

Using project management principles to improve research projects

After reading this article, you should be able to:

- Understand the principles of project management and how they can be applied to clinical trials;
- Identify the tools that can be used for research project management;
- Know the role of the pharmacist in these processes.

Introduction

Research is an integral component of any modern health service that incorporates evidence-based practice, where clinical decisions are made based on available research to ensure balanced and appropriate clinical guidance (Ref). The current high standards of medical care are partly attributable to the clinical studies that have been conducted under the guidance and funding of regulatory bodies such as the National Institute of Health Research (NIHR) and the UK Medical Research Council. In addition to testing new drugs and devices, clinical trials provide a scientific basis for advising and treating patients contributing immensely to safe and effective clinical practice.

Pharmacists play a vital role in the clinical trial process. They are often responsible for dispensing medications and as well as ensuring that the study protocol is followed correctly. Additionally, pharmacists can provide valuable input in the design of clinical trials, particularly in areas related to medication dosing and drug interactions. They can also assist with data collection and analysis, which is essential for evaluating the safety and efficacy of new medications.

Knowledge of research project management is essential for pharmacists as it enables them to better understand and critique the evidence presented in research studies. This knowledge can help them make informed decisions about the efficacy and safety of medications, as well as help them communicate effectively with other healthcare professionals and patients.

Managing clinical trials

The achievement of a successful clinical trial requires organisation and execution of activities and tasks within given timelines in a step-wise manner and must be managed meticulously in order to avoid unnecessary delays and problems. It can be a time-consuming, difficult, and challenging task that must be fulfilled within a finite budget, therefore, requires careful planning and organisation

from the onset. An analysis of 114 multicentre clinical trials showed that 45% failed to reach 80% of the prespecified sample size required to obtain significant data, and around a third were unable to recruit study participants within the time specified and had to extend, costing more time and resources (3).

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Box 1: Clinical trial phases

Clinical trials are divided into four phases, each with its own purpose and design.

Phase 1 trials are the first step in testing a new drug or treatment in humans. They are conducted to evaluate the safety of the drug and determine the appropriate dosage. Typically, phase 1 trials involve a small group of healthy volunteers who are closely monitored for adverse effects. Phase 1 trials can last several months, and the results are used to inform the design of subsequent trials.

Phase 2 trials are conducted to evaluate the effectiveness of the drug or treatment in a larger group of patients. These trials can last several years and involve hundreds of participants. Phase 2 trials are designed to assess the safety and efficacy of the drug or treatment, as well as to determine the optimal dosage and any potential side effects.

Phase 3 trials are the largest and most expensive phase of clinical trials. They are designed to confirm the safety and efficacy of the drug or treatment in a large, diverse population. Phase 3 trials can involve thousands of participants and can last several years. The results of phase 3 trials are used to support an application for approval by regulatory authorities, such as the U.S. Food and Drug Administration (FDA).

Phase 4 trials are conducted after a drug or treatment has been approved by regulatory authorities and is on the market. These trials are designed to monitor the long-term safety and efficacy of the drug or treatment in a larger, more diverse population. Phase 4 trials can also be used to explore new uses for the drug or treatment or to compare it to other treatments.

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Applying project management principles to clinical trials

We propose that clinical trials can be conducted more efficiently using project management principles. Large or small clinical trials can be classified as a 'project' whereby a project is any temporary endeavour with a clear beginning and end, has clear boundaries, and is creating something new that did not previously exist. Factors that limit projects include, scope, time, people and resources. In this article, the main principles of project management will be applied to research projects in health settings, using a clinical trial as an example of a complex project in a multi-centred setting.

The Project Management Body of Knowledge (PMBOK) guide (4, 5) explains project management in terms of five steps:

1. Initiation
2. Planning
3. Executing
4. Controlling and monitoring
5. Closing

These principles were initially developed for engineering and construction-based disciplines; however, the application of the theory can be applied to academic research projects (6), pharmaceutical industries (7), and in particular, prospective studies such as clinical trials. By applying the above set of project management principles as a systematic process it is possible to eliminate costly mistakes, prevent budget overruns, improve quality, and save time (8, 9).

There are very few clinical trials that have applied the principles of project management to guide and implement the full process from inception to completion. The Obsessive Compulsive Treatment Efficacy Trial (OCTET), funded by the NIHR, is one of the few studies that investigated the application of research project management tools throughout the entirety of the trial. The purpose of the study was to evaluate whether adoption of the key principles of project management would lead to the successful completion and greater satisfaction for the staff involved in the day-to-day operation. It was concluded that developing trial management and methods was key to the success of clinical trials (10). Another example of the successful application of the above principles to a clinical study related to the *Alcohol and Pregnancy study (2006-2008)* where the researchers comprehensively endorsed project management and agreed that it contributed substantially to the research outcome (9).

Step 1: Initiation

The study proposal is the formal initiation of a clinical trial project and is the conceptual phase where the research question must be transformed into a hypothesis supported by literature to identify and justify the gap in research that the project will contribute to answering. It will set the background for the research project and describe the transformation of the research question/hypothesis into the actual study.

The study proposal will include the following (5, 11):

- What the trial is trying to achieve (i.e. objectives, the study intervention and the differences in treatment sought)
- Sample population
- Eligibility criteria
- Study intervention
- Sample size
- Differences in the treatment effects that are sought
- How data will be collected
- Data collection and analysis according to Good Clinical Practice guidelines (12)
- How will the project be monitored and controlled to ensure the project will be delivered on time
- How the trial results will be reported and disseminated
- Quality assurance to ensure reliable and reproducible results of the highest standards

Ethical approval must be sought at this stage, and a 'steering committee' is set-up, chaired by the principal investigator who created the study idea and other members who will provide guidance and advise, but are not involved in the implementing of the project on a practical level. Finally, applications must be submitted to a funding organisation to seek approval, which will give the green-light for the next phase of the project.

Step 2: Planning

A clear plan must be formulated consisting of the project protocol that involves every aspect of the vision and scope of the project, including the management of the day-to-day running of the trial. This is the most important phase of the project that allows the researchers and investigators to formulate a clear plan on how to manage the process according to the scope of the study, within a

designated timeframe and within budget. The major features of this phase of the project management are:

Study protocol

A plan of how the overall study is managed by estimating a realistic time schedule of what can be achieved. It allows the investigators and all individuals involved to keep the project on time and within budget. The key features are:

- The timings for grant submission and grant approval
- Site activation
- Study subject recruitment
- Data collection and data analysis
- Outlining the timing and sequence of each major event within the study
- The sequence of events required to meet the study objectives
- Defines the persons responsible for activities and tasks
- Establishes method of communication between the steering committee and the Independent Data Safety and Monitoring committee

Study budget

The budget is finite; therefore, the cost of resources must be considered relating to the milestones of the project and timescale. This involves the breakdown of tasks and assignment of responsibilities for timely completion. Key features of budgeting and costs are:

- Estimating the budget and cost for each major milestone within the project lifecycle
- Itemised budget for staff salaries (researchers, investigators, database programmers, statisticians etc.)
- Site payment for contributing hospitals and study intervention costs
- Costs set aside for contingency purposes if events do not follow the protocol

Study manuals, documentation, and software

Particularly for clinical trials involving several sites (multicentred), study manuals ensure all staff receive training consistent with the same guidelines and all staff members will conduct the study in the same way. For drugs being investigated as part of the study, a pharmacy manual is essential to specify preparation, storage, routes of delivery to the body, and destruction. Finally, the blind

randomisation of study participants to different treatment arms in a confidential manner requires the use of software systems that must be acquired and established.

Source documentation relating to all aspects of the clinical trial is essential and should be recorded, monitored and archived in accordance with good clinical practice guidelines (12, 13). Good Clinical Practice (GCP) is a quality standard for designing, conducting, recording, and reporting trials that involve the participation of human subjects. Compliance with this standard provides public assurance that the clinical trial data are credible. Source documentation includes the clinical history and medical records of all study participants before, during, and after the trial ends, records relating to staff training, handling of all drugs used, standard operating procedures, laboratory reports etc. This will ensure safety of study participants, accountability, and high-quality results. An audit in 2010 by the U.S FDA cited 6 out of 10 clinical trials did not keep adequate documentation (13).

Step 3: Execution

The successful execution of clinical trials is a multidimensional and multi-faceted operation. At the execution stage, the study plan is implemented, and the actual clinical trial commences. The main features of this phase are (9, 14, 15):

- Various teams are acquired, developed and managed
- Allocation of resources and support is provided to team members to ensure that assigned tasks are completed
- Quality assurance is performed (see 'Step 4: Monitoring and controlling')
- The deliverables are developed and completed to meet the requirement of the project aims and objectives
- Communication links are established with the clinical teams and stakeholders (pharmaceutical companies, funders, regulatory agencies, study participants, research institutions)
- Research is conducted (e.g. analysing samples, synthesising and analysing data)
- Dissemination of educational resources to health professionals, stakeholders, and the general public

Step 4: Controlling and monitoring

This process occurs alongside the execution phase, focussing on measuring project progression and performance in line with previously agreed goals and timelines. The project plan determines and

specifies the quality assurance, control, monitoring and risk assessment of activities conducted while the clinical study is in progress. This includes, but is not limited to:

- Onsite monitoring and audits e.g. looking through medical records and cross-checking data against case report forms (CRFs)
- Reviewing the study manuals and files to ensure essential documents are up-to-date
- Review all manuals including, staff training manuals and standard operating procedures (SOPs)
- Making sure research is conducted in accordance with GCP (12) and Medicines and Healthcare Products Regulatory Agency (MHRA) (16) for research with human participants
- Regularly reviewing the tasks and activities associated with each milestone
- Data management e.g. data checking, ensuring the data is void of errors
- Results of interim data analysis
- Safety monitoring

The outcomes of control and monitoring is compared to the original study plan and adjustments can be made if necessary.

A good clinical trial study will have a contingency plan set in place, that was developed before the execution phase, which is incorporated into the study plan. It will specify the risks that may occur, the likelihood of them occurring, the potential impact on the project and the course of action recommended should the risk occur.

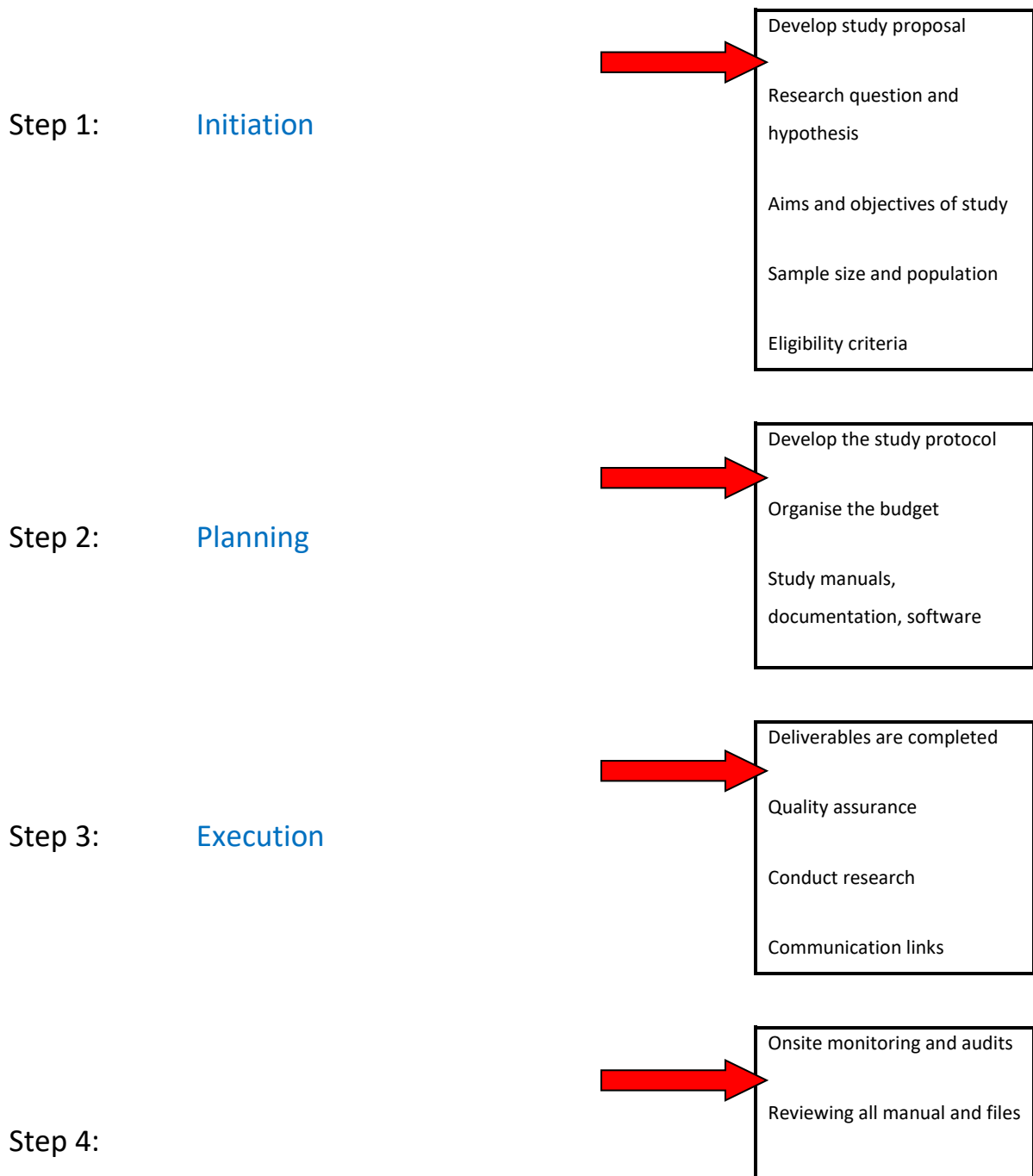
Step 5: Closing

Towards completion of the research project, the main activities involve:

- Final analysis of the data
- Reporting of the data (e.g. presentations or a manuscript in a peer-reviewed journal)
- Study sites are formally closed
- Ethics committee and staff are informed of completion
- Final reports are submitted to funding bodies
- Study participants/patients are informed of completion of the clinical trial and the outcomes
- Records are archived in accordance with the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use Good Clinical Practice

guidelines (ICH GCP) that state that all documentation should be kept for at least three years after completion of the clinical trial (12)

In addition, it is optional for a post-trial review to be conducted where management of the clinical trial is evaluated to determine strengths and weaknesses in the process, such that future clinical trials can be conducted more effectively (15).



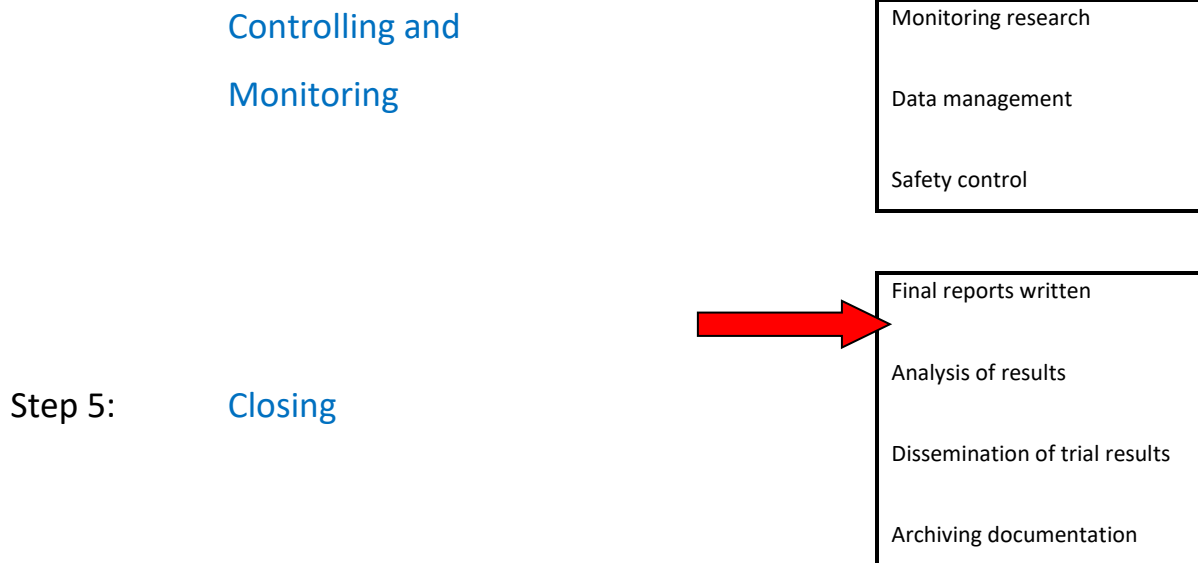


Figure 1: The steps of clinical trial management

Role of the pharmacist in clinical trials

Pharmacists play a crucial role in clinical trial management, particularly in the areas of drug preparation, dispensing, and management of adverse drug reactions. They are responsible for ensuring that the investigational drug is properly handled and administered to trial participants, and that any adverse events or drug interactions are documented and reported appropriately.

According to the ICH, pharmacists' expertise can be utilized in the planning and conduct of clinical trials, particularly in the following areas:

1. Investigational medicinal product (IMP) management: preparation, labelling, storage, temperature monitoring, dispensing, and accountability of the investigational drug. This includes ensuring that the drug is handled and stored in accordance with the trial protocol and applicable regulations.
2. Drug safety: monitoring trial participants for any adverse drug reactions or interactions, and for reporting these events to the study team and regulatory authorities as required.
3. Compliance monitoring: Pharmacists can support for ensuring that trial participants comply with the dosing regimen and other requirements of the trial protocol, and for providing education and counselling as needed to ensure proper adherence.
4. Quality control: general check of documentation including checking proper population of informed consents and other legal documents.

5. Data management: Pharmacists are responsible for maintaining accurate records of drug dispensing and adverse event reporting, and for ensuring that these records are kept confidential and secure.

The success and failure of clinical trials

There are many challenges associated with the management of clinical trial projects. One of the main problems encountered in clinical trials that has been cited repeatedly, is the difficulty in registering an efficient sample size of patients in a timely fashion (2, 17). Among the factors observed more often, in trials that recruited successfully, was having a dedicated trial manager (18). Another challenge in multicentre studies is to identify appropriate clinical sites and set up realistic recruitment expectations. However, the key challenge is to implement and maintain effective management systems and techniques in response to the needs of the trial project.

Here are our Top Tips to overcome some of these challenges:

1. Define project scope: Clearly define the scope of your project, including the goals, objectives, and deliverables.
2. Develop a project timeline: Create a detailed project timeline that outlines the key milestones and deadlines for your project.
3. Communicate regularly: Establish regular communication channels with all stakeholders involved in the project, including team members, sponsors, and other relevant parties.
4. Monitor project risks: Identify potential risks to the project and develop contingency plans to address them.
5. Use project management tools: Consider using project management tools such as Gantt charts, project management software, and risk management tools to help manage your project effectively.

Project management in health and medical research may substantially benefit both the managerial and scientific aspects of clinical trial projects. It is also suggested that project management could reduce a proportion of fund waste (ref). Staff members on the *Alcohol and Pregnancy Project (2006-2008)* found that the use of project management assisted in the process of communicating and integrating project work across multiple organisations and professions, in clarifying and agreeing goals, in assisting in the delivery of defined project outcomes, and in ensuring accountability for results and performance (Ref).

It is worth noting that although this article has focused on the application of project management principles to clinical trials, these principles can be applied to any pharmacy project, whether research-related or not. For instance, project management principles can be applied to clinical audits, quality improvement initiatives, and other projects that aim to improve patient care and healthcare outcomes. By utilizing project management principles, pharmacists can ensure that their projects are completed on time, within budget, and to the desired quality standards. As such, this knowledge is highly relevant to anyone involved in a pharmacy project, regardless of its specific focus. By incorporating project management principles into their work, pharmacists can enhance the quality and impact of their projects, ultimately improving patient care and healthcare outcomes.

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