Determining research priorities for clinician-initiated trials in infectious diseases

Randomised controlled trials (RCTs) are accepted as the best type of study to assess the effects of health care interventions and therefore have a pivotal role in evidence-based medicine.1 A new paradigm is emerging whereby RCTs are now being undertaken by a network of clinicians.2

Clinician-initiated RCTs have several features that differentiate them from industry-sponsored studies. They are more likely to compare generically available, off-patent medications, or to study processes of care or non-pharmacological interventions. As clinician-initiated trials are financially independent of industry, with their funding source being governmental research organisations (e.g., the National Health and Medical Research Council [NHMRC]), the results are viewed by clinicians as more credible.3 The NHMRC has already demonstrated a willingness to fund clinician-initiated RCTs, as shown by the success of networks such as the Australian and New Zealand Intensive Care Society Clinical Trials Group.4-7 The impact of their successfully completed trials on practice change, cost savings and improved patient outcomes has not been formally measured but is likely to be significant.

Another key advantage is that clinician-initiated RCTs tend to investigate issues that clinicians find most important and relevant to their practice. Moreover, the process of engagement with other clinicians is a crucial one. If investigator-initiated studies are to successfully recruit patients, there needs to be an appreciation by other clinicians that the studies have realistic comparators and clinically significant end points.

To facilitate physician engagement and training in clinical trials methodology, the Australasian Society for Infectious Diseases Clinical Research Network (ASID CRN) was established in 2009. This report summarises the results of an online survey of infectious diseases physicians, conducted by the ASID CRN, to establish its research priorities.

Methods

In 2012, a self-reported online questionnaire-based survey was administered on behalf of the steering group of the ASID CRN. The survey was developed by the ASID CRN steering group, who compiled a list of more than 100 potential studies: 42 potential randomised controlled trials, 20 epidemiological studies and 40 observational studies registries. These studies pertained to bacterial infections (69 of the nominated studies), viral infections (18), fungal infections (10), mycobacterial infections (3) and general aspects of clinical infectious diseases practice (3).

A “short list” of these studies was selected by the ASID CRN steering group to be sent to the entire community of members of ASID, comprising most practising infectious diseases physicians in Australia and New Zealand. The ASID members were asked to rate the proposed studies within each group: (a) RCTs, (b) epidemiological studies, and (c) registries of specific infectious diseases, using a numerical scale (with 1 being of little likely clinical significance and 5 being of greatest clinical significance). To determine the feasibility of the proposed studies, the physicians were also asked to estimate the number of patients seen at their hospital in the past year with each of the conditions relevant to the proposed clinical trial. Additionally, they were asked to describe barriers to enrolment of study patients at their hospital.

Results

Of the 550 clinicians approached online, 122 (22%) responded to the survey. The RCTs ranked by the ASID members as having most potential clinical significance are listed in Box 1. Foremost among these were RCTs investigating prosthetic joint infections, native joint septic arthritis or osteomyelitis, Staphylococcus aureus bloodstream infections, diabetic foot infections and the treatment of serious multiresistant, gram-negative bacterial infections. Lack of funding was the most important perceived barrier to participation in clinician-initiated RCTs.
The surveyed clinicians also supported further study of emerging infections (eg, multi- or extensively drug-resistant tuberculosis or unexplained encephalitis) by way of registries or epidemiological studies.

Barriers to performance of clinician-initiated studies are listed in Box 2. The most commonly perceived barrier was lack of funding for conducting studies, followed by absence of infrastructure or study personnel, and lack of time owing to clinical commitments.

**Discussion**

A number of features dominated the research preferences of Australian and New Zealand infectious diseases physicians. RCTs investigating optimal treatment of commonly encountered infections were highly ranked, highlighting the lack of well-conducted RCTs in this area. Investigations into optimal therapy of antibiotic-resistant organisms were also identified as a priority.

Clinician-initiated research presents a number of advantages over research sponsored by pharmaceutical companies. The primary focus of clinician-initiated research is to answer problems of direct clinical relevance, while that of pharmaceutical companies is to obtain regulatory approval for new, patented products. Additionally, the impact of clinician-focused research is, in many cases, cost-savings to the health care system, while that of company-initiated research is the introduction of new and often expensive drugs or devices. As an example, the four highest-ranked RCTs proposed by Australian and New Zealand infectious diseases physicians dealt with reducing the duration of courses of intravenous antibiotics (Box 1). RCTs whereby medications are used less are unlikely to be of interest to industry. RCTs that allow the rigorous evaluation of recommendations in guidelines are likely to be of particular value to clinicians, and those that reduce the duration of intravenous antibiotic courses are likely to reduce costs for governments and, potentially, reduce adverse events for patients.

Steering groups, comprising both researchers and clinicians, have now been established to develop protocols, seek funding for the trials and initiate the studies most highly ranked by clinicians.

Could the methodology and results of our survey of infectious diseases physicians be of use to other clinicians? More than 90 research networks of collaborating clinicians currently exist in Australia (http://australianclinicaltrials.gov.au/). Some of these networks are well established and have been highly productive, completing a number of high-impact studies. Others are nascent, like our own, and may seek to replicate our methodology.

There are significant challenges in the initiation and conduct of clinician-initiated studies. Foremost of these is funding, which was regarded in our survey as the single largest barrier to studies being conducted. Other potential difficulties included time-consuming processes for (and cost of) ethical approval, and lack of support and infrastructure in cash-strapped hospital systems. Innovative solutions to these barriers should be sought — other research networks (eg, Australian and New Zealand Intensive Care Society Clinical Trials Group) have received funding from foundations.
and the NHMRC. In addition, the private hospital system may be an untapped resource for clinician and administrative support.

A limitation of our study was the low response rate of 22%. This is to be expected given the nature of online surveys. The research priorities chosen may not necessarily reflect those of all members of ASID.

We have described here a method for giving practising clinicians a central role in the selection of clinical studies. We hope that this will facilitate not just the planning and conduct of these studies, but also their rapid implementation into clinical practice.

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