Trial Registration and Abstracts from the American Society of Anesthesiologists
Meetings 2010-2013: a retrospective observational study of methods

Population of interest: Randomised Controlled Trials (RCTs) with abstracts presented at the American Society of Anesthesiologists (ASA) Meetings 2010-2013.

Primary Hypothesis: That trials that are not prospectively registered (but have a reported outcome) are more likely to have a positive outcome.

- To determine this:
  o What proportion of abstracts were registered prior to being presented at the meeting?
  o Of those that were registered, what proportion presented a 'positive primary finding' in the abstract?
  o Of those that were not registered, what proportion presented a 'positive primary finding' in the abstract?

Secondary Questions

1) What proportion of these trials were registered?

= Trials in our defined population that were registered / All trials in our defined population

2) What proportion of these trials were prospectively registered?

= Trials in our defined population that were prospectively registered / All trials in our defined population
3) What proportion of these trials with trial registration, displayed major discrepancies between their trial registration entry and their published paper?

= Trials in our defined population that were registered AND displayed a major discrepancy between their trial registration entry and their published paper / All trials in our defined population that were registered

Major Discrepancies are defined as:

- 1) **Selective Outcome Reporting**
  - Includes primary outcome discrepancies:
    - Addition or Omission of primary outcomes
    - Change in definition
    - Downgrading of primary outcome to secondary outcome OR upgrading of secondary outcome to primary outcome

- 2) **Sample Size change without adequate explanation**

- 3) **Study Intervention change**

**Methods:**

All abstracts from the 2010-2013 ASA Annual Meeting will be identified from the ASA Abstracts website. We will use this timespan as it allows at least 6 years to have elapsed for subsequent publication of studies in the peer reviewed literature, and findings from our recent review demonstrated that at 6 years post abstract presentation, 97.4% of the positive abstracts and 96.3% of the negative abstracts that went on to publication, had been published (1).

All abstracts performed as RCTs in humans will be included in a database constructed with Microsoft Excel 2016 (Microsoft Corporation, Redmond, WA, USA). We will use the same
methods to estimate publication bias in the post compulsory trial registration abstracts as we did in our previous review (1). A trial will be considered to be an RCT if the individuals in the trial were prospectively assigned to one of two or more alternative forms of healthcare using a random method of allocation (2). Studies will firstly be assessed as either “positive” or “negative”. Positive studies will be defined as studies showing a statistically significant result in the direction of the experimental treatment for the primary outcome compared to the control treatment in the conference abstract. Where the primary outcome is not clearly defined, the first reported outcome will be utilized. Studies showing no difference in outcome between treatment groups will be counted as positive if the stated objective was to show treatment equivalence or non-inferiority. We will define negative studies as those that failed to show a statistically significant difference in the direction of the experimental treatment over the control treatment, or failed to show equivalence or non-inferiority if that was the stated aim. Some abstracts comparing interventions may have no clear “experimental” and “control” group but will be considered positive if a difference was shown between the groups. If there is initial uncertainty over whether the result of the abstract was positive or negative, two authors will discuss and make a consensus decision guided by the above definitions.

A systematic literature search will then be performed via PubMed and Medline to identify any subsequent publication of the study. The search strategy will include seven separate searches in the order of the first author’s name, the second author’s name, the last author’s name, the first author’s name AND keywords, the second author’s name AND keywords, the last author’s name AND keywords, and keywords alone.
The following baseline characteristics will be recorded: the month and year of presentation of the conference abstract (Note: the ASA Meeting is held in October each year) and of the journal publication if published, the author details, and reported study size. Whether a study that proceeded to journal publication had completed full recruitment at the time of conference abstract will be noted by comparison of sample sizes in meeting abstract and subsequent publication. Studies which do not state that full recruitment has occurred explicitly will be classified by us as uncompleted at the time of conference presentation if the number of participants in the final journal publication is different to that of the conference abstract.

A systematic search for trial registration of the abstract will then be performed. Where the trial registration number is available, this will be used to examine the corresponding trial registry entry. If this is not present, the clinicaltrials.gov website (United States Trial Registry website), the International Standard Randomised Controlled Trial Number Register (ISRCTN), and the World Health Organization International Clinical Trials Registry Platform will be searched.

Following on from above, the search strategy to be employed on the trial registry databases will involve conducting separate searches in the order of the first author’s name, the second author’s name, the third author’s name, through to the last author’s name, the first author’s name AND keywords, the second author’s name AND keywords, the last author’s name AND keywords, and keywords alone.

The following characteristics will be examined from the trial registry websites: date of registration, date of commencement, primary and secondary outcomes, sample size estimation, study population, study intervention, and country of origin.
Statistical Analysis:

Proportions as stated above, with 95% Confidence Intervals. These will be compared with logistic regression.

For the primary hypothesis:

The primary endpoint will be a comparison between the proportion of positive outcome trials which did not have prospective registration versus the proportion of positive outcome trials with prospective registration. We define a 20% reduction in positive outcomes as clinically significant when comparing trials without prospective registration to trials with prospective registration.

Sample size calculation: Using the database from our previous study (1), 1052 RCT abstracts were identified for inclusion from the 4 year period studied, of which 73% had positive outcomes. Based on pilot data conducted, the trial registration rate is estimated to be roughly 20-25%.

Calculations from STATA:

90% power to show a 20% reduction in positive outcomes from 73% to 58% overall.

 Estimated sample size for two-sample comparison of proportions:
Test Ho: p1 = p2, where p1 is the proportion in population 1

and p2 is the proportion in population 2

Assumptions:

\[
\text{alpha} = 0.0500 \text{ (two-sided)}
\]

\[
\text{power} = 0.9000
\]

\[
p1 = 0.7300
\]

\[
p2 = 0.5800
\]

\[
n2/n1 = 1.00
\]

Estimated required sample sizes:

\[
n1 = 223
\]

\[
n2 = 223
\]

References:


Author/s:
Chong, Simon; Peyton, Philip; Imberger, Georgina; Simons, Koen; Bianco, Anthony; Liskaser, Grace; Burggraf, Millicent

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