The TARGET Pain Study – Lessons from a painful marathon.

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OT, GK, DT, DF, DF, JF, SJ, SMacD, HM, JR, JT, CG, and DC conceived the paper, contributed to and reviewed the manuscript and were investigators in the original trial. All authors take responsibility for the final version.

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Abstract

This perspective article summarises the experience of conducting a multi-centre research project. We describe expected and unexpected hurdles we experienced as well as suggesting possible solutions for researchers embarking on multi-centre studies.

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INTRODUCTION

The benefits of investigator driven multi-centre research are many. The ability to answer questions relevant to clinicians, recruit more participants, decrease selection bias, increase external validity and attract funding make it a worthwhile endeavour. However, every gain has a cost and increasing the number of different jurisdictions greatly increases the complexity of the task in terms of leadership, communication, logistics, ethical and governance processes. The Australasian College for Emergency Medicine Clinical Trials Group (ACEM CTG) has recently completed TARGET, a national, multi-centre, cluster randomised clinical trial (1). The aim was to provide 'adequate analgesia' and determine the effect on patient satisfaction. The study intervention was a range of educational activities to encourage the ED staff to provide 'adequate analgesia' to their patients, that is, to reduce their patients' triage pain score by ≥ 2 points and to < 4 . While the project was a success, it was not without its difficulties. The purpose of this article is to highlight some of the many and varied barriers we encountered undertaking this trial and to assist researchers in the preparation of future multi-centre studies.

Getting Ready

The trial was run under the auspices of the CTG and the majority of members had previously collaborated successfully. Using ACEM distribution pathways, new collaborators outside the CTG were invited to participate, with a good response. Increasing the number of Emergency Departments and clinicians that are engaged in clinical research is a key role for groups such as the CTG (2). For us, the development

of the research protocol (written by the lead investigator and reviewed by other investigators) was a straightforward initial process.

The participating sites varied in their research infrastructure. Some had well-established units with research nurses/assistants available, while others had clinical staff prepared to commit their clinical support time/unpaid overtime to the study. There was minimal funding available for the trial – just enough to support central administration costs. The trial was wholly dependent on in-kind support and without this support our trial would have foundered.

The Warm Up

The National Approach to Single Ethical Review of Multi-Centre Research (3) was adopted by the NHMRC following a request in 2006 from the Australian Health Ministers' Advisory Council. The concept was that a single Human Research Ethics Committee (HREC) approval of a project would be accepted by all participating sites in Australia. However, in 2012, when our study underwent ethical review, all interstate sites insisted on local HREC review. Aside from the obvious delays this caused, we required completion of ethics/governance processes at all sites prior to revealing the site randomisations. Delays at one site translated into delays for all.

The governance requirements in Queensland were particularly time-consuming. The trial required telephone follow up with patients who had not previously consented to this contact (in an effort to control bias). Approval had to be obtained under the relevant legislation (Public Health Act, PHA)(4), to access the medical records for participants' phone numbers. The governance process was further complicated when one site had their Research Governance Unit transition into a new purpose built

facility. Unfortunately, this was accompanied by the loss of numerous documents and a lengthy and piecemeal notification process of which documents had been misplaced.

The interstate differences in governance were exemplified again when the three Queensland Health (QH) sites required a Clinical Trial Agreement (CTA) with the lead site. All three CTAs had different requirements, complicating the contract process. Overall, the QH governance requirements delayed commencement of the trial by six months compared to other states. Queensland governance requirements continue to add complexity relative to the rest of the country. Recent legislation establishing Queensland Hospital and Health Services requires the health service to obtain Treasury approval prior to taking on unknown financial liabilities. Unfortunately, this currently includes the indemnity requirements of the CTA. The mechanisms for obtaining this approval are, as yet, unclear.

Getting Started

Capturing the interest of clinical staff and then maintaining that momentum is a problem across all clinical research in the ED. Our trial required ongoing staff education regarding the rationale behind the intervention as well as the phrasing of the questions that constituted the intervention. Many EDs have several hundred clinical staff with constant turnover further increasing the number of individuals requiring engagement. The local researchers championed this research and facilitated staff education and data collection. Several sites also experienced turnover in their research staff, with one site unable to find an appropriate replacement and withdrawing from the study.

While staff turnover is a commonplace event in the ED that can be planned for, hospital turnover is not an everyday event. One consequence of the multiple (governance) delays was that one site moved into an expanded green-field site in the middle of a data collection period. Prior to the move there was an enormous amount of effort required of the staff in terms of learning new processes and adapting to a new environment. The move was accompanied by a significant increase in clinical load resulting in a huge impact on this site's ability to conduct clinical research. One unexpected bonus of this process anecdotally was an increase in the receptiveness of staff to new ideas, a potential aid to our study.

Up and Running

Our experiences are likely comparable to other ED clinical research around the world. Project interest from clinical staff varied greatly from the start and enrolments varied accordingly. The presence of investigators within the department was often reflected with increased enrolment, even though they tried to keep a low profile and not influence clinician behaviour. In particular, our trial relied on the triage nurse flagging potential participants. Since triage nurses are often very busy with several competing interests, we anticipated problems with enrolment, despite each site requiring 'only' 50 patients in each of the three data collection periods. Once enrolled, we experienced the typical difficulties in data collection during, and following, a patient visit – patients were unavailable due to transport to medical imaging, other departments or other hospitals. Incorrect contact details lead to inability to follow up many patients. An unexpected difficulty encountered by many sites was the telephone follow up. It is common for hospital telephone numbers in Australia to be blocked from display on the receiving telephone, which frequently lead to patients not answering the phone

calls. This was so prevalent that some sites began using prepaid mobile phones to overcome it.

Crossing The Finish Line

Difficulties in getting research published are neither new nor isolated. Most of the investigators are experienced researchers, well versed in the peer review process (including rejection of manuscripts). However the experiences we encountered in getting our paper accepted for publication were out of the norm. Editors' responses to our submission varied from prompt and utterly appropriate to the delayed and in our opinion, quite unreasonable. One prominent journal rejected our paper on the basis that our aim to achieve early adequate analgesia was encouraging drug addiction in participants.

Coaches' post mortem

The hypothesis underpinning the project had widespread support. As a clinically relevant knowledge translation project, the study goal was to achieve an immediate improvement in patient care and patient satisfaction. This identification with the research question by all researchers at all sites was vital in overcoming the incessant delays, maintaining clinical staff interest and persisting with publication efforts in the face of numerous rejections. Our trial had minimal financial support and absolutely relied on in-kind support and staff goodwill at each site.

Areas that we could have improved on are summarized in Table 1.

Participating sites were spread across the country (Vic, NSW, WA, Qld). We used email as our primary means of communication but, in retrospect, regular monthly teleconferences/telephone contact may have worked better, even among investigators

who had previously collaborated successfully. Teleconferences should also coincide with major milestones such as recruitment periods.

The need for dedicated ED research appointments was highlighted by this project. We recommend these be at both departmental and ACEM level. At the ACEM Research Forum in February 2015 a proposal for a formal Director of Emergency Medicine Research scheme was put to ACEM.(5) ACEM must take the lead on this, as without encouragement, individual hospitals are unlikely to fund these positions, especially when faced with constant budgetary difficulties. We also recommend that ACEM consider the creation of a central clinical trials centre. The variable resources available to participating sites and experience of researchers provide a strong argument for the establishment of an ACEM run clinical trials unit that can provide the necessary support for multi-centre studies. Dedicated research support within the ED, ie research nurses, is an essential component of an effective research culture.

Summary

Well conducted, investigator driven, multicentre research is an essential feature of efforts to improve outcomes for patients. As investigators we can do many things to improve how we conduct this research. Unfortunately many issues were beyond our direct control. The difficulties presented by multiple HREC approvals were recognized in 2006(3). Nine years later we still do not have an effective national single HREC approval process and the governance requirements are becoming so varied, complex and prolonged that they are almost prohibitive. We urgently need to create structures to help FACEM investigators overcome these barriers, mentor new

investigators and lobby at Health Department levels and above for ongoing improvements to the system of research.

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References

1. Taylor DMcD, Fatovich D, Finucci D et al. Best-practice Pain Management in the ED: a multi-centre cluster-randomised, controlled, clinical intervention trial. Emerg. Med. Australas. DOI: 10.1111/1742-6723.12498
2. Oakley E., Taylor D. McD, Coats T., Davidson A., Fry A., Babl F.E. [A primer for clinical researchers in the emergency department: Part IV: Multicentre research](#) Emerg. Med. Australas. 2012 24:5 (482-491)
3. NHMRC.org.au. Canberra. The National Approach to Single Ethical Review for Multi-Centre Research. National Health and Medical Research Council. Available from URL:<https://hrep.nhmrc.gov.au/national-approach> (Accessed 20/10/15)
4. Public Health Act 2005 (Valid as of 1 Sept 2015), Chapter 6, Part 4. Available from URL:<https://www.legislation.qld.gov.au/LEGISLTN/CURRENT/P/PubHealA05.pdf>, (Accessed on 20/10/2015)
5. Taylor DMcD, Cohen D, Epstein J, Freeman P, Gosbell A, Judkins S, Mowatt E, O'Reilly G, Vinen J. Development of a productive research culture in Emergency Medicine: Report of the outcomes of a Research Forum. Emerg. Med. Australas. DOI: 10.1111/1742-6723.12504

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Table 1. Summary of problems experienced and proposed solutions.

Issue	Problem encountered	Predictability	Possible solution/Lesson learnt
Team gathering	Teams with varying experience and infrastructure	Predictable, even desirable	Provide clear research mentor arrangement
Ethics/Governance	No interstate recognition, varying requirements even within same jurisdiction Loss of documentation	Duration rather than occurrence of delays was unexpected	Build delays into planning Need for dedicated research staff/appointments #1 Need for ACEM clinical trials centre #2 ACEM advocacy for uniform national governance processes and requirements #3 Support for matched funding for research officers/project managers Keep copies of documents, particularly pages with signatures
Staff Turnover	Site lost due to	Unexpected	Build redundancy into number

	loss of research champion		of sites participating in cluster study.
Data collection	Incorrect contact details Inability to contact patient Variable staff engagement	Predictable	Need for uniform compulsory patient database for ED research Call from recognisable number (mobile rather than hospital phone) – justifiable cost inclusion in budget Establish clinical research in ED as core function
Publication	Inconsistent reviews	Expected	Nature of peer review. Take it with a pinch of salt, most of it is constructive. Persistence is essential!
Communication	Tyranny of distance and shift work	Predictable	Clinical trials centre coordination Telephone vs email Regular schedule

#1,2 and 3 refer to recommended priorities for actions likely to ease the difficulties associated with multicentre research. #2 and 3 are medium to long term propositions.

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