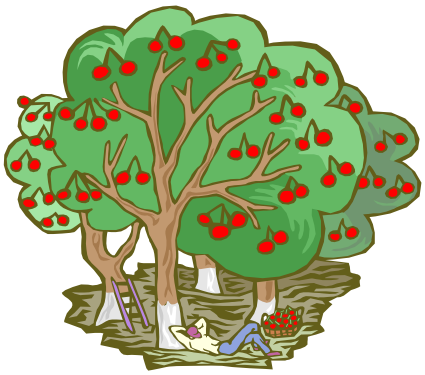
AUCKLAND WOMEN'S HEALTH COUNCIL

NEWSLETTER

APRIL 2013



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The AllTrials Campaign

An international campaign has been mounted for the publication of the results from all clinical trials – past, present and future – on all treatments currently being used. (1)

Currently companies and researchers can withhold the results of clinical trials even when they are asked for them. It has been like this for a very long time, and it has resulted in poor treatment decisions, patients being harmed or dying, law suits, drug company scandals, and a waste of health dollars.

The problem is well documented. The current best estimate is that half of all the clinical trials that have been completed have never been published in academic journals. Trials with positive results are twice as likely to be published as others while many trials with negative results are simply swept under the carpet.

It goes without saying that doctors and regulators need the results of all clinical trials to make informed decisions about which treatment is best. Without all the evidence it is impossible to know what the real risks and benefits of a particular drug or medical device are. It results in ridiculously absurd situations whereby patients are at risk of being exposed to unnecessary harm through being prescribed the wrong treatment or their doctor prescribes an expensive new drug when an older cheaper one is actually more effective.

Ben Goldacre gives a personal example of why missing data matters so much in his latest book "*Bad Pharma*." (2) He describes how several antidepressants had done nothing for one of his patients, so he and his patient decided to try something new. Ben Goldacre writes: "I'd read the trial data before I wrote the prescription, and found only well-designed, fair tests, with overwhelmingly positive results. Reboxetine [the anti-depressant] was better than a placebo, and as good as any other antidepressant in head-to-head comparisons...Reboxetine was clearly a safe and effective treatment. The patient and I discussed the evidence briefly, and agreed it was the right treatment to try next."

Subsequent investigation by a group of researchers, a long process that involved searching in academic journals, arduous requesting of data from the manufacturers and gathering documents from regulators, revealed a very different picture. Out of seven trials comparing reboxetine against a placebo only one, conducted in 254 patients, had a positive result. It was the only study that was published in an academic journal. The other six trials involving almost ten times as many patients were never published as they showed that reboxetine was no better than a dummy sugar pill.

The trials comparing reboxetine against other drugs produced the same result. The three small studies involving 507 patients that showed that reboxetine was just as good as any other drugs were published, but the other studies which involved 1657 patients were not published as they showed that patients on reboxetine did worse than those on other drugs. Patients on reboxetine were also more likely to have side effects, more likely to dropout of taking the drug, and more likely to withdraw from the

trial because of side effects. Ben Goldacre writes: “I did everything a doctor is supposed to do. I read all the papers, I critically appraised them, I understood them, I discussed them with the patient, and we made a decision together, based on the evidence. In the published data, reboxetine was a safe and effective drug. In reality, it was no better than a sugar pill, and worse, it does more harm than good, As a doctor, I did something which, on the balance of all the evidence, harmed my patient, simply because unflattering data was left unpublished.”

As stated on the AllTrials website (1), the problem of the missing data also affects some very expensive drugs. Governments around the world spent billions on an antiviral drug called Tamiflu. The UK spent £500 million on this one drug in 2009 which was 5% of the total of the National Health Services’ drugs budget of £10 billion. Roche, the manufacturer of Tamiflu, published fewer than half of the clinical trials conducted on it, and continues to withhold important information about these trials from doctors, researchers and the Cochrane Collaboration, the large international non-profit academic collaboration that produces rigorous systematic reviews. The result is that we don’t know if Tamiflu is any better than paracetamol.

A number of initiatives have been introduced to try to fix this problem, but they have all failed. Since 2008 in the USA the FDA has required the results of all clinical trials to be posted within a year of completion of the trial. However an audit published in 2012 has shown that 80% of trials failed to comply with this law. Despite this fact, no fines have ever been issued for non-compliance. However, since most currently used drugs came onto the market before 2008, the trial results that are most important for current medical practice would not have been released even if the FDA’s law was fully enforced.

The AllTrials campaign is calling on governments, regulators and research bodies to implement measures to ensure the publication of the results of all clinical study reports.

It is also calling for all universities, ethics committees and medical bodies to enact a change of culture, recognise that underreporting of trials is misconduct and police their own members to ensure compliance.

The AllTrials website features a petition which states:
“*Thousands of clinical trials have not reported their results; some have not even been registered.*

Information on what was done and what was found in these trials could be lost forever to doctors and researchers, leading to bad treatment decisions, missed opportunities for good medicine, and trials being repeated.

All trials past and present should be registered, and the full methods and the results reported.

We call on governments, regulators and research bodies to implement measures to achieve this.”

Check out the website and sign the petition.

References

1. http://www.alltrials.net/
2. Ben Goldacre. *Bad Pharma*. Fourth Estate. 2012.

BEN GOLDACRE IN AUCKLAND

Ben Goldacre is a medical doctor, non-fiction author and, since 2003, a columnist for the UK newspaper, *The* Guardian. He has also made various documentaries for BBC Radio 4.

Ben is a man on a mission, that mission being to teach the public about good science by talking about bad science. His first book *"Bad Science"* was first published in 2003. *"Bad Pharma"* was published in 2012.

His work focuses on unpicking the evidence behind misleading claims from journalists, the pharmaceutical industry, alternative therapists, and government reports.

He will be in Auckland in May for the Auckland Writers and Readers Festival, and will be giving two lectures.

Clinical Trials: The Whole Truth and Nothing but the Truth
Wednesday 15 May 12.30-1.30pm University of Auckland, Grafton Road campus.

Bad Science, Bad Pharma
Saturday 18 May 5.30-6.45pm ASB Theatre, Aotea Centre

See the Auckland Writers and Readers website for information and to make bookings:
www.writersfestival.co.nz/Home/WritersAZ/BenGoldacre/tabid/807/Default.aspx

Further information about Ben Goldacre is available on his website:
www.badscience.net/

A SEQUEL TO THE STORY OF HENRIETTA LACKS

The June 2010 issue of the AWHC's newsletter featured a review of Rebecca Skloot's book, "The Immortal Life of Henrietta Lacks," which told the amazing story of the life and death of a poor Southern tobacco farmer in the USA whose cancer cells were the first human tissue samples to be successfully grown in culture.

In 1951 Henrietta, a young black mother of five children, died of cervical cancer at the age 31. Her cancer cells were removed without her knowledge as she lay dying in the John Hopkins Hospital in Baltimore. Her cells, known as HeLa cells, changed the history of medicine, and became the world's most famous human cell line.

As the book about Henrietta makes clear, her children and grandchildren on the other hand still struggle to understand the incredible legacy of their mother's and grandmother's cancer cells. While cell banks and biotech companies made millions from HeLa cells, her children couldn't afford health insurance.

Last month scientist Lars Steinmetz and his group at the European Molecular Biology Laboratory in Heidelberg, Germany published the HeLa cell genome which resulted in a bioethical storm. While the team of scientists saw the HeLa cell genome as a helpful resource for their work examining how gene variants influence basic biological functions, as well as the countless other scientists studying the same cell line, Henrietta Lack's descendants objected to this latest development in the incredible

story of Henrietta's cells. Some of their objections related to the possibility that the published genome may reveal genetic traits carried by the surviving members of her family.

Other scientists and bioethicists were also critical of the decision to publish the sequence, noting that this debate has opened up a morass of unresolved ethical issues surrounding HeLa cells as well as genetic privacy and the use of archival tissue samples in genomic studies.

Lars Steinmetz subsequently pulled the genomic data from public databases, but pointed out that researchers have been generating and publishing genetic data on HeLa cells for decades. Taking the data off doesn't change anything, he said. "There are more data already out than what we generated in our study."

In order to prove that point, Joseph Pickrell, a geneticist at Harvard Medical School in Boston, spent a couple of hours gathering publicly available genetic data on HeLa cells. From the data he retrieved he was able to assemble a draft of the HeLa cell genome.

Even more data may soon become available as another team of researchers presented work at the annual meeting of the American Society for Human Genetics held in November 2012 in San Francisco, creating an even more detailed analysis of the HeLa genome.

In many ways Henrietta's cells pose a unique dilemma. While the donors of most other human cell lines are anonymous, hundreds of thousands of people know that HeLa is derived from the cells of Henrietta Lacks. Lars Steinmetz and other scientists have no legal obligations to obtain permission to sequence and publish the HeLa cell genome. The tissues from which the cells were obtained were discarded in 1951, and no laws at that time prevented the taking and use of a person's cells without their knowledge or consent. Even today, countries and individual institutions differ on whether researchers must obtain consent before using tissue removed in the course of a health care procedure.

Privacy and other bioethical issues
However, the can of worms that the HeLa genome has opened up has revealed a number of issues that need to be resolved. Recent work has shown that anonymised participants in large genomics projects can be identified by cross-referencing their genomes with genealogy databases. Guidelines are needed around the publication of such data which limits access to the data and preserves the privacy of the individuals involved.

Other archived tissue such as that held in museums present similar problems.

Another issue that needs to be addressed is whether family members have the right to override the wishes of individuals who choose to share their genetic data, and whether scientists are obligated to disclose a person's genetic information, such as disease risk, to family members.

For Henrietta's family, these are painful issues as they believe that having sequenced Henrietta's cells the scientists have sequenced them.

www.guardian.co.uk/world/2013/mar/31/henrietta-lacks-cancer-research-genome

PREVALENCE OF HPV TYPES PRE GARDASIL

Prior to the introduction of the Gardasil vaccination programme a number of women's health groups called for baseline research to be undertaken in order to identify the current HPV prevalence rates. Several articles appeared in the AWHC newsletter (1), and the Federation of Women's Health Councils wrote letters to the media pointing out the need for such a study in order to be able to monitor the impact of the Gardasil vaccine in NZ.

The results of a study of the types of HPV (human papillomavirus infection) in women aged 20-69 years who had cervical smears as part of the NZ National Cervical Screening Programme (NCSP) and were subsequently diagnosed with CIN2 or 3 (cervical intraepithelial neoplasia) or AIS (adenocarcinoma *in situ*) was recently published in BioMed Central's journal, *BMC Infectious Diseases*. (2)

One of the aims of the study was to measure the prevalence of oncogenic (cancer causing) HPV infection in women prior to the introduction of the HPV vaccination programme in New Zealand in 2008.

The second aim of the study was to compare oncogenic HPV prevalence in women with high grade cervical cell abnormalities or neoplasia with those in Australia and other regions.

The Gardasil vaccine offers protection against two types of HPV infection – 16 and 18 – that are responsible for the majority of cases of CIN2 and CIN3, as well as against HPV types 6 and 11 that cause genital warts. The vaccination programme involves girls aged 12-13 years receiving three shots of Gardasil, with the option of a catch-up for females aged up to 19 years who choose to be vaccinated later than 12 years of age.

The study found that among women with a high grade cytology report and a valid HPV test, the most common HPV types detected were HPV 16 (44%), followed by HPV 52 (16.8%), HPV 31 (15.2%) and HPV 18 (11.2%).

HPV 16 was the most common type in both New Zealand (51.4%) and Australia (51.4%), with HPV 18 infection rates being 12.1% in New Zealand and 9.2% in Australia. Significantly higher rates of HPV types 52, 58 and 68 were observed in New Zealand compared with Australia. The prevalence of HPV 52 was reported as 13.9% in Australia compared to 18.8% in New Zealand.

The NZ study revealed that for HPV types 16 and 18 prevalence peaked among women aged 20 – 29 years and fell with increasing age. The paper reports that "this age-related pattern of infection supports a proposed model of disease development that contends that HPV 16 is more likely to progress to CIN3 precancerous disease within a shorter period, whereas other types progress slowly and less frequently to precancerous abnormalities."

This study is important because it goes some way towards providing a baseline measure of oncogenic HPV prevalence in a population of New Zealand women, as well as providing a baseline for future similar surveys to assess the benefits of the Gardasil vaccination programme. The authors

state "our findings imply that the current HPV vaccination program in New Zealand, which involves delivery of a vaccine against HPV types 16/18, could prevent up to 62% of high grade lesions." They go on to list a number of assumptions that such estimates are based on, one of them being that HPV 52, 31 and 33 were not responsible for the development of the majority of high grade lesions in their study. They admit that if these assumptions do not hold "then the proportion of vaccine-preventable high grade lesions could be considerably lower." Quite.

There are a number of other factors that must also be taken into account when assessing the effectiveness of the Gardasil vaccination programme. These include the duration of the protection against HPV 16/18 offered by the vaccine, the possibility that other oncogenic types of HPV not included in the Gardasil vaccine take over as lead cervical cancer causing agents, and the fact that most HPV infections are cleared spontaneously with clearance occurring within one year for about 70% of HPV-infected women, and within two years for 90% of women. (3)

References

1. http://www.womenshealthcouncil.org.nz/Features/Hot+Topics/Gardasil.html
2. http://www.biomedcentral.com/1471-2334/13/114
3. Abby Lippman et al. "Human papillomavirus, vaccines and women's health: questions and cautions." *Canadian Medical Association Journal.* 28 August 2007; 177(5)

Australasian Association of Bioethics & Health Law Conference

11-14 July 2013

2013 is an auspicious year. It is:

- 25 years since the Cartwright Inquiry into the treatment of cervical cancer
- 21 years since the decision of Roger vs Whitaker which enshrined the doctrine of informed consent into Australian law
- 21 years since the High Court's decision in Marion's case which transformed the nature of parental consent to medical treatment in Australia
- 18 years since the creation of the NZ Code of Consumers' Rights.

This conference will provide a forum for discussion of several core concerns within bioethics and health care law.

For more information visit the conference website: www.cdesign.com.au/aabhl2013

UP AND COMING EVENTS

DISTRICT HEALTH BOARD meetings for May 2013:

Waitemata DHB (Website address: www.waitematadhb.govt.nz)

The **combined Waitemata DHB and Auckland DHB** Community & Public Health Advisory Committee meeting starts at 2pm on Wednesday 1 May 2013.

Waitemata Hospital Advisory Committee meeting starts at 11am on Wednesday 22 May 2013 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.

Auckland DHB (Website address: www.adhb.govt.nz)
The Hospital Advisory Committee meeting will be held at 9.30am on Wednesday 15 May 2013 followed by the Full Board meeting at 2pm. Both meetings will be held in The Marion Davis Library at Auckland City Hospital.

Counties Manukau DHB (Website address: www.cmdhb.org.nz)
The Hospital Advisory Committee meeting will be held at 9am on Tuesday 23 April 2013 and will be followed by the Community & Public Health Advisory Committee meeting at 12.30pm at 19 Lambie Drive, Manukau.

The Counties Manukau DHB Full Board meeting will be held at 1pm on Wednesday 1 May 2013 at 19 Lambie Drive, Manukau City.

'Australia-New Zealand Roundtouble on Genomics'

Sunday 4th August 2013 12 noon to 4pm in Queenstown

Ethical, Social and Legal Aspects of Next-Generation Methodologies, with particular reference to managing incidental findings and issues relating to prenatal diagnosis will be discussed at the 4th Australia-New Zealand Roundtable on Genomics.

This year, the Roundtable is jointly organised by the International Centre for Society, Governance and Science (SoGoS), led by the Faculty of Law - University of Otago, and the Ethics and Social Issues Committee (ESIC) of the Human Genetics Society of Australasia (HGSA). The sponsors include NZ Genomics Ltd and ESIC.

The Roundtable is open to the public. Registration is required as seating is limited, but there is no charge. Contact Richman Wee at richman.wee@otago.ac.nz or 021 623 622.