An Introduction to Research for Primary Dental Care Clinicians

Part 6: Stage 7. Piloting the methodology and project management

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Introduction

This paper, the sixth in the series, will address the seventh of the ten stages of a research project suggested in the first paper in the series. The ten suggested stages are:

1. The initial idea (asking a research question).

2. Searching the literature.

3. Refining the research question.

4. Planning the study.

5. Writing a protocol.

6. Obtaining ethical approval and funding.

7. **Piloting the methodology and project management**.

8. Collecting data.

9. Analysing the data.

10. Writing up and disseminating the results.

A previous paper1 outlined how to write a protocol, which provides the blueprint for a project. Once ethical approval and funding have been obtained, the next stage is to pilot (test) the project and manage it.

Stage 7. Piloting the Methodology and Project Management

This paper serves to expand the reader's understanding of research operations; that is, the preparation and deployment of the project in a manner directed toward accomplishment of the research objectives. The principles are the same, no matter the size or location of the project, whether a general dental practice or the laboratories of a large international pharmaceutical company. There is always the possibility for even the best-designed protocol to go drastically wrong, rendering the data that have been collected meaningless. This usually occurs as a result of mistakes in a single critical step in the implementation of the study methodologies embedded within the protocol. Piloting a study's methodology and managing the study attentively are crucial for success. The underlying concept is to minimise bias,

trying at all times to ensure that results are as valid as possible. In addition, any study involving humans or samples taken from humans (for example, studies in a pathology laboratory) must be conducted in a manner compliant with the regulations governing clinical research.[2,3] As discussed in a previous paper,[4] codes of ethical behaviour are designed to protect study participants and people that might eventually benefit from the treatment being investigated. Elements of project management facilitate the scientific aspects whereas other elements focus on participant protection and regulatory aspects.[3,5] The subsequent sections of this paper will outline and explain simple procedures and practical steps proven to minimise bias during a study, while also facilitating participant protection. The paper aims to highlight the importance of these two key operational aspects of clinical research.

A. Piloting the methodology

First and foremost in setting the framework for any study is the piloting of all aspects to confirm the feasibility of the operational aspects. Piloting should ideally incorporate elements of training, calibration, definition of scheduling, systems to obtain the supplies needed, and testing of recruitment procedures, as well any support activities of external collaborators, be they administrative, technical, clinical or laboratory in nature.[6] Although an ideal protocol seems overtly clear when written, research projects are conducted by individuals, not machines. The actual implementation of even the most detailed protocol may give rise to unexpected issues, which may become apparent only after piloting. The most well-deliberated plan may overlook some highly undesirable surprises. The following procedures need to be followed:

A1. Training

All individuals involved in a project should be thoroughly familiar with their defined tasks, beyond knowing how to perform the study correctly. The target is that the task should be so practised that not only can it be performed correctly, but it is very unlikely to be performed incorrectly. In addition, consistency between individuals is vital. For example, in certain epidemiological studies, persons responsible for gathering data should be trained to the same consistent standard with any potential investigator who is an outlier with regard to his/her observations to be excluded. It therefore follows that all persons responsible for carrying out any given task should be trained to the same gold standard, simultaneously if at all possible. This small step minimises variation (and thus bias) in explanations or understanding of key elements of potentially technique-sensitive measurements or procedures.

A2. Calibration

Many procedures incorporated in research projects are already well known to clinicians. Even in the case of qualitative research, healthcare professionals often have pre-existing routines, habits or approaches when performing what are normally thought of as standard techniques. Calibration is a part of piloting methodologies that serves to confirm that the planned procedures are highly repeatable. It often serves to ‘reprogram’ researchers to perform common tasks in a more consistent manner. It is a form of training aimed at reaching a level that ensures that when repeating the same task many times, the data are within the defined limit of error (repeatability). Repeatability refers to the level at which a single individual can repeat the same task in a consistent way, minimising variation. This is referred to as calibrating against oneself (intra-examiner repeatability). Calibration may also be between two or more individuals (inter-examiner calibration and repeatability).[7] Calibration of

examiners is performed in a manner that quantifies the variation between the two sets of measures employed. This variability can later be taken into account during analysis and interpretation of the study data. Calibration may also refer to agreement on and duplicate practice of any study procedure; for example, the style in which interview questions are asked in obtaining quantitative data, or the consistency with which impression materials are mixed as a procedure in a prosthetics project, or the technique used for suturing a site in a surgical study.

A3. Schedules

All aspects of scheduling and timing should also be piloted before a study commences to facilitate definition of time required for each aspect included as a part of a single study visit. Accurate definition of 'time per task' serves to facilitate overall predictions of time required and also defines the overall clinic and administrative time. Timing of each step also allows study coordinators to see imbalances or bottlenecks in the flow of a study appointment. This can be particularly important in scenarios where a participant is seen by multiple researchers during a study visit. For example, there may be one examiner assessing gingival health using one index and a second person assessing plaque using another. In the context of the overall project, efficient use of time is a critical element of study implementation because each project normally has set funding that needs to be used wisely in order to meet defined budgets.

A4. Supplies

Piloting of the project is also useful in characterising the quantity and nature of supply requirements. Any products to be used should be identical, including instruments, materials, and pharmacological and cosmetic agents. For example, different brands of periodontal probes may have small differences in gradations that could introduce variability of measurements. Biological products such as periodontal membranes or toothpastes should be supplied from the same production lot for the entire study. Another less frequent example might be saliva tubes, which are available in various shapes and sizes with some more suitable for storage and others more suitable for collecting the sample. Only when one tries to spit into a small tube does one realise how important the design of the tube can be to the amount collected. In a study assessing plaque, the strength of differing disclosing agents might affect the ease and consistency of assessments performed, and therefore results.

A5. Recruitment

Recruitment strategies are one of the most important aspects of any study and require piloting before the study commences.[7,8] Recruitment spans from the first approach made to inform a patient of a project, to the steps in explaining the study, to following up to confirm a patient's interest to participate and obtaining informed consent. Participants are only considered recruited once they have signed the informed consent form. Bottlenecks or unanticipated challenges in any of these steps can impact on overall recruitment rates substantially. If difficulties are encountered at one stage, the entire study can be delayed, which in turn can increase costs. For example, the delicate manner in which the study objectives or procedures are explained may significantly impact the willingness of potential participants to consider participation. If it is feasible and within the current regulations, an opt-out approach enables greater numbers to be recruited than an opt-in approach. That is to say, participants may tentatively be included and proceed to the next step of scheduling with the condition that if

they call to withdraw after consideration of information provided, then the tentative appointment will be cancelled. Approaches and systems such as this should be tried and defined based on experiences encountered during piloting. In any explanation, there can be the glass-half-full or the glass-half-empty approach. The challenge is to discern how the patient would see the glass half full when considering study participation. This can be quite different to a clinician's view of the benefits of study participation. Piloting is an opportunity to sound out patient views.

A6. Support requirements

Steps in the conduct of a research study often rely on external collaboration or support. These partnerships should also be tested before a study commences to ensure that the services that are to be provided are commensurate with the study protocol and are delivered in a timely manner. For example, a study investigating the effects of different impression materials on the characteristics of crown margins would depend upon partnership with dental technicians and a laboratory. In such a case, it might be desirable to have all the work done by one clinician and one technician to minimise variability, and this might have implications for laboratory production time. Ensuring that a back-up person is trained, should the designated person be unable to carry out the task, is part of testing the system. Piloting of external partnerships can be even more important than those internal to the study setting, because the study principal investigator often has little control of factors that may affect the external collaborators who work within the team.

B. Project management (logistical elements)

For ease of discussion, project management is presented in two sections: the first focuses on logistical elements and the second on those elements defined by regulatory guidelines. However, to a degree these aspects overlap and are in no way mutually exclusive. For example, logistical elements should promote conduct that minimises bias while maximising efficiency in every aspect. Regulatory guidelines state that a study conducted in a disorganised, inefficient manner with little attention to consistency is an unethical study and puts participants at risk.[4] Therefore, although discussed separately here, whether an operational aspect of the study management is driven by regulatory guidance or by logistical elements, it cannot help but facilitate the other. Project management is ultimately the responsibility of the study principal investigator. However, this is normally delegated to a study coordinator for implementation on a day-to-day basis. It is a defined role in itself, as it is time-consuming and requires exhaustive focus on detail.[9]

B1. Project initiation

The first step in managing a project is the study initiation, which begins with a study initiation meeting. The initial meeting is held with all members of the study team present, including the principal investigator and the statistician. It should be held prior to piloting study methodologies and serves to confirm final agreement and understanding by all study team members of every aspect of the project. It informs each member of aspects of the study which might be beyond their own role or responsibility. Roles are confirmed and defined to the final level of detail. The agenda of the meeting is defined largely by the protocol, with the normal format being simply to go step by step through each page of the protocol, clari fying methods, roles, supplies and so forth that pertain to each step. A thorough initiation meeting generally requires a minimum of three hours, depending on the size and complexity of the

protocol and the size of the research team. Imagine it to be an enactment of the study visits. It may involve role-playing, to provide examples of study recruitment conversations, during which a clinician explains facets of study participation to an individual unaware of the project details. Elements of the training mentioned earlier may be combined with study initiation, and this may require as much time as two or more days. The meeting is led by the study coordinator, with those in other key roles leading pertinent sections. For example, the study examiner might coordinate discussions of study assessments with treatment clinicians leading discussions of study treatments and so forth. Beyond defining roles and tasks, the study initiation meeting is a time to define and set practical systems in place that will orchestrate consistent and smooth running of the study project. Unless the defined systems are linked together as in a chain, the risks of problems in the study are high. Any break in the chain can put the quality of the data at risk.

B2. Participant recruitment

Following study initiation, the subsequent project management focus is around study recruitment. The techniques used should serve to focus on potential calculation of the recruitment rate. Logs should be kept of all participants deemed suitable for inclusion in a given project. Furthermore, suitable potential participants should be logged and provided with an information sheet that invites them to participate in the study. As participants agree or decline to participate, this is noted in the log, together with the reason if it is declined. The number of participants recruited divided by the number approached provides the recruitment rate, an element critical to study resources and flow. For example, if one out of every five people approached agrees to participate, the impact on recruiting time is far greater than if one person agreed out of every ten approached. Use of such logs allows researchers to discern whether any difficulties in recruitment are related to too few suitable participants or too few suitable individuals agreeing to participate.

B3. Participant flow and retention

Once patients are enrolled in the research study, the demands of management increase because it is vital to ensure that all study visits or other aspects, such as the return of questionnaires, occur within timeframes defined in the study protocol. It is essential that as many participants as possible are retained until the end of the study. Various computer programs facilitate tracking of study visits from the use of a simple spreadsheet to complex databases, designed specifically for this purpose. It is important that every visit is logged in a form that allows easy identification of any visit that may have been missed, thus preventing a participant from ‘falling through the cracks’. For example, when a study appointment is cancelled, it should normally be rescheduled as soon as possible. It is very easy to forget a patient who has simply left a message on a voicemail system. Too many drop-outs may cause a tremendous bias in the study results, particularly if all of the participants lost during follow-up were part of the same group within the study, such as a test or control group.

B4. Project monitoring and quality assurance

The Oxford Advanced Learner’s Dictionary definition of ‘monitoring’ is ‘to watch and check something over a period of time in order to see how it develops, so that you can make any necessary changes’.[10] In the context of clinical research, monitoring is carried out throughout a study, essentially in the same way as an ongoing audit of all other aspects, to ensure study compliance with the protocol and regulatory guidelines.[3,5] Monitoring includes observation of

each task, including all clinical and laboratory procedures and administrative aspects, to verify consistency with the initial training or systems agreed upon during study initiation. It can be easy for clinicians to drift back to previous clinical habits over time; therefore, constant follow-up serves to remind the study team of details previously agreed. Without ongoing monitoring, small critical changes can be overlooked. For example, imagine a scenario related to the saliva samples mentioned earlier. During the study initiation, it was agreed that saliva should be placed immediately into a -20 freezer (a freezer that can freeze to -20°C) The -20 freezer is in an area some distance from the clinic area. After some weeks of the study commencement, the member of the study team who normally stores the sample initially realises that there is a refrigerator closer to the clinic area. For pragmatic reasons, they decide to store all samples collected from the morning session in the 4°C refrigerator before taking them all to the -20°C in a batch at midday, to avoid losing time walking back and forth to the -20 freezer. A simple time-saving step becomes a disaster for the samples because they change in content with each minute that passes by before being frozen. Such an error can occur so easily without notice. In the scenario cited, regular monitoring of study activity and tasks picked up the change, and the study was quickly reverted to the original plan.

Constant communication within the study team is not only essential but also an easy way to monitor all activity. Again depending on project complexity, project size, duration and the size of the study team, study meetings may be held weekly, bi-weekly or monthly. Less frequently than monthly is not advised because small errors have the potential to have significant impact on the study data if not discovered early. Evaluation and discussion of each step with potential to impact on study data or study efficiency, at regular intervals, allows the study team to capitalise on things that are working and alter approaches. Efficiency in all aspects of the study implementation is vital, hence the need for ongoing assessment of operational elements.

Monitoring of study data-collection forms and study files can also highlight areas where the team may have slowly digressed away from the study protocol. This may be performed internally by members of the study team or alternatively by a person external to the team. In many studies funded by an industrial sponsor, the sponsor will often monitor all aspects of the study.

B5. Contingency plans

Contingency plans are part of good project management. In the same manner, well-defined project plans must be in place before a study begins, together with a good contingency plan to cope with the unexpected. This is most pertinent in respect to the personnel of the study team, each member of which has a particular responsibility. As discussed previously, some may be very specifically trained; therefore, a plan should be in place for someone to cover, should one of them be unable to carry out their defined role.

C. Project management (regulatory elements)

As highlighted previously, project management carries with it many requirements defined by regulatory bodies. Although these can be time-consuming and are often criticised for their impact on timeliness of study conduct, they are essential and ultimately improve the quality of all aspects of study management. Regulatory guidance requires documentation of all study activities to a level that would enable the project to be re-enacted, much like a theatre play,

should any issue arise around a treatment or product at the time it is implemented on a wider scale in clinical practice. It defines the systems that should be in place to ensure accurate archiving of critical information related to the study.

C1. Project initiation

Regulatory requirements at the time of study initiation include full documentation of all steps that have been taken to ensure appropriate training of members of the study team. These form the contents of the study initiation minutes/report. The main study file, sometimes referred to as the investigator file, is started at this point. It contains a copy of all documents such as the protocol, information sheet, consent form, all communication with ethics committees, and sample data collection forms. It also includes sample signatures of all individuals who may sign study forms, curricula vitae of study team members, and professional registration details of all clinicians.

C2. Project duration

Throughout the duration of the study, regulatory elements of study management are focused on communication with the ethics committee with attention to two main elements related to participant safety. The first is a system for reporting any adverse events that may be experienced by participants during the study. All adverse events must be documented in the study forms with an assessment of the nature of the event, the seriousness and possible relation to the study. In the rare event of a major problem with a patient, particular attention must be given to adverse events that result in hospitalisation. These must be reported to the principal investigator within 24 hours and to the ethics committee within a defined limit of time, normally 14 days maximum, in addition to the usual procedures following such incidents within the clinic or practice. Repeat occurrence of a similar adverse event may require a study to be stopped in order to protect participants; thus, this is a vital step of study management and documentation.

The second important regulatory aspect is communication with the ethics committee regarding any changes to the protocol. It is very often the case that there is a need or desire to make alterations to a study protocol, sometimes for logistical reasons, such as to improve study recruitment, or sometimes due to new scientific knowledge that has become available since study initiation. Amendments are only allowed following approval by the original ethics committee that approved the project before it started. Again, this formal process for any alterations to the initial protocol facilitates consistency in study procedures.

D. Conclusions

Irrespective of the location of the research, whether it is in a primary dental care practice, a teaching hospital, or a laboratory, attention to minimising bias is situated at the heart of a robust study. Piloting of methodologies and project management emerge as indispensable aspects of performing research. A well-constructed blueprint (protocol) is essential but in itself is insufficient to achieve valid results. Piloting of methodologies and project management demand equal, if not more, time and effort as construction of the plan. Therefore, a well-defined strategy and resources should be set from the outset to ensure that operational aspects are not overlooked.

E. Suggested further resources

• Pocock SJ. Clinical Trials. A Practical Approach. Chichester: Wiley; 1983.

• Association of Clinical Research Professionals. Available at: www.acrpnet.org/

• Department of Health. Clinical Trials Toolkit. Available at www.ct-toolkit.ac.uk/

• Department of Health. Research Governance Framework for Health and Social Care. Available via: www.dh.gov.uk/en/publications

• Giannobile W, Burt B, Genco R, editors. Clinical Research in Oral Health. New York: Wiley-Blackwell

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