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Embarking on a research project…or research for the absolute novice

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ABSTRACT Research can be a difficult area for the novice to break into. A number of different obstacles face the new researcher, starting with selecting a suitable supervisor, writing a workable protocol and obtaining permissions from all the relevant organisations. This beginner's guide walks the fledging researcher through the required steps, including formulating a research question, designing a protocol and completing the Integrated Research Application System form to obtain the required permissions. The aim is to demystify the terms used in research and expose some of the pitfalls the authors experienced so that others can avoid them! Although challenges can arise throughout the research process, we aim to help you get underway.

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EDUCATION

> So, the Labyrinth is a piece of cake, is it? Well, let's see how you deal with this little slice…*(Jareth [David Bowie] Labyrinth)*

THE IDEA

You may have an idea or perhaps you have inherited someone else's idea. This might be stating the obvious but, whatever this idea is, it needs to be something that you are genuinely interested in. If an idea doesn't seem like a good one at this stage, it never will. The best ideas for clinical research address a clinical need. One method developed by the James Lind Alliance involves asking patients and carers what their priorities for research are.[1] It has recently been successfully applied to a wide range of conditions including Parkinson's disease[2] and stillbirth.[3] Even if this kind of exercise is beyond the scope of your research, it pays to know if one has been done for the condition you are studying; this kind of patient input is grant-writing gold. Remember too that some of the best ideas are also very simple.

For quantitative research, there needs to be a clearly defined hypothesis. This is usually stated as a 'null hypothesis'; that is, an assertion that you can disprove, as it is impossible to absolutely prove a hypothesis. An example of a Null Hypothesis would be that alcohol does not cause tongue cancer. The next stage is to make sure your research methods will allow you to meet your research aims.

THE SUPERVISOR

Often there is one person who is the natural choice of research supervisor; however, before making a decision it is worth considering their track record, in terms of getting their students through their project and publishing papers and whether students then were offered consultant jobs in their chosen specialty/subspecialty. An ideal supervisor is both on the conference circuit – with their finger on the pulse – and hands-on, guiding you through day-to-day practicalities such as Integrated Research Application System (IRAS) forms and formulating protocols. In reality, time constraints mean that most favour one or the other and it is worth thinking about how relationships with colleagues and mentors can help fill the gaps.

In either case, a good set of colleagues at a similar stage is invaluable. They may already have a phone book with all those crucial contacts you don't even know you need yet! They can help translate 'research-ese', which can be as dense and impenetrable as clinical-speak is to a medical student. Table 1 is a jargon-buster to get you familiar with some key terms. While we aim to demystify the research project, the local landscape is always different; fellow travellers are indispensable to help guide and encourage you on the path ahead.

PROTOCOL

The protocol is your project's DNA. It has to be detailed enough for colleagues to carry out your project without

TABLE 1 A guide to terms and abbreviations commonly used in clinical research

CI	Chief Investigator. Person with overall responsibility for the conduct of a research project. Often the same person as the PI in single site studies.
CTIMP	Clinical Trial of an Investigational Medicinal Product. Will require a Clinical Trial Authorisation from the Medicines and Healthcare Products Regulatory Agency and a EudraCT number (European Clinical Trials Database).
GCP	Good Clinical Practice. This training seeks to prepare individuals involved in research to carry out their duties. Can be done face-to-face or online.
HRA approval	A new approval that is being rolled out for research in the NHS in England. Consists of REC review plus an assessment to make sure the study meets the required standards for regulatory and legal purposes. The assessment was done by each NHS organisation undertaking the study, but will now be carried out once, by the HRA. The HRA manages the REC service in England.
IRAS	Integrated Research Application System
PI	Principal Investigator. Responsible for a piece of research at a particular site.
PIC	Participant Identification Centre. Identifies potential participants, e.g. through clinics or registries, but does not take part in the research study itself
PIS	Patient Information Sheet. Explains the research, why a person is eligible, risks and benefits and contact information for more information. Should contain version numbers so consent form refers to appropriate PIS.
PPI	Patient and public involvement, is the vogue term for involving patient groups and other members of the public in the design and execution of a study.
Portfolio study	A study which has been included on the NIHR Clinical Research Network Portfolio, which provides resources for recruiting patients.
PR	Proportionate Review. Projects which represent a 'minimal risk, burden or intrusion for research participants' can be reviewed within 14 days by a REC sub-committee.
REC	Research Ethics Committees are convened to discuss the ethics of potential studies, using the information in the IRAS form and supporting documentation (e.g. consent forms).
Site specific master file	A site specific file must be created for every site at which research will take place. Must contain key information relating to research such as consent forms, participant information forms, protocol, communications with sponsor, funding information and insurance/indemnity information. This is in the process of being replaced with a Schedule of Events/Statement of Activities
Schedule of Events/ Statement of Activities	This gives a guide to the potential resource implications of becoming involved in a trial, so that potential research sites can assess their capacity to deliver the research. The details of implementation are still being worked out at time of going to press.
Sponsor	Company, University or Hospital trust responsible for the study and for ensuring that appropriate standards are adhered to.
SSI Form	Site Specific Information Form. A specific version of the IRAS form that contains information about the planned research at a specific site. It may not be required for your study so check IRAS for guidance.

your having to lift a finger and for ethics committees and funders to be completely confident in your methods. It is time-consuming to get right and the best place to start is to look at successful protocols from your institution.

The traditional format is:

Background

Start with the published research in your field leading to how your proposed project fits in. Define research questions, making sure that it is possible to answer them.

Study design

This has to be detailed enough for someone else to pick up the protocol and take over if need be, and should outline all the steps required. Often pilot data or trial runs will be necessary in order for this to be accurate. This section will need to justify the methods used, usually by referencing to the previous work of your group or others.

Include:

- Participant selection or recruitment; including who will approach potential participants, and whether in clinic or by letter. How representative will the sample be? Any inclusion or exclusion criteria need to be stated and justified
- Consent process
- Randomisation, if required
- Any clinical tests being carried out and what you will do with the results if abnormal
- Details of any intervention if appropriate

- Details of any data being collected with justification. How will it be stored and who will have access to it?
- Outcomes – what is being measured? What are the primary and secondary outcomes?
- Statistics – brief plan for how you plan to analyse the data. You are likely to need to perform a power calculation, which determines the minimum number of participants you would need to have to detect a genuine difference between the groups
- Staff – if any – and their skill sets. Are they (and you) sufficiently trained to carry out the procedures proposed?
- Costing – detailed breakdown of all the costs are required at this stage to ensure the project is viable
- Legal – does the study meet all the current legal and regulatory requirements?
- Ethics – are there any relevant ethical issues, such as potential for harm or distress? What have you done to minimise the harm? Is the risk justified?
- Realistic timetable for the recruitment of participants, experiment, data analysis and write up and the time it will take to get ethical approvals, etc.

PATIENT-PARTICIPANT INVOLVEMENT

Involve potential participants in every stage of the study design. They will think of practicalities that will never occur to you. Beware that this feedback can be bracing and can dramatically alter your project, so ensure you seek it early on in the design process. Some institutions have Dragon's Den-style project pitches where research novices can get feedback from established researchers and interested members of the public.

IRAS

What is it?

The IRAS form is designed to be a single online application for approval by the Research Ethics Committee (REC), Health Research Authority (HRA) and the Medicines and Healthcare products Regulatory Agency. The form focuses on the legal, ethical and regulatory aspects of your study and requires detailed information about how your study will fulfil the requirements on a daily basis.

Why?

Previously, separate forms had to be completed to get permissions for a research project. Even within IRAS, some crossover is apparent. Therefore, you shouldn't panic if you feel your answer to question 51 is fairly similar to the content to question 52, they may well be read by different people.

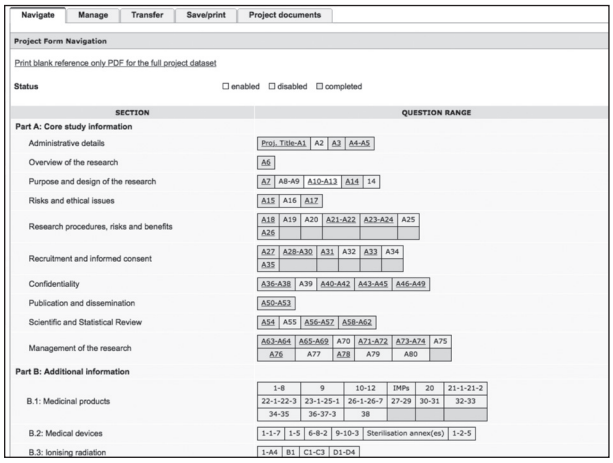

FIGURE 1 IRAS navigation screen showing the project filter

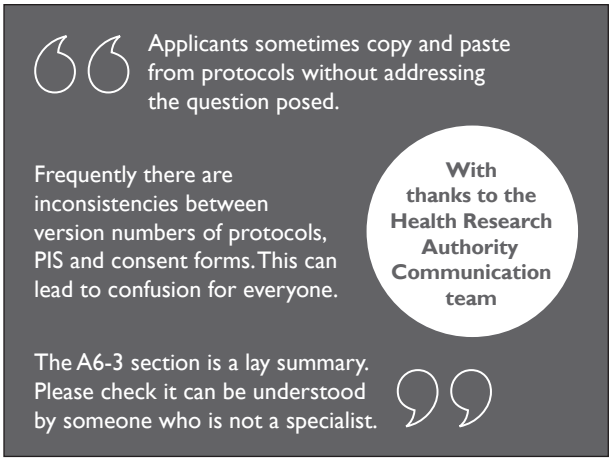

FIGURE 2 REC comments[4]

Where do I start?

There is an IRAS e-guide, to get you started and the green 'i' icons, will give you an idea of what information is expected from that question. Some RECs may have particular accreditation in certain situations such as CTIMPS or approval under the Mental Capacity Act.[4] The local REC may allow you to observe a REC meeting to get a feeling for the experience. The authors would strongly advise this as it would have been helpful for us to have had this chance.

Troubleshooting

Another tip is to print off your blank form (after using the filter) and speak to your supervisor. Anything you don't understand or haven't confirmed with your supervisor can be worked out over a coffee, saving endless email enquiries. Make sure you know who will be the CI and the PI. Will there be Participant Identification Centres as well as your main site? Who is the sponsor? See Table 1. At present, separate forms for each site (Site Specific Information Forms) are being phased out in favour of a document that sets out what would be

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TABLE 2 The Caldicott Principles[5]

1	Justify the purpose – of each aspect of data you intend to use
2	Do not use identifiable information unless necessary – assigning anonymised research codes are the common means of achieving this in research
3	Only use minimum identifiable information – if you don't need certain demographics, don't collect them
4	Access to patient-identifiable information should be on a strict need-to-know basis
5	Everyone should be aware of their responsibilities - a delegation log is the best way to do this
6	Understand and comply with the law

expected of a particular type of site (resources, time, recruitment, space, etc.), i.e. sites that only recruit participants or that undertake part of the study.

ADDITIONAL DOCUMENTS

As well as completing the IRAS form, you will need to produce the documents for use in your project so they can be reviewed by the relevant bodies. These include invitation letters, GP information letters (it's only polite, especially if you need to call them later when your research participants need GP input), participant information sheets and consent forms. You also need to provide any scales or questionnaires you want to use (and have permission to use them…it could be potentially very embarrassing if you don't).

Versions and dates could leave you on a sticky wicket. Make sure you link all sheets to each other and be assiduous regarding version control (all forms need title, IRAS number, date and version footers). So if you change one of your patient information sheets, the consent form should reflect this. Always make sure any version updates are approved by the REC and version numbers/dates change accordingly, e.g. I consent to taking part and have read and understood the information in the participant information sheet - 05/06/15, version 2.0

The creation of the protocol and completing the IRAS form forces you to examine the mundane and everyday issues you will face in a research project.

SUBMISSION

When you have completed the body of your IRAS form, have a friend who is familiar with the process look through it, as well as your supervisor. Once you are satisfied, upload your documents, contact the REC central line to inform them of your application and make any last minute additions. Once you are ready,

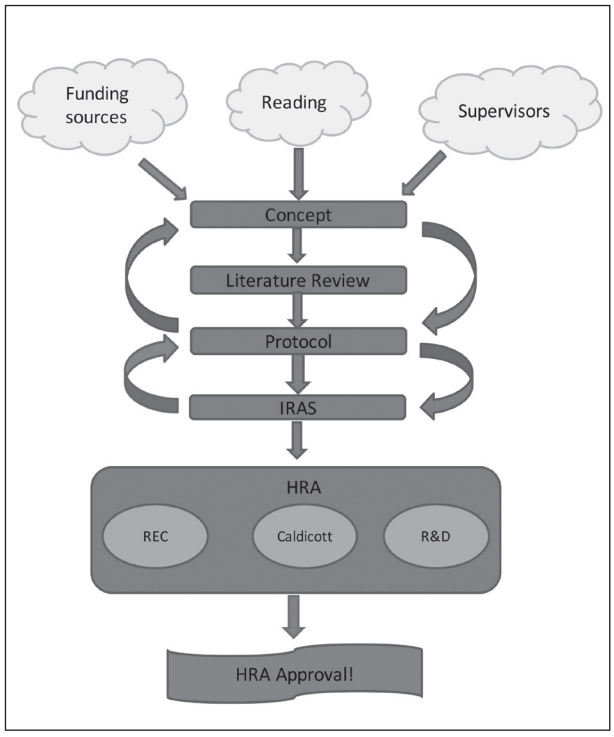

FIGURE 3 Flow chart of project procedure

submit your form for electronic signing by your CI and sponsor's representative. Check in advance your supervisor is available and has a working IRAS account; you have until the end of the working day to submit after booking through REC. You **cannot** modify your form after it is signed: it will void the electronic signatures.

AMENDMENTS

If you want to change any part of your protocol you **cannot** do this after you have attended your REC meeting and received permission. You can submit an amendment after discussing the details with the sponsor and CI/PI but in the interim you can only carry out the protocol you have permission for. One author on this paper (LW) wanted to add a questionnaire but could not use it until the amendment was approved, so continued with the original protocol until the amended permission came though.

RESEARCH AND DEVELOPMENT/CALDICOTT

Caldicott principles (Table 2) are designed to protect patient confidentiality and ensure that information is used and stored appropriately and safely. Overall responsibility within an NHS organisation lies with an appointed Caldicott Guardian. Different Trusts have different requirements; discuss with your local R&D office to see whether your project requires Caldicott

permission. The easiest way to complete the Caldicott form is to review the information you intend to collect, store or transfer against the Caldicott principles.

Each Trust's Caldicott form was historically different, but having these principles to hand and contrasting your plans for patient information against these, coupled with an understanding of how data is safely and responsibility stored in your facility (locked filing cabinets, secure encrypted computer systems etc.) allowed you to complete them. Now, the same HRA-approved forms for this purpose will be submitted to each site which is much more convenient! Caldicott and R&D approval are being integrated into the HRA process (though principles for completing these sections still apply).

ADAPT WITH THE TIMES

Remember that the research world, like the clinical one, is always changing. Though we hope the principles and guidance in this paper will stand you in good stead, even now there are changes ongoing to research applications. Ensure you have the latest information by checking the HRA website (http://www.hra.nhs.uk) and speaking to colleagues who have recently gone through the process.

SUMMARY

We hope that this summary will help you get a feeling for how to go about negotiating the labyrinth of applying for permissions for a clinical research project. Remember to take one step at a time, make use of the expertise around you and grasp how a particular site functions, as this is invaluable. The late, great David Bowie in the film *Labyrinth*, talked about taking little slices of the cake: breaking it up into manageable chunks will hopefully allow your application to be a piece of cake.

LEARNING POINTS

1. Ensure your research idea is relevant, will add to current understanding and that you are genuinely interested in it.
2. Make sure your supervisor has a reputation in the area and that you both have similar goals for your project.
3. Start with a good, working protocol. This will make ethics and R&D applications much more straightforward.
4. Print your IRAS (HRA) form out and go through it with your supervisor to expedite the process.

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