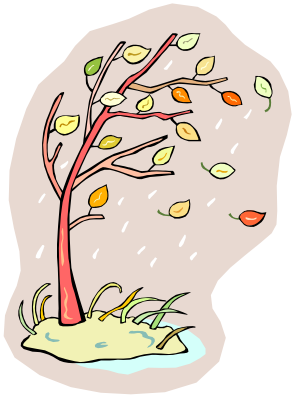
AUCKLAND WOMEN'S HEALTH COUNCIL

NEWSLETTER

MAY 2014



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ENROLLING UNCONSCIOUS PATIENTS IN CLINICAL TRIALS

If there was any remaining doubt about how NZ Ministry of Health's ethics committees are now firmly focused on paving the way for clinical trials to go ahead rather than focusing on protecting the rights of patients it was firmly dispelled at the March and April meetings of the Northern A ethics committee.

In March one of the research proposals discussed during the Northern A ethics committee meeting involved a study of a new antibiotic which would be tested on unconscious, critically ill patients unable to give prior informed consent before being enrolled in the study. It subsequently emerged that the practice of enrolling unconscious patients in these sorts of trials has been going on in New Zealand for a decade or so. In fact, in 2004 during a review of the HDC Act and Code of Consumers' Rights there was an attempt by Ron Paterson who was the Health & Disability Commissioner at the time to get something added to the Code of Rights about the practice but his recommendation was not actioned by the government.

The current ethical dilemmas facing Ministry of Health's ethics committees are the result of a number of events and changes both here in New Zealand and in the USA.

FDA changes the rules

Behind the latest research proposals for studies on the use of new antibiotics lies another fascinating tale about an antibiotic approved by the FDA in 2004 which was later linked to liver failure, the ensuing scandal that exposed the FDA's failure to listen to its own advisors, the subsequent development of strict clinical guidelines for antibiotic development and the exodus of the pharmaceutical industry from the development of new antibiotics. (1) (2)

In May 2012 the FDA acknowledged the looming public health crisis of antibiotic resistance and the need for the agency to "reboot antibiotic development" by changing the rules again around clinical trial designs in order to entice the drug companies back into developing urgently needed new antibiotics. (2)

NZ changes its ethics committees

Over the past five years the current government has driven major changes to the structure and operating procedures for the Ministry of Health's ethics committees. Alarm bells were sounded by women's health groups, the Otago Bioethics Centre, academics and researchers and reported in the February and July 2012 issues of the AWHC newsletter. (3)

The changes effectively spelt the end of the purpose, role and function of ethics committees that were set up in the wake of the Cartwright Inquiry. The ethics committees that were established in the early 1990s were designed to provide extensive safeguards for patients. The changes that were introduced in 2012 have totally undermined these safeguards, and have resulted in a significant and worrying departure from international standards.

The motives driving the changes were financial and economic ones as the Minister of Health had been led to believe that New Zealand was missing out on millions of dollars to be had by getting more involved in the clinical trials industry. The focus needed to shift from protecting patients or “research participants” as they are now referred to – it was interfering with speedy access to the clinical trial industry – to smoothing the pathway for fast-tracked approval of research by the ethics committees.

Ethics committees can no longer be counted on to put patients first as they are now operating under new rules that do not permit them to insist on the various safeguards that were once part of their brief, or question the design and power or scientific merit of the studies that are submitted for their approval. Prior to the changes introduced in 2012 ethics committee chairpersons wanted greater protections for those enrolled in trials sponsored by international pharmaceutical companies; now they have deadlines that must be met, and enabling researchers to get those patients enrolled one way or another is the priority.

New Zealand has become known internationally for being one of the best countries to go to for getting fast-tracked and speedy approval for research studies – New Zealand is now “the first cab off the rank,” even for Phase I first-in-humans research proposals.

Testing new antibiotics

The research proposal that came before the Northern A ethics committee in March was for a study that compared treatment with a new antibiotic with an existing antibiotic. It is part of a non-inferiority trial, so there is no power in the study to prove the new antibiotic is better than the antibiotic it is being compared with.

The acceptability of non-inferiority trials is one of the changes made by the FDA who are now working to fast track approval of the introduction of new antibiotics. The study is a phase III trial. Phase II testing had shown that the new antibiotic is safe.

However, the major stumbling block to the trial obtaining ethics committee approval was the fact that nearly all of the patients being used to test the “non-inferiority” of the new antibiotic would be unable to consent to being involved in the trial until they had regained consciousness and were well enough to absorb and under-stand the information they were given about the study and give retrospective consent to being enrolled in the trial.

The current problem was that Crown Law had now become involved, and it was their opinion that patients who are unable to give consent cannot be enrolled in studies unless the study involves a life-saving treatment, and a Court order has been obtained which authorised the participation of the unconscious patient in the clinical trial.

As the testing of the antibiotic is part of a trial that is not designed to show if the new antibiotic is better than the current antibiotic, let alone a life-saving treatment, there was no prospect of getting permission through the court system. Besides, no researcher wants to have to get a court order to enrol each patient in a clinical trial.

Patients

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Following a lengthy discussion with the researcher the Northern A ethics committee decided by consensus to defer a decision, “while it seeks further information.” It was painfully clear during the discussion that the committee was focused on the need to find a way round the obstacles being put in place to prevent the enrolment of unconscious patients in clinical trials.

Ignoring the lessons of history

There was little evidence that anyone in the room was focused on the rights of patients being enrolled in non-therapeutic clinical research. The legacy of the Cartwright Inquiry with its emphasis on ethics and patient rights, informed consent and clinical research was forgotten. Judge Silvia Cartwright’s recommendations that non-therapeutic clinical research should not be undertaken on patients without their “free consent,” and then only after they have been fully informed about the study and given written consent, were consigned to the dustbin of history. (4) Nor was there any mention of Right 7 of the Code of Consumers’ Rights – the right to make an informed choice and give informed consent.

It didn’t get any better when the Northern A ethics committee reconvened in April and began the meeting with another discussion on the vexed issue of enrolling unconscious patients and getting their consent later. Following the March meeting the Ministry of Health’s Health Legal team had written to the ethics committees advising them that ethics committees cannot give consent for individuals to be involved in clinical trials, and informing them the test that must be met is that it must be in the best interests of the patient. There must be a restoration of Right 7(4) of the Code of Rights – which begs the question as to exactly when was it dismissed?

But dismissed it certainly had been – thousands of patients in ICUs (Intensive Care Units) have been enrolled in both drug company-sponsored studies as well as non-commercial studies.

What followed next was further discussion on how best to comply with Health Legal’s letter but make it possible for the clinical trials on patients unable to give informed consent that are currently underway to continue, and for the proposed trial to go ahead. Various arguments were suggested by the ethics committee members as to why unconscious patients should continue to be enrolled in clinical trials. While some were rejected it didn’t take them very long to come up with quite a list:

- The researchers believe it is in the patients’ best interests to be included in these sorts of studies
- Patients get better care when they are involved in clinical trials
- Patients enrolled in clinical trials get more tests and are more likely to get an accurate diagnosis
- Patients are all happy to be included in clinical trials; they say they want to be included, (once they have regained conscious-ness, that is)

All that needed to be done now was to change the Patient Information Sheet (PIS) by removing the sentence saying the study did not offer any direct benefit to the patient, and pitch it to the patient’s relative, rather the patient. The ethics committee then

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gave it provisional approval without a thought for where this might lead.

This saga around what happened with this research proposal is just one example of what has happened to NZ's former watchdog ethics committees. Drug companies now see New Zealand as a soft touch for getting fast-tracked ethics committee approval for their studies. The sponsor's demands are outrageous and are definitely not in keeping with the hard-won rights of patients or "research participants."

Biobanking is now part of nearly all research trials with tissue samples usually being sent overseas.

The Patient Information Sheets are incompatible with patient rights in New Zealand and the sponsors won't agree to the researchers changing them unless the ethics committees demand changes as a condition of obtaining ethics committee approval.

The drug companies also attempt to restrict patient access to their own health information, and to insist on research participants filling in a form or writing to the study's chief investigator should they decide to withdraw from the research trial. The Northern A ethics committee has, so far, refused to comply with either of these conditions.

It's definitely time for an inquiry!

References

1. http://www.nature.com/news/fda-under-pressure-to-relax-drug-rules-1.11936
2. http://aac.asm.org/content/57/10/4605.full.pdf
3. http://www.womenshealthcouncil.org.nz/Features/Hot+Topics/Ethics+Committees.html
4. Judge Silvia Cartwright. *The Report of the Cervical Cancer Inquiry*. 1988. Chapter 7 "Ethics and Patient Rights." Page 133.

SWISS MEDICAL BOARD ADVOCATES ABOLISHING MAMMOGRAPHY SCREENING

A "Perspective" on mammography screening published in the *New England Journal of Medicine* on 16 April 2014 describes a review undertaken by the Swiss Medical Board, an independent non govern-mental body which resulted in a recommendation that "no new mammography screening programs be introduced and that a time limit be placed on existing programs."

The Swiss Medical Board's report was published on 2 February 2014. In their report the Board acknowledged that systemic mammography screening might prevent about one death attributed to breast cancer for every 1000 women screened, even though there was no evidence to suggest that overall mortality was affected. The Board found that for every breast-cancer death prevented in US women over a 10-year course of annual screening beginning at 50 years of age, 490-670 women are likely to have a false positive mammogram with repeat examinations; 70-100 women would have an unnecessary biopsy; and 3 – 14 an overdiagnosed breast cancer that would never have become clinically apparent.

The authors of the NEJM opinion piece, a medical ethicist and a clinical

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epidemiologist, stated “we were struck by how non obvious it was that the benefits of mammography screening outweighed the harms.”

http://www.nejm.org/doi/pdf/10.1056/NEJMp1401875

TISSUE-BASED CANCER RESEARCH IN NZ

An all-day forum took place at Auckland University on Thursday 17th April whose aim was to explore how to go about developing a cohesive national ethical framework for the collection and storage of human cancer tissues for future research in New Zealand.

AWHC member Jo Fitzpatrick was there to present the social and ethical considerations of some of the patient views on this form of biobanking. What follows is a summary of some the points she made during her presentation at the forum:

“In many ways we are working at the cutting edge of science and unlocking the potential for a new future. Old concepts and ideas are a good starting point but they are not enough to meet our needs going into a dynamic future.

The issues we are dealing with are dynamic and fast moving. We must ensure that our mechanisms for the inclusion and engagement of consumers as partners in this process reflect this and can serve our needs - as consumers, researchers, clinicians and society.

There’s money in the bank

People generally want to help, to be of use. There is public goodwill in the idea of Biobanks and helping to progress the cause of science in the public good. There is money in the bank and most people want to invest.

But we have already made some withdrawals. The Cartwright Inquiry, the library of baby hearts at Greenlane hospital, and the warrior gene are all out there in the public mind, and they are highly charged and emotive.

We cannot afford to add to this list. My fear is that another serious incident will see a run on the currency we have left. And to extend the banking analogy, we need to consider whether Biobank tissues are 'donated' or merely on loan.

Consumer participation is too often seen as a hurdle, a problem, and expensive. But what happens if we reframe it as an opportunity?

My view is that it is a partnership. In the Maori experience a lot of attention is paid during the courtship. Promises are made. People are careful to tick all the boxes, say all the right things, work hard to get what they want. But sometimes it ends badly.

So I want to reinforce some key points for discussion:

- It isn’t an option to NOT include

consumers. We may not reach nirvana but we must continually strive for it. We cannot move forward without going beyond the ethics committees. Using ethics committees

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as a de facto method for consumer involvement is just not good enough. Right 7(10) may be useful for retrospective studies but prospective studies need active and meaningful consumer involvement.

- Participation needs to be embedd-

ed at all levels and at all points in the Biobank pathway – in all governance structures and on all steering and working groups.

These are some useful starting points to consider –

- survey current levels of consumer

participation in Biobanks and their experiences of these

- join up existing consumers in the

system and include Ethics Committees in this network

- involve consumers in the develop-

ment of principles and guidelines

- national autonomy is crucial and

important. We cannot cede to international mores and pressures which do not match the standards we set for ourselves. Ignorance is not an excuse for negligence

- the benefits must always fall to all.

Commercialisation and the locking up of data or technologies developed from donated material is a breach of trust and faith

- actions speak louder than words

in consumer partnerships. They need funding and commitment. They are about building respectful relation-ships, not paying lip service to worthy ideas we wish we could implement if we only had time.

Today is the day to start conversations and decide on what the issues are, and where we need further discussion and action.

AWHC GENERAL MEETING 1 May 2014

Detailed minutes of this meeting are available on request. Matters discussed included:

- Financial reports
- Grant applications
- Bowel cancer screening pilot
- Breast cancer screening
- Northern A ethics committee
- 2015 Cartwright conference

Further information on some of the topics listed above is contained in this issue of the AWHC newsletter.

AWHC NEWSLETTER

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UP AND COMING EVENTS

DISTRICT HEALTH BOARD meetings for May/June 2014:

Waitemata DHB (Website address: www.waitematadhb.govt.nz)
The Waitemata Hospital Advisory Committee meeting starts at 11am on Wednesday 21 May 2014 and will be followed by the DHB Full Board meeting which starts at 1.30pm. Both meetings will be held in the DHB Boardroom, Level 1, 15 Shea Terrace, Takapuna.

The **combined Waitemata DHB and Auckland DHB** Community & Public Health Advisory Committee meeting starts at 2pm on Wednesday 11 June 2014.

Auckland DHB (Website address: www.adhb.govt.nz)
The Hospital Advisory Committee meeting will be held at 9.30am on Wednesday 14 May 2014 followed by the Full Board meeting at 2pm. Both meetings will be held at the Marion Davis Library, Building 43, Auckland City Hospital.

Counties Manukau DHB (Website address: www.cmdhb.org.nz)
The Community & Public Health Advisory Committee meeting will be held at 1.30pm on 21 May 2014 at 19 Lambie Drive, Manukau City.

The Hospital Advisory Committee meeting will be held at 9am on Wednesday 11 June 2014 at Ko Awatea and will be followed by the Full Board meeting at 1.30pm.

ETHICS COMMITTEE meetings – dates for the four new ethics committees are at: http://www.ethics.health.govt.nz/about-committees/meeting-dates-venues-minutes

Waitakere Health Link is holding an NGO Health Network Forum at 9am on Wednesday 28 May. The topic is "***The history and future development of Maternity Services in West Auckland***" at the Kelston Community Centre, West Auckland. This is a unique opportunity for NGOs and consumers to talk to the people from the Waitemata DHB, independent midwives and the Maternity Services Consumer Council, and will include a discussion panel of questions and answers.

For further information phone 839-0512, or email: office@waitakerehealthlink.org.nz