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Variation in Human Research Ethics Committee and governance processes throughout Australia – a need for a uniform approach
Australian Experience of Multicentre Surgical Research Ethics Application Processes

Short running head: Australian ethics application process

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ABSTRACT

Background: In Australia, ethics committees across different states vary in application, requirement and process for the ethical review and approval for clinical research. This may lead to confusion and delays in the enablement of multicentre research projects. This study explores the effect of differing processes for Ethics and Governance in the establishment of the CovidSurg-Cancer study during the global COVID-19 pandemic.

Methods: An anonymous, structured web-based questionnaire was designed using the Research Electronic Data Capture application (REDCap) platform to capture consultant surgeons, fellows, and trainees experience in the ethics application process. “CovidSurg-Cancer” was an international multicentre collaborative study to assess the impact of COVID-19 on the outcomes of patients undergoing cancer surgery. The ethics process to set up this observational study was used as to explore the differing processes applied across Australia.

Results: The CovidSurg-Cancer study was successfully set up in fourteen hospitals. Four hospitals approved the study directly as an audit. Of the remaining sites, ten ethics applications underwent HREC review following which two (14%) were subsequently approved as an audit activity and eight hospitals (57%) were given formal ethical approval with waiver of consent. Ethics application acceptance from another Australian HREC was provided with six applications, however, only three were reciprocated without the requirement for further agreements. A third of (30%) respondents suggested that the details of the application pathway, process and documentation were unclear.

Conclusion: Ethics processes are varied across Australia with considerable repetition. A centralised, harmonised application process would enhance collaborative research.

Keywords: Collaborative research; research ethics; governance; surgical research

INTRODUCTION

Research and Audit are fundamental to the development and implementation of knowledge in medical practice. Research is broadly defined as additional data gathered on patients leading to new or substantially improved insights and developments. (1) Clinical research involves undertaking a systematic investigation related to a patient that is not current practice with the aim to seek new knowledge and ask ‘what should we be doing’ to improve. In contrast, Audit asks the question of whether the practices that medical staff undertake are in keeping with current standards or guidelines. This process involves routine testing and analysis of materials, components, and processes, for example, comparisons of local performance compared to national standards, as distinct from the development of new analytical techniques. Audit does not create new knowledge rather it tests process and management and asks, ‘what are we doing’.

In Australia, research involving patients requires ethical review and approval by Human Research Ethics Committees (HRECs). (2) HRECs make sure research is conducted in accordance with the National Statement on Ethical Conduct in Human Research (the National Statement) issued by the National Health and Medical Research Council (NHMRC). The National Statement defines the types of human research that are required to undergo ethics review. (3) Audit does not necessarily require ethical review, but the differentiation between audit and research can be confused. For instance, a common misconception is that the publication of data in a medical journal requires HREC approval when in fact it is the work undertaken to generate the data that does require the relevant regulatory approval, whether HREC approval or audit registration. Hence, the classification of a study as research or audit relies on interpretation of the study protocol and distinction between them can be influenced by individual opinion. (4) In some Health Districts, the HREC also functions as the audit committee, adding to the confusion of approach. Additionally, lack of a centralised or harmonised HREC application system, of reciprocal approvals between sites, and differing laws and interpretations between states exacerbates this confusion. This results

in concerns that the ‘paperwork’ can be unduly cumbersome resulting in unnecessary delays to improvements in patient care. (5,6)

In an era in which practice changing research requires multicentre collaborative studies, inconsistent approaches to HREC and audit applications across multi-state, multi-centre projects have become a barrier to delivering better clinical outcomes in Australia. (7)

The onslaught of the COVID-19 pandemic necessitated swift action from the research community to inform public health responses, and examine interventions to manage infected individuals, and improve the systemic response to the disease. (8) The World Health Organization’s (WHO) 2009 report on Research Ethics in International Epidemic Response recommended streamlining the ethics review processes, with appropriate, flexible mechanisms and procedures for ethical oversight not limited to traditional HREC systems during a pandemic. (9) One of the key aspects affected by the COVID-19 pandemic has been the interruption of normal clinical management pathways highlighted by cancellation of elective surgery. In order to gather data about the impact of COVID-19 on cancer surgery a large international study was developed. (10) The study was observational, with no intervention and used de-identified patient data. Hence the study could reasonably be regarded as an audit involving only documentation of pathways and outcomes. However, others may regard this as research, as it required collection of patient data and described the consequences of an intervention which in this case was the disruption of the pandemic, and thus necessitating a full HREC review with either waiver of consent or full ethics approval.

The aim of this study was to explore Australian surgical researchers’ experiences of the HREC application process for CovidSurg study during the global COVID-19 pandemic.

METHODOLOGY

Setting

A two-stage iterative review was performed utilising the Royal Australasian College of Surgeons Clinical Trials ANZ (CTANZ) Network. CTANZ is an umbrella organisation developed to promote trainee-led Australasian surgical collaborative networks (11,12). The CTANZ network's aim is to build multi-centre network approaches with rapid recruitment of large numbers of study participants across Australian and New Zealand.

A working group was set up within the CTANZ to identify themes and key factors involved in research experience that were likely to impact HREC applications. Subsequently, after an in-house pilot testing phase, a final questionnaire was developed that incorporated a total of 70 questions, divided into three sections: i) experiences of the CovidSurg-Cancer application *during* the pandemic, ii) individuals experiences of HREC application processes *before* the pandemic and iii) a section to invite researchers comments on how HREC processes might evolve or be improved. Survey questions were closed multiple choice questions with branching logic and free text responses. The survey can be viewed at: <https://is.gd/NEAPstudy>.

The population surveyed included consultant surgeons, surgical fellows, accredited and unaccredited surgical trainees in Australia who had previous experience in ethics application processes for research projects. The survey was disseminated through email lists and surgical societies (e.g., *General Surgeons Australia [GSA]*, *Australia New Zealand Hepatic, Pancreatic and Biliary association [ANZHPBA]*, *Australia & New Zealand Gastric and Oesophageal Surgery Association [ANZGOSA]*), CTANZ, surgical research collaboratives (e.g., VERITAS, STARC) and, via social media (Twitter, WhatsApp). The survey was kept open to participants over a 3-week period (22/4/2020 to 13/05/2020). Participation in the questionnaire was voluntary and without any personal incentive.

Data collection and analysis

Data from this survey was collected using REDCap tools hosted at the University of Adelaide, Australia. (14) Data were analysed using descriptive statistics.

RESULTS

Of the 112 respondents, 80 (71%) completed the section of the survey on pre-pandemic applications, 73 (65%) on their experience with COVIDSurg applications, and the last section on suggestions for improvement was completed by 50 (45%).

Fifty-eight respondents (n=80, 72.5%) had previous ethics application experience. The majority, 52 (90%) had submitted to a public hospital HREC and almost half of them 28 (48.3%) were for multi-centre studies. Overall, a third of these respondents were “beginner’s” having had submitted 1-3 applications (16, 28%), a third with “intermediate” experience of 4-8 applications (20, 35%), and a third with “advanced” experience of > 8 applications (22, 38%).

Experience with CovidSurg ethics applications

Twenty-three (32%) respondents were involved in COVIDSurg ethics application submissions for 17 hospitals, of which 14 (82%) hospital sites were finally approved to start the study. The applications went through three different pathways to achieve approval. Four hospitals (29%) had the study approved as an audit activity. The remaining 10 required a HREC review, following which two (14%) were subsequently approved as an audit activity and eight hospitals (57%) were given formal ethical approval with waiver of consent. The median timeline taken for approval through these pathways were: audit activity without HREC 5.5 (3-7 days), audit activity with HREC 9.5 (4-15days), and HREC pathway 6 (5-10 days). The level of risk attributed to the same study application, irrespective of approval outcome by different ethics committees varied between low or negligible risk in 10 (n=17, 59%) applications, and seven (n=17, 41%) each as low risk and greater than low risk studies.

Ethics application acceptance from another institutional HREC was provided as supporting documentation in six applications. Four (n=6, 66%) of these approved ethics applications originated

from outside the respondent's home state and three (75%) among them did not require a collaboration, research, data, or material transfer agreement. Interstate differences in the CovidSurg ethics application approval processes are illustrated in **Figure 1a-b** and **Figure 2**.

A third of respondents (30%) suggested that the details of the application pathway, process and documentation were unclear. Overall, 16 (n=17, 94 %) of the COVIDSurg applications submission had no associated costs. Of the six percent of applications incurring a fee, <\$500 was charged. Amendments were required in 29% of COVIDSurg applications with one revision in 80% of them. The most common reasons for application revision in COVIDSurg are shown in **Table 1**. No cost was charged for revisions in these applications.

Experience with ethics applications before the pandemic

Fifty-eight (n=80, 72.5%) respondents were involved in submitting applications to their ethics committee for research projects before the pandemic. These applications were for audit activity in 24 (n=58, 41%), for HREC review in 47 (n=58, 81%), and for site-specific approval for a project already been given ethics approval in 41 (n=58, 71%). Of the nineteen projects approved as an audit activity, nine of them (47%) were subjected to a full HREC review even though almost 80% of them were considered negligible risk studies. Less than half of the projects approved as an audit activity (n=19, 42%) were for collaborative studies and ethics approval from another institutional HREC was provided as supporting documentation to support these applications in 88% (n=8) of them. Four of these approvals (n=7, 57%) originated from interstate committees and three (n=4, 75%) of them required a collaboration, research, data, or material transfer agreement to proceed further with the research project. The median timeline taken for approval for these projects were: audit activity without HREC 30 (12-105 days) and audit activity with HREC 60 (22-135 days).

Suggestions for improvement

Most respondents (n = 50, 84%,) considered that ethics, research governance and audit applications could be improved. Comparisons between ethics application experiences in pre-COVID-19 projects and COVIDSurg were provided by 25 (50%) of respondents. They indicated an increased ease of ethics approval and turnaround for COVIDSurg compared with previous studies. Almost 80% of respondents were enthusiastic to present study applications via video conference to HREC to expedite applications. Other suggestions for improvement were to have a clear distinction between pathways for audit/quality improvement studies and research studies, succinct application instructions on a central online portal, open and transparent communication channels between researchers and the HREC early in the application process, and a national streamlined and standardised system governing all jurisdictions (other suggestions for improvement are listed in **Table 2**).

DISCUSSION

We conducted a survey to explore Australian surgical researchers' experiences of the HREC application process before and during the global COVID-19 pandemic. This survey found a significant variation in review and approval processes for applications across Australian sites. For example, even though the ethics is approved at one site by a HREC, this is not necessarily 'useable' approval across the rest of the country. There is an urgent need to formalise this process to avoid the repetitive paperwork submission process that potentially delays and discourages Australian multi-site research. We report here that a single multicentre audit application took three different pathways, but the outcome was, in the end, identical i.e., all applicants got approval for an audit type project with waiver of consent.

The time taken from application to ethics approval varied depending on the pathway taken during the approval process. This finding is corroborated by previously published reports in Australia, which suggested the timeline could vary between 33–165 days for HREC applications. (15-17) White *et al.* also showed that this process gets further delayed in applications for multi-centre, collaborative studies originating interstate, and this could take between 2 and 18 weeks for approval. (7) The reasons for the delay in HREC processing times for studies involving the same design, in similar settings, is unclear. The expeditious processing of applications during the pandemic is to be expected, given the pressure of the circumstances. Whilst it is unlikely that HREC offices could maintain this expediency long-term, our results clearly demonstrate that more efficient processes are achievable.

An important finding of our study is that, despite being a cohort of experienced surgical researchers (38% had previously submitted >8 ethics applications), investigators were unable to definitively select the most appropriate approval pathway an application should follow. This was attributed in part from the lack of a pathway for quality improvement activities, such as clinical audit, which are to be conducted across multiple sites in multiple jurisdictions. Projects of this nature default to being

classified as research and suffer a protracted review and interrogation process that is not relevant to an audit project. This is supported by our finding that, of the 43% of CovidSurg-Cancer applications that were finally approved as an audit activity, more than a third of these applications had been subject to an initial full HREC review.

There have been repeated calls for improvements in ethics application processes over the last two decades. In principle, NSW, Queensland and Victoria began interstate acceptance of a single HREC review for multi-centre research in 2011, this agreement was superseded by the National Mutual Acceptance (NMA) scheme in 2013. (18) A single NHMRC-certified HREC can approve an application without further local ethics review. Individual sites would then apply a local research governance review, “Site Specific Assessment” (SSA). (18) Whilst encouraging in spirit, NMA is far from delivering the national, streamlined multi-centre HREC review process it promised as shown in our study. For the CovidSurg-Cancer project, researchers had to submit applications for a full HREC approval locally, despite providing evidence of HREC approval from another site, in 50% of sites. Many reported that the complexity of NMA applications and the significant delayed turnaround times acted as a major disincentive to be pursuing these applications.

The landscape of surgical research across Australasia is evolving as shown in this study. The success of the COVIDSurg collaborative is a testament to the value of engaging multi-centred sites with greater capacity to recruit and reach project targets in the shortest time possible. (10)

The authors acknowledge that any perceived criticism of current processes should not lead to a relaxation of standards and protections for individuals contributing to research, even for low-risk cohort studies focussing on clinical outcomes. Process-driven delays should be addressed separately to HREC application issues raised by the ‘*genuine normative requirements*’ of human ethics research. (17) However, we posit that whilst HRECs have a duty to appraise the risks/benefits for any research

project, they also have a moral and ethical obligation to conduct that review within a reasonable time frame. They need to be cognisant that delaying appropriate research may result in adverse clinical outcomes caused by delays in the implementation of improved clinical care. Without a much-needed evolution of the HREC processes, Australia is in danger of being left behind the rest of the world in terms of developing impactful surgical outcome-based research relevant to our healthcare setting.

The most significant limitation of this study is that, without an in-depth investigation into the unique circumstances of each HREC application reported, it is impossible to ascertain whether HREC applications were delayed due to genuine ethical concerns, process-driven delays or delays that relate to the applicant. However, by employing a ‘control’ study – CovidSurg-Cancer – that utilised an identical study protocol (and would therefore presumably raise the same normative issues) across the nation we have highlighted differences in HREC processes and geographic variability during the pandemic.

CONCLUSION

Ethics and governance processes are varied across Australia with considerable repetition. With evolving collaborative, multi-centre models of surgical research worldwide, current HREC process needs to move towards a centralised and streamlined mechanism to enhance collaborative research.

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Table 1. Financial costs, revisions involved with applications and concerns raised during revisions during the CovidSurg Study.

HREC/RG applications for COVIDSurg	
Financial cost involved for ethics/RG application	
Yes	3 (10.7%)
AUD\$ 101-250	1 (33.3%)
AUD\$ 251-500	2 (66.7%)
AUD\$ 501-750	-
≥ AUD\$ 750	-
No. of applications requiring amendments	
	5 (29.4%)
No. of revisions required (n=5)	
One revision	4 (80%)
≥ 2 revisions	1 (20%)
Concerns raised for revision	
Lack of documents required for submission	2 (40%)
Data storage	2 (40%)
Sharing of patient data with third party	4 (80%)
Patient confidentiality	2 (40%)
Unclear inclusion/exclusion criteria	1 (20%)
Other concerns	1 (20%)

Table 2. Perceived barriers to ethics applications and suggestions on how processes could be improved.

<i>Barriers</i>
Lack of clarity regarding level of risk stratification of project and which institution to apply through.
Convolved, lengthy information on selection of pathways
Uncertainty where to access information or who to clarify concerns with resulting in difficulty with trouble shooting.
Inconsistencies between jurisdictions regarding paperwork required for acceptance of projects under NMA scheme.
Unnecessary repetitive nature in the process of submission of applications.
Inconsistent and uncertain advice from RGO/HRECs regarding correct submission pathway.
Inconsistent and inconsequential reasons to delay progression by RGO/HREC.
<i>Suggestions for improvement</i>
Improved clarity of application pathway and processes.
Availability of clear centralised published online instructions
Development of national guidelines for the conduct of multicentre non-research projects (audit).
Standard agreements for data transfer, collaboration, intellectual property and authorship.
Increased open communication between researchers and RGO/HREC early in application process.
Streamlined, nationalised and standardised system across all jurisdictions.
Improved efficiency, reducing delay and repetition under NMA scheme.
Increasing use of online platforms (ERM) or tele/video conferencing for expediting the process.
Fast-track resolution of amendments and revisions.

Figure 1 (a and b). Differences in the CovidSurg ethics application process across Australian states.

Figure 2. Time taken for study approval for the COVIDSurg project across interstate hospitals at different Australian jurisdictions.