Risk communication in clinical trials: how does it influences decisions to participate and what are the best methods to improve understanding in a trial context?

1. Introduction

Understanding, or more often mis-understanding, of risk information related to trials has been shown to influence decisions about participation in a range of trials.[1,2] Preliminary findings from recent work from our group have shown that stakeholders have varied preferences about how probabilistic information relevant to trial participation (e.g. estimates of the likelihood of benefit and/or harm associated with trial interventions, from here on referred to as 'probabilistic trial information') is communicated.[3] Spiegelhalter *et al* have shown that probabilities are '*notoriously difficult to communicate effectively*' to lay audiences in various contexts, including health, but no research has looked specifically at how to communicate probabilities for trial participation, where uncertainties will usually be greater.[4] However, there is research from treatment and screening decisions on methods to present probabilistic information to improve patient understanding and decision making.[5,6] Our research has shown that stakeholders recognise the importance of including probabilistic trial information in decision aids, and agree that insights from research in treatment decision aids should be used.[4] Yet, surprisingly, the methods shown to be effective to improve treatment decision making are not routinely employed in written participant information leaflets for trial participation.[7]

Therefore, further investigation of methods for presenting probabilistic trial information and the influence this has on the decision to participate is warranted. To address this, this research plans to conduct a systematic review of the literature reporting any aspect of presentation of probabilistic information or understanding of risk by potential trial participants. Specifically we will search for:

1. Comparative effectiveness studies testing different presentations of probabilistic information on potential trial participants understanding and/or decision to participate;
2. Qualitative studies reporting participant perspectives about probabilistic information in trial information or how their understanding of the trial 'risk' impacts on their decision to participate.

2. Methods

2.1 Criteria for consideration of included studies

Types of studies

Evaluative studies that have investigated the methods for presenting probabilistic information within participant information leaflets for a clinical trial will be included. Studies will include systematic reviews with/without meta-analyses, randomised controlled trials, case controlled trials, case series, and prospective cohorts. Specifically, the nature of intervention must focus on optimising understanding (or another plausible outcome linked to decision making for trial participation) of probabilistic information within the context of a clinical trial. Exploratory studies (using observations, interviews, focus groups and other methods) that have explored aspects of the RCT decision process (for adults with capacity) will also be included if they discuss any aspect of risk or risk communication as bring important in the decision making process. At this stage we will include both real and hypothetical decisions about trial participation.

Exclusion criteria

Papers or articles (both explanatory and exploratory) that present findings on risk communication in a treatment or screening context or consider the decision to participate in research studies that are not definitive effectiveness RCTs.

3.2 Search methods for identification of studies.

A search strategy will be designed by the Senior Information Scientist (CF), refined through discussion with the Chief Investigator (KG) and informed by previous work conducted in this area. The search for explanatory studies will focus on interventions targeting presentation of probabilistic information in participant information leaflets for clinical trials. Specific search strategies will be designed to capture the explanatory studies and exploratory studies separately. The exploratory searches will exclude the records retrieved by the explanatory search to avoid duplication of the results. Searches will be applied to, MEDLINE(from 1946), EMBASE (from 1947), and CINAHL (from 1981) to current for both sets of literature and in addition CENTRAL and the Cochrane Methodology Register will be search for explanatory studies. It is likely that some of these articles will also be identified through reference linking of known articles and those identified in the quantitative and qualitative search. The review will be reported in accordance with PRISMA guidelines.

A search for additional studies will be undertaken by checking the references of the included studies. Citation searches of the included studies will also be performed using Scopus, Science Citation Index and the Social Science Citation Index.

Eligibility of studies

Citations identified through the search will be independently assessed by one reviewer (MC) with a second reviewer (KG) screening a random 10%. Full text papers will be obtained for those studies that on initial screening are considered potentially relevant and will be further assessed for inclusion. Any studies not meeting inclusion criteria will be excluded. The eligible full text papers will be assessed independently by two reviewers with a third reviewer acting as an arbiter is there is any disagreement. Reference lists of all included studies will be examined for further relevant studies.

Data extraction

Information from primary studies will be extracted by one reviewer with a random sample assessed y a second reviewer. The following summary data will be extracted and summarised from each study: study type; study aim; author details; year and journal of publication; and where relevant, parent study context (e.g. condition, trial design, intervention(s)). Specific details on the intervention(s) being evaluated and study outcomes will be extracted. These will include: comparative methods of disseminating probabilistic information to potential trial participants using different communication tools/aids. These methods of communication may include numerical presentations (percentages and frequencies), graphical and tabular representations, and qualitative risk descriptors to illustrate the risks and benefits of trial participation. Modes of intervention delivery (i.e. paper, computer, verbal) will also be considered. Study outcomes to be extracted include; cognitive outcomes i.e. potential trial participant comprehension of probabilistic information and subsequent risk perception; affective outcomes i.e. participant preferences and/or satisfaction with communication methods, and level of decisional conflict and concern; behavioural outcomes i.e. willingness to participate in clinical trial. Verbatim data (Both participant quotes and authors interpretations) will be extracted from included qualitative studies and coded into discrete themes, which will be generated iteratively through discussion. Study authors will be contacted if published data is unavailable or unclear.

Data analysis

Data will be summarised and presented in tabular form. Where appropriate we will conduct meta-analysis but due to the scarcity of comparative effectiveness studies in this area it is more likely the results will be presented in narrative form.

3. Outputs

This review will provide evidence about how risk information is perceived but potential trial participants and how it influences their decision to participate. It will also collate what is known about methods to present probabilistic trial information within trial information leaflets. Taken together this information will be used to inform a statement about presentation of probabilistic information on participant information leaflets and directly inform, future research in this area.

References

1.McCann S, *et al.* Trials. 2010; 11:31

2.Linden H, *et al.* Cancer Nurs. 2007;30(4):261.

3. Gillies K et al, BMJ Open. 2014; 4:8.

4. Spiegelhalter D, *et al.* Science. 2011;333(6048):1393.

5. Fagerlin A, *et al.* J Natl Cancer Inst. 2011;13(3):e54.

6. Thomson R, *et al.* Clin Med.

7. Gillies K et al, Trials. 2014; 15:62.