Changing the face of clinical trials

Drawn to palliative care because relatively little empirical work has been done with the terminally ill in the primary care setting, UC’s Professor Philip Schluter believes there is a wealth of research that needs to be done in this area in New Zealand and elsewhere.

“Ethics is always a consideration with these patients and the emphasis on evidence-based research in a biomedical framework often demands a more detached, rather than human approach, which may not always be in the best interests of the patients,” says Schluter, Head of the School of Health Sciences.

Moreover, most of the thinking, analysing and structuring of clinical research designs is currently predicated on the fact that the studied condition deteriorates in a predictable fashion over the course of the trial. This is not the case in palliative care and we need to recognise this and include it in the way we understand and present information so we get a better reflection on response or not.”

One of Schluter’s areas of expertise is in methodological development with particular skill in n-of-one trials, or single patient clinical case studies. These trials, compared to randomised controlled trials (RCTs), represent individualised medical care and provide stronger evidence about the effectiveness of a treatment for an individual patient. This gives a better reflection of response for informing palliative care and we need to recognise this and include it in the way we understand and present information so we get a better reflection on response or not.

One problem with conventional RCTs is that they can only deliver a group response, which doesn’t necessarily apply to the individuals within the group,” says Schluter.

“One of our recent n-of-one trials used psychostimulants to address chronic fatigue in advanced cancer patients. Many were highly respondent, some were not and a few had a negative reaction.”

“However, if this were to have been done as a conventional RCT, no difference would have been observed and therefore the treatment not supported. The strength of the n-of-one trial is that it can show the treatment did work for some, but not for others, meaning we can recommend continuing the treatment for a responsive sub-group.”

Schluter says that this evidence can frequently only be indicative, and needs to be integrated with other indications before a conclusion can be drawn.

“This encourages clinicians to find additional information to define what a responder is and if a treatment should be pursued which, in itself, is a welcome shift away from wholly evidence-based medicine approach or thinking.”

“Within the old hierarchy of evidence, clinical experience used to be on the bottom of the pyramid, and has now been removed altogether. Empirical evidence is definitely important, but it is only one tool in the decision-making arsenal. Things like the patient history and profile, past experience and discussions with colleagues, particularly when a patient presents a complex case, need to be integrated in a coherent decision-making framework.”

Schluter says single patient trials are not a new concept.

“Although its formal uptake in medicine has only been recent, its principles have been employed throughout the ages and it’s actually very similar to what happens whenever we consult a GP with a condition. The GP will often suggest some treatment and, if we respond, that’s great. If not, then they’ll likely suggest something else. It could be a change of medication, a different dose, some change in environmental effects or another factor entirely. N-of-one trials introduce rigour into these investigations in a controlled research framework.”

Schluter first became involved in single patient trials research at the Queensland Clinical Trials & Biostatistics Centre at the University of Queensland (UQ) in Australia, which was created to formalise n-of-one trials and find a scientifically rigorous way to assess single patient consultations.

Schluter’s collaboration with the UQ centre continues, alongside Queensland Health, through joint clinical trials, particularly in the palliative care area. He was recently part of an international collaboration with researchers from England, Australia and elsewhere that was formed to establish guidelines for n-of-one trials to support the Consort Statement — an international body that sets standards for good quality research and reporting. This group is now drafting a textbook on the subject.

Through his work, Schluter has also developed a passionate interest in the health and wellbeing of marginalised peoples. Until his appointment as Head of UC’s School of Health Sciences, Schluter co-directed the Pacific Islands Families Study, a longitudinal study that started in 2000.
The cohort comprises 1,500 mothers, fathers and children, and the study has followed the children through from their birth to their present day ages of 13 to 14 years.

While no longer a co-director, Schluter is still actively involved in this highly collaborative work, which involves researchers from the Auckland University of Technology, Victoria University of Wellington and Otago University, as well as overseas universities including Harvard University.

“Work going forward in population health really benefits from strong collaborative teams,” says Schluter.

“That’s how advances will be made, especially in areas like epigenetics. This is the international trend and what I’m part of — bringing together the different expertise needed, which can include clinicians, epidemiologists, health economists, sociologists, anthropologists, coroners and others, all working alongside each other to improve all people’s health outcomes and negate inequality.”

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By Jann O’Keefe