Intensive and Critical Care Nursing (2013) 29, 300—309

Available online at www.sciencedirect.com

SciVerse ScienceDirect

journal homepage: www.elsevier.com/iccn

ORIGINAL ARTICLE

Enhancing the informed consent process for critical care research: Strategies from a thromboprophylaxis trial☆

Orla M. Smith[a,1], Ellen McDonald[b,1], Nicole Zytaruk[b,1], Denise Foster[c,1], Andrea Matte[d,1], France Clarke[b,1], Suzie Fleury[e,1], Katie Krause[f,1], Tracey McArdle[g,1], Yoanna Skrobik[h,1], Deborah J. Cook[b,i,*,1]

[a] *Critical Care Department and Keenan Research Centre, Li Ka Shing Knowledge Institute, St. Michael's Hospital, Toronto, Canada*
[b] *Department of Clinical Epidemiology & Biostatistics, McMaster University, Hamilton, Canada*
[c] *Division of Critical Care, Vancouver General Hospital, Vancouver, Canada*
[d] *University Health Network, Toronto, Canada*
[e] *Division of Critical Care, Kingston Hospital, Kingston, Canada*
[f] *Division of Critical Care, St John's Mercy Hospital, St Louis, USA*
[g] *Division of Critical Care, Ottawa Hospital, Ottawa, Canada*
[h] *Division of Critical Care, Hôpital Maisonneuve Rosemont, Montreal, Canada*
[i] *Department of Medicine, McMaster University, Hamilton, Canada*

Accepted 26 April 2013

KEYWORDS
Clinical research;
Critical care;
Informed consent;
Intensive care;
Randomized trials;
Studies;
Substitute decision-makers

Summary
Background: Critically ill patients lack capacity for decisions about research participation. Consent to enrol these patients in studies is typically obtained from substitute decision-makers.
Objective: To present strategies that may optimise the process of obtaining informed consent from substitute decision-makers for participation of critically ill patients in trials. We use examples from a randomised trial of heparin thromboprophylaxis in the intensive care unit (PROTECT, clinicaltrials.gov NCT00182143).
Methods: 3764 patients were randomised, with an informed consent rate of 82%; 90% of consents were obtained from substitute decision-makers. North American PROTECT research coordinators attended three meetings to discuss enrolment: (1) Trial start-up (January 2006); (2) Near trial closure (January 2010); and (3) Post-publication (April 2011). Data were derived from slide presentations, field notes from break-out groups and plenary discussions, then analysed inductively.

* Corresponding author at: Department of Medicine, McMaster University Health Sciences Center, Room 2C11, 1200 Main Street West, Hamilton, Ontario, Canada L8N 3Z5. Tel.: +1 905 525 9140x22162; fax: +1 905 524 3841.
E-mail address: debcook@mcmaster.ca (D.J. Cook).

[1] For the North American PROTECT Research Coordinators and the Canadian Critical Care Trials Group.

0964-3397/$ — see front matter
http://dx.doi.org/10.1016/j.iccn.2013.04.006

Results: We derived three phases for the informed consent process: (1) Preparation for the Consent Encounter; (2) The Consent Encounter; and (3) Follow-up to the Consent Encounter. Specific strategies emerged for each phase: Phase 1 (four strategies); Phase 2 (six strategies); and Phase 3 (three strategies).
Conclusion: We identified 13 strategies that may improve the process of obtaining informed consent from substitute decision-makers and be generalisable to other settings and studies.

Implications for clinical practice

- Informed consent for research is an ongoing process.
- Optimising informed consent for research participation is a multi-phase process that starts before a study is implemented and involves the inter-professional ICU clinical team.
- Implementation of these 13 strategies may help to improve the integrity of the informed consent process, minimise SDM decisional burden and maximise timely enrolment of eligible patients into clinical studies in the ICU.

Introduction

Clinical research in the intensive care unit (ICU) is essential to improve the outcomes of critical illness (Luce et al., 2004; McRae and Weijer, 2002; Yarborough, 1993). Timely completion of randomised trials and the generalisability of study results are contingent upon recruitment of the majority of eligible patients (Wade et al., 2009; Watson and Torgerson, 2006). While deferred or waived consent models have been employed in ICU trials of urgent interventions (Annane et al., 2002; NICE-SUGAR Investigators et al., 2009; Roberts et al., 2004), interventional trials typically require a priori informed consent. Most critically ill patients are incapable of research decision-making (Fan et al., 2008), such that substitute decision-makers (SDMs) are typically approached to consider research opportunities on their behalf (Arnold and Kellum, 2003). SDM consent to research is the preferred enrolment approach of ICU survivors (Chenaud et al., 2009; Scales et al., 2009), ICU family members (Barrett et al., 2012; Chenaud et al., 2009; Perner et al., 2010), research ethics board (REBs) (Duffett et al., 2011; Gong et al., 2010) and the public (Burns et al., 2011).

Ethical and procedural guidelines require research consent to be informed, voluntary, documented and ongoing (Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, and Social Sciences and Humanities Research Council of Canada, 2010; International Conference on Harmonisation, 1997; National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1979; Nuremburg code, 1996; World Medical Association, 1997). Researchers are obligated to disclose risks and benefits of participation to decision-makers, and to ensure understanding of the research purpose and procedures. Making a decision about research participation in the ICU may be difficult for SDMs for several reasons. First, enrolment is often time-sensitive, sometimes even requiring a decision within hours (Burns et al., 2009). For example, in two recently published international randomized controlled trials, the eligibility criteria dictated that patients be enrolled within 24 hours of demonstrating signs of septic shock (Guntupalli et al., 2013; Ranieri et al., 2012). Second, most SDMs are unaware of patient wishes regarding research (Chenaud et al., 2009; Ciroldi et al., 2007; Coppolino and Ackerson, 2001) and must balance their understanding of patient values with knowing how trial interventions may cause more harm than good, or introduce risk without benefit. Third, comprehension of SDMs regarding medical issues and research in the ICU is limited (Azoulay and Pochard, 2002; Rodriguez et al., 2008). Finally, SDMs are anxious, and involvement in research decision-making may increase psychological burden (Wendler and Rid, 2011) or induce post-traumatic stress (Azoulay et al., 2005). In this unique context, research coordinators approach SDMs, inviting their consideration of research opportunities for critically ill patients.

SDMs may agree to, or decline, a request for a critically ill patient to participate in research. High rates of refusal can decrease the generalisability of trial results if non-consenting participants are systematically different than consenting participants, even if the desired sample size is achieved (Chertow et al., 2003; Crowley et al., 2008). In observational research, it has been suggested that the requirement for informed consent can lead to biased results due to the systematic exclusion of some individuals (Gershon and Tu, 2008; Tu et al., 2004). Recruitment rates vary across studies; however, rates can also differ among centres recruiting patients into the same trial (Smith et al., 2012) underscoring how several factors may influence enrolment, just one of which is the informed consent process (Table 1). Although systematic reviews have addressed patient recruitment strategies outside the ICU setting (Caldwell et al., 2010; Mapstone et al., 2007; Watson and Torgerson, 2006), literature is sparse on how to improve the informed consent process for research involving critically ill patients.

The objective of this report is to present strategies that may optimise the process of obtaining informed consent from SDMs for participation of critically ill patients in randomised trials. To illustrate some strategies, we use the example of PROTECT (the Prophylaxis for ThromboEmbolism in Critical Care Trial) an international trial of heparin thromboprophylaxis for medical-surgical critically ill patients (clinicaltrials.gov NCT00182143).