Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/burns

Review

Burn clinical trials: A systematic review of registration and publications

Sarthak Sinha [a,b], *Grace Yoon* [b], *Wisoo Shin* [b], *Jeff A. Biernaskie* [b], *Duncan Nickerson* [c,d], *Vincent A. Gabriel* [a,d,*]

[a] *Division of Physical Medicine and Rehabilitation, Departments of Clinical Neurosciences, Pediatrics and Surgery, Faculty of Medicine, University of Calgary, Alberta,Canada*
[b] *Department of Comparative Biology & Experimental Medicine, Faculty of Veterinary Medicine, University of Calgary, Canada*
[c] *Section of Plastic Surgery, Department of Surgery, University of Calgary, Alberta, Canada*
[d] *Calgary Firefighters' Burn Treatment Centre, Canada*

ARTICLE INFO

Article history:
Accepted 2 November 2017

Keywords:
Clinical trial
Burns
Industry
Publication quality
Trial termination

ABSTRACT

Background: Randomized controlled clinical trials (CTs) are gold standard tools for assessing interventions. Although burn CTs have improved care, their status, publication frequency, and publication quality are not known.
Objectives: (1) Characterize burn CTs by analyzing location, completion status, temporal trend, and funding sources. (2) Assess quality of trial reporting.
Data sources: CT records were obtained from ClinicalTrials.gov and WHO's CT Registry (searched May 2017). Publications were obtained from PubMed, Google Scholar, OVID MEDLINE, and ClinicalTrials.gov (searched June 2017).
Publication appraisal: 23-item rubric adapted from CONSORT and ICH E3 guidelines.
Results: 738 burn CTs were identified globally, of which majority were publically-funded (77%), ongoing (52%), and assessed behavioral, pharmacological, device-based, dietary-based, and biological/procedural interventions. Amongst the ended trials, 69 (28%) published their findings. Significantly fewer industry-funded trials published findings (14% vs 33% publically-funded). Quality of reporting was suboptimal, and most underreported categories were trial phase, severity, and sample size estimation.
Limitations: Incomplete, outdated, and non-registered CTs which are difficult to track.
Conclusions: Burn trials are proliferating in number, location, and interventions assessed. Only a small proportion are published and quality of reporting is suboptimal.
Implications of key findings: Burn researchers should aim to register and report on all clinical trials regardless of outcome. Superior a priori design can reduce precocious termination and mandatory reporting of data fields can improve quality of reporting.
Systematic review registration number: CRD42017068549.

* *Corresponding author at*: Room AC122 SSB, Foothills Medical Centre, 1403 29 Street NW, Calgary, AB T2N 2T9, Canada.
E-mail addresses: sarthak.sinha@mail.utoronto.ca (S. Sinha), grace.yoon2@ucalgary.ca (G. Yoon), wshin@ucalgary.ca (W. Shin), jabierna@ucalgary.ca (J.A. Biernaskie), duncan.nickerson@ahs.ca (D. Nickerson), vincent.gabriel@ucalgary.ca (V.A. Gabriel).
https://doi.org/10.1016/j.burns.2017.11.001

Contents

1. Introduction

The earliest record of burn treatment comes from ancient Egyptian Ebers Papyrus where wounds were treated with mud, excrement, oil, plant extracts, and fermented goat dung [1]. Hippocrates, in fourth century BC, was the first to use wound dressings impregnated with pig fat, resin, and bitumen to treat open wounds [1]. With growing recognition that medical practitioners are also investigators seeking to improve wound care, the way burns are treated has evolved with our understanding of burn pathophysiology and careful analysis of experimental therapies. Critical to this endeavour has been randomized controlled clinical trials (CTs), which are the gold standard tools for evaluating interventions. However, the utility of CT is contingent on the adherence to prescribed guidelines and whether findings from a trial are published.

There have been numerous studies across many medical disciplines which have assessed the success of CTs, from conception to publication and beyond, and most have returned empty handed [2–8]. Four significant problems have emerged from these studies. First, many CTs are not registered in government databases and evade all attempts at surveillance. This practice remains sustainable as a survey by the OPEN Project found that only 30% of journals requested trial registration when findings were submitted for editorial consideration [3]. Second, among the registered CTs, many are precociously terminated or suspended. Although discontinuation of CTs may be favored if the intervention inflicts harm, most trials are discontinued for reasons which could have been avoided with a more careful study design and an a priori evaluation of budget and patient enrollment [6]. Third, non-publication and delayed publication of completed CTs remains a persistent problem across diverse disciplines [2,4,5]. Chapman and colleagues assessed 395 surgical trials registered in ClincialTrials.gov and found that 21% were discontinued and 34% of completed trials were never published [2]. Fourth, trials publish distorted evidence by selectively reporting outcomes and inflating coverage on benefits while underreporting risks and harms [7,8].

Taken together, these studies have been instrumental in developing superior guidelines to regulate CTs and mitigate participant risk before and during trials. Promoting registration of clinical trials has been enforced by editorial boards of medical journals and by country-specific legislations. For example, in 2005, the International Committee of Medical Journal Editors mandated that trials involving human participants must be registered prior to participant enrollment to be considered for publication [9]. Shortly after, an international policy was initiated by the World Health Organization (WHO) in 2006 which encouraged registration and publication of trial results globally [10]. Subsequently, in 2007, the passage of FDA Amendments Act expanded ClinicalTrials.gov to include a database of trial results so investigators can submit trial results through a non-peer reviewed stream [11]. A timeline on events, policies, and laws relating to registering CTs in the US and around the world can be found at: https://clinicaltrials.gov/ct2/about-site/history and https://clinicaltrials.gov/ct2/manage-recs/background.

Although burn CTs have identified strategies that have been incorporated into clinical recommendations to improve cutaneous wound healing and scar quality [12], the status, publication rate, and the quality of publications generated from these CTs are not known. This is the first report to provide a comprehensive and systematic assessment of CTs listed in worldwide trial registries involving experimental therapies for burns. It has two aims. First, to characterize the global landscape of burn-related CTs by analyzing the geographical location, completion status, temporal trend, and funding sources of all trials registered. Second, to assess the extent to which publications generated from completed, terminated and suspended CTs reflect the Consolidated Standards of Reporting Trials' (CONSORT) best practice guidelines.