

Gathering Preliminary Data

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Abstract:

Prior to any large-scale basic science or clinical research project being funded, it is important for researchers to gather preliminary data. This is essential for providing evidence for the feasibility of research projects and helping to design larger scale studies. When gathering preliminary data one needs to consider how much data are required, how this work is to be funded and where and when the data will be generated. Most importantly researchers should ensure that the planned data collection will be meaningful, serve its intended purpose and follow the principles of good clinical practice.

What are preliminary data?

Preliminary data are the data generated from small-scale research projects to evaluate feasibility, prior to conducting full research studies. Preliminary data are used to test approaches using small sample sizes, provide proof of concept or evidence to support a working hypothesis or they are used as pilot data for grant funding applications. As such they are useful for showing the progression of an idea and likely success of future research projects. In addition preliminary data may also be used to demonstrate the significance or potential impact of a research project. In some cases, preliminary data

can also be combined with data from the full research project to generate a larger data set.

Why do you need to gather preliminary data?

Preliminary data are useful when designing a research project as they can confirm that a planned approach is likely to succeed and has the potential to answer the questions of the research project. These data do not usually provide conclusive proof as they are limited by the size and nature of these small-scale or pilot studies. They are useful for highlighting flaws in design, sample collection, data generation or analysis.

Consequently they enable troubleshooting and the design of full research studies to be improved.

In clinical trial research there are a number of reasons why one might want to gather preliminary data, usually via a feasibility or pilot study. Clinical trials are generally very expensive, resource intensive and time-consuming. Going straight into a large fully powered clinical trial may be wasteful if for example patients would unlikely to be willing to take part in the study, if there are not enough eligible patients available to be recruited in a timely manner or if it is more difficult to deliver the clinical trial interventions than originally anticipated.

To address these issues, preliminary data may be gathered on the acceptability of the trial interventions to patients, the number of eligible patients the proposed trial unit sees per month and the practicalities of the clinicians performing the trial interventions at the trial unit. The preliminary data may confirm that patients are willing to accept the trial interventions, that there needs to be more than the originally anticipated number of centres to complete recruitment in a timely manner and that adjustments for instance in theatre availability are required to be able to practically deliver the interventions planned. A more expansive list of reasons for gathering preliminary data in clinical trial research is given in Table 1:

Examples of reasons for gathering preliminary data for clinical trial research

Plan sample size calculation of the main study – e.g. estimate standard deviation of the primary outcome measure

Assess the willingness of clinicians to participate in the trial

Assess the willingness of participants to be randomised in a trial

Assess the number of eligible patients for the trial

Assess recruitment rate

Assess adherence to trial protocol

Assess whether the randomization process works well

Assess whether the trial interventions can be practically delivered

Table 1: Reasons for gathering preliminary data in clinical trial research, adapted from the National Institute for Health UK¹

Preliminary data are usually gathered prior to obtaining funding for a full research project. They are an essential and usually mandatory part of a funding application, providing supporting data and context for the proposed research.

In basic science research, gathering preliminary data may involve generating laboratory reagents and resources or collecting clinical samples and so can indicate the feasibility of the research approach and the team's ability to deliver. Preliminary data can demonstrate the suitability and applicability of novel methodologies and technologies, particularly if these are challenging or risky. They can also demonstrate technical ability and competence of the research team.

In some cases it may also be possible to publish preliminary data in small research articles or present the data at research conferences. As it is usually part of a smaller project, this is usually a more accessible route for those interested in experiencing research than a larger scale study. This can help one determine whether this is something they enjoy and want to commit to spending more time on.

How much preliminary data should you gather?

Preliminary data are gathered from small-scale initial experiments designed to provide critical pieces of evidence that will support a research idea. They do not need to be a complete piece of research but the data should be meaningful. For example basic science preliminary data do not necessarily need to reach statistical significance but they should not be underpowered so as to produce useless results that cannot inform on the full research study. It is important to consider how small a sample one needs to generate preliminary data and how many replicates are required. Inadequate preliminary data are often the result of over-interpretation and insufficient sample sizes.

For clinical trial research, although it can be challenging to decide how many patients a feasibility or pilot study should have, a sample size should be set *a priori*, with clear reasoning for the size chosen relating to the outcomes that the researcher wants to obtain. This is a complex topic and a good starting point for sample size calculation for clinical trial pilot studies can be found in work by Thabane *et al.*,². A realistic and achievable piece of research should be planned that generates preliminary data in a reasonable time frame and addresses the purpose for which it was intended.

It is also important not to generate so much preliminary data for a grant application that it looks like you have already done the majority of the work and answered your research questions.

Demonstrating how power calculations in the main study can be influenced by preliminary data

In a full study, power calculations are necessary to decide how many data points one needs to collect or how many participants one needs to recruit to be able to observe a statistically significant difference between two groups. Very simply they are based on knowing firstly the level of significance needed (usually $p=0.05$ for scientific research in medicine), the approximate effect change between groups i.e if two treatments are being compared: A vs B and A has a predicted 10% efficacy compared to B which has a predicted 50% efficacy then the difference is 40% or 0.40. This information on predicted efficacy is what is usually obtained from preliminary data gathering or prior studies. Finally, knowing how much one wants their study to be powered (80% power is commonly used) allows one to input these parameters into a formula to work out how many data points or participants are needed to appropriately power the main study.

As can be expected if two conditions show a very small effect change between them then the number of patients or samples required to adequately power a study needs to be far greater in order to detect a significant difference. Further to this the more accurately one can estimate the treatment effect from preliminary data or other studies the more accurate the power calculation will be. This highlights the importance of conducting an adequate literature review, as discussed in another article from this series of publications³. Further information and online power calculators can be found at ClinCalc.com⁴.

Knowledge of the estimated sample size helps researchers to plan their future study and decide whether it is feasible to run at all. For instance a longer timeline may be planned if it is realised that a power calculation estimates over 1000 patients are required, compared to initial thoughts of 100 patients. This is why most funding bodies will ask for a power calculation when considering whether to fund a particular study. Extremely large clinical studies without a large enough clinical network to run the study in may be deemed as non-feasible by trial funders. Questions will be raised about the importance of such a large study if the estimated treatment differences are small.

How to fund gathering preliminary data?

There are a variety of informal and formal mechanisms to fund the collection of preliminary data. These include using existing grant funding to generate preliminary data for a new research project, where an idea or hypothesis stems from data generated during the funded research project. In addition there are funding opportunities designed explicitly for gathering preliminary data. In the UK these include seed corn funding, pump-priming funding, pilot and small research grants, as well as pre- and post-doctoral research bursaries for clinical trainees and starter grants for clinical lecturers (Table 2).

Funding Type	Funder	Purpose
Seed corn	Rosetrees Trust ⁵ Royal Society ⁶	Obtaining data for applications to major funders Purchasing specialised equipment and consumables (early career researchers)
Pump-priming	Royal College of Surgeons ⁷	Assisting newly appointed consultants and senior lecturers in their independent research careers

	Royal College of Surgeons of Edinburgh ⁸	Funding small research projects within the College's priority area (surgical trainees and recently appointed consultants)
Small research grants	<p>Bowel and Cancer Research⁹</p> <p>Carnegie Trust¹⁰</p> <p>Chief Scientist Office¹¹</p> <p>Tenovus Scotland¹²</p>	<p>Funding proof-of-principle studies to collect data for applications to major funders</p> <p>Funding stand alone or initial studies that lead to more extensive work</p> <p>Funding for short projects to provide key supporting evidence to underpin applications to major funders</p> <p>Funding for innovative, patient-related projects and particularly to preliminary "pump priming" studies leading to</p>

	The Urology Foundation ¹³	applications to major funders Funding for projects that seek to improve services and treatments and communications with patients and carers
Research bursaries	Cancer Research UK ¹⁴ Cancer Research UK ¹⁵	Short-term funding to get involved in research projects (early career) Funding for research costs for a small research project (post PhD clinical trainees)
Starter grants	Academy of Medical Sciences ¹⁶	Supporting clinical lecturers to develop and strengthen their research careers

Table 2: Examples of funders who provide small research grants

How to get involved in gathering preliminary data?

The key to gathering preliminary data is to have a clear idea of the overarching research question and how the preliminary data fits into the package of research planned to answer the research question. A good way to get involved is to contact an

established University-affiliated research unit, which will help with the research question and research package and may have opportunities to get involved in the gathering of preliminary data. They will also have familiarity with the funding streams available for funding preliminary data collection and main studies. Opportunities for medical professionals can be taken alongside clinical training (e.g. Academic Clinical Fellow / Clinical Lecturer / in one's free time), out of programme in a dedicated research period (e.g. MD/PhD/MSc) or as a medical student (e.g. BSc) (see the article on non-clinical laboratory based research¹⁷ that is part of this series of publications). These opportunities are often competitive and it is important to contact the research unit that one is interested in to meet with them and signal interest.

Research governance and good clinical practice (GCP)

When working with any clinical data adherence to local Research and Development (R&D) policies and an understanding of Good Clinical Practice (GCP) are essential in order to protect patients' welfare and confidentiality and to ensure any data can be considered part of future publications. These steps can sometimes be seen as barriers but local R&D teams provide far more support than just registration and ethical approval, with advice on data analysis and potential collaborations (see the article on getting to grips with clinical research¹⁸ and setting up clinical research studies in the

NHS in England¹⁹ that are part of this series of publications). GCP training can be accessed either locally by attending courses (through your local R&D department) or via online e-learning provided by the National Institute of Health Research (NIHR)²⁰.

Using existing databases as an alternative source of preliminary data

Carrying out new experiments or clinical studies is a common way to obtain preliminary data. However there are alternative sources of data that can be used, such as mining data from existing databases. Clinicians are constantly exposed to patient data that could be used as preliminary data. A hospital is essentially an amalgam of biochemical, pathological, microbiological and medical physics imaging laboratories. By working with audit departments, biobanks, data repositories and other departments such as radiology and microbiology and pathology it is possible to access many forms of retrospective clinical data which can be analysed to help generate some preliminary data for a research proposal.

Take a laparoscopic nephrectomy, a common urological procedure, as an example. Just a single elective procedure produces a large amount of data, which may be gathered to answer a clinical question. Data available pre-operatively include biopsy histopathology, staging scans, blood tests and patient parameters such as blood

pressure and body mass index measured in pre-assessment clinic. Intra-operatively, parameters such as procedure time and blood loss are available. Post-operatively data on tumour grading, staging, follow-up scans and survival data are available. These data can be analysed to look for associations between variables and outcomes, which may help provide preliminary data for a research proposal in the field of nephrectomy.

With over 900 nephrectomies reported in the 2009 BAUS audit²¹, it can be clearly seen that the volume of data produced by routine procedures alone is huge. The collection of preliminary data may be aided by these large public datasets, which have far greater statistical power than smaller cohorts.

Take home messages:

- Preliminary data are generated from small-scale research projects
- Gathering preliminary data is useful for testing the likely success of a future research project

- Preliminary data are necessary for applying for research funding
- Existing clinical databases can be an alternative source of preliminary data
- Preliminary data should be meaningful and offer insight to the main study
- Research governance and ethical approval are essential for gathering preliminary data

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