Avoiding pitfalls in conducting hand surgery research

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Avoiding pitfalls in conducting hand surgery research: the feasibility analysis

Abstract
This paper is intended to support hand surgeons who, at the beginning of their research career, are planning a clinical study. Besides establishing the research methodology of the study, the organizational planning of the work itself is essential. A feasibility analysis carried out before or during the writing of the study protocol helps to estimate the required resources and duration of a project. We highlight some tips and tricks as well as provide checklists that outline the important points to consider before starting a study.

Keywords
Feasibility, patient selection, study planning, checklist, recruitment

Introduction

Discontinuation of clinical trials is a common issue in research. In orthopaedic surgery, 40% of randomized controlled trials remain incomplete (Shepard et al., 2023). The most common reasons for discontinuation are insufficient recruitment, lack of funding or administrative problems (Chapman et al., 2014; Shepard et al., 2023). This discontinuation of approved research projects represents a waste of resources and raises ethical concerns because relevant data collected from patients having been exposed to potentially harmful interventions remain unpublished (Chapman et al., 2014; Shepard et al., 2023).

To avoid a waste of research resources, thorough planning is fundamental. At the outset, the methodological definition of a study should be well described in the study protocol. Nonetheless, it is crucial to outline an organized plan of how the study will be undertaken; a well-planned research project will more effectively achieve its set goals. Before or during the writing of the study protocol, a feasibility analysis helps to estimate the resources needed to execute a study project as well as create a realistic budget and schedule for its completion. The aim of this paper is to support hand surgeons who are at the beginning of their research career and wish to plan a clinical study. We provide various tips and tricks as well as checklists to address the aspects and considerations before a study is initiated.

Study planning: the feasibility analysis

In the course of specifying the methodological aspects of a study in the study protocol, there are substantial benefits in carrying out a thorough feasibility analysis. This ensures successful completion of the project and avoids the production of research waste in the form of incomplete data and misused resources.

Larger institutions usually have a quality management system including relevant standard operating procedures (SOPs) that can assist the feasibility checks. The principles from these SOPs can be distilled into a checklist that includes important points to consider in a feasibility analysis (Figure 1).

Recruitment of patients

Patient recruitment is one of the most challenging parts of a clinical trial; delayed or poor patient recruitment is the main reason for stopping a study (Chapman et al., 2014; Shepard et al., 2023). Before study inception, the number of potential eligible patients needs to be estimated. It is quite unreliable to depend on a colleague's statement that a specific number of patients are operated in a certain time frame because, often, only a small fraction of the estimated patients is actually available for a trial. This well-known phenomenon was first described by the clinical pharmacologist Louis Lasagna and is

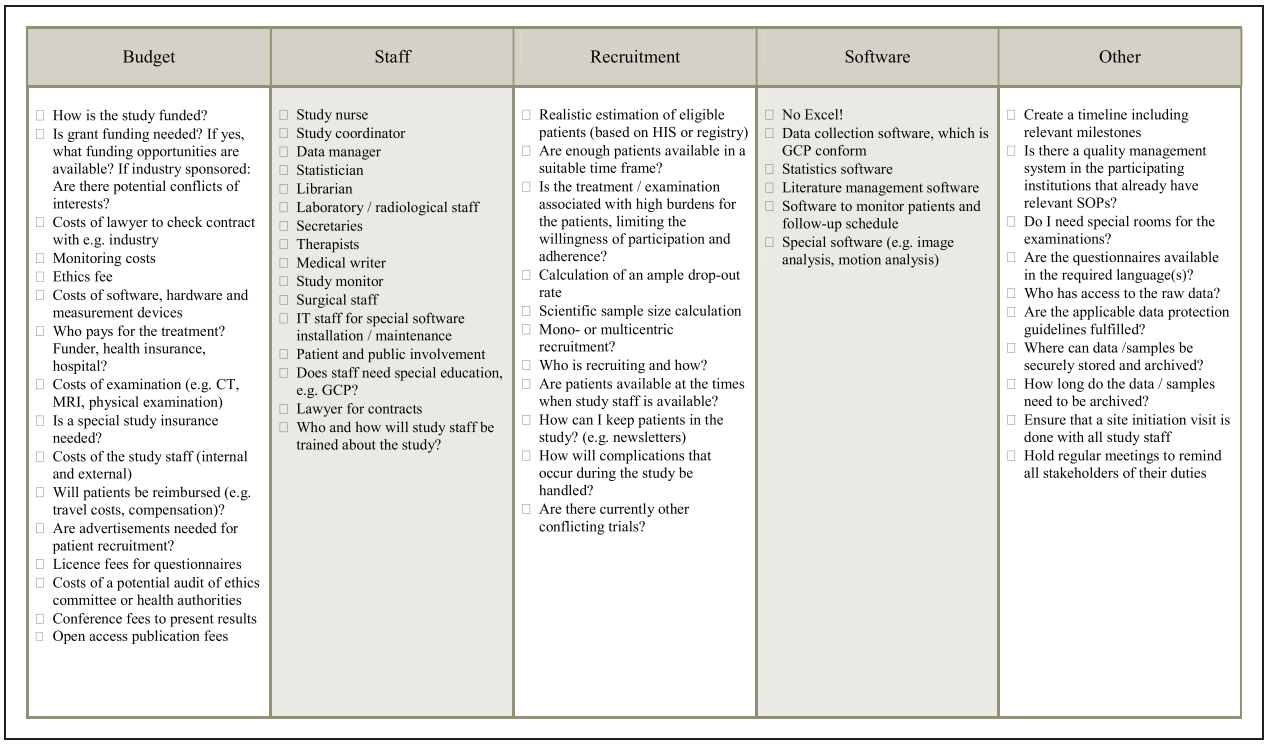

Figure 1. Feasibility checklist. CT: computed tomography; GCP: good clinical practice; HIS: hospital information system; IT: information technology; MRI: magnetic resonance imaging; SOP: standard operating procedures.

known as Lasagna's law (Lasagna, 1979). The small percentage of patients who are actually eligible or available remains a problematic aspect in the execution of a clinical trial (Bogin, 2022).

It is advantageous to allocate sufficient time for realistic recruitment planning. If possible, the number of patients that can potentially be included in a trial should be estimated with the help of the hospital's information system or available registries. In complex trials, it might be of greater value to undertake a pilot phase in which recruitment, its issues and possible improvements are analysed before the main trial begins (Bertram et al., 2019).

There are some pertinent recruitment issues to consider in hand surgery studies, for example, the age of the patient matters. Older and retired patients are more likely to participate in studies, complete questionnaires and return to follow-up visits. For any study focused on a disease with greater prevalence in younger patients, anticipate that recruitment will be slower and the drop-out rate higher. It has to be considered that working patients are often unavailable during office hours, which limits the study-specific visits to either the evenings or weekends.

Second, for studies requiring all patients to attend a follow-up visit after receiving a certain rare intervention, it is useful to contact these candidates before writing the protocol so as to better estimate whether enough patients are willing to participate. However, care must be taken to determine whether such pre-screening is permitted from a regulatory perspective and who is authorised to do so (e.g. only the treating physician and not the study nurse). And again, having Lasagna's law in mind, not all patients who have given their non-binding consent will finally be included.

Third, it is useful to estimate the drop-out rate during the sample size calculation. If there is a lack of internal experience, one can compare published studies with similar patients and the medical setting to gauge the potential number of lost to follow-up patients and the associated reasons.

If the burden for the patient is high, e.g. there are many follow-up visits or the trial includes unpleasant or harmful examinations, the likelihood of participation and adherence is reduced. For example, a study including five computed tomography scans scheduled in 1 year and several questionnaires for completion, the risk of patient withdrawal is high at any point during the study period. Furthermore, it is usual that the responsible ethics committee will likely request revising the protocol. Therefore, it is important to consider and justify whether all investigations and data collections are scientifically necessary.

Although randomized controlled trials are still regarded as the gold standard for generating high-quality evidence, it is important to note these are complex and expensive. Recruitment is usually slower than in observational trials because the inclusion and exclusion criteria are strictly defined, and patients are generally critical about the randomization process. In some cases, it can also be considered unethical to randomize patients. If one can assume that the test intervention yields better outcomes than the control intervention, it would be ethically unsound to deny some patients access to the superior treatment (Djulbegovic, 2007). In such circumstances, cohort studies are more useful.

Budget planning

Similar to the effect of Lasagna's law in patient recruitment, there is also a known phenomenon that studies are usually more expensive than expected. In 2018, the costs of industry-sponsored clinical trials with medical devices were in the range of 5000–9000 Canadian dollars (equivalent to €3200–€5700 based on 2018 exchange rates) per enrolee, and this excluded the cost for the medical device itself (Akpinar et al., 2019). Due to increased regulatory restrictions, inflation rates and overall cost expansion, the current values might have considerably increased. As the costs of a clinical trial increase with higher sample sizes, more study visits, longer duration and more participating sites (Martin et al., 2017), maintaining a balance between the efforts involved in a clinical trial and its scientific value is crucial.

A thorough feasibility analysis helps in estimating the total cost of a trial. Study funding can be secured by applying for grants from national hand surgery societies, Federation of European Societies for Surgery of the Hand (FESSH), local or international funding agencies, foundations or the industry. Many funding agencies also require the submission of a feasibility analysis report in addition to the study protocol before endowing their support.

Staffing for the study

The planning and conduct of high-quality studies are quite complex and time-consuming. It is impossible for all this to be done by a hand surgeon alone. A multidisciplinary team comprising a hand surgeon(s), project leader, methodologist, study nurse, medical writer, monitor and librarian (for reviews) is necessary. A clear definition of the different roles and inclusion of different professionals enhances the study quality. As a consequence, the administrative complexity as well as associated costs will increase and, therefore, doing research without adequate funding is barely feasible (Marks and Herren, 2017).

One also needs to consider that the probability of errors or problems arising during implementation increases with the number of team members involved. Therefore, everyone should be involved in the study and process planning from the very beginning. Responsibilities and duties have to be defined in a binding delegation log.

Data management and monitoring

Data management and monitoring are critical parts of a study and should be defined in the study protocol to ensure reliability and validity of the collected information. For data collection, a professional database that conforms with international laws and regulations and protects patient data should be used. The use of Excel for research is outdated and usually does not meet regulatory requirements for data traceability and protection (International Organization for Standardization, 2020), since data can be easily manipulated or accidentally misplaced.

Regular monitoring of the study is essential to ensure that the study is conducted, recorded and reported in accordance with the study protocol, good clinical practice guidelines and applicable regulatory requirements (International Organization for Standardization, 2020). Although it is not obligatory for every type of study, monitoring supports high data quality and patient safety. The monitoring is usually performed by a study-independent person who systematically checks the completeness and accuracy of the case report forms, that informed consent has been obtained from participants and any adverse events have been recorded. Monitoring can be accomplished on-site and/or remotely through centralized monitoring. While up to 100% of all source data were traditionally verified by the monitor, there has been a more recent shift towards risk-based monitoring, which relies on an initial risk assessment completed before study initiation to assess the level of monitoring required (Beever and Swaby, 2019; International Organization for Standardization, 2020). This practice enables more efficient data checks such that high-risk studies would generally require more frequent site visits over low-risk projects that require only a few checks.

Patient and public involvement (PPI)

One method to increase recruitment is PPI. PPI means that patients, carers, organizations, people

who may be patients in the future or recipients of health services are involved in the study. Involvement can take place at different stages of the trial. PPI can suggest research topics, assist in defining the study protocol, support the writing of the informed consent form, help with recruitment, help with the interpretation of study results, communicate research findings to different audiences and help with implementation into practice (University of Oxford, 2024). PPI has now become part of routine practice in academic and NHS-sponsored UK-based surgical trials (Crocker et al., 2019) and an increasing number of funding agencies now require PPI as a prime consideration before approving grants. On the whole, PPI is relatively poorly applied in orthopaedics and especially in hand surgery (Owyang et al., 2021), but it has the potential to improve study participant enrolment (Crocker et al., 2018). Arumugam et al. (2023) published some practical tips and a useful checklist to get started with PPI in research.

Study execution

Regardless of a thoroughly planned strategy, issues can still arise during the course of the study, such as delayed recruitment, change in the study team, availability of products and funding.

The creation of a timeline that includes all relevant milestones allows regular evaluations of whether the targets are met. If there is a fall behind schedules, the study team can discuss what actions can be taken. If recruitment is slower than expected, alternative recruitment strategies need to be considered, such as involving other centres or adapting the inclusion criteria. The study protocol may need to be revised and reapproved by the ethics committee. In addition, if there are funding issues, efforts should be made to secure additional funding in a timely manner.

All stakeholders of the study should be kept engaged and positively reminded of their duties. This can be done with regular meetings or newsletters. Sometimes it helps to bring extrinsic incentives (e.g. cake) when dealing with colleagues who may overlook their study-related activities. Celebrating milestones together with the study team recognizes their work and provides further motivation for the next steps in the study. Finally, it is worth remembering that patients are also interested in information regarding the study's course and results, and issuing regular patient newsletters can certainly help to elevate study adherence.

Table 1. Eight tips to avoid obvious errors when preparing a manuscript.

Tips	Steps to take when preparing a manuscript
1	Check that data in the abstract match the data presented in the results and tables/figures.
2	Check that the same nomenclature is used throughout the entire manuscript.
3	Ensure all data/numbers in the patient selection flow chart are consistent with data in the main text.
4	Ensure figures and tables are correctly numbered and cited in the text and that the legends are also positioned correctly within the manuscript.
5	Check the formatted references for their correctness. Although reference management software is advantageous in producing your bibliography, a final manual inspection of citations can avoid, for example, the erroneous presentation of upper- and lowercase letters or journal name abbreviations.
6	Before submission, allow an independent colleague to check the final document
7	Mistakes may occur during the review process, particularly when reviewers advise a change, e.g. in the nomenclature or data analysis. In revising the selected parts in the results, it is important to ensure revision of any corresponding sections within the abstract, methods or discussion.
8	The proof presents a final opportunity to check whether the entire manuscript content is correct. It is the duty of all co-authors to read the proof carefully and thoroughly cross-check all data.

Publication

The most common pitfall in the publication process is the definition of authorship. To avoid conflict during manuscript preparation, it is useful to define authorship before writing begins and, ideally, already at study inception where it is clearly outlined in the study protocol. Only those people meeting the International Committee of Medical Journal Editors (2023) criteria for authorship can be listed as authors (Boeckstyns et al., 2020). This includes those who may have entered the study at a later stage, e.g. a statistician, but had contributed significantly to the paper. Conversely, those who have contributed to the work but do not explicitly meet the authorship criteria, must be mentioned as non-author contributors or in the acknowledgements (J Hand Surgery Eur, 2024). Making it clear who will be an author or contributor from the start will avoid major issues concerning authorship later on.

After a long study process, researchers are generally eager to publish their findings. It is crucial to give the final step, the writing, submission and publication itself, the same level of attention as in all previous stages. Despite careful planning and execution, errors can still occur during the final stages.

While recently conducting a literature review (Neumeister et al., 2024), we found that 11% of the included studies contained erroneous data regarding sample sizes and treatments for thumb carpometacarpal osteoarthritis. Specific flaws included: reports of more patients than thumbs operated on; different sample sizes stated throughout the abstract, text and tables; inconsistencies in nomenclature; or differences in numbers and numbers written out in full. Even though these errors might have been a slip of the pen, readers might question the overall quality of such studies as well as the correctness of the data and statistical methods.

To err is human and even the best researcher is not immune to mistakes. What can be done to avoid such inaccuracies? From our publishing experience, we summarize the most common neuralgic points where errors can occur by providing tips on avoiding these when preparing and submitting a manuscript (Table 1).

It is the ultimate duty of authors, reviewers, editors and publishers to work with the highest level of quality. Otherwise, serious (intentional or unintentional) mistakes can be overseen and, in the worst case, lead to retraction of the article and damage to scientific reputation. If a mistake is detected after publication, despite careful checks from all parties involved, publishing a corrigendum should be encouraged, for the sake of other researchers, healthcare providers and patients.

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