SWAT 233: Behavioural nudges to increase responses from residents in England to a postal invitation from NHS England to take part in the Antiplatelet Secondary Prevention International Randomised study after INtracerebral haemorrhaGe (ASPIRING)

Objective of this SWAT
The primary objective is to determine the effects on responses to a nudge in letters of invitation to take part in the ASPIRING study. The secondary objective is to determine whether the effects differ between sub-groups of people who are often underrepresented in randomised trials.

Additional SWAT Details
Primary Study Area: Recruitment
Secondary Study Area: Document design and delivery; Prompts
Who does the SWAT intervention target: Carer/Parent; Participants
Estimated resources needed to conduct the SWAT: Low
Estimated cost of the SWAT (£):

Findings from Implementation of this SWAT
Reference(s) to publications of these findings:
Primary Outcome Findings:
Cost:

Background
The REstart or STop Antithrombotics Randomised Trial (RESTART) found that antiplatelet therapy seemed safe for survivors of stroke due to an intracerebral haemorrhage (ICH), who are at high risk of major adverse cardiovascular events (MACE) [1]. However, RESTART did not meet its recruitment target, and recruited just one in 12 eligible patients at sites that kept screening logs. There were multiple reasons for patients not being randomised beyond the exclusion criteria for the trial and almost half of the eligible people who were not recruited might have been included if they were approached directly, after they had been discharged from hospital [2]. There was a sex disparity in recruitment: two-thirds of people recruited were male. It is also known that people with multiple morbidities are less likely to take part in randomised trials. For example, an analysis of 116 phase 3/4 trials of novel drug therapies for chronic medical conditions found that participants had fewer health conditions than the average person with the index condition [3]. Nationwide recruitment by post, identifying potentially eligible patients using healthcare systems data, might reduce recruitment disparities and improve access to randomised trials for under-represented groups.

ASPIRING (ISRCTN16705062) aims to determine if antiplatelet monotherapy is of overall net benefit in reducing the incidence of MACE, compared to avoiding antiplatelet therapy for adults with a history of spontaneous ICH. The trial aims to recruit 4148 participants, including 2828 in England, Scotland and Wales. NHS England will support recruitment to ASPIRING in England, using healthcare systems data to identify all ICH survivors in England and send letters of invitation to potential participants.

‘Nudge’ interventions seek to modify the social and physical environment to enhance capacity for subconscious behaviours that align with the intrinsic values of an individual, without actively restricting options. A nudge could be as simple as intentionally designing the order in which options are laid out, changing the default choice a user can make to increase the chances of them selecting this choice, or adjusting the way language is framed.

The content and format of the letter of invitation to participate in a randomised trial may influence the response to the letter. A randomised implementation trial, NUDGE-FLU, used nine different electronic flu vaccination invitation letters sent to one million individuals aged ≥65 years in Denmark [4]. Compared with a standard government issued email, a letter emphasizing potential cardiovascular benefits led to an absolute increase in the proportion receiving flu vaccination of 0.9%. A systematic review of strategies to improve recruitment to randomised trials included two

randomised trials which found specific wording of SMS messages increased recruitment to a host trial of smoking cessation [5].

Preliminary testing:
Before undertaking this Study Within a Trial (SWAT), we performed a preliminary pilot survey of stroke survivors and carers to test letter variants via an online survey. Participants were asked, on viewing the letter, how likely they were to (a) read the accompanying leaflet it refers to, (b) visit the website it refers to and/or to contact the trial team, and (c) to take part in the study described. Responses were received from 1458 stroke survivors and 801 carers. For stroke survivors, the nudge most likely to prompt all three actions was the “individualistic plus norms” nudge: 85% of stroke survivor respondents said they would likely read the leaflet, 84% would likely visit the trial website and 79% said they were likely to take part in the study. For stroke survivors, a control letter without a nudge gave responding proportions of 86%, 81% and 76% in these three categories. Importantly, responses were maintained across subgroups of interest, including people with two or more long term health conditions and carers.

Host Trial Population: Adults
Host Trial Condition Area: Neurological Conditions

Interventions and Comparators
Intervention 1: Standard 2-page letter of invitation without any nudges (comparator).
Intervention 2: Standard 2-page letter of invitation with an individualistic plus norms nudge: ‘‘As someone who has a health condition, you are uniquely placed to help with this trial. Your help has the potential to transform the lives of people like you, who have this health condition.”
Intervention 3: Standard 2-page letter of invitation with a physical safety nudge: “Safety is at the core of this study. The pill in this study seems to be safe after a stroke due to bleeding.”

Method for Allocating to Intervention or Comparator: Randomisation

Outcome Measures
Primary Outcomes: Response to postal invitation letter via ASPIRING study website.
Secondary Outcomes: Recruitment and randomisation in the ASPIRING study by a study site.

Analysis Plans
Intervention and comparator: The SWAT will compare the effects of two randomly assigned nudges embedded in the wording of invitation letters to a randomised trial sent direct to patients, with invitation letters without these nudges. The outcomes will be the proportion of invitees who respond to these invitations and the proportion of invitees who are recruited to the host study.

People identified as eligible to participate in ASPIRING by NHS England searches of healthcare systems data will be approached in batches at regular time intervals, according to their residential postcode and the planned order of site activations. NHS England will use computerised randomisation to assign each invitee to one of the three SWAT groups with a 1:1:1 ratio.

Analysis plan: We will measure the number of invitees and their primary and secondary outcomes for each nudge group and the control group. We will describe the characteristics of invitees for each nudge group and the control group. We will describe the responding proportions overall and compare these proportions between groups. Due to the randomized design and large sample size, we expect all measured and unmeasured confounders to be balanced between the SWAT groups. We will perform the following pairwise comparisons: control vs individualistic plus norms; control vs physical safety; and individualistic plus norms vs physical safety. Outcomes will be considered statistically significant if $p<0.05$.

We will use exploratory tests of interaction to assess consistency of effects among subgroups on the primary outcome. Subgroups to be investigated are age, sex, deprivation status, polypharmacy and multimorbidity.

Possible Problems in Implementing This SWAT
Healthcare systems data may be inaccurate for identifying people with ICH and cannot identify patients' ethnicity and mental capacity.

Older people, or their nearest relatives, may not have the skills or technology required to register interest in participating via the ASPIRING study website.

A respondent's hospital may not be activated as a trial site soon after they register their interest.

Although the sample size will be large, if there are high response rates overall (>10%) ASPIRING will not be sufficiently powered to detect differences in nudge effects.

References Cited in This Outline
1. Al-Shahi Salman R, Minks DP, Mitra D, et al. Effects of antiplatelet therapy on stroke risk by brain imaging features of intracerebral haemorrhage and cerebral small vessel diseases: subgroup analyses of the RESTART randomised, open-label trial. Lancet Neurol 2019; 18(7): 643-52.
2. Maxwell AE, MacLeod MJ, Joyson A, et al. Reasons for non-recruitment of eligible patients to a randomised controlled trial of secondary prevention after intracerebral haemorrhage: observational study. Trials 2017; 18(1): 162.
3. Hanlon P, Hannigan L, Rodriguez-Perez J, et al. Representation of people with comorbidity and multimorbidity in clinical trials of novel drug therapies: an individual-level participant data analysis. BMC Medicine 2019; 17(1): 201.
4. Johansen ND, Vaduganathan M, Bhatt AS, et al. Electronic nudges to increase influenza vaccination uptake in Denmark: a nationwide, pragmatic, registry-based, randomised implementation trial. Lancet 2023; 401(10382): 1103-14.
5. Treweek S, Pitkethly M, Cook J, et al. Strategies to improve recruitment to randomised trials. Cochrane Database of Systematic Reviews 2018; (2): MR000013.

References to This SWAT

Source of This SWAT
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