to avoid leading language.

To mitigate response bias and ensure the coverage of both anticipated and emergent issues, the guide was designed to begin with broad, open-ended questions (e.g., *'What are your first impressions of the template?'),* followed by more specific prompts (e.g., *'Do you anticipate using this template regularly or in future trials?'*). I was careful in designing the wording, sequencing, and structure of the questions to avoid leading participants, and to allow spontaneous comments to arise. The design of the guide aimed to balance structure and flexibility, enabling in-depth exploration while avoiding imposing pre-existing assumptions on participants. Feedback on the draft interview guide was obtained from my supervisory team and piloted with two PhD students at MRC CTU to ensure clarity, neutrality, and logical flow.

Qualitative and thematic analysis

Swain et al explains that qualitative methods of analysis can be notoriously varied and complex (Swain, 2018). There are at least 50 distinct types of analysis to choose from, including content analysis, interpretative phenomenological analysis, template analysis, discourse analysis, narrative analysis, and conversation analysis (Harry, 1994; Swain, 2018). Thematic analysis, as the most widely used qualitative analytic method in the social sciences, offers considerable flexibility, making it applicable across various epistemological and ontological positions (Braun & Clarke, 2006). While this flexibility is an advantage, it can also lead to challenges in ensuring methodological consistency and rigor, particularly when it comes to the interpretation of themes. Furthermore, the subjective nature of thematic analysis means that it relies heavily on the researcher's interpretations, which may introduce biases. Despite these potential limitations, I chose thematic analysis for this chapter due to its adaptability

and its suitability for capturing patterns across diverse data sources, allowing for a comprehensive exploration of the research question.

A common criticism of thematic analysis however is that there are no clear guidelines for how it should be carried out, making it challenging to make judgements about the quality of the analysis (Antaki et al., 2003). Several qualitative analysis methods also fall under the heading of 'thematic', questioning what makes this method unique (Madill & Gough, 2008). However, having no strict guidelines to conduct thematic analysis makes it a more flexible approach for researchers to use as a data analysis tool.

Furthermore, thematic analysis allows flexibility in coding data and developing themes, a feature highlighted by (Braun & Clarke, 2006). They describe theoretical coding as being *'driven by the researcher's theoretical or analytical interest in the area,'* which enables researchers to focus on specific research questions. While this flexibility allows for a tailored analysis that can align with the researcher's theoretical framework, it also introduces the potential for researcher bias. The process of selecting which themes to focus on can be subjective, and the researcher's preconceptions or theoretical interests may shape the outcomes of the analysis. This subjectivity can be both a strength, in terms of providing rich, focused insights, and a limitation, as it may limit the exploration of unexpected or alternative themes.

Hybrid Approach to Thematic Analysis

Fereday et al. specifically focus on a hybrid methodology for thematic analysis, which combines elements of both deductive and inductive approaches (Fereday & Muir-Cochrane, 2006). After reviewing the literature, I found this hybrid method, used by researchers such as (Swain, 2018), to be the most appropriate for my study. The hybrid approach offers flexibility in data analysis, allowing for a structured yet adaptive process. The **deductive** approach is theory-driven, beginning with predefined themes or codes based on the research aims, questions, and interview content (Swain, 2018). In this approach, the researcher tests specific theories or hypotheses by seeking data that either supports or challenges the predetermined categories. This is particularly useful when the research is guided by specific questions or hypotheses. In contrast, the **inductive** approach is driven by the data itself, allowing themes to emerge naturally from the raw data without being constrained by preconceived frameworks

(Braun & Clarke, 2006). Researchers adopting this approach work closely with the data, allowing patterns, categories, and themes to evolve from participants' responses in an open-ended, exploratory manner. The combination of these two approaches in a hybrid methodology allows for a more nuanced and comprehensive analysis, incorporating both theory and data-driven insights.

The researcher is not neutral in thematic analysis (Swain, 2018). The position they take comes from their role as an agent interpreting the *"thing(s)"* they find in the world, in their reality. The researcher acts as a mediator, influencing data/findings, by constantly making choices and selections on how and what to code, and how and why data/findings are presented and re-presented (Swain, 2018). Weber et al., argues that not one objective reality exists but instead as many realities as there are individuals and their subjective experiences (Weber et al., 1947).

I acknowledge that each participant's experience is unique and that individuals interpret their experiences in various ways, leading to the observation of multiple realities from their accounts. From an interpretivist perspective, this study does not aim to generalise individual experiences but rather to explore patterns in participants' accounts that may reveal successful monitoring practices and areas for improvement. While the findings are rooted in the experiences of the participants, the ultimate goal of this research is to develop a tool i.e., the TMP template that can be applied across different CTUs. This tool is designed to provide a flexible framework that can be adapted to diverse trial contexts, based on commonalities identified in the participants' experiences, and encourages CTUs to implement practices that are informed by these insights.

Justification for choice of methodology

The thematic analysis following the method outlined by (Fereday & Muir-Cochrane, 2006) enabled me to use pre-defined questions, in addition to those emerging from the data, in the analysis process. (Fereday & Muir-Cochrane, 2006) describe thematic analysis as being "a search for themes that emerge as being important to the description of the phenomenon" (p. 82). This method is suitable when the data collection method is relatively structured, and clusters of themes can be anticipated, but also allows for the incorporation of the unexpected. This approach allowed me to ask pre-defined questions rather than conducting an open-ended, free-ranging

interview. As a result, I was able to focus on specific themes related to the research question, gathering participants' responses for each. At the same time, it also provided me with the opportunity to discover insights I had not anticipated. All the details for step-by-step analysis with illustrative examples from the data will be discussed more in the result section.

Instant reaction interviews

The instant reaction interviews were conducted between Dec 2023 and March 2024. The plan was to conduct the interviews until there are no more changes being suggested to the template by the participants (Fusch, 2015). These interviews with the aim to collect data were carried out iteratively, which meant I interviewed 3 participants, gathered their feedback and insights, made template improvements, and then repeated the interview process with another 3 participants. I continued this iterative process until I reached 12 participants, and no more changes were being suggested to the template. The iterative process enabled me to gradually enhance the template and achieve a refined final product. This approach was used in previous researches successfully by (Busert et al., 2018).

Twelve instant reaction qualitative interviews were conducted with individuals from nine UK CTUs, including the following: NHS Blood & Transplant Cambridge CTU, Oxford CTU, Northern Ireland CTU (NCTU), Cardiff Cancer Division CTU, Sheffield CTU, Cancer Research UK & UCL Cancer Trials Centre, Sutton CTU, MRCCTU at UCL, and the Intensive Care National Audit and Research Centre (ICNARC).

The participants came from diverse clinical trials backgrounds, including trial management, monitoring, quality assurance, and head of operations. They had varying levels of experience, ranging from a few years to extensive experience in their respective fields.

Pilot interviews

Pilot interviews ran from mid-April 2024 to February 2025. Interviews were set with the trial manager shortly after they confirmed the completion of the TMP template for the specific trial, followed by another one after the piloting period. The CTUs that participated in piloting were Southampton, Plymouth, Bristol, Northern Ireland, Exeter, and Cambridge NHS Blood and Transplant CTUs.

Interview Process for both instant reaction and pilot interviews

Each interview began with me introducing myself and providing participants with an overview of my PhD project and its aim, followed by the specific purpose of the interview. I informed them that there are no right or wrong answers, and they can skip any questions they do not want to answer, and they can stop the interview at any point. I also shared a brief explanation of my trial management experience to establish rapport and context. Additionally, I reminded them of the approximate length of the interview to ensure they had sufficient time for the discussion, and to avoid any sense of being rushed.

Participants were provided with a Participant Information Sheet (PIS) and a consent form at least one week before the interview. At the start of each session, I confirmed that they had read and understood the PIS and addressed any questions they had. I ensured I had a signed copy of their consent form before proceeding. Participants were also given the opportunity to ask questions before the interview began.

For instant reaction interviews, once they confirmed they were ready, the TMP template was emailed to them for review. They were allowed to examine it at their own pace, and the interview questions commenced once they were ready to discuss it. For pilot interviews the interview started after participants asked any questions they had.

Interviews were scheduled for 50 minutes, though their duration ranged from 25 to 45 minutes. Predefined questions guided the discussions; however, the order of the questions was occasionally adjusted to maintain a smooth conversational flow (Swain, 2018). Probing questions were used to obtain more information or clarify participants' point of view.

In line with (Yardley, 2003) recommendations for ensuring reflexivity and confirmability, I made a conscious effort to verify participants' perspectives throughout the interviews. For instance, I regularly used prompts like, *'You mentioned this—have I understood you correctly?'* to ensure I was accurately interpreting their responses. This not only helped build rapport but also maintained the rigor of the data collection.

To further ensure rigor, I kept a reflexive journal throughout the research process. In this journal, I recorded my thoughts on non-verbal cues and the dynamics of the interviews that might influence how I interpreted the data. Immediately after each

interview, I made entries in the journal, reflecting on my own reactions, assumptions, and how these might have affected my understanding of the data. This practice allowed me to remain aware of my own influence as a researcher. Later, when revisiting the journal during the analysis phase, I was able to reflect critically on these insights to ensure that my interpretation of the data was as unbiased and self-aware as possible (Braun & Clarke, 2006; Creswell, 2018).

At the end of each interview, I thanked participants for their time and contributions. I also invited them to ask any additional questions or share further comments. Participants were informed that they could contact me for further involvement in the study or to request a copy of the finalised TMP template.

Each interview transcript was pseudonymised and cleaned prior to data analysis. This is explained in further detail in the result section.

Ethics and consent

A Participant Information Sheet (PIS) (Appendix 13) and a consent form (Appendix 14) were created for the study participants. These documents, along with the interview questions, were reviewed and approved by UCL Research Ethics Service. Each participant received the PIS and consent form at least one week prior to their scheduled interview. Consent forms were collected before the interviews commenced. Participants were fully aware their participation was voluntary, and they could withdraw whenever they wanted without giving a reason

Participants consented to having their names collected for the purpose of acknowledging their participation in the publication, while ensuring that their views would remain anonymous. I also collected participants' email addresses to disseminate the study results, with the option to opt out of both the acknowledgment and receiving the results.

They also consented to their interviews being audio recorded, with the understanding that the results would be handled pseudonymously. Recording the interviews was essential to ensure rigorous and ethical data collection processes, meaning I took necessary precautions to maintain data integrity and quality throughout the research process (Kvale & Brinkmann, 2009). This included accurate transcription leading to accurately documenting the conversations and ensuring participants' responses were

correctly captured. Recording the interviews helped to verify the accuracy of the data and allowed for thorough analysis. Therefore, participants who declined to be recorded could not be included in the study. However, I did not encounter any participants that objected to being recorded.

I pseudonymised personally identifiable data to ensure it could not be linked to the interview data by anyone else. This was achieved by assigning each participant a study ID and removing any identifiable information, such as institute or staff names from interview transcripts.

All participants I interviewed were individuals with whom I had no prior personal relationship and very limited professional interaction. We shared similar professional backgrounds, which helped to create a sense of equality and mutual understanding during the interviews. This reduced the likelihood of any power imbalance influencing the responses. At the start of each interview, I explained that their honest and critical feedback was not only welcome but essential to improving the template. I made it clear that disagreement with any aspect of the template would not cause offense and that there were no 'right' or 'wrong' answers. Despite these efforts, it is possible that some participants may have hesitated to voice more negative views. Nonetheless, several participants did offer critical insights, which were valued and subsequently incorporated into further template refinements.

3.6 Data Analysis

This section describes the data analysis for both instant reaction interviews and pilot interviews. The results, however, are presented separately.

(Braun & Clarke, 2006) guidelines for thematic analysis have been used widely by researchers conducting qualitative analysis. I have used this guideline as a framework for thematic analysis. Each stage of the framework is described in detail below.

Figure 3.3: Six steps of thematic analysis based on Braun and Clarke (2006). Diagram created by the author using AI-assisted design.

Familiarisation with the data

After completing each interview, I pseudonymised and cleaned the transcripts whilst listening to the interview recording. This was conducted to ensure that there were no inconsistencies between what the participants had said and what was automatically generated by Microsoft Teams (Braun & Clarke, 2006). Each transcript was read twice, and errors were checked against the recording.

Generating Codes

Each transcript was read line by line and codes were generated for segments or whole sections of the transcript (Swain, 2018). I chose a hybrid approach for analysis which incorporated two main contrasting philosophical methods of reasoning: top-down, deductive, theoretical process and a bottom-up, inductive, data-driven process (Swain, 2018). Using the deductive approach, a set of *a priori codes* were generated (Crabtree & Miller, 1999; Swain, 2018). These codes reflected the research aim and questions and the interview questions. After reading the interview transcripts, a set of *a posteriori codes* were generated, as a result of examining the data (R. E. Boyatzis, 1998; Swain, 2018). Once the transcripts were read, I prepared an excel sheet of the *a priori* and *a posteriori* codes from examining the interview data. The process was organic, iterative, and ongoing and required me as the researcher to be reflexive (Swain, 2018). My interpretation of the interview transcripts was reflexive as I analysed

what I was reading with my own experience of the monitoring processes in clinical trials. Quotations were given as many codes as were appropriate to cover the content of the quotation. I also regularly referred to my reflective journal which I had been maintaining during and after each interview in order to ensure I have a holistic understanding of the data. During coding process, I ensured to keep an open mind about what the participants were saying and reflect on the meaning of the data with the aim to improve the TMP template based on user feedback.

I used an excel spreadsheet to develop my codes. Each participant was given a study ID number, consisting of P01 (with "P" standing for participant). Study ID was written on the first row, and the information and codes were written down each column under the participant's ID. Demographic information was also collected as part of the interviews. This included information such as their job role and the length of monitoring experience they have. This information helped put their feedback into context.

The a priori codes were generated using the research aim, questions, and interview questions. These included overall impressions, clarity and understanding, customisation, usefulness, suggestion for improvement, comparison to alternative, and future use. Reading each interview transcript, I would code any parts of the conversation that indicated these initial codes (a priori codes). I would also search for patterns and meanings in conversations and create a posteriori codes. This was an ongoing process and continued until all the interview transcripts had been read through. The analysis was circular meaning once I had been through all the interview transcripts and coded them, I went back to the early transcripts to ensure that I did not miss applying codes from the full set of the a posteriori codes (Swain, 2018). The full set of codes can be found in Appendix 15. The a priori codes are distinguished from a posteriori codes. A posteriori codes are written in italic. An example of a posteriori code that was generated from interview transcript is *'comprehensive'*. I generated this code based on the latent content going beyond the surface level to interpreting meaning (R. Boyatzis, 1998).

12 instant reaction interviews, 6 initial pilot interviews together with 1 follow up pilot interviews created 86, 80 number of codes respectively. I printed off the list of codes and cut them up, so each code was on a separate piece of paper. I then moved around the pieces of paper until the individual codes were grouped into initial themes, where

each of the codes in the group related to a core concept. For example, in instant reaction interviews all the codes that related to *'ease of understanding'* and *'ease of following the document through various sections'*, were grouped into a theme called *'Clarity and Understanding'*. Similarly in pilot interviews all the codes in *'ease of use'* and *'user experience'* were merged, as they included a lot of the same data. This process of grouping codes allowed me to identify that there were several duplicate codes, which covered the same concept but were named differently. I checked for overlapping codes, underused codes, or too broad/narrow codes that might need refining. I then grouped the codes manually (after checking that the data in both codes to be merged really did relate to the same concept).

To ensure accurate coding of my transcripts, I joined the MRC CTU Qualitative Research Group. This group includes colleagues with extensive experience in qualitative research as well as PhD students learning about qualitative research. The group meets bimonthly and organises data clinics.

Prior to one of these data clinics, I shared one of my transcripts and asked group members to code a section of it. I then compared and discussed their coding with mine, finding it mostly consistent. In cases where inconsistencies arose, I sought further clarification and resolved the differences.

Following this exercise, I reviewed all my transcripts to ensure that the insights gained from the discussion were applied consistently throughout my analysis.

Searching for themes

During analysis for instant reaction interviews, once all the codes were generated and all the transcripts were checked against the codes, I started to search for themes. I started doing this by NVivo14; however, I switched to doing this manually as I found that I can connect with my data better if I have them written down in pieces of sticky notes on a big plain wall. This manual approach allowed me to visually connect with the data in a way that felt more intuitive. Before making this switch, I consulted with my supervisory team and colleagues at the MRC CTU, and I also attended a training on thematic analysis. These steps reassured me that moving away from NVivo would not compromise the credibility of the analysis. However, there was a gap of approximately nine months between analysing the data from the instant reaction interviews and the pilot interviews. During this time, I worked part time as a research

assistant in qualitative analysis at the MRC CTU, where I used NVivo to code qualitative data. This experience allowed me to gain more familiarity with NVivo and receive feedback from a senior member of staff. As a result, I decided to use NVivo for coding the pilot interviews, given my improved proficiency with the software. I coded my transcripts using NVivo; however, when reviewing the codes and identifying themes, I realised once again that I cannot connect with my data without visually seeing them in a larger space. Consequently, I reverted to manually searching for themes, similar to how I approached the instant reaction interviews.

In organising the themes and subthemes, I adopted a hierarchical approach based on the relationships between the codes derived from the qualitative data. Initially, I used sticky notes on a wall to visually map out all the codes, allowing me to rearrange them until coherent themes were developed. This method enabled me to take a holistic view of the data, which helped group related codes into overarching themes and, where applicable, subthemes. I documented this process to ensure transparency and coherence in the thematic analysis. Any codes that did not fit within the identified themes were placed in a 'miscellaneous' category. However, after reviewing themes, codes in miscellaneous category were reassigned to other more relevant themes.

To ensure that my themes were correct and consistent, I sought feedback from a colleague at MRC CTU with experience in thematic analysis. I selected a section of my codes that I had already grouped into themes and asked her to review this portion of the analysis. I spent time explaining the reasoning behind my thematic groupings, describing how I had arrived at each theme and subtheme. My colleague then reviewed the codes within these themes and raised questions that prompted me to reconsider the placement of certain codes. For example, she pointed out that one code, initially placed under the theme *‘Clarity and understanding’*, could more appropriately be placed under the subtheme *‘Overall impression’* based on its specific context in the data. This discussion led to a more refined categorisation, with several codes being reassigned to themes or subthemes that more accurately reflected their meanings. Through this process, I was able to enhance the clarity and consistency of the theme structure, ensuring a more robust and grounded analysis.

Reviewing Themes

Reviewing the themes consisted of two parts. First, after finding themes within the data, I read all data extract for each theme to ensure that a coherent pattern was formed. For example, for the theme *'clarity'* I categorised this to three further sub-themes, which were *'clarity of the TMP template as a whole'*, of the *'TMP template instructions'* and *'TMP template tables'*. Therefore, an overarching theme *'clarity'* was created.

The second part of reviewing the themes was to review the thematic maps (Appendix 16) and ensure it represents the entire data set. To achieve this, I reviewed the spreadsheet for my codes and NVivo, which contained data extracts from interview transcripts for instant reaction interviews and pilot interviews, respectively. I reflected on what was suggested by the participants. This also provided me with the opportunity to review all data extracts from the interview transcripts and decide whether any further coding was needed. This step produced some extra data under each theme.

Designing and naming themes

The last step of the analysis was to review the themes and sub-themes names and ensure they convey clear meaning and representative of the participants' feedback. At this stage I reflected carefully about the research aim and questions. Each theme and sub-theme clearly represented why I did the qualitative interviews and thematic analysis and linked back to the research objectives.

3.7 Quality Assurance

(Lincoln & Guba, 1985) describe the difference between research conducted by post-positivist approach and one conducted by interpretivist approach. The former focuses on an objective understanding of reality through rigorous scientific methods, blending both qualitative and quantitative approaches. The later focuses on subjective experiences and co-constructed meaning, using qualitative methods to deeply explore human contexts and interactions. Therefore, research underpinned by an interpretivist approach such as social constructivism, confirm quality assurance by examining dependability, credibility and confirmability (Lincoln & Guba, 1985). These three aspects are explored in detail below for both instant reaction and pilot interviews.

Dependability

(Guba & Lincoln, 1981) describe dependability in qualitative research as a stage towards quality assurance. At this stage the researcher evaluates whether the same findings would have been produced if another researcher undertook the study. (Guba & Lincoln, 1981) explain that triangulation across researchers can be used to confirm dependability. Auditing can also be carried out to allow another researcher to follow the audit trail generated by the original researcher.

It is important to note that this thesis accepts that findings are unlikely to be exactly replicable given the nature of multiple social realities. (Yardley, 2003) explains that qualitative researchers *''would not expect their findings to be exactly replicated in any other sample or context but would hope that the insights they derived from studying one context would prove useful in other contexts that had similarities.''*

This qualitative analysis of the monitoring plan template aimed to validate the TMP template and provide CTUs with a comprehensive TMP template based on feedback from experienced individuals, which will contribute to a positive change in the monitoring community. This was achieved by implementing participant feedback, resulting in a refined TMP template. Furthermore, the qualitative interviews aimed to test the template's usability, credibility, understandability, usefulness, future use, and comparison with the current monitoring plan available to CTUs.

Credibility

(Guba & Lincoln, 1981) explain credibility in qualitative research as research participants feel that the findings represent their experiences. Steps to take to make it more likely that research produces credible findings include but not limited to prolonged engagement with participants (Lincoln & Guba, 1985), peer briefing (Yardley, 2003), reflexivity (Guba & Lincoln, 1981), audit trail (Lincoln & Guba, 1985), and member validation (Morrow, 2005). The aim of checking credibility is to ensure correspondence between the realities expressed by the research participants and the researcher's interpretation of what was said. I took all the above steps to ensure research credibility. These are explained below:

I ensured I spend enough time with the participants to understand the context of their experiences. This allowed me to build trust and gain deeper insights into the participants' perception of the TMP template. Furthermore, I engaged in discussions

with MRC CTU Qualitative Research Group about the data analysis, and interpretation processes. This allowed them to review the research process and findings, offering an external perspective to ensure the research is credible. Additionally, I ensured to stay transparent about my own biases, assumptions, and values, and how they may influence the research process. I did this by keeping a reflexive journal which allowed me to track my thoughts and how these might shape data collection and analysis. Finally, to ensure that I get closer to the participants' reality and to eliminate my own misconceptions, I summarised participants answers to questions that were more ambiguous and asked them *'is this what you mean?'* or *'could you give me an example'* or *'could you elaborate more'*. If a participant was very brief with their answers, such as just *'Yes'* or *'No'*, I'd encourage them to speak more with giving them an example about the subject and ask them *'do you agree with this'* or *'could you tell me more'* or *'could you give me an example in your own CTU that you have used'*. To complement this step, after interviewing every three participants and making changes to the TMP template, I sought feedback on these updates from the next set of participants. This iterative approach allowed me to continuously refine the TMP template based on ongoing input and ensure that the changes were well-informed and aligned with participants' perspectives.

Confirmability

According to (Guba & Lincoln, 1981) confirmability is checking if the research findings are a product of participants' responses and not the researcher's biases, motivations, interests or perspectives. (Guba & Lincoln, 1981) suggests that a transparent report of the findings (with signposted reflexivity) makes confirmability easier to evaluate. As the interviews were conducted on Teams and the transcripts were produced automatically, I made notes of my own reflections and understandings as I was interviewing each participant. (Yardley, 2003) suggests ''seeking others'' perspectives with regard to interpretation of data and maintaining a reflexive approach as steps to ensure confirmability.

To establish confirmability of my research I triangulated my perspective of the data with other researcher's perspective. This was to ensure that I have coded the transcripts correctly and did not miss any important or obvious themes. The support of the MRC CTU Qualitative Research Group was particularly valuable during this stage, as they assisted by coding a section of one of my transcripts. I compared their codes

with my own, and the results were largely consistent, clearly reflecting the study's aims. In instances where discrepancies arose, I discussed these differences with the other researchers. It was apparent that the differences resulted from my deeper involvement in the research, giving me a more in depth understanding.

Reflexivity

(Rohleder & Lyons, 2017) encourages the researchers to ask themselves ‘how is the research shaped by them? And how is the research shaped and received by the people who are investigated in the research?’ (Rohleder & Lyons, 2017) write ‘‘personal reflexivity involves the researcher looking inwards to see how they themselves have informed the research’’.

I have been a trial manager since 2015, during which time I have worked on numerous trials and conducted various monitoring activities. When conducting interviews with participants, I introduced myself as a PhD student at UCL working on improving monitoring practices in the UK. I also shared a brief description of my experience in trial management and monitoring to provide them with background about myself. Most importantly, I emphasised that the purpose of the interviews was to enhance the TMP template for the benefit of everyone. I encouraged participants to be as honest and open as possible, assuring them that I would not take any negative comments personally. Instead, I conveyed that all feedback would be taken seriously and used constructively to improve the template. Additionally, I assured participants that there were no right or wrong answers.

To create a comfortable and supportive atmosphere, I maintained eye contact and smiled regularly to help participants feel at ease. As an introvert who enjoys listening to people, I was comfortable allowing silences during the interviews, giving participants the time to think and provide additional insights. This approach often revealed valuable perspectives that might have been missed if I had moved too quickly to the next question.

I spent over a year constructing the TMP template and was emotionally invested in the work I had done. However, I kept an open mind about the feedback I received from participants. I approached every comment as constructive, even if it was critical. Most of the changes suggested by participants were implemented to enhance the template. The only changes I did not incorporate were those specific to the unique practices of

individual CTUs. In these cases, I informed participants that they could adapt the template to meet their specific needs.

Conducting the qualitative interviews with experienced members of the monitoring community provided me with a different perspective to the trial monitoring plan template. During the qualitative interviews I gained a better understanding of what the TMP template looks like to end users. Whilst analysing the qualitative interviews data, I employed reflexivity using my own trial management and monitoring experiences. While interviewing participants and during the data analysis stage, I frequently referred to my reflexive journal to reflect on the participants' responses. The journal allowed me to document my thoughts immediately after each interview, ensuring that I did not forget any important reflections. During the coding process and the creation of themes, I revisited my journal for additional context on specific interviews.

The journal also helped me capture key information that may not have been recorded during the interview. For example, if a participant shared something significant after the recording had ended, I noted it in my journal to ensure it was not overlooked in the analysis.

Transparency

Transparency refers to the clarity of the research report and whether another researcher could attempt to replicate the research method. It also refers to whether the reader can grasp how the research data support the research findings and conclusion (Guba & Lincoln, 1981) (Rohleder & Lyons, 2017). (Yardley, 2003) explains transparency as ‘paper trail’ so that the final report can be linked back to raw data. As all my qualitative interviews were conducted on Microsoft Teams, recorded, and automatically transcribed, all the transcripts (pseudonymised) as well as my reflection notes have been kept securely on my UCL drive.

3.8 Results

3.8.1 Instant Reaction Interviews Results

This section describes the themes and sub-themes that were developed from the coding process of instant reaction interviews. Each theme represents the aims of conducting the qualitative interviews which was to assess the overall impressions,

clarity and understanding, customisation, usefulness, suggestion for improvement, comparison to alternative, and future use of the TMP template.

Each theme and subthemes are explained below. Table 3.1 overleaf presents themes and sub-themes derived from the thematic analysis. To enhance transparency and rigour, each theme is presented with illustrative participant quotations and an indication of its prevalence among the interviewees. Each quotation includes the participant's role and their years of monitoring experience. Aligned with an interpretivist view, it is important to remember that each individual's experience is unique, so each quotation reflects a single participant's reality, which might not be true for others. This reflection includes the participant's role in clinical trials (Figure 3.2), such as whether they are a monitor or a trial manager who also conducts monitoring, as well as their years of experience in monitoring clinical trials. It is important to consider each participant's statements in relation to their specific role and experience. The interview questions were formulated to assess overall impressions, clarity and understanding, usefulness, suggestion for improvement, customisation, comparison to alternative and future use. After analysing the data 'customisation' was assigned to 'suggestion for improvement' as a subtheme. A full list of all the additional changes that were made to the TMP template can be found in Appendix 17.

Themes	Sub-themes
1. Overall Impressions	Comprehensive
	Length
	User friendly
2. Clarity and understanding	Clarity and understanding of the introduction and purpose
	Clarity and understanding of the template content
	Confusing
3. Usefulness	Template provides useful guidance for monitoring needs
4. Suggestions for improvement	Formatting suggestion
	Customisation suggestion
	Content suggestion
	Order of sections
5. Comparison to alternative	Clarity
	Layout
	Helpful examples
	Comprehensive
	Anything set this template apart?
6. Future use	Anticipate using this template regularly or in future trials?
	Anything that would prevent you from continuing to use this template?
	Limitations in using the template.

Table 3.1: Themes and sub-themes developed from thematic analysis of instant reaction interviews.

Theme One: Overall Impressions

This theme is an important theme which aimed to capture the first and overall impression the reader gets from seeing the template and starting to engage with it. All participants began by expressing a positive impression about the template. They then went into more details and described how they feel about it as we discussed things furthermore. Subthemes are highlighted in bold font.

Comprehensive

Participants shared generally positive impressions of the TMP template. Three key sub-themes developed from this theme: its comprehensiveness, its length, and its user-friendliness. While experiences varied slightly, the overall sentiment reflected a recognition of the template's value in enhancing the structure and consistency of monitoring plans across trials.

Many participants described the template as highly comprehensive, particularly when compared to other documents used within their CTUs. This was seen as a strength that could reduce the likelihood of missing important aspects of trial monitoring.

'I like that I can find all information in one document.' (Monitor, 6 years of monitoring experience)

'I think it usefully brings together everything that you would need to think about when monitoring a trial.' (Monitor, 12 years of monitoring experience)

'You've included certain things that I've spotted that I haven't seen on monitoring templates before.' (Trial Manager, 5 years of monitoring experience)

The consolidation of key elements into a single, structured tool was especially valued by participants who had previously worked with fragmented or overly brief monitoring documents.

Length

Out of the 12 participants that were interviewed, 5 of them mentioned that the TMP template is very long. They mentioned most of the monitoring plans they have seen are more brief. However, all 5 participants expressed that the length of the document is not a negative point, instead, the length was often framed as necessary and justified by the breadth of content, especially given the template's flexible format.

'It's long, but it needs to be long.' (Trial manager, 18 months monitoring experience)

'It's a long document, but it is not unique to this template, it is the nature of this document.' (Senior Trial Manager, over 10 years of monitoring experience)

'Long and detailed' (Monitor, 6 years of monitoring experience)

These comments suggest that comprehensiveness was understood and accepted, and that length was not perceived as a barrier to implementation so long as the content remained adaptable to different trial contexts.

User Friendly

Most of the participants agreed that the TMP template is user friendly and easy to follow. This sub-theme was repeated in other themes, such as formatting and clarity. One participant suggested to remove some of the table and leave as blank text box, however the others all agreed that the box format of the template is what makes it user-friendly.

'I really like the boxes; it feels neat and keeps everything intact.' (Quality assurance manager, 5 years of experience)
'I would remove the boxes for monitoring report, as this is more free text, but then again we can amend it to what works for us'. (Trial Manager, 6 years of monitoring experience)

Overall, the template's design was considered intuitive and adaptable, making it suitable for both experienced staff and those newer to monitoring roles.

Theme two: Clarity and understanding

This theme captures participants' reflections on how clearly the TMP template conveyed its purpose, structure, and instructions. Feedback was grouped under three sub-themes: clarity of the introductory section, clarity of the content, and points of confusion. Overall, the TMP template was considered clear and accessible by all participants, even to those with limited monitoring experience.

Clarity and understanding of the introduction and purpose

Participants consistently stated that the introductory section of the TMP template was clear and helpful in setting expectations. Many contrasted it favourably with previous templates, noting that the instructions made it easier to understand how to complete the document and adapt it to their needs.

'I really like this section. With a lot of monitoring plans, you open them and you left guessing what to do'. (Monitor, 6 years of monitoring experience)

‘Yes, it's clear the instruction is saying you can use what's useful to you.’ (Quality assurance manager, 5 years of experience)

Minor formatting suggestions were offered, including a correction to the wording around highlighted text. These were easily addressed during the revision process.

‘You've said that certain instructions are highlighted in red, but they are red text not highlighted, so it maybe just changed the wording slightly.’ (Trial Manager, 6 years of monitoring experience)

Clarity and understanding of the template content

The main body of the template was also regarded as clear and accessible. Several participants appreciated the use of colour-coded guidance and straightforward language, which helped draw attention to key sections and reduced the risk of misinterpretation.

‘I really like having instructions in a different colour throughout. I find that quite easy because it's really easy to just pick out what bits you need immediately.’ (Trial Manager, 6 years of monitoring experience)

‘It's quite straightforward and used lay language. So, it's easier for people that have not had any monitoring experience to understand.’ (Monitor, 6 years of monitoring experience)

This level of clarity was noted as particularly beneficial for less experienced staff, suggesting that the design of the template could support wider and more consistent use across teams with varying levels of expertise.

Confusing

This was one of the most useful sections of the qualitative interviews. In this part, one participant pointed out that we do not need a specific section for ‘routine monitoring.’ She explained that monitoring is either routine or triggered, and can be conducted onsite, remotely, or centrally. I removed the ‘routine monitoring’ section from the TMP template and replaced it with a question to specify whether the monitoring strategy for the trial is routine or triggered, along with another question on the frequency of routine monitoring. This change was implemented after the first three participants were interviewed. The subsequent nine participants were asked if they agreed with the

change, and they all did. This change was also discussed with my supervisory team. Other than this, no additional concerns were raised. The remaining participants confirmed they did not find any part of the template confusing, reinforcing the perception that the TMP template was generally accessible and logically structured.

Theme Three: Usefulness

This theme explores participants' reflections on the usefulness of the TMP template, particularly in terms of the structured guidance it offered for planning and delivering trial monitoring activities. The general consensus was that the template helped clarify expectations, standardise practices, and prompt critical thinking about monitoring needs, particularly for those less experienced in this area.

Template provides useful guidance for monitoring needs

Participants agreed that the TMP template served as a helpful guide for ensuring comprehensive monitoring coverage. Many appreciated its structured layout, examples, and prompts, which encouraged them to think critically about their trial's monitoring requirements.

'Yes, you can go through it one by one and each section. You can be sure that you're not going to leave out anything important.' (Monitor, 10 years of monitoring experience)

'Absolutely. Example in onsite monitoring visits it says it should include the following checklist and there's like 3 bullet points and one of them is just the adhere into the study protocols etcetera. And I think that's really helpful.' (Monitor, 10 years of monitoring experience)

'Triggered monitoring especially is quite useful.' (Senior Trial Manager, over 10 years of monitoring experience)

This level of structure was seen as particularly valuable for those developing or revising their monitoring plans, helping ensure consistency across trials and teams.

Although most participants found the template broadly applicable, one participant noted that the document may function better as a guidance resource rather than a direct replacement for existing institutional templates. This view highlights the importance of local adaptation and organisational context in the implementation of standardised tools.

'I think that is how it would be most helpful for us—as a guidance rather than actually using the template. Some of the activities that are listed in here as monitoring are not currently considered as monitoring in our processes.' (Senior Trial Manager, over 10 years of monitoring experience)

Rather than suggesting a limitation, this comment reflects a pragmatic approach to integrating new tools within existing frameworks and practices. Other participants also expressed interest in adapting the TMP template locally.

'We're very keen to adapt to this template when it's available.' (Senior Trial Manager, over 10 years of monitoring experience)

The TMP template was also recognised for fostering consistency across different trials and teams, especially by offering a shared framework that could be understood and used across CTUs. This was considered particularly useful for new staff or ensuring team alignment.

'Understanding what other people do or that there is a kind of consensus in monitoring activities and that way working consistently is helpful.' (Senior Trial Manager, over 10 years of monitoring experience)

'The guidance is helpful for those with less monitoring experience.' (Operational Manager, over 10 years of monitoring experience)

Overall, the feedback demonstrated that the TMP template offers both practical support and educational value. It helped participants feel more confident in the completeness of their monitoring planning and provided reassurance that their practices aligned with broader expectations.

Theme Four: Suggestion for improvement

This theme aimed to capture suggestions made by participants to enhance the TMP template. These included aspects of formatting, content, layout, and opportunities for customisation to suit the specific needs of individual CTUs.

Formatting suggestion

Several participants provided useful formatting suggestions, such as bolding section titles, adding a contents page, and inserting page numbers. These changes were implemented to improve the document's navigation and readability. Although one

participant suggested switching the format to landscape, this was not adopted to preserve flexibility across CTUs.

'I like the table formats, it makes things more clear and easy to follow.' (Trial Manager, 3 years of monitoring experience)

Overall, participants viewed the layout as clear and functional, with formatting improvements making the document feel more professional and accessible.

Customisation Suggestions

Participants were encouraged to think about the way they would customise this TMP template for their own CTUs. This section of the interviews was particularly important to ensure that the TMP is clearly implying that CTUs can take some sections of the template and use it in their own monitoring plan, or they can use it entirely. From the answers it was clear that this message was conveyed. Some participants thought that they would take some sections of the template and use it in their own monitoring plan with the aim to improve their documentation.

'Tables would be useful for some of the sections and that we would use in our monitoring plans.' (Trial Manager, 3 years of monitoring experience)

'We can customise by removing sections we don't need for the trial.' (Monitor, 6 years of monitoring experience)

One participant thought about customising the template to better suit their monitoring scope.

'We would need to customise it as the scope is now wider than our plan scope.' (Senior Trial Manager, over 10 years of monitoring experience)

'Fairly straightforward to amend the text in the tables, or even add rows, delete rows if they're not going to be applicable to the unit. So, I think it seems good.' (Monitor, 6 years of monitoring experience)

These insights reflected that the template was flexible enough to be adopted across diverse trials while still offering enough structure to ensure completeness.

Content suggestion

Most participants felt that this monitoring plan is very comprehensive and includes more information that a typical monitoring plan usually includes. However, one participant suggested adding one more additional section on sponsor monitoring to demonstrate sponsor oversight. This was added and discussed with the following participants, and they all agreed to add the section, and CTUs can remove it if necessary. All other changes to the content were mainly word changes and minor additions. A full list of these content changes can be found in Appendix 17.

Order of sections

Participants were asked to consider whether the section order in the template followed a logical structure. Several adjustments were suggested early on and were subsequently validated by later interviewees. One key change involved moving the *'Site Initiation Visit (SIV)'* section to the beginning to better align with the chronological flow of trial processes. Another participant recommended placing the monitoring report section after the monitoring visit sections but before *'close-out'* and *'archiving'*.

'I think monitoring report should be at the end of all monitoring.' (Monitor, 10 years of monitoring experience)

These revisions contributed to improving the coherence and user flow of the document.

Theme Five: Comparison to alternative

This theme explores how participants compared the TMP template to the existing monitoring plans used at their CTUs. Understanding these comparisons was essential to determine whether the new template could bring about a meaningful shift in monitoring practices. Participants highlighted several ways in which the TMP template differed and often improved on what they were accustomed to.

Clarity

Participants widely agreed that the TMP template improved clarity by explicitly outlining expectations for each section. Compared to more ambiguous documents used in their CTUs, the structured explanation in the TMP template left less room for misinterpretation.

‘You're explaining each point a little bit more, so there is less room for ambiguity.’ (Trial Manager, 18 months monitoring experience)

‘I prefer the format that you have here because it's easy to understand.’ (Monitor, over 6 years of monitoring experience)

This perceived clarity was particularly valued by those with less monitoring experience, who appreciated how the template broke down complex tasks into comprehensible components.

Layout

Participants commented positively on the template’s layout, particularly its consistent use of tables to organise content. Compared to other plans that relied heavily on text or combined tables with unstructured narrative, the table format was seen as clearer and more user-friendly.

‘I really like the table formatting because our is a combination of tables and a lot of just text in between.’ (Trial Manager, 18 months monitoring experience)

‘You've got layer by layer all the different types of monitoring there, we don't have that at the moment.’ (Senior Trial Manager, over 10 years of monitoring experience)

The layout encouraged better engagement with the content and was considered more accessible for different roles across the trial team.

Helpful examples

The embedded examples throughout the TMP template were frequently mentioned as a unique strength. These examples helped clarify what kind of information should be included, reducing uncertainty and offering reassurance.

‘Without example I'm worried I'm answering wrong.’ (Trial Manager, 18 months monitoring experience)

‘Examples are very helpful, especially if someone is new to the monitoring role.’ (Senior Trial Manager, over 10 years of monitoring experience)

This feature stood out as particularly helpful for less experienced staff and those adapting from less structured documentation.

Comprehensive

Many participants commented on how comprehensive the template is and how they like having all the information they need in one document. Two participants mentioned having this information on other documents within their units. One participant mentioned the depth of the template being different to their own unit's monitoring plan.

'Our monitoring plan has a lot less depth and so almost looks like one large table just with a couple of bullet points.' (Senior Trial Manager, over 10 years of monitoring experience)

'Much more detailed than our units current monitoring plans. More structured.' (Operational manager, over 10 years of monitoring experience)

'Ours is not as detailed as this and focuses mainly on central monitoring.' (Trial Manager, 6 years of monitoring experience)

Even those who mentioned duplication noted that the consolidation of information was useful and would likely streamline their processes.

Anything set this template apart?

When asked what set the TMP template apart from existing tools, participants emphasised its level of detail, structure, and embedded examples. These aspects not only distinguished it from current templates but were seen as features that could enhance trial oversight and documentation quality.

'I think on the monitoring templates I've used before; there has been a lot of comments. I think if it's as stringent as this, yeah, we wouldn't have as many comments.' (Trial Manager, 18 months of monitoring experience)

'It's really detailed. It's covered more things than I've probably put into my monitoring plans.' (Monitor, over 6 years of monitoring experience)

'Yes, this is the most detailed I've seen.' (Trial Manager, 6 years of monitoring experience)

Taken together, these reflections suggest that the TMP template not only compares positively to existing documents but may represent a step forward in promoting more consistent and comprehensive monitoring practices across CTUs.

Theme Six: Future Use

This theme explores participants' views on whether they would adopt the TMP template in future trials. As the ultimate aim of this research is to promote uptake of a more consistent and structured approach to trial monitoring, participants' willingness to use the template and any foreseeable barriers provides important insight into its potential for wider implementation.

Anticipate using this template regularly or in future trials?

All participants expressed a willingness to use the TMP template in future work. Several highlighted specific ways the template could support their current practices, either by fully adopting it or by integrating certain sections into existing documentation.

'Yeah, I do think it would be useful, and I would just be something to get used to compared to the one we use at the minute.' (Monitor, over 10 years of monitoring experience)

'Yes, we can take sections and use in our plans.' (Operational manager, over 10 years of monitoring experience)

'Yes, there are a few things that we don't specifically cover in our template and that I think it would be helpful to consider.' (Senior Trial Manager, 6 years of monitoring experience)

Participants also appreciated the structure and comprehensiveness of the template, which they believed could improve both individual and team-level monitoring practices.

Anything that would prevent you from continuing to use this template?

While there was broad enthusiasm for future use, most participants noted that adoption would depend on institutional processes, such as CTU-level approval and alignment with CTU SOPs. Concerns were not related to the quality or usability of the template itself, but rather to administrative and governance structures.

'I don't think so, as long as sponsor is happy.' (Senior Trial Manager, 6 years of monitoring experience)

'I need to check with our QA team that we are able to use a non-validated quality control document. Imagine that would be fine, because this is for research, and we are a trials unit.' (Monitor, over 10 years of monitoring experience)

'I guess just adoption of it at CTU level, obviously we have to follow our local SOP's and our templates that are associated with those approved SOPs providing our unit is happy then. I don't think it would be any other barriers.' (Senior Trial Manager, 6 years of monitoring experience)

'We're quite small unit. My managers certainly happy for me to take this forward and from looking through the template I can't see anything that would prevent us from using it from a practical point of view.' (Senior Trial Manager, over 10 years of monitoring experience)

These insights suggest that while the template was positively received, successful implementation will depend on institutional support, SOP revision, and broader organisational buy-in to avoid duplication and ensure compliance with local quality control frameworks.

3.8.2 Pilot Interviews Results (First Interviews)

The CTUs that participated in piloting phase of the TMP template were Southampton, Plymouth, Bristol, Northern Ireland, Exeter, and Cambridge NHS Blood and Transplant CTUs. However, only Northern Ireland CTU was able to start using the template on a trial and complete the process with a follow up interview after 6 months. Southampton, and Plymouth CTUs both used the template and continued to use the template beyond the pilot period. Southampton CTU used the template to conduct 1 monitoring visit during the pilot period. When I contacted them after 6 months for a follow up interview, they informed me that the initial visit was carried out as per their own TMP as the trigger to go to site was the same. Furthermore, they added that as they combined a TMP, Data Monitoring Plan (DMP), Targeted Source Data Verification (TSDV) plan to ensure everything is captured in the data team and the monitoring team, it did feel like they were duplicating in some areas. They did not want to carry out the second interview, as they did not feel there were any further feedback to provide, given that they only conducted one monitoring visit.

Plymouth CTU also informed me that they are using the template, and they don't have any further comments to add, and therefore a second interview was not conducted with them. However, they informed me that they are planning to use the TMP template on another trial, as they found it to be useful on their pilot experience.

Exeter CTU informed me that their trial was yet to open (as of February 2025) due to significant delays with the Investigational Medicinal Product (IMP), so they had not yet begun monitoring their sites. The trial manager I was liaising with was due to go on sabbatical leave for the months of April and May 2025, with other colleagues covering the trial. Therefore, this CTU was also unable to pilot the template in real time and to provide further feedback.

Bristol CTU experienced significant and unexpected delays in opening their study. An MHRA sponsor inspection further postponed progress, requiring protocol updates and revisions to several other documents. As a result, the trial manager had not been able to use the template in practice as of March 2025. However, they remained hopeful that the study would commence soon and had planned to implement the template, though no confirmed start date was available.

The results presented in this section for the pilot interviews, therefore, represents the 6 initial interviews conducted with CTUs after completion of the first initial draft of the template for their trial. This is followed by the final interview conducted with the Northern Ireland CTU which completed the pilot phase.

This section describes the themes and sub-themes that were developed from the coding process of pilot interviews. Each theme represents the aims of conducting the qualitative interviews which was to assess the *''overall impressions, clarity and understanding, usefulness, suggestion for improvement, customisation, comparison to alternative, ease of use, user experience, fit for purpose and future use"* of the TMP template.

Each theme and subthemes are explained below. Table 3.2 overleaf presents the themes and sub-themes derived from the thematic analysis of the pilot interviews. Each theme also includes illustrative quotations from participants. Each quotation also includes the participant's role and monitoring experience. Aligned with an interpretivist view, it is important to remember that each individual's experience is unique, so each quotation reflects a single participant's reality, which might not be true for others. This reflection includes the participant's role in clinical trials, such as whether they are a monitor or a trial manager who also conducts monitoring, as well as their years of experience in monitoring clinical trials, and whether it is their first time completing a TMP document. It is important to consider each participant's statements in relation to

their specific role and experience. The interview questions were formulated to assess overall impressions, clarity and understanding, usefulness, suggestion for improvement, customisation, comparison to alternative, ease of use, user experience, fit for purpose and future use. There were many similarities between the results of the instant reaction interviews and the pilot interviews. In fact, as a researcher, I saw the pilot interview results as a confirmation of my findings from the instant reaction interviews. Additionally, the pilot interviews provided further insights by allowing a real-time review of key aspects such as customisation, comparison to alternatives, ease of use, and fit for purpose. Moreover, because the template had been implemented in practice, the pilot interviews gave me a clearer understanding of its potential for future use.

Themes	Sub-themes
1. Overall Impressions	Comprehensive
	Well structured
	Helpful tool
2. Clarity and understanding	Clarity and understanding of the template instructions
	Clarity and understanding of the template content
3. Customisation	Adaptation strategies and recommendations
4. Ease of Use	User friendly and clarity
	Formatting
5. Comparison to alternative	Through and detailed
	Ease of use and efficiency
	Structured guidance vs. free text
	Difference in content
	Integration with existing workflows
6. Fit for Purpose	Structured Guidance for Confidence and Completeness
	Support for less experienced users
7. Suggestion for improvement	Content suggestions
8. Usefulness	Guidance and prompts for comprehensive monitoring
9. Future use	Anticipate using this template regularly or in future trials?
	Anything that would prevent you from continuing to use this template?
	Limitations in using the template.

Table 3.2: Themes and sub-themes developed from thematic analysis of the pilot phase interview.

Theme one: Overall Impression

This theme aimed to explore participants' overall impressions of the TMP template after piloting it within their CTUs. All participants offered broadly positive feedback,

often noting the comprehensive nature of the template and its utility in supporting structured monitoring practices.

Comprehensive

Participants consistently described the TMP template as covering all the necessary components of monitoring. This was seen as particularly valuable given the complexity of trial oversight. Several felt reassured that the document included everything required, reducing the risk of missing key elements. This sentiment was especially prominent among less experienced users, who described the template as instilling confidence and offering a solid foundation for drafting their first monitoring plan.

'The template covers all the elements of monitoring a trial.' (Trial Manager, 5 years of trial management and monitoring)

'After going through it, I was trying to think if there was anything else like that I hadn't covered. And I couldn't really think of anything.' (Trial Manager, 8 years of trial management and monitoring)

'My initial thoughts were I thought it very comprehensive, more so than what we're currently using, so it added quite a lot of extra detail that we found would be a benefit and useful for a monitoring plan.' (Operational Manager, 8 years of monitoring clinical trials)

'I'm confident that I have covered everything… if this is going to be a standard one, I do know that somebody's already done a lot of research… so that was a bit of a confidence for me.' (Trial Manager, limited experience of monitoring, never completed a monitoring plan before.)

Overall, participants regarded the template as thorough and reliable, reducing the likelihood of oversight and offering reassurance during plan development.

Well Structured

About half the participants explicitly stated that the TMP was well-structured, while others affirmed this when prompted. They appreciated the logical order of the sections and found the format easy to follow. For those new to the process, the structure offered reassurance and clarity, acting almost as a step-by-step guide.

'I think it was really well structured.' (Trial Manager, 5 years of experience)

'My initial thoughts are actually it's my first time doing a monitoring template, so I thought this is a little bit more easy for me to kind of follow a structure is there.' (Trial Manager, limited experience of monitoring, never completed a monitoring plan before.)

This indicates that the template's layout contributed to usability, particularly for first-time users.

Helpful Tool

Several participants, particularly those with less experience in monitoring, described the template as a helpful tool. While brief positive comments such as *'helpful'* or *'useful prompts'* were common, these may reflect polite agreement or social desirability bias. Nonetheless, their responses suggest that the template may provide additional structure and guidance for those less familiar with monitoring processes. This was especially evident in how they engaged with the prompts and reflected on how the template could support risk-based monitoring.

'I found it overall very helpful as a tool.' (Trial Manager, 8 years of monitoring experience)

Overall, the TMP was perceived as a practical aid, especially beneficial for guiding staff with less monitoring experience.

Theme Two: Clarity and Understanding

When asking participants about clarity and understanding, I wanted to know about the clarity and understanding of the instructions of the template, as well as the clarity and understanding of the content of the template. Additionally, I wanted to determine whether they found the template's order logical and if anything about its content or flow was confusing.

Clarity and understanding of the template instructions

I asked all participants whether they found the template instructions clear, as this was a crucial factor for me. It was important to ensure they understood both the purpose of the template and how to use it. Since this was a yes/no question, all participants responded 'yes.' However, while some initially provided no further details, additional probing encouraged them to share more feedback. Participants were asked to provide

any suggestions for improving the instructions; however, no comments were made to refine them further.

'I think the guidance was really clear actually.' (Trial Manager, 8 years of experience)

'I just kind of removed the instructions as I went along so that was really helpful to go through.' (Trial Manager, 8 years of experience)

'I think it sort of explains enough in the instructions of how to use the document as well as sort of the clearly set out tables.' (Trial Manager, 5 years of experience)

'Just scrolling through it was very I mean it was clear what information it was asking for.' (Trial Manager, 5 years of experience)

'I think it sort of explains enough in the instructions of how to use the document as well as sort of the clearly set out tables.' (Monitor, over 10 years of monitoring experience)

'The information that it's asking for is quite clear.' (Monitor, over 10 years of monitoring experience)

In the following quote, the interviewee asked for further clarification on the list of attendees for the Site Initiation Visit, and this was clarified with them. Since this was the second interviewee, I had the opportunity to ask the subsequent participants whether they felt the sentence needed further clarification, but all confirmed that it was easily understood.

'But then I was confused about attendance and the instructions say list of attendees in person or online. I'm not sure exactly what went in there, whether it was just asking if it wanted a list or whether it would be recorded, or whether it was sort of Yes/No answer maybe.' (Trial Manager, 5 years of experience)

'Yeah, yeah, the first few pages are very clear. Quite clear. Yeah.' (Trial Manager, limited experience of monitoring, never completed a monitoring plan before.)

Clarity and understanding of the template content

I asked all participants whether they found the content of the template as well as the flow of the document clear.

‘I thought it was very thorough and very comprehensive. I didn't have any particular issues filling it out. I, you know, I understood what was being asked. So yeah, it’s good to use so.’ (Operational Manager, 8 years of monitoring experience)

‘It was really sort of clear to navigate through.’ (Monitoring Lead, over 10 years of experience)

‘No, I thought it flowed quite nicely because they're starting obviously with the site initiation visit and then going on and then flowed through the actual process rather than jumping all over the place. So, I thought I thought that was quite good.’ (Monitoring Lead, 10 years of experience)

‘Like I said, a lot of them are self-explanatory.’ (Monitoring Lead, over 10 years of experience)

Theme Three: Customisation

This theme explores how participants adapted the TMP template to meet the specific needs of their trials and CTU procedures. Given the diversity of trial designs and monitoring requirements, the ability to tailor the template was crucial. Participants generally found the template adaptable, though opinions differed on the best way to customise it without compromising its integrity.

Adaptation Strategies and Recommendations

Most participants reported removing sections that were not relevant to their specific trial, such as those dealing with site visits in centrally monitored studies. They recognised that the template's comprehensive nature made it adaptable across various trial types but also noted that this required careful tailoring.

This feedback highlights both a limitation and a strength of the template. While its comprehensive scope may not suit every trial *‘as is’*, its adaptability was viewed positively. Participants appreciated having the autonomy to modify the tool, suggesting that a flexible, modular design supports broader applicability across diverse trial types.

‘There was a lot on there that wasn't particularly applicable to our trial. So, we did end up removing a lot of the sections based on obviously the trial.’ (Trial Manager, 5 years of experience)

‘So, our trial is just going to be monitored centrally, so we took out a lot of information.’ (Trial Manager, 8 years of experience)

There's quite a lot of it, as I said that would be taken out. But I guess you know that would happen because there's so many different types of trial. (Operational Manager, 8 years of experience)

While the need for adaptation was seen as a limitation by some, participants appreciated the flexibility of the template and its modular design, which allowed them to shape it around their specific needs.

The following quotation illustrates that even though the template was approved for use, it did not replace the sponsor’s formal monitoring plan. Instead, it was perceived as an additional requirement. While this may have created a degree of duplication, it was also reassuring to see that the sponsor still recognised the value of engaging with the template. This demonstrates that while the template is valuable, integration with sponsor SOPs may be necessary to avoid duplication of effort.

‘Our sponsor did approve us to use this, but it was very much in addition to theirs, rather than to replace their plan.’ (Monitor, over 10 years of monitoring experience)

The following quotation suggested that the template include a summary page, allowing monitors to review key information before a monitoring visit rather than reading the entire document. I explained that since the template contains sections that can be modified depending on the trial, creating a generic summary page would be challenging. Instead, I suggested that trials generate a summary page upon completing the template for their specific trial. This was discussed with other participants, who all agreed that a summary page would be useful. However, they felt it would be more appropriate to create it after completing the full document, based on the trial and risk assessment.

‘Maybe you need a monitor summary page. So that they could just read that and go. Then almost need this checklist and you can't do that over a 26 page document.’ (Monitoring lead, over 10 years of experience)

This idea prompted reflection on how to make the template more accessible for monitoring visits without compromising detail. Participants valued the flexibility of tailoring such features post-completion.

The following quotations from two participants with considerable monitoring experience stood out to me. They both suggested in different ways that CTU not to remove sections that are not applicable to the trial from the template. They suggested that CTUs could mark those sections as not applicable. The reasons they used can be seen in the quotations below but to summarise it was to show that the section was considered for the trial but not used as not applicable, and to avoid changing the main skeleton of the template so much that it would no longer be recognised as the template once was created. I thought this was a very good suggestion. In most templates and forms you have the option to skip the questions that don't apply to you, but the body of the template remains the same.

'Yeah, I haven't removed them because I just want to keep everything there and just sort of say it's not applicable. So that it can demonstrate that we considered it, but it's not applicable to the trial.' (Operational Manager, 8 years of experience)

'Because the template is so thorough, someone could end up removing so much that it no longer resembles the original. It needs a basic skeleton to preserve its structure.' (Monitoring lead, over 10 years of experience)

This suggestion led to a small change in the guidelines of the template at the beginning of the document. The implemented change guides the document user to answer the first question in each section, which determines whether that section is applicable to the trial. If the answer is *'No*' the subsequent questions are removed. For example, if the trial does not involve sample monitoring, the first question, *'Does this study involve the collection of biological samples?'*, would be answered *'No'* and the related questions would be removed. This process demonstrates that sample monitoring was considered for the trial but, as it was not applicable, the questions were not answered.

Theme Four: Ease of use

This theme explores participants' experiences with using the TMP template in practice. During the interviews, participants were asked about how intuitive they found the template and whether the formatting supported or hindered their workflow. After reviewing the transcripts and codes, the sub-themes *'ease of use'* and *'user experience'* were combined under this broader theme, reflecting their close overlap.

User Friendly and Clarity

Participants described the template as user friendly and easy to follow. Several highlighted the clear layout and consistent structure as factors that made the template accessible. Both experienced monitors and those with limited exposure to monitoring templates found it intuitive.

'The structure was really consistent throughout.' (Trial Manager, 5 years of experience)

'It was really user friendly […] it's divided up into very clear sections […] it was really sort of clear to navigate through.' (Monitor, over 10 years of monitoring experience)

Overall, the clear structure and layout were highly valued, with the template seen as particularly helpful for those with less experience in monitoring documentation.

Formatting

Most participants were satisfied with the formatting of the template and found it aligned with their expectations, especially those who had worked with similar monitoring templates before. The boxed layout was seen as familiar and easy to navigate.

'I think it's fairly accessible and they were the formats exactly as I'd expected.' (Monitoring lead, over 10 years of experience)

'No, I'm used to doing formats like this for monitoring plans in Word. I quite like the boxes being separated out and just under the different sections.' (Monitoring lead, over 10 years of experience)

'So definitely this is a lot more easy to write down and you know like follow but I don't how it will be in the long run but yeah it looks good to follow.' (Trial Manager, limited experience of monitoring, never completed a monitoring plan before.)

One participant did note minor issues, such as the difficulty of manipulating certain tables, which occasionally shifted when being edited. These concerns were addressed by adjusting the table layout in the final template version.

'So definitely I found it a little tricky to the formatting wise, but that's only a small thing.' (Trial Manager, limited experience of monitoring, never completed a monitoring plan before.)

Overall, formatting was generally seen as acceptable and familiar. Minor usability issues were noted and addressed during the piloting process, reinforcing the iterative nature of template refinement.

Theme Five: Comparison to Alternative

An important aspect of evaluating the TMP template was understanding how it compared to alternative monitoring plans already in use within CTUs. Participants were asked to reflect on whether the template provided any advantages or improvements over their existing monitoring plans and whether it aligned with or enhanced their current practices. By comparing the template to alternative approaches, I aimed to assess its usability, efficiency, and added value in clinical trial monitoring. Additionally, understanding how the template integrated with different CTUs' workflows provided insights into its adaptability and potential for standardisation. Participants referred to the tabular format of the template and guidance provided making it a lot easier to complete as well as providing assurance to the user that they have not missed anything.

Through and detailed

Participants generally felt that the TMP template was more detailed than the monitoring plans they typically used. This level of detail provided reassurance that nothing important would be overlooked.

*‘Compared to the one I used before, this is a lot more thorough in a very good way.’ (*Trial Manager, 5 years of experience)

‘My initial thoughts were I thought it was very comprehensive, more so than what we're currently using.’ (Operational Manager, 8 years of experience)

‘The one I had (referring to CTU monitoring plan) actually for a study was very detailed when it's probably 50 pages. So I find this is really good for a small study like mine.’ (Trial Manager, limited experience of monitoring, never completed a monitoring plan before.)

Overall, the template was perceived as more complete or appropriately scoped compared to existing alternatives, depending on the size and nature of the trial.

Ease of use and efficiency

The TMP template was found to be more user-friendly and efficient, with clear guidance that made the process faster and easier compared to alternative templates.

'I think the one I used before was a lot more simpler and a lot more blank space for you to fill in. So, I think the detail on this one and the individual rows with guidance for each was just made it much quicker process and it's not relying on you to remember things to fill in.' (Monitor, over 10 years of monitoring experience)

This feedback suggests that the structure and guidance within the TMP helped reduce cognitive load and potential omissions, especially when compared to more open-ended templates.

Structured guidance vs. free text

Participants noted that the TMP provided more structured prompts than their current templates, which relied heavily on free-text entries. This made the TMP more accessible and easier to navigate.

'I've seen many different structures and it is takes a second to figure out what you're where to look for the information you need.' (Trial Manager, 8 years of experience)

'We can go through each section […] if someone only needs one area, they can easily find it.' (Monitor, over 10 years of monitoring experience)

'This template asks specific questions rather than just a free text […] it guides you more, which is helpful.' (Operational Manager, 8 years of experience)

In essence, this structure was seen as a strength, improving usability and consistency in reporting.

Difference in content

Some participants compared the template's content to their own and found that the TMP covered different or additional areas. They noted how some sections were broader, while others were more specific to their own CTU practices.

'Our monitoring plan focuses more on just the monitoring […] it goes into more detail about which tasks belong to whom.' (Monitoring lead, over 10 years of experience)

'We saw that it did have more information than we felt was lacking in our current monitoring plan template.' (Operational Manager, 8 years of experience)

This illustrates that the TMP's scope may differ from unit to unit, but its content was often seen as adding value by prompting consideration of areas that may have been overlooked.

Integration with existing workflows (established practices)

While participants generally recognised the value of the TMP template, some highlighted tensions between its structure and their existing workflows. In particular, aspects of staff training and delegation were viewed as overly rigid or misaligned with routine monitoring practices. One experienced monitor explained that delegation and training records are not formally reviewed at fixed intervals, but rather in response to staff changes, reflecting a more dynamic and practical approach. The quote below captures both the procedural logic and informal pragmatism that shaped their interpretation of the template:

'We don't routinely monitor training docs. Because if they're delegated, they should be trained […] so we're monitoring it essentially monthly or something.' (Monitoring lead, over 10 years of experience)

'I think for how we operate as a CTU, number of those points that need completing in the TMP are captured either like in the risk assessment or in the data management plan rather than in the TMP so.' (Monitoring lead, over 10 years of experience)

These responses highlight the challenge of balancing standardisation with local flexibility. While the TMP template offers a structured approach, its integration into existing workflows may require negotiation or adaptation within CTUs.

Theme Six: Fit for Purpose

This section of the interview explored whether participants felt the TMP template was fit for purpose in guiding monitoring strategy planning. While I was personally invested in the development of the template, I remained mindful of the potential for response bias and took care to invite open and critical feedback. Participants were explicitly encouraged to share areas of concern or confusion.

All participants indicated that the template was fit for purpose in its current form. Three participants ranging from a senior monitoring lead to an operational manager and a less experienced trial manager commented that the template would be especially

useful for those with less monitoring experience. It was encouraging to see that the tool's usability was recognised across different levels of expertise.

That said, the development process was intentionally iterative. Earlier feedback led to several refinements, and it is possible that the positive responses reflect the improved version presented in the later interviews. I acknowledge that my dual role as both researcher and developer of the tool may have influenced how feedback was framed or delivered, and I have tried to remain reflexive about this throughout the study.

Structured guidance for confidence and completeness

Several participants valued the structured nature of the TMP template. They noted that it provided prompts that made it easier to navigate complex monitoring requirements, reducing the risk of omissions and increasing users' confidence that all necessary elements had been addressed.

'*So, kind of introduces you to what you're going to be working through. Yeah, I don't think I would change anything major.'* (Trial Manager, 5 years of experience)

'In most monitoring plans you would just have to write in there what you're going to do, whereas this guides you a bit more which is helpful I think because it asks a question then you've got more guidance, rather than just expecting you to write that information in.' (Operational Manager, 8 years of experience)

Support for less experienced users

Participants across all levels of monitoring experience endorsed the TMP template as fit for purpose, but their reasons for doing so reflected their varying backgrounds. Less experienced users valued the template as a structured guide, helping them gain confidence in drafting a monitoring plan:

'Because it's my first time, I felt I could rely on this one […] I'm confident that if I can fit everything in here, I have covered everything.' (Trial Manager, limited experience)

This highlights the template's role not only as a planning tool, but also as a learning scaffold. It reduces the likelihood of omissions by guiding new users through key domains of monitoring.

In contrast, more experienced participants recognised the template's value in prompting less experienced staff to consider essential elements:

'I think it's quite good for those who aren't as familiar with monitoring plans […] it covers the things we need to be thinking about.' (Operational Manager, 8 years of experience)

'It's very much aimed at people who are learning to become a trial manager, to ensure they don't miss anything.' (Monitoring Lead, 10+ years of experience)

These comments suggest that for senior staff, the template serves a dual purpose as both a quality control mechanism and a tool for capacity-building among junior colleagues.

Theme Seven: Suggestions for Improvement

Participants were asked if they had any suggestions to improve the content or layout of the template. All participants agreed that nothing was missing from the content. Two suggestions were made regarding the layout of the tables and having a summary page on the document during the discussion on ease of use, which were addressed earlier. One participant recommended replacing the term 'subject' with 'participant' in clinical trials to keep in line with latest changes in ICH GCP guidelines, which was implemented in the template. This same participant also suggested including links to relevant guidelines, such as the 'Monitoring Triggers and Metrics Tool' created by the task and finish group at UKCRC. While this suggestion was considered, I decided against it. Guidelines can change or be updated and linking to them would require the template to be regularly updated and redistributed to CTUs. As I will not be actively monitoring the template or updates to the guidelines, I wanted to avoid the risk of including outdated information. Instead, the template guidelines advise users to refer to the latest ICH GCP guidelines, as well as any other relevant guidelines and unit SOPs. Another participant suggested to add the sponsor and CI name to the template. These were the items that were considered during reviewing items for the template. I decided to have three trial identifiers on the template. These three identifiers were, *'ISRCTN',* '*ClinicalTrials.gov'* and '*EudraCT Number'* which were those that were mostly used and internationally recognised. Therefore, the more local identifiers were left to be used under the discretion of the CTU.

Content Suggestions (Refinements)

While participants generally found the content of the template appropriate, several offered constructive suggestions for refinement. These suggestions tended to focus

on minor content-level improvements rather than major structural changes, suggesting overall satisfaction with the core design.

One participant flagged the use of the term *'subject'*, noting its diminishing use in light of recent ethical guidance. This was an important point, and it was implemented in the template.

'Really minor points, sorry to be picky, but there's the use of the term subject […] the Declaration of Helsinki is being updated to stop using that term.' (Trial Manager, 5 years of experience)

Others recommended adding specific fields or supportive resources to improve clarity during completion. For example, some participants suggested including trial identifiers, such as the sponsor or CI details. These fields were considered during the initial design of the template phase, but I decided not to include them in the core template to allow CTUs the flexibility to add trial-specific information as needed.

'The registration things—I would expect to see somewhere to log the sponsor and the CI.' (Operational Manager, 8 years of experience)

Together, these comments suggest that while the content was generally well-received, participants valued the opportunity to ensure that the template remained ethically current and practically useful. They also highlighted the need for regular updates and the importance of allowing flexibility in how the tool is adapted to meet local requirements, while still retaining a minimum standard of expected content.

Theme Eight: Usefulness (of the template)

This theme explores the overall usefulness of the TMP template, particularly in shaping participants' monitoring practices. While earlier parts of the interview had already hinted at its value, this section focused explicitly on whether participants felt the template made a tangible difference. When asked directly, most elaborated on specific features they found especially beneficial. As expected, some of the codes and quotations in this theme overlapped with those in the Overall Impression section, but the responses here provided more targeted reflections.

Prompts and Guidance for Comprehensive Planning

Several participants noted that the template served as a helpful prompt, guiding them through aspects of monitoring they might otherwise overlook:

'There were definitely a few points in there that hadn't come into my mind already.' (Monitor, 10 years of experience)

Clarity Through Structure and Examples

Participants also valued the clarity provided by the template's structure particularly the inclusion of examples and optional tables. These elements were seen as practical supports, helping users interpret expectations more easily and fill out the document with confidence.

'The examples in that column really helped me to see what was intended.' (Monitor, over 10 years of experience)

Reinforcing Monitoring Best Practices

For more experienced staff, the template served to reinforce good practice by making expectations more explicit and prompting reflection on frequency and approach to monitoring tasks.

'The bit about the regularity of the visits and what we need to do […] that's the bit that's useful to me.' (Monitoring Lead, over 10 years of experience)

Overall, these insights suggest that the usefulness of the template extended beyond its individual components. It acted as a planning scaffold, clarifying expectations, reinforcing best practices, and offering structured guidance. This was particularly valuable for those seeking either reassurance in their process or a practical tool to support consistent monitoring strategies.

Theme Nine: Future Use

In the final part of the interview, participants reflected on whether they would use the TMP template in future trials and what might influence their decision. Broadly, there was enthusiasm for adopting the template particularly due to its perceived comprehensiveness and standardised structure. However, participants also raised some operational and procedural barriers to implementation.

Anticipate using this template regularly or in future trials?

Many participants saw value in using the template more widely. The idea of a standardised format was particularly appealing, especially for those working across different trials or institutions:

'I think having an overall standard approach is helpful […] sponsors would probably find it helpful as well.' (Trial Manager, 8 years)

Some participants had already shared the template with colleagues or incorporated it into ongoing work, signalling early adoption and peer endorsement:

'I've sent this formatted one to another team member of mine […] she said it was helpful so she might be using this template as well.' (Trial Manager, limited experience)

Anything that would prevent you from continuing to use this template?

Despite the positive feedback, several participants identified potential barriers to adoption primarily related to internal processes and standard operating procedures (SOP)s. Some noted that using the template would require formal approval and integration into controlled document systems:

'We currently have our own process […] we've completed a sort of deviation from our SOPs to enable us to use this document […] We just need to get it listed as our controlled document.' (Operational Manager, 8 years)

Another challenge was resistance from staff who might feel the template duplicates information already recorded elsewhere, potentially increasing their workload:

'I would get resistance […] if I'm asking them for information they've already put into a document.' (Monitoring Lead, over 10 years of experience)

These insights suggest that, although the template was generally well-received, its successful implementation within existing trial units would depend on broader institutional support. Specifically, participants highlighted the need for alignment with existing standard operating procedures (SOPs), and recognition of the template as a controlled document. Additionally, user buy-in would be essential, particularly from trial managers who may perceive the template as duplicating existing documentation. Addressing these concerns would likely involve streamlining how information is captured across documents, ensuring clarity on the distinct purpose of the template,

and offering practical guidance on how to integrate it into current workflows without adding unnecessary burden.

3.8.3 Pilot Interview Results (second interview at the end of piloting phase)

Once the pilot phase was completed at a CTU, I planned to conduct a follow up qualitative interview with them to gather their hands on experience of using the template. However, as mentioned earlier, only the Northern Ireland CTU was able to fully complete the process. During the interview in October 2024, they informed me that they had also begun using the template for another trial scheduled to commence recruitment in January 2025. Furthermore, they found the template so useful that they planned to amend their own monitoring plan to incorporate elements of the TMP template. In their own words, they wanted to use the TMP template as a *'hybrid template'*.

This section reflects the views of a single interviewee. However, it was an exceptionally rich interview, as the participant provided extensive insights. Unlike the other interviews, this discussion focused on real-life experiences of using the TMP template in practice. I was particularly keen to listen, allowing the participant to lead the conversation in their own way. They covered many of my intended questions without prompting, which reassured me as a researcher that I had designed an appropriate and effective set of questions. I also found that a lot of the data in this interview transcript was interchangeably used for various themes. Examples of this will be seen below. The interview was conducted with a Senior Clinical Research Monitor, with over 10 years of monitoring experience.

Theme one: Overall Impressions

In this post-pilot interview, the participant began by sharing their overall impressions of the TMP template. One of the first observations they made was about the length of the document. After completing all the relevant sections, they found the template to be quite extensive:

'So what we found initially was that it is very long because you're trying to incorporate everything.'

Despite its length, the participant expressed a positive view of the template's utility. They described it as a comprehensive and effective tool that served as a checklist to ensure nothing important was missed during planning:

'But what we thought it was, it's a very good checklist to ensure that you're not missing any key areas in your plan. So it's very comprehensive.'

Their comments reflect a recognition of the template's depth and thoroughness, acknowledging its value in supporting complete and consistent planning, even if the detailed nature of the document made it feel lengthy.

Theme Two: Clarity and Understanding

In this part the participant reflected on the clarity of the template and how easy it was to understand the instructions as well as various sections of it. I specifically asked them if they found anything confusing about the template.

'I think there was a few bits that I thought was maybe a bit repetitive, you know, but I didn't think it was confusing, if you know what I mean. It was fairly straightforward. It was laid out quite clearly.'

In particular, the clear section headings appeared to support a more efficient and focused approach to developing the monitoring plan. The participant described how these prompts helped maintain momentum and clarity throughout the drafting process:

'I knew the sections that I needed to include, so I actually think it was really useful and kind of speeding up the development because there were very clear headings, and it just kept me focused on this is what I need to include, or I don't need to include.'

Overall, the participant's feedback suggested that the clarity and structure of the template were effective in supporting both understanding and efficient completion.

Theme Three: Customisation

The participant reflected on their experience of customising the template to suit the specific requirements of both their CTU and the trial it was being used for. They demonstrated a clear understanding that the template could be adapted, and described the process of tailoring it as straightforward and flexible:

'So what we found initially was that it is very long because you're trying to incorporate everything, but obviously it can be edited.'

‘So if a section isn't applicable, that can be removed.’

The participant also discussed how their approach to customisation evolved with increased familiarity. Using the template for a second time significantly reduced the time required for completion, as they had developed a clear strategy for adapting it to their preferred format:

‘What I did was populated the template as is, so populated exactly your template and I found it was really long. And I sat down with my manager and we kind of looked at it and we came to the decision that right let's lift the sections and put them into our format.
That worked really well. So when we were developing the 2nd monitoring plan, it was much faster then.’

They also described how the clear layout and structure helped them identify relevant sections for inclusion or exclusion, which not only supported customisation but also enhanced efficiency:

‘I knew the sections that I needed to include, so I actually think it was really useful and kind of speeding up the development because it was in a very clear, and it just kept me focused on.’

Overall, the participant’s comments underscored the flexibility of the template and its adaptability to different trials, while highlighting that familiarity with the format made subsequent use more efficient.

Theme Four: Ease of Use

The participant discussed the ease of using the template throughout the interview, describing its structured layout as a particular strength. The clear division into distinct sections and headings was seen as beneficial, especially in supporting practical use during monitoring visits. They explained that the layout helped streamline navigation and made the document more user-friendly, particularly when differentiating between remote and on-site activities.

In describing feedback from a colleague who used the template during a monitoring visit, the participant noted:

‘Once it was in use, I had discussions with [name of monitor removed] the monitor who's using it, she actually found it quite useful before going out for the visit to read through, it was much easier to see different sections. She said this is exactly what I need to do when I'm out on an onsite visit versus our old template.’

They added that the defined structure made it easier for the monitor to locate specific sections quickly:

‘How the template is laid out into the very defined sections, again, much easier for the monitor then to go specifically to that section. So, if they're going on an on-site visit, they could go straight there.’

These reflections suggest that the format not only improved usability but also supported real-time, task-specific reference, enhancing the practicality of the template in routine monitoring work.

Theme Five: Comparison to Alternative

This theme captured the participant’s thoughtful reflection on how the TMP template compared to their CTU’s existing monitoring plan. The comparison process appeared to be instrumental in shaping their appreciation of the new template and ultimately influenced their intention to adopt it for future trials.

The participant acknowledged that the TMP template highlighted several gaps in their current monitoring documentation:

‘It covered all of the key areas and there were definitely a few areas in it that we wouldn't have thought about in our template.’

‘So for example, the central monitoring section was very comprehensive and that was definitely something in our template that I know we were lacking.’

‘I think what we were struggling with before the template was trying to incorporate central monitoring and remote monitoring because we were working off an original template that didn't really cover that.’

They also commented on the table format of the template, noting how it differs from their own free-text, paragraph-based format. While this largely comes down to personal preference, some participants found the table format easier to follow, whereas others preferred the non-table structure. The main drawback of the table

format is that it increases the overall length of the template. However, its advantage lies in making the content easier and quicker to locate, which is particularly useful when a monitor needs a quick reference before a monitoring visit.

'That was probably the thing that we changed most was the format in that table format, but again it was purely because our template runs just more like pros really and paragraphs. So yeah, if you looked at your template versus the plan that we've developed, it looks very different in that we didn't use the table format.'

Despite modifying the structure, the participant highlighted the strength of the TMP template's content, particularly when presenting it to sponsors:

'It just was much more comprehensive than what we usually would have presented to the sponsor.'

Additionally, they reflected on the layout of the template, noting that it is much easier to work with than their own monitoring plan. This ultimately improves accessibility for monitors and reduces the likelihood of important information being overlooked.

'And then how the template is laid out into the very defined sections. Again, much easier for the monitor then to go specifically to that section. So, if they're going on an onsite visit, they could go straight there. Whereas I think our old plan was getting a bit muddled and confused, and the monitors often had to read the entire document in case there was something buried in a section that didn't jump out at them, you know, but this is a very defined, you know, I'm doing remote monitoring.'

These reflections underline how direct comparison with an existing monitoring plan helped the participant appreciate the structure, comprehensiveness, and navigability of the TMP template. While some formatting changes were made to suit local preferences, the content and clarity of the template were seen as a clear improvement.

Theme Six: Fit for Purpose

This theme explored whether the participant an experienced trial manager felt the TMP template was fit for purpose in guiding monitoring strategy planning. In earlier pilot interviews, all participants agreed that the template was fit for purpose, with some specifically noting its value for individuals with limited monitoring experience. This interview provided an opportunity to assess its perceived value from the perspective

of someone with considerable monitoring expertise who had applied the template in practice.

The participant affirmed that the template was fit for purpose, particularly praising its structured layout and how it allowed for targeted use:

'It is easy to find sections, say this is what I need to do. I'm doing STV. This is what I need to do. So yeah, I would say it was fit for purpose.'

'This is exactly what I need to do when I'm out on an onsite visit versus our old template. She liked the format of it being laid out as remote, onsite etc.'

One particularly powerful example shared by the participant highlighted how the template helped communicate a monitoring strategy to a Chief Investigator (CI) who was particularly interested in remote and onsite monitoring. They explained that before having access to the template, they would have struggled to structure these sections effectively. However, the template provided the necessary guidance, making the process much more straightforward, and the final version of the monitoring plan was something that the CI was happy with and approved. This was very important to me and made me feel that the template has served its purpose, at least with this CTU.

'The CI for our new study is very keen on remote or central monitoring. So that was one of the key things that she wanted included in the plan. I think before the template I probably would have struggled to figure out how to word that in the plan, but this definitely helped to keep my thought process very clear, and it helped to lay everything out. So, when I presented it to her, she could clearly see. Yep, that's exactly what I want. So, it really helped with that.'

This account strongly supports the template's intended purpose, not only as a practical planning tool but also as a framework for clear communication with stakeholders. The participant's ability to confidently structure and present a plan tailored to a CI's expectations serves as further evidence of the template's utility, even among highly experienced staff.

Theme Seven: Suggestions for improvement

In this part of the interview, the participant was invited to offer any suggestions for improving the TMP template. They confirmed that no changes were necessary. The participant emphasised that the strength of the template lies in its adaptability,

highlighting that it is designed to accommodate a range of study types. This flexibility was seen as a key feature, not a limitation:

'No, I don't think that's required, because it's a template and you have to kind of plan for all different types of studies. So no, I didn't think there was anything that would need to change or amend.'

This feedback reinforces the value of the template's structure as sufficiently broad to support diverse trial needs without requiring modification.

Theme Eight: Usefulness

The participant spoke positively about the usefulness of the TMP template throughout the interview. They described how it supported both the development and practical application of monitoring plans. The structured layout made it easier to review before monitoring visits and allowed monitors to quickly locate relevant sections.

'I had discussions with [name removed] the monitor who's using it, she actually found it quite useful before going out for the visit to read through.'

'And it's definitely made our plans much more comprehensive.'

'I do think it definitely was a useful document. Took a little while just to get my head around new sections really on things that we wouldn't have previously written about.'

One particularly meaningful reflection came when the participant described their intention to revise their CTU's monitoring plan, stating that the TMP template had helped clarify areas such as central and remote monitoring. They acknowledged that the template had directly contributed to a change in practice within their unit:

'I was probably going to have to just go away and completely redo our template. But it really helped to bring the central monitoring and the remote monitoring into our plans because before that we were trying to include it, but it just it didn't sit as clearly as it does now. So, it really helped the change of practise.'

Theme Nine: Future Use

By the time this question was addressed in the interview, it was already evident that the CTU intended to continue using the TMP template and adapt it into a format that best suited their internal processes. The participant expressed confidence in the

template's value and confirmed their plans to revise their own monitoring plan template using its content.

An important point raised was the initial challenge of working with a new format. Although this specific concern was not mentioned in earlier interviews, it resonated with my own reflections on feedback from other CTUs. Adopting new documentation often involves an adjustment period, requiring both time and, in some cases, formal approval from sponsors. The participant captured this sentiment well:

'I think the main thing was just getting started with it because with anything new, you're kind of sitting down thinking, oh, this is so different from what I'm used to. But once we'd kind of worked through it, it worked well.'

They also acknowledged that some sections initially felt unfamiliar, but noted that once they had completed it once, it became easier to use:

'Took a little while just to get my head around new sections on things that we wouldn't have previously written about. But once we've done it once, it's become much easier now. So yeah, I will be using it again.'

Finally, the participant confirmed their intention to revise their CTU's existing monitoring plan by incorporating all sections of the TMP template while adapting the layout to suit their preferred format. This statement reaffirmed their long-term commitment to using the tool:

'Yeah, I think what we'll do is we will definitely go away and redo our monitoring plan template using your plan. And it will probably become a kind of a hybrid plan where we've got all of your sections in it, but it will just be laid out in a slightly different format.'

These reflections confirmed that the template was not only usable but adaptable and had already begun influencing practice in a meaningful way.

The final version of the TMP template, which was also published as part of the paper can be found in Appendix 18.

3.9 Chapter Summary and Discussion

This chapter analysis provides a comprehensive understanding of participants' perceptions, highlighting both the strengths of the TMP template and areas for potential improvement. The aim of this research was to ensure that the TMP template aligns with its intended purpose which is enhancing clinical trial monitoring practices among UK CTUs and promoting standardisation in an evidence-based manner.

A key aim of this research was to develop a structured and practical monitoring plan template that could support standardised trial monitoring practices across UK CTUs and beyond. This work builds on prior standardisation efforts in clinical trials, such as the SPIRIT guidelines for protocols (Chan et al., 2025) and recommendations for statistical analysis plans (Gamble et al., 2017).

The findings can be understood within the wider movement to improve trial conduct through structured, evidence-informed tools. Frameworks such as TIDieR (Hoffmann et al., 2014) , Trial Forge (Treweek et al., 2015) , and Quality-by-Design (QbD) (CTTI Quality by Design (QbD) toolkit, 2014) illustrate how iterative, consensus-based development can enhance clarity, efficiency, and proportionate focus on quality. The TMP template extends these principles to the domain of trial monitoring, operationalising them through concise prompts and examples tested with end-users. Like methodological programmes such as COMET (Williamson et al., 2017) and COS (Prinsen et al., 2016) , the refinement process combined quantitative indicators from the Delphi with qualitative feedback to achieve both consistency and contextual relevance.

Integrating these distinct forms of evidence required reflection on how findings from different methods interacted. Mixed methods research frequently exposes areas of tension between quantitative consensus and qualitative nuance (Creswell & Plano Clark, 2018; Fetters et al., 2013). Following the integrative principles described by these authors, apparent contrasts such as items rated highly important in the Delphi but viewed as less feasible in consensus meeting were treated not as contradictions to resolve but as opportunities to clarify meaning and contextualise application. This iterative comparison strengthened the final template by aligning empirical consensus with practical feasibility and demonstrates how mixed-methods integration can enrich methodological tool development.

Building on the insights gained through mixed-methods integration, further lessons were drawn from established methodological frameworks to guide dissemination and practical implementation. Trial Forge (Treweek et al., 2015) demonstrates the value of accessibility and embedding new tools in routine trial processes, while QbD (CTTI Quality by Design (QbD) toolkit, 2014) reinforces a focus on *"errors that matter"* when prioritising content. Drawing on these insights, the revised TMP template emphasises brevity, clarity, and risk-proportionate actions to support uptake across CTUs. Collectively, these connections position the TMP template within the evolving methodological landscape of trial design and monitoring, showing how consensus and empirical testing can be combined to produce tools that are both rigorous and usable.

Co-design approaches in healthcare stress that credible tools emerge when evidence generation and experiential knowledge are integrated through structured, transparent, and inclusive processes (Bate & Robert, 2006; Sanders & Stappers, 2008). Frameworks such as Experience-Based Design (EBD) (Bate & Robert, 2006) and the James Lind Alliance (NIHR, 2021) illustrate how stakeholder diversity can be balanced through defined stages of engagement, clear decision rules, and open communication. Reflecting on these principles, this study sought to value multiple professional perspectives by using pre-circulated materials, open and transparent discussions, explicit consensus criteria, and anonymous electronic voting, to reduce dominance effects while maintaining discussion and ensured that differing operational perspectives were represented in the final tool. Future iterations could further strengthen inclusivity by incorporating earlier contributions from patients or public partners, particularly in refining examples and usability guidance. Such integration would extend the co-design ethos of this work and ensure that the template remains both methodologically rigorous and grounded in the realities of trial delivery.

These principles of inclusivity and balanced contribution extended beyond the consensus phase into piloting and dissemination. I actively engaged with a wide range of CTUs across the UK and professional roles through national presentations including the national monitoring meetings in 2023, 2024 and 2025, conference presentations, pilot testing, and unit-based seminars. These interactions broadened participation and created further opportunities for iterative feedback, reinforcing the collaborative and co-designed nature of the TMP's ongoing refinement.

Beyond this study, mixed methods approach that *combine Delphi with qualitative enquiry* are increasingly used to develop methodological tools in trials. For example, programmes developing core outcome sets commonly pair Delphi consensus with interviews or focus groups to refine domains and clarify wording before finalisation (Keeley et al., 2016; Young & Bagley, 2016). Similar approaches are used in checklist and template development, where Delphi-derived items are iteratively tested with qualitative user feedback to enhance usability and contextual fit (Diamond et al., 2014; Tong et al., 2007). Including such exemplars underscores that my integration of Delphi findings with interview-based refinement follows established practice in methodological tool development and helps situate the TMP within this trajectory of evidence-informed co-design.

During the interview phase of the study, all participant feedback were valued and carefully considered. Where suggestions were not implemented, it was primarily due to CTUs having the flexibility to adapt the template to their specific trials by adding or omitting sections as needed. Feedback from the piloting interviews did not result in changes to the content or format of the TMP template. The analysis process was reflexive, iterative, and transparent, ensuring that the final template reflects the needs and perspectives of its users. Appendix 17 shows the detailed list of all the changes that were implemented as a result of the interviews. As (Yardley, 2003) noted, qualitative researchers would not expect their findings to be exactly replicated in every context but would hope that the insights they derived from studying one context would prove useful in other contexts that had similarities.'

A crucial aspect of this research was to capture participants' genuine thoughts and experiences with the TMP template. While positive feedback was welcomed, constructive criticism was equally valued, as both played a key role in refining and improving the template. A participant's comment during the pilot interviews captured the intended impact of this work:

"If this is going to be a standard one, I do know that somebody's already done a lot of research or put a lot of thought into it and made sure that everything is there. So that gave me confidence to say that I can use this template without worrying that I might have missed something important."

This quote reaffirmed that the research had achieved its goal which is creating a structured, well thought out template that could positively impact monitoring practices in clinical trials.

During the instant reaction interviews, numerous suggestions were made, leading to refinements in the template. The revised version was then tested in the pilot phase. Interestingly, fewer suggestions were made during the pilot phase, which led me to reflect on the reasons for this.

The instant reaction interviews evaluated a version of the template developed from a Delphi survey and consensus meeting. Although these processes involved participants with monitoring experience, they assessed the template as a whole. However, the instant reaction interview participants reviewed the template in the context of their own practical reality and monitoring practices. By the time of the pilot phase, the template had already undergone extensive revisions, so I did not expect significant further changes. Instead, my focus was on determining whether CTUs viewed the template as fit for purpose and whether they saw its potential for future use.

Although some useful recommendations were made during the pilot phase (some of which were implemented, as discussed in the results), the overall response indicated a willingness to adapt a standardised document. The comment on the value of a standardised template emerged in direct response to a question asking participants whether they would consider adopting this template within their own CTU. While some interview questions were intentionally structured to explore participants' openness to standardisation, others allowed space for unprompted reflections. Notably, several participants spontaneously raised the benefits of harmonisation across CTUs without direct prompting, suggesting that standardisation is a relevant and salient concern within the monitoring community. As one participant noted:

"I think having an overall standard approach is helpful because then when you're moving around or imagine sponsors would probably find it helpful as well."

This comment highlights how a standardised approach benefits not only monitors but also sponsors, especially when staff transition between CTUs and need to familiarise themselves with different monitoring plans.

Another CTU acknowledged that the template contained a lot of information missing from their current monitoring plan. As a result, they decided to pilot it and deviated from their SOPs to see how well it worked in practice. Although this CTU was unable to participate in a follow-up interview after the pilot, they expressed strong interest in getting the template formally approved by their sponsor for ongoing use. I continued to follow up with them to understand whether they had succeeded in making the template an official document, but I have not yet received a response.

Another CTU also mentioned that they found the template to be useful and comprehensive, and it has been passed down to another trial manager to use. The experience of the trial manager piloting the template was positive, leading to further discussions among colleagues who expressed interest in adopting the template for their own trials. The CTU that completed the piloting process also noted that the TMP template addressed gaps in their existing monitoring plan. Reflecting on these comments from CTUs regarding deficiencies in their monitoring plans further reinforces the importance of this research. It highlights how a standardised approach can enhance monitoring standards in clinical trials and bring significant benefits to the field.

This research developed a monitoring plan template based on an extensive review of 32 monitoring plans used across the UK, alongside input from experienced monitoring staff via a Delphi survey and a consensus meeting. Ensuring that the template effectively served its purpose was essential, and qualitative interviews and piloting played a crucial role in testing its usability and gathering user feedback. Overall, based on participants' reflections and my own observations, the template was generally well received. However, this finding should be interpreted with some caution. It is possible that the participants many of whom were already engaged with or interested in monitoring practices may have been more receptive to the idea of a standardised template. Additionally, some interviews were conducted shortly after initial use, and longer-term feedback might yield different perspectives. Despite these limitations, the research highlights a growing interest in standardising monitoring practices in clinical trials. While further evaluation is warranted as more CTUs implement the template, there is strong potential for its continued use both within the UK and internationally.

Throughout the instant reaction interviews, participants offered a range of constructive suggestions, which informed several iterative refinements to the TMP template. During the subsequent pilot phase, fewer suggestions for improvement were made. This reduction may indicate that the earlier revisions addressed many of the initial concerns. It could also reflect the increased clarity, usability, and completeness of the template by the time it was piloted. While it is important to acknowledge that time constraints or participant familiarity with the topic may have also influenced the depth of feedback, the more limited critique in the pilot phase was encouraging and suggested growing acceptance of the template in its refined form.

3.10 Chapter Limitations

One limitation of this study is the inherent nature of instant reaction interviews. One-to-one instant reaction interviews can be restrictive, as participants have limited time to engage with the instrument under review. Although a think-aloud protocol was considered, it was ultimately deemed unsuitable. This method would have required participants to attempt to complete the TMP template while reflecting on it. However, as the TMP template is lengthy and cannot be completed in one sitting, potentially requiring several days, a think-aloud protocol was not feasible.

Furthermore, although the TMP template was piloted at six CTUs across the UK, this number may not fully capture the diversity of trial monitoring practices. Differences in organisational structures, funding, and trial types may have influenced how the template was implemented and perceived. However, I attempted to mitigate this limitation by including a diverse mix of CTUs. Although, the extent to which each CTU engaged with the TMP template and integrated it into their monitoring processes also varied. Some CTUs had a more flexible approach, using the template in its entirety, while others were restricted to using it alongside their existing, approved monitoring plans. As CTUs faced limitations in piloting the template, I needed to adopt a flexible approach, allowing them to use the template either as it was or alongside their approved monitoring plans.

Additionally, participants' recollections of their experiences with the template may have been influenced by the time elapsed between their first and second interviews during the pilot phase. This could have impacted the accuracy of their feedback regarding usability, challenges, and perceived benefits. However, all participants referred to

notes they had made while using the template, suggesting they had reflected on it throughout the process.

When designing the pilot process, I planned to conduct an initial interview with each CTU at the start of the piloting phase, followed by a second interview within 6–9 months. This approach assumed that CTUs would be able to use the template in at least one of their trials and apply it to a minimum of two monitoring visits within that period. Although these expectations were clearly communicated to and confirmed by the CTUs, only one out of the six CTUs was able to complete the pilot phase. While all six CTUs completed the TMP template initially with the intention of using it for one of their trials, in reality:

- Only Northern Ireland and Plymouth CTUs completed the pilot phase with two monitoring visits.
- Southampton CTU completed the pilot phase, but with only one monitoring visit.
- The remaining three CTUs could not use the template in practice due to trial setup delays discussed earlier.

Although piloting the template at three CTUs was a successful endeavour, only Northern Ireland CTU provided two qualitative interviews. Southampton and Plymouth offered feedback via email, stating they had nothing further to add beyond the first interview. Since these CTUs piloted the template as part of my research, I did not want to pressure them into additional commitments. Thus, I accepted what feedback they could provide via email. However, I acknowledge that a full qualitative interview with probing questions would have provided more in-depth insights than email responses alone.

This outcome, however, did not surprise me. Delays in setting up clinical trials are common (Biggs et al., 2020; Ratnayake et al., 2024), and I have frequently encountered them in my experience as a trial manager. While the CTUs had planned and intended to pilot the template, practical constraints made this challenging. Reasons cited for delays included issues such as delays in producing the IMP and competing trial commitments. Moreover, changes in staff turnover or shifting priorities at CTUs may have affected participation and continuity between the two interviews. Factors such as workload pressures, competing priorities within CTUs, or

organisational changes may have influenced how the TMP template was implemented and evaluated, potentially affecting the depth of feedback received.

Furthermore, reflecting on the interview questions and my discussions with qualitative researchers at the MRC CTU, I realised that some of my instant reaction interview questions were likely to elicit *'Yes'* or *'No'* answers, potentially limiting the depth of participants' responses and requiring additional probing. For instance, the question *'Do you find the template instructions and purpose clear?'* could be interpreted as leading, as it implies an expected answer and restricts the opportunity for more expansive reflection. A more effective approach might have been to ask, *'What do you think about the template instructions and purpose?'* to encourage participants to articulate their views in their own words.

Although I addressed this limitation by using follow-up prompts to explore participants' responses in greater detail, this reflection has reinforced the importance of phrasing questions in a way that minimises bias and supports richer qualitative data collection. Fortunately, participants were generally forthcoming and eager to provide detailed feedback. For those who needed more prompting, I carefully encouraged further elaboration while remaining sensitive to their comfort levels. If a participant appeared reluctant to expand on a response, I respected their cues and did not insist. These reflections also informed the design of the pilot interview questions, which incorporated more open-ended prompts and facilitated more nuanced discussions.

Furthermore, all participants I interviewed I did not know or had very limited professional interaction with. There was no element of power influence involved as the participants, and I had similar professional backgrounds. In each interview, I clearly explained that the participants' views are extremely valuable for improving the template and assured them that no offense would be taken if they disagreed with any part of it. Despite this, some participants may have hesitated to share negative feedback. Nevertheless, some did provide critical insights, which were taken into account and led to changes.

"Not everything that can be counted counts, and not everything that counts can be counted." (Cameron, 1963)

Chapter Four: Structured interviews with CTUs to systematically explore the role of metrics in risk-based monitoring, identify challenges, and propose practical solutions to enhance their adoption in clinical trial units.

4.1 Chapter Overview and Scope

Objective 3 of this thesis focuses on the role of metrics in risk-based monitoring of clinical trials, and the challenges UK Clinical Trials Units (CTUs) face in implementing metrics in their monitoring practices. This was achieved by conducting interviews with staff at six UK CTUs to understand their current practices, identify barriers or hesitations around using metrics and finally uncover potential interest or willingness to adopt a metrics-based approach within UK CTUs.

Risk-based monitoring (RBM) has become a cornerstone of modern clinical trial oversight, offering a more efficient, targeted alternative to traditional exhaustive monitoring approaches. RBM involves identifying and focusing on the areas of greatest risk to trial integrity, participant safety, and data quality, rather than applying uniform oversight across all sites and processes (Bakobaki et al., 2012; TransCelerate, 2013). Central to RBM is the use of metrics which are quantitative indicators used to monitor key aspects of trial conduct and performance. These may include data query rates, protocol deviation frequency, site recruitment performance, and timeliness of data entry (Brosteanu et al., 2017; Tudur Smith et al., 2014). Metrics enable trial teams to detect anomalies, assess risk levels in real time, and make informed decisions about where to focus monitoring efforts.

The European Medicines Agency's Risk-Based Quality Management Reflection Paper (Agency, 2022) explicitly encourages sponsors to *'define the metrics that will allow oversight of the trial'* and supports regular metrics-based monitoring through statistical methodologies (CluePoints' Commentary, 2013). Similarly, the FDA's guidance on risk-based monitoring endorses the use of centralised monitoring systems and

data-driven metrics to enhance trial quality and oversight (US Food & Drug Administration, 2023).

Although the use of metrics in trial oversight is increasingly discussed, their implementation remains inconsistent across organisations and studies (Love et al., 2020). International initiatives such as (TransCelerate, 2013), empirical work by Yorke-Edwards et al. (Yorke-Edwards et al., 2023), and methodological reflections by Whitham et al. (Whitham et al., 2018) and the European Medicines Agency (Agency, 2022) highlight continuing uncertainty regarding which indicators best reflect trial quality, how they should be defined, and how results should inform decision-making. Within the UK context, there is still no agreed framework or common set of monitoring metrics across Clinical Trials Units, and inspection reports identify marked diversity in current practice (MHRA, 2023). This absence of standardisation creates challenges for benchmarking, proportionate oversight, and quality assurance. The work presented in this chapter therefore addresses this gap by exploring how monitoring metrics are defined and used across UK CTUs, and by proposing a structured framework for their integration into trial oversight.

In practice, CTUs vary widely in how metrics are embedded within their monitoring systems. Some have developed quantitative dashboards to track site performance or data quality, while others rely more heavily on narrative reports and professional judgement. Through the work undertaken in this chapter, it became evident that this variability is not merely procedural but reflects deeper differences in how CTUs conceptualise ‘risk’ and operationalise quality oversight. This heterogeneity has been acknowledged in methodological and regulatory literature (Whitham et al., 2018) (MHRA, 2023; TransCelerate, 2013; Yorke-Edwards et al., 2023), but limited empirical research has examined the underlying reasons for such differences. Understanding this variability is therefore essential for identifying which metrics are most meaningful, feasible, and transferable across trial contexts.

Recognising the diversity in how CTUs interpret and apply metrics, it was important to return to the purpose of clinical trial monitoring and consider how metrics can meaningfully support that purpose. The conceptual grounding for this chapter draws on Love et al.’s *What is the purpose of clinical trial monitoring?* (Love et al., 2022), which defines three core aims of monitoring: (1) protecting participant safety, (2)

ensuring the integrity and reliability of trial data, and (3) supporting the overall credibility of trial findings. As Love et al. argue in their related work on “errors that matter”, metrics can help identify processes most vulnerable to critical mistakes, providing a structured way to align monitoring activities with key risk pathways and trial priorities. When applied proportionately, metrics can therefore act as indicators linked to these objectives, for example, recruitment timeliness and protocol deviations relate to participant protection, whereas query rates and delays in data entry relate to data integrity. Framing the findings in this way positions the metrics discussed in this chapter not merely as operational measures, but as tools that reflect, reinforce, and help operationalise the fundamental aims of clinical trial monitoring.

This chapter aims to contribute to the evidence base by exploring the broader role of metrics in monitoring within UK CTUs.

4.2 Research question/aim and objectives

Aim

This chapter aims to explore the challenges faced by UK Clinical Trials Units (CTUs) in implementing and using metrics for trial monitoring.

Objectives

This chapter has three objectives, and these are:

1) Understand current practices: Examine how UK CTUs currently use metrics in trial monitoring, including their role in decision-making, risk assessment, and trial oversight.
2) Identify barriers and hesitations: Investigate challenges, concerns, and limitations that hinder the adoption or effective implementation of metrics in trial monitoring, including strategies that CTUs have implemented to overcome the barriers.
3) Explore potential interest and willingness to adopt metrics-based approaches: Assess the attitudes of CTU staff toward increasing the use of metrics, including factors that may encourage or discourage adoption.

4.3 Research Design

Analytical method and research paradigm

This chapter aims to explore the challenges faced by UK Clinical Trials Units (CTUs) in implementing and using metrics for trial monitoring. I used semi-structured interviews to get an in-depth understanding of CTUs monitoring practices, including the use of metrics in their monitoring practices. To analyse the qualitative data collected from six interviews with CTU staff, Framework Analysis was selected as the most appropriate method. This section justifies the choice of framework analysis by comparing it with thematic analysis and content analysis, outlining their advantages and limitations in the context of this chapter.

Framework Analysis (FA) is a matrix-based method of qualitative data analysis that allows researchers to organise data into key themes and categories while maintaining a clear link to the original source material (Gale et al., 2013). It is particularly well-suited for applied policy research, where comparisons across cases or groups are needed. More detail on framework analysis is covered in section 4.5 of this chapter.

The choice of Framework Analysis over other methodologies like thematic analysis and content analysis is justified based on its structured approach, which allows for both in-depth exploration and cross-case comparison. Framework Analysis enables the systematic organisation and analysis of data, making it particularly useful when dealing with multiple CTUs, each with its own monitoring practices. This method also provides flexibility, allowing for both predefined and emerging themes to be explored, which aligns with the interpretivist paradigm of this study (Gale et al., 2013). Notably, Framework Analysis has been effectively used in previous clinical trials methodology research for example, by (Murphy et al., 2024), who successfully used the method to analyse trial staff insights on retention strategies across different trial sites.

To further clarify the choice of Framework Analysis for this chapter, I reflected on my choice of research paradigm in the previous qualitative research chapter, and considered various paradigms (Creswell, 2018). I decided that this chapter fits well within an interpretivist paradigm, which recognises that knowledge is constructed through subjective experiences and social contexts (Lincoln & Guba, 1985). Since the aim of this chapter was to explore the perspectives of CTU staff regarding the use of metrics in clinical trial monitoring, an interpretivist approach seemed appropriate. This

paradigm allows for an in-depth understanding of individual and organisational experiences, rather than assuming an objective, one-size-fits-all reality (Pervin & Mokhtar, 2022).

Through an interpretivist lens, the researcher aims not to identify a single objective truth but rather to uncover the diverse ways participants make sense of their experiences (Merriam & Tisdell, 2015). This approach allows for a flexible, responsive research design that prioritises participants' voices and centres their subjective experiences (Merriam & Tisdell, 2015). Given my research's focus on understanding participants' perspectives in their natural settings, interpretivism seemed a suitable match as it provides a framework that facilitates rich, contextually grounded insights (Merriam & Tisdell, 2015).

Additionally, the interpretivist paradigm underscores the co-constructed nature of knowledge, recognising that the researcher's values, background, and interactions with participants influence data collection and interpretation (Otani, 2020). This epistemological stance enables the researcher to engage reflexively with the data, ensuring that findings are understood as products of collaborative meaning-making rather than objective observations (Otani, 2020).

Interpretivism is ideal for research that seeks to explore individual perceptions, interpretations, and meaning-making processes (Merriam & Tisdell, 2015). It supports the idea that people's experiences and responses are socially and contextually constructed (Lincoln & Guba, 1985; Otani, 2020). The interpretivist paradigm also supports the goal of generating deep insights rather than seeking to generalise findings to a broader population (Pervin & Mokhtar, 2022). Since my research was centred around understanding the participants' diverse perspectives on the use of metrics in monitoring clinical trials, this paradigm seemed well-aligned with my objectives.

4.4 Research Methodology

To achieve the objective of this chapter, I conducted qualitative interviews with monitoring staff at various UK CTUs and asked them a series of questions (Appendix

19) to understand their monitoring practices and any use of metrics for monitoring. The interviews were conducted online via Microsoft Teams.

Sample size for metrics interviews

As explained in the previous qualitative research chapter, there are no strict rules for determining sample size in qualitative research, as it is often shaped by the study's scope, available resources, and time constraints (Cohen, 2011). To achieve the aim of this chapter, I needed to interview a diverse range of CTUs, including those that have actively adopted metrics for trial monitoring and those that aspire to use them but currently lack the means. I aimed to speak with at least 1 staff member from each CTU who have experience in monitoring trials, such as trial managers, monitors, or quality assurance personnel.

In line with Malterud's concept of *information power* (Malterud et al., 2016), the adequacy of a sample is determined not by quantity alone but by the relevance and richness of the data in relation to the study aim. Based on ongoing interactions with UK CTUs, I developed an informal understanding of the variation in how metrics are used or considered across units. This informed my decision to include six CTUs three currently using metrics and three not yet doing so. This sample was both feasible within the remaining timeframe of my PhD and sufficient to allow meaningful comparisons between the two groups, enabling exploration of differing practices, barriers, and perspectives regarding the use of metrics in trial monitoring.

I planned to start conducting the metrics interviews from January 2025 until the end of February 2025.

Recruiting for metrics interviews

To recruit CTUs for this research, I explained in all communications that the study aimed to explore the role of metrics in risk-based monitoring and to understand challenges and opportunities from the perspective of those involved in monitoring practice. I emphasised that I was interested in hearing from CTUs regardless of whether they currently used metrics and assured participants that their views would remain anonymised.

An initial email was sent to all UK CTU monitoring leads in December 2024, followed by a reminder in January 2025. The email included a simple Microsoft Teams form for interested participants to complete. However, this method did not yield any responses.

In addition to the blanket email approach, I reached out directly to several CTUs and invited them to participate. This proved to be a more successful strategy, leading to recruitment from the following CTUs: Plymouth, Leeds, Warwick, North Wales Organisation for Randomised Trials in Healthcare and Social Care (NWORTH), Cambridge, and Nottingham CTUs. I had no prior personal or professional relationships with the participants; their decision to take part reflected their interest in contributing to methodological research in clinical trials.

4.5 Methods of data collection and analysis

The Semi-structured interviews

To collect data for this chapter I considered various methods. Conducting a survey was considered but rejected because it did not provide an opportunity for open-ended conversations with participants. A survey would have limited my ability to seek further clarification on responses, reducing the depth of understanding. Additionally, surveys tend to generate surface-level responses that would not allow for the exploration of nuanced experiences or reasoning behind metric adoption or resistance (Weller et al., 2018). A focus group was also considered but rejected because I wanted to discuss individual CTUs' practices with their staff without concerns about speaking openly in a group setting. The potential influence of group dynamics and confidentiality concerns (if there was any) could have led to participants withholding critical insights. Creating focus groups involving participants with widely differing perspectives can cause participants to hesitate to speak openly and create unpleasant situations for the members of the group and a level of conflict that may prevent the debate from developing (Acocella, 2012; Bloor et al., 2001). I ultimately chose qualitative interviews as it allowed for a more interactive and flexible form of data collection (Swain, 2018). Through semi-structured interviews, I was able to engage in discussions where meanings were co-constructed between myself (the researcher) and the participants. This approach provided the depth needed to explore individual and organisational experiences regarding metric use in clinical trials. Semi-structured interviews also enabled me to adapt questions dynamically based on participants' responses,

ensuring that key themes were explored thoroughly while allowing for the emergence of unexpected insights (Fereday & Muir-Cochrane, 2006). Furthermore, given the potentially diverse experiences across different CTUs, individual interviews provided a more tailored approach to understanding specific organisational challenges. By using semi-structured interviews, I had the flexibility to probe on certain topics with more open ended and follow up questions (Swain, 2018).

I conducted interviews online via Microsoft Teams and they were digitally recorded, transcribed, pseudonymised and analysed. I ensured that data was always handled in a confidential manner and stored on UCL drives that only relevant staff (i.e., myself) have had access to.

The interview questions were designed to align with the research aim, focusing on the use of metrics in monitoring practices, challenges and barriers faced in using metrics, potential interest in using metrics, and perception of using metrics in monitoring. The questions were reviewed by the supervisory team for suitability prior to start of the interviews. The interviews began by exploring each CTU's general approach to monitoring. This not only helped ease interviewees into the conversation, but also allowed me, as the researcher, to build a picture of each CTU's monitoring practices. It also provided an opportunity to tailor follow-up questions based on whether the unit actively used metrics as part of their monitoring strategy.

Another reason for using semi-structured interviews was to allow participants to guide discussion towards issues more relevant to them, reducing researcher influence over the points discussed and keeping in line with the interpretivist view of getting as close to the participant's reality as possible (Cohen, 2011).

The interviews were relatively structured, with a series of questions that was asked to each participant. However, the order of questions asked were not necessarily the same for each participant as the individuals were encouraged to elaborate on any areas, they felt they had more to contribute (Swain, 2018). If a participant responded to questions with short answers such as yes or no, they were encouraged to give more details with follow up questions and examples.

When designing the interview questions, I applied the skills developed in the previous qualitative research chapter. I ensured that the questions were open-ended, beginning

with *‘why’, ‘how’,* or *‘what’* to encourage detailed responses rather than simple yes/no answers. This approach allowed for richer discussions and deeper insights. Compared to my previous interviews, I found these questions to be more effective in eliciting meaningful conversations with participants. The depth and quality of these discussions are further explored in the results and discussion sections of this chapter.

Interviews were scheduled for 50 minutes, though their duration ranged from 40 to 60 minutes. Predefined questions guided the discussions; however, the order of the questions was occasionally adjusted to maintain a smooth conversational flow (Swain, 2018). Probing questions were used to obtain more information or clarify participants’ point of view.

Each interview was scheduled for approximately 50 minutes to strike a balance between obtaining in-depth insights and respecting participants’ limited availability due to their professional responsibilities. This duration allowed sufficient time to explore key areas of interest such as current monitoring practices, perceptions of metrics, and implementation challenges, without overwhelming participants or risking fatigue. The length also aligned with standard practice for semi-structured interviews in applied health and trials research, where 45–60 minutes is often considered optimal for depth and engagement without diminishing data quality (Adams et al., 2015; Kallio et al., 2016). Participants were informed of the estimated duration in advance, ensuring they could allocate adequate time and engage fully in the discussion.

In line with Yardley’s recommendations for ensuring reflexivity and confirmability (Yardley, 2003), I regularly verified participants' perspectives during the interviews. For example, I used prompts such as, *'You said this—have I understood you correctly?'* to ensure accurate interpretation and uphold data rigor. Additionally, to further maintain rigor, I kept a reflexive journal where I recorded notes on non-verbal cues and the interview dynamics that could influence interpretation (Creswell, 2018). Immediately after each interview, I wrote in my journal, and I reflected on these experiences. These notes were later revisited during the analysis phase to ensure a thorough, self-aware, and unbiased interpretation of the data (Braun & Clarke, 2006; Creswell, 2018).

At the end of each interview, I thanked participants for their time and contributions. I also invited them to ask any additional questions or share further comments. Participants were informed that they could contact me for further involvement in the

study. They were also informed that the result of the chapter will be presented at the National Monitoring Meeting in June 2025 and will be published in the form of a paper.

Framework Analysis and justification for its use

To analyse the qualitative data collected from six interviews with CTU staff, Framework Analysis was selected as the most appropriate method. This section justifies the choice of framework analysis by comparing it with thematic analysis and content analysis, outlining their advantages and limitations in the context of this study.

Framework Analysis is a structured, yet flexible qualitative research method widely used in applied health research (Gale et al., 2013; Huberman et al.; Ritchie, 2013). It is particularly well-suited for studies that require a balance between systematic data organisation and interpretative depth. Framework Analysis was chosen for this chapter as it enabled systematic comparisons across different CTUs, allowing for the identification of common themes and unique challenges related to metric use. Framework analysis, also known as *'the framework approach'*, *'the framework technique'* and *'the framework method'*, is an inherently comparative form of thematic analysis which employs an organised structure of inductively- and deductively-derived themes (i.e., a framework) to conduct cross-sectional analysis using a combination of data description and abstraction (Goldsmith, 2021; Ritchie, 2014). Furthermore, the structured approach of framework analysis involves creating a framework matrix that organises responses across key themes, making it easier to visualise patterns and differences (Gale et al., 2013). Additionally, while some themes are expected based on literature and prior research (or in this chapter based on research aim) (deductive), framework analysis allows new themes to be generated naturally from the data (inductive). The step-by-step structure of framework analysis also ensures rigor and transparency in data interpretation, making it a suitable approach for this chapter. Framework analysis can be used to methodically describe a population of interest including the notable variation contained within that population (Goldsmith, 2021).

I also considered using thematic analysis for this chapter due to its flexibility in identifying patterns within qualitative data (Braun & Clarke, 2006). However, I decided to choose framework analysis in the end because thematic analysis does not support structured comparisons across cases or groups (Gale et al., 2013), making it less effective for identifying variations across CTUs. Furthermore, thematic analysis

primarily relies on narrative-style analysis, which makes it harder to present data in a clear, tabular format for easy comparison. Finally, since thematic analysis was used in the previous chapter, applying a different method, framework analysis, for this study introduces methodological diversity and allows for a more structured, matrix-based approach to comparing perspectives across multiple CTUs. This avoided repeating the same analytical approach and provided a fresh lens tailored to the aims of this chapter.

Content Analysis was also considered because of its systematic approach to coding qualitative data (Hsieh & Shannon, 2005). However, it was not selected due to the following limitations. Content analysis emphasises counting occurrences of words or themes rather than exploring their contextual meaning, which is not suitable for this study's exploratory nature (Hsieh & Shannon, 2005). Additionally, in an evolving field like metrics-based monitoring, where the terminology is not yet fully standardised, there is a risk that important insights could be missed if the analysis focused primarily on word frequency. Furthermore, unlike framework analysis and thematic analysis, content analysis would not provide insights into underlying challenges and perceptions surrounding the use of metrics. Finaly, content analysis is more commonly used in large-scale qualitative research where patterns can be quantified across numerous transcripts (Hsieh & Shannon, 2005), whereas this chapter only contains six data transcripts.

Ethics and consent

An amendment to the previous ethics approval was submitted to UCL Ethics Services in December 2024 to include the data collection for the use of metrics in this chapter. Participants were fully aware their participation were voluntary, and they could withdraw whenever they wanted without giving a reason

Participants consented to having their names collected for the purpose of acknowledging their participation in the publication, while ensuring that their views and name of their CTU would remain anonymous. I also collected participants' email addresses to disseminate the study results, with the option to opt out of both the acknowledgment and receiving the results.

Interviews in this phase followed the same ethical procedures as outlined in Chapter 3, including informed consent, audio recording, pseudonymisation, and secure data

handling in line with UCL guidelines. No participants declined to be recorded. Each interview transcript was pseudonymised and cleaned prior to data analysis. This is explained in further detail in the results section of this chapter (4.8).

4.6 Data Analysis

Framework analysis consists of two major components: creating an analytic framework and applying this analytic framework. These two major components occur through five steps (1) *data familiarisation*; (2) *identifying a thematic framework*; (3) *indexing* all study data against the framework; (4) *charting* to summarise the indexed data; and (5) *mapping and interpretation* of patterns found within the charts (Goldsmith, 2021; Ritchie et al., 1994). These five steps are all explained below. It is important to mention that I had a very specific topic in mind to understand the challenges of using metrics in monitoring clinical trials. These challenges were: Use of metrics at CTU, barriers to using metrics (non-users), perception of metrics in monitoring, future use of metrics and potential interest in a pilot project to demonstrate the practical benefits of metrics. Under each theme were interview questions to facilitate answering the research question. These are discussed further.

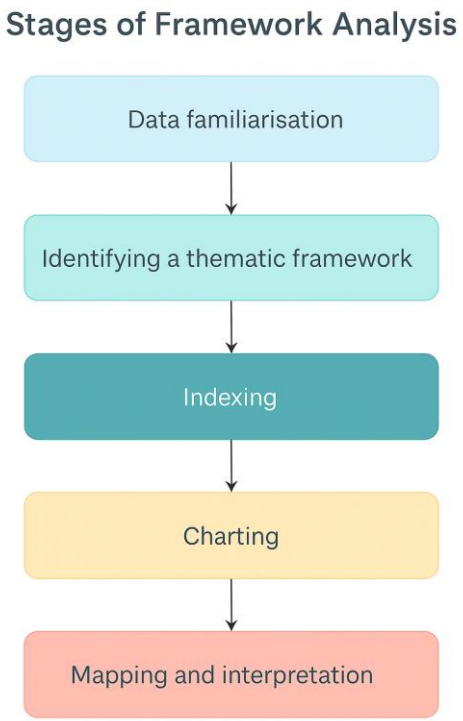

Figure 4.1: Stages of framework analysis, created by the author.

Familiarisation with the data

As (Goldsmith, 2021) explains, the first step of data familiarisation provides the researcher with an initial, purposeful understanding of the data. I conducted all the interviews myself, therefore I already had a good understanding of the data, however the step to clean the data provided me with the opportunity to immerse myself in the data (Goldsmith, 2021). Interviews were recorded on Microsoft Teams and transcripts were automatically generated. After completing each interview, I pseudonymised and cleaned the transcripts whilst listening to the interview recording. This was conducted to ensure that there were no inconsistencies between what the participants had said and what was automatically generated by Microsoft Teams (Braun & Clarke, 2006). Each transcript was read twice, and errors were checked against the recording. Furthermore, when analysing the data, I read the transcripts again and again to ensure that I was fully immersed in the data and making notes of all the themes that were presented in the data.

Reading and cleaning the transcripts as well as referring to my reflexive journals and taking notes whilst listening to the interviews provided me with the opportunity to understand major themes in the data. These major themes included topics related to the research questions and those that recur across the data (Goldsmith, 2021; Ritchie & Lewis, 2003). For example, advantages of using metrics described by CTUs, challenges experienced or foreseen by CTUs in implementing metrics in their monitoring practices and training needed for staff to be able to use metrics. As I had a relatively small dataset to work with, I was able to complete the familiarisation step with all my transcripts and find a few themes that recur in the transcripts (Goldsmith, 2021).

Identifying a thematic framework

In this step, key themes and concepts were identified based on the research aims and generated from the data itself. Since I had specific themes in mind (e.g., challenges, training needs), my framework was predefined, focused on answering my research questions. These themes served as an initial coding framework, which was refined throughout the analysis. This framework organised the data into a structure that helped summarise it meaningfully and supported answering the research question (Gale et

al., 2013). Typically, frameworks consist of major themes and concepts, which are then elaborated on or subdivided by supporting themes and concepts (Goldsmith, 2021).

These themes were specifically chosen because they directly address the core challenges identified in the research question, particularly understanding how CTUs engage with metrics and what prevents or motivates them to adopt these practices. For example, *'Training Needs'* was included as a theme because the research question asked about the support required by CTU staff to integrate metrics into monitoring practices.

While familiarising myself with the data, I had the opportunity to further develop the framework by identifying additional major themes from the data. During the creation of this predefined framework, I referred to the interview questions, designed to answer the research question, and included these in the framework. Like thematic analysis, identifying a framework in this approach is an iterative process. As (Ritchie et al., 1994) describe, an initial framework is tested against a manageable portion of the data and refined as necessary to move from simple description to conceptual abstraction. Refining the framework involves renaming themes, identifying new themes, removing irrelevant themes, and collapsing others (Goldsmith, 2021; Ritchie et al., 1994).

For example, one of the interview questions was, *“Are there any aspects of your monitoring process that you feel are currently underserved by the available tools or frameworks?”* However, this question did not yield much new data, as most CTUs had already addressed this issue in response to other questions. Similarly, in the early stages of coding, I created a theme titled *‘Positive Talk About Metrics’*. As the analysis progressed, I found that all content initially assigned to this theme was better captured under *‘Advantages of Using Metrics in Monitoring Clinical Trials’*. This process highlights the iterative nature of qualitative analysis and the importance of refining themes to best represent the data. Goldsmith, 2021 and Ritchie et al. highlight the importance of flexibility in qualitative analysis, which aligns with my iterative process of refining themes (Goldsmith, 2021; Ritchie, 2014). Their framework for identifying and refining thematic categories helped guide my decision-making in merging or renaming sub-themes, as seen in the transition from *'Positive Talk About Metrics'* to *'Advantages of Using Metrics in Monitoring Clinical Trials'*. The bullet points below

show the predefined framework created based on the research question and interview questions.

- **CTU Monitoring Strategy:** To focus on the overall approach taken by Clinical Trial Units (CTUs) to monitor clinical trials.
- **Use of Metrics at CTU:** To explore how CTUs integrate metrics into their monitoring practices. To understand the types of metrics used (e.g., recruitment rates, safety data), how they are applied to assess trial performance, and whether metrics influence decision-making processes.
- **Barriers to Using Metrics:** To identify the obstacles and challenges CTUs face in implementing metrics for trial monitoring. Barriers may include technical issues (e.g., lack of suitable software or infrastructure), human factors (e.g., resistance to change or lack of training), and organisational constraints (e.g., limited resources or institutional support).
- **Perceptions of Metrics in Monitoring:** To investigate the subjective views of CTU staff regarding the use of metrics in monitoring. It captures both the perceived advantages (e.g., improved data quality, enhanced efficiency) and the concerns (e.g., reliability, over-reliance on data).
- **Adaptations & future directions:** To examine the adjustments and changes CTUs have made, or are planning to make, in their monitoring practices over time. It focuses on how CTUs have evolved their use of metrics and monitoring strategies to improve trial oversight, and the steps they are taking to refine these practices.
- **Potential Interest in Metrics:** To explore the willingness and interest of CTUs to adopt or expand the use of metrics in their monitoring practices.

When setting up the interview topic guide, I developed slightly different questions for CTUs based on whether they currently used metrics or not, to ensure that the discussion remained relevant to their operational context. This distinction informed the initial framework, which included separate codes for motivators to adopt metrics among users and non-users. While an alternative approach might have been to code motivators under a single category and explore differences by case characteristics during analysis, I chose to reflect the structure of my interview guide within the initial coding framework. This allowed me to retain clarity and alignment between the

questions asked and the themes analysed, particularly as my aim was to explore both shared and divergent motivations across these two groups.

Indexing (Coding the Data to the Framework)

Once a reasonable framework was identified, the next step in framework analysis was to systematically apply the framework to all of the study data (Ritchie et al., 1994). This process, known as indexing, resembles the creation of the index in a book (Goldsmith, 2021; Ritchie et al., 1994). Segments of text were systematically coded under relevant themes, using NVivo to manage the data.

Having used NVivo14(*QSR International. (2022). NVivo Version 14*) previously for another research project during my time as a research assistant between Oct 2024 to Mar 2025, where I applied a Theoretical Domain Framework (TDF) approach to data analysis, I felt confident using NVivo for this PhD chapter. The software facilitated the organisation of interview transcripts, enabling efficient indexing and retrieval of data across the framework matrix. In retrospect, NVivo was the correct choice for indexing, as it provided an effective and systematic way to store, organise, and access the data for analysis (Gale et al., 2013). This was particularly useful, given the richness of the dataset and my aim to ensure that all data was accurately captured. NVivo facilitated a transparent approach to coding, making it easier to revisit decisions and demonstrate the analytical process during write-up.

Using NVivo, I developed parent codes based on the predefined thematic framework *(e.g., 'CTU Monitoring Strategy', 'Use of Metrics at CTU', 'Barriers to Using Metrics', 'Perceptions of Metrics in Monitoring', 'Adaptations and Future Directions', and 'Potential Interest in Metrics').* Each parent code also included child codes that were developed as part of the initial framework design, enabling structured indexing from the outset. For example, the parent code *'Barriers to Using Metrics'* contained child codes such as *'Anticipated challenges in using metrics'* and *'Staff capability to use metrics'*, which helped further explore specific obstacles faced by CTUs. Table 4.1 overleaf shows these parent and child codes in detail.

Parent Codes	Child Codes	Description
1. CTU monitoring strategy	Data quality & patient safety methods and tools	A description of the CTU's approach to monitoring in general.
	Monitoring approach	
	Site performance assessment	
2. Use of metrics at CTU	Actions taken for high scores	Insights into how metrics are applied or not applied at the CTU.
	Benefits of using metrics	
	Changing metrics score	
	Experiences using metrics	
	Factors influencing metric use	
	Reasons for not using metrics	
	Types of metrics used	
	Views on predefined metrics	
3. Barriers to using metrics	Anticipated challenges using metrics	Challenges faced by CTUs in adopting metrics.
	Contexts where metrics are (in)effective	
	Experienced challenges using metrics	
	Staff capability to use metrics	
	Training or resources provided to CTU staff to start using metrics	
4. Perceptions of metrics in monitoring	Concerns about metrics reliability	Participant views on the benefits or drawbacks of metrics.
	Perceived advantages of metrics	
	Stakeholder perceptions of metrics	
5. Potential interest in metrics	Motivators for adopting metrics (non-users)	Thoughts on motivation on use of metrics.
	Motivators for adopting metrics (users)	
	Perceived valuable metrics	
	Willingness to use metrics with tools or training	
6. Adaptations and Future Directions	Steps to improve metrics usability or recommendation	Thoughts and recommendations on ways to improve metrics use and willingness to explore further.
	Willingness to explore metrics pilots	

Table 4.1: A list of parent and child codes and their description

After completing the indexing using NVivo, I also incorporated regular reflections from my reflexive journal. This process allowed me to maintain a balance between systematic coding and personal awareness, ensuring that my interpretations remained grounded in the data.

As discussed in the previous chapter, reflexivity was central to the qualitative components of this research. In this chapter, I continued to reflect on how my role and prior experience may have shaped both data interpretation and participant interaction. I revisited my reflexive notes during analysis to support transparency and minimise bias. Reflexivity is a critical aspect of qualitative research, particularly when it involves subjective interpretation and data analysis. It requires the researcher to engage in ongoing self-examination, acknowledging how personal experiences, assumptions, and biases can influence the research process from data collection to analysis (Braun & Clarke, 2006; Ritchie & Lewis, 2003). As (Dingwall, 1998) explain, by reflecting on these influences, researchers can ensure that their findings are grounded in the data and more accurately reflect the participants' perspectives, rather than being shaped by the researcher's preconceptions or emotional responses.

In the context of my research, reflexivity played a key role in shaping the interpretation of data, especially in relation to the themes of *'Barriers to Using Metrics'* and *'Perceptions of Metrics in Monitoring'*. As I analysed the data, I made deliberate efforts to document my personal reflections on how my experiences and assumptions might affect my interpretation. This was done through regularly consulting my reflexive journal, which allowed me to critically assess how my own background and expectations were influencing the analysis.

For instance, in examining the *'Barriers to Using Metrics'* theme, I noticed recurring mentions of *'lack of tools'* and *'staff training'* as significant obstacles faced by CTUs. Initially, I was inclined to place more weight on template or guidance related barriers, based on my own experiences in clinical trials where lack of templates was a frequent issue. However, upon reviewing my reflexive journal, I recognised that this focus might be a result of my prior involvement with similar challenges related to template implementation. Acknowledging this bias, I revisited the transcripts with an open mind and gave equal consideration to the training-related challenges, which were equally prominent but had initially been overlooked.

Similarly, when analysing the *'Perceptions of Metrics in Monitoring'* theme, I found that CTUs that had not yet implemented metrics still expressed a positive outlook on their future use. Initially, I interpreted this as a sign of growing enthusiasm for incorporating metrics into their practices, which may well be true. However, after reflecting on my own positive views about metrics in my reflexive journal, I recognised that my interpretation might have been influenced by social desirability bias. Respondents may have wanted to appear progressive rather than express doubts or resistance to change. This insight prompted me to adjust my analysis to acknowledge the complexity and potential tensions in their perceptions.

The reflexive journal helped me remain vigilant about these biases and ensured that my interpretations were more balanced and nuanced. By constantly reflecting on my personal assumptions, I was able to refine my analysis and ensure that it was rooted in the data rather than coloured by preconceived ideas. This practice of reflexivity allowed me to construct a more rigorous and accurate analysis of the data, contributing to the depth and reliability of the findings.

In qualitative research, reflexivity is not only about recognising personal biases but also critically questioning the role of the researcher in shaping knowledge. Authors like (Finlay, 2002) and (Gergen et al., 2001) have highlighted the importance of reflexivity in improving the validity of research by pushing researchers to examine the power dynamics, ethical considerations, and impact of the research process. This process of ongoing self-reflection and acknowledgment of potential biases ultimately strengthened the credibility of my analysis and allowed me to stay true to the data while remaining self-aware of my own influence on the interpretation of the findings.

By reflecting on my own assumptions, I was able to adjust the framework to better capture the complexities of the data and ensure that the themes I identified were not unduly influenced by my own perspectives.

The process of indexing revealed that the data largely aligned with my predefined framework, with no major unexpected patterns emerging. All data segments were appropriately indexed into the themes that had been identified during the familiarisation and thematic framework stages. However, as I reviewed the indexed data, I assessed whether similar ideas had been grouped correctly, and I considered whether any codes needed to be merged, split, or renamed for clarity. For example,

early in the coding process, I had created a theme titled *'Positive Talk About Metrics'*. Upon further analysis, I found that the content I had assigned to this theme was better captured under the theme *'Advantages of Using Metrics in Monitoring Clinical Trials'*. This iterative process of refining and adjusting themes underscored the flexibility and adaptability required during the framework analysis process.

Once the indexing was completed, each code was thoroughly reviewed alongside the associated segments from the transcripts. This allowed me to ensure consistency in my indexing decisions and further refine the thematic structure of the data. The result was a comprehensive, nuanced set of codes that would provide a solid foundation for the next step in the framework analysis: charting the data into a framework matrix.

Charting the Data into a Framework Matrix

Once the data was indexed, I created a framework matrix that organised responses based on the themes (columns) and CTUs (rows). Each cell in the matrix contained a concise summary of the participant's relevant responses, rather than raw transcript extracts, allowing for easier comparison across cases and themes (Gale et al., 2013). For example, when analysing *'Perceived Benefits'* I summarised and grouped all positive feedback about metrics from each CTU to see if any patterns were developed. This visual aid helped identify recurring benefits such as *'improved data quality'* and *'better resource allocation'* which I could then connect to the CTUs' overall perceptions of metrics. Framework matrices enable researchers to visualise patterns, relationships, and contradictions within the data in a clear and accessible format (Ritchie, 2013). At this point I was able to see a clear picture of the findings across the dataset which helped me compare the data based on different themes. This also allowed me to group similar data together, making it easier to identify patterns or trends. By grouping and categorising the data in the framework matrix, I was able to directly address the research questions, particularly in relation to understanding the perceived benefits and challenges of using metrics in monitoring clinical trials. However, as I was dealing with a massive excel spreadsheet (exported from NVivo), I printed the spreadsheet and cut up each theme and the summaries of the themes. I was then able to move them around and group them into meaningful data groups under each theme to create the final framework matrices which contributed to clarifying relationships or patterns within the data. The final framework matrix is shown in

Appendix 20, which visualises the relationships between the themes and provides a structured comparison of the data across the CTUs.

Once the data was indexed, it was summarised and placed into a framework matrix. During this stage, some of the sub-themes within the themes were combined to provide a more coherent analysis. These are explained below.

In the *'Use of Metrics at CTU'* the two sub-themes *'Benefits of Using Metrics'* and *'Experiences Using Metrics'* were merged due to their thematic overlap. Both sub-themes described CTUs' perceptions of metrics and their practical application, which made it logical to combine them into one broader category. This allowed for a more streamlined and meaningful interpretation of the data, as it highlighted the shared insights from the participants regarding both the advantages and real-world usage of metrics in clinical trials. The decision to merge these themes was based on my observation that the practical experiences participants described aligned closely with the perceived benefits of metrics. This overlap led me to combine them into one cohesive theme to better capture the data's essence.

Furthermore, within the category of 'Use of Metrics at CTU,' two sub-themes were generated during indexing: 'Actions Taken for High Scores' and 'Changing Metrics Score.' These sub-themes both described the actions a CTU might take when a metric consistently scores high during review at a Trial Management Group (TMG) meeting. Specifically, they addressed the decision-making process regarding the potential adjustment of metrics scores or amending the protocol. Given the thematic overlap between these two sub-themes, they were grouped together to provide a more coherent interpretation of how CTUs address high metric scores. As a result, this combined sub-theme was named *'Actions Taken for High Scoring Metrics'.*

Furthermore, another category was initially named *'Steps to Improve Metrics Usability'* during the development of the thematic framework. However, as I read through the data, it became clear that many of the responses were thoughtful and practical recommendations from CTUs that could be beneficial for others in the field. As a result, I renamed the theme to *'Recommendations for Using Metrics in Monitoring'*, which I felt better captured the intent and potential impact of the participants' insights. This iterative process of reviewing and merging themes allowed me to refine my analysis, ensuring the final themes best represented the data.

Similarly, in the theme *'Barriers to using metrics'*, I initially created two sub-themes: *'Anticipated challenges using metrics'* and *'Experienced challenges using metrics'*. The aim was to capture the views of CTUs that do not use metrics, focusing on the anticipated challenges they foresee in setting up metrics. On the other hand, the second sub-theme aimed to understand the lived challenges of those CTUs that do use metrics in their monitoring practices. However, there was insufficient data in the first sub-theme, and considerable overlap with the second. As a result, I decided to combine these two sub-themes into a single theme titled *'Challenges of using metrics'*. Additionally, a sub-theme titled *'Willingness to use metrics with tools or training'* was initially created under the theme *'Potential interest in metrics'*. However, because there was a similar sub-theme, *'Willingness to explore metrics pilots'*, under the theme *'Adaptations & Future Directions'*, it was removed to avoid duplication. Once all the themes and sub-themes were reviewed, I decided to change the name of the theme *'Adaptations & Future Directions'* to *'Future Work'*. I felt that this was a better fit for the themes considering the data were included in this theme. The theme *'Potential interest in metrics'* was changed to *'Motivators for using metrics'* as I felt this was also a better title for this category. *'Perceived valuable metrics',* was also removed from this theme as data about what participants perceived as valuable data was capture better in *'Types of metrics used'*. Table 4.2 overleaf shows the final set of codes and parent codes when renaming and grouping was completed.

Parent Codes	Child Codes	Description
1. CTU monitoring strategy	Data quality & patient safety methods and tools	A description of the CTU's approach to monitoring in general.
	Monitoring approach	
	Site performance assessment	
2. Use of metrics at CTU	Benefits of using metrics	Insights into how metrics are applied or not applied at the CTU.
	Reasons for not using metrics	
	Types of metrics used	
	Views on predefined metrics	
3. Barriers to using metrics	Contexts where metrics are (in)effective	Challenges faced by CTUs in adopting metrics.
	Challenges using metrics	
	Training or resources required	
4. Perceptions of metrics in monitoring	Concerns about metrics reliability	Participant views on the benefits or drawbacks of metrics.
	Stakeholder perceptions of metrics	
5. Motivators for using metrics	Motivators for adopting metrics (users)	Thoughts on motivation on use of metrics.
6. Future Work	Recommendations for Using Metrics in Monitoring'	Thoughts and recommendations on ways to improve metrics use and willingness to explore further.
	Willingness to explore metrics pilots	

Table 4.2: Final set of codes and parent codes.

Mapping and Interpretation

(Goldsmith, 2021) describes the final stage of framework analysis, mapping and interpretation, as the process of synthesising insights gained from the previous steps and systematically exploring patterns within the data. In this stage, I thoroughly

immersed myself in the data, reviewing the framework matrices and revisiting the indexed data to identify key patterns, relationships, and contradictions that emerged across the dataset. By doing so, I was able to refine my understanding and generate deeper insights into the data. In the final stage, I printed out the framework matrix and physically moved sections of data under each theme to make sure they aligned with the emerging patterns. This manual process helped me visualise the relationships between themes, ensuring that themes like *'Barriers to Using Metrics'* and *'Perceived Benefits'* were adequately represented. Once all themes were grouped together, I reviewed the matrix to confirm the consistency of my thematic structure, leading to the finalisation of the framework.

At this point, I grouped and organised the matrices that had overlaps, carefully considering variations across and within the units of analysis (CTUs) to explore the richness of the data. This process allowed me to identify overarching patterns, trends, and emerging themes. To assist in this, I asked myself critical questions such as: What are the key insights from each theme? For example, regarding the theme *'staff training needs',* what specific gaps were identified in training, and how did these gaps affect the implementation of metrics? Similarly, in the theme *'barriers to using metrics'* what were the most common challenges CTUs faced in adopting metrics?

During this mapping process, I was able to integrate developing themes into the analysis, refining the structure of my findings. I used predefined themes as a guide while ensuring that I remained open to discovering new patterns in the data. This process included comparing differences across CTUs, identifying subgroups, and recognising clusters of data. The framework matrices visually represented the relationships between themes and patterns across the CTUs, providing a clear picture of the findings. This matrix allowed me to compare data points under each theme and better understand how different CTUs approached and perceived metrics.

To ensure credibility in my findings, I also consulted with a colleague at the MRC CTU who had extensive experience in qualitative research. This step provided an additional layer of scrutiny and helped ensure that my interpretation of the data was accurate. Moreover, during the interviews, I made efforts to check my understanding of participants' views by occasionally using clarifying prompts such as, *'If I understood you correctly, you said this […]'*. While this approach can help surface

misinterpretations and promote mutual understanding, it does not eliminate the risk of researcher bias or distortion through paraphrasing. Such forms of real-time checking can enhance credibility, but they must be used cautiously, with an awareness of the researcher's interpretive influence (Lincoln & Guba, 1985). I therefore treated these prompts as opportunities for clarification rather than confirmation, recognising the co-constructed and interpretive nature of qualitative interviews.

During the interviews, I made efforts to check my understanding of participants' views by occasionally using clarifying prompts such as, "If I understood you correctly, you said this…". While this approach can help surface misinterpretations and promote mutual understanding, it does not eliminate the risk of researcher bias or distortion through paraphrasing. As noted by (Lincoln & Guba, 1985), such forms of real-time checking can enhance credibility, but they must be used cautiously, with an awareness of the researcher's interpretive influence. I, therefore, treated these prompts as opportunities for clarification rather than confirmation, recognising the co-constructed and interpretive nature of qualitative interviews.

Through this process of mapping and interpretation, I identified specific patterns in the data, particularly regarding the challenges CTUs faced in using metrics for monitoring clinical trials. This mapping and interpretation process allowed me to construct a coherent narrative that not only captured the data's structure but also highlighted the dynamic interactions between different themes, providing a comprehensive understanding of the challenges and potential for metrics in clinical trial monitoring.

4.7 Quality Assurance

To ensure the rigour and trustworthiness of the qualitative findings presented in this chapter, I followed the same procedures outlined in Chapter 3 section 3.7. These included steps such as maintaining reflexivity, involving peer review of coding, and using a systematic analysis framework. Full details of these procedures are provided in Chapter 3 to avoid unnecessary repetition here.

4.8 Results

This section presents the findings from the six interviews conducted with UK Clinical Trials Unit (CTU) staff regarding the use of metrics in trial monitoring. The results section outlines the key findings from the data analysis, which was guided by the

predefined thematic framework. The analysis focused on identifying the challenges, perceptions, and potential benefits of using metrics in monitoring clinical trials, as well as understanding CTUs' current practices and their openness to adopting new metric-based approaches. In some theme similarities and differences of the CTUs practices are highlighted, whereas other themes present the overall agreement that was observed in the data. Where relevant, illustrative quotes from participants are included to provide deeper insight into the experiences and perspectives shared. To keep participant anonymity, the illustrative quotes do not mention the names of the CTUs. However, they do include information about the participant's role within the CTU and their years of experience.

Theme One: CTU Monitoring Strategy

The CTU Monitoring Strategy was a theme I wanted to explore at the beginning of the interview, as it is a critical component of clinical trial management. It directly influences how effectively clinical trials are monitored, data is captured, and patient safety is ensured, especially considering that monitoring practices can vary across different CTUs. This theme explored the approaches taken by CTUs in monitoring their clinical trials, including the tools, methodologies, and processes they employ. To me as researcher it was essential to understand these strategies as they provide insight into the broader practices surrounding trial monitoring, especially in relation to the use of metrics.

From the data gathered, it became clear that all six CTUs have a risk-based monitoring approach, with varying emphasis on central, remote, and on-site methods. The monitoring strategy of each CTU is shaped by factors such as available resources, the complexity of the trials being conducted, trial risk level, trial sponsor requirements and the regulatory requirements they need to meet. By examining the responses from participants, this theme aims to highlight the similarities and differences in monitoring strategies across CTUs, as well as to identify the effectiveness and limitations of the approaches used.

In this section, I will explore the different monitoring strategies identified in the data, focusing particularly on the sub-themes which are how CTUs evaluate and manage data quality and patient safety, the role of site performance assessment, and monitoring approach. This analysis will provide a deeper understanding of the practical

implications of monitoring strategies and the role of metrics in shaping these strategies.

Sub-theme one: Monitoring Approach

All six CTUs mentioned using a risk-based approach to monitoring their trials, guided by a trial monitoring plan developed during early stages of the trial set up. The following will discuss CTUs monitoring approaches similarities and differences in detail, followed by a summary of it all.

Similarities:

All CTUs follow a risk-based monitoring strategy. The use of predefined risk factors and thresholds for triggering monitoring visits is a common approach. CTUs conduct monitoring visits based on the risk assessment performed at the start of the trial, with the frequency and intensity of visits tailored to the trial's risk profile.

All the CTUs emphasise flexibility in their monitoring approach. This flexibility allows them to adapt to emerging challenges, changing trial circumstances, and the available resources. For example, some CTUs prioritise on-site visits during the early stages of trials when recruitment is active and may shift to remote or central monitoring as the trial progresses.

Across all CTUs, monitoring is focused on high-risk areas, sites, or activities. For example, sites with poor performance, high recruitment rates, or high missing data rates are given particular attention. Monitoring is also adapted to specific trial needs, such as monitoring critical data points like pharmacokinetics or IMP procedures.

Most of the CTUs have a set of predefined metrics used to assess the trial’s progress and guide the monitoring approach. These metrics include recruitment rates, data quality, site performance, and non-compliance reports, which are central to triggering monitoring visits or remote assessments.

All CTUs aim to optimise resource use by focusing on high-priority sites and activities. This is especially evident in CTUs like Nottingham, which performs most monitoring centrally and resorts to on-site visits only when necessary. Similarly, CTUs like Leeds and Warwick emphasise the importance of efficient resource allocation, particularly when budgets are limited in the later stages of trials.

Differences:

The use of technological tools to support risk-based monitoring varies among CTUs. For example, Warwick CTU use a central Excel-based tool for tracking risk items and metrics, while Cambridge focus on predefined risk factors for specific trial milestones, Leeds work with an in-house bespoke monitoring tracker and Nottingham use the recently developed UKCRC monitoring triggers and metrics tool. On the other hand, NWORTH use an approach with more flexibility in tailoring their monitoring process to the individual needs of each trial.

In terms of type of monitoring, while most CTUs follow a combination of central, remote, and on-site monitoring, the emphasis varies. Some CTUs, like Leeds, Warwick, Plymouth, Cambridge and Nottingham, rely more on central monitoring, particularly for low-risk trials, while others, like NWORTH, are more focused on on-site visits, particularly for underperforming sites. A quote from a participant who prefers more on-site visits was very interesting to note:

'I think it's nice (to conduct on-site visits) because it gives us a bit of a face to face, and you get a bit of a rapport with the site.' (Monitor, over 20 years of experience)

The quote below is from a different CTU. In here the participant explains the different approaches of monitoring based on the trial phase:

'Again, if it's an early phase trial, we may want to do 100% SDV of each participant at a specific time point. If it's a later phase trial, which is a lot larger with a lot of sites and a lot of participants, we might do more selected.' (Monitor, 10 years of experience)

The quote below is from another CTU which explains with an example how the focus of monitoring can change depending on the trial:

'For instance, if the trial is using a new IMP, we will focus on pharmacy processes and the unblinding process at a monitoring visit. If they're doing pharmacokinetics analysis, as part of the primary endpoint, we would focus on lab aspects for the monitoring visits.' (Quality Assurance officer, over 10 years of experience)

Another interesting point that was also raised by a few CTUs (e.g., NWORTH and Warwick) was the emphasis on early on-site visits within the first six months to engage with the site team and identify issues proactively. This early engagement helps build

rapport and ensure smooth trial operations. Cambridge and Leeds CTUs also use specific triggers early on, but their focus is on milestone events or high recruitment rates.

'For instance, a common trigger will be high recruitment rates, the highest recruiting sites we would do on site monitoring visits for.' (Quality Assurance officer, over 10 years of experience)

Warwick CTU has notably adapted its processes post-COVID, adopting remote-friendly processes that align with evolving trial needs. Other CTUs like Leeds and Nottingham also consider remote engagement but do not mention COVID-related changes as explicitly.

While non-compliance is a common trigger for further monitoring, the way each CTU addresses it differs. Leeds CTU use an in-house bespoke trigger spreadsheet to track non-compliance, while Plymouth CTU discusses these issues in trial management meetings. Nottingham CTU, on the other hand, take a more tailored approach, only initiating on-site visits, when necessary, based on the metrics and triggers tool's output.

In summary, the monitoring strategies across the CTUs share a common risk-based framework, with flexibility built in to adapt to the trial's progress and resource availability. However, differences arise in the specific tools used, the emphasis on on-site versus remote monitoring, and the handling of non-compliance and early engagement. These differences reflect the varied contexts and needs of the trials each CTU supports, with some prioritising early engagement and others focusing on efficiency and adaptability throughout the trial lifecycle.

Theme Two: Use of metrics at CTUs

Sub-theme one: Benefits of using metrics

Similarities:

All CTUs using metrics described a recent and established use of metrics in their practices. For example, Leeds, Nottingham, Plymouth and Warwick CTUs all describe a recent shift to more formalised metrics-based monitoring, which is still evolving. However, it's important to note that some CTUs described that they have been using metrics as part of their centralised monitoring, but they have only recently started using

the metrics to inform their monitoring approach. The quote below, is shown as an example.

'We have always done the central monitoring. We've always, monitored metrics centrally, but we haven't always used that to inform monitoring if that makes sense.' (Lead clinical trials associate, over 6 years of experience)

All CTU using metrics in their monitoring approach highlighted the efficiency and targeted nature of metrics-based monitoring. This seems to be the biggest and most important benefit of using metrics by CTUs. The participants describe how metrics allow for more focused and context-sensitive decisions in monitoring (Cambridge CTU), whether that's addressing missing data, recruitment targets, or site-specific issues (Leeds CTU). By using metrics, CTUs can focus on critical areas and avoid a blanket approach, which improves the relevance of their actions. Some quotes from participants are shown below:

'Using a metrics-based approach, the monitor has a lot more focus on what the issue is and then know what to look for in terms of root causes. Which I think is really beneficial to us and to site rather than doing a blanket approach of sort of going to site and just choosing a random patient doing SDV, but then we're not necessarily finding the cause of the issue. (Monitor, over 10 years of experience)

The use of metrics results in a more strategic allocation of resources, ensuring that time and effort are concentrated on the areas that matter most, especially in larger, late-phase trials (Leeds). This results in a more cost-effective and practical approach to monitoring, as opposed to traditional resource-intensive methods like routine site visits (Plymouth).

'Where we found it really useful is these larger late phase trials because we don't have the monitoring resource to visit every site. We need to really take a risk-based approach. And so obviously using central monitoring using these metrics to guide where the risks actually are, which sites actually require monitoring, has been really beneficial for the trials that we've used it on.' (Quality Assurance Manager, over 20 years of experience)

CTUs highlight metrics provide a clearer view of site-specific challenges, allowing CTUs to adjust their monitoring efforts according to the issues identified (Leeds and

Plymouth CTUs). For example, targeted visits based on high recruitment or non-compliance rates ensure that resources are focused on areas that need the most attention (Cambridge and Leeds CTUs).

Ultimately, they viewed metrics as tools to identify potential problems early, with on-site or remote monitoring then used to confirm issues and develop Corrective And Preventive Actions (CAPAs). Without this approach, monitoring would be more random and less effective in safeguarding trial quality and integrity.

'So, for example, if a site has scored high on those pharmacy triggers, then we know that we need to do a longer pharmacy visit and that can be a lot more fruitful.' (Lead clinical trials associate, over 6 years of experience)

'So, for example, we have some issue of non-compliances with a particular trial and then we may look at that again at another point and see if that's reduced as well.' (Monitor, over 10 years of experience)

Furthermore, learning and refining the use of metrics is acknowledged by many CTUs. As CTUs gain more experience with metrics, they become better at identifying the most critical indicators that impact trial outcomes. The learning curve mentioned in Plymouth and Leeds highlights the evolving understanding of what metrics are most relevant and how to interpret them effectively.

'And again, once you get used to looking at it (metrics), you know what's important and what's not, so you can end up with lots of metrics. But it's knowing what's the important metric and what's not. You know what's going to affect the outcome of your study and what is not.' (Monitor, over 10 years of experience)

This sub-theme also emphasises that the use of metrics allows for data-driven decisions, which are more flexible and adaptive to changing circumstances. For example, Leeds CTU emphasise that metrics trigger more focused, actionable responses, while Cambridge describes how metrics lead to informed decisions about when to trigger site visits.

Differences:

Leeds CTU mention that metrics allow for a proportionate response and targeted interventions, ensuring that resources are used efficiently. For instance, monitoring

visits might be avoided or replaced with other forms of engagement if the issue isn't critical.

Warwick CTU, by contrast, describes a more adaptive, evolving approach, where thresholds are continuously reviewed and adjusted based on ongoing performance and contextual factors. This adaptability helps the CTU respond to real-time data, suggesting a more dynamic and continuous approach to using metrics.

In summary the similarities between the experience and benefits of using metrics show that both offer substantial improvements in trial monitoring through enhanced efficiency, focus, and data-driven decisions. The differences primarily relate to the stage of adoption, flexibility in metric use, and challenges in determining the most relevant metrics for each trial. Overall, metrics offer benefits across all CTUs, but the degree to which they are embedded in practices and the approach to their use varies depending on the specific context of the CTU.

Sub-theme two: Types of metrics used

Similarities:

Across all CTUs, there is a strong emphasis on monitoring patient safety and data quality as part of their core metrics. This includes monitoring Serious Adverse Events (SAEs), non-compliance, series breach and protocol deviations (Nottingham, Plymouth, Warwick, Cambridge, Leeds CTUs). These metrics are consistently used to track the integrity of the trial, ensure compliance with protocols, and monitor the safety of participants. Additionally, data quality checks such as the accuracy of consent forms, screening logs, and tracking patient recruitment are widely used (e.g., Plymouth, Nottingham CTUs).

Furthermore, recruitment rates are a common metric used across CTUs as a trigger for monitoring activities. Cambridge, Plymouth, and Leeds CTUs all highlight recruitment as a primary metric, with recruitment issues such as high recruitment rates or loss to follow-up prompting site visits or further investigation (Cambridge, Plymouth CTUs).

Non-compliance is a critical metric across all CTUs. Whether it's missing data, missed visits, or late reported consent forms, non-compliance is closely tracked and can trigger further investigation or action (Cambridge, Nottingham, Leeds CTUs). The

CTUs also use non-compliance data to evaluate site performance and identify underlying issues that may require intervention.

Trial-specific metrics are employed in each CTU to cater to the unique characteristics of different studies. For example, Leeds CTU use trial-specific metrics such as monitoring metrics for drugs with particular risks to track dose reduction and whether re-evaluation of the drug triggers a monitoring visit. Similarly, Warwick and Leeds integrate site-specific metrics such as CRF return rates, adapting to each trial's risk profile.

Differences:

Some CTUs (like Warwick and Leeds) incorporate a flexible approach to metrics, where monitoring plans are adjusted based on trial-specific characteristics and risk profiles. For example, Warwick varies its monitoring metrics based on site performance and CRF return rates, while Leeds allows trial teams to carefully select metrics relevant to each study's specific needs. In contrast, Nottingham CTU uses a more structured set of core metrics, with predefined checks for SAEs, data quality, and site performance.

Leeds CTU is particularly focused on the adjustment of metric thresholds based on real-world data and outcomes, such as modifying thresholds when metrics consistently score high or low. This ongoing refinement helps ensure that the metrics remain relevant and accurate. Warwick and Plymouth CTUs, however, do not seem to emphasise on adjusting thresholds but use the established metrics to evaluate and monitor trial progress.

Plymouth CTU emphasises the trend analysis of key metrics, particularly looking for patterns in SAEs over time, focusing on recurrent issues or issues of special interest. This trend-based approach contrasts with Cambridge CTU, which uses high recruitment rates and protocol-specific milestones (e.g., cycle one in dose escalation studies) as primary triggers for monitoring visits. The focus on trends in Plymouth CTU offers a more dynamic and data-driven approach, while Cambridge CTU focuses more on milestone-based monitoring.

Leeds CTU places significant emphasis on the role of remote data entry and electronic systems in streamlining the use of metrics and improving data access. In comparison,

while other CTUs such as Nottingham, Cambridge and Warwick mention digital tools like (Research Electronic Data Capture) REDCap and non-compliance systems, the use of electronic systems is not as heavily emphasised. Leeds CTU's focus on technology highlight how digital transformation can drive metrics-based monitoring, making data analysis faster and more efficient.

A few quotes below from some of the participants help put some of the items discussed above into perspective:

'So, whenever I'm trying to get new sites to use these metrics, I'm always trying to encourage sites to really think about how they're setting those different metrics and what they want to think about in terms of what's important, what's a higher risk, what's low, what's medium.' (Lead clinical trials associate, over 6 years of experience)

'That's the first metric we ever look at is recruitment. And obviously, as a study runs, the other important thing is the loss to follow up as well.' (Quality Assurance Manager, over 20 years of experience)

'Obviously, noncompliance and what we're looking is whether this is a trend. And I mentioned SAEs, yes, obviously an SAE I'm looking for trends there as well.' (Quality Assurance Manager, over 20 years of experience)

'For instance, a common trigger will be high recruitment rates, the highest recruiting sites we would do on site monitoring visits for but also for let's say I have a dose escalation study where the data has to be monitored at the end of cycle one, because there's a committee that bases their decision for dose escalation on that data, we have to review all of that data at the end of cycle one.' (Quality Assurance officer, over 10 years of experience)

In summary across all CTUs, core metrics related to patient safety, data quality, and non-compliance are consistently used, forming the backbone of their monitoring strategies. The key difference lies in the flexibility and adaptability of these metrics, with CTUs like Leeds and Warwick offering more customised, trial-specific metrics, while others like Nottingham maintain a more standardised set of metrics. Furthermore, some CTUs, particularly Leeds, emphasise the adjustment of thresholds for specific metrics, whereas others focus more on trend analysis and milestone-based triggers. Additionally, the use of technology in data collection and remote monitoring is

more prominent in Leeds CTU, aligning with the more dynamic approach to metrics. Overall, while the core metrics remain consistent across CTUs, their application, focus, and technology integration reflect the varied practices across different research environments.

Sub-theme three: Reasons for not using metrics

This sub-theme is discussed in detail, particularly in relation to NWORTH, but also includes the views of other CTUs on the challenges that hindered the adoption of metrics in the monitoring practices, where relevant. The summary combines the data without breaking it down into similarities and differences, as the available data is limited and does not warrant such a detailed analysis.

Some CTUs shared common challenges that have hindered the adoption of metrics in their monitoring practices. A primary factor is the historical lack of use within some CTUs, where metrics have simply not been part of their standard operating procedures. The absence of a tradition of using metrics led to no significant push for their implementation, despite the potential benefits. However, a recent change in leadership in one particular CTU, including the appointment of a new director with a statistical background, has created optimism for incorporating metrics in the future, especially if suitable tools become available.

Additionally, the nature of the studies managed by the CTUs plays a role in their stance to adopt metrics. Many trials are non-CTIMPs and lower risk, often focusing on complex interventions rather than Investigational Medicinal Products (IMPs). As such, there is a perception that metrics may not be essential or necessary in these settings. At NWORTH, their involvement in trials typically includes providing services such as statistics, IT, and quality assurance, while overall trial management is usually led by external sponsors or collaborators. This hybrid model further complicates the adoption of metrics, as the CTU is required to follow the sponsor's monitoring plans, which may not include metrics.

'I think as well, a lot of our studies aren't CTIMPs well. So, I think that probably plays quite a big role in it. So, we do a lot of non-CTIMP non-drug studies probably more lower risk but complex intervention studies. So, I think that probably plays quite a big part in it.' (Monitor, over 20 years of experience)

'So, for quite a lot of our studies, we offer more discrete aspects of work. So, we'll maybe just provide the IT side of things, the stat side, quality assurance for some of the studies, the sponsor lies elsewhere, and they request that we followed their SOPs.' (Monitor, over 20 years of experience)

Another significant challenge is the confusion and difficulty in selecting appropriate metrics for each trial. Some CTUs expressed uncertainty about which metrics are necessary and how they should be aligned with the trial's risk level. The number of available metrics further complicates the selection process, creating challenges in determining which metrics should be tracked on a monthly basis or cumulatively. This uncertainty has been exacerbated by insufficient training on the effective use of metrics, leading to difficulties in prioritising the right metrics and excluding less relevant ones. This further highlights the importance of appropriate training and tools to be provided to trialists.

'People get confused as to which ones they need for their trial. And which ones are appropriate according to risk?' (Monitor, 10 years of experience)

'You add as much as you can to aid the person that's picking it up to just choose what they need, but then I think what I found is there's too much in there because they don't know which ones they don't need, if that makes sense. I think we're struggling with that at the minute. And I think that's partly down to training.' (Monitor, 10 years of experience)

Overall, these reasons highlight the complexity and barriers CTUs face when incorporating metrics into their monitoring processes, with historical practices, study types, limited resources, and confusion about metric selection all playing key roles.

Sub-theme four: Views on predefined metrics

I was interested in understanding participants' views on using predefined metrics in monitoring clinical trials, and the majority of responses were in agreement.

Overall, participants agreed that predefined metrics can serve as useful guidelines. However, they caution that these metrics should only be included in the monitoring plan if they directly relate to the risks identified during the risk assessment phase. Predefined metrics should not be rigid but flexible and adaptable to the specific needs and characteristics of each trial.

There was a strong emphasis on the need for flexibility. One participant noted that predefined metrics should be introduced at the start of a trial during the risk assessment stage, with the option to modify or introduce new metrics as the study progresses. This flexibility ensures that the metrics remain relevant and aligned with the trial's objectives and evolving needs. The scoring system is also adaptable, which allows for adjustments based on real-time monitoring outcomes.

'I mean we do that sort of approach. I think it's important to have some metrics that are defined at the start of the trial. I guess it depends on how predefined they are really, I think we would almost predefine them at the stage of risk assessment rather than before that.' (Lead clinical trials associate, over 6 years of experience)

Some participants, citing concerns from the MHRA, expressed that predefined metrics could be too prescriptive and rigid. The caution here is that what may work well for one trial, especially a low-risk study, may not be appropriate for another, particularly a higher-risk trial such as phase one oncology trials. As a result, some CTUs have removed predefined metrics altogether, preferring to tailor each trial's monitoring plan to its specific context.

'Knowing what the MHRA said about as predefining certain things in our metrics tool. They were very much against it because it was too prescriptive to give trials units.' (Monitor, 10 years of experience)

Despite concerns, there was agreement that some core predefined metrics, such as recruitment, data quality, participant safety, serious breach and protocol deviations are essential to the success of any study. These metrics are foundational and reliable indicators of a trial's progress and performance. However, participants acknowledged the challenge in defining appropriate metrics for all types of studies and emphasised that flexibility is needed in the selection and application of these metrics.

'So basically, the only things that really undermine your study are kind of the recruitment, quality of data and safety. So, if you've got minimum those three metrics you know you've got a reasonable metric to measure what you think you're measuring.' (Quality Assurance Manager, over 20 years of experience)

'I would say an ongoing challenge is just being prescriptive enough for the metrics to be worthwhile, but not so prescriptive that it becomes a job in itself. Yeah, doesn't double workload.' (Monitor, 10 years of experience)

The opinion is also that the use of predefined metrics should depend on the specific risk profile of each trial. Larger, more complex trials may require different metrics than smaller, less risky studies. This is particularly important as the size, number of sites, and type of trial will determine which metrics are appropriate.

'It depends a little bit on the risk profile of the study, the number of sites, the size and scale of the studies in that way. But we would have a similar structure for all with the same route.' (Monitor, over 20 years of experience)

In summary, the majority of participants recognise the value of predefined metrics but stress that they should not be rigidly applied across all trials. Flexibility, contextual relevance, and adaptability are essential. Predefined metrics are seen as helpful when they are directly tied to the specific risks and characteristics of a trial, but they should not be used to constrain the monitoring process. Moreover, some participants prefer to tailor the monitoring plan and metrics based on the unique context and needs of each trial, rather than relying on a one-size-fits-all approach.

Theme Three: Barries to using metrics

Sub-theme one: Challenges of using metrics

CTUs face a range of challenges when adopting and using metrics in clinical trial monitoring. Anticipated challenges often revolve around the technical infrastructure and resource limitations, sponsor requirement and type and risk of trials. For instance, CTUs like Cambridge and NWORTH highlighted the importance of having the right tools and systems, with Cambridge CTU noting difficulties in extracting data from their database due to technical limitations (relying on programmers to do so) and NWORTH pointing to the lack of previous experience and the influence of sponsor requirements as barriers to integrating metrics.

'So, although we've shifted to risk-based monitoring to be honest at the minute our tools to set the triggers and to monitor the things are quite difficult. We use Macro at the minute, and if we needed to get any reports from it, we would have to go to a programmer and then maybe a statistician to like extract the report in a meaningful

manner and then like pull out figures.' (Quality Assurance officer, over 10 years of experience)

Similarly, Leeds CTU identified funding and resource constraints, especially for large trials, while Nottingham CTU highlighted the lack of clarity around selecting the right metrics and the need for more training. Another CTU further explained that although metrics save a lot of time once all set up and running, the process to setting them up can be time consuming.

'We've implemented this triggered monitoring, which has been a positive, but the drawback is that we just don't have that much time.' (Lead clinical trials associate, over 6 years of experience)

Leeds and Warwick CTUs both noted that the complexity of interpreting metrics and the challenges of balancing the amount of data with actionable insights were significant hurdles. Nottingham CTU, on the other hand, highlighted operational overload due to the use of multiple reporting tools and a lack of role clarity, which made managing metrics difficult. Plymouth CTU also highlighted that paper records previously was a hurdle to using metrics effectively.

'You know, somebody had to transcribe data into an electronic system (from paper), then you had to verify it. And if you then actually exported that to do metrics as well, you then have to have another check just to make sure that whatever you'd exported was correct as well.' (Quality Assurance Manager, over 20 years of experience)

'I think it caused a lot of confusion. It was all implemented alongside a lot of other things like reports and stuff to try and help staff just be able to pick it up and use it. But like I say, I think there's too much there now and we need to try and streamline it. And it's not just the metrics that have complicated, it's all the different reports, but obviously the different reports are where all the metrics are held.' (Quality Assurance Manager, 10 years of experience)

Overall, the data shows challenges focus largely on preparation of tools, resource allocation, and practical struggles CTUs face once metrics are implemented. The key issues often relate to infrastructure limitations, the need for training, and the adaptation of existing workflows to accommodate new processes. These ongoing challenges

underline the importance of proactive planning, resource allocation, and continuous training to ensure the successful use of metrics in clinical trials.

Sub-theme two: Contexts where metrics are (in)effective

In this sub-theme I was exploring with participants whether they can think of any situations where use of metrics is more effective or ineffective. The responses were similar across the board; therefore, I have summarised the data as a whole. In the responses from the CTUs, the effectiveness of metrics in clinical trial monitoring was primarily influenced by the type and scale of the trial, as well as the risk profile of the study.

Metrics are universally regarded as highly valuable in monitoring safety, especially in clinical trials involving investigational medicinal products (CTIMPs). Most CTUs such as Leeds, Nottingham, NWORTH and Warwick emphasised that safety metrics play an essential role in ensuring ongoing regulatory compliance and are crucial for tracking and responding to safety issues effectively. This sentiment was echoed by Plymouth CTU, which also highlighted the use of safety metrics as a core part of drug trials, especially for regulatory bodies like the MHRA.

However, the usefulness of metrics is considered to be strongly context-dependent, and this was agreed by all CTUs. Larger, later-phase trials benefit from the application of centralised metrics, which help to identify sites requiring closer attention. CTUs like Cambridge and Leads described how centralised metrics are useful for managing large-scale trials with multiple sites. These metrics help to focus monitoring efforts and resources on the areas where they are most needed, making them particularly valuable in larger studies where resource constraints are a significant consideration.

‘Certainly, for drug studies, metrics are very useful. And it kind of satisfies the MHRA that what you're looking at, you know, makes them feel confident that you are kind of following a risk-based strategy.’ (Quality Assurance Manager, over 20 years of experience)

In contrast, smaller and early-phase trials present different challenges when applying metrics. For these trials, especially those with fewer than 10 sites, the monitoring visits are already frequent and detailed. As a result, metrics can become less applicable and may not provide additional value. This was highlighted by CTUs like Leeds and

Cambridge, which pointed out that in these cases, the signal-to-noise ratio of metrics is too low, and the frequent site visits make the application of metrics less necessary.

'I don't think it's particularly effective for smaller trials. So, we have quite a few early phase trials and we don't use this approach on our smaller early phase trials, so trials that only have maybe under 10 sites maybe under 100 participants. I think the signal to noise ratio in the data is too difficult to unpick.' (Monitor, 10 years of experience)

The effectiveness of metrics in lower-risk trials was also discussed. CTUs like Nottingham and Plymouth discussed that for lower-risk trials or observational studies, the need for metrics is less critical. In these cases, other validation methods may be more suitable. For instance, in qualitative research, Plymouth CTU suggested that metrics are less applicable, as non-interventional research typically uses different methods for ensuring data quality. Nottingham CTU also emphasised that in these studies, metrics should be applied pragmatically, focusing only on data that directly informs critical decisions or monitoring needs.

Ultimately, CTUs acknowledged the importance of using metrics selectively and adapting their application based on the specific needs of each study. While safety metrics are crucial across all trial types, the application of centralised or risk-based metrics should be adapted to suit the size, scope, and phase of the trial. This ensures that the use of metrics is both efficient and meaningful.

'I think the riskier the trial you've got in terms of you know whether you've got like an IMP involved and that kind of stuff they are more useful and more critical to your data because you're going to be wanting to look at safety more and you know compliance and that kind of thing.' (Senior Quality Assurance Manager, over 10 years of experience)

Sub-theme three: Training and resources required

Across all the CTUs, I observed a clear recognition that training is essential for the successful implementation and use of metrics in trial monitoring. However, the level of training and resources required, as well as the stage of training implementation, varies. Due to this variation, I have broken down the requirements for each CTU below and will compare their similarities and differences.

NWORTH: The CTU described a proactive culture towards learning and skill development. They have a structured training process in place, but there is an openness to external support for additional training, particularly regarding metrics. This suggests that NWORTH staff are already well-equipped for general training, but specific training on metrics is still a developing area.

Cambridge CTU: Similar to NWORTH, Cambridge acknowledged the necessity for staff training on metrics, particularly with their transition to using the REDCap system to facilitate the better use of metrics. Training efforts are underway, starting with system training and expanding to more advanced metrics-based training. This indicated that Cambridge CTU is in the early stages of embedding metrics-related training into their processes.

Leeds CTU: Leeds CTU provides extensive and structured in house training on metrics to their staff. They have developed their own tools for monitoring and have trained staff on how to use them. The training includes detailed sessions on how metrics are applied in monitoring, emphasising practical skills. Leeds CTU seemed to be more advanced in integrating training on metrics into their workflows, with internal tools and recorded sessions available for continuous learning.

Nottingham CTU: Nottingham CTU recognises the lack of sufficient training as a barrier to effective use of metrics. They are taking steps to address this by creating a new job role dedicated to monitoring processes and staff training. The CTU plans to provide training on both the tools and the contextual application of metrics, suggesting a more structured approach is in development.

Plymouth CTU: Plymouth CTU staff are described as proactive and capable of using electronic systems like REDCap for data management, which suggests they have the necessary skills for metrics-based monitoring. However, there is no specific mention of formal training, suggesting that the CTU may rely more on informal, on-the-job learning or that they are already proficient with the available tools.

Warwick CTU: Warwick CTU emphasises that training must not only cover technical aspects but also practical guidance on integrating metrics into daily workflows. This includes clarifying roles, responsibilities, and actions to take when metrics indicate issues. Warwick CTU is integrating training within broader trial processes, making it part of the overall monitoring framework rather than focusing on metrics alone.

I now look more deeper into comparing the similarities and differences between these CTUs.

Similarities:

All CTUs emphasise the importance of training, particularly regarding the use of metrics for monitoring. Whether they are at the beginning stages or more advanced, they recognise that training staff is essential to ensure successful adoption and implementation of metrics.

Most CTUs integrate training into their existing trial and monitoring workflows, whether by developing new roles (e.g., Nottingham CTU), updating existing sessions (e.g., Warwick CTU), or embedding training into system rollouts (e.g., Cambridge CTU).

Differences:

Some CTUs, like Leeds, already have well-established training programs on metrics, while others like Plymouth and NWORTH are in the early stages of developing or expanding their training. Nottingham and Cambridge CTUs are also actively working on embedding training into their systems, and their current focus is on developing roles and systems for training.

Leeds and Warwick CTUs provide comprehensive, structured training that covers not just the technical aspects of metrics but also how they are integrated into trial processes. Warwick CTU places particular emphasis on practical, hands-on training and clarifying roles and responsibilities. In contrast Cambridge, and Nottingham CTUs are still focusing on foundational training and systems integration, with varying levels of resource allocation.

Cambridge and Plymouth CTUs specifically mention the use of electronic tools like REDCap to aid in metrics implementation, suggesting that training may be more tool specific. In contrast, Leeds and Warwick CTUs focus more broadly on the principles and practices behind metrics-based monitoring, not limiting training to specific technologies.

In summary, training and resources required for metrics usage are recognised across the CTUs as essential for effective monitoring. While some units have advanced training structures in place, others are still working on integrating training within their

existing systems and workflows. The emphasis on practical application and the integration of training into the trial's broader monitoring plans is becoming a key feature for most CTUs.

Theme Four: Perceptions of metrics in monitoring

Sub-theme one: Concerns about metrics reliability

This theme aimed to explore the perceptions of metrics among CTU staff, regardless of whether they currently use metrics in their monitoring practices. I was particularly interested in understanding whether there was general positivity towards the concept of metrics, as well as any concerns about their reliability and stakeholder perceptions. My findings indicate that there is indeed widespread support.

Overall, my observation was that there is a shared understanding across CTUs that the reliability and usefulness of metrics depend heavily on the trial context, including the type of study, the nature of the intervention, and the operational environment. For example, NWORTH and Cambridge CTUs highlighted the importance of these contextual factors, suggesting that metrics must be adapted to reflect the unique needs and characteristics of each trial.

Both Cambridge and Warwick CTUs discussed the evolving nature of metric reliability. Cambridge notes that the true usefulness of metrics often becomes apparent only once the trial is underway, as issues or risks may emerge that were not foreseen in the initial planning stages. This aligns with Warwick's perspective, which advocates for a measured, investigative approach to interpreting metrics, especially safety-related data, suggesting that initial impressions of metric reliability should be carefully reassessed throughout the trial.

Nottingham CTU expressed a more confident stance on the reliability of metrics. The participant there emphasised the automated, data-driven nature of their system, relying on data input directly from the source and statisticians' analysis. This confidence suggests a more streamlined and established approach to metric use within their CTU, which may reduce concerns about the accuracy of metrics over time.

'Not really, no, because they're not particularly manual metrics. We use REDCap and everything is very data driven. And inputted at source if you like. And the statisticians do a good job of, you know, running reports on those kinds of things. So, I know that

doesn't really concern me, to be honest.' (Senior Quality Assurance Manager, over 10 years of experience)

Some CTUs, such as Leeds, Plymouth, and NWORTH, did not report specific concerns about metric reliability. While NWORTH acknowledged the importance of trial context, there was no indication of active issues or concerns with the accuracy of metrics within the unit.

Overall, the data suggested a broad recognition that metrics reliability is influenced by trial-specific contexts and the adaptive nature of the trial process. While some CTUs like Nottingham have a more automated and streamlined approach, others like Cambridge and Warwick emphasise the need for ongoing updates and contextual understanding to ensure metrics remain relevant and accurate throughout the trial. The overarching understanding is that while CTUs generally trust metrics, there is an acknowledgement that the selection, interpretation, and use of metrics must be carefully managed and continuously adapted to trial developments.

Sub-theme two: Stakeholder perceptions of metrics

Across the majority of CTUs, there is a general belief that stakeholders (such as funders, sponsors, and regulators) view metrics positively.

NWORTH and Leeds CTUs emphasise that sponsors and funders are likely to be receptive to metrics, particularly because they align with risk-based monitoring, improve monitoring efficiency, and help meet regular reporting requirements. Warwick also shared a similarly optimistic view, anticipating that stakeholders view metrics as a positive addition to trial monitoring.

'I think that they're quite positive about this. I mean it's more targeted way of doing monitoring.' (Lead clinical trials associate, over 6 years of experience)

Despite the positive views, some CTUs such as Cambridge and Leeds noted that stakeholders, particularly sponsors and regulators, may require some persuasion or evidence before fully embracing metrics. Cambridge CTU pointed out that stakeholders may need to be shown clear examples of how metrics improve cost-effectiveness and streamline site visits.

'I think we can prove to them (regulators) that it would be better to look at the metrics centrally and use that to tailor to go out to site. So, I think they might need a bit of

persuasion. They might need some evidence like examples.' (Quality Assurance officer, over 10 years of experience)

Nottingham CTU stood out with its more cautious approach, highlighting that regulators generally view metrics as useful, but they are wary of being too prescriptive in their use. Regulators prefer flexibility and context-sensitive approaches rather than rigid numerical thresholds. This suggests a desire for metrics to remain adaptable to the unique characteristics of each trial, rather than imposing one-size-fits-all standards.

'I think regulators think that they are useful, but to not guide like I say CTUS into how they use them prescriptively. They were very much sort of against giving figures against them.' (Senior Quality Assurance Manager, over 10 years of experience)

Plymouth CTU added an interesting perspective by emphasising the advisory role CTUs play in shaping the metrics used by sponsors. The participant from Plymouth CTU suggested that there is a collaborative relationship between CTUs and stakeholders, where CTUs help determine which metrics are most relevant and how they should be implemented. This contrasts with a more top-down view of stakeholders imposing metrics on CTUs.

Overall, there is broad agreement that stakeholders, particularly sponsors and regulators, see metrics as beneficial for trial monitoring, improving efficiency, and supporting risk-based monitoring. However, the level of enthusiasm and the extent of support vary. While NWORTH, Leeds, and Warwick CTUs express confidence that stakeholders view metrics positively, Cambridge and Plymouth CTUs note that persuasion and evidence may be necessary to win full support. Nottingham CTU brings a cautionary perspective, with regulators preferring flexibility in how metrics are used. Ultimately, there is a general trend towards increasing acceptance of metrics, but the degree of support and the conditions under which metrics are adopted may vary across different stakeholders.

Theme Five: Motivators for using metrics

Sub-theme one: Motivators for adopting metrics

This theme aimed to explore the motivators for CTUs to use metrics. While it shares some similarities with the advantages of using metrics, it specifically focuses on the

factors that initially drove CTUs to adopt metrics in their monitoring practices, rather than the ongoing benefits experienced after adoption.

A major motivator for CTUs for the adoption of metrics is the potential for more efficient central monitoring. This includes using metrics to verify whether critical tests have been completed (for example laboratory test for primary outcome measures) and to target specific sites for visits based on their performance or risk factors. Cambridge CTU, for instance, highlighted that the ability to leverage pharmacovigilance data from their databases can help identify safety issues (e.g., the ratio of SAEs to recruitment) and guide monitoring priorities.

Several CTUs, including Nottingham and Plymouth, highlighted cost and time savings as key motivators. The reduction in the need for on-site visits was noted as a significant advantage, especially when using a risk-based monitoring approach. Metrics help identify which sites require attention, thereby reducing unnecessary visits and extensive travel. This also translates into more manageable and efficient monitoring processes, as seen in Nottingham and Plymouth CTUs.

'Yeah, well, it's certainly helped in the costs. You know, cause, obviously you don't have all these monitoring visits and travelling around the country to look at the data.' (Quality Assurance Manager, over 20 years of experience)

Furthermore, the ability to use data-driven approaches to inform monitoring decisions is another motivator. Cambridge particularly pointed out how limitations in existing clinical trials data management systems like MACRO led to a shift towards more flexible platforms such as REDCap, which support more efficient metrics-driven approaches. The desire to make better use of available data to improve monitoring is a recurring theme.

A motivator for some CTUs, particularly Nottingham, is the ability to conduct remote monitoring. While metrics add some complexity to the documentation process, they offer the opportunity to monitor sites without the need for frequent on-site visits. This shift aligns with a more flexible, adaptable approach to monitoring and supports better use of resources.

In Plymouth CTU, the participant emphasised the importance of risk-based monitoring. Metrics are particularly useful for providing insight into site activity and performance,

which directly informs risk-based decisions on which sites need more focus. This approach is seen as both cost-effective and efficient, as it allows for targeted monitoring rather than blanket oversight.

Overall, these motivators show a clear trend towards improving efficiency, reducing costs, and making better use of data to optimise clinical trial monitoring practices. The shift towards more flexible and adaptable monitoring systems is also highlighted as a significant driving force behind adopting metrics.

Theme six: Future work

Sub-theme one: Recommendations for Using Metrics in Monitoring

This theme aimed to explore recommendations from CTUs currently using metrics to inform their monitoring practices, with the goal of helping other CTUs that are considering or planning to implement metrics in the future. Additionally, the theme explored CTUs' interest in participating in a potential pilot project to implement metrics in their monitoring practices, to assess how such an initiative might benefit their operations and inform their broader adoption of metrics in future trials. By gathering these insights, the study sought to identify practical guidance to the adoption of metrics across a wider range of CTUs. To improve clarity and readability, this theme has been broken down into numbered subcategories. This structure makes the practical implications of the findings more accessible.

1. Tool Improvement and Independence

The transition from a database that is more programmer dependent such as MACRO to one that can be managed more independently by the CTU such as REDCap was viewed as a step toward greater independence in generating reports. One CTU recommended moving to more flexible platforms like REDCap that enable teams to generate their own reports without relying on programmers. They also emphasised the importance of providing the right infrastructure and training to staff, ensuring that both the tools and the knowledge to use them effectively are in place.

This recommendation highlights the need for CTUs to have both the right tools, and the appropriate skill sets to make the most out of their metrics-based systems. It stresses the importance of making metrics actionable by ensuring staff have the resources to interpret the data.

2. Template Development and Customisation

Another CTU suggested that CTUs should work collaboratively with groups like the UKCRC to improve and customise monitoring templates. It was also recommended that CTUs avoid using templates without fully understanding their purpose or adapting them to the specific context of each trial.

This recommendation reflects the importance of not taking a one-size-fits-all approach to metrics. By customising monitoring tools to meet the unique needs of each trial, CTUs can avoid inefficiencies and ensure that metrics are applied in the most effective way possible.

3. Training and Awareness

Another CTU suggested that more training would be beneficial for staff to identify and implement relevant metrics effectively. Specifically, the newly released UKCRC metrics and triggers tool was noted as a useful resource that could be more widely adopted if there was additional support for training teams on how to use it.

This recommendation underscores the importance of continuous education and upskilling. Effective training is key to empowering staff to use metrics accurately, confidently and efficiently, which in turn will lead to better-informed decision-making about escalation.

4. Visual Tools and Dashboards

Another CTU suggested adopting a dashboard with colour-coded indicators (e.g., red-amber-green) to highlight studies or sites requiring attention. They also recommended incorporating visual tools like pie charts to make metric data more accessible and digestible for trial teams.

This recommendation focuses on making metrics more accessible for a wide range of trialists through effective visual representation. Visual tools help staff quickly grasp key insights without the need for extensive analysis, which improves the speed and clarity of decision-making.

5. Risk-Based and Incremental Approach

Another CTU recommended that CTUs adopt a top-down approach when implementing metrics, starting with a study's risk profile and reviewing existing data to

determine the most appropriate monitoring strategy. They also suggested a gradual, step-by-step implementation of metrics, starting with small-scale trials or scenarios, to build confidence and avoid overwhelming staff.

This recommendation highlights a thoughtful and gradual approach to implementing metrics. By starting small and building upon existing knowledge and data, CTUs can avoid challenges such as resistance to change and the overcomplication of workflows. This ensures that teams are more likely to embrace metrics and use them effectively.

Sub-theme two: Willingness to explore metrics pilot project

The data overall indicated a strong willingness among CTUs to explore future initiatives related to clinical trial monitoring and the use of metrics. However, there are varying degrees of openness depending on the level of existing infrastructure, current resources, and the practical challenges each CTU faces. All the CTUs, including NWORTH, Cambridge, Plymouth, Nottingham, Leeds and Warwick, expressed openness to future initiatives involving metrics in monitoring. The willingness was not only about participating in pilot projects but also about contributing to the development of more standardised approaches to trial monitoring. This indicates a shared recognition of the potential benefits of using metrics for improving monitoring practices across CTUs.

NWORTH, Cambridge, and Plymouth CTUs expressed interest without significant hesitation, which reflects a general enthusiasm for engaging with future metrics initiatives.

Warwick CTU was similarly open but acknowledged the challenge of introducing new approaches into established systems, highlighting the practical constraints of existing workflows.

Leeds specifically highlighted the potential benefit of a pilot project that could contribute to the standardisation of monitoring practices across CTUs. This willingness to standardise the process suggests an understanding of how shared tools and processes can enhance the efficiency and consistency of monitoring practices across different units.

The emphasis on standardisation suggests that a common set of tools, metrics, and guidelines could lead to better-coordinated and more comparable monitoring practices across CTUs, benefiting the wider clinical trials community.

Nottingham CTU expressed a desire to evaluate the long-term impact of recent initiatives like the UKCRC metrics and triggers tool. This reflects a thoughtful approach where CTUs wish to see tangible results from past efforts before fully committing to larger-scale implementation of metrics. The willingness to assess the impact of previous efforts shows a cautious but practical attitude toward adopting new practices.

Nottingham CTU's cautious approach contrasts with the more enthusiastic responses from other CTUs, emphasising the importance of evaluating the effectiveness of current tools and strategies before scaling them up.

Warwick CTU raised concerns about the challenges posed by existing systems and time constraints when introducing new approaches. This recognition of barriers indicates that while there is willingness, there is also an awareness that successful implementation requires careful planning, training, and adaptation of current processes.

Warwick CTU's acknowledgment of the practical challenges faced when introducing new tools into established systems suggests a more gradual and considered approach to integrating metrics, where training and infrastructure would need to be addressed alongside the introduction of new tools.

Across the CTUs, there was an implicit understanding that for any pilot project to be successful, the appropriate tools such as the Monitoring triggers and metrics tool (UKCRC, 2024) and training would be required. CTUs like Cambridge CTU specifically mentioned the need for proper training to interpret and leverage metrics effectively, highlighting the importance of ensuring that staff are equipped with the right knowledge and tools.

The integration of tools and training was a common theme, reflecting a shared recognition that simply adopting metrics is not enough. Successful adoption requires staff to be adequately trained in both the technical aspects of the tools and the interpretive skills to make data-driven decisions.

One CTU expressed a strong willingness to use metrics, provided that appropriate tools and training are available. They stressed the importance of having user-friendly tools, such as a working spreadsheet that allows easy data entry and clearly defined scoring ranges. However, they cautioned against overly simplistic ‘plug and play’ tools, noting that users still need to engage thoughtfully with the data and its implications. They also emphasised the value of peer support and shared experiences, suggesting that when experienced staff openly discuss how metrics work and demonstrate their benefits, it can encourage wider uptake among trial teams. Overall, the participant showed a clear enthusiasm for implementing and improving metric tools, indicating they would be keen to adopt and advocate for them with the right support.

In summary, the willingness to explore metrics pilots across CTUs is high, with a shared understanding of the importance of standardising practices. However, there are varying levels of readiness based on existing systems, time constraints, and the desire to see concrete results from earlier efforts. The key drivers for engaging with metrics initiatives include the potential for improved efficiency, the desire for standardisation, and the recognition that appropriate tools and training are crucial for success. Addressing these practical considerations and ensuring that metrics are implemented in a way that aligns with each CTU's specific needs will be critical for the successful adoption of metrics-based monitoring practices.

4.9 Chapter Summary and Discussion

This chapter analysis explored how metrics are currently defined, selected, and used to inform trial monitoring across UK Clinical Trials Units. The findings highlighted substantial variation in the types of metrics collected and the purposes they serve. Most CTUs reported using recruitment and data-entry timeliness as primary indicators of performance, but definitions and thresholds differed considerably between units. Participants described challenges in determining which metrics were most meaningful and expressed concern that some indicators risked driving undesirable behaviours or misrepresenting trial quality. Despite these differences, there was broad agreement that metrics can add value when interpreted alongside contextual information and professional judgement. Collectively, these findings illustrate both the perceived utility and the current limitations of metric-based monitoring within UK academic trials.

One of the challenges of this chapter was conducting the interviews. Although by this stage in my PhD I had gained more experience with qualitative interviewing, I still needed to ensure that I managed the conversations effectively and recognised when participants were drifting away from the topic. A key lesson I learned through this process was the importance of keeping participants focused. While I was keen to gather as much insight as possible, it was equally important to gently steer the discussion back on track when necessary. I found this particularly challenging with two of my participants, where I had to politely redirect the conversation to ensure my questions were fully addressed. Despite this, all interviews were data-rich, and each participant contributed valuable insights to the study.

These interviews felt more relaxed compared to those in the previous chapter, perhaps because participants were not in a position to judge anyone else's work. However, I was still aware that some participants were conscious of how they spoke about their own CTU's practices and may have avoided making overtly negative comments. My introverted nature was, once again, helpful in this context. I was comfortable holding space and listening quietly while participants shared their views. I also found it useful to allow pauses, giving them time to reflect further rather than rushing into the next question. At the same time, I remained actively engaged during the interviews by maintaining eye contact, nodding, and using other non-verbal cues to show that I was listening. I also used probing questions to clarify and deepen my understanding for

example, by paraphrasing a point and checking: *'You said this, have I understood you correctly?'*. These techniques helped create a sense of dialogue while ensuring that participants felt heard and that their perspectives were accurately captured.

In addition to managing bias through reflexivity, I also recognise that my background in clinical trial management and monitoring may have positively contributed to the research. My familiarity with the terminology, processes, and challenges discussed by participants allowed me to understand their perspectives more quickly and to ask more meaningful follow-up questions. Rather than being a source of bias alone, my prior knowledge helped build rapport and enriched the quality of the interviews and subsequent analysis.

This chapter provides an in-depth analysis of the integration of metrics in UK Clinical Trial Units (CTUs), focusing on the implementation, benefits, challenges, and recommendations for the use of metrics in clinical trial monitoring. Through a framework analysis approach, I examined the perceptions, practices, and experiences of CTUs with respect to the use of metrics. The framework analysis allowed me to organise and interpret the data in a structured way, focusing on the themes of training, resources, and the various challenges CTUs face when adopting metrics. The findings demonstrate a clear move towards adopting metrics across most CTUs, though the depth of integration and standardisation varies.

While all six CTUs I interviewed reported using a risk-based approach to monitoring, four CTUs have fully integrated metrics into their monitoring strategies, while two do not use them routinely but still recognise their potential value. The consensus across all units was that metrics can significantly improve monitoring efficiency, particularly by identifying key areas such as recruitment, safety, and data integrity. Notably, all CTUs expressed support for future initiatives to explore metrics-driven monitoring practices and pilot projects to further standardise practices.

As a researcher, I was able to draw from my previous experience conducting qualitative interviews to gather rich data. I recognised the importance of carefully managing these interviews, ensuring that the conversations remained on track while allowing participants the space to reflect on their own practices. A key learning for me throughout this process was the importance of flexibility and adaptability in the research process. I found that while I had a structured framework in place for my

analysis, the iterative nature of framework analysis allowed me to refine my interpretation of the data based on emerging themes and insights from participants.

In terms of methodology, framework analysis proved to be highly effective for organising and interpreting the data. It provided a clear structure for identifying key themes related to the use of metrics, including the role of predefined metrics, the importance of flexibility, and the need for continuous training and support. These themes were generated as critical elements for the successful adoption of metrics in clinical trials. The framework also allowed me to explore variations across CTUs, including differences in the use of tools, the integration of metrics into existing systems, and the different levels of readiness for adopting new approaches to monitoring.

A significant challenge highlighted in the data was the need for continuous training and infrastructure support. The findings revealed that while some CTUs have already established solid training frameworks, others are still in the early stages of developing these processes. There is a clear recognition that effective use of metrics requires not only the right tools for data collection but also the skills to interpret and act on the data. This was a key motivator behind the willingness of CTUs to explore pilot projects, as they recognised the need for more training and a more robust infrastructure to support the effective use of metrics.

Context was also an important consideration when analysing the data. The use of metrics is not a one-size-fits-all approach; rather, it is influenced by the type of trial, the resources available, and the level of engagement with trial sites. For instance, the challenges faced by smaller trials differ significantly from those experienced by larger, more complex studies. In this way, framework analysis allowed me to highlight how the data differed across the CTUs and how these differences were rooted in the specific needs and contexts of each unit.

The analysis presented in this chapter complements the development of the Trial Monitoring Plan template by providing insight into how metrics are currently interpreted and applied across UK Clinical Trials Units. Rather than proposing a new framework, this work highlights the diversity of existing approaches and the challenges of defining common indicators of trial quality and risk. These findings inform the practical implementation of the TMP by illustrating where metrics can realistically support proportionate decision-making and where reliance on contextual judgement remains

necessary. Linking the findings from this chapter to the TMP therefore strengthens its applicability in real-world settings, ensuring that the proposed monitoring processes reflect the operational realities and constraints experienced by CTUs. Together, these insights bridge the gap between theory and practice, illustrating how the principles of risk-proportionate monitoring outlined in the TMP can be informed by empirical evidence on how CTUs currently use and interpret monitoring metrics.

In addition to informing how metrics can be integrated into risk-proportionate decision-making, these findings also highlight several practical implications for the future use of the TMP template. First, the variation in how CTUs currently define and apply metrics suggests that the TMP template could be further adapted for local use, for example through CTU-specific versions that include pre-filled metric definitions or routinely collected indicators. Second, by offering a structured and consistent format, the TMP template has the potential to promote greater alignment in the selection, interpretation, and reporting of metrics both within and between CTUs. Finally, the TMP template provides a convenient and neutral vehicle for facilitating discussion about metric use across teams, helping to surface differing assumptions, improve shared understanding, and support more coherent monitoring practices across the UK trial community.

In conclusion, while there is widespread agreement across CTUs on the benefits of using metrics, there are also significant differences in their implementation, largely driven by factors such as trial type, resources, and institutional culture. The flexibility of predefined metrics was emphasised as essential, with CTUs suggesting that metrics should be adapted to the specific context of each trial. Moreover, the importance of continued training, resource allocation, and the adaptation of existing systems to support metrics-driven approaches were developed as central themes. My role as a researcher in this chapter has been to synthesise these findings and explore how framework analysis helped to draw out key insights, providing a coherent understanding of the challenges and opportunities for integrating metrics in clinical trial monitoring across CTUs.

Ultimately, for the successful implementation of metrics-based monitoring, it is crucial to maintain flexibility in their application, ensuring that they are aligned with each trial's unique needs and characteristics. The willingness of CTUs to engage in future pilot

projects, along with the recognition of the importance of training and infrastructure, will be key to optimising the use of metrics in clinical trial monitoring.

4.10 Chapter Limitations

While this chapter provides valuable insights into the integration of metrics in clinical trial monitoring across UK Clinical Trial Units (CTUs), several limitations should be acknowledged.

The sample for this chapter consists of six CTUs, which provided a diverse range of perspectives across different contexts. While the findings are not intended to be statistically generalisable, they offer in-depth, context-rich insights into how metrics are perceived and implemented in trial monitoring. As is typical of qualitative research, the aim was not to produce universally applicable conclusions but to generate findings that may be *transferable* to similar settings (Lincoln & Guba, 1985). Future studies could build on this work by involving a larger number of CTUs to examine whether these patterns are reflected more broadly across the UK clinical trials landscape.

The participants in this study came from different roles within their respective CTUs, which could influence their perspectives on the use of metrics. For instance, the insights from data managers or trial managers may differ from those of statisticians or monitoring team leads. Although this variation in roles provides a multifaceted view, it may also contribute to differing perceptions of the same issues, such as the challenges of using metrics or the need for training. More focused participant selection, with a clearer understanding of role-specific perspectives, could provide further insights into how different roles influence the adoption of metrics.

As the researcher, my own background and experiences in clinical trials management and data collection likely influenced my approach to the interviews and analysis. While I took conscious steps to remain neutral and objective, my prior knowledge of the field may have subtly shaped the framing of questions or interpretation of responses. Reflexivity played a critical role in managing these influences, and I regularly engaged in self-reflection to minimise bias. Nonetheless, it is important to acknowledge that my interpretations are inevitably shaped by my own experiences. In future research, involving a more diverse research team could help to broaden perspectives and further enhance interpretive rigour.

This study focused exclusively on UK-based CTUs, which means the findings are context-specific and may not directly transfer to settings in other CTUs where regulatory frameworks, resources, and institutional structures differ. Future research

involving CTUs from a broader range of countries or regulatory environments could help explore how international contexts influence the adoption and use of metrics in clinical trial monitoring.

While this chapter provides a comprehensive overview of the benefits, challenges, and motivators for using metrics, there is limited exploration of the actual implementation challenges faced by CTUs. For instance, the difficulties in transitioning from paper-based to electronic systems, or the specifics of adapting existing monitoring systems to integrate metrics, were only briefly touched upon. Further research could focus specifically on the practical challenges and barriers to implementing metrics at the operational level, providing more detailed guidance for CTUs looking to adopt or optimise their use of metrics.

The use of metrics in clinical trial monitoring is an evolving practice, and the findings from this chapter may be subject to change as more CTUs adopt metrics or refine their approaches. Metrics-related practices may also shift with ongoing advancements in technology, regulatory changes, or broader industry trends, such as the growing use of remote monitoring. As such, the findings in this chapter represent a snapshot of current practices but may not reflect future developments in the field.

Chapter Five: Thesis summary, conclusion and future work

This thesis has explored the development and implementation of a Trial Monitoring Plan (TMP) template designed to standardise clinical trial monitoring practices across UK Clinical Trial Units (CTUs). It highlights the significant variation in the monitoring plans currently in use across UK CTUs, with many units duplicating efforts and lacking a uniform approach to high-quality, consistent monitoring. The research in this thesis demonstrates the value of a standardised TMP template that could streamline processes, improve efficiency, and reduce resource waste across CTUs. Developed through extensive expert consultation and iterative refinement, the template reflects national consensus on core monitoring principles while maintaining the flexibility needed to accommodate diverse trial contexts.

A key contribution of this research is the development of a comprehensive, evidence-based TMP template to promote consistency and efficiency in clinical trial monitoring. The template provides a structured yet adaptable framework, supporting proportionate oversight across diverse trial contexts. Its development was shaped by expert consensus, which helped define the essential monitoring domains and ensure flexibility in their application. The consensus process also highlighted the importance of dialogue and transparency in refining monitoring practices and addressing differing interpretations of what constitutes proportionate monitoring.

Collectively, these studies revealed a strong willingness among CTUs for greater harmonisation of monitoring practices, while also identifying structural and operational barriers that limit consistency. The findings emphasise that effective standardisation requires balance, providing clear guidance while allowing flexibility to adapt to differing trial contexts, resources, and risk levels. Overall, the thesis demonstrates both the need and the practical feasibility of a coordinated approach to monitoring across UK CTUs.

Despite the widespread interest in improving monitoring practices, this research identified persistent challenges faced by CTUs, particularly limited resources and competing operational demands. Feedback gathered across the Delphi survey, consensus discussions, and pilot interviews provided valuable insights into the TMP's usability, revealing both its strengths and areas for refinement. Importantly, many CTUs expressed a genuine interest in adopting a standardised TMP, recognising its

potential to harmonise monitoring practices and enhance efficiency across the UK network.

The findings also highlight the importance of flexibility and continuous adaptation in trial monitoring, recognising that monitoring practices must evolve alongside advances in trial design, regulation, and technology. While the TMP template was developed to improve standardisation and consistency, it must remain dynamic and responsive to emerging needs. Ongoing engagement with CTUs will therefore be crucial to ensure the template's continued relevance, usability, and effectiveness in practice.

These findings contribute to a small but growing body of empirical research on trial monitoring, complementing earlier work that has primarily examined the concept from a regulatory or theoretical standpoint (Love et al., 2022; Whitham et al., 2018). Beyond monitoring, this research aligns with methodological innovations in process and template design such as SPIRIT (Chan et al., 2013), TIDieR (Hoffmann et al., 2014), Trial Forge (Treweek et al., 2015) and COMET (Williamson et al., 2017). Like the TMP, these initiatives promote transparency, reproducibility, and stakeholder engagement through structured, consensus-based tools. This thesis extends those principles to an area of trial methodology that has remained underdeveloped, establishing a foundation for future evidence-informed approaches to monitoring.

The research also discusses the dissemination of the TMP template, which has been made publicly available through an open-access publication in Trials Journal. It highlights the widespread interest in the research findings within the clinical trials community, evidenced by invitations to present at monitoring and other research events and ongoing discussions about the template's potential adoption. Additionally, pilot projects at various CTUs have shown positive engagement, with some units already considering the template for official adoption.

Furthermore, this thesis highlights the importance of user feedback in refining the TMP template and the ongoing process of refining clinical trial monitoring practices. The research emphasises the role of reflexivity and iterative feedback in improving the template's design and ensuring that it meets the needs of CTUs. The overall aim of this work was to contribute to the standardisation of clinical trial monitoring across the UK and internationally, ensuring that future trials are conducted with enhanced quality, efficiency, and patient safety in mind.

In addition to the TMP template, the research delves into the use of metrics in trial monitoring, highlighting the benefits and challenges of adopting a metrics-based approach across CTUs. Through framework analysis, this research presents a clear picture of the perceptions, practices, and experiences of CTUs in integrating metrics into their monitoring strategies. The findings revealed that while many CTUs support the use of metrics, their implementation varies widely due to factors such as trial type, resources, and institutional culture. Continuous training and infrastructure support are identified as key components for the successful integration of metrics into monitoring practices.

In conclusion, this research has made a significant contribution to the standardisation of trial monitoring practices across UK CTUs. By developing a comprehensive, evidence-based TMP template, the study has provided a valuable tool for improving trial monitoring efficiency, reducing resource waste, and promoting consistency across clinical trials. The iterative, consensus-driven approach to developing the TMP template has ensured that it aligns with both regulatory requirements and best practice standards, while maintaining the flexibility to accommodate the diverse needs of CTUs.

The findings of this study have highlighted the growing recognition within the clinical trials community of the need for standardisation in trial monitoring. While there are challenges to its widespread adoption, the research suggests that the TMP template has strong potential for enhancing monitoring practices, not only within the UK but also internationally. The ongoing engagement with CTUs, alongside continued refinement and adaptation of the template, will be essential for ensuring its effectiveness and relevance as clinical trial monitoring practices evolve.

The research also emphasises the importance of integrating metrics into trial monitoring and the need for continuous training and infrastructure support to facilitate the successful implementation of metrics-driven approaches. As such, the TMP template should be seen as a key step in the broader effort to improve clinical trial monitoring and ensure the quality, safety, and integrity of clinical trials moving forward. Future work could involve a formal evaluation of the template's impact on monitoring efficiency, data quality, and risk detection across a range of trial types and settings, including both academic CTUs and industry-led trials. This may include multi-site

implementation studies, feedback from trial managers and monitors, or integration with digital monitoring platforms. Furthermore, involving regulatory bodies such as MHRA with the research could enhance the template's efficiency and relevance from a regulatory perspective. Such work will be crucial in evaluating the template's performance in real-world applications and ensuring its continued evolution in response to changing trial designs and regulatory landscapes.

As a researcher, I made a conscious effort to share my research with the monitoring and clinical research community, actively seeking opportunities to disseminate my findings. Every opportunity to give a presentation or attend a conference was greatly valued. I delivered an oral presentation at the Society of Clinical Trials conference in May 2024, when the template's first draft was completed, and I was beginning the pilot phase. Later, in September 2024, I delivered an oral presentation at the Operational Research Society conference as the template and its associated paper neared publication. This conference sparked interest in piloting the template at NWORTH. Although they were ultimately unable to participate in the pilot study, they did contribute to the metrics aspect of my research. Furthermore, I presented a poster at the International Clinical Trials and Methodology Conference in October 2024, further extending the reach of my research.

Additionally, following the publication of my paper, I was invited by North Wales Organisation for Randomised Trials in Healthcare and Social Care (NWORTH), within the North Wales Medical School at Bangor University, to deliver a one-hour presentation on my research in February 2025. Attendees included research staff from North Wales (Bangor), Mid Wales (Aberystwyth), and South Wales (Cardiff), as well as NHS Wales staff. This was a significant dissemination opportunity. I have also an invited speaker at the National Monitoring Meetings in 2023, 2024, and 2025. Furthermore, I have delivered presentations internally within ICTM such as PhD Symposium (June 2023), ICTM Seminar (May 2024), ICTM All Staff Cancer Meeting (December 2024).

Recommendations and Future Work

The TMP should remain flexible and adaptable rather than prescriptive. Future work should evaluate real-world implementation of the TMP template across diverse trial portfolios and iterations could include exemplar templates for different trial designs, embedded guidance on risk assessment, and integration with electronic systems. Dissemination through the UKCRC CTU Network, NIHR, and training initiatives would encourage consistent adoption. Collaboration with regulatory bodies such as MHRA and international CTUs could ensure adaptability and broader adoption.

Metrics should complement, not replace, professional judgement. Standardised definitions and a shared repository of metrics could improve comparability across CTUs. Pilot studies could test the impact of metrics-driven monitoring on efficiency, data quality, and participant safety. Integration with digital dashboards and training programmes should also be explored to sustain long-term change. In line with the suggestions raised in Chapter 4, future work should also focus on developing practical tools, such as a metrics template, clearer guidance, and visual dashboards, to support consistent interpretation and implementation across CTUs.

Collectively, these recommendations provide a roadmap for enhancing monitoring practice and guiding the next phase of methodological development in this field.

While this research has made significant strides in standardising trial monitoring practices across UK CTUs, further work is necessary to ensure the TMP template's continued relevance and effectiveness. Future efforts will focus on testing and validating the TMP template in real-world clinical trial settings. This phase could involve ongoing collaboration with both academic CTUs and industry-led trials to assess how the template performs under varying trial conditions and whether it can be seamlessly integrated into diverse trial protocols and practices. Feedback from these trials will be crucial in identifying any areas where the template can be refined or adapted to meet evolving needs.

A key aspect of future work will involve expanding the template's application to both CTIMP and non-CTIMP trials across different trial phases. As clinical trial designs and regulatory requirements evolve, the TMP template must be adaptable to these changes. A critical component of future research will be to assess the template’s

adaptability to new methodologies, technologies, and regulatory frameworks, ensuring it remains a dynamic and useful tool for CTUs.

In addition, engagement with international CTUs will be a priority, to explore the potential for the TMP template to be adapted and adopted beyond the UK. The insights gained from CTUs outside of the UK will provide valuable information on how the template could be adapted to different healthcare settings, considering local regulatory, operational, and cultural differences. This international collaboration could lead to broader standardisation of trial monitoring practices and further improve the quality and consistency of clinical trials worldwide.

The integration of new metrics and data analysis tools into clinical trial monitoring is another area for future research. As trial monitoring becomes increasingly data-driven, the role of real-time data, machine learning, and other advanced tools will be crucial in enhancing the efficiency and accuracy of trial monitoring. Future work should explore how these tools can be incorporated into the TMP template to further improve monitoring strategies and outcomes.

Finally, ongoing professional development and training initiatives will be essential to ensure that CTU staff are equipped with the skills and knowledge necessary to effectively implement and use the TMP template. Continued research into the best ways to provide training and support to CTU staff will help optimise the use of the template and ensure that trial monitoring standards are maintained across the board.

In summary, future work will focus on the practical implementation of the TMP template, its adaptation to new trial designs and international contexts, and the integration of advanced tools and training initiatives to further improve clinical trial monitoring practices. By addressing these areas, this research will continue to contribute to the evolution of trial monitoring and the enhancement of clinical trials worldwide.

References

2004, M. f. H. U. C. T. R. (Medicines for Human Use (Clinical Trials) Regulations 2004). Medicines for Human Use (Clinical Trials) Regulations 2004. https://www.legislation.gov.uk/uksi/2004/1031/contents

(ICH), I. C. f. H. (International Council for Harmonisation (ICH)). *ICH E6 (R3) Good clinical practice - Scientific guideline 2025* (European Medicines Agency, Issue. https://www.ema.europa.eu/en/documents/scientific-guideline/ich-e6-r3-guideline-good-clinical-practice-gcp-step-5_en.pdf

Acocella, I. (2012). The focus groups in social research: advantages and disadvantages. *Quality & Quantity*, *46*(4), 1125-1136. https://doi.org/10.1007/s11135-011-9600-4

Adams, E. (2010). The joys and challenges of semi-structured interviewing [Article]. *Community Practitioner*, *83*, 18+. https://link.gale.com/apps/doc/A229720174/HRCA?u=anon~ed9f9f7e&sid=googleScholar&xid=b3f97338

Adams, W. C., Hatry, H. P., Newcomer, K. E., & Wholey, J. S. (2015). Conducting Semi-Structured Interviews. In (pp. 492-505). John Wiley & Sons, Inc. https://doi.org/10.1002/9781119171386.ch19

Agency, E. M. (2022). *Reflection paper on risk-based quality management in clinical trials*. Retrieved 29/10/2025 from https://www.ema.europa.eu/en/documents/scientific-guideline/reflection-paper-risk-based-quality-management-clinical-trials_en.pdf

Agrafiotis, D. K., Lobanov, V. S., Farnum, M. A., Yang, E., Ciervo, J., Walega, M., Baumgart, A., & Mackey, A. J. (2018). Risk-based Monitoring of Clinical Trials: An Integrative Approach. *Clinical Therapeutics*, *40*(7), 1204-1212. https://doi.org/https://doi.org/10.1016/j.clinthera.2018.04.020

Ahmed, J., Mehmood, S., Rehman, S., Ilyas, C., & Khan, L. U. R. (2012). Impact of a structured template and staff training on compliance and quality of clinical handover. *International Journal of Surgery*, *10*(9), 571-574. https://doi.org/https://doi.org/10.1016/j.ijsu.2012.09.001

Antaki, C., Billig, M., Edwards, D., & Potter, J. (2003). Discourse Analysis Means Doing.

Bakobaki, J. M., Rauchenberger, M., Joffe, N., McCormack, S., Stenning, S., & Meredith, S. (2012). The potential for central monitoring techniques to replace on-site monitoring: findings from an international multi-centre clinical trial. *Clin Trials*, *9*(2), 257-264. https://doi.org/10.1177/1740774511427325

Barnes, B., Stansbury, N., Brown, D., Garson, L., Gerard, G., Piccoli, N., Jendrasek, D., May, N., Castillo, V., Adelfio, A., Ramirez, N., McSweeney, A., Berlien, R., & Butler, P. J. (2021). Risk-Based Monitoring in Clinical Trials: Past, Present, and Future. *Ther Innov Regul Sci*, *55*(4), 899-906. https://doi.org/10.1007/s43441-021-00295-8

Bate, P., & Robert, G. (2006). Experience-based design: from redesigning the system around the patient to co-designing services with the patient. *Qual Saf Health Care*, *15*(5), 307-310. https://doi.org/10.1136/qshc.2005.016527

Becker, G. E., & Roberts, T. (2009). Do We Agree? Using a Delphi Technique to Develop Consensus on Skills of Hand Expression. *Journal of Human Lactation*, *25*(2), 220-225. https://doi.org/10.1177/0890334409333679

Biggs, K., Hind, D., Gossage-Worrall, R., Sprange, K., White, D., Wright, J., Chatters, R., Berry, K., Papaioannou, D., Bradburn, M., Walters, S. J., &

Cooper, C. (2020). Challenges in the design, planning and implementation of trials evaluating group interventions. *Trials*, *21*(1), 116. https://doi.org/10.1186/s13063-019-3807-4
Bloor, M., Frankland, J., Thomas, M., & Robson, K. (2001). *Focus Groups in Social Research*. SAGE Publications Ltd. https://doi.org/10.4135/9781849209175
Boulkedid, R., Abdoul, H., Loustau, M., Sibony, O., & Alberti, C. (2011). Using and Reporting the Delphi Method for Selecting Healthcare Quality Indicators: A Systematic Review. *PLOS ONE*, *6*(6), e20476. https://doi.org/10.1371/journal.pone.0020476
Bowen, G. A. (2008). Naturalistic inquiry and the saturation concept: a research note. *Qualitative Research*, *8*(1), 137-152. https://doi.org/10.1177/1468794107085301
Boyatzis, R. (1998). Transforming Qualitative Information: Thematic Analysis and Code Development.
Boyatzis, R. E. (1998). *Transforming qualitative information : thematic analysis and code development / Richard E. Boyatzis*. SAGE Publications.
Braun, V., & Clarke, V. (2006). Using thematic analysis in psychology. *Qualitative research in psychology*, *3*(2), 77-101. https://doi.org/10.1191/1478088706qp063oa
Brosteanu, O., Schwarz, G., Houben, P., Paulus, U., Strenge-Hesse, A., Zettelmeyer, U., Schneider, A., & Hasenclever, D. (2017). Risk-adapted monitoring is not inferior to extensive on-site monitoring: Results of the ADAMON cluster-randomised study. *Clin Trials*, *14*(6), 584-596. https://doi.org/10.1177/1740774517724165
Busert, L. K., Mütsch, M., Kien, C., Flatz, A., Griebler, U., Wildner, M., Stratil, J. M., Rehfuess, E. A., & on behalf of Cochrane Public Health, E. (2018). Facilitating evidence uptake: development and user testing of a systematic review summary format to inform public health decision-making in German-speaking countries. *Health Research Policy and Systems*, *16*(1), 59. https://doi.org/10.1186/s12961-018-0307-z
Cameron, W. B. (1963). *Informal Sociology: A Casual Introduction to Sociological Thinking*. Random House. https://books.google.co.uk/books?id=I6JIAAAAMAAJ
Campbell, M. https://libguides.ucd.ie/harvardstyle/harvardtwitter
Chan, A.-W., Boutron, I., Hopewell, S., Moher, D., Schulz, K. F., Collins, G. S., Tunn, R., Aggarwal, R., Berkwits, M., Berlin, J. A., Bhandari, N., Butcher, N. J., Campbell, M. K., Chidebe, R. C. W., Elbourne, D. R., Farmer, A. J., Fergusson, D. A., Golub, R. M., Goodman, S. N.,…Hróbjartsson, A. (2025). SPIRIT 2025 statement: Updated guideline for protocols of randomised trials. *PLOS Medicine*, *22*(4), e1004589. https://doi.org/10.1371/journal.pmed.1004589
Chan, A.-W., Tetzlaff, J. M., Gøtzsche, P. C., Altman, D. G., Mann, H., Berlin, J. A., Dickersin, K., Hróbjartsson, A., Schulz, K. F., Parulekar, W. R., Krleža-Jerić, K., Laupacis, A., & Moher, D. (2013). SPIRIT 2013 explanation and elaboration: guidance for protocols of clinical trials. *BMJ : British Medical Journal*, *346*, e7586. https://doi.org/10.1136/bmj.e7586
Chaudhari, N., Ravi, R., Gogtay, N. J., & Thatte, U. M. (2020). Recruitment and retention of the participants in clinical trials: Challenges and solutions. *Perspect Clin Res*, *11*(2), 64-69. https://doi.org/10.4103/picr.PICR_206_19

ClinicalTrials.gov. Retrieved 20/11/2023 from https://clinicaltrials.gov/about-site/about-ctg

CluePoints' Commentary. (2013). EMA Reflection Paper On Risk Based Quality Management In Clinical Trials,. https://cluepoints.com/cluepoints-commentary-ema-reflection-paper-on-risk-based-quality-management-in-clinical-trials/?utm_source=chatgpt.com

Cohen, L., Manion, L., & Morrison, K. . (2011). *Research Methods in Education* (7th ed.). Routledge. https://doi.org/https://doi.org/10.4324/9780203720967

Crabtree, B. F., & Miller, W. L. (1999). *Doing Qualitative Research*. SAGE Publications. https://books.google.co.uk/books?id=MEd2AwAAQBAJ

Creswell, J. W., & Plano Clark, V. L. (2018). *Designing and conducting mixed methods research / John W. Creswell, Vicki L. Plano Clark* (Third edition. ed.). SAGE Publications. Inc.

Creswell, J. W. a. P., C.N. . (2018). In *Qualitative Inquiry and Research Design Choosing among Five Approaches* (4th ed.). SAGE Publications. https://books.google.co.uk/books?hl=en&lr=&id=DLbBDQAAQBAJ&oi=fnd&pg=PP1&dq=Creswell,+J.+W.,+%26+Poth,+C.+N.+(2018)&ots=-iq287JWNw&sig=38r0NGWRow4_XOdfM-36o3b7xR0#v=onepage&q&f=false

CTTI Quality by Design (QbD) toolkit. (2014). *Clinical Trials Transformation Initiative. (n.d.). Quality by Design (QbD) toolkit*. Retrieved 29/10/2025 from https://ctti-clinicaltrials.org/about/ctti-projects/quality-by-design/qbd-quality-by-design-toolkit/

Daniels, N., Teagarden, J. R., & Sabin, J. E. (2003). An ethical template for pharmacy benefits. *Health Aff (Millwood)*, *22*(1), 125-137. https://doi.org/10.1377/hlthaff.22.1.125

de Manincor, M., Bensoussan, A., Smith, C., Fahey, P., & Bourchier, S. (2015). Establishing key components of yoga interventions for reducing depression and anxiety, and improving well-being: a Delphi method study. *BMC Complementary and Alternative Medicine*, *15*(1), 85. https://doi.org/10.1186/s12906-015-0614-7

de Meyrick, J. (2003). The Delphi method and health research. *Health Education*, *103*(1), 7-16. https://doi.org/10.1108/09654280310459112

Department of Health. (2005). The research governance framework for health and social care (2nd ed). https://assets.publishing.service.gov.uk/media/5a7a0d41ed915d6eaf153692/dh_4122427.pdf

Diamond, I. R., Grant, R. C., Feldman, B. M., Pencharz, P. B., Ling, S. C., Moore, A. M., & Wales, P. W. (2014). Defining consensus: A systematic review recommends methodologic criteria for reporting of Delphi studies. *Journal of Clinical Epidemiology*, *67*(4), 401-409. https://doi.org/https://doi.org/10.1016/j.jclinepi.2013.12.002

Dingwall, R. (1998). Silverman, D. (ed.) "Qualitative Research. Theory, Method Practice" (Book Review). In (Vol. 20). Henley-on-Thames: Routledge and Kegan Paul.

Fereday, J., & Muir-Cochrane, E. (2006). Demonstrating Rigor Using Thematic Analysis: A Hybrid Approach of Inductive and Deductive Coding and Theme Development. *International Journal of Qualitative Methods*, *5*(1), 80-92. https://doi.org/10.1177/160940690600500107

Fetters, M. D., Curry, L. A., & Creswell, J. W. (2013). Achieving integration in mixed methods designs-principles and practices. *Health Serv Res*, *48*(6 Pt 2), 2134-2156. https://doi.org/10.1111/1475-6773.12117
Finlay, L. (2002). “Outing” the Researcher: The Provenance, Process, and Practice of Reflexivity. *Qualitative Health Research*, *12*(4), 531-545. https://doi.org/10.1177/104973202129120052
Fox, L., Love, S. B., Fitt, L., Upton, L., Leslie, R., Carrilho Britto, J., Mooney, C., & Dight, E. (2021). *UKCRC Registered CTU Network – Monitoring of clinical trials: a handbook*. Retrieved 01/11/2023 from https://ukcrc-ctu.org.uk/guidance-for-ctus/
Fusch, P. I. P. D. a. N., Lawrence R. (2015). "Are We There Yet? Data Saturation in Qualitative Research". *Walden Faculty and Staff Publications.*, 1408-1416. https://scholarworks.waldenu.edu/facpubs/455
Gale, N. K., Heath, G., Cameron, E., Rashid, S., & Redwood, S. (2013). Using the framework method for the analysis of qualitative data in multi-disciplinary health research. *BMC Medical Research Methodology*, *13*(1), 117. https://doi.org/10.1186/1471-2288-13-117
Gamble, C., Krishan, A., Stocken, D., Lewis, S., Juszczak, E., Doré, C., Williamson, P. R., Altman, D. G., Montgomery, A., Lim, P., Berlin, J., Senn, S., Day, S., Barbachano, Y., & Loder, E. (2017). Guidelines for the Content of Statistical Analysis Plans in Clinical Trials. *Jama*, *318*(23), 2337-2343. https://doi.org/10.1001/jama.2017.18556
Gergen, K. J., McNamee, S., & Barrett, F. J. (2001). TOWARD TRANSFORMATIVE DIALOGUE. *International journal of public administration*, *24*(7-8), 679-707. https://doi.org/10.1081/PAD-100104770
Goldsmith, L. J. (2021). Using Framework Analysis in Applied Qualitative Research. *The Qualitative Report, 26(6), 2061-2076.*, 2061-2076. https://doi.org/https://doi.org/10.46743/2160-3715/2021.5011
Greatorex, J., & Dexter, T. (2000). An accessible analytical approach for investigating what happens between the rounds of a Delphi study. *J Adv Nurs*, *32*(4), 1016-1024.
Guba, E. G., & Lincoln, Y. S. (1981). *Effective evaluation / Egon G. Guba, Yvonna S. Lincoln*. Jossey-Bass.
Guba, E. G., & Lincoln, Y. S. (1994). Competing paradigms in qualitative research. In *Handbook of qualitative research.* (pp. 105-117). Sage Publications, Inc.
Guest, G., Bunce, A., & Johnson, L. (2006). How Many Interviews Are Enough?: An Experiment with Data Saturation and Variability. *Field Methods*, *18*(1), 59-82. https://doi.org/10.1177/1525822X05279903
Harry, F. W. (1994). *Transforming Qualitative Data* [Description, Analysis, and Interpretation]. SAGE Publications.
Hasson, F., Keeney, S., & McKenna, H. (2000). Research guidelines for the Delphi survey technique. *J Adv Nurs*, *32*(4), 1008-1015.
Hoffmann, T. C., Glasziou, P. P., Boutron, I., Milne, R., Perera, R., Moher, D., Altman, D. G., Barbour, V., Macdonald, H., Johnston, M., Lamb, S. E., Dixon-Woods, M., McCulloch, P., Wyatt, J. C., Chan, A. W., & Michie, S. (2014). Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. *Bmj*, *348*, g1687. https://doi.org/10.1136/bmj.g1687
Holey, E. A., Feeley, J. L., Dixon, J., & Whittaker, V. J. (2007). An exploration of the use of simple statistics to measure consensus and stability in Delphi studies.

BMC Medical Research Methodology, *7*(1), 52. https://doi.org/10.1186/1471-2288-7-52
HRA. (2017). *UK policy framework for health and social care research*. Retrieved 29/01/2024 from https://s3.eu-west-2.amazonaws.com/www.hra.nhs.uk/media/documents/Final_Accessibility_uk-policy-framework-health-social-care-research_.pdf
Hsieh, H.-F., & Shannon, S. E. (2005). Three Approaches to Qualitative Content Analysis. *Qualitative Health Research*, *15*(9), 1277-1288. https://doi.org/10.1177/1049732305276687
Huberman, A., Miles, M., Ritchie, J., & Spencer, L. Qualitative Data Analysis for Applied Policy Research. In.
IRAS. Retrieved 24/04/2024 from https://www.myresearchproject.org.uk/Signin.aspx
Jones, J., & Hunter, D. (1995). Consensus Methods For Medical And Health Services Research. *BMJ (Online)*, *311*(7001), 376-380. https://doi.org/10.1136/bmj.311.7001.376
Kadam, R. A., Borde, S. U., Madas, S. A., Salvi, S. S., & Limaye, S. S. (2016). Challenges in recruitment and retention of clinical trial subjects. *Perspect Clin Res*, *7*(3), 137-143. https://doi.org/10.4103/2229-3485.184820
Kallio, H., Pietilä, A. M., Johnson, M., & Kangasniemi, M. (2016). Systematic methodological review: developing a framework for a qualitative semi-structured interview guide. *Journal of advanced nursing*, *72*(12), 2954-2965. https://doi.org/10.1111/jan.13031
Keeley, T., Williamson, P., Callery, P., Jones, L. L., Mathers, J., Jones, J., Young, B., & Calvert, M. (2016). The use of qualitative methods to inform Delphi surveys in core outcome set development. *Trials*, *17*(1), 230. https://doi.org/10.1186/s13063-016-1356-7
Kruk, M. E., Gage, A. D., Arsenault, C., Jordan, K., Leslie, H. H., Roder-DeWan, S., Adeyi, O., Barker, P., Daelmans, B., Doubova, S. V., English, M., García-Elorrio, E., Guanais, F., Gureje, O., Hirschhorn, L. R., Jiang, L., Kelley, E., Lemango, E. T., Liljestrand, J.,…Pate, M. (2018). High-quality health systems in the Sustainable Development Goals era: time for a revolution. *Lancet Glob Health*, *6*(11), e1196-e1252. https://doi.org/10.1016/s2214-109x(18)30386-3
Kvale, S., & Brinkmann, S. (2009). *InterViews : learning the craft of qualitative research interviewing / Steinar Kvale, Svend Brinkmann* (2nd ed.). SAGE.
Lincoln, Y. S. (1995). Emerging Criteria for Quality in Qualitative and Interpretive Research. *Qualitative Inquiry*, *1*(3), 275-289. https://doi.org/10.1177/107780049500100301
Lincoln, Y. S., & Guba, E. G. (1985). *Naturalistic Inquiry*. SAGE Publications. https://books.google.co.uk/books?id=2oA9aWlNeooC
Linstone, H. A., & Turoff, M. (Eds.). . (1975). *The Delphi method: Techniques and applications*. Addison-Wesley.
Love, S. B., Yorke-Edwards, V., Lensen, S., & Sydes, M. R. (2020). Monitoring in practice – How are UK academic clinical trials monitored? A survey. *Trials*, *21*(1), 59. https://doi.org/10.1186/s13063-019-3976-1
Love, S. B., Yorke-Edwards, V., Ward, E., Haydock, R., Keen, K., Biggs, K., Gopalakrishnan, G., Marsh, L., O'Sullivan, L., Fox, L., Payerne, E., Hood, K., & Meakin, G. (2022). What is the purpose of clinical trial monitoring? *Trials*, *23*(1), 836. https://doi.org/10.1186/s13063-022-06763-2

Madill, A., & Gough, B. (2008). Qualitative research and its place in psychological science. *Psychological Methods*, *13*(3), 254-271. https://doi.org/10.1037/a0013220

Malterud, K., Siersma, V. D., & Guassora, A. D. (2016). Sample Size in Qualitative Interview Studies:Guided by Information Power. *Qualitative Health Research*, *26*(13), 1753-1760. https://doi.org/10.1177/1049732315617444

McKee, A. (2003). *Textual analysis: a beginner's guide*. Sage Publications.

Medicines and Healthcare products Regulatory Agency. https://www.gov.uk/mhra

Medicines and Healthcare products Regulatory Agency. (2021). *GCP INSPECTIONS METRICS REPORT*. https://assets.publishing.service.gov.uk/media/602a8e3cd3bf7f03190cbe43/GCP_INSPECTIONS_METRICS_2018-2019_final_12-02-21.pdf

Mentimeter. (2025). https://www.mentimeter.com/

Merriam, S. B., & Tisdell, E. J. (2015). *Qualitative research: a guide to design and implementation* (Fourth edition. ed.). Wiley.

MHRA, M. a. H. p. R. A. (2023). *Good Clinical Practice (GCP) Inspection Metrics*. https://assets.publishing.service.gov.uk/media/64357bfe89f19f00133cfb40/GCP_inspection_metrics_2019-2020.pdf?utm_source=chatgpt.com

Morgan, D. L., & Nica, A. (2020). Iterative Thematic Inquiry: A New Method for Analyzing Qualitative Data. *International Journal of Qualitative Methods*, *19*, 1609406920955118. https://doi.org/10.1177/1609406920955118

Morrow, S. L. (2005). Quality and trustworthiness in qualitative research in counseling psychology. *Journal of Counseling Psychology*, *52*(2), 250-260. https://doi.org/10.1037/0022-0167.52.2.250

MRC/DH/MHRA. (2011). *MRC/DH/MHRA Joint Project: Risk-adapted approaches to the management of clinical trials of investigational medicinal products.* Retrieved 15/10/2023 from https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/343677/Risk-adapted_approaches_to_the_management_of_clinical_trials_of_investigational_medicinal_products.pdf

Murphy, E., Gillies, K., & Shiely, F. (2024). Retention strategies are routinely communicated to potential trial participants but often differ from what was planned in the trial protocol: an analysis of adult participant information leaflets and their corresponding protocols. *Trials*, *25*(1), 372. https://doi.org/10.1186/s13063-024-08194-7

Murphy, E., Shiely, F., & Treweek, S. (2022). How much is the lack of retention evidence costing trial teams in Ireland and the UK? *Trials*, *23*(1), 396. https://doi.org/10.1186/s13063-022-06223-x

Murphy, M. K., Black, N. A., Lamping, D. L., McKee, C. M., Sanderson, C. F., Askham, J., & Marteau, T. (1998). Consensus development methods, and their use in clinical guideline development. *Health Technol Assess*, *2*(3), i-iv, 1-88.

Myers, M. D., & Newman, M. (2007). The qualitative interview in IS research: Examining the craft. *Information and Organization*, *17*(1), 2-26. https://doi.org/https://doi.org/10.1016/j.infoandorg.2006.11.001

NHS R&D Forum. (May 2011). *How to prepare for an inspection for good clinical practice by the MHRA: a guide for organisations that sponsor or host non commercial clinical trials of medicinal products.* Retrieved 24/11/2023 from

https://www.rdforum.nhs.uk/content/wp-content/uploads/2014/05/RDFguidance-MHRA.pdf
NIHR. (2021). *The James Lind Alliance Guidebook*. Retrieved 29/10/2025 from file:///C:/Users/rehbsta/OneDrive%20-%20University%20College%20London/Downloads/jla-guidebook-version-10-march-2021.pdf
Otani, T. (2020). Functions of qualitative research and significance of the interpretivist paradigm in medical and medical education research. *Fujita Med J*, *6*(4), 91-92. https://doi.org/10.20407/fmj.2020-018
Patton, M. Q. (1990). *Qualitative evaluation and research methods / by Michael Quinn Patton* (2nd ed.). Sage Publications.
Pervin, N., & Mokhtar, M. (2022). The Interpretivist Research Paradigm: A Subjective Notion of a Social Context. *International Journal of Academic Research in Progressive Education and Development*, *11*. https://doi.org/10.6007/IJARPED/v11-i2/12938
Prinsen, C. A. C., Vohra, S., Rose, M. R., Boers, M., Tugwell, P., Clarke, M., Williamson, P. R., & Terwee, C. B. (2016). How to select outcome measurement instruments for outcomes included in a "Core Outcome Set" – a practical guideline. *Trials*, *17*(1), 449. https://doi.org/10.1186/s13063-016-1555-2
QSR International. (2022). NVivo Version 14 (https://www.qsrinternational.com/nvivo-qualitative-data-analysis-software/home
Ratnayake, I., Do, A. T., Gajewski, D., Pepper, S., Ige, O., Streeter, N., Lin, T. L., McGuirk, M., Gajewski, B., & Mudaranthakam, D. P. (2024). Evaluating the impact of delayed study startup on accrual in cancer studies. *Res Sq*. https://doi.org/10.21203/rs.3.rs-3660904/v1
Research Ethics Committee review. Retrieved 20/11/2023 from https://www.hra.nhs.uk/approvals-amendments/what-approvals-do-i-need/research-ethics-committee-review/
Research, N. I. f. H. a. C. (2019, 01 January 2019). *What does NIHR mean by dissemination?* Retrieved 12/10/2023 from https://www.nihr.ac.uk/documents/how-to-disseminate-your-research/19951
Ritchie, J. (2013). *Qualitative research practice: A guide for social science students and researchers* (Second edition ed.). SAGE Publications.
Ritchie, J., & Lewis, J. (2003). *Qualitative research practice : a guide for social science students and researchers / edited by Jane Ritchie and Jane Lewis*. Sage.
Ritchie, J., Spencer, L., Burgess, R. G., & Bryman, A. (1994). Qualitative data analysis for applied policy research. In (1 ed., pp. 173-194). Routledge. https://doi.org/10.4324/9780203413081-10
Ritchie, J. e. a. (2014). *Qualitative research practice : a guide for social science students and researchers / [edited by] Jane Ritchie ... [et al.]* (2nd edition ed.). SAGE.
Rohleder, P., & Lyons, A. (2017). *Qualitative Research in Clinical and Health Psychology*. Bloomsbury Publishing. https://books.google.co.uk/books?id=PiNHEAAAQBAJ
Rubin, H. J., & Rubin, I. (2011). *Qualitative interviewing : the art of hearing data* (3rd ed.). SAGE Publications, Inc Thousand Oaks.
Salman, R. A.-S., Beller, E., Kagan, J., Hemminki, E., Phillips, R. S., Savulescu, J., Macleod, M., Wisely, J., & Chalmers, I. (2014). Increasing value and reducing

waste in biomedical research regulation and management. *The Lancet*, *383*(9912), 176-185. https://doi.org/10.1016/S0140-6736(13)62297-7
Sanders, E. B. N., & Stappers, P. J. (2008). Co-creation and the new landscapes of design. *CoDesign*, *4*(1), 5-18. https://doi.org/10.1080/15710880701875068
Schulz, K. F., Altman, D. G., Moher, D., & for the, C. G. (2010). CONSORT 2010 Statement: Updated Guidelines for Reporting Parallel Group Randomised Trials. *PLOS Medicine*, *7*(3), e1000251. https://doi.org/10.1371/journal.pmed.1000251
Schwandt, T. A. (1994). Constructivist, interpretivist approaches to human inquiry. In *Handbook of qualitative research.* (pp. 118-137). Sage Publications, Inc.
Shamseer, L., Hopewell, S., Altman, D. G., Moher, D., & Schulz, K. F. (2016). Update on the endorsement of CONSORT by high impact factor journals: a survey of journal "Instructions to Authors" in 2014. *Trials*, *17*(1), 301. https://doi.org/10.1186/s13063-016-1408-z
Smith, C. A., Grant, S., Lyttleton, J., & Cochrane, S. (2012). Using a Delphi consensus process to develop an acupuncture treatment protocol by consensus for women undergoing Assisted Reproductive Technology (ART) treatment. *BMC Complementary and Alternative Medicine*, *12*(1), 88. https://doi.org/10.1186/1472-6882-12-88
SPIRIT Endorsement. https://spirit-statement.org/about-spirit/spirit-endorsement/
Swain, J. (2018). *A Hybrid Approach to Thematic Analysis in Qualitative Research: Using a Practical Example* https://doi.org/10.4135/9781526435477
Taheri, S., Yorke-Edwards, V., Sydes, M. R., Isaacs, T., & Love, S. B. (2024). A new trial monitoring plan (TMP) template for clinical trials: output from a Delphi process. *Trials*, *25*(1), 748. https://doi.org/10.1186/s13063-024-08601-z
Tong, A., Sainsbury, P., & Craig, J. (2007). Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. *International Journal for Quality in Health Care*, *19*(6), 349-357. https://doi.org/10.1093/intqhc/mzm042
TransCelerate. (2013). *Risk-based monitoring methodology*. TransCelerate BioPharma. Retrieved 20/10/2023 from http://www.transceleratebiopharmainc.com/wp-content/uploads/2017/01/RBM_InteractiveGuide.pdf
Trevelyan, E. G., & Robinson, P. N. (2015). Delphi methodology in health research: how to do it? *European Journal of Integrative Medicine*, *7*(4), 423-428. https://doi.org/https://doi.org/10.1016/j.eujim.2015.07.002
Treweek, S., Altman, D. G., Bower, P., Campbell, M., Chalmers, I., Cotton, S., Craig, P., Crosby, D., Davidson, P., Devane, D., Duley, L., Dunn, J., Elbourne, D., Farrell, B., Gamble, C., Gillies, K., Hood, K., Lang, T., Littleford, R.,…Clarke, M. (2015). Making randomised trials more efficient: report of the first meeting to discuss the Trial Forge platform. *Trials*, *16*(1), 261. https://doi.org/10.1186/s13063-015-0776-0
Tudur Smith, C., Hickey, H., Clarke, M., Blazeby, J., & Williamson, P. (2014). The trials methodological research agenda: results from a priority setting exercise. *Trials*, *15*(1), 32. https://doi.org/10.1186/1745-6215-15-32
US Food & Drug Administration. (2023). *A Risk-Based Approach to Monitoring of Clinical Investigations Questions and Answers*. US FDA. Retrieved 05/07/2023 from https://www.fda.gov/regulatory-information/search-fda-guidance-documents/risk-based-approach-monitoring-clinical-investigations-questions-and-answers

von der Gracht, H. A. (2012). Consensus measurement in Delphi studies: Review and implications for future quality assurance. *Technological Forecasting and Social Change*, *79*(8), 1525-1536. https://doi.org/https://doi.org/10.1016/j.techfore.2012.04.013

Ward, L., Stebbings, S., Sherman, K. J., Cherkin, D., & Baxter, G. D. (2014). Establishing key components of yoga interventions for musculoskeletal conditions: a Delphi survey. *BMC Complementary and Alternative Medicine*, *14*(1), 196. https://doi.org/10.1186/1472-6882-14-196

Weber, M., Henderson, A. M., & Parsons, T. (1947). *The theory of social and economic organization, 1st Amer. ed*. Oxford University Press.

Weller, S. C., Vickers, B., Bernard, H. R., Blackburn, A. M., Borgatti, S., Gravlee, C. C., & Johnson, J. C. (2018). Open-ended interview questions and saturation. *PLOS ONE*, *13*(6), e0198606. https://doi.org/10.1371/journal.pone.0198606

Whitham, D., Turzanski, J., Bradshaw, L., Clarke, M., Culliford, L., Duley, L., Shaw, L., Skea, Z., Treweek, S. P., Walker, K., Williamson, P. R., Montgomery, A. A., Bevan, S., Bradshaw, L., Clarke, M., Culliford, L., Devall, A., Duley, L., Fairbrother, K.,…On behalf of the Site Performance Metrics for Multicentre Randomised Trials, C. (2018). Development of a standardised set of metrics for monitoring site performance in multicentre randomised trials: a Delphi study. *Trials*, *19*(1), 557. https://doi.org/10.1186/s13063-018-2940-9

Williamson, P. R., Altman, D. G., Bagley, H., Barnes, K. L., Blazeby, J. M., Brookes, S. T., Clarke, M., Gargon, E., Gorst, S., Harman, N., Kirkham, J. J., McNair, A., Prinsen, C. A. C., Schmitt, J., Terwee, C. B., & Young, B. (2017). The COMET Handbook: version 1.0. *Trials*, *18*(3), 280. https://doi.org/10.1186/s13063-017-1978-4

Yardley, L. (2003). *Qualitative psychology: A practical guide to research methods*. Sage Publications, Inc.

Yorke-Edwards, V., Diaz-Montana, C., Murray, M. L., Sydes, M. R., & Love, S. B. (2022). Monitoring metrics over time: Why clinical trialists need to systematically collect site performance metrics. *Research Methods in Medicine & Health Sciences*, 26320843221147855. https://doi.org/10.1177/26320843221147855

Yorke-Edwards, V., Diaz-Montana, C., Murray, M. L., Sydes, M. R., & Love, S. B. (2023). Monitoring metrics over time: Why clinical trialists need to systematically collect site performance metrics. *Research Methods in Medicine & Health Sciences*, *4*(4), 124-135. https://doi.org/10.1177/26320843221147855

Young, B., & Bagley, H. (2016). Including patients in core outcome set development: issues to consider based on three workshops with around 100 international delegates. *Research Involvement and Engagement*, *2*(1), 25. https://doi.org/10.1186/s40900-016-0039-6

Appendices

Appendix 1: All CTU templates extracted information (textual analysis)

All CTU templates extracted information (textual analysis) 31Mar2022.xlsx

Appendix 2: Final list of Delphi Round 1 (66 items)

1. Study details
Purpose
CTIMP/non-CTIMP
2. Introduction to the trial: Summary of study design/Trial overview
Overall recruitment target
Primary outcome measures
Secondary outcome measures
Duration of patient recruitment
Duration of follow up: (choose as appropriate) ☐ Per patient ☐ The trial
Intervention(s)
Is the trial placebo or standard of care controlled?
Describe any specific regulatory requirements: e.g., The intervention is/is not being used in a licensed indication OR The data from the trial will/will not be used to support a licensing application OR The trial is/is not supporting a license change. <include details of international regulation e.g., FDA, Medical Devices, or other specific regulations>
Describe other issues specific to the treatment under study
3. Monitoring
Who will monitor the study? e.g., Sponsor/sponsor delegate
What will be the first monitoring time-point?
4. Central Monitoring Activities
Review of IMP shipment and delivery documentation
Review of IMP dosage calculations
If medical device trial SADEs reported to manufacturer (if not delegated to CTU)
Out-of-hours emergency cover arrangements- Where participants are provided with out of hours contact details for site staff (e.g., on a Participant ID card or PIS)

indicate how this will be verified (e.g., for high-risk trials a test procedure may be put in place).
4.1 Data Checks
Checks for missing or invalid data (range and consistency checks)
Hard-copy CRFs and patient completed questionnaires validation: e.g., Where the CRF is a hard-copy, the content of approximately 10% of case report forms (CRFs) and patient questionnaires entered at sites will be checked (or double entered) to ensure the accuracy of data input. **(An error rate of <3% will require no further action, however if the error rate is >3%, a 100% check of forms will be undertaken.)**
4.2 Protocol Deviation
Review of Visit Window Thresholds

Other- Specify (e.g., Central review of adherence to the protocol and plausibility of the data, review of any questionnaires for completeness, time of randomisation and intervention consistent with clinical context, expected variability in items such as age, disease severity etc.)
5. On-Site Monitoring activities
Checking understanding and adherence to study protocol, procedures, and governance requirements (including any conditions in regulatory or ethics approval)
Review Medical/study records and results of eligibility assessments for <X%> of participants to confirm participant eligibility
Verification that resources and facilities remain adequate
Verification of appropriate oversight and documented delegation by the local investigator
Is the Site Delegation Log the original of the latest copy filed in Site Master File?
Has the Site Visit Log been completed at each visit?
Availability of completed source documents and CRF for the monitoring visit.
Source document completion in accordance with the ALCOA principles check.

5.1 Protocol Deviation and Compliance
Verification of missing visits, examinations, or tests.
Verification of lab reports reviewed, signed, and dated appropriately.
Have protocol deviations been reported appropriately?
Have any new protocol deviations and/or regulatory or GCP deviations occurred at site since the last visit?
5.2 Site Staff Discussion
Discussions with site staff and review of site staff training requirements (current documents and training present, staff changes documented, CVs, GCP, delegation log).
Other- Add any additional checks to be performed during on-site monitoring visits for this trial.
5.3 Documents and systems to be reviewed
Completion of annual progress and safety reports (as appropriate)
Randomisation processes
Recruitment rates
Screen failure
Withdrawal rates
6. Source Data Verification (SDV)
Is any SDV to be performed? Yes/no
Which patients need SDV and how will you select them? e.g., number/percentage of patients and how you will select them, first patient at each site.
What data needs SDV? e.g., eligibility, outcome data, or all data
Question for Delphi respondents: Do you want a prompt list of data to SDV on the template?
Describe what source data will be available as a hard copy, and what will be available electronically and how access arrangements will be set up.
7. Routine Monitoring Visits

Selection criteria for participants to be reviewed during Routine Monitoring Visits- This may be on request of the TMG or following review of central monitoring reports, (e.g., participants who have a high number of SAEs reported) or on a percentage of participants (e.g., 10% selected at random).
8. Remote monitoring activities
Ongoing training/motivation meetings and teleconferences.
Completion of annual progress and safety reports (as appropriate).
9. Metrics
Question for Delphi Respondents: Do you want to see a prompt list of metric examples on the template?
Or do you want to have the option to use your unit specific list of metrics?
10. Site Initiation Visit
List of trainings to occur during the site initiation visit
Request for submission of Trial Equipment calibration records
Confirmation of Critical Documentation held– both regulatory and trial/site specific
Obtaining confirmation that the site staff have completed the trial-specific training and are made aware of the operational requirements
11. Close out visit
Definition of end of trial
The Investigator Site File must be reviewed and confirmed as complete by the Trial Manager, prior to archiving.
All outstanding payments must be reviewed and invoiced
12. Pharmacy Monitoring (Ordering and Storage of IMP)
Are there adequate stocks within expiry dates for the planned patients?
Are storage temperatures adequately monitored by pharmacy staff?
Have any temperature excursions occurred?
Have any temperature excursions been appropriately managed?
13. Trial oversight of vendor
Onsite vendor monitoring

Central monitoring of vendor duties
Review of vendor related deviations (if required)
Completion of Vendor status reports

Appendix 3: Study flow from item generation to post-meeting decisions

Stage	Actions and decision rules	Item counts (where applicable)
Item generation	Textual analysis of 31 CTU monitoring documents; extraction into spreadsheet; grouping into 38 sections.	745 items across 38 sections.
Preliminary reduction	Supervisory review items, combine those with similar meaning and classify into three categories: • include directly • send to Delphi • • exclude. Priority to items common across CTUs and essential to monitoring practice.	Preliminary TMP template consolidated to 412 items. Followed 66 items to be included in the Delphi and 267 items to be excluded.
Delphi round 1	66 items requiring consensus rated on 9-point scale (1–3 not important; 4–6 important; 7–9 critical). Participants could comment/suggest items.	66 items; 47 participants (including 3 partial responses). Six additional items suggested for round 2.
Delphi round 2	All round-1 items plus six new suggestions; controlled feedback provided (round-1 distributions/medians).	72 items; 40 participants responses (plus 3 partial responses).
Round-to-round change	Agreement threshold: ≥70% rating 7–9 for inclusion and ≤70% rating 1-3 for exclusion. Stability criterion: IQR ≤2.	Items ≥70% critical increased from 22/66 (33%) to 37/72 (51%). Items with IQR ≤2 increased from 29 to 56.
Consensus meeting	Two sessions; discussion and votes on items without Delphi consensus and on select additions/wording. Voting guided by relevance to monitoring, availability of information elsewhere (e.g., protocol), and brevity.	32 non-consensus items voted; 18 excluded, 14 included. Additional late items adjudicated (Table 2.8–2.10).
Finalisation for testing	Template wording refined (e.g., 'overview of the trial design'; replacing fixed	Finalised for piloting (see Chapter 3).

	error rates with 'X'; clarifying 'early cessation').	

Appendix 4: Alignment of this Delphi with recommendations from methodological reviews.

Topic	Recommendations from reviews	Approach in this study
Panel definition	Define 'expert' and justify inclusion criteria.	Practitioners with direct clinical trial monitoring expertise across UK CTUs and industry; roles included trial managers, monitors, QA, statisticians, investigators (see Figures 2.1–2.2).
Rounds and burden	Justify number/length of rounds; minimise fatigue while allowing iteration.	Two rounds planned a priori to balance iteration with burden; 2-week interval; retention strategies implemented between rounds.
Controlled feedback	Provide structured, non-coercive feedback between rounds.	Round-2 items presented with round-1 distributions and medians for reflection; wording refinements presented back to participants.
Consensus definition	Pre-specify quantitative thresholds.	Consensus defined a priori as ≥70% rating 7–9 'critical' and <15% rating 1–3 'not important', following prior trials methodology Delphis (Gamble et al., 2017; Whitham et al., 2018).
Agreement statistics	Use robust statistics; report stability.	Medians and IQRs used; IQR ≤2 treated as consensus/stability indicator (von der Gracht, 2012); stability examined across rounds.
Response reporting	Report response and attrition per round.	Round-1 n=47 (91% complete); Round-2 n=40 (93% complete) (see Results). Retention actions described.
Transparency of item generation	Describe how items were generated and refined.	Items derived from textual analysis of 31 CTU templates (745 items across 38 sections),

		refined with supervisory review and Delphi comments.
Post-Delphi adjudication	If used, describe meeting structure and voting.	Structured consensus meeting (two sessions) with voting on non-consensus items; procedures and outcomes reported (Figures 2.6–2.7; Table 2.10).

Appendix 5: Participant Information Sheet Delphi Survey

Participant Information Sheet

For monitoring staff, monitoring experts or those with an interest in clinical trial monitoring running trials in the UK

UCL Research Ethics Committee Approval ID Number: 24121.001

YOU WILL BE GIVEN A COPY OF THIS INFORMATION SHEET

Title of Study: Uplifting the standard of monitoring in clinical trials – developing evidence and tools

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Department: MRC Clinical Trials Unit at UCL Institute of Clinical Trials and Methodology (ICTM)

Name and Contact Details of the Researcher(s): Ms Shiva Taheri, s.taheri@ucl.ac.uk

Name and Contact Details of the Principal Researcher: Sharon Love, s.love@ucl.ac.uk

1. Invitation Paragraph

This study is a PhD research project to look at how we can improve trial monitoring by creating a trial monitoring plan template based on knowledgeable input. This information sheet is to help you understand why the research is being done and what it will involve for you if you decide to take part. Please take time to read this information and ask us if there is anything that is not clear to you, or if you would like more information. Taking part in the study is entirely voluntary. If you agree to take part, you are free to withdraw at any time without giving a reason. Take time to decide whether or not you wish to take part. Thank you for your interest in this study and taking time to read this information sheet.

2. What is the project's purpose?

Background

Clinical trials are conducted to answer a question in health or science. Monitoring clinical trials is important to ensure patient safety, data integrity and trial integrity. Central, remote, and on-site monitoring brings quality assurance to the design and conduct of research, mitigates risk, and detects issues at early stages. Trial Monitoring Plans detail the trial aspects to be monitored and the actions required centrally, remotely, and on-site. Trial monitoring plans are written based on the research risk level and are reviewed regularly.

A Clinical Trials Unit (CTU) is the main hub for clinical trials management, and each follows their own trial monitoring plan template. However, there is no trial monitoring plan template available to standardise monitoring process within all CTUs. The benefits of a trial monitoring plan template are:

- Maintain consistency in monitoring standards across all CTUs, resulting in higher monitoring standards overall.
- Provide an evidence based, efficient and effective trial monitoring plan across all CTUs.
- Provide a cohesive trial monitoring plan for all CTUs.

Aim

The aim of this project is to improve monitoring of clinical trials.

Objectives

To create a trial monitoring plan template based on knowledgeable input from people working in clinical trials.

We will collect trial monitoring plans from each of the UKCRC (Clinical Research Collaboration) registered CTUs and create a comprehensive list of items that could be included in the trial monitoring plan template. We will also survey people with monitoring experience and expertise in those CTUs, and people at regulatory authorities. We will use a Delphi survey with up to 3 rounds to gain consensus on as

many items as possible to be included in the trial monitoring plan template. This Delphi survey will begin in Q2 2023. There will be 6 weeks between each round, with participants having 4 weeks to complete the first round, and 3 weeks to complete the subsequent rounds. The data collection should end in Q3 2023.

When the survey rounds are all completed, we will call together a group of people with experience and expertise from CTUs and regulatory authorities to a consensus meeting. You will have an opportunity to register your interest to be a part of the consensus meeting at the end of the Delphi survey. We will finalise the content for the trial monitoring plan template, based on the survey results and input from the meeting. This should be completed in Q4 2023.

We will hold the consensus meeting in person, with an option for attendees to join online via MS teams as well. The meeting will be recorded on teams. You will sign a consent form prior to joining the meeting to confirm your consent for being recorded. The meeting will last approximately 3 hours with some break times.

What is a Delphi Survey?

A Delphi survey collects views of a group with experience or expertise on a particular subject to reach a group consensus. The group are typically asked to rate how important they think something is, in this case how important a list of items is to be included in a trial monitoring plan template. The responses are collected and aggregated by the researcher. In this case, this will be done in 3 rounds, with 6 weeks between each round, and participants will have 4 weeks to complete the first round and 3 weeks to complete the subsequent rounds. It is expected that each round will take no longer than 30-45 minutes to complete. You do not have to complete the questionnaire in one sitting, you can save and return to it later. Email reminder will be sent out weekly.

The group members will be aware of the views of the other members; however, they will not know who made which comment. In this way anonymity is kept, which will allow members to express their views without being influenced by group member

status or perceived expertise. Members will be able to change their answer if they wish to.

In this study in round 1, you will be asked to rate how critical you think a list of items are to be included in a trial monitoring plan template, using a 9-point rating scale. You will be given the opportunity to briefly justify your choice (this is optional, you do not have to do this) and change item wordings and/or suggest new items if you wish to do so.

In round 2 and 3, you will be provided with a summary of scores from other participants along with your own score. You will then be given the chance to change your rating or keep with your original decision. Those items that reach a certain criterion (for example, 70% of the group rate the items as being 'Critical', scoring it 7-9), will be assumed to have reached consensus and therefore considered for inclusion in the final list of items in a trial monitoring plan template.

Proposed key dates:

First round of survey: Mid-April 2023

Second round of survey: End of May 2023

Third round of survey: Mid-July 2023

3. Why have I been chosen?

We are inviting people involved in monitoring of clinical trials across the UK to take part. Whether you are a trial manager, monitor, statistician, or someone interested in monitoring clinical trials and improving methodology, you can take part.

4. Do I have to take part?

No. It is up to you to decide whether or not to take part in this research. If you do decide to take part, we will send you the survey link to complete. This is an anonymous survey and by submitting a response to the survey, you confirm consent to taking part. You can withdraw at any time without giving a reason and without any

negative consequences. However, if you do decide to withdraw, any data already collected via survey cannot be withdrawn.

5. What will happen to me if I take part?

You will take part in a Delphi survey. All data will be collected online, using a software program called DelphiManager. We will provide you a link and clear instructions on how to complete the survey. Taking part in the survey is straightforward and does not require access to any specialist equipment/programs. You will have 4 weeks to complete the first survey round and three weeks to complete the two subsequent rounds. If you complete the first survey round, you will be invited to take part in the second round. If you complete the second round, you will be invited to the third and final round. Email reminders will be sent out two weeks before the survey round closes. The survey takes about 30-45 minutes to complete.

6. Will I be recorded and how will the recorded media be used?

The consensus meeting will be recorded on MS teams. You will be consented before joining the recorded meeting. The recording will be saved on UCL's secure IT network and only accessed by authorised research team i.e., PhD student or supervisors. The recording will be used to write up the final trial monitoring plan template and PhD thesis. No other use will be made of them without your written permission, and no one outside the project will be allowed access to the original recordings.'

7. What are the possible disadvantages and risks of taking part?

There are no anticipated risks in taking part in this study. No potentially sensitive information will be collected, and data will be shared anonymously. There will be the option to save and return to the survey to reduce time burden.

8. What are the possible benefits of taking part?

There are no immediate benefits to you or others participating in the project. However, we intend this work will improve conduct of clinical trials by improving monitoring and thereby benefiting research and patients.

Additionally, the final trial monitoring plan template can maintain consistency in monitoring standards across all CTUs, resulting in higher monitoring standards and consequently, higher research quality. It will also provide a cohesive and easy to follow trial monitoring plan template for all CTUs, enabling trial monitoring plan completion more comprehensively and earlier in a study. This will consequently prevent resource waste for funders and CTUs.

We would like to acknowledge those who contribute to this research by completing the Delphi survey. We plan to report the names of the Delphi participants as an appendix to our reports. We will ask you after the final Delphi questionnaire if you would like to be included in the list of contributors. We will make it clear that participation in the Delphi does not necessarily mean agreement with the final guidelines and that participants had a range of views. If you would prefer to not be included in the list of names, that is fine as well.

9. What if something goes wrong?

If you have any concerns about this project, please contact the PhD student Shiva Taheri via

s.taheri@ucl.ac.uk or the PhD supervisor Sharon Love via s.love@ucl.ac.uk, who will do their best to answer your query. However, if you feel that your concern has not been handled to your satisfaction by the research team, you can contact the Chair of the UCL Research Ethics Committee via ethics@ucl.ac.uk.

10. Will my taking part in this project be kept confidential?

All the information that we collect about you during this research will be kept strictly confidential. You will enter your name and email address into the Delphi software when you first access the database. The database will then automatically generate a study ID. This will ensure anonymity of the data therefore your answer will not be linked back to you. Only authorised members of the research team will have access to the database and any data collected from you.

DelphiManager is a bespoke web-based software. The system itself is hosted on a dedicated server which is hosted in the University of Liverpool data centre. The DelphiManager server sits behind the University firewall. Access to the DelphiManager software instance is set up by the IS team and then password protected administrator accounts are managed by the study team. Any data entered into the individual instance of DelphiManager can be extracted by the study team administrators, which will then be saved safely on UCL's secure IT network.

Email addresses collected from survey participants will be kept so that you can be told about the result of the research unless you tell us that you don't want to know. Your name is collected so that we can acknowledge your contribution to the study in an appendix to our reports, unless you don't want to.

Consensus meeting recording will only be used to complete the final trial monitoring plan template and write up the PhD thesis. No other use will be made of them without your written permission, and no one outside the project will be allowed access to the original recordings.'

11. Limits to confidentiality

Please note that assurances on confidentiality will be strictly adhered to unless evidence of wrongdoing or potential harm is uncovered. In such cases the University may be obliged to contact relevant statutory bodies/agencies.

12. What will happen to the results of the research project?

The result of this research will be written up for a PhD dissertation, publication(s) and disseminated at conferences as well as to all CTUs around the UK. If you withdraw from the study, we will need to keep and use the data collected up to your withdrawal. The study will also be published on Open Science Framework https://osf.io/, to enable free and widely available sharing of the study. We will also send you the final trial monitoring plan template.

13. Local Data Protection Privacy Notice :

The controller for this project will be University College London (UCL). The UCL Data Protection Officer provides oversight of UCL activities involving the processing of personal data, and can be contacted at data-protection@ucl.ac.uk

This 'local' privacy notice sets out the information that applies to this particular study. Further information on how UCL uses participant information can be found in our 'general' privacy notice:
here

The information that is required to be provided to participants under data protection legislation (GDPR and DPA 2018) is provided across both the 'local' and 'general' privacy notices. The categories of personal data used will be as follows:

- Name
- Email address

The lawful basis that would be used to process your *personal data* will be performance of a task in the public interest.

Your personal data will be processed so long as it is required for the research project. If we are able to anonymise or pseudonymise the personal data, you provide we will undertake this and will endeavour to minimise the processing of personal data wherever possible.

If you are concerned about how your personal data is being processed, or if you would like to contact us about your rights, please contact UCL in the first instance at data-protection@ucl.ac.uk.

14. Who is organising and funding the research?

The study is being organised and coordinated by the MRC Clinical Trial Unit at UCL Institute of Clinical Trials and Methodology (ICTM). The funding for the study is provided by the Medical Research Council (MRC) and UK Research and Innovation (UKRI).

14. Contact for further information

Should you need further assistance with regards to this study please see contact details below:

PhD Student: Shiva Taheri s.taheri@ucl.ac.uk

PhD supervisor: Sharon Love s.love@ucl.ac.uk

MRC Clinical Trials Unit at UCL

Institute of Clinical Trials and Methodology

90 High Holborn

2nd Floor

London

WC1V 6LJ

Thank you for reading this information sheet and for considering taking part in this research study.

Appendix 6: Delphi survey participant recruitment advert

UNIVERSITY COLLEGE LONDON

Are you involved or interested in monitoring clinical trials?

MRC Clinical Trials Unit, Institute of Clinical Trials and Methodology (ICTM)

Calling everyone with clinical trial monitoring experience, expertise, or a desire to improve monitoring processes to complete a Delphi survey to choose the contents of a trial monitoring plan template.

My name is Shiva, and I am a PhD student at MRCCTU. I worked as a trial manager for a number of years before starting my PhD.

UNIVERSITY COLLEGE LONDON

Are you involved or interested in monitoring clinical trials?

MRC Clinical Trials Unit, Institute of Clinical Trials and Methodology (ICTM)

The aim of my PhD is to improve monitoring trials by creating a trial monitoring plan template based on knowledgeable input.

I have put together a comprehensive list of items that could be included in a trial monitoring plan template after reviewing templates sent to me by CTUs around the UK.

I've created a Delphi survey to gain consensus on as many items as possible to be included in a trial monitoring plan template. Scan the QR code to find out more. Your contribution to this research is highly appreciated.

The deadline to complete the survey is **25th May**. If you are interested to take part in this survey, please scan the QR code or go to : https://delphimanager.liv.ac.uk/TMPtemplate/. For further information about this study, please contact **Shiva Taheri on s.taheri@ucl.ac.uk.**

Appendix 7: List of items that had reached consensus during the Delphi survey.

	TMP template item	% of participants responding 7-9 (critical)
	Study Details	
1	Purpose	81%
2	CTIMP/nCTIMP	91%
	Introduction to the trial: Summary of study design/Trial overview	
3	Primary Outcome Measures	86%
	Monitoring	
4	Who will monitor the study? e.g., Sponsor/sponsor delegate	86%
5	What will be the first monitoring time-point?	95%
	Central Monitoring Activities	
6	Review of IMP shipment and delivery documentation.	74%
7	Review of IMP dosage calculations.	76%
	Data Checks	
8	Checks for missing or invalid data (range and consistency checks).	90%
9	Hard-copy CRFs and patient completed questionnaires validation: e.g., Where the CRF is a hard-copy, the content of approximately 10% of case report forms (CRFs) and patient questionnaires entered at sites will be checked (or double entered) to ensure the accuracy of data input. (An error rate of <3% will require no further action, however, if the error rate is >3%, a 100% check of forms will be undertaken.):	81%
	Protocol Deviation	
10	Other- Specify (e.g., Central review of adherence to the protocol and plausibility of the data; review of any questionnaires for completeness; time of randomisation and intervention consistent with clinical context; expected variability in items such as age; disease severity etc.)	74%
	On-Site Monitoring activities	
11	Checking understanding and adherence to study protocol; procedures; and governance requirements (including any	90%

	conditions in regulatory or ethics approval.)	
12	Review Medical/study records and results of eligibility assessments for <X%> of participants to confirm participant eligibility.	100%
13	Verification that resources and facilities remain adequate.	76%
14	Verification of appropriate oversight and documented delegation by the local investigator.	95%
15	Availability of completed source documents and CRF for the monitoring visit.	98%
16	Source document completion in accordance with the ALCOA principles check.	71%
	Protocol Deviation and Compliance	
17	Verification of missing visits; examinations; or tests.	88%
18	Verification of lab reports reviewed; signed; and dated appropriately.	88%
19	Have protocol deviations been reported appropriately?	95%
20	Have any new protocol deviations and/or regulatory or GCP deviations occurred at site since the last visit?	88%
	Documents and systems to be reviewed	
21	Randomisation processes	71%
	Source Data Verification (SDV)	
22	Is any SDV to be performed? Yes/no	93%
23	Which patients need SDV and how will you select them? e.g., number/percentage of patients and how you will select them; first patient at each site.	90%
24	What data needs SDV? e.g., eligibility; outcome data; or all data	95%
	Routine Monitoring Visits	
25	Selection criteria for participants to be reviewed during Routine Monitoring Visits- This may be on request of the TMG or following review of central monitoring reports; (e.g., participants who have a high number of SAEs reported) or on a percentage of	78%

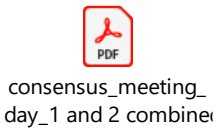
	participants (e.g., 10% selected at random).	
	Site Initiation Visit	
26	List of training to occur during the site initiation visit.	78%
27	Confirmation of Critical Documentation held both regulatory and trial/site-specific.	78%
28	Obtaining confirmation that the site staff have completed the trial-specific training and are made aware of the operational requirements.	80%
	Close out visit	
29	Definition of end of trial.	78%
30	The Trial Investigator File must be reviewed and confirmed as complete by the Trial Manager; prior to archiving.	85%
	Pharmacy Monitoring (Ordering and Storage of IMP)	
31	Are there adequate stocks within expiry dates for the planned patients?	98%
32	Are storage temperatures adequately monitored by pharmacy staff?	98%
33	Have any temperature excursions occurred?	100%
34	Have any temperature excursions been appropriately managed?	100%
	On-site monitoring activities	
35	To review consenting process and document completion	74%
36	Review of consent forms to ensure completed correctly.	95%
37	Have all SAEs been reported by site within the reporting timelines?	93%

Appendix 8: List of 32 items that did not reach consensus in the Delphi survey.

	TMP Item	% of participants responding 7-9 (critical)
1	Overall Recruitment Target	42%
2	Secondary outcome measures	40%
3	Duration of patient recruitment	33%
4	Duration of follow up (Per patient)	40%
5	Duration of follow up (The trial)	19%
6	Intervention(s)	64%
7	Is the trial placebo or standard of care controlled?	55%
8	Describe any specific regulatory requirements: e.g., The intervention is/is not being used in a licensed indication OR The data from the trial will/will not be used to support a licensing application OR The trial is/is not supporting a license change. Include details of international regulation e.g., FDA; Medical Devices; or other specific regulations.	40%
9	Describe other issues specific to the treatment under study.	17%
10	If medical device trial SADEs reported to manufacturer (if not delegated to CTU).	62%
11	Out-of-hours emergency cover arrangements- Where participants are provided with out of hours contact details for site staff (e.g., on a Participant ID card or PIS) indicate how this will be verified (e.g., for high-risk trials a test procedure may be put in place).	62%
12	Review of Visit Window Thresholds	67%
13	Is the Site Delegation Log the original of the latest copy filed in Site Master File?	57%
14	Has the Site Visit Log been completed at each visit?	21%
15	Discussions with site staff and review of site staff training requirements (current documents and training present; staff changes documented; CVs; GCP; delegation log.)	66%

16	Other- Add any additional checks to be performed during on-site monitoring visits for this trial.	32%
17	Completion of annual progress and safety reports (as appropriate)	68%
18	Recruitment rates	32%
19	Screen failure	27%
20	Withdrawal rates	34%
21	Question for Delphi Respondents: Do you want a prompt list of data to SDV on the template?	46%
22	Describe what source data will be available as a hard copy; and what will be available electronically and how access arrangements will be set up.	46%
23	Ongoing training/motivation meetings and teleconferences.	15%
24	Completion of annual progress and safety reports (as appropriate).	43%
25	Question for Delphi Respondents: Do you want to see a prompt list of metric examples on the template?	20%
26	Or do you want to have the option to use your unit specific list of metrics?	45%
27	Request for submission of Trial Equipment calibration records.	35%
28	All outstanding payments must be reviewed and invoiced.	55%
29	Onsite vendor monitoring.	20%
30	Central monitoring of vendor duties.	48%
31	Review of vendor related deviations (if required).	55%
32	Completion of Vendor status reports.	18%

Appendix 9: Delphi graphs and consensus meeting voting



consensus_meeting_day_1 and 2 combined.pdf

Appendix 10: TMP template finalised after consensus meeting

<study name> Trial Monitoring Plan Template			
Version			
Effective date			
Reviewer	**Position**	**Signature**	**Date**
Approved by			

Introduction to this trial monitoring plan template for Clinical Trial Units (CTUs): [remove this page once the template is finalised]

This document provides a monitoring plan template suitable for both CTIMP and non-CTIMP studies. Please tailor the template to align with your study's specific requirements and risk levels. Alternatively, you may choose to incorporate relevant sections into your CTU template. It's essential to highlight that this template is not a standalone document and should be used in conjunction with the clinical trial protocol, CTU's study-specific SOPs, and any other work instructions specified by the CTU. Any template sections that do not pertain to the trial or CTU can be omitted as needed.

Important note: Throughout the template, you will find tables with a column called 'Trial Specific Notes' which should be used for tailoring the template to the specific requirements of the trial. These tables also include examples and guidance Trial Specific Notes in italic font which you have the flexibility to choose whether to remove, retain, or enhance based on the trial's risk level or any specific regulations pertinent to the CTU. The template also includes checklists in various sections. Certain instructions are highlighted in red and should be deleted once the template is in its final form.

List of Acronyms

Acronyms	Definitions
CRO	Contract Research Organization
CTIMP	Clinical Trial of an Investigational Medicinal Product
CTU	Clinical Trials Unit
DMEC	Data Monitoring and Ethics Committee
eCRF/CRF	Electronic/Case Report Form
FDA	Food and Drug Administration
GCP	Good Clinical Practice
IMP	Investigational Medicinal Product
ISF	Investigator Site File
non-CTIMP	Clinical Trial that does not involve an Investigational Medicinal Product
PSF	Pharmacy Site File
QA	Quality Assurance
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SDV	Source Data Verification
SmPC	Summary of Product Characteristics
SOP	Standard Operating Procedure
TMG	Trial Management Group
TMP	Trial Monitoring Plan

Contents

Purpose

[This refers to the purpose of the TMP template. Enter a description of the purpose of this document based on the local SOPs and study protocol.]

The Trial Monitoring Plan (TMP) template outlines a comprehensive set of planned and systematic measures designed to ensure that the <INSERT Study Name> is conducted, and data are created, recorded, and reported in accordance with Good Clinical Practice (GCP) and relevant regulatory standards. This plan is formulated based on the study-specific Risk Assessment and thus may be subject to modifications as the study risks evolve. Regular review of the TMP is advisable on an annual basis, with more frequent revisions warranted in the event of changes to the study's Risk Assessment.

The purpose of this template is to document the procedures for monitoring before, during and at the end of <Study Name> including central monitoring, site visits, report writing and archiving.

Study Details

Complete the table below to give a description of the study details.

	Study details
Study acronym/short name	
ClinicalTrials.gov identifier	
EudraCT number	
ISRCTN number	
CTIMP/non-CTIMP	
Is there blinding in the study?	
Who is blinded (give role) and what are they blinded to?	
Randomisation procedure (for confirming that randomisation is performed according to the protocol and investigational plan)	e.g., comparison of randomisation and CRF data to assess whether the subject was administered or dispensed the assigned product.
Definition of end of trial	

An overview of the trial design

[Complete the table below to give a description of the study design and trial overview.]

	Trial Specific Notes
Study design	
Primary Outcome measures	
Describe any specific regulatory requirements:	(e.g., The intervention is/is not being used in a licensed indication OR The data from the trial will/will not be used to support a licensing application OR The trial is/is not supporting a license change. Include details of international regulation e.g., FDA, Medical Devices, or other specific regulations)
Describe other issues specific to the treatment under study (anything that is not covered by inclusion/exclusion criteria).	(e.g., participants need to fast for the intervention, or the treatment has a 12-hour life)

Summary of the trial risks

The table below is a summary of the trial risk assessment. Please follow your local risk assessment procedures and complete any relevant documents accordingly. Please note this should not replace the risk assessment for the trial, instead, it should be used as a snapshot of the main risk assessment of the trial.

Monitoring for this trial will be carried out using a risk-based approach. The risks to participants associated with the trial intervention(s) have been assessed in relation to standard care for the participant group concerned. Is the monitoring of this trial carried out on a risk-based approach? Yes ☐ No ☐ If CTIMPT, The trial has been assessed as: A **Type A** trial requiring a **low** intensity of monitoring ☐ A **Type B** trial requiring a **moderate** intensity of monitoring☐ A **Type C** trial requiring a **high** intensity of monitoring ☐

If non-CTIMP please indicate the risk level:
Justification of risk category selected:
Add justification of risk category selected, e.g., Impact of participation/administration of IMP compared to standard care, current licence vs. current off label use, oversight of IMP administration, side effects, safety monitoring.

Monitoring

The following monitoring approaches can be used based on the trial's risk category and the trial specific risks identified within the risk assessment:

Central monitoring –Central monitoring is a remote evaluation carried out by sponsor personnel or representatives (e.g., clinical monitors, data management personnel, or statisticians) at a location other than the sites at which the clinical investigation is being conducted. Central monitoring processes can provide many of the capabilities of on-site monitoring as well as additional capabilities.

On-site monitoring – On-site monitoring will involve a visit to a site/s by a member of the CTU and can be carried out for the following reasons: Site Initiation Visit (SIV) (to train site staff), Triggered Monitoring Visit (TMV), and Close Out Visits (COV) (to close the site).

Remote monitoring- Remote monitoring is when monitors don't visit the site to review the data. Instead, data monitoring is done virtually. With the use of digital technology, CROs and study sponsors/stakeholders can see the data from wherever they are located.

These types of monitoring can be carried out as part of:

Triggered Monitoring- Triggered monitoring in clinical trials is a risk-based monitoring approach where triggers specify the extent, timing, and frequency of monitoring visits.

Routine Monitoring- routine monitoring occurs at pre-decided times rather than in response to a concern.

Important note: All trial monitoring activities should be conducted in accordance with the local SOPs. The frequency of monitoring and who carries out the task should be indicated where possible for all monitoring tasks.

Trial/Study Monitoring Approach: choose the monitoring approach for the trial. (Tick all that apply)	Central ☐ Onsite ☐ Remote ☐
Type of monitoring (Tick all that apply)	Triggered ☐ Routine ☐
Who will monitor the study?	e.g., Sponsor/sponsor delegate
What will be the first monitoring time-point?	e.g., after first participant is randomised

Central Monitoring Activities

The table below lists activities to be completed during central monitoring. Please complete this table considering the local SOPs and trial protocol.

	Trial Specific Notes
Frequency of central monitoring	
Consent and eligibility	
Checking consent is taken correctly.	e.g., Completion of Informed Consent Forms (ICFs) for X participants (X is determined based on the trial risk), checking the signature, dates are contemporaneous, and counter signatory on the delegation log.
Additionally, consent and eligibility should include the following checklist: (Add/Delete as appropriate to the trial) • Eligibility checks before randomisation. • Review of trial eligibility criteria sign-off by local PI.	
Site Delegation and training	
Indicate how staff training and delegation of responsibilities will be monitored including the frequency of review.	(e.g., collection and review of CVs, training logs and delegation logs)
IMP accountability **(For more details on IMP please see the pharmacy monitoring section in this TMP)**	

Will IMP accountability be done for all participants or for a sample from each site?	
How will this be done if an external service provider is being utilised?	
How frequently should the accountability log be sent to the trial office?	e.g., every 6 months
How frequently should the dispensing log be sent to the trial office?	e.g., every 6 months
Additionally, IMP accountability should include the following checklist: (Add/Delete as appropriate to the trial) • Review of IMP shipment and delivery documentation. • Review of IMP dosage calculations.	
AE, SAE, and SADE	
Adverse Events	e.g., central review or reconciliation of SAE forms and reporting timelines.
If medical device trial, indicate if SADEs are reported to the manufacturer or delegated to CTU.	
Out-of-hours emergency cover arrangements- Where participants are provided with out of hours contact details for site staff.	(e.g., on a Participant ID card or PIS) indicate how this will be verified (e.g., for high-risk trials a test procedure may be put in place).
Data Checks	
Checks for missing or invalid data (range and consistency checks)	
Checks for unusual data patterns/Suspected fraud.	e.g., audit trail end digit review.
Protocol Deviation	
Review of Visit Window Thresholds	
Other- Specify (Add any protocol deviation which is to be checked centrally)	(These examples are not an exhaustive list. e.g., Central review of adherence to the time

	of randomisation and intervention consistent with protocol.)
Site File Review	
Site File and Pharmacy File: Indicate the procedures for checking the site file.	e.g., A checklist of documents contained within the site file and site pharmacy file will be sent out for self-completion by the sites as appropriate. The Trial Office will monitor these on return and implement remedial action as and when appropriate.

Central Quality Checks

Central quality checks should include the following checklist:

(Add/Delete as appropriate to the trial)

- Completion of a site questionnaire/assessments or to confirm that they can fulfil the safety requirements and perform the required trial assessments.
- Sites are requested to return anonymised screening logs every X months (X is determined based on the trial risk) for review at CTU.
- Chief Investigators and Principal Investigators sign an Investigator Statement agreeing to their roles and responsibilities during the trial.
- Screening and Enrolment log review before each IDMC, or every X months (X is determined based on the trial risk).
- Signed receipts to confirm receipt of any updated documents (e.g., Protocols, Investigator Brochures (IBs) etc.) as required.
- Other central quality control procedures to be conducted centrally by trial team members [add as applicable].

Metrics

The table below is about the use of metrics in monitoring trials, sometimes termed "site performance metrics". Add more rows as needed.

Metrics If applicable, list the metrics used for this trial.	**Thresholds** If applicable, list the metrics thresholds for this trial.

Escalation	
Consider the action of escalation proportionate to central monitoring findings, linked to specific metrics crossing a threshold if appropriate. A general concern with a site based on correspondence or other incidents may also be a reason to escalate. Add action of escalation for trial in here i.e., when meetings will be held to discuss an action.	

Onsite Monitoring Visit

The table below lists activities to be completed at onsite monitoring visits. Please complete this table considering the local SOPs and study protocol.

	Trial Specific Notes
Frequency of on-site monitoring	
Choose the applicable option from the two following options and delete the one that is not needed: On-site monitoring will be carried out for this trial in the form of routine monitoring visits with additional triggered monitoring visits where applicable OR Routine on-site monitoring will not be carried out for this trial. Triggered monitoring visits will be conducted in response to the triggers stated in the protocol or on request of the trial oversight committees or the Senior Trial Manager/QA Manager at the CTU.	
Availability of completed source documents and CRF for the monitoring visit.	Indicate how this will be done prior to visit
Selection criteria for participants to be reviewed during On-site Monitoring Visits- This may be on request of the TMG or following review of central monitoring reports.	(e.g., participants who have a high number of SAEs reported or on a percentage of participants e.g., 10% selected at random).

Review of consent forms to ensure completed appropriately.	e.g., Completion of Informed Consent Forms (ICFs) for X participants (X is determined based on the trial risk), checking signature, dates are contemporaneous, and counter signatory on the delegation log.
Serious Adverse Event / Serious Adverse Device Effect report(s) check: Check all serious adverse events are accurately documented and reported by site within the reporting timelines.	To be performed for <X> number /% of participants (X is determined based on the trial risk), at each monitoring visit alongside medical records and database entries/logs of SAEs.
Review Medical/study records and results of eligibility assessments to confirm participant eligibility.	for <X%> of participants (X is determined based on the trial risk).
Investigator Site File - presence and completion of all (OR a selection of) trial documents, security, and location of files.	List all the documents to be checked. (e.g., Delegation logs, Training logs (including the trial-specific training), CVs and GCP certificates).
Source document completion in accordance with the ALCOA principles check. *ICH E6 4.9.0 -The investigator/institution should maintain adequate and accurate source documents and trial records that include all pertinent observations on each of the site's trial subjects. Source data should be attributable, legible, contemporaneous, original, accurate, and complete. Changes to source data should be traceable, should not obscure the original entry, and should be explained if necessary (e.g., via an audit trail).	
Additionally, the onsite monitoring visit should include the following checklist: (Add/Delete as appropriate to the trial) • Checking understanding and adherence to study protocol, procedures, and governance requirements (including any conditions in regulatory or ethics approval). • Verification that resources and facilities remain adequate. • Verification of appropriate oversight and documented delegation by the local investigator.	
Protocol Deviation and Compliance	

Additionally, protocol deviation and compliance should include the following checklist:

(Add/Delete as appropriate to the trial)

- Verification of missing visits, examinations, or tests.
- Verification of lab reports reviewed, signed, and dated appropriately.
- Verification of protocol deviations reported appropriately.
- Verification of any new protocol deviations and/or regulatory or GCP deviations that occurred at the site since the last visit, reported appropriately.

Site staff discussion

Site staff discussion should include the following checklist:

(Add/Delete as appropriate to the trial)

- Discussions with site staff regarding staff training requirements (current documents and training present, staff changes documented, CVs, GCP, delegation log).
- Time at the end of the monitoring visit for discussion with the site staff to resolve any issues where feasible. Key points to be recorded in the monitoring visit report. Issues not resolved during the visit should be recorded in the report for resolution prior to the next monitoring visit.

Documents and systems to be reviewed

Deviation logs	e.g., frequency of checks
Screening logs	e.g., frequency of checks
Completion of previously raised findings and actions (as appropriate).	Indicate how this will be checked
Randomisation processes	e.g., date of randomisation recorded on the CRF and randomisation service e.g., sealed envelope if applicable, and appropriateness of trial team member according to the site delegation log.
Screening procedures	
Early cessation of participation in trial (treatments, procedures, and/or data)	
Hard-copy CRFs and patient completed questionnaires validation.	The amount of content to be checked and the error rate (X) is determined based on the trial risk. Where the CRF is a hard copy, the content

	of approximately X% of case report forms (CRFs) and patient questionnaires entered at sites will be checked (or double entered) to ensure the accuracy of data input. An error rate of <X% will require no further action, however, if the error rate is >X%, a 100% check of forms will be undertaken.
Visit to other departments	
Will the monitor visit the PI, Research team, Lab, and Pharmacy? If yes, complete the relevant sections of this template.	
Source Data Verification (SDV)	
Is any SDV to be performed? Yes/no	
If applicable, which participants need SDV and how will you select them?	e.g., number/percentage of participants and how you will select them, e.g. First X patient(s) at each site.
If applicable, what data needs SDV?	e.g., study arm, outcome data, or all data.
Describe what source data will be available as a hard copy, and what will be available electronically and how access arrangements will be set up. (Refer to source data location agreement if applicable)	

Remote Monitoring Visit

[The table below lists activities to be completed during remote monitoring visits. Please complete this table considering the local SOPs and study protocol.]
Remote Monitoring serves as a valuable resource for the CTU trial management team, allowing them to adopt a risk-based strategy for minimizing on-site monitoring and addressing situations where physical presence at the trial site is not feasible. It is crucial to prepare adequately for remote monitoring, ensuring that all necessary information and documentation are obtained from the trial site for the monitoring visit. This may include using self-monitoring questionnaires, administered in accordance with a risk-based approach, which the trial site team completes and submits to the CTU for confirmation. If

requested documentation contains personal information, this should be redacted and managed accordingly i.e., no patient personal details will be retained by the CTU.

	Trial Specific Notes
Frequency of remote monitoring.	
Determine how the trial issue will be resolved.	e.g., telephone, email
X should be determined based on the trial risk. **Monitoring will consist of X% monitoring of the following:**	
Patient informed consent forms completed correctly.	
CRF/eCRF completion and data cleaning	
Recording and reporting of AE's and SAE's	
Source data verification facility/all CRF entries can be verified either in electronic or paper format (see SDV section for more details).	

Monitoring will also consist of monitoring the following items as appropriate to the trial:

(Add/Delete as appropriate to the trial)

Localised PIS and consent form

Delegation log (updated version to be sent if additional study team leave or join)

CV's, GCP certificates and training logs

Monthly screening and recruitment logs (anonymised)

Deviation logs

eCRF audit logs

Local approval documents

Investigator Site File Contents (e.g., newsletters, significant communication with the site)

Pharmacy Site File Contents (see pharmacy section for more details).

IMP (request/shipment request, accountability logs, destruction logs, temperature logs).

Triggered Monitoring

The table below is to be completed for triggered monitoring. Examples and guidance are given to help with developing trial triggered monitoring strategies. Please complete this table considering the local SOPs and study protocol. Please note this sections lays out the process leading to triggered monitoring. Once this is established, the monitoring will be done either centrally, on-site, or remote, in which the relevant sections should be completed for the visit.

A weekly/monthly/quarterly triggered monitoring report (produced by the Data Management team) will be generated to include data around specific trigger categories. For this trial, <xx> number of triggers in a <xx> (X is determined based on the trial risk) period will require further investigation by the TMG and, where necessary, may trigger an on-site visit. Any triggered monitoring visits will be documented internally within a monitoring report.

Thresholds and associated actions/escalation plan:

(What specific findings/thresholds would necessitate an action in response? What would the immediate corrective actions be and what is the escalation process if the issue is not resolved within a specified timeframe?)

The types of issues identified through monitoring that would trigger immediate issue escalation:

This is not an exhaustive list, items can be added or removed as appropriate.

- A high level of findings through central monitoring oversight.
- A high number of protocol deviations.
- Low or High SAE reporting rate compared with other sites.
- Poor data quality (long data entry delays, high query rate and high percentage of missing data, constant outstanding data, particularly relating to primary endpoint or safety data).
- Concerns over IMP or sample management processes.
- Concerns over consent procedures.

Routine Monitoring Visit

[The table below is to be completed for routine monitoring visits. Please complete this table considering the local SOPs and study protocol.]

	Trial Specific Notes
Frequency of routine visits	
Type of monitoring	i.e., remote, or onsite
Selection criteria for participants to be reviewed during Routine Monitoring Visits-	This may be on request of the TMG or following a review of central monitoring reports, (e.g., participants who have a high number of SAEs reported or on a percentage of participants e.g., 10% selected at random).

Pharmacy Monitoring

[The table below lists activities to be completed during pharmacy monitoring visits. Please complete this table considering the local SOPs and study protocol.]

	Trial Specific Notes
Is Pharmacy involved in the study? Yes/No	
Planned Frequency of Pharmacy Monitoring Visits	
Will Pharmacy visits be timed with the main visits?	
Ordering and Storage of IMP	
Description of the necessary transport and storage conditions, if applicable with reference to the study protocol or another respective document.	
Additionally, ordering and storage of IMP should include the following checklist: • Checks to verify if IMP is being stored appropriately and in a secure location. • Checks to verify the availability of adequate stocks within expiry dates for the planned participants. • Checks to verify storage temperatures adequately monitored by pharmacy staff. • Checks for any temperature excursions. • Checks to verify any temperature excursions have been appropriately managed.	

IMP Accountability	
IMP accountability should include the following checklist: • Checks to determine supplied IMP dispensed at the protocol-specified dose(s)/schedule. • Checks for any IMP returned or destroyed at the monitoring visit? (e.g., expired, or damaged). • Checks to verify the disposal of IMP at the site is appropriately documented. • Checks to verify study medication is appropriately documented. • Checks for any discrepancies in IMP accountability logs.	
Pharmacy File	
Pharmacy File: Indicate the documents to be checked for the pharmacy file.	e.g., Is the current version of Investigator Brochure/SmPC, IMP handling/pharmacy guidelines (if applicable) and current approved protocol held in the Pharmacy File?

Medical Device Monitoring

The table below lists activities to be completed during medical device monitoring. Please complete this table considering the local SOPs and study protocol.

	Trial Specific Notes
Does this study involve Medical Devices? Yes/No	
Ordering and Storage of the devices	
Description of the necessary transport and storage conditions, if applicable with reference to the study protocol or another respective document.	
Device Accountability	
Monitoring device accountability should include the following checklist: • Allocation/return • Storage • Expiry • Documentation	

Sample Monitoring

The table below lists activities to be completed during sample monitoring. Please complete this table considering the local SOPs and study protocol.

	Trial Specific Notes
Does this study involve the collection of biological samples? Yes/No	
Are the samples processed locally or centrally?	
Sample Monitoring Procedure	
Sample monitoring procedure should include the following checklist: • Sample log completion checks • Sample delivery log checks (if samples are sent off-site for processing). • Other documentation related to sampling.	
Storage of samples	
Description of the necessary transport and storage arrangements for samples collected for the study if applicable, with reference to the study protocol or another respective document.	
How often will the labs be visited?	
Where the lab section of the ISF will be held and who will maintain this?	
Which procedures should be followed where deviations occur?	
Procedures to take place during the close-out visit.	
Sample Accountability	
Sample accountability should include the following checklist: • Storage conditions • Sample tracking • Laboratory reports • Expiry	

Site Initiation

The table below lists activities to be completed during the site initiation visit. Please complete this table considering the local SOPs and study protocol.

	Trial Specific Notes
Remotely within the CTU or via on-site visits? Describe the rationale for the chosen method of Site Initiation. Where SIV is to be carried out via on-site visits, indicate how many sites are to be visited.	(Format on-site visit/teleconference/video conference e.g., MS teams meeting).
Determine site staff members who need to be present at the initiation visit.	(e.g., principal investigator, investigator, study assistant, pharmacist, etc.).
Attendance to be documented.	
List of trainings to occur during the site initiation.	
Site-specific documentation reviews.	List all the documents to be checked. (e.g., Delegation logs, Training logs (including the trial-specific training), CVs and GCP certificates).
Arrangements for study medication, documentation (CRFs, Investigator Site File) and further study material delivery to sites(s).	(e.g., drug supply, schedule of assessments, treatment schedule, biological sample collection/ processing/ shipment).
Additionally, site initiation should include the following checklist: • If applicable, a review of the Pharmacy facilities (see pharmacy section of the template). • Request for submission of Trial Equipment calibration records. • Confirmation of Critical Documentation held both regulatory-specific, trial, and site-specific.	

Site Close Out

The competent authority and research ethics committee should be notified within 90 days of the end of the trial. A summary report of the research is to be sent to the competent authority and research ethics committee within 12 months of the end of the trial. The funder is to be provided a final report at the end of the trial. An official close-out letter will be sent by the

trial manager to each participating site once outstanding queries are finalised, and all data has been received.

	Trial Specific Notes
Will visits be conducted remotely from CTU, on-site or centrally?	
% and number of sites expected to be visited for Site Close-out.	
Document how site close-out will be conducted for those sites that are not visited.	(e.g., via teleconference, emails, and letters to sites).
The proposed timing of Close-out visits.	(X weeks from the end of the study).

Additionally, close out visit should include the following checklist:

- The Trial Site File must be reviewed and confirmed as complete prior to archiving.
- All outstanding payments must be reviewed and invoiced.
- Drug accountability.
- Ensure all SAEs are correctly reported including SDV if required.
- Final review of Investigator Site File (ISF)/Pharmacy Site File (PSF).

Monitoring reports

The monitoring report is intended to summarise the monitoring visit. It will facilitate the recording of the items reviewed, any findings (such as non-compliance, deviations, deficiencies, or data anomalies), and recommended corrective actions. Furthermore, the report will enable the documentation of findings and details of any meetings conducted during the visit, which encompasses the feedback meeting. The full follow-up letter should include the following components:

- Actions Resolution Document
- Date of visit
- Name of the monitor(s)
- Site name
- Name of the investigator

- A brief review of any additional meetings that took place, in particular the feedback meeting.
- Sites response and implementation of corrective actions where appropriate.

Additionally, timelines should be allocated for:

- Internal review of the written report.
- Written report submitted to sites.
- Sites response and implementation of corrective actions where appropriate.

Archiving

[Archiving plan for the trial should be drawn here following the local SOPs.]

Appendix 11: One to one instant reaction semi-structured interview questions

Qualitative Interview questions for one-to-one instance reactions:

1. Overall Impressions

What are your initial thoughts on the template?

How would you describe your initial reaction to the template?

2. Clarity and Understanding

Do you find the template instructions and purpose clear?

Are there any parts of the template that you found confusing or unclear?

Can you suggest any improvements to the formatting of the template?

3. Customisation

What are your suggestions for customising the template to better suit your specific needs?

Are there any limitations or challenges in customising the template?

4. Usefulness

Do you think the template provides useful guidance for your monitoring needs?

5. Suggestions for Improvement

Are there any changes or additions you would recommend making the template more user-friendly or effective?

Do you have any further suggestions for improving the template's design, layout, or content?

6. Comparison to Alternatives

How does the template compare to the one used in your CTU?

Does anything set this template apart from other options available to you?

7. Future Use

Do you anticipate using this template regularly or in future trials?

Is there anything that would prevent you from continuing to use this template?

8. Additional Comments

Is there anything else you'd like to share about your experience today?

Appendix 12: Pilot semi-structured interview questions

Qualitative Interview questions after piloting the template at a CTU:

1. Overall Impressions

What are your initial thoughts on the template?

How would you describe your initial reaction to the template?

2. Clarity and Understanding

Do you find the template instructions and purpose clear?

Are there any parts of the template that you found confusing or unclear?

Can you suggest any improvements to the formatting of the template?

3. Ease of Use*

How easy or difficult was it for you to find your way through different sections and use the template?

Were there any specific features or functions that you had trouble with?

4. Fit for Purpose*

Did the template meet your needs for a trial monitoring template in your CTU?

Were there any aspects of the template that didn't align with your expectations?

Were there any aspects of the template that didn’t align with your CTU’s requirements and practices?

Did you experience any challenges in using the template?

5. Customisation

What are your suggestions for customising the template to better suit your specific needs?

Are there any limitations or challenges in customising the template?

6. Usefulness

Do you think the template provides useful guidance for your monitoring needs?

Are there any elements of the template that you found particularly lacking in utility? *

7. Suggestions for Improvement

Are there any changes or additions you would recommend making the template more user-friendly or effective?

Do you have any further suggestions for improving the template's design, layout, or content?

8. User Experience*

Can you describe your overall experience using the template in terms of satisfaction and usability?

Were there any aspects of using the template that stood out to you, positively or negatively?

Do you think this template brings any additional value to your monitoring practices?

9. Comparison to Alternatives

How does the template compare to the one used in your CTU?

Does anything set this template apart from other options available to you?

10. Future Use

Do you anticipate using this template regularly or in future trials?

Is there anything that would prevent you from continuing to use this template?

11. Additional Comments

Is there anything else you'd like to share about your experience today?

Appendix 13: Participant Information Sheet (Instant reaction interviews)

Participant Information Sheet

For monitoring staff, monitoring experts or those with an interest in clinical trial monitoring running trials in the UK

UCL Research Ethics Committee Approval ID Number: 24121.002

YOU WILL BE GIVEN A COPY OF THIS INFORMATION SHEET

Title of Study: Uplifting the standard of monitoring in clinical trials – developing evidence and tools

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Department: MRC Clinical Trials Unit at UCL Institute of Clinical Trials and Methodology (ICTM)

Name and Contact Details of the Researcher(s): Ms Shiva Taheri, s.taheri@ucl.ac.uk

Name and Contact Details of the Principal Researcher: Sharon Love, s.love@ucl.ac.uk

1. Invitation Paragraph

This study is a PhD research project to look at how we can improve trial monitoring by creating a trial monitoring plan template based on knowledgeable input. This information sheet is to help you understand why the research is being done and what it will involve for you if you decide to take part. Please take time to read this information and ask us if there is anything that is not clear to you, or if you would like more information. Taking part in the study is entirely voluntary. If you agree to take part, you are free to withdraw at any time without giving a reason. Take time to decide whether or not you wish to take part. Thank you for your interest in this study and for taking the time to read this information sheet.

2. What is the project's purpose?

Background

Clinical trials are conducted to answer a question in health or science. Monitoring clinical trials is important to ensure patient safety, data integrity, and trial integrity. Central, remote, and on-site monitoring brings quality assurance to the design and conduct of research, mitigates risk, and detects issues at early stages. Trial Monitoring Plans detail the trial aspects to be monitored and the actions required centrally, remotely, and on-site. Trial monitoring plans are written based on the research risk level and are reviewed regularly.

A Clinical Trials Unit (CTU) is the main hub for clinical trial management, and each follows its own trial monitoring plan template. However, there is no trial monitoring plan template available to standardise the monitoring process within all CTUs. The benefits of a trial monitoring plan template are:

- Maintain consistency in monitoring standards across all CTUs, resulting in higher monitoring standards overall.
- Provide an evidence based, efficient and effective trial monitoring plan across all CTUs.
- Provide a cohesive trial monitoring plan for all CTUs.

Aim

The aim of this project is to improve the monitoring of clinical trials.

Objectives

To actively disseminate the Trial Monitoring Plan (TMP) template created from knowledgeable input and encourage CTUs to use it. Investigate the use of the monitoring template by conducting qualitative interviews and updating it as necessary.

In the first part of this PhD, we created a TMP template. This template is created following a comprehensive review of monitoring templates received from 31 UKCRC registered CTUs. We subsequently conducted two rounds of Delphi survey and organised a two-day consensus meeting to refine the template. The template is now

ready to be disseminated and tested to assess its utility and usability. We would like to conduct the following activities with any CTUs or members of the CTUs interested in collaborating with the project:

- Conduct one-on-one, informal, in-person qualitative interviews lasting 30-45 minutes with individuals involved in monitoring within CTUs. During these interviews, participants will be presented with the template, and I will pose a series of qualitative questions to capture their immediate impressions and insights of the template. These interviews will take place at the CTUs' locations.
- Piloting the template at any interested CTU for 6-9 months for 1 or more of your trials, followed by feedback on usability and any changes.

3. Why have I been chosen?

We are inviting people involved in the monitoring of clinical trials across the UK to take part. Whether you are a trial manager, monitor, statistician, or someone interested in monitoring clinical trials and improving methodology, you can take part.

4. Do I have to take part?

No. It is up to you to decide whether or not to take part in this research. If you do decide to take part, we will arrange a date for the qualitative interview to take place in person (or online if inperson is not an option). Additionally, if CTUs are interested in piloting the template an appointment will be arranged to organise this activity. You can withdraw at any time without giving a reason and without any negative consequences. However, if you do decide to withdraw, any data already collected cannot be withdrawn. Qualitative interviews will be recorded on Microsoft Teams. The meeting transcripts and recordings will be stored on the student's Microsoft UCL account. More details about this can be found further in the next section.

5. What will happen to me if I take part?

Piloting the template at the CTU will be for 6-9 months for 1 or more of your trials, followed by feedback on usability and any changes you suggest being made to the TMP template at the end of the piloting phase. You will be contacted every 2 months during the piloting to ask for feedback to mitigate against any potential

risks/oversights identified in the TMP throughout the piloting. You will take part in a qualitative interview with the PhD student. You will be provided with the TMP template and asked to review it for a few minutes. You will then a asked a series of questions which ask about your instant thoughts on the template. The interview will be recorded on Microsoft Teams. We record the meeting to have a transcript and for the due diligence of the analysis. The interview will last about 45 minutes. The result of the interview will be written up without mentioning your name or any identifiable information. The report will be given a participant's ID.

6. Will I be recorded and how will the recorded media be used?

The qualitative interview will be recorded on MS teams. You will be consented before joining the recorded meeting. The recording will be saved on UCL's secure IT network and only accessed by authorised research team i.e., PhD student or supervisors. The recording will be used to write up the final qualitative interview analysis and report and PhD thesis. No other use will be made of them without your written permission, and no one outside the project will be allowed access to the original recordings.'

7. What are the possible disadvantages and risks of taking part?

There are no anticipated risks in taking part in this study. No potentially sensitive information will be collected, and data will be shared anonymously for research output purposes.

8. What are the possible benefits of taking part?

There are no immediate benefits to you or others participating in the project. However, we intend this work will improve the conduct of clinical trials by improving monitoring and thereby benefiting research and patients.

Additionally, the final trial monitoring plan template can maintain consistency in monitoring standards across all CTUs, resulting in higher monitoring standards and consequently, higher research quality. It will also provide a cohesive and easy to follow trial monitoring plan template for all CTUs, enabling trial monitoring plan

completion more comprehensively and earlier in a study. This will consequently prevent resource waste for funders and CTUs.

We would like to acknowledge those who contribute to this research by completing qualitative interviews or piloting the template in their CTU. We plan to report the names of the participants as an appendix to our reports. We will ask you during the qualitative interview session if you would like to be included in the list of contributors. If you would prefer to not be included in the list of names, that is fine as well.

There will be a prize draw at the end of the interview rounds for one £25 love-to-shop voucher. This is to say thank you for your participation.

9. What if something goes wrong?

If you have any concerns about this project, please contact the PhD student Shiva Taheri via

s.taheri@ucl.ac.uk or the PhD supervisor Sharon Love via s.love@ucl.ac.uk, who will do their best to answer your query. However, if you feel that your concern has not been handled to your satisfaction by the research team, you can contact the Chair of the UCL Research Ethics Committee via ethics@ucl.ac.uk.

10. Will my taking part in this project be kept confidential?

All the information that we collect about you during this research will be kept strictly confidential.

The reports and data analysis will only include a study ID. This will ensure anonymity of the data therefore your answer will not be linked back to you. Only authorised members of the research team will have access to the interview transcripts and any data collected from you will be saved safely on UCL's secure IT network.

We will use Microsoft Teams to record qualitative interviews. Microsoft Teams uses encryption to protect data in transit and at rest. This means that data, including recorded meetings, is encrypted during transmission and while stored on Microsoft

servers. Microsoft Teams employs strong authentication methods, including multi-factor authentication, to help ensure that only authorised users can access and record meetings.

Email addresses collected from participants will be kept so that you can be told about the result of the research unless you tell us that you don't want to know. Your name is collected so that we can acknowledge your contribution to the study in an appendix to our reports unless you don't want to.

Any meeting recording will only be used to complete the final qualitative analysis report and write up the PhD thesis. No other use will be made of them without your written permission, and no one outside the project will be allowed access to the original recordings.'

11. Limits to confidentiality

Please note that assurances on confidentiality will be strictly adhered to unless evidence of wrongdoing or potential harm is uncovered. In such cases, the University may be obliged to contact relevant statutory bodies/agencies. Please note that confidentiality cannot be guaranteed in group settings.

12. What will happen to the results of the research project?

The result of this research will be written up for a PhD dissertation, publication(s) and disseminated at conferences as well as to all CTUs around the UK. The results of the qualitative interviews will be written as a report in which no participants will be identified. If you withdraw from the study, we will need to keep and use the data collected up to your withdrawal. The study will also be published on Open Science Framework https://osf.io/, to enable free and widely available sharing of the study. We will also send you the final trial monitoring plan template.

13. Local Data Protection Privacy Notice

Notice:

The controller for this project will be University College London (UCL). The UCL Data Protection Officer provides oversight of UCL activities involving the processing of personal data, and can be contacted at data-protection@ucl.ac.uk

This 'local' privacy notice sets out the information that applies to this particular study. Further information on how UCL uses participant information can be found in our 'general' privacy notice:
here

The information that is required to be provided to participants under data protection legislation (GDPR and DPA 2018) is provided across both the 'local' and 'general' privacy notices. The categories of personal data used will be as follows:

- Name
- Email address

The lawful basis that would be used to process your *personal data* will be performance of a task in the public interest.

Your personal data will be processed so long as it is required for the research project. If we are able to anonymise or pseudonymise the personal data, you provide we will undertake this and will endeavour to minimise the processing of personal data wherever possible.

If you are concerned about how your personal data is being processed, or if you would like to contact us about your rights, please contact UCL in the first instance at data-protection@ucl.ac.uk.

14. Who is organising and funding the research?

The study is being organised and coordinated by the MRC Clinical Trial Unit at UCL Institute of Clinical Trials and Methodology (ICTM). The funding for the study is provided by the Medical Research Council (MRC) and UK Research and Innovation (UKRI).

15. Contact for further information

Should you need further assistance with regard to this study please see the contact details below:

PhD Student: Shiva Taheri s.taheri@ucl.ac.uk

PhD supervisor: Sharon Love s.love@ucl.ac.uk

MRC Clinical Trials Unit at UCL

Institute of Clinical Trials and Methodology

90 High Holborn

2nd Floor

London

WC1V 6LJ

Thank you for reading this information sheet and for considering taking part in this research study.

Appendix 14: Consent form instant reaction interviews

CONSENT FORM FOR

Anyone with experience or expertise wishing to join the qualitative interviews to discuss the trial monitoring plan

template for the PhD research study

Please complete this form after you have read the Information Sheet and/or listened to an explanation about the research.

Title of Study: Uplifting the standard of monitoring clinical trials – developing evidence and tools
Department: MRC Clinical Trials Unit at UCL, Institute of Clinical Trials and Methodology
Name and Contact Details of the Researcher(s): Shiva Taheri, s.taheri@ucl.ac.uk
Name and Contact Details of the Principal Researcher: Sharon Love, s.love@ucl.ac.uk
Name and Contact Details of the UCL Data Protection Officer: data-protection@ucl.ac.uk
This study has been approved by the UCL Research Ethics Committee: Project ID number: 24121.002

Thank you for considering taking part in this research. The person organising the research must explain the project to you before you agree to take part. If you have any questions arising from the Information Sheet or explanation already given to you, please ask the researcher before you decide whether to join in. You will be given a copy of this Consent Form to keep and refer to at any time.

I confirm that I understand that by ticking/initialling each box below I am consenting to this element of the study. I understand that it will be assumed that unticked/initialled boxes means that I DO NOT consent to that part of the study. I understand that by not giving consent for any one element that I may be deemed ineligible for the study.

		Tick Box
1.	*I confirm that I have read and understood the Information Sheet for the above study. I have had an opportunity to consider the information and what will be expected of me. I have also had the opportunity to ask questions which have been answered to my satisfaction and would like to take part in a qualitative interview to discuss the final trial monitoring plan template as part of a PhD Research Project.	

2.	I understand that I will be able to withdraw at anytime without giving a reason. I understand if I withdraw from the study, the research team will need to keep and use the data collected up to my withdrawal.	
3.	I consent to participate in the study. I understand that my personal information *(full name and email address) will* be used for the purposes explained to me. I understand that according to data protection legislation, 'public task' will be the lawful basis for processing.	
4.	**Use of the information for this project only** I understand that my data gathered in this study will be stored securely. I understand my name will be on the qualitative interview recording until the recordings are deleted. I agree for my name to appear in the acknowledgement sections of any publication related to this study. I understand my comments will be presented anonymously.	Yes/ No
5.	I understand no promise or guarantee of benefits have been made to encourage me to participate.	

6.	I understand that the data will not be made available to any commercial organisations but is solely the responsibility of the researcher(s) undertaking this study.	
7.	I understand that I will not benefit financially from this study or from any possible outcome it may result in in the future.	
8.	I wish to receive a copy of the published report that contains the information I have submitted (this is optional).	Yes/ No
9.	I consent to the qualitative interview meeting being audio/video recorded and understand that the recordings will be: - Stored securely, using password-protected software, and will be used for training, quality control, audit and specific research purposes.	
10.	I am aware of who I should contact if I wish to lodge a complaint.	
11.	I voluntarily agree to take part in this study.	
12.	I understand no data that can identify a participant will be shared, and the video recordings as well as any information kept from me such as my name and email address will be deleted 6 months after the completion of the PhD project.	

If you would like your contact details to be retained so that you can be contacted in the future by UCL researchers who would like to invite you to participate in follow up studies to this project, or in future studies of a similar nature, please tick the appropriate box below.

	Yes, I would be happy to be contacted in this way	

	No, I would not like to be contacted	

_____	_____	_____
Name of participant	Date	Signature
_____	_____	_____
Name of witness (If applicable)	Date	Signature

Appendix 15: List of codes and thematic analysis (instant reaction interviews)

Thematic Analysis instant reaction interviews.xlsx

Appendix 16: Instant reaction interviews thematic map

Theme	Sub-theme	Example of Codes
7. Overall Impressions	Comprehensive	• Very thorough • Very detailed • Covers all bases • much more detailed than our units current monitoring plans. • More structured
	Length	• Very long • It needs to be long
	User friendly	• Easy to follow • Easy to understand • Easy to cross reference with • Not a lot of text to read
8. Clarity and understanding	Clarity and understanding of the introduction and purpose	• Very clear • Easy to understand • Not complicated • Very helpful to have this at the beginning
	Clarity and understanding of the template content	• Very clear • Lay language used • Easy to follow • Good examples • Each section well explained • Quite straight forward • A good guide for people with less experience in monitoring
	Confusing	• Routine monitoring is confusing. We don't need it as there are onsite and remote and triggered monitoring. • Order of sections could be changed. •
	Order of sections	• SIV to come to the beginning, followed by routine and then triggered.

		• SIV to come closer to beginning. • Pharmacy to go in with onsite monitoring. • To put metrics with triggered in one section. • Monitoring report at the end of all monitoring visits section.
9. Limitations		• We need to follow our SOPs • It's ok as long as we can remove sections we don't need. • It's ok as long as document is not locked so I can edit. • No, nothing I can envisage
10. Usefulness	Template provides useful guidance to monitoring needs	• The examples are very useful. • Prompt monitor to think • Helpful for those with less monitoring experience • Triggered monitoring section very useful. • Metrics sections very useful.
11. Suggestion for improvement	Formatting suggestion	• Make titles bold. • Give page numbers. • Metrics, threshold and escalation all alongside each other rather than separate. • It's easy to navigate, no suggestions. • Like the tables more than big chunks of text. • A good layout which means you can be sure you won't leave anything out. • May be change to landscape. • Very user friendly. • The approver table on the first page to have bigger heights to fit the signature. • First page looks a bit empty, maybe add some colour.

	Customisation suggestion	• Easy to remove sections we don't need or add things we need. • I'd add a section on sponsor monitoring. • The scope of this template is wider than our plan scope, so we need to customise.
	Content suggestion	• A summary page might be useful. • Add in summary of the overall monitoring. Say the overview of how this study would be monitored. • Add sponsor monitoring section to demonstrate sponsor oversight. • Trial specific notes change to Trial Specific information to be clearer. • Change central monitoring to centralised monitoring to reflect what is written on the ICH GCP. • Add frequency of pharmacy visit. • Add how many randomisation arms there are. • Add sample identifier and temperature log to sample monitoring. • Add a version of the TMP template and then a version for the CTU's document. • Make the risk assessment section clearer so that the reader knows ABC categories refers to CTIMP trial.
12. Comparison to alternative	Clarity	• This template is clearer. • I prefer the format that you have here because it's easy to understand. • The colour coding makes things clearer. •
	Layout	• Ours has a different layout • I like this better • No big chunks of text

		• All sections are divided up which makes it very easy. •
	Helpful examples	• Without example I'm worried I'm answering wrong • Yes, which we don't have in our one. •
	Comprehensive	• Very comprehensive. We have a lot of this information in other documents. • It brings together information that is already held elsewhere in our processes. •
	Anything set this template apart?	• Specific sections for everything • Very stringent • Less chance of making mistakes
13. Future use	Anticipate using this template regularly or in future trials?	• Yes, it would be just something to get used to. • Yes, we can take sections and use in our plans. • Yes, there's a few things that we don't specifically cover in our template and that I think it would be helpful to consider. • •
	Anything that would prevent you from continuing to use this template?	• No, as long as sponsor is happy. • No, just need it to be approved at higher level.

Appendix 17: A full list of all the additional changes made to the TMP

First Cohort:

1: titles to be bold (currently is) and as well as underlined.

2: routine monitoring to go before triggered monitoring

3: SIV to come to the beginning of the template before central monitoring.

4: to put pharmacy, lab and medical device monitoring with onsite. (this was not done as everyone else said that they would like to see these at the end of the template)

Second Cohort:

5: give each section a number (not applied as sections can be removed for some CTUs and this will create extra unnecessary work for CTUs to renumber sections).

6: p1: summary table added: short title, long title, CI, IRAS ID, Eudract, version and date.

7: page number 1 of x added

8: Sponsor oversight (p20) added

9: DMEC responsibilities (not added as beyond the scope of this document)

10: routine monitoring section removed, the frequency of routine monitoring added to table in p8 and the selection criteria for patients added to the to remote monitoring table too (p14).

11: risk category section has been split into CTIMP and non-CTIMP to remove confusion about category selection (p6&7)

12: p2: certain instructions are ‘highlighted in red’. This has changed to ‘coloured in red text’ instead, as it is not highlighted rather it’s red text.

13: p15, frequency of metrics checks added to the table.

14: p16, triggered monitoring. The following sentence has been added to show an example that the triggered monitoring is not always as a result of a central

monitoring report or a data extract: Triggered monitoring visits can also happen as a result of other events such as a phone call with the site.

15: applies to all tables: 'Trial Specific Notes' is changed to 'Trial Specific Information' for easier understanding of the purpose of this section.

16: p2: the following sentence is added to explain the scope of the document: The template includes sections on site initiation and close out visits, and various monitoring visits such as central, onsite, remote, routine and triggered. The template also includes sections on pharmacy, medical device, and sample monitoring visits.

17: p19, monitoring report is moved to the end of monitoring section after sample monitoring. (previously it was after site close out).

18: p5: the following sentence has changed **from** *Regular review of the TMP is advisable on an annual basis, with more frequent revisions warranted in the event of changes to the study's risk assessment* **to** *Regular review of the TMP is advisable on an annual basis, with more frequent revisions warranted in the event of changes to the study's risk assessment or a protocol amendment.*

18: metrics section is moved to be together with the triggered monitoring section.

19: p:16 the following changes is made to the sentence to include more options for report generating: A *weekly/monthly/quarterly* triggered monitoring report (produced by the *Data Management team* OR *manually from the database by the study team*). The CTU will delete the option that is not applicable to them.

Third Cohort:

20: p5: medical device is added to CTIM and non-CTIMP row on the table

21: p5: Randomisation arms (if applicable) is added to the table

22: throughout the document central monitoring is changed to centralised monitoring to be consistent with the term that is used in ICHGCP guideline.

23: p16 the following is added to the table: Frequency of pharmacy monitoring visits?

24: p19: the following is added to the table: (this is not an exhaustive list)

25: p19: the following is added to the table: (the words if applicable) Written report submitted to sites (if applicable). (some CTUs don't submit a report to site after monitoring).

26: p1, a table is added to summarise the changes made to the previous version of the TMP template in case of an amendment.

27: p11: the words or the sponsor is added to the table as sometimes this is requested by the external sponsor.

28: p19: the following are added to the table: Sample labels of trial identifiers and Temperature logs

29: p20 the following is added to the table: Ensure all data queries are addressed and closed.

Fourth Cohort:

30: p1: the TMP template effective date is changed to Version of TMP template Date to clarify this date refers to the version of template date rather than the date the TMP is written for the trial.

31: p8: the word site is added to the 'What will be the first site monitoring time-point?' this is to specify that monitoring doesn't just begin with patient recruitment, and to highlight that SIV is also a type of monitoring.

32:p8: the following is added to the table as example of the first time point of monitoring: after the IMP is shipped to site (to emphasise again that monitoring doesn't just start with randomised participants).

33: p10: the following is added to the table under data checks: Other- Specify (Add any other data checks to be done centrally)

34: p8: the following is added to the table as example for attendance to be documented: list of attendees and in person or online etc.

Appendix 18: Final version of the TMP template

<study name> Trial Monitoring Plan

Trial Information	
Trial Short Title/Acronym	
Trial Long Title	
ClinicalTrials.gov identifier	
EudraCT number	
ISRCTN number	

This monitoring plan was created from the Trial Monitoring Plan (TMP) Template Version 2, dated 06Mar2024.

Trial Monitoring Plan Information			
TMP Version			
TMP Date			
Reviewed by	**Position**	**Signature**	**Date**
Approved by			

Summary of the changes made to the previous version

Introduction to this trial monitoring plan template for Clinical Trial Units (CTUs): [remove this page once the template is finalised]

This document provides a monitoring plan template suitable for both CTIMP and non-CTIMP studies. The template includes sections on site initiation and close out visits, and various monitoring visits such as centralised, onsite, remote, routine and triggered. The template also includes sections on pharmacy, medical device, and sample monitoring visits.

Please tailor the template to align with your study's specific requirements and risk levels. Alternatively, you may choose to incorporate relevant sections into your trial monitoring plan. It's essential to highlight that this template is not a standalone document and should be used in conjunction with the clinical trial protocol, CTU's study-specific SOPs, and any other work instructions specified by the CTU. Any template sections that do not pertain to the trial or CTU can be omitted as needed.

Important note: Throughout the template, you will find tables with a column called 'Trial Specific Information' which should be used for tailoring the template to the specific requirements of the trial. These tables also include examples and guidance for 'Trial Specific Information' column in italic font which you have the flexibility to choose whether to remove, retain, or enhance based on the trial's risk level or any specific regulations pertinent to the CTU. The template also includes checklists in various sections. Certain instructions are coloured in red text and should be deleted once the template is in its final form.

List of Acronyms

Acronyms	Definitions
CRO	Contract Research Organization
CTIMP	Clinical Trial of an Investigational Medicinal Product
CTU	Clinical Trials Unit
DMEC	Data Monitoring and Ethics Committee
eCRF/CRF	Electronic/Case Report Form
FDA	Food and Drug Administration
GCP	Good Clinical Practice
IMP	Investigational Medicinal Product
ISF	Investigator Site File
non-CTIMP	Clinical Trial that does not involve an Investigational Medicinal Product
PSF	Pharmacy Site File
QA	Quality Assurance
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SDV	Source Data Verification
SmPC	Summary of Product Characteristics
SOP	Standard Operating Procedure
TMG	Trial Management Group
TMP	Trial Monitoring Plan

Table of Contents

Purpose

[This refers to the purpose of the TMP template. Enter a description of the purpose of this document based on the local SOPs and study protocol.]

The Trial Monitoring Plan (TMP) template outlines a comprehensive set of planned and systematic measures designed to ensure that the <INSERT Study Name> is conducted, and data are created, recorded, and reported in accordance with Good Clinical Practice (GCP) and relevant regulatory standards. This plan is formulated based on the study-specific risk assessment and thus may be subject to modifications as the study risks evolve. Regular review of the TMP is advisable on an annual basis, with more frequent revisions warranted in the event of changes to the study's risk assessment or a protocol amendment.

The purpose of this template is to document the procedures for monitoring before, during and at the end of <Study Name> including centralised monitoring, site visits, report writing and archiving.

Study Details

Complete the table below to give a description of the study details.

	Trial Specific Information
CTIMP/non-CTIMP/Medical Device	
Is there blinding in the study?	
Who is blinded (give role) and what are they blinded to?	
Randomisation procedure (for confirming that randomisation is performed according to the protocol and investigational plan)	e.g., comparison of randomisation and CRF data to assess whether the subject was administered or dispensed the assigned product.
Randomisation arms (if applicable)	
Definition of end of trial	

An overview of the trial design

[Complete the table below to give a description of the study design and trial overview.]

	Trial Specific Information
Study design	
Primary Outcome measures	
Describe any specific regulatory requirements:	(e.g., The intervention is/is not being used in a licensed indication OR The data from the trial will/will not be used to support a licensing application OR The trial is/is not supporting a license change. Include details of international regulation e.g., FDA, Medical Devices, or other specific regulations)
Describe other issues specific to the treatment under study (anything that is not covered by inclusion/exclusion criteria).	(e.g., participants need to fast for the intervention, or the treatment has a 12-hour life)

Summary of the trial risks

The table below is a summary of the trial risk assessment. Please follow your local risk assessment procedures and complete any relevant documents accordingly. Please note this should not replace the risk assessment for the trial, instead, it should be used as a snapshot of the main risk assessment of the trial.

Monitoring for this trial will be carried out using a risk-based approach. The risks to participants associated with the trial intervention(s) have been assessed in relation to standard care for the participant group concerned.

Is the monitoring of this trial carried out on a risk-based approach? Yes ☐ No ☐

For CTIMP trials (remove if a non CTIMP trial)
The trial has been assessed as:
A **Type A** trial requiring a **low** intensity of monitoring ☐
A **Type B** trial requiring a **moderate** intensity of monitoring☐
A **Type C** trial requiring a **high** intensity of monitoring ☐

For CTIMP trials (remove if a non CTIMP trial)

Justification of risk category selected:

Add justification of risk category selected, e.g., Impact of participation/administration of IMP compared to standard care, current licence vs. current off label use, oversight of IMP administration, side effects, safety monitoring.

If a non-CTIMP trial, please indicate the trial risk level and justification of risk level: (remove if a CTIMP trial)

Monitoring

The following monitoring approaches can be used based on the trial's risk category and the trial specific risks identified within the risk assessment:

Centralised monitoring –Centralised monitoring is a remote evaluation carried out by sponsor personnel or representatives (e.g., clinical monitors, data management personnel, or statisticians) at a location other than the sites at which the clinical investigation is being conducted. Centralised monitoring processes can provide many of the capabilities of on-site monitoring as well as additional capabilities.

On-site monitoring – On-site monitoring will involve a visit to a site/s by a member of the CTU and can be carried out for the following reasons: Site Initiation Visit (SIV) (to train site staff), Triggered Monitoring Visit (TMV), a Standard monitoring visit (for example to conduct Source Data Verification (SDV) checks), and Close Out Visits (COV) (to close the site).

Remote monitoring- Remote monitoring is when monitors don't visit the site to review the data. Instead, data monitoring is done virtually. With the use of digital technology, CROs and study sponsors/stakeholders can see the data from wherever they are located.

The above list of monitoring approaches can be carried out as part of:

Triggered Monitoring- Triggered monitoring in clinical trials is a risk-based monitoring approach where triggers specify the extent, timing, and frequency of monitoring visits.

Routine Monitoring- routine monitoring occurs at pre-decided times rather than in response to a concern. **Important note:** All trial monitoring activities should be conducted in accordance with the local SOPs. The frequency of monitoring and who carries out the task should be indicated where possible for all monitoring tasks.	
Trial/Study Monitoring Approach: choose the monitoring approach for the trial. (Tick all that apply)	Centralised ☐ Onsite ☐ Remote ☐
Type of monitoring (Tick all that apply)	Triggered ☐ Routine ☐
Frequency of routine monitoring visit?	
Who will monitor the study?	e.g., Sponsor/sponsor delegate
What will be the first site monitoring time-point?	e.g., after first participant is randomised, after IMP is shipped to site

Site Initiation

The table below lists activities to be completed during the site initiation visit. Please complete this table considering the local SOPs and study protocol.

	Trial Specific Information
Remotely within the CTU or via on-site visits? Describe the rationale for the chosen method of Site Initiation. Where SIV is to be carried out via on-site visits, indicate how many sites are to be visited.	(Format on-site visit/teleconference/video conference e.g., MS teams meeting).
Determine site staff members who need to be present at the initiation visit.	(e.g., principal investigator, investigator, study assistant, pharmacist, etc.).
Attendance to be documented.	list of attendees in person or online etc.
List of trainings to occur during the site initiation.	

Site-specific documentation reviews.	List all the documents to be checked. (e.g., Delegation logs, Training logs (including the trial-specific training), CVs and GCP certificates).
Arrangements for study medication, documentation (CRFs, Investigator Site File) and further study material delivery to sites(s).	(e.g., drug supply, schedule of assessments, treatment schedule, biological sample collection/ processing/ shipment).
Additionally, site initiation should include the following checklist: • If applicable, a review of the Pharmacy facilities (see pharmacy section of the template). • Request for submission of Trial Equipment calibration records. • Confirmation of Critical Documentation held both regulatory-specific, trial, and site-specific.	

Centralised Monitoring Activities

The table below lists activities to be completed during centralised monitoring. Please complete this table considering the local SOPs and trial protocol.

	Trial Specific Information
Frequency of centralised monitoring	
Consent and eligibility	
Checking consent is taken correctly.	e.g., Completion of Informed Consent Forms (ICFs) for X participants (X is determined based on the trial risk), checking the signature, dates are contemporaneous, and counter signatory on the delegation log.
Additionally, consent and eligibility should include the following checklist: (Add/Delete as appropriate to the trial) • Eligibility checks before randomisation. • Review of trial eligibility criteria sign-off by local PI.	
Site Delegation and training	
Indicate how staff training and delegation of responsibilities will be monitored including the frequency of review.	(e.g., collection and review of CVs, training logs and delegation logs)

IMP accountability **(For more details on IMP please see the pharmacy monitoring section in this TMP)**	
Will IMP accountability be done for all participants or for a sample from each site?	
How will this be done if an external service provider is being utilised?	
How frequently should the accountability log be sent to the trial office?	e.g., every 6 months
How frequently should the dispensing log be sent to the trial office?	e.g., every 6 months
Additionally, IMP accountability should include the following checklist: (Add/Delete as appropriate to the trial) • Review of IMP shipment and delivery documentation. • Review of IMP dosage calculations.	
AE, SAE, and SADE	
Adverse Events	e.g., centralised review or reconciliation of SAE forms and reporting timelines.
If medical device trial, indicate if SADEs are reported to the manufacturer or delegated to CTU.	
Out-of-hours emergency cover arrangements- Where participants are provided with out of hours contact details for site staff.	(e.g., on a Participant ID card or PIS) indicate how this will be verified (e.g., for high-risk trials a test procedure may be put in place).
Data Checks	
Checks for missing or invalid data (range and consistency checks)	
Checks for unusual data patterns/Suspected fraud.	e.g., audit trail end digit review.
Other- Specify (Add any other data checks to be done centrally)	
Protocol Deviation	

Review of Visit Window Thresholds	
Other- Specify (Add any protocol deviation which is to be checked centrally)	(These examples are not an exhaustive list. e.g., Centralised review of adherence to the time of randomisation and intervention consistent with protocol.)
Site File Review	
Site File and Pharmacy File: Indicate the procedures for checking the site file.	e.g., A checklist of documents contained within the site file and site pharmacy file will be sent out for self-completion by the sites as appropriate. The Trial Office will monitor these on return and implement remedial action as and when appropriate.

Centralised Quality Checks

Centralised quality checks should include the following checklist:

(Add/Delete as appropriate to the trial)

- Completion of a site questionnaire/assessments or to confirm that they can fulfil the safety requirements and perform the required trial assessments.
- Sites are requested to return anonymised screening logs every X months (X is determined based on the trial risk) for review at CTU.
- Chief Investigators and Principal Investigators sign an Investigator Statement agreeing to their roles and responsibilities during the trial.
- Screening and Enrolment log review before each IDMC, or every X months (X is determined based on the trial risk).
- Signed receipts to confirm receipt of any updated documents (e.g., Protocols, Investigator Brochures (IBs) etc.) as required.
- Other centralised quality control procedures to be conducted centrally by trial team members [add as applicable].

Onsite Monitoring Visit

The table below lists activities to be completed at onsite monitoring visits. Please complete this table considering the local SOPs and study protocol.

	Trial Specific Information
Frequency of on-site monitoring	

Choose the applicable option from the two following options and delete the one that is not needed: On-site monitoring will be carried out for this trial in the form of routine monitoring visits with additional triggered monitoring visits where applicable OR Routine on-site monitoring will not be carried out for this trial. Triggered monitoring visits will be conducted in response to the triggers stated in this trial monitoring plan or on request of the trial oversight committees, or the Senior Trial Manager/QA Manager at the CTU or the sponsor.	
Availability of completed source documents and CRF for the monitoring visit.	Indicate how this will be done prior to visit
Selection criteria for participants to be reviewed during On-site Monitoring Visits- This may be on request of the TMG or following review of centralised monitoring reports.	(e.g., participants who have a high number of SAEs reported or on a percentage of participants e.g., 10% selected at random).
Review of consent forms to ensure completed appropriately.	e.g., Completion of Informed Consent Forms (ICFs) for X participants (X is determined based on the trial risk), checking signature, dates are contemporaneous, and counter signatory on the delegation log.
Serious Adverse Event / Serious Adverse Device Effect report(s) check: Check all serious adverse events are accurately documented and reported by site within the reporting timelines.	To be performed for <X> number /% of participants (X is determined based on the trial risk), at each monitoring visit alongside medical records and database entries/logs of SAEs.
Review Medical/study records and results of eligibility assessments to confirm participant eligibility.	for <X%> of participants (X is determined based on the trial risk).
Investigator Site File - presence and completion of all (OR a selection of) trial documents, security, and location of files.	List all the documents to be checked. (e.g., Delegation logs, Training logs (including the trial-specific training), CVs and GCP certificates).

Source document completion in accordance with the ALCOA principles check. *ICH E6 4.9.0 -The investigator/institution should maintain adequate and accurate source documents and trial records that include all pertinent observations on each of the site's trial subjects. Source data should be attributable, legible, contemporaneous, original, accurate, and complete. Changes to source data should be traceable, should not obscure the original entry, and should be explained if necessary (e.g., via an audit trail).	

Additionally, the onsite monitoring visit should include the following checklist:

(Add/Delete as appropriate to the trial)

- Checking understanding and adherence to study protocol, procedures, and governance requirements (including any conditions in regulatory or ethics approval).
- Verification that resources and facilities remain adequate.
- Verification of appropriate oversight and documented delegation by the local investigator.

Protocol Deviation and Compliance

Additionally, protocol deviation and compliance should include the following checklist:

(Add/Delete as appropriate to the trial)

- Verification of missing visits, examinations, or tests.
- Verification of lab reports reviewed, signed, and dated appropriately.
- Verification of protocol deviations reported appropriately.
- Verification of any new protocol deviations and/or regulatory or GCP deviations that occurred at the site since the last visit, reported appropriately.

Site staff discussion

Site staff discussion should include the following checklist:

(Add/Delete as appropriate to the trial)

- Discussions with site staff regarding staff training requirements (current documents and training present, staff changes documented, CVs, GCP, delegation log).
- Time at the end of the monitoring visit for discussion with the site staff to resolve any issues where feasible. Key points to be recorded in the monitoring visit report. Issues not

resolved during the visit should be recorded in the report for resolution prior to the next monitoring visit.	
Documents and systems to be reviewed	
Deviation logs	e.g., frequency of checks
Screening logs	e.g., frequency of checks
Completion of previously raised findings and actions (as appropriate).	Indicate how this will be checked
Randomisation processes	e.g., date of randomisation recorded on the CRF and randomisation service e.g., sealed envelope if applicable, and appropriateness of trial team member according to the site delegation log.
Screening procedures	
Early cessation of participation in trial (treatments, procedures, and/or data)	
Hard-copy CRFs and patient completed questionnaires validation.	The amount of content to be checked and the error rate (X) is determined based on the trial risk. Where the CRF is a hard copy, the content of approximately X% of case report forms (CRFs) and patient questionnaires entered at sites will be checked (or double entered) to ensure the accuracy of data input. An error rate of <X% will require no further action, however, if the error rate is >X%, a 100% check of forms will be undertaken.
Visit to other departments	
Will the monitor visit the Lab, and Pharmacy? If yes, complete the relevant sections of this template.	
Source Data Verification (SDV)	
Is any SDV to be performed? Yes/no	

If applicable, which participants need SDV and how will you select them?	e.g., number/percentage of participants and how you will select them, e.g. First X patient(s) at each site.
If applicable, what data needs SDV?	e.g., study arm, outcome data, or all data.
Describe what source data will be available as a hard copy, and what will be available electronically and how access arrangements will be set up. (Refer to source data location agreement if applicable)	

Remote Monitoring Visit

[The table below lists activities to be completed during remote monitoring visits. Please complete this table considering the local SOPs and study protocol.]

Remote Monitoring serves as a valuable resource for the CTU trial management team, allowing them to adopt a risk-based strategy for minimizing on-site monitoring and addressing situations where physical presence at the trial site is not feasible. It is crucial to prepare adequately for remote monitoring, ensuring that all necessary information and documentation are obtained from the trial site for the monitoring visit. This may include using self-monitoring questionnaires, administered in accordance with a risk-based approach, which the trial site team completes and submits to the CTU for confirmation. If requested documentation contains personal information, this should be redacted and managed accordingly i.e., no patient personal details will be retained by the CTU.

	Trial Specific Information
Frequency of remote monitoring.	
Selection criteria for participants to be reviewed during Remote Monitoring Visits	This may be on request of the TMG or following a review of centralised monitoring reports, (e.g., participants who have a high number of SAEs reported or on a percentage of participants e.g., 10% selected at random).
Determine how the trial issue will be resolved.	e.g., telephone, email
X should be determined based on the trial risk. **Monitoring will consist of X% monitoring of the following:**	
Patient informed consent forms completed correctly.	

CRF/eCRF completion and data cleaning	
Recording and reporting of AEs and SAEs	
Source data verification facility/all CRF entries can be verified either in electronic or paper format (see SDV section for more details).	

Monitoring will also consist of monitoring the following items as appropriate to the trial:
(Add/Delete as appropriate to the trial)

Localised PIS and consent form
Delegation log (updated version to be sent if additional study team leave or join)
CV's, GCP certificates and training logs
Monthly screening and recruitment logs (anonymised)
Deviation logs
eCRF audit logs
Local approval documents
Investigator Site File Contents (e.g., newsletters, significant communication with the site)
Pharmacy Site File Contents (see pharmacy section for more details).
IMP (request/shipment request, accountability logs, destruction logs, temperature logs).

Metrics

The table below is about the use of metrics in monitoring trials, sometimes termed "site performance metrics". Add more rows as needed.

Metrics If applicable, list the metrics used for this trial.	**Thresholds** If applicable, list the metrics thresholds for this trial.	**Frequency of metric checks**
Escalation		
Consider the action of escalation proportionate to centralised monitoring findings, linked to specific metrics crossing a threshold if appropriate. A general concern with a site based on correspondence or other incidents may also be a reason to escalate. Add action of escalation for trial in here i.e., when meetings will be held to discuss an action.		

Triggered Monitoring

The table below is to be completed for triggered monitoring. Examples and guidance are given to help with developing trial triggered monitoring strategies. Please complete this table considering the local SOPs and study protocol. Please note this sections lays out the process leading to triggered monitoring. Once this is established, the monitoring will be done either centrally, on-site, or remote, in which the relevant sections should be completed for the visit.

A weekly/monthly/quarterly triggered monitoring report (produced by the Data Management team OR manually from the database by the study team) will be generated to include data around specific trigger categories. For this trial, <xx> number of triggers in a <xx> (X is determined based on the trial risk) period will require further investigation by the TMG and, where necessary, may trigger an on-site visit. Triggered monitoring visits can also happen as a result of other events such as a phone call with the site. Any triggered monitoring visits will be documented internally within a monitoring report.

Thresholds and associated actions/escalation plan:
(What specific findings/thresholds would necessitate an action in response? What would the immediate corrective actions be and what is the escalation process if the issue is not resolved within a specified timeframe?)

The types of issues identified through monitoring that would trigger immediate issue escalation:
This is not an exhaustive list, items can be added or removed as appropriate.

- A high level of findings through centralised monitoring oversight.
- A high number of protocol deviations.
- Low or High SAE reporting rate compared with other sites.
- Poor data quality (long data entry delays, high query rate and high percentage of missing data, constant outstanding data, particularly relating to primary endpoint or safety data).
- Concerns over IMP or sample management processes.
- Concerns over consent procedures.

Pharmacy Monitoring

[The table below lists activities to be completed during pharmacy monitoring visits. Please complete this table considering the local SOPs and study protocol.]

	Trial Specific Information
Is Pharmacy involved in the study? Yes/No	
Planned Frequency of Pharmacy Monitoring Visits	

Frequency of pharmacy monitoring visits?	
Will Pharmacy visits be timed with the main visits?	
Ordering and Storage of IMP	
Description of the necessary transport and storage conditions, if applicable with reference to the study protocol or another respective document.	
Additionally, ordering and storage of IMP should include the following checklist: • Checks to verify if IMP is being stored appropriately and in a secure location. • Checks to verify the availability of adequate stocks within expiry dates for the planned participants. • Checks to verify storage temperatures adequately monitored by pharmacy staff. • Checks for any temperature excursions. • Checks to verify any temperature excursions have been appropriately managed.	
IMP Accountability	
IMP accountability should include the following checklist: • Checks to determine supplied IMP dispensed at the protocol-specified dose(s)/schedule. • Checks for any IMP returned or destroyed at the monitoring visit? (e.g., expired, or damaged). • Checks to verify the disposal of IMP at the site is appropriately documented. • Checks to verify study medication is appropriately documented. • Checks for any discrepancies in IMP accountability logs.	
Pharmacy File	
Pharmacy File: Indicate the documents to be checked for the pharmacy file.	e.g., Is the current version of Investigator Brochure/SmPC, IMP handling/pharmacy guidelines (if applicable) and current approved protocol held in the Pharmacy File?

Medical Device Monitoring

The table below lists activities to be completed during medical device monitoring. Please complete this table considering the local SOPs and study protocol.

	Trial Specific Information
Does this study involve Medical Devices? Yes/No	

Ordering and Storage of the devices	
Description of the necessary transport and storage conditions, if applicable with reference to the study protocol or another respective document.	
Device Accountability	
Monitoring device accountability should include the following checklist: • Allocation/return • Storage • Expiry • Documentation	

Sample Monitoring

The table below lists activities to be completed during sample monitoring. Please complete this table considering the local SOPs and study protocol.

	Trial Specific Information
Does this study involve the collection of biological samples? Yes/No	
Are the samples processed locally or centrally?	
Sample Monitoring Procedure	
Sample monitoring procedure should include the following checklist: • Sample log completion checks • Sample delivery log checks (if samples are sent off-site for processing). • Other documentation related to sampling.	
Storage of samples	
Description of the necessary transport and storage arrangements for samples collected for the study if applicable, with reference to the study protocol or another respective document.	
How often will the labs be visited?	
Where the lab section of the ISF will be held and who will maintain this?	

Which procedures should be followed where deviations occur?	
Procedures to take place during the close-out visit.	
Sample Accountability	
Sample accountability should include the following checklist: • Storage conditions • Sample tracking • Sample labels of trial identifiers • Laboratory reports • Expiry • Temperature logs	

Monitoring reports

Use this section to populate the monitoring report following a monitoring visit.

The monitoring report is intended to summarise the monitoring visit. It will facilitate the recording of the items reviewed, any findings (such as non-compliance, deviations, deficiencies, or data anomalies), and recommended corrective actions. Furthermore, the report will enable the documentation of findings and details of any meetings conducted during the visit, which encompasses the feedback meeting. The full follow-up letter should include the following components: (this is not an exhaustive list)

- Actions Resolution Document
- Date of visit
- Name of the monitor(s)
- Site name
- Name of the investigator
- A brief review of any additional meetings that took place, in particular the feedback meeting.
- Sites response and implementation of corrective actions where appropriate.

Additionally, timelines should be allocated for:

- Internal review of the written report.
- Written report submitted to sites (if applicable).
- Sites response and implementation of corrective actions where appropriate.

Site Close Out

The competent authority and research ethics committee should be notified within 90 days of the end of the trial. A summary report of the research is to be sent to the competent authority and research ethics committee within 12 months of the end of the trial. The funder is to be provided a final report at the end of the trial. An official close-out letter will be sent by the trial manager to each participating site once outstanding queries are finalised, and all data has been received.

	Trial Specific Information
Will visits be conducted remotely from CTU, on-site or centrally?	
% and number of sites expected to be visited for Site Close-out.	
Document how site close-out will be conducted for those sites that are not visited.	(e.g., via teleconference, emails, and letters to sites).
The proposed timing of Close-out visits.	(X weeks from the end of the study).
Additionally, close out visit should include the following checklist: • The Trial Site File must be reviewed and confirmed as complete prior to archiving. • All outstanding payments must be reviewed and invoiced. • Drug accountability. • Ensure all SAEs are correctly reported including SDV if required. • Ensure all data queries are addressed and closed. • Final review of Investigator Site File (ISF)/Pharmacy Site File (PSF).	

Sponsor Oversight

This section is optional. Please remove if this is covered by the CTU's audit SOPs.

[sponsor name] is sponsor of the study and has delegated sponsor responsibilities to [CTU name] CTU, whose main roles and responsibilities are: (Remove or include additional responsibilities as per the Sponsor – [CTU name] CTU arrangement.)

If [sponsor name] is not the sponsor please adapt the above sentence. [remove this sentence if not necessary]

- The provision of trial management
- Inclusion of a medical expert into the Trial Management Group (TMG)
- The holder of the Trial Master File (TMF)
- Regulatory document collection

- Site selection and monitoring
- Site contracts
- CRF design and distribution
- Resolution of site compliance and performance issues
- Oversight of drug supply and management
- Data management (for centralised monitoring)
- The oversight of safety assessments & onward reporting to investigators and authorities
- Database development and maintenance, including program for randomisation
- Data analysis
- Preparation of study report and manuscripts

External Vendor Oversight

[For details on monitoring external vendors please follow the local SOPs and sponsor guidelines if necessary or remove this section otherwise.]

Archiving

[Archiving plan for the trial should be drawn here following the local SOPs and sponsor guidelines.]

Appendix 19: Metrics interview questions

Qualitative Interview Questions (Metrics)

General Questions about Clinical Trial Monitoring

1. Can you describe the current approach your unit uses for monitoring clinical trials?
2. What tools or methods do you typically use to ensure data quality and patient safety during monitoring?
3. How do you assess the performance of trial sites during the monitoring process?

Specific Questions about Metrics Usage

4. Do you use any metrics (e.g., data quality indicators, protocol adherence) in your monitoring process? If so, which ones?
5. If you use metrics in your monitoring strategy, what are your experiences?
6. If you don't use any metrics, can you expand why?
7. What are your thoughts on using predefined metrics to guide clinical trial monitoring?
8. What factors have influenced your decision to rely or not to rely heavily on metrics in monitoring?
    - (e.g., lack of tools, difficulty interpreting data, cost, uncertainty about effectiveness)

Barriers to Using Metrics

9. What challenges do you foresee in implementing a metrics-based approach for monitoring clinical trials? (if not using metrics)
10. What challenges did you have in implementing a metrics-based approach for monitoring clinical trials? (if using metrics)
11. Are there specific types of trials or scenarios where you think metrics would be less/more effective or less/more applicable?

12. Do you believe your staff have the necessary training or resources to use metrics effectively for monitoring? Why or why not?
13. What training or resources did you need to provide to your staff to start using metrics effectively for monitoring? (if using metrics)

Potential Interest in Metrics

14. If provided with appropriate tools and training, would your unit consider incorporating metrics into your monitoring process? Why or why not?
15. Are there any particular metrics you think could be most valuable for your trials if implemented?
16. What improvements or changes in trial monitoring processes would motivate you to adopt metrics in your monitoring framework? (if not using metrics)
17. What improvements or changes in trial monitoring processes motivated you to adopt metrics in your monitoring framework? (if using metrics)

Perceptions of Metrics in Monitoring

18. What do you see as the biggest advantage of using metrics in trial monitoring?
19. Do you have any concerns about the accuracy, reliability, or interpretation of metrics in guiding decisions during trials?
20. How do you think sponsors, regulators, or other stakeholders perceive the use of metrics in clinical trials?

Closing Questions

21. What steps do you think would be necessary to make metrics-based monitoring more practical and appealing for clinical trial units?
22. Are there any aspects of your monitoring process that you feel are currently underserved by the available tools or frameworks?
23. Would you be willing to explore pilot projects demonstrating the value of metrics in clinical trial monitoring?

Appendix 20: Final Framework Matrices

Framework Matrices .xlsx