INTERNATIONAL JOURNAL OF ORTHOPLASTIC SURGERY

Hendrickson, S, et al. The Only Way is Ethics: Obtaining Approvals for NHS Clinical Research Projects. *International Journal of Orthoplastic Surgery.* 2019; 2(3), pp. 80–83. DOI: https://doi.org/10.29337/ijops.42

REVIEW

The Only Way is Ethics: Obtaining Approvals for NHS Clinical Research Projects

Susan Hendrickson*, Sadie McKeown-Keegan*, Thomas Wright* and David Carpenter†

Setting up and running a research project can be a daunting endeavour, especially for clinicians for whom there is a professional aspiration and expectation to publish in the scientific literature despite often lacking a formal research degree and allocated time for research activity. This article aims to give NHS clinicians a step-by-step guide to obtaining governance and ethics approval.

Keywords: Research ethics; Ethical review; Research governance

Introduction

Setting up and running a research project can be a daunting endeavour, especially for clinicians for whom there is a professional aspiration and expectation to publish in the scientific literature [7] despite often lacking a formal research degree and allocated time for research activity. One particular challenge is navigating the myriad processes and procedures required to obtain governance and ethics approval to carry out research, which can be extremely complex and time-consuming even for projects seemingly entirely devoid of ethics pitfalls [8, 9]. This article aims to give NHS clinicians a step-by-step guide to the basic processes and procedures required to obtain governance and ethics approval for these seemingly straightforward studies.

For the relatively new and emerging field of orthoplastic surgery, it is especially important for clinicians with expertise or a subspecialist interest in this field to contribute to the international body of evidence. There remain many unanswered questions relating to the care of these complex injuries, and national guidelines are based largely on level III, IV and V evidence [1]; Nanchahal *et al.*, 2009; National Institute for Health and Care Excellence, 2016). Systematic reviews of available evidence do exist (Whitehouse *et al.*, 2017), but most conclude that larger studies or randomised controlled trials are needed. Although randomised controlled trials have become increasingly common in orthopaedic surgery, there are few relating to orthoplastic surgery (a study by [2] is a notable recent example, examining the impact of initial negative pressure wound therapy on patient reported outcome measures in open lower limb fractures). This leaves many elements of the orthoplastic patient pathway open for discussion, leaving orthoplastic departments without a robust evidence base to support decision-making and service funding. Although in depth discussion of the law and processes relating to more ethically complex studies (for instance involving (poly)trauma patients lacking capacity to consent, children, or testing of new drugs or medical devices) falls outside the scope of this article, it provides a basic a framework with which to approach simpler studies including observational cohort studies and randomised controlled trials comparing standard treatments for which there is no evidence base.

Despite the catchy title of this article, it is worth pointing out that ethics review is just one part of the approval process, which comprises of governance approval from the Health Research Authority (HRA) and the local 'sponsor' (for instance the NHS Trust where the research is taking place), and, where applicable, a 'favourable opinion' from a specialist committee tasked with reviewing the ethics of the proposed research (a Research Ethics Committee, REC). The information presented here should be used in conjunction with meeting with your local trust Research and Development (R&D) or Research and Innovation (R&I) department and with the information found on the HRA website.

Write a Clear and Relevant Research Question

Detailed advice on formulating a good research question and designing a good study fall outside the remit of this article, but both will aid the approval process. Important considerations include systematically reviewing the existing scientific literature to ensure the question has not already been answered, and choosing an appropriate study design. Examples include case series/case note review, cohort observation, controlled trial without randomisation, epidemiology, qualitative research, observational research and randomised controlled trials. The authors recommend all researchers complete Good Clinical Practice (ICH-GCP)

* North Bristol NHS Trust, Bristol, GB

† Research and Ethics, GB

Corresponding author: Susan Hendrickson (susan.hendrickson@nhs.net)

training – this is an international quality standard that is provided by the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) [6]. The HRA requires the Principal Investigator (usually the senior author) to provide an up-to-date certificate as evidence of Good Clinical Practice training. Often your R&D department can help organise this training for you and your principal investigator via an online or short taught course.

Is It Research?

Once you have decided your research question and method, the next step is to determine if your project falls under the category of research, audit, service evaluation or defining usual practice: research usually requires HRA approval and often requires a 'favourable opinion' from a Research Ethics Committee (REC), whereas audit, service evaluation and defining usual practice usually do not [5]. The definition of research as per the UK Policy Framework for Health and Social Care Research is "…the attempt to derive generalisable or transferable new knowledge to answer or refine relevant questions with scientifically sound methods." Importantly, the definition goes on to say that research "…includes activities that are carried out in preparation for or as a consequence of the interventional part of the research, such as screening potential participants for eligibility, obtaining participants' consent and publishing results. It also includes noninterventional health and social care research (i.e. projects that do not involve any change in standard treatment, care or other services), projects that aim to generate hypotheses, methodological research and descriptive research" [3, 4]. The scope of this definition means that even projects which appear to have little or no ethical concerns may still require HRA approval, which in some cases includes an ethics review by a REC.

The Medical Research Council has created an online tool to assist researchers in determining whether a project is 'research', which is available here: http://www.hra-decisiontools.org.uk/research/. Once identified as research, another online tool can be used to assess whether NHS ethics review by a REC is required (http://www.hra-decisiontools.org.uk/ethics/). The local trust R&D department can assist in this process to ensure the correct decision is made. If your project is not research it most likely does not need HRA approval, you can stop reading here. If your project is research, read on.

Write a Protocol

The next step is to write a protocol. This will be submitted to your local trust R&D department, so it is best to liaise with them prior to writing one to ensure you meet their requirements. Generic templates for study protocols can be found on the HRA website: https://www.hra.nhs.uk/planning-and-improving-research/research-planning/protocol/. Your R&D department may also ask for a data management plan, which will delineate how you plan to store data to ensure compliance with data governance, including the European Union General Data Protection Regulation (GDPR), and protection of patient confidentiality. Although these documents take a bit of work to prepare properly, they will come in handy when subsequently preparing the application to the HRA for approval, so the work will not be wasted.

Study Registration

Certain kinds of studies should be registered in a publicly accessible database, to ensure transparency. Registration of some studies, especially clinical trials, is a prerequisite to achieving HRA approval. There are a number of different online databases where studies can be registered, and which one you choose depends on the type of study. Clinical trials for instance can be registered at https://ClinicalTrials.gov, and systematic reviews, meta-analyses, and observational or cohort studies can be registered at https://www.ResearchRegistry.com. Your local R&D team may be able to help you register your study on an appropriate registry.

Funding

Not all projects require formal funding, and particularly if you are performing a simple prospective or retrospective case note review and you are happy to put the unpaid time in, you are not likely to need any. Larger projects requiring specific equipment, medicines, medical devices, or research assistance such as dedicated research nurses will likely need funding. There are many possible avenues for funding and an in-depth discussion of this is outside the scope of this article, but a good starting point for assistance on this (and many other elements of research) is the National Institute for Health Research (NIHR) website (https://www.nihr.ac.uk/funding-and-support/funding-opportunities/) as well as your local R&D department who have often specialist staff to assist with this. Funding applications can be lengthy processes and this may introduce a significant additional delay.

The Integrated Research Application System (IRAS) Form

Once the study protocol and data management plan have been accepted by your local R&D department, you can begin work on HRA documents in order to obtain approval. The mainstay of this a lengthy online application process called the Integrated Research Application System (IRAS) form, found at https://www.myresearchproject.org.uk/. The first step in completing the form is the Project Filter, which will ensure you only see the questions that you need to complete for your specific project type. It is important to choose the correct filters before starting so that the correct data set is generated. If the wrong filters are selected, important information will be missing, governance assessment and ethics review may not be possible, and you may need to start over. Additional sections will need to be completed, for instance, for projects involving use of tissue, ionising radiation, or children as research participants, to name a few, but these more complex study types fall outside of the scope of this article. Any work done on the form can be saved at any point, so it does not have to be done all at once. The information gathered in the systematic literature review,

the study protocol and the data management plan will all help contribute to completing the IRAS form as many of the questions will overlap. Your local R&D department should also be able to help with the wording to increase the likelihood of success. You will need to declare the 'Chief Investigator' on the project, which is likely to be the senior/supervising author, and who then needs to upload a copy of their CV to the IRAS form. As mentioned above, they also need to provide evidence of up-to-date GCP training. In addition, you will need to declare a 'sponsor', which is usually your NHS Trust, your university if the project is part of an educational degree, or it could be an industry body for some clinical trials. Your local R&D department can help you determine who should be the Chief Investigator and sponsor. If you are collecting data at multiple centres, details for all centres and all senior corresponding study collaborators will should be listed on the form.

Statement of Activities and Schedule of Events

If your study involves multiple sites, a Schedule of Events (a tabulated description of the events and research activities planned throughout the execution of the project and at each site) and the Statement of Activities (a tabulated description of the research activities that will take place) need to be submitted to the HRA alongside your IRAS form. Your R&D department should guide you as to how to complete them. One Schedule of Events needs to be created for each site type. In some cases, all participating sites will perform all of the same activities, in which case, just one Schedule of Events is needed. In contrast, one Statement of Activities document needs to be created for each participating centre. These are used to help the study sponsor, for instance your NHS Trust R&D department, ensure you have the appropriate capacity and capability to carry out the research and monitor your research activity, to ensure you are sticking to the planned protocol and there are no practical or ethical concerns with the execution of the research.

Submission to the HRA and Other Regulatory Bodies

When you have finished all of the paperwork, it is submitted electronically to the HRA via the IRAS website. Make sure all documents submitted to HRA have a version number, full document date, and IRAS ID number included at the top. Lack of this information is one of the most common reasons applications are not validated. If you also require submission to the MHRA (for Clinical Trials of Investigational Medicinal Products or clinical investigation of a medical device studies), ARSAC (for administration of radioactive substances) or Confidentiality Advice Group (where access to confidential patient information is required without consent) this can be submitted via IRAS in parallel to the HRA approval process.

Research Ethics Committees (REC) Review

Whilst all research in the NHS requires HRA assessment to gain HRA approval, not all studies require review by a REC (such as studies recruiting only staff, or retrospective data review by the clinical care team where the data was received as part of clinical care and subsequently anonymised).

If REC review is required, the IRAS application is sent to volunteer (lay and expert) committee members, who will review the application prior to the committee meeting. Studies with fewer ethical issues may undergo Proportionate Review, which has a quicker turnaround than a full REC review (usually less than 21 days), and the researcher is not normally required to attend. The researcher is encouraged to attend a full review meeting, ideally in person, and students should attend with an academic supervisor. The turnaround for a full review is less than 60 days (it usually takes about 30 days). The REC assesses the proposed project for a number of ethical domains, including research design, welfare and dignity of research participants, risk-benefit ratio, and data protection, to name a few. The Ethical Opinion is then issued within maximum 60 days. This can be: 'favourable', 'favourable with additional conditions', 'provisional opinion' or 'unfavourable opinion' (this is rare). The commonest reason for provisional opinions is missing documents. Documents sometimes require substantial revisions and occasionally the research design needs to be changed.

HRA Approval

HRA Approval will be given once the application has received a favourable ethical opinion from the REC, and any other approvals, including addressing any points raised by the HRA Approval Manager. Once HRA approval is granted, notify the lead R&D department so that they can start setting up the sites. They will need the Chief Investigator's signed and dated CV, evidence of valid GCP status (see above) and the Statement of Activities. Once all documents have been approved, the R&D department at each participating site must be contacted so that these sites can be 'set up' prior to beginning recruitment. Usually, some of the paperwork already generated earlier in the process needs to be forwarded on to each site, but exactly what is required varies.

Finally, at the end of the study (for instance, when data collection is complete or a different defined end point), let your local R&D department know that the study has been completed. Send them copies of any presentation or publication arising from the project to attach to the records. An end of study report must also be sent to the HRA.

Conclusion

Obtaining approval to carry out even the simplest research projects can be time-consuming and daunting, especially for medical and surgical trainees who lack formal guidance or training in the process. This guide aims to demystify this process and provide helpful pearls and pitfalls in navigating the required approvals.

Glossary of Terms

- **Health Research Authority (HRA):** A national body that aims to protect patients and the public by ensuring research is ethically reviewed and approved, and promoting transparency in research, among other roles.

- **Research Ethics Committee (REC):** A designated committee of lay and expert volunteers tasked with providing an opinion about the ethics of the proposed project. These committees are governed by the Governance Arrangements for Research Ethics Committees (GAfREC), most recently updated in 2018 (Health Research Authority, 2018).
- **Research and Development (R&D) or Research and Innovation (R&I) departments:** Most NHS Trusts and Universities have a designated department for overseeing and assisting with local research activity. They are a fount of knowledge and should be your first port of call when designing a research project and beginning the approvals process.
- **National Institute Health Research (NIHR):** The NIHR was established in 2006 by the government to support individuals within the NHS to undertake high level research, including funding opportunities.
- **Sponsor:** The body responsible for the oversight of the study, usually the health/social care provider for clinicians or university/college if you're a student.

Acknowledgements
The authors would like to gratefully acknowledge Tom Lucas and Charlotte Allen of the HRA for their contribution to the title of this paper.

Funding Statement
There was no funding received for this paper.

Competing Interests
The authors have no competing interests to declare.

Author Contributions
- S. Hendrickson: primary manuscript author
- S. McKeown-Keegan: expert input, editing
- T. Wright: senior input, editing
- D. Carpenter: expert input, editing, accuracy and fact-checking

Guarantor
Susan Hendrickson is the guarantor for this work.

Peer Review
This is a non-commissioned paper that has undergone external peer review according to journal policy.

References
1. **British Orthopaedic Association and British Association of Plastic Reconstructive and Aesthetic Surgeons.** 'BOAST 4: the management of severe open lower limb fractures'; 2009.
2. **Costa, ML,** et al. 'Effect of Negative Pressure Wound Therapy vs Standard Wound Management on 12-Month Disability Among Adults With Severe Open Fracture of the Lower Limb'. *JAMA*. 2018; 319(22): 2280. DOI: https://doi.org/10.1001/jama.2018.6452
3. **Health Research Authority.** *Defining Research Table*; 2017a. Available at: http://hra-decisiontools.org.uk/ethics/ [Last accessed: 9 June 2019].
4. **Health Research Authority.** *UK policy framework for health and social care research*, *Health Research Authority*; 2017b.
5. **Health Research Authority.** *Governance arrangements for research ethics committees: 2018 edition*; 2018. Available at: https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/governance-arrangement-research-ethics-committees/ [Last accessed: 9 June 2019].
6. **International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH).** *Integrated Addendum to ICH E6(R1): Guideline for Good Clinical Practice E6(R2)*, *ICH Harmonised Guideline*; 2016.
7. **Joint Committee on Surgical Training.** (no date) *JCST Quality Indicators*. July 2018. Available at: https://www.jcst.org/quality-assurance/quality-indicators/ [Last accessed: 9 June 2019].
8. **Petrova, M** and **Barclay, S.** 'Research approvals iceberg: how a "low-key" study in England needed 89 professionals to approve it and how we can do better'. *BMC Medical Ethics*. 2019; 20(1): 7. BioMed Central. DOI: https://doi.org/10.1186/s12910-018-0339-5
9. **Thompson, AGH** and **France, EF.** 'One stop or full stop? The continuing challenges for researchers despite the new streamlined NHS research governance process.' *BMC health services research*. 2010; 10: 124. BioMed Central. DOI: https://doi.org/10.1186/1472-6963-10-124

How to cite this article: Hendrickson, S, McKeown-Keegan, S, Wright, T and Carpenter, D. The Only Way is Ethics: Obtaining Approvals for NHS Clinical Research Projects. *International Journal of Orthoplastic Surgery*. 2019; 2(3), pp. 80–83. DOI: https://doi.org/10.29337/ijops.42

Submitted: 11 April 2019 **Accepted:** 18 June 2019 **Published:** 05 July 2019