SWAT 161: ‘Principled’ versus usual approach for sharing information about potential benefits and harms of trial interventions in patient information leaflets

Objective of this SWAT
To determine the effects on reported adverse events, recruitment and retention of a stakeholder-informed way of sharing information about potential benefits and harms of trial interventions in patient information leaflets (PILs).

Study area: Recruitment, Retention, Outcomes
Sample type: Participants
Estimated funding level needed: Very Low

Background
The second most important question listed in the Prioritising Recruitment in Randomised Trials (PRioRiTy) project (http://priorityresearch.ie/) is: ‘What information should trialists communicate to members of the public who are being invited to take part in a randomised trial to improve recruitment to the trial?’ Our SWAT aims to address this question by testing a new way of sharing information about potential benefits and harms of trial interventions. We will compare standard PILs with PrinciPILs: patient information leaflets developed with extensive input on benefit and harm presentation from stakeholders (including patients, research ethics committee members, clinicians and senior trial managers).

Our recent qualitative analysis of 33 PILs from UK placebo-controlled trials registered between 2016 and 2019 revealed wide variability in how information about potential benefits and harms of trial interventions are shared in PILs.(1) Roughly a third (10/33) did not contain any information about potential intervention benefits. By contrast, all (33/33) contained information about potential harms. The relative lack of information about potential benefits could cause information-induced adverse events (‘nocebo effects’). Supporting this hypothesis, our systematic review found that 49.1% (interquartile range 25.7% to 64.4%) of trial participants in placebo groups reported at least one adverse event (AE).(2) One in 20 (5%, interquartile range 2.3% to 8.4%) dropped out due to a reported AE. Information-induced AEs could also affect recruitment and retention.

Additionally, because guidance regarding how to balance the presentation of potential benefits and harms of trial interventions does not exist, scarce resources are wasted. Currently, every principal investigator (PI) must negotiate their own method for presenting balanced information about benefits and harms within PILs.

Possible ethical concerns also arise from the way that information about potential benefits and harms of trial interventions are shared. If information about potential harms can be done honestly, while reducing information-induced AEs, then it could be an ethical requirement to do so (based on the principle of non-maleficence).(3)

Interventions and comparators
Intervention 1: Standard PIL (the one designed by the host trial)
Intervention 2: PrinciPIL (designed by the PrinciPIL team)

Index Type: Participant Information

Method for allocating to intervention or comparator
Randomisation

Outcome measures
Primary: difference in reported AEs
Secondary: difference in recruitment and retention rates, and differences in specific Aes

Analysis plans
The primary analysis is the comparison of the proportion of participants who report adverse events in the different randomised groups. The secondary analysis will be a comparison of recruitment

and retention rates. These analyses will be done in the context of a living meta-analysis of PrinciPIL SWATs.

Possible problems in implementing this SWAT
It may be more difficult to use both PILs and PrinciPILs at the same recruitment site than it is to use just one. This difficulty can be overcome by using cluster randomisation. We are also dependent on the availability of a sufficient number of host trials.

References
1. Kirby N, Shepherd V, Howick J, Betteridge S, Hood K. Nocebo effects and participant information leaflets: evaluating information provided on adverse effects in UK clinical trials. Trials 2020;21:658.
2. Howick J, Webster R, Kirby N, Hood K. Rapid overview of systematic reviews of nocebo effects reported by patients taking placebos in clinical trials. Trials 2018;19:674.
3. Howick J. Unethical informed consent caused by overlooking poorly measured nocebo effects. Journal of Medical Ethics 2020;47:590-4.

Publications or presentations of this SWAT design

Examples of the implementation of this SWAT

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