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Heterogeneity of Human Research Ethics Committees and Research Governance Offices across Australia: An observational study

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RESEARCH

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ABSTRACT

Background

Conducting ethically grounded research is a fundamental facet of all investigations. Nevertheless, the administrative burdens of current ethics review are substantial, and calls have been made for a reduction in research waste.

Aims

To describe the heterogeneity in administration and documentation required by Human Research Ethics Committees (HRECs) and Research Governance Offices (RGOs) across Australia.

Methods

In establishing a nationwide study to investigate the molecular aetiology of Giant Cell Arteritis (GCA), for which archived pathological specimens from around Australia are being recruited, we identified variation across separate HREC and RGO requirements. Submission paperwork and correspondence from each collaborating site and its representative office for research were reviewed. This data was interrogated to evaluate differences in current guidelines.

Results

Twenty-five pathology departments across seven Australian States collaborated in this study. All states, except Victoria, employed a single ethics review model. There was discrepancy amongst HRECs as to which application process applied to our study: seven requested completion of a "National Ethics Application Form" and three a "Low Negligible Risk" form. Noticeable differences in guidelines included whether electronic submission was sufficient. There was variability in the total number of documents submitted (range five to 22) and panel review turnaround time (range nine to 136 days).

Conclusion

We demonstrate the challenges and illustrate the heavy workload involved in receiving widespread ethics and governance approval across Australia. We highlight the need to simplify, homogenise, and nationalise human ethics for non-clinical trial studies. Reducing unnecessary administration will enable investigators to achieve research aims more efficiently.

Key Words

Ethics administration, Australian Offices for Research; Multisite Medical Research, Human Research Ethics Committees, Regional Governance Offices

What this study adds:

1. What is known about this subject?
Previous published papers have illustrated the administrative burdens of medical research.

2. What new information is offered in this study?
We demonstrate key logistical impediments to conducting non-interventional research on a national scale. We suggest changes and support nationalising ethics for non-clinical trial studies.

3. What are the implications for research, policy, or practice?
Streamlining ethics nationally will prevent unnecessary duplication of work by researchers, allow investigators to achieve research goals quicker, and reduce administrative load on research officers.

Background

Ethics approval is an essential prerequisite to conducting a human research study. The Declaration of Helsinki stipulates that all medical research be submitted to and approved by an ethics committee before a study commences.[1] While there is a need for a thorough review process to prevent unethical research, the resulting administrative workload required for applications is substantial and this is often multiplied in multi-centre studies.

In 2007, the National Health and Medical Research Council (NHMRC) of Australia developed the National Approach to Single Ethical Review of Multi-Centre Research, previously known as Harmonisation of Multi-Centre Ethical Review (HoMER) project.[2] It was designed to facilitate effective ethics approval processes for multi-site research projects where a lead Human Research Ethics Committee (HREC) would review the project and provide an approval sign-off recognised by other research sites. However, until very recently, the process of "streamlining ethics review" was only operated on at state level. Prior to 14 December 2015 there was no streamlined national process for obtaining ethical approval for non-clinical trials across Australia.[2]

While establishing a nationwide study to investigate the molecular aetiology of Giant Cell Arteritis (GCA), we identified differences and inconsistencies amongst HREC and Research Governance Office (RGO) requirements in Australia. Our study has the primary aim to investigate the genetic architecture of GCA by genotyping samples of patients with this disease. Unfortunately, given the age at which patients with GCA are diagnosed, retrospective recruitment of blood samples is difficult. However, the gold standard method to diagnose GCA is through temporal artery biopsy,[3] and these archived pathological specimens represent a rich resource for genomic studies.[4] As such, our proposed work seeks to use re-identifiable biopsies currently stored in pathology centres around the country. We have established a network of collaborating centres and investigators to facilitate access to such archived specimens.

Given the research framework in Australia at the time of establishing our national study, numerous ethics and research governance applications were made to cover each participating site. Significant discrepancy was noted with regard to the practices of these committees across the country and in this manuscript we seek to highlight and explore the impediments to conducting non-interventional clinical research. We demonstrate the differences amongst HREC and RGO guidelines, as well as highlight the challenge and workload involved in obtaining ethics and governance approval for a national non-clinical trial study.

Methods

All submission paperwork and email correspondence from each collaborating site and its representative HREC and RGO were reviewed. This information was used to evaluate differences in interpretations and practices.

We documented the nature of the ethics and/or governance application procedures for the various sites. We recorded whether ethics committees requested a National Ethics Application Form (NEAF) versus a Low Negligible Risk (LNR) form and whether the requested form was to be completed and submitted via the https://neaf.gov.au or https://au.ethicsform.org websites. We documented whether RGOs requested a Site Specific Assessment (SSA) form and the formatting requirements. The need for detailed budget declarations prior to submission and for formal written research agreements were also recorded.

For some analyses, when possible, we grouped the results from the HREC and RGO of a collaborating site. This allowed us to determine the efficiency and overall performance of a site's "office for research" as a whole rather than the HREC or RGO independently. The requested submission formats, whether electronic or hardcopy, requested by each site's office for research were documented. We took note of any paperwork required by HREC and/or RGO that was specific in its request and not previously submitted to any other site. These included pathology forms, special checklists, as well as specific requested letters on special letterhead.

When applications were not yet submitted or review not complete, these were excluded from some of the analyses.

Details relating to the number of ethics and governance committee panels reporting an "issue" regarding our application were recorded. An issue raised was defined as any documented query or concern that required a direct response by the investigators. When pre-submission inquiries were performed, we only considered the issues derived after full committee review.

The total number of documents submitted as part of one complete ethics and/or governance application for each site was calculated. When RGOs requested the provision of the original ethics documents and corresponding approval letter received from a previously approved HREC, these were also included. The duration of each collaborating site's ethics and/or governance review process was calculated from the time of complete application submission to the time of final approval. When ethics and governance applications were sent as one, only the duration of the ethics review was calculated. When available, the cost of an office for research administration was also recorded.

Results

Twenty-five anatomical pathology departments across Australia collaborated in our GCA study in 2014 and 2015. These departments were either part of public Australian hospitals or independent private pathology centres.

For the purpose of our study, all states, except Victoria, employed the single ethics review model, with one application covering ethics approval for all sites within that state. An individual ethics application was completed for seven of the eight participating study sites within the state of Victoria. One Victorian application is awaiting signatures and is still to be submitted. A total of six ethics applications were submitted to cover the rest of the study sites across the country.

Table 1 outlines the item requirements in each ethics application submitted varied across HRECs. There was no overall consensus regarding which type of ethics application best suited our study. Opinions varied between HRECs as to whether our study protocol required a full NEAF application or whether our study could instead be classified low risk and hence require an LNR application.

In total, three HRECs requested an LNR application, including the lead NSW HREC for our study. Their reasoning was justified as: "There is no likelihood for incidental findings or other findings that will impact on individual patients or their families and therefore there will be no need to contact them down the track ... Our decision is based on sections 3.5 (Human Genetics p41 & 42) of the NHMRC National Statement".[5] However, the majority of the HRECs deemed that a full NEAF was necessary in view of the fact that we were employing tissue for genetic purposes and that data collected were re-identifiable. Other HRECs judged that our study did not meet low-risk criteria as a waiver of consent was requested, and hence a full NEAF was deemed more appropriate. Two ethics applications were submitted prior to the release of the web-based NEAF proforma in 2010.[6] All other applications were submitted after January 2014.

Table 1: Nature and modality of ethics and governance applications requested by HRECs and RGOs

Ethics Applications: Number of HRECs[a] requesting NEAF[b], LNR[c] or prior approval recognition	
NEAF	7
Original NEAF website	4
Online forms website	3
LNR (online forms website)	3
Previous acceptance form	3
Form predating web based ethics proforma	2
Total ethics applications	**15**
Governance Applications: Number of RGOs[d] requesting SSA	
SSA[e]	21
Online forms website	14
Individual Site Assessment form	7
No SSA	4
Total Governance applications	**21**

[a]HREC=Human Research Ethics Committee; [b]NEAF=National Ethics Application Form; [c]LNR = Low Negligible Risk Form; [d]RGO=Research Governance Office; [e]SSA=Site Specific Assessment Form
Original NEAF website: https://www.neaf.gov.au; Online forms website: https://au.ethicsform.org

Three HRECs bypassed the need for a full formal ethics application through NEAF or LNR, and performed an expedited ethics review based on the fact that former ethics approval had been granted by other HRECs across the country.

HREC guidelines differed in regard to which proforma should be used to complete the ethics form. Some HRECs requested the NEAF form be completed and downloaded from the https://www.neaf.gov.au website, while others requested completion of either a NEAF or LNR from https://au.ethicsform.org (Table 1). For the three HRECs suggesting an expedited review through a "former acceptance form", this unique application form was available on their own website rather than one of the two aforementioned generic ethics websites.

A total of 21 governance applications were completed, and as such only four sites did not require a specific governance review (Table 1). Detailed budgets were required by 16 (64 per cent) of the RGOs prior to submission. A formal research agreement was required by 12 (48 per cent) RGOs, of which nine requested a material transfer agreement (MTA) (Table 2).

Table 2: Differences in guidelines and procedures amongst offices for research; number of offices for which the analyses apply

Analysis of applications	Number of offices for research
Ethics review turn around time	
≤ 2 weeks	2
> 2–4 weeks	2
> 1–2 months	7
> 2–3 months	1
> 3 months	2
Governance review turnaround time	
≤ 2 weeks	1
> 2–4 weeks	8
> 1–2 months	2
> 2–3 months	2
> 3 months	1
Necessity of research agreement & type	
Yes	12
MTA[a]	*7*
RCA[b] alone	*1*
MTA & RCA	*2*
MIA[c]	*2*
None	12
Total number of documents requested	
≤ 5	3
6 to 7	4
8 to 9	13
10 to 20	3
≥ 20	1
Electronic or hard copy submission	
Electronic	6
Hard copy	18
Number of issues raised at ethics and/or governance review	
0	11
1–3	5
4–5	5
6–7	0
8–9	2
>10	1

[a]MTA=Material Transfer Agreement; [b]RCA=Research Collaboration Agreement; [c]MIA=Multi-Institutional Agreement.

Fourteen offices for research required the submission of a document or form unique in their guidelines and which had not been submitted elsewhere. Two states, Victoria and Western Australia, requested the completion of a state specific special study module as part of their ethics application process.

Electronic submission of documents by email was accepted for seven offices for research. The majority of offices for research, either by their HREC, RGO or both, required some form of hard copy submission (Table 2). Most offices requested anywhere between one and three hard copies of documents. One Victorian office for research requested eight copies of all submitted paperwork.

The total number of documents submitted to each research office, whether HREC, RGO, or both ranged from five to 22 documents. The majority of offices for research requested a submission pack containing between eight to nine types of documents (Table 2). Most RGOs requested submission of all documents provided by the initial ethics approval.

Eleven committees neither identified any issues nor required any changes to be made to our application. However, 13 committees required amendments or clarifications. The total number of issues raised by each committee was noted (Table 2); the majority had three or four, but a few required detailed answers to more than eight issues. Three offices for research requested resubmission of the entire application. The topics of issues raised by committee panels in response to our application are categorised in Table 3.

Table 3: Topics raised in response to our ethics and governance applications; Number of offices for research raising each topic

Topics raised in response letters	Number of offices
Study protocol-related queries	
Confidentiality, sample ID & storage	9
Waiver of consent	7
Risk or benefit to patient or their family	3
Medical records & database access	1
Role future research & use of data	3
Collaboration-related queries	
Research agreement	5
Material transfer between sites/states	3
Administration-related queries	
Additional documents required	4
Signature on documents	4
Phrasing of document/wording	2
Staff training for project	1
Financial issues	4

Turnaround time for ethics and governance reviews varied substantially. The median/mean turnaround time for ethics review was 43 days (range nine to 136 days). Governance review time varied from 12 to 147 days (Table 2). The administration costs by offices for research differed substantially. Administration charges varied from AUD $0 to $660. Costs were not always clearly stated at the time of application.

Discussion

This study highlights the heterogeneity of HREC and governance practice in Australia. In 2009, Thompson et al. pleaded for an improvement in the way ethics for national studies was conducted across Australia.[7] Thompson et al. mentioned differences in HREC reporting timeframes and submission practice with regard to digital signatures and faxing of documents being allowed. Six years later, we found that many of these problems remained and that there is great opportunity to harmonise ethical review of research across Australia.

The longest ethics review turnaround time in our study was 136 days. According to a review published by Hunter[8] in 2015, in New South Wales the average total time that ethics applications spent in review was 77 days in 2012. His findings were in agreement with ours in that there was a large variation in time spent at review, from 33–165 days.[8,9] Negative experiences with regard to costs, inefficiency, tardiness, duplication, as well as the inconsistent nature of ethical practice for the same study by ethics committees have also been reported in the United States and United Kingdom.[10–14]

The Australian National Mutual Acceptance (NMA) programme, implemented in November 2013, enabled multi-centre clinical trials taking place in one or more of the participating states, to be eligible for single ethical review. While previously limited to the review of clinical trials only, as of December 2015, the NMA broadened its scope to incorporate the review of all multi-centre human research proposals.[2] However, the NMA only covers full NEAF applications and does not apply to LNR applications.

Although this latest NMA reform was implemented too late to benefit the conduct of our national study, it is promising to see the realisation of a nationalised ethics review system for human non-clinical trial studies in Australia. Future studies that will benefit from these recent reforms include studies requiring access to archived pathological specimens such as ours, as well as observational studies needing access to medical records or databases across multiple sites and states. Rationalising and streamlining ethics nationally will prevent a huge burden on researchers and unnecessary duplication of their work.[7,14–16] HREC energy and resources can be spent on other matters.

Current states participating in the NMA programme are New South Wales, Queensland, South Australia, and Victoria.[2] Although other sites in non-participating states may accept an interstate multisite ethics approval or possibly use it to fast track their local ethics application, a separate ethics application for their site may still be required. In addition, the NMA policy only covers studies performed in publicly funded health services.[2] A private health institution might accept the NMA multisite ethics approval, but this decision remains at the discretion of the participating private health centre's ethics committee. As such, researchers collaborating with both sites in participating and non-participating NMA states, and/or public and private health services, may still experience duplication of work in establishing their multisite non-clinical trial research study.

Prior to the recent NMA expansion to nationalise ethics for all medical research, the process of "streamlining ethics review" for non-clinical trial studies took place in certain states across Australia. This meant that a research project, taking place across multiple sites within a jurisdiction actioning this reciprocal approval model, only required one ethical and scientific review conducted by a NHMRC certified HREC within that state. During the time course of our study, most jurisdictions, other than Victoria, allowed for this single ethics review model. It was only as of January 2015 that the Victorian Streamlined Ethical Review Process (SERP) was extended to include all health and medical research.[2] This single ethics model for a study carried at multiple sites within the same state is still in place in states such as Western Australia, which does not take part in the NMA.

Our study also highlights inconsistencies amongst governance applications. In 2007, the reform to centralise ethics review in some states resulted in decoupling research governance processes from human ethics. This has meant that governance approval still needs to be obtained for each separate research site, hence delaying overall approval to include a site.[17] The lack of communication between HRECs and RGOs, whether at the same site or amongst different healthcare districts, created duplication of work within our research study.

Although there has been some effort made to improve the conduct of ethics application processes, we suggest improvements can be made to current practice for offices for research (Figure 1). Our study highlights that HRECs were not always clear or in agreement as to how to interpret the guidelines of the National Health and Medical Research Council (NHMRC) National Statement on Ethical Conduct in Human Research. The interpretation of these guidelines, in particular chapters 3.4 (ethical considerations specific to the use of bio-specimens in laboratory based research) and 3.5 (ethical considerations with regard to human genetic research) varied significantly between discrete HRECs. Their understanding of the national

statement guidelines determined which ethics pathway we were guided down for our study, whether NEAF or LNR.

Figure 1: Suggestions for improving ethics and governance for multisite non-clinical trial studies

- To elaborate the NMA to include all jurisdictions and states in Australia (sites currently not participating include TAS, ACT, NT, WA): Approval by one NHMRC-approved HREC would suffice and cover ethics across multiple sites in all Australian jurisdictions.
- To expand the NMA to include LNR as well as full NEAF applications. Low, negligible-risk applications should be less difficult to assess, require less HREC review and input. As such, they warrant inclusion in a nationalised ethical review system.
- The NHMRC could consider clarifying its national statement guidelines on ethical conduct to prevent less subjective interpretation by HRECs. As it stands, the submission documents and application format required may differ depending on which lead HREC you allocate to review your initial multisite ethics application.
- To homogenise offices for research website pages and guidelines, particularly in reference to their governance applications. To streamline the number of forms required, review timeframes, and administration costs.
- For all offices for research, including HRECs and RGOs, to accept digital signatures and electronic submissions of applications.

Some HRECs automatically considered our study "high risk" as it involves research of genetic nature. As such, some HRECs deemed a full NEAF application necessary for our study. Other HRECs felt that, as our research did not impact the future health of the individual participant, nor their families or communities, nor would it generate sensitivities for the individual, the research would be suitable for as a "low-risk" ethics application and be exempt from full HREC review. Clearly, there was inconsistency in the interpretation of the guidelines and as such we suggest that the NHMRC could clarify these, as this would hopefully allow less subjective interpretation by HRECs. This is even more important now that the NMA covers NEAF but not LNR applications. Based on our study findings, in the current state, depending on which HREC researchers choose to appoint as their lead HREC, the type of initial ethics application may vary.

Another suggestion for improving current ethics practice is to homogenise offices for research website guidelines, timeframes, and administration costs amongst public hospitals. Although RGOs might keep some individuality, as each site may have certain hospital protocol differences, these should not be too dissimilar from one another. We noticed that the administration cost of each office for research was not necessarily reflected in its efficiency and speed of review. In addition, detailed study budget declarations required by some governance committees prior to submission should be allowed retrospectively as costs invariably change as the project emerges.

Additionally, we advocate the acceptance of digital signatures and electronic submissions on applications. This is especially relevant for nationwide studies requiring multiple signatures on the same documents from individuals located across the country. We noted that the majority of offices for research today still required hard copy submissions which in this day and age are redundant and excessive, especially if eight copies are required.

Conclusion

In summary, this work demonstrates the heterogeneity in administration amongst offices for research, including HRECs and RGOs, across Australia. The administrative burdens we faced for ethics review were substantial. We emphasise the key logistical impediments we experienced while conducting a non-interventional research study. We hope the recent reforms of the NMA to include non-clinical trial studies will simplify the ethics application process and review of such future studies. We reveal that there is still room for improvement and suggest further changes are warranted. Reducing unnecessary administration will help investigators achieve research aims more quickly and effectively as well as reduce the administrative burden currently experienced by offices for research.

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PEER REVIEW

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CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

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ETHICS COMMITTEE APPROVAL

Multiple ethics committee approvals for this national study were provided as described in this observational study.