It’s not the evidence, it’s the way you use it: is clinical practice being tyrannised by evidence?

My experience with the PBAC and evidence-based practice

Kathy Stiller

“Good doctors use both individual clinical expertise and the best available external evidence, and neither alone is enough. Without clinical expertise, practice risks becoming tyrannised by evidence, for even excellent external evidence may be inapplicable to or inappropriate for an individual patient.”1 (p. 72)

I am a senior physiotherapist and clinical researcher and in the comparatively early stages of a sero-negative spondyloarthropathy that may well develop into full blown ankylosing spondylitis (AS). The severity of my symptoms was such that in 2005 I had to relinquish the full-time position I had held for 21 years and reduce my working hours to 12 hours per week in a non-clinical role. To set the picture of my symptoms at their worst, I was unable to sit for more than a few minutes a day because of severe axial pain, forced to do all work in kneeling, standing or lying positions, with social activities likewise restricted. In order to sleep I often needed strong analgesia and icepacks, only to wake 2–3 hours later. Life was pretty tough. After little response to conventional medications, I started a tumour necrosis factor α (TNF-α) blocker (Infliximab) in March 2007 with a significant and dramatic response. As well as markedly decreasing my pain and fatigue, and improving range of movement, function and quality of life, Infliximab has enabled me to commence some additional part-time work as a medical writer.

Despite my positive response to Infliximab, I do not even come close to meeting the criteria for Pharmaceutical Benefits Scheme (PBS)-funded Infliximab or any other TNF-α blocker, and thus have to pay for it myself. Because of the high cost, I initially tried a low dosage regimen, but after a few months it became clear that this was not sufficient and I am now on the full recommended dosage regimen of Infliximab for AS, which I will need indefinitely. This is costing me about $20,000 per year, which is proving very difficult financially. In this article I discuss some of my impressions regarding the way in which the Pharmaceutical Benefits Advisory Committee (PBAC) makes decisions regarding the PBS listing of drugs. While I have written the article from my personal perspective, I am also writing on behalf of other Australians who are in a similar position and do not have a “voice”. While the sentiments expressed in this article are somewhat negative, I have had many positive experiences during my illness, in particular encountering some truly kind and empathetic health care professionals, often in the most unexpected settings, and friends who have been supportive when it really counts, but that is another story, for another time perhaps.

In an attempt to defray the costs of Infliximab, I wrote to, among other bodies, the PBAC. The reply was sympathetic, but essentially unhelpful, and included the comment that “The PBAC and the Government are committed to using sound evidence-based principles to identify the scope of PBS listings . . .” Despite this assurance, Australian rheumatologists have noted that the current strict criteria used to assess eligibility for PBS-funded TNF-α blockers for AS are not evidence based, favouring patients with established disease yet denying treatment to patients with shorter disease duration, even though younger patients are the

Kathy Stiller. PhD, BAppSc(Physio), Adelaide, SA.
Correspondence: Dr Kathy Stiller. kathys@internode.on.net
ones most likely to have best outcomes and achieve the disease modifying effects of TNF-α blocking therapy.\(^2\) Also, it would seem that the PBAC require clinical evidence for the effectiveness of medications for each specific condition and every clinical scenario before they will list a drug on the PBS for that specific condition.\(^3\) As someone with a long-standing career in clinical research and many publications, I know only too well that clinical research necessitates tightly defined inclusion criteria in order to achieve an homogenous study sample. However, surely this does not mean that the results of the research are only applicable to patients who meet the exact or very similar criteria? Moreover, while the PBAC state that all levels of evidence will be considered, they note that direct randomised clinical trials are most influential in submissions.\(^3\) To quote Sackett et al\(^1\) (p. 72): “Evidence based medicine is not restricted to randomised trials and meta-analyses. It involves tracking down the best external evidence with which to answer our clinical questions … if no randomised trial has been carried out for our patient’s predicament, we must follow the trail to the next best external evidence and work from there”. While I do not dispute the value of randomised controlled trials, and fully understand why the PBAC look first at such data, isn’t it unrealistic to expect high-level evidence to cover the use of TNF-α blockers in every clinical scenario? Shouldn’t the lessons learnt from the evidence that is currently available (eg, for advanced AS) be translated to other similar clinical scenarios when conventional treatment has failed, even though there may be no direct high-level evidence? For some patients with unusual presentations or who are early in the disease process, high-level evidence will never be available. Indeed, highly respected text books such as Harrisons Principles of Internal Medicine\(^4\) recommend the use of TNF-α blockers for a much wider range of spondyloarthropathies than is currently covered by the PBS, as do most rheumatologists in everyday clinical practice.

It would also seem that the PBAC rely almost exclusively on clinical evidence in isolation to recommend/decline drugs for PBS listing.\(^2\) Evidence-based practice (EBP), as noted by Sackett et al,\(^1\) requires the integration of best available clinical evidence from systematic research and individual clinical expertise. By only considering research-based evidence, the PBAC are disregarding the role of clinical expertise as a linchpin of true EBP.\(^1\) Sackett et al\(^1\) noted (p72): “External clinical evidence can inform, but can never replace, individual clinical expertise, and it is this expertise that decides whether the external evidence applies to the individual patients at all and, if so, how it should be integrated into a clinical decision.” While I understand that the PBAC cannot themselves use clinical expertise in their decision-making process, perhaps true EBP could be achieved by the PBAC working in closer collaboration with rheumatologists?

The letter from the PBAC also noted that, “The system would be unworkable if patients were assessed individually for PBS eligibility or the merits of individual circumstances were judged on a case-by-case basis”. I fully agree that the same requirements should be applied to all cases to ensure consistency and fairness in the PBS-eligibility process and indeed it would be inappropriate to make exceptions in individual cases. However, the criteria that are currently required for AS patients to receive PBS-funded TNF-α blockers already require individual patient assessment in rheumatology clinics. Would it not be possible to devise broader criteria to cover patients like me who fall outside the current strict requirements? For example, potential patients could be identified by their rheumatologists, have a clinical condition severe enough to significantly impact on quality of life and functional ability (measured using standard outcome measures), with an inadequate response to conventional medications. Perhaps such patients could demonstrate a willingness (and hence sufficient desperation) to fully self-pay for a TNF-α blocker for a trial period of at least 6 months (means tested). The degree of clinical response to treatment with a TNF-α blocker could be measured (using the same outcome measures). An independent review board could be set up to screen patients for eligibility, and an audit system established to
ensure the system is not misused. While broad criteria such as these rely on individual assessment of patients by rheumatologists, they could be applied consistently and fairly, and would be no more unworkable than the current requirements to obtain PBS funding for TNF-α blockers. They would provide hope to “outlier” patients like me who, as my case clearly demonstrates, have as much, if not more, potential to benefit from TNF-α blockers as those currently receiving PBS-funded treatment. In the Republic of Ireland, patients with a sero-negative spondyloarthropathy receive funded treatment with TNF-α blockers based totally on the discretion of the prescribing rheumatologist (personal communication; Oliver FitzGerald, Newman Clinical Research Professor, Dublin; Ronan Kavanagh, Consultant Rheumatologist, Galway; Douglas Veale, Professor of Medicine and Consultant Rheumatologist, Dublin; 2007). Interestingly, a recent study comparing patients with rheumatoid arthritis in Ireland and The Netherlands (where prescription of TNF-α blockers is tightly regulated) showed that selection of patients for TNF-α blockers in Ireland was more stringent, and the clinical response greater, despite the absence of strict regulatory conditions.5

I note on the front page of the PBAC Outcomes website that “The PBS ensures that all Australian residents have access to necessary and lifesaving medicines at an affordable price”.6 Is Infliximab a necessary medicine for me? Is $20,000 a year an affordable price? If the unwillingness of the PBAC to expand the conditions eligible for PBS-funded TNF-α blockers is primarily due to the high cost of these drugs, which would be understandable, couldn’t the PBAC/PBS look at a shared-funding arrangement with the patient (means tested)?

In conclusion, in clinical practice rheumatologists in Australia, using best available clinical evidence and their clinical expertise, recommend treatments such as TNF-α blockers to spondyloarthropathy patients like me with disabling symptoms who have had an inadequate response to conventional therapy. Rheumatologists are best placed to identify these patients and make this recommendation — it is not made lightly and is done with the knowledge that these drugs may not be PBS funded and that their extremely high cost will put them beyond reach of most patients. Rather than forcing Australian rheumatologists to practice with one hand tied behind their backs, couldn’t the PBAC support and empower rheumatologists by working in closer cooperation with them, in keeping with the true meaning of evidence-based principles, namely using best available clinical evidence and clinical expertise? This would ensure that all patients who would benefit from TNF-α blockers, in terms of quality of life and productivity, could receive them at an affordable price and go some way towards resolving the current inequalities in delivery of health care to Australian patients with AS and other spondyloarthropathies.

To re-quote Sackett et al1 (p. 72), “Without clinical expertise, practice risks becoming tyrannised by evidence, for even excellent external evidence may be inapplicable to or inappropriate for an individual patient.” Are the PBAC tyrannising clinical practice by the way they interpret evidence and EBP? There is little doubt that there are other Australian patients with sero-negative spondyloarthropathies whose quality of life could, like mine, be markedly improved by PBS-funded TNF-α blockers. But for us, the PBAC is impenetrable. Is there any way to encourage the PBAC to reconsider their stance on this issue?

Competing interests
The author declares that she has no competing interests.

References


5 Radovits BJ, Ng CT, Klevit W, et al. Differences in selection criteria and clinical outcomes to anti-TNFα therapy in patients with rheumatoid arthritis in two European countries. American College of Rheumatology/Association of Rheumatology Health Professionals Annual Scientific Meeting; 2007 Nov 6-11; Boston, USA. Available at: http://www.rheumatology.org/annual/07wrapup.asp (accessed Jan 2008.)


(Received 6/02/08, accepted 5/03/08)