Building a bridge from the swamp to the ivory tower

Conducting randomised controlled trials in general practice

Clare Heal, Jennifer Banks, Pranav Divakaran, Petra Buttner

Background

Primary care research is underfunded. Few randomised controlled trials (RCTs) are conducted in a primary care setting. However, it is important that clinical practice be informed by adequate primary care evidence so general practitioners (GPs) have tools and guidelines applicable to the patients they see.

Objective

The aim of this article is to describe and reflect on the experience of conducting five RCTs between 2003 and 2017 in a general practice setting with minimal funding, in North Queensland.

Discussion

Enabling factors include using grassroots research questions and engaging practice nurses. Barriers include ethics applications and insufficient funding. Recommendations to reduce study costs include compensating practice nurses rather than GP time. The findings are designed to encourage grassroots GPs to consider participating in pragmatic, feasible projects. The success of the projects was underpinned by the fact that they were established by a group of GPs who had interesting questions that were relevant to their clinical practice and not answered by current evidence.

PRIMAR HEALTHCARE SYSTEMS must be evidence-based in order to be both streamlined and effective and, therefore, must be supported by rigorous research. It is important that clinical practice be informed by adequate primary care evidence. Otherwise general practitioners (GPs), the end users of the research process, who attempt to practise evidence-based medicine, may have flawed tools, and the guidelines they use may not be applicable to the patients they see or the processes they use.1,2

Medical research in Australia has mostly been conducted in tertiary hospital settings, but as the majority of illnesses are managed in primary healthcare settings,4 there is a need for a change in focus.4 Funding allocated to primary care research has a greater potential population impact, compared with research in other specialties,5 with 82% of the population visiting their GP in the past 12 months.6 There is compelling evidence that the strength of a primary care system in a region or country predicts the health status of the population.7 Studies suggest that stronger primary care systems, and investment in primary care research, lead to better health outcomes at a lower cost.7–9 However, despite outstripping other areas of research in value for money and clinical importance, funding for primary care research in Australia is disproportionately low, particularly when compared with the UK and the Netherlands, with only 2% of National Health and Medical Research Council (NHMRC) grants awarded to primary care research between 2000 and 2008.10

Primary care and general practice research in Australia have been criticised for conducting mainly small-scale descriptive and survey-based studies.11 Few large randomised controlled trials (RCTs) are conducted in a primary care setting;12 RCTs comprised 5% of general practice research projects conducted in Australia in the 1990s.13 RCTs have been reported as being methodologically and practically difficult to conduct in general practice.13,14

Barriers to GP research participation include lack of training in research methods, absence of clearly defined clinical research career pathways, underdeveloped research infrastructure and inadequate project funding.15 While The Royal Australian College of General Practitioners (RACGP) and other professional bodies in Australia are working to overcome some of these barriers, there is a lack of government funding to support these activities.

Some specialist training programs mandate trainee research, but there are no specific requirements as part of current GP training. There does not appear to be a ‘culture’ of research in general practice, and GPs do not see themselves as potential researchers.14 Grassroots general practice research has been described as the ‘swamp’ and academia the ‘ivory tower’;17 as such, there is a need to bridge the gap between these two institutions in order to create a culture of research.

The aim of this review is to describe and reflect on the experience of conducting a series of five successful RCTs in a general practice setting, with minimal funding, in North Queensland, Australia.10–21 Enabling factors and barriers are identified (Tables 1, 2), as well as recommendations to reduce study costs (Table 3). The lessons learned from these experiences
CONDUCTING RANDOMISED CONTROLLED TRIALS IN GENERAL PRACTICE

The research process

Background
Between 2003 and 2017, five randomised controlled trials were conducted in Mackay, North Queensland (Table 4). Mackay is a provincial town in tropical North Queensland with a population of 125,000. In 2017 there was a total of 104 GPs practising in the Mackay region. Between one and four general practices were involved in the five trials; one practice was involved in all five trials.

Establishment of research group
Before commencing the first project, there had been a long-established GPs’ evidence-based medicine group, which met on a monthly basis. The history of how this group was established is unclear, although the group had existed since the early 1990s (Del Mar, personal communication). Around 15 GPs attended these meetings on a regular basis, with a rotating chairperson. The meeting room and catering were funded as in-kind support by the local private hospital. Meetings involved the delivery of conference reports, discussion of interesting cases, or presentation of evidenced-based medicine literature reviews, and GPs were awarded professional development points for their attendance. Research questions were generated and GPs and general practices were recruited for the trials through these meetings. Unfortunately, the evidence-based medicine meetings ceased in 2014. However, the North Queensland Practice-Based Research Network evolved out of this group and still remains actively engaged in research in 2017.

Research career of principal author/investigator
The principal author/investigator of the RCTs first embarked on a research project in 2000, shortly after gaining fellowship of the RACGP, with a Primary Health Care Research, Education and Development (PHCRED) novice research fellowship. She was awarded additional project funding from the RACGP registrar research fund. She then gained a fractional university position, and incorporated the first two of the five RCTs in her masters and PhD programs. She progressed to a full-time university position, and a promotional chair. The final three RCTs were conducted by medical students undertaking the Honours program under her supervision.

Choosing a research question generated by clinicians
Practical questions and clinically relevant questions were generated by grassroots GPs. The ‘wetting sutures’ research question evolved from two senior group members while driving to an evidence-based medicine meeting. A heated discussion ensued regarding the topic (whether wetting and uncovering sutures in the first 48 hours following minor excisions could increase infection rate) and gave rise to the first trial.20 The sterile gloves project evolved from doctors at a single medical centre differing in the type of gloves that they used for minor procedures, and wishing to resolve their disagreement.21

For the AVALANCHE trial, local clinicians were first consulted to decide which antiseptics were most relevant to clinical practice. Most clinicians did not use betadine because of perceptions of ‘messiness’ and skin staining. Therefore, the investigators designed the project to examine the difference between alcoholic and aqueous chlorhexidine, rather than comparing the relative efficacy of chlorhexidine and betadine.22

Choosing a unique research theme
Skin excisions form a large proportion of Australian GP workload and this is greater in Queensland, which has the highest incidence of skin cancer in the world.23 This is further magnified in regional towns such as Mackay, where there are no permanent dermatologists or plastic surgeons. All of the trials focused on management of skin excisions in general practice, which increased the feasibility of recruitment. Additionally, the high infection rate in the tropical setting meant sample size requirements were attainable.

Research funding
The projects received small grants from PHCRED or RACGP Research Foundation (Table 1). Funding was available quickly (within three months of application), in contrast to a possible 12-month turnaround for competitive grant schemes such as those of the NHMRC.

Ethics approval
Although ethics processes are becoming more streamlined, and ethics committees can now often give multicentre approval, ethics clearance still took a minimum of three months for each project.

Project planning and design
The research design and methods were developed by the group of co-investigators, including GPs and practice nurses, led by the principal author. Sometimes, the design was modified for the sake of pragmatism, and the protocol had to be acceptable to all practices involved. For instance, in the first trial doctors refused to use a random number table and opaque envelopes, perceiving the process as too complicated, so patients were consequently randomised by pulling labelled pingpong balls out of a bag.

Minimise work for GPs
The studies involved very little extra work for participating GPs – they were not responsible for data collection, but were required to have knowledge of the process in order to answer any possible queries.

Use of practice nurses
Practice nurses were responsible for data collection, and were paid on a fee-for-service basis for each of the trials ($5–10) to complete data on each patient.

Acknowledgement of all contributions
All contributors were acknowledged appropriately in the form of co-authorship or acknowledgements.
Reducing study costs
Tips for low-cost research are presented in Table 3, highlighting areas where costs can be saved without sacrificing rigour. For instance, self-made envelopes for randomisation rather than a telephone randomisation service were used in all five trials. Well-motivated medical students can provide an alternative to employing project officers and managers.

Conclusion
Grassroots GPs working in clinical practice have been shown to support the need for relevant clinical research. However, in the past, many projects focused predominantly on health service organisation rather than clinical problems. The success of the five RCTs we conducted was underpinned by the research questions being established by a group of GPs with an interesting series of questions relevant to their clinical practice and not answered by current evidence. In order to bridge the ‘swamp’ with the ‘ivory tower’, GPs should not merely collect data for large research projects designed by university academic departments. If GPs ‘own’ their research project, which is relevant to their clinical practice, it is more likely to succeed.

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References

Table 1. Recommendations relating to enabling factors

<table>
<thead>
<tr>
<th>Enabler</th>
<th>Recommendation</th>
</tr>
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<tbody>
<tr>
<td>Research question</td>
<td></td>
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<tr>
<td>Research topic devised and chosen by a group of clinicians</td>
<td>Grassroots questions are likely to be more clinically relevant and result in more commitment from clinicians than research topics imposed by ‘outsiders’</td>
</tr>
<tr>
<td>GPs ‘own’ projects, and are co-investigators and co-authors, not participants and data collectors</td>
<td>Facilitate ownership by local stakeholders. Be inclusive with co-authorship and acknowledgements</td>
</tr>
<tr>
<td>Research question was locally feasible because of high incidence of skin cancer</td>
<td>Build on unique local strengths</td>
</tr>
<tr>
<td>Funding</td>
<td></td>
</tr>
<tr>
<td>Small RACGP foundation and PHCRED novice research grants</td>
<td>Category 1 grants are difficult to obtain and have a lengthy turnaround. Focus on smaller grant schemes that foster novice research</td>
</tr>
<tr>
<td>Research team</td>
<td></td>
</tr>
<tr>
<td>Practice nurses as co-researchers</td>
<td>Engage practice nurses as co-researchers. Can lead to greater commitment to project and data collection rigour</td>
</tr>
<tr>
<td>Design and methods</td>
<td></td>
</tr>
<tr>
<td>Project design and method developed by GPs as group of co-researchers, while involving a methodologist early in the study design.</td>
<td>Ensure that the project remains practice-based and clinically relevant, but also that it is methodologically sound</td>
</tr>
<tr>
<td>Project design always kept as simple as possible</td>
<td>Concentrate on important primary outcome</td>
</tr>
<tr>
<td>Data collection</td>
<td></td>
</tr>
<tr>
<td>Work for participating GPs minimised</td>
<td>GPs time poor and unlikely to devote time to data collection</td>
</tr>
<tr>
<td>Practice nurses engaged to collect data collectors</td>
<td>Use and fund practice nurses to collect data</td>
</tr>
<tr>
<td>Analysis</td>
<td></td>
</tr>
<tr>
<td>Principal researcher established local clinician with university appointment and long-term collaboration/mentorship from experienced statistician/epidemiologist/methodologist</td>
<td>Adequate academic support is required ‘Build bridge between the swamp and the ivory tower’ ensures commitment to project and clinical relevance of question, methods and results.</td>
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</tbody>
</table>

GP, general practitioner; PHCRED, Primary Health Care Research, Education and Development; RACGP, The Royal Australian College of General Practitioners
Table 2. Recommendations relating to barriers

<table>
<thead>
<tr>
<th>Barrier</th>
<th>Recommendations</th>
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</thead>
<tbody>
<tr>
<td><strong>Method</strong></td>
<td></td>
</tr>
<tr>
<td>Primary care research underfunded</td>
<td>See tips for low-cost research</td>
</tr>
<tr>
<td>It is difficult to ‘sell’ clinical rigour to GPs</td>
<td>Use pragmatic RCT&lt;sup&gt;25&lt;/sup&gt; – key RCT principles, but tailored to meet the reality of GP setting</td>
</tr>
<tr>
<td>Ethics process lengthy and onerous, particularly for high-risk projects</td>
<td>Know ethics committee requirements and ensure all information provided first time. Be prepared for at least eight week turnaround.</td>
</tr>
</tbody>
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**Analysis and publication**

- There may be lengthy delays for journal decisions; rejection is common
  - Be aware of timelines, have realistic expectations regarding publication, be resilient

- GPs may not see themselves as researchers
  - Build a culture of research in general practice that starts at registrar level
  - Develop a research user culture, such as a GP journal club

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Table 3. Tips for reducing costs

<table>
<thead>
<tr>
<th></th>
<th>Expensive option</th>
<th>Cheaper option</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Randomisation</strong></td>
<td>Randomisation service</td>
<td>Computer-generated random number tables, make up envelopes</td>
</tr>
<tr>
<td>Research support</td>
<td>Employ project officer, clinical trial staff</td>
<td>Engage medical students to complete honours projects</td>
</tr>
<tr>
<td>Obtaining trial medication</td>
<td>Use industry to make intervention and control medication</td>
<td>Use compounding pharmacists to make medications</td>
</tr>
<tr>
<td>Practice payments</td>
<td>Payment to GPs to compensate for time</td>
<td>Payment to practice nurses to compensate for time</td>
</tr>
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</table>

<sup>25</sup> RCT, randomised controlled trial

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Table 4. RCTs conducted in general practice

<table>
<thead>
<tr>
<th>Question/intervention</th>
<th>Funding</th>
<th>Outcome</th>
<th>Journal (impact factor)</th>
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<tbody>
<tr>
<td>Wetting of sutures19</td>
<td>PHCRED Novice Researcher Fellowship $20,000</td>
<td>931 patients; wetting equivalent to not wetting</td>
<td>BMJ (14)</td>
</tr>
<tr>
<td>Topical chloramphenicol18</td>
<td>RACGP Chris Silagy Scholarship $20,000</td>
<td>1000 patients; absolute reduction in infection rate after application of topical chloramphenicol was statistically but not clinically significant</td>
<td>BMJ (14)</td>
</tr>
<tr>
<td>Cephalexin 2 g for lower limb excisions21</td>
<td>PHCRED funding $15,000</td>
<td>72 patients; cephalexin significantly superior</td>
<td>BMJ Open (2.5)</td>
</tr>
<tr>
<td>Sterile versus non-sterile gloves20</td>
<td>RACGP Family Medicine Scholarship $20,000</td>
<td>400 patients; non-sterile gloves non-inferior</td>
<td>MJA (4.5)</td>
</tr>
<tr>
<td>Alcoholic versus aqueous chlorhexidine22</td>
<td>RACGP Family Medicine Scholarship $20,000</td>
<td>912 patients; alcoholic chlorhexidine not superior</td>
<td>Canadian Medical Journal (7)</td>
</tr>
</tbody>
</table>

BMJ, British Medical Journal; MJA, Medical Journal of Australia; RACGP, Royal Australian College of General Practitioners; PHCRED, Primary Health Care Research, Education and Development; RCTs, randomised controlled trials.