(Four) highways through uncertainty

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I thought my research career had started in 1984 when I published a review on episiotomy in the *Canadian Family Physician*. However, I was asked to give a talk in Adelaide in 2005 on my research journey and I realised, when I was preparing for that talk, that my research career had actually started with a question in 1974. At that time I was a medical student in my second year at the University of Auckland. Part of the course involved a child and family study, which involved meeting a woman who was pregnant, attending the delivery and then following the mother and child for two years. I had met the mother at the outpatient clinic in National Women's Hospital. At 2am on a cool May morning in 1974 I received a telephone call telling me that the study mother was in labour at National Women's Hospital and that I should make my way there. I was a little sleepy when I arrived at the delivery suite and, never having seen a live birth, I was somewhat overwhelmed by the atmosphere of the hospital, the bright lights, warm rooms and people running around in a busy state. I was not sure what was happening for most of the second stage, but just as the baby was about to be born, the registrar injected the perineum with local anaesthetic and picked up a pair of scissors and performed an episiotomy. I was completely unprepared for this procedure and, while the mother and baby were fine, I needed 'resuscitating'. I was completely 'shocked' by this procedure. The interesting aspect of this was that I did not discuss what had happened with my fellow students and have often wondered how often health professional students have traumatic experiences that they don't talk about.

National Women's Hospital 1980

In 1980 I started the Diploma of Obstetrics at National Women's Hospital. At that time it seemed that every woman having a baby would have an episiotomy. At the same time there was a home birth movement that was reasonably active in Auckland where virtually no woman received an episiotomy. To me this was difficult to explain. I asked many of the consultants and they defended the episiotomy procedure saying that while it was possible to preserve the perineum without performing an episiotomy the woman was likely to experience incontinence later in life. This was partly but not completely convincing to me.

McMaster University Canada 1981 Family Medicine Programme

I had been interested in the undergraduate medical programme at McMaster Medical School as a medical student as I knew it was problem based and that they had no examinations. In 1980 I was keen to do some training overseas and was looking at doing a Masters programme. I wrote to a number of programmes and one of the few that acknowledged me was the Family Medicine Department at McMaster University in Hamilton, Ontario. They said that they did not think I was ready for a Masters programme but would I consider being a resident (registrar) in family medicine. Needless to say I jumped at the idea of being able to work in Canada. While I was there one of the tutors was Brian Hutchinson who ran a course on critical appraisal. These papers became the 'how to read clinical journals' in the *Canadian Medical Association Journal*.[1] It turned out that McMaster was the centre of clinical epidemiology, which later became known as evidence-based medicine. This course gave me some rudimentary skills in critical appraisal.

Lillooet – Central British Columbia

After leaving McMaster University I worked in Fort St James in northern British Columbia in Canada and, after about 10 months there, moved to Lillooet in south central British Columbia. There I worked with three other family doctors and we ran a small (about 20 bed) hospital. The two senior doctors did anaesthetics and surgery, as was common in small towns in Canada at the time. During

the evenings and in my spare time I started to research the issue of episiotomy. To get the literature searches and articles that I needed I had to write to the Library of the College of Family Physicians of Canada, which was 3000 miles away in London, Ontario. They were very supportive and sent me the requests for articles. I could find no clinical trials of episiotomy and it appeared to have become a standard practice in the 1920–30s based on a 'good idea' rather than on any evidence. I even found a number of articles from Washington State that reported a number of deaths from necrotising fasciitis as a result of episiotomy. In 1984 I published an article titled *'Episiotomy in low risk patients'* in the *Canadian Family Physician*. It was my first publication that I had written.[2] At the time I did not know that there was a prize, known as the literary prize, for the best article in the *Canadian Family Physician*. My paper won it and I often feel that I am like a gambler who wins a big prize early on and goes on to be a problem gambler. This was the case with me, in that I came to like doing systematic reviews and have done many in my career. About the time my paper was published, the first randomised controlled trial was completed and this found that a restrictive policy for episiotomy was no more harmful in the short-term than a non-restrictive policy.[3] I did not realise at that time that the final author on that randomised trial was Iain Chalmers whom I was to meet 10 years later in Canberra where he was helping the Australians set up their Cochrane Centre. Iain is one of the truly admirable people that I have met in my clinical career. Later research showed that there did not seem to be any long-term problems in terms of incontinence or anything else. Ironically, my first paper received more dissemination than any article I have since written, as a Canadian newspaper chain reported the article and it went to every province in Canada.

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First highway through uncertainty

A Cochrane review on the topic of episiotomy reported that there appeared to be a number of benefits to a restrictive policy of episiotomy in terms of pain, suturing and posterior vaginal trauma with an increase in anterior vaginal trauma.[4] I present the Cochrane database as an example of an electronic reference source that provides clinicians with a pathway through uncertainty.

Biography

I was born in Devonport in Auckland, not in the Navy hospital as I had thought but in a private obstetric home. Such places no longer exist. I attended Murray's Bay Primary and Intermediate School and then went to Westlake Boys High School. I did first and second professional engineering studies at Auckland University then changed to the Auckland Medical School. Following two years as a house surgeon in Auckland I went to McMaster University in Hamilton, Ontario. I then worked in rural British Columbia and moved to Vancouver in 1985 where I completed a Masters degree in Clinical Epidemiology. In 1987 I taught in the Fairmont Family Practice supervising Family Medicine Residents for the University of British Columbia. In 1988 I started a PhD in the Department of Community Health under the supervision of Robert Beaglehole. I joined the Department of General Practice in 1991 and have been there ever since. In 2005 I became the Head of Department.

Antibiotics and respiratory tract infections

In 1996 my brother-in-law had a cold and went to his doctor. He was given the broad spectrum antibiotic Augmentin. Two days later he still had symptoms of his cold but now had diarrhoea from the Augmentin. I decided at that point that my mission in life would be to decrease the use of antibiotics for respiratory tract infections. The situation has improved considerably since 1996 when there were 1.2 million prescriptions of Augmentin filled in New Zealand. By 2003 it had decreased to 0.6 million. The cost of antibiotics in 1998 was $36m and by 2003 had fallen to $16m. This was a decrease in both volume and unit cost and a tribute to the efforts of Pharmac (*Pharmac Annual Report* 2003).

The antibiotic state of the nation

This is possibly not as good as it could be. A study conducted by Pauline Norris at the School of Pharmacy at Otago University found that 42% of the population of a small New Zealand town (population about 12 000) collected a prescription for antibiotics in 2002.[5] I found this figure quite alarming and discussed it with Professor Chris van Weel from Neimegen University in the Netherlands. He thought the rate of antibiotic use in his country was about 3% and thought that was too high. I am not sure what the ideal level is, but I suspect it should be less than 10%.

Our Department has done some work on the patient and GP issues for antibiotics. In a comparison of patients, 82% saw a GP in 1998 to get an antibiotic for a respiratory tract infection and this had decreased to 57% in 2003.[6] A survey of GPs over the same period found that 77%

were prescribing fewer antibiotics than in 1998, 2% more and 21% no change.[7] These are encouraging trends. This work triggered interest in the use of delayed prescriptions. We have since published a randomised controlled trial,[8] a systematic review,[9] an editorial[10] and a qualitative study[11,12] on this topic. The most interesting part of the systematic review was the 75% reduction in the use of antibiotics for otitis media in children aged over the age of two years. This has led to a major change in the practice of giving a routine antibiotic in patients with acute otitis media.

Our group conducted a qualitative study on patients who had been in our delayed prescription randomised trial. This was my first involvement with a qualitative study. Two insights emerged from this. We found two GPs who no longer used delayed prescriptions as they had already 'trained' their patients not to expect antibiotics for respiratory symptoms. These two GPs would have appeared in a regular questionnaire as non-users and we would not have been aware that there is the opportunity to train a practice. The other insight was that resistance to antibiotics by micro-organisms was an issue for doctors but not for patients.

Augmentin-free office

As a result of this work, Dr Tana Fishman and I have created the 'Augmentin-free office' where, if a doctor wants to prescribe Augmentin, he or she needs to explain the clinical circumstances to a colleague to get their 'permission' to prescribe it. This reinforces with students that it is a very broad spectrum drug that should be used with caution.

The second highway through uncertainty – pre-test probabilities

There is an issue that I am keen to get across to colleagues and medical students and that is the issue of pre-test probabilities. This sounds like a fancy name for what is really the prevalence of an illness. When an individual patient presents to us in clinical practice they have a point prevalence of a number of conditions. For example, on average 5% of patients presenting to us have a major depression. The pre-test probability is a little higher for anxiety. From work I have done with a PhD student, Natalie Khin, we know that 25% of Maori women will have a major depression on any one day. This is a startlingly high figure. Diagnosis is all about probability and when I teach diagnostic tests I ask the audience if they have done a diagnostic today. Unless they are practising clinicians the answer is invariably no. However, I then say that if you asked someone how he or she is, you have just done a diagnostic test. Every question and examination we ask or do to patients is a diagnostic test. The way this works is that when a patient presents to me for any condition, if I ask how they are and they say terrible they score a positive for major depression and their risk goes up from the 5% to say 10%. If they say they are feeling fine their risk goes down to say 3%.

Table 1. This table explains 'all' of clinical medicine

	Low prevalence	Medium prevalence	High prevalence
	(screening every one we see e.g. mammography)	(assessing patients with a breast lump)	(patient with suspected disseminated breast cancer)
Problem	False +ve	Tests work well	False -ve
Strategy	Do another test or gold standard or delay intervention if safe to do	Biopsy Treat +ve don't treat -ve	Scan for metastases Treat or perform gold standard

When I teach diagnostic tests I ask the audience if they have done a diagnostic today. Unless they are practising clinicians the answer is invariably no. However, I then say that if you asked someone how he or she is, you have just done a diagnostic test

I have a story to tell about a friend of mine. She is a 52-year-old European woman who had a cold for a week and during that time she developed bilateral ear pain. She went and saw a young doctor at an accident and medical clinic (whom I hope may have been a house surgeon moonlighting). He could not see her ear drums and said, *'I think you have an ear infection'*. She was given a week of amoxicillin and given careful instructions on how to take it. She was very satisfied with her care. She called me one week later to say that her ear pain had not gone away and on the phone I told her that she did not have an ear infection and the antibiotics would have done nothing for her. I went around to her place to see her and both her ear drums looked perfectly normal and she had probably never had an ear infection in her life. When I tell students this story I say that she died on day two from the antibiotics (this is not true) to highlight the fact that every year in New Zealand about one to two people die from everyday antibiotics that we use, i.e. trimethoprim, doxycycline, amoxicillin and augmentin to name a few. The causes are usually due to effects on the bone marrow or liver rather than due to allergy (the CARM group have not reported results since 1997 but up until then there were at least one or two deaths each year). In terms of pre-test probabilities my friend

had a 0.000001% chance of having an acute otitis media while her chances of having a bilateral eustachian tube dysfunction would be about 99.999999%. Unless the clinician saw a bulging drum this would not change the situation. Where do these pre-test probabilities come from? They come in my case from experience or from the literature. For the young doctor I can only presume that 'all' the cases of ear pain that he had seen were probably otitis media as he would be unlikely to see eustachian tube dysfunction in a hospital setting.

I like to say that Table 1 explains all of clinical medicine and if you understand it this may keep your name off the front page of the *NZ Herald*. It shows that the purpose of taking a history is to take presenting individuals with a low initial pre-test probability, via a series of questions and examinations, to a medium prevalence when tests such as blood tests and radiography can be done, or to a high prevalence, when treatment can be initiated. In low prevalence settings such as screening for breast cancer we expect false positives. There is no way around this unless you are using the gold standard, i.e. it is a mathematical certainty. If you do tests in a high prevalence setting and these show a negative result, you need to be careful about false negatives. A good example of this is a patient with suspected streptococcal tonsillitis who has a temperature of 39°C, tender anterior cervical neck glands, no cough, aged under 14 years and who has swollen tonsils with pus on them. The pre-test probability of a streptococcal tonsillitis is about 50%, so the risk here would be doing a throat swab and getting a negative result, which in this case would likely be a false negative.[13]

We can mean quite different things with words that we think are communicating what we are thinking

The third highway through uncertainty – numbers needed to treat

Our young doctor in the after hours clinic may have found it helpful to know that the numbers needed to treat to reduce pain at day two in a child with otitis media is 17. If he had thought that is what my friend had had he may have been less enthusiastic about giving her an antibiotic. There is no data in adults as it is such a rare condition. I recently had a medical student say to me that a treatment was moderately effective for the condition we were discussing. My reply to this was what did he mean by 'moderately effective'. I would like to suggest that we sometimes need numbers to communicate effectively with our colleagues. There is evidence for this from a letter from the *New England Journal of Medicine* in 1980.[14] There they asked physicians what they thought the per cent risk would be if a person had a moderate risk and they answered between 20% and 75%. For pathognomonic (which I always thought was absolutely certain) the range was 55% to 100%. For high probability this was 55% to 95%. So you can see that we can mean quite different things with words that we think are communicating what we are thinking. There is controversy about using numbers needed to treat as these can differ considerably from study to study for similar conditions. However, for a person who has had a heart attack or angina, 11 people need to take the powerful cholesterol lowering drug, simvastatin, to prevent one new cardiovascular event.[15] This is a medication that most doctors think is a fantastic drug, yet most individuals taking it will not benefit from it. The same goes for antidepressant medication, for which about eight patients need to take an antidepressant for eight to 12 weeks to get a remission, so again, most people will not benefit.[16] About half of those eight will get better as a result of the placebo and, potentially, there are another three who may not benefit from this treatment but may get better from something else. There are some who may not get better from any treatment. I like to mention to students that most people don't get better from most medications, as I feel there is an impression among students and

Table 2. Summary of 'Four highways through uncertainty'

Resources	Examples	What we learn
1. Electronic resources such as the Cochrane Library		Good summaries of evidence
2. An understanding of the prevalence of conditions in our setting. Pre-test probabilities is the term used for this	E.g. 52 year old adults rarely get otitis media	That a diagnosis is likely or unlikely to be correct depending on the prevalence
3. Numbers needed to treat	E.g. 11 patients who have coronary heart disease need to be treated with a statin for five years to prevent another vascular event	That most patients do not benefit from most medications
4. Electronic clinical textbooks	Four clicks on uptodate.com to get a complete updated list of treatments	That with good resources we can get fast evidence-based information and that textbooks are only useful during power cuts

colleagues that 'everyone' gets better with antidepressants or antibiotics. I will present an example of some work Dr Tim Kenealy and I have done on acute purulent rhinitis. You may wonder why we are interested in coloured mucus coming from the nose. It is because this is the major predictor of antibiotic use in the United States. We recently published a systematic review on antibiotics for this condition in the *BMJ*.[18] The numbers needed to treat to improve this condition is between seven and 15. Our recommendation was that as this is not usually a serious condition we would suggest not using antibiotics initially. As with the other medications most people do not benefit from treatment.

The fourth and final highway

In terms of finding a way through the uncertainty of clinical work, the electronic clinical textbooks are providing a solution. There are a number of these. One of the best known is *Clinical Evidence*. There are also three other freely available UK textbooks. The best ones from our limited assessment are the three from the USA that cost variable amounts of money. They are uptodate.com, mdconsult.com and dynamicmedical.com and we are currently conducting a randomised controlled trial on the one most preferred by GPs and their use of this over three to four months. Their cost ranges from about $US490 for the first to about $US200 for the last one. From the GP point of view a good clinical textbook needs to be comprehensive, valid and quick to access. If it is not comprehensive then time is wasted going to the website only to find no answer. I can confidently say that for almost any reasonably common problem you can find an answer in a few minutes. I recently had a reporter with me and I made this claim. She suffers from Rosacea, which is an acne like condition that affects individuals in middle age. I went to uptodate.com and in about four clicks of the mouse was able to show her two summarised pages on treatments for this condition. The article has numbered references and if you click on the number you are taken to a page on which there is an abstract from Pubmed. If you wish to find out the details of a medication you click on the name of it and you are taken to an electronic page with all the details of the medication including the US names of all the medication, the indications, doses and adverse effects. I next went to patient.co.uk and printed out two very patient-oriented handouts on Rosacea. All this was accomplished in about four minutes. I had all the answers I needed and she had all the information she needed. In a real consultation the next step would be negotiation.

In terms of finding a way through the uncertainty of clinical work, the electronic clinical textbooks are providing a solution

So, in summary, we need 'pathways' through the clinical uncertainty in both general practice and hospital settings. I have mentioned four tonight (summarised in Table 2): Cochrane, pre-tests, NNTs and electronic text. If we can use these concepts and tools then I see a very high standard of clinical care in the future.

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