HREC Leaders '22 Summit. 26 October 2022

Speakers and workshop discussion notes

The Summit sessions posed questions for discussion. The aim of the discussions was to share expertise, approaches and experience around the Summit topics. The notes reflect the questions asked and discussions that followed. What is included and the variety of styles in the notes about each session reflect the session scribe's note taking approach.

Morning Keynote Address

Prof Ingrid Winship AO

Noted that Australia has a good research reputation globally.

1. The three peaks of project ethical oversight:
   - Ethics review
   - Governance or site specific assessment activities
   - Post approval monitoring and oversight

Ethics review in the continuum of scientific merit review, ethics review and governance oversight. Is the balance being applied appropriately?

2. Is there a better way to do ethics review? Acknowledging low and negligible risk research; 'research' that isn't research; review that is done largely because of journal requirements for proof of some prior oversight; audit versus research; and considering what level of risk is involved. What does and doesn't work? What is the way forward?

3. Are specialist HRECs a good or bad mechanism? A properly constituted HREC can bring in expertise when needed.

4. How do we approach the ethical challenges being raised by new technologies, eg genetics, precision medicine, AI, Big Data, biobanks, the climate crisis, infection and pandemics?

5. Do we need all HRECs to be accredited to undertake National Mutual Acceptance?

6. Should we move away from institutional based HRECs to centralised or global HRECs?

- Advantages include ending potential conflicts of interest and providing greater choice for researchers as to where they assign their applications.
- Should we disband all 54 NSW HRECs and have 1 HREC meeting multiple times per week?
- Should HRECs be owned by departments of health rather than institutions?
- Why do we have state by state HRECs when research and ethics review principles cut across state boundaries?
- Is there a potential role for the Research Translation Centres in a new model of HRECs which are institution agnostic?

7. Should all HREC members receive a sitting fee?

8. What are the roles and responsibilities of ethics committees; what is the key role of providing guidance?
- The importance of balanced and appropriate membership, diversity of membership and appropriate expertise.
- The changing nature of ethics in society and therefore the ethics implications of research and the review considerations of HRECs. What may have been acceptable even 5 years ago may no longer be so.

9. Questions to ponder

- Can post research outcomes be attributed to the processes that lead up to it?
- Do we have the right framework and the right balance?
- How do we better promote the ethical conduct of research?
- How do we take more notice of what the community think – a matter of public interest.

10. Principles to take forward

- Alignment of ethics and governance
- Be pragmatic
- End parochialism
- Stakeholder focus – especially CCI involvement
- Training
- Continuous improvement.

Workshop – Session 1.

The pros and cons of inviting researchers to HREC meetings

Facilitator: Prof Murray Killingsworth. Pre workshop input Annamarie D'Souza.

Discussion

1. NHMRC HREC Terms of Reference encourages open communication between researchers and HRECs, noting the desirability of providing ready accessibility of review bodies and their staff to researchers. Technology is now available to do it – Teams, Zoom etc.

2. Implementation – how is this to be done? Issues of workload
- Taking up HREC committee members time with extra discussion with researchers
- Taking up the researcher's time waiting to appear at the HREC meeting

- Anonymity of the reviewers – do we need to protect them?
- Implementation – timing in an already crowded monthly schedule?
- How to structure the process?
- Do we want to invite researchers for every project?
- How do we select who to invite? Criteria?
- Can this be done by the Research Office manager?
- How far in advance should researchers be requested?

3. Pros
- Open lines of communication; increased transparency and collegiality, researchers working in partnership with the committee
- Increased understanding of committee and researcher
- Ability to make full use of the committee's skills - more than just a gatekeeper role, an asset for the project as well.

4. Cons
- Increased risk of conflict of interest
- The anonymity of reviewers is impacted
- Can be confronting for the researcher and not a good use of their time
- Researchers need to be able to clearly communicate in writing and not rely on being able to clarify things at a meeting. It is also important to have written records for accountability.

5. Practicalities of three different models of implementation
- Researcher present for whole discussion and review of their application e.g. Bellberry – General consensus - NOT liked
- Researcher present to answer a summary of questions regarding ethical issues after discussion and review by committee has been completed – Liked, most common option now in place
- Researcher to be able to pitch argument (or rebuttal) to the committee before or after receiving their formal review? - After review - YES / Before review - NO

Are there other models? None emerged.

Workshop – Session 1.

How to determine what is a clinical trial, and how to assess clinical trials and research design quality
Facilitators: Dr Tony Skapetis and Kellie Hansen

Discussion

1. Defining a Clinical Trial
- There is no one definition for a clinical trial. Requirements are different from country to country and between jurisdictions.
- Some organisations have developed clinical trial decision tools to assist with determining whether a study is a CT.
- Although time consuming, engaging with researchers and asking them to justify why their research is (or is not) a clinical trial can be helpful.
- TGA colleagues may also be a good point of contact to offer advice about whether a study is a clinical trial.
- University of Sydney and UNSW have clinical trial decision tools –guides to assist people if they are confused about whether a project is a CT. See University of Sydney attachment: Is my research study a clinical trial?

- Patient information sheets and consent forms/processes are where it should be clear what is being done in the research and therefore whether it is a CT.
- WSLHD ask researchers to prepare an executive summary which is provided to patients with their patient information consent form Some organisations have a pre-review process before the study is submitted to the HREC.
- Investigated initiated CTs can be very time consuming projects for HRECs to review.

2. How to ensure research design and quality of a clinical trial

- If there is expertise on the committee it is deferred to them. If no one on the committee has expertise in the subject area, then the HREC could reach out to someone in the district (LHD or organization) to review the study design and methodology. Involve local experts to review methodology of the study.
- Some organisations have a peer review process. This is coordinated by a central office who distributes the study to the relevant Faculty for peer review by subject matter experts. This ensures that the HREC can focus on ethics, not methodology. The HREC should only review methodology if it impacts ethics. If HREC is concerned about peer review, they go back to the Faculty to discuss further. HREC may provide suggestions to improve methodology, rather than making adherence to comments a requirement before approval.

Workshop – Session 1.

So many ways to say 'yes'. An in-depth look at the issue of consent

Facilitators: Assoc Professor Helen Mitchell and Mr Alan Hales

Discussion around helping researchers understand their obligations around the National Statement when writing an ethics application.

The groups discussed 4 scenarios involving consent of an infant to participate in a clinical trial, power imbalance, voluntary participation, reimbursement, limited disclosure, the use of social media, waiver of consent and data collection from social media sites.

Discussion

1. Clinical Trial involving a newly diagnosed infant's parents asking to consent to the child participating in a clinical trial. The clinical trial has a reimbursement of $2000 and the infant meets the inclusion criteria.
- Ethical issues in consent of a child to a paid clinical trial.
- Doctor patient relationships.
- Reimbursements – National Statement 2.2.10.
- Advertisement should not show the amount of reimbursement for participation.
- Unequal relationships Doctor/patient – power balance National Statement 2.2.9.
- Benefits to the doctor or benefits to research.
- Refer investigators to the National Statement for clarification.
- Easy for a doctor to ask a patient to participate and hard for the patient to say no. Patients trust their clinicians. Patients need options. Relationships and connections often bring people into a clinical trial
- Question around vulnerability – newly diagnosed condition in a child, emotional time.
- Coercion – voluntary consent to participate – National Statement 2.2.1 and 2.2.2.
- Very dependent upon type of trial - is it an intervention or short-term study i.e. a sample of blood?
- Recruitment process different to consent process.

- Clinician or Researcher – who does what and when?

2. Research project around concealment and deception using survey responses. Participants will be told the focus is on shopping habits and loyalty, although the instrument is aimed at supply chains. (Modern slavery to influence the decision making of consumers).
- Weigh up the value of deception and the outcomes of research.
- Identify natural behaviours using deception – limited disclosure National Statement 2.3.2.
- Identify vulnerable groups – different cultures and provide adequate services to support people at risk or harm.
- What can be disclosed and still retain the integrity of data being collected?
- Are the surveys anonymous or identifiable?
- Technology can allow the use of data from surveys.
- Getting researchers to think about the risk/benefit and management.
- Is it a waiver of consent? - need to identify the merit of the research.

3. Observational research – A researcher proposes to undertake observational research in a private performance venue focusing on interactions between the audience and performers of entertainment associated with social stigma. What are the challenges?
- Participant groups – performers, audience and event organisations
- Consent – is it the organisation responsible for the venue – explicit consent? National Statement 2.2.2
- Performers – explicit/waiver of consent? National Statement 2.2.10
- Audience – explicit/waiver of consent?
- What is the type of venue?
- Who are the audience?
- Who are the performers?
- Is it an illegal activity?
- Does the venue need signage to let patrons know research is being undertaken?
- What are the benefits/risks?
- DO they have permission?
- Privacy and confidentiality considerations
- What are they observing for?
- What will the data be used for in the future?
- How do you opt-out of a video consent?
- If you are paying for a service, are you automatically consenting?

4. A researcher proposes to undertake research into hate speech involving data collection from posts on nationalist social medial sites. What are the challenges in obtaining consent?

- Consent from the owners of the social media platform (terms and conditions).
- Owners of the websites.
- Arguments the site is already in the public domain.
- How will the data be accessed?
- Reputational harm.
- Disclosure to users or deception.
- Can users be identified?
- Use of direct quotes may identify individuals.
- Is it a closed forum? - privacy regulations
- Permission is often given when accepting the terms and conditions of a site

- Burden of seeking consent for data that has already been given away by the user – do you really need it?
- Is it ethically right to do so – refer to the National Statement on use of Public Data 3.1.52

Workshop – Session 1.

The challenges raised by genetic research
Facilitator: Prof Ingrid Winship

Discussion

1. Difference between genomics and genetics. Are we missing things on the HREC because we don't understand the difference?

2. What to do about incidental findings?
- If a researcher finds something other than what was the research focus, do we communicate that too?
- Family members may want to dictate what can and can't be told.
- Duty of care to protect someone – to inform about imminent danger. What constitutes clear and imminent danger?
- The consent form – 'you can tell x and y but not z'. Repercussions for family – do you tell or not? The right of an individual to say they didn't want to know. If its medically actionable do you want to know?
- Could a strategy be to advise researchers not to look for other things? Keep the research 'clean' and not try and do everything with one study?

3. Privacy and re-identification of data
- Can't have de-identified data when it comes to genetics in 2022 but lots of people have lots of samples; there are lots of databases with DNA – who are they on-selling this to? With rare disorders it's re-identifiable. Not an easy answer but must be very protective of our data and data governance. In clinical trials importance of monitoring and good data and data protection.
- Issue of journals wanting raw data. The emphasis of research has moved from the 'publish or perish' – now more about patient outcomes and translation and impact. Journals are asking for primary data - consent was given to the researcher, not the journal.

4. Children in research
- Raises challenges which are different to adults. The way we analyse genes creates much more raw data than the data we can use. Who owns the raw data and who can access it?
- Need clarification around children re-consenting and informing adults about research done when they were a child.
- Clinical trials require that the data is kept until the child is an adult.
- If the investigator lives longer than the child how is the data stored and accessed?

Workshop – Session 2.

Best practice involvement of consumers in research design
Facilitators: Carrie Hayter, Health Consumers NSW and Brian Dalton

Materials provided for the workshop:
Good Practice in Consumer Involvement - handout

Discussion

- Meaningful consumer involvement in research is varied. Some researchers see consumer involvement as an obstacle, some fear consumer involvement as they don't know where to start, some see the benefits of it as it makes translation easier. But there seems to be an appetite for change, and it is now seen as a "superior form of research".
- Consumers should be involved in defining the research question and leading the research from the beginning, and throughout the project. Researchers should be looking to communities to determine what the research question should be.
- Meaningful consumer involvement may include consumers being listed as Chief Investigators in the protocol. Communities should be acknowledged in the research team.
- Institutional level structures – consumer advisory groups enable consistency.
- It is sometimes difficult for HRECs to push back on projects which they don't believe include meaningful consumer involvement, especially if the project has already been approved for grant funding.
- HRECs should pay attention to detail when reviewing the terms of reference e.g. membership of the steering committee and whether it enables meaningful consumer involvement.
- Research should involve diverse consumer perspectives.
- It was suggested that it is difficult for HRECs to have a one size fits all approach for consumer involvement due to the diversity of health and medical research.
- There should be prompts as part of HREC submission documentation, to at least prompt researchers to think about consumer involvement.

Workshop – Session 2.

Collaboration, connection and innovation in a data economy
Facilitator: Assoc Prof Angela Todd

Discussion

- Health information is an under-used asset
- Data literacy variable, including how patient info is stored
- Storage – from unsophisticated to highly secure. There is an opportunity to increase the
- standards across the health sector. Standards can be put in place in but can safety ever be
- guaranteed?
- Consent process – move to open data, more sharing and dynamic consent (data is not
- static)
- Emerging issues – deidentification (need to look more closely at this) - identifiability
- impacts re-use; offshore data management, social media (public data and consent issues)

Workshop – Session 2.

Adaptive designs - embracing the trials and avoiding the tribulations
Facilitators: Prof Tom Snelling and Dr Lucy Coupland.

Materials provided pre workshop:

- Protocol for the controlled evaluation of angiotensin receptor blockers for COVID-19 respiratory disease (CLARITY): a randomized controlled trial.
- Link to https://drive.google.com/file/d/14qyp47B567EA3q776fVNNafssbTx0Rju/view

Discussion

1. Adaptive trials undertake pre-specified analysis as the research progresses that may lead to an adaptation of the methodology.

There are a number of aspects that could be adapted. The:

- intervention
- sample size – with an open ended sample size the analysis can evaluate the probability of effectiveness and you can continue to adapt until you have enough evidence to determine effectiveness, or not.
- targeted disease
- the ratio of different treatments being evaluated.

The adaption may be planned with pre-specified analysis outcomes triggering adaption and there may be a stopping rule.

Adaptive trials need a large input of statistical expertise to establish and as they progress.

2. Possible advantages:

- Most CTs fail to be conclusive in their results. An adaptive design may improve the likelihood that the trial may be conclusive; and/or may stop a trial when additional participants would clearly not be useful.
- Adaptive trials can provide advantages to efficiency by allowing the research to focus on the best performing treatment.
- Participants might have more chance of getting an effective treatment.
- Less participants might be involved overall.
- Fewer participants may be exposed to risk.
- There is community advantage if a treatment can be proven and rolled out sooner.

3. Adaptive trials can raise ethical issues such as:

- Q. Does it need a form of adaptive consent, given that these trials evolve? A. A patient may consent to different domains of intervention.
- If the adaptations change the risk/benefit analysis, how is that accounted for?
- Do adaptive trials provide a chance for a patient to get a more effective treatment arm?
- Are biases introduced? There is the potential risk of response adaption introducing the possibility of bias; there can be bias when the data is looked at multiple times. There may be an over estimation of the benefit of the intervention.
- Because these trials can be run over a long period, standard of care could change during the life of the project, the nature of the disease being studied could change, a medical approach to treatment of the disease could change/become available. (Covid 19 provided as an example of these last points.)
- These studies have different and complex study designs which may make it more difficult for an HREC to review.
- The safety of the participant and the robustness of the consent process must be considered and may be impacted by the adaption.

4. Funding implications

Q. Do HRECs query funding for the trial? A. They want to know about the source of funding and generally they are quite happy if the study is able to be stopped sooner than might have been suggested.

Q. What would happen if funds were exhausted before the study has a definitive result? A. Funding may be conditional on evaluation outcomes and even a promising result may not receive funding.

Workshop – Session 2.

SUCCESS: What lessons can be learned from the world's first randomized placebo-controlled surgical trial of lumbar spinal stenosis?

Facilitators: Prof Manuela Ferreira and Pauline Hanrahan.

Materials provided for the workshop:

- *Randomised placebo controlled trials of surgery* – handout
- *Considerations and methods for placebo controls in surgical trials (ASPIRE guidelines)* – journal article

Discussion

1. General

- There is a need to produce evidence to prove efficacy of surgical procedures and determine if they are needed or not. Even if thousands of people have had a surgery, what evidence is there that it is beneficial, or not, and that it is safe and effective?
- Do we need a review of the guidelines for SHAM surgery to ensure safety and efficacy?
- ASPIRE guidelines discussed and Levels of fidelity – Placebo with High fidelity – High fidelity
- https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(19)33137-X/fulltext
- Problems in who and how payment is made, eg Government cannot pay for placebo
- If different bills for treatment and placebo are provided, participants and researchers may be unblinded.
- Health Economics – there may be health dollar savings if we stop undertaking non effective surgeries.

Canadians developing a framework called *"Practice Change Framework"*

2. Design of Placebo Surgery

- To ensure participant protection studies need a surgeon working group – for co-design.
- Independent Data Monitoring Committee (IDMC) required for stopping rules, list of recommendations with clear definition of design.
- Surgeon and participation interaction.
- Explain why they are using SHAM or low fidelity, high fidelity. Why are they doing this? Is this for blinding? Is it for decreasing risk? Is it to improve care?

3. Other

- For the project used as a starting point for discussion at this workshop, the researchers employed an ethicist to work on the protocol. The ethics application HREC was approved on first review.
- Governance can be problematic – do not understand the trial design.
- Many surgeons are not willing to participate in these trials.

AFTERNOON SPEAKERS' SESSIONS

Same Rules, Different Outcomes – 'Tricky issues' that arise in ethics review

Speaker: Dr. Karolyn White

Summit delegates were asked to provide a 'tricky issue' they would like discussed on the day. The speaker grouped them and posed a number of questions for discussion.

Discussion

1. Risk

Q. What level of risk committee are we willing to accept?

- Different committees may have different risk appetites. May vary by project and population (e.g. children)
- Needs to be considered with respect to the benefits.
- Risk in relation to what can be achieved. Are there any other ways to achieve the projects aims?
- Consent process and mitigation strategies are very important. Participants need to understand the risk.
- Question of whether HRECs should consider the risk to the organisation and the researcher as well as the participant.

Q. Do HRECs use empirical evidence to assess risk? Does the committee research the issue prior to approval? Should the HREC ask the researcher for that kind of detail?

- Suggestion to develop a portfolio of skilled reviewers who can be called up for specialist review as needed. Some use a lead and secondary reviewer and choose those whose experience lines up with the skill sets required to review the application.
- Suggestion to do research on the sponsor of a Clinical Trial for verification of its reputation/work.
- Some HRECs conduct a light review if the researcher's references are old (i.e. 10 years), but also ask the researcher to update their references.

Discussion around applications that get amended many times ('death by amendment'). When do you stop allowing so many amendments?

Q. Should HRECs consider the risk to the researcher in their ethics reviews?

- There was a range of opinions on whether it is the HRECs responsibility to consider this and/or whether responsibility lies with other sections of the organisational hierarchy.
- Is it the PI's job to determine risk for the project team? What responsibilities are there for a less experienced and/or student researchers? Is it the role of the HREC and/or PI to veto research based on risk to the researcher?
- A soon to be expected revision to the National Statement may address this issue.

Q. Is there a point where the HREC is over-extending their subjective view of the risk assessment?

- It was suggested that the institution has the duty of care for the researcher. The HREC may flag the risk with the Chief Executive for a risk assessment.
- There was general agreement that it is the duty of the CI first, but duty of the HREC to bring this up with the researcher in their comments.
- Have HRECs moved from ethical principles to risk mitigation and protecting the institution? Has it moved from ethics to governance?
- Have to be careful that we don't re-invent the wheel. HREA is designed to address the ethical principles.
- Risk mitigation has to start with the participants but also the institution as well.

2. Social Media

- Ethical issues around recruiting international participants via social media.
- Payment is an ethical issue and difficult to manage. One HREC says participants should be paid minimum wage.

- Issues with participant age in that it can't be confirmed.
- Privacy and risk for involved 'non research participants'. Eg researchers being able to view the posts of participant 'friends'. One HREC felt they needed to protect the 'friends' and sought advice from the Privacy Commissioner. Decision was to have a separate research assistant remove the posts of the 'friends' before the researchers viewed the data.

Q. Are there any ethical issues accessing data from social media for research purposes?

- Example – Cornell Facebook Study – the decision handed down was that there were implications.
- Questions raised about whether a researcher can join a public account for their research (e.g. posing as someone else). Who do the HRECs ask when they have questions like this? Often there is anxiety associated with making this decision.

3. Data Management

Should Data Stewards be members of HRECs? Data stewards can advise committees and researchers on how research data can be made safely accessible for reuse and on security of storage.

The value-add of human research ethics committees

Speakers: Assoc Prof Sarah Garnett and Prof Barbara-Ann Adelstein.

Discussion

- The importance of asking for the qualifications of the research team. Having this information can help meet many queries around potential risk and likelihood of a successful project.
- The line between research ethics committee and clinical ethics committee. Research ethics committees focus on research. In clinical care, the risk/benefit is for an individual who is 'unwell' whereas research can involve people who are 'healthy' (controls).
- The duty of the HREC to protect the integrity of science (integrity, methodology).
    - Noting that student projects may not have definitive results and that the National Statement acknowledges the benefit of student research.
    - Some researchers think that HRECs are out of their remit to comment on study methodology. It was suggested this is a misunderstanding of good research practice.
- Ethics committees provide an external review of the protocol and can help researchers to better develop and articulate how they will conduct the research and what they will measure.
- The ethics review process, when done properly, can lessen the workload of writing up the final paper – much of the information required will have been articulated in the ethics application.
- The practice of 'HREC shopping'. Ie choosing an HREC based on the expectation that the application will get through that HREC easily; or taking an already reviewed application to another committee because of unfavourable comments. Generally not considered ethical. It was noted that in the case where the HREC is reviewing as well as, and after, ethics approval has been gained from another HREC, some HRECs will do a minimisation review, rather than a full review.
- Criticism of the committee – the process of HREC review is not always appreciated
    - Researchers on the whole think they are proposing a project that can be considered ethical. The HREC may need to translate the guidance contained in the National Statement. Ethics is also a continually moving benchmark.
    - Need to promote that the HREC is helpful. The focus should be on improving the health and research environment.
- HRECs don't have the resources to extend the role of back and forth for coaching the students/researchers. Should the HREC be 'teaching' people how to do research?

- There should be a dialogue with the researchers and opportunity to provide a rebuttal to the comments from the HREC. HRECs should be open to informed debate with the researcher.
- Based on their broad view and experience with reviewing studies, HRECs are used to identifying risks that researchers may not have considered.
- Q. What is the most important positive interaction with researcher? A. Good communication to avoid the back and forth with the researcher. A 'face-to-face' conversation, especially if the protocol will potentially be rejected.
- Examples of value of ethics review – stories from researchers who were appreciative of the feedback. Discussed the option of transparency with the researchers and if the committee is comfortable, with researchers joining meetings.
- Sometimes it is useful to invite 'difficult' researchers to join the HREC.
- Do we need a campaign to profile HRECs as key research partners? Do we need 'Research Champions'?

Afternoon Wrap-up and Summit Close

Speaker: Assoc Prof Angela Todd

- Reflected on the history of research in Australia.
- Australia is recognised as having high quality research and ethics committees contribute to make research better and provide an important 'value add'. The HRECs are part of why Australian research is respected around the world.
- There has been a massive injection of money through MRFF for more research – so HRECs are busier now than previously. Requirements for multi-site research may make ethics review more complex for HRECs.
- Researchers may not know that HRECs are made up of volunteers.
- Given these complexities, there is education needed for researchers around the issues they see as impediments.
- The journey of a researcher is also hard. Applying for and getting a grant when approx. 18% of applicants are awarded funding under some schemes; the journey through ethics and governance when they are working to a funding deadline; post completion, peer review and acceptance for publication of the research.
- Consistency for multi-site approvals is challenging, although HRECs have come a long way with standardising ethics applications. Governance is also challenging, and SHP is working with partner sites to improve consistency.
- SHP and SPHERE have collaborated with PRAXIS Australia to develop and provide HREC learning modules for its partner organisations.
- Thank you to the HRECs who took time to join today and share their ideas through the workshops.