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Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

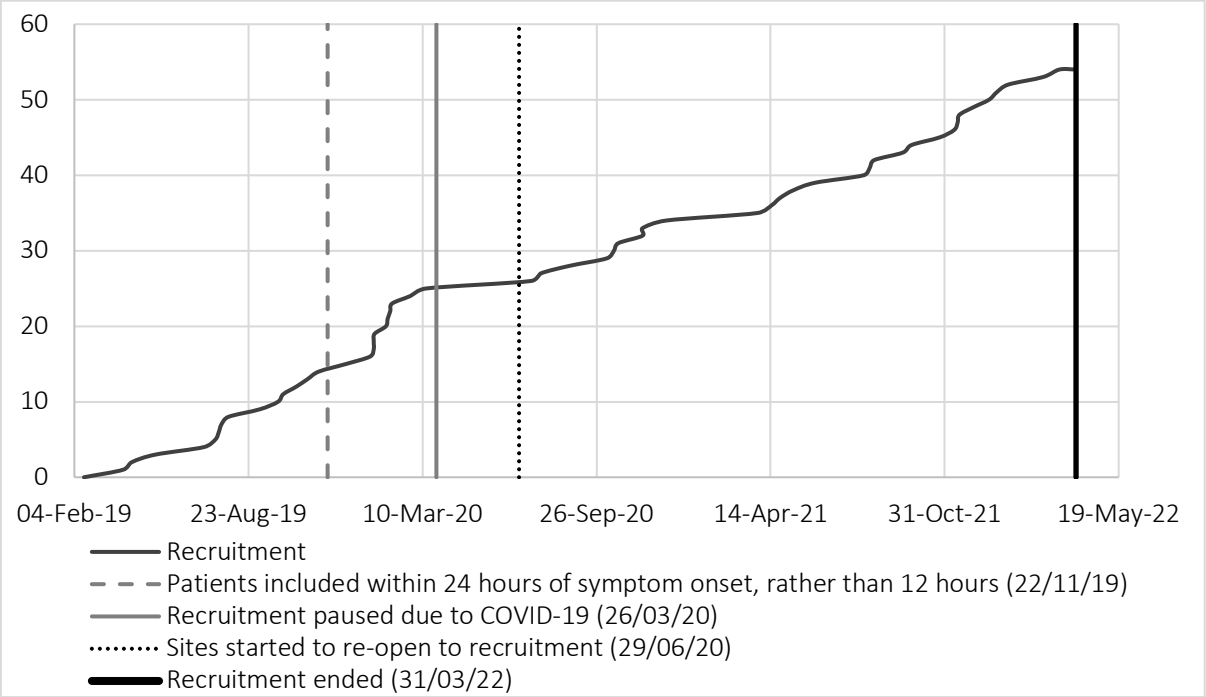
Supplement to: Desborough MJR, Al-Shahi Salman R, Stanworth SJ, et al. Desmopressin for patients with spontaneous intracerebral haemorrhage taking antiplatelet drugs (DASH): a UK-based, phase 2, randomised, placebo-controlled, multicentre feasibility trial. *Lancet Neurol* 2023; **22:** 557–67.

Desmopressin for patients with spontaneous intracerebral haemorrhage taking antiplatelet drugs (DASH): a multi-centre phase II blinded randomised controlled feasibility trial

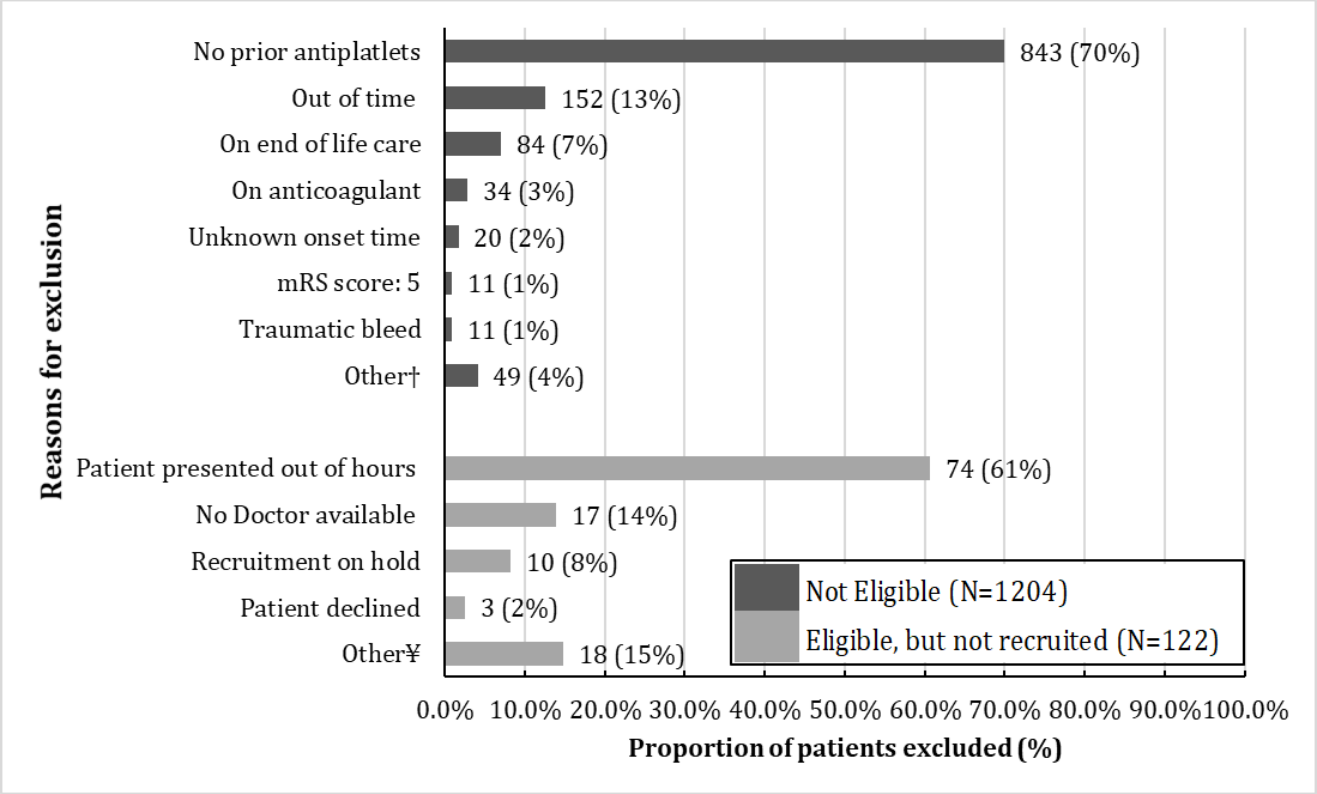
Supplementary figures and tables

Contents

Supplementary Figure 1. Cumulative recruitment .



Supplementary Figure 2. Reasons for exclusion

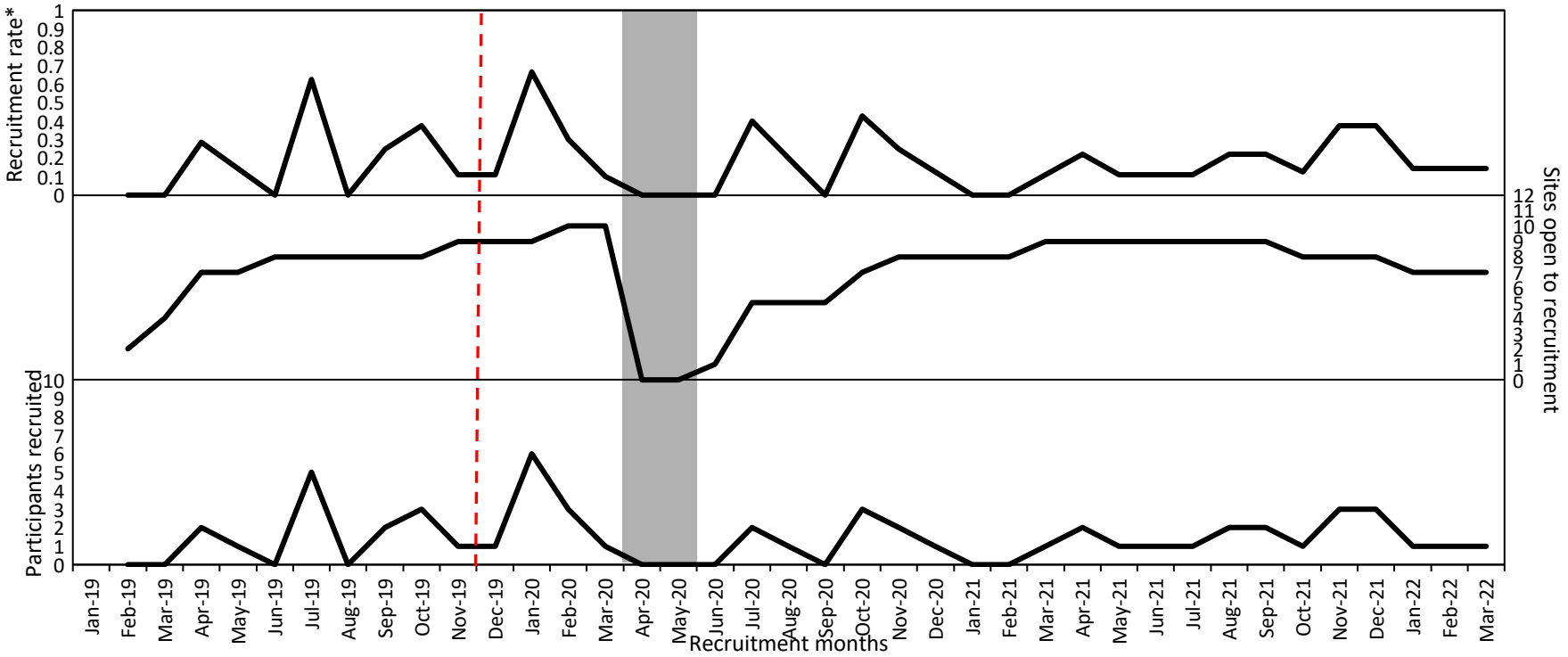


Other categories are summations of categories where total is <10 patients, with the exception of patient declined.

† Categories include infarct/transformation, GCS<5, intracranial aneurysm, critically unwell/poor diagnosis, ambiguity regarding antiplatelets, drug-eluting stent, status epilepticus, secondary bleed, other clinical, subdural haematoma or subarachnoid haemorrhage, amyloid angiopathy, simultaneous heart attack, incorrect screening, cardiac failure and vaccine induced thrombotic thrombocytopenia.

¥ Categories include language barrier, surgery, recruitment to other trial, dementia, no assent available, no capacity to recruit, overseas patient, patient put on 'psych hold', COVID-19 positive diagnosis and patient missed.

Supplementary Figure 3. Site recruitment between the first site opening (Feb 2019) and the trial closing (Mar 2022)



*Recruitment rate calculated as number of participants recruited/number of sites open to recruitment

Amendment SA/03/19 (participants eligible for randomisation within 24 hours of symptom onset [previously 12 hours])

Recruitment paused due to COVID-19

Supplementary Figure 3 illustrates monthly recruitment totals and rates, in conjunction with the number of sites open to recruitment for the trial duration. An increase in recruitment is evident following the implementation of amendment SA/03/19 and prior to the pause in recruitment due to COVID-19 (March – June 2020). Sites re-opened after the pandemic according to limited local capacity, but this took several months, and one site did not re-open at all. Consequently, recruitment did not return to the level seen post-amendment/pre-pandemic.

Supplementary Table 1. Reasons for exclusion of participants who were eligible

Eligible but not recruited	**122**
Patient arrived out of hours	74 (61%)
No doctor available to take consent	17 (14%)
Recruitment on hold	10 (8%)
No capacity at hospital to recruit	3 (2%)
Patient declined	3 (2%)
Language barrier	3 (2%)
Surgery	2 (2%)
Dementia	2 (2%)
No assent available	2 (2%)
Recruitment to other trial	2 (2%)
COVID-19 positive diagnosis	1 (1%)
Patient put on 'psych hold'	1 (1%)
Overseas patient	1 (1%)
Patient missed	1 (1%)

Supplementary text. P-Selectin

P-selectin is derived from alpha-granules within platelets and becomes exposed on the platelet surface membrane when platelets are activated. Measurement of surface expression of P-selectin was performed using commercial kits sensitive to aspirin or clopidogrel (Platelet Solutions). Citrate anticoagulated blood was kept at 37°C once collected using a dry heat pad and insulation pouch, then incubated with platelet stimulants: arachidonic acid 0.5 mM for aspirin testing; ADP 10 μM for clopidogrel testing; and an unstimulated sample for baseline expression. After 5 min of incubation, a fixative (PAMFix) was added and the fixed samples were transferred to the Nottingham flow cytometry laboratory for processing. Fixed blood was incubated with fluorescent antibodies to identify platelets (CD61) and P-selectin (CD62P). Median fluorescence was recorded for platelet surface expression of P-selectin for each sample. Arachidonic acid was used to assess aspirin with mean fluorescence of 500 or less considered to be appropriate inhibition of platelet function by aspirin. ADP used to assess clopidogrel with median fluorescence of 860 or less considered to be appropriate inhibition of platelet function by clopidogrel

The first 28 patients recruited into the DASH trial would have been eligible for P-Selectin testing and 14 (50%) had the tests done. The manufacturers of the P-Selectin tests, Platelet Solutions Ltd., closed to business before the end of the trial, so these tests were not available for the last 26 patients recruited to DASH.

Baseline, pre-treatment samples were available for 14 patients: nine taking aspirin and six taking clopidogrel (one patient was on both drugs)

Negative controls (no agonist) and positive controls (thrombin as agonist) all worked appropriately

Anti-platelet drug	Inhibited	Not inhibited	Total patients
Aspirin	3 (33%)	6 (67%)	9
Clopidogrel	4 (67%)	2 (33%)	6

There is no validated cut-off for the P-Selectin test for determining resistance to antiplatelet drugs. It is possible that these results may show high rates of either antiplatelet drug resistance or non-compliance. However the small numbers of patients who had these tests run and limitations of the sensitivity and specificity of these tests also must be considered. As the manufacturer, Platelet Solutions Ltd., closed to business part way through the DASH trial, further validation and analysis was not possible.