

What a year 2023 was!

Welcome to the RUSH newsletter, brimming with updates about people in the team and their projects in 2023.

We'll start by highlighting how well our people are doing, and then move on to the projects...

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***Nesh Samarasekera
awarded a Stroke
Association senior
clinical fellowship***

Dr Nesh Samarasekera is already a consultant neurologist who combines clinical practice



with research and has worked with the RUSH team since 2010. She applied for a senior clinical lectureship

from The Stroke Association in open competition, and got 5 years of funding for this post in the Autumn. No mean feat!

Stroke
Association

Nesh is excited to devote more of her work life to better understanding the inflammatory response to brain haemorrhage. She aims to find a drug treatment to improve outcome.

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Welcome to the team, Alice Hosking

Alice is a doctor in training who moved to Edinburgh from London a few years ago, and started a 1-year research fellowship with the RUSH team this year. She has developed a proposal for a PhD and is hoping to obtain funding to stay with the team for three more years.

Here is Alice with her little boy, Ruaridh.



Alice has already been successful with her application to the British Heart Foundation Data Science Centre who supported her project: *Improving*

the accuracy, equity and efficiency of using healthcare systems data for recruitment to a clinical trial.



Led by Health Data Research UK

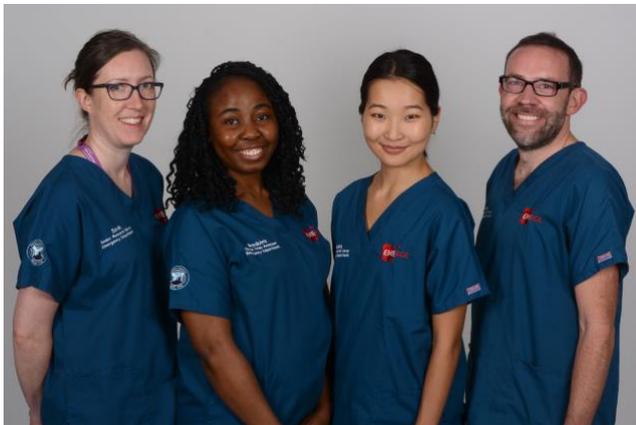
She has enjoyed being an integral part of the team to start a new study, called PLINTH. You can read more about it below.

Alice also really enjoyed running the Edinburgh half marathon with the several members of the RUSH team, in aid of The Stroke Association... so much so that she has signed up for a full marathon next year!

Welcome to our new EMERGE nurses

Mairi Macdonald and Jess Teasdale moved on to pastures new this year, and they have been succeeded by Anuka Boldbaatar and Ikeoluwa Adekoya. Allan Macraird

continues to lead the team with panache, pictured left to right: Sarah Risbridger, Ikeoluwa Adekoya, Anuka Boldbaatar, and Allan MacRaild...



The EMERGE nurse team in the Cerebrovascular Research Group nurse team continue to recruit to a varied portfolio of stroke studies, including the following studies for people with intracerebral haemorrhage (ICH):

1. *EdoxabaN foR IntraCranial Hemorrhage survivors with Atrial Fibrillation (ENRICH-AF)*
2. *Triple therapy prevention of Recurrent Intracerebral Disease EveNts Trial (TRIDENT)*

3. *Tranexamic acid for hyperacute spontaneous IntraCerebral Haemorrhage (TICH-3)*

One of the benefits for participants in clinical trials with long-term follow-up is the development of significant therapeutic relationships. Both participants and the team can attest to the value of these deeper connections within the search for ICH treatments.

We attended the EMERGE annual meeting, dinner and ceilidh. Rustam spoke about the future of clinical trials in acute care research, with a focus on sustainability (so he 'cycled there) – don't the team scrub up well (Rustam's cycling shoes are hidden, though!)?



Tom Moullaali



Dr Tom Moullaali continues to support the RUSH team each Wednesday. Tom helped design the PLINTH feasibility study and now supports the RUSH team with recruitment. Looking forward to 2024, Tom intends to lead a project to

determine characteristics (e.g. a person's health problems, brain scan findings, genetics) that predict the risk of serious bleeding and/or serious blood clots after ICH. This might help doctors personalise decisions about long-term treatment after ICH.

As you can see from his portrait this year, Tom also did some fundraising for The Stroke Association by running the Edinburgh half marathon – further details below.

Rustam Al-Shahi Salman

Rustam hasn't been slacking this year, which has involved the usual pleasurable mix of clinical work in the stroke service, grant writing, publications, and supporting the next generation of stroke researchers. However, his leadership roles have reminded him that surviving your 50s is all about resilience and succession planning, and that he can't do it without two amazing women behind him: **thanks Elaine and Rosemary!**



Rustam was honoured to be asked by the European Stroke Organisation to organise the 2023 and 2025 European Stroke Science workshops at the Hotel Eibsee in [Garmisch Partenkirchen](#) near the Alps in Bavaria. This invitation-only academic retreat for 120 people

was a little too elitist for Rustam's tastes, so he introduced:

- an open application process for early-mid career researchers, 30 of whom applied, and 5 of whom won awards.
- opportunities for families to join those with caring responsibilities, and
- a "fun run"



As you can see, snow made the pace of the run 'gentle', but sadly it kept on falling, leading to the closure of Munich airport and many delegates being stranded for up to five days. I bet the 'select invitees' weren't so chuffed with their invitation then!

Finally, Rustam was appointed as one of a small number of medical Trustees of The Stroke Association. He looks forward to guiding the charity and learning from other Trustees from diverse backgrounds.

Stroke
Association

Visitor from Italy



In June, we were pleased to host Dr Raffaele Ornello from the University of L'Aquila in Italy on a European Stroke Organisation 'department to department visit programme, so that he could experience the way we look after people with stroke, and our approach to conducting clinical research.

Disseminating our research



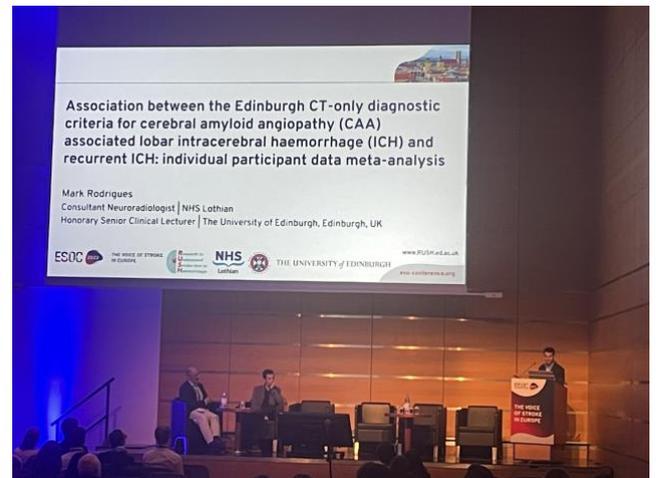
24-26 MAY 2023
MUNICH, GERMANY

Almost all of us were in Munich in May at the European Stroke Organisation Conference, including our research nurses (who are never shy of a photo), as you can tell from this selfie below (left-to-right: Allan, Mairi, and Sarah).



Rustam gave a talk to prepare the delegates for ASPIRING (more details below). More

importantly, our mid-career researchers had a good outing, as you can see from Mark Rodrigues presenting his work on the association between the Edinburgh CAA diagnostic criteria and outcome...



...and Nesh presenting on inflammation after ICH...



In October, Rustam made himself work hard for the trans-

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Atlantic airfare, presenting work at three conferences in Canada:

World ICH conference (WICH)



World Congress of Neurology



WCN 2023
XXVI WORLD CONGRESS
OF NEUROLOGY
MONTREAL, 15-19 OCTOBER, 2023



World Stroke Congress (WSC)



Rustam presented his most important publication of the year at the World Stroke Conference, which was published at the same time in *The Lancet Neurology* (<https://pubmed.ncbi.nlm.nih.gov/37839434/>). This was the result of a global collaboration of researchers doing randomised

controlled trials to try to work out whether powerful blood thinning treatments (oral anticoagulation) are safe and beneficial for people with an irregular heart rhythm (atrial fibrillation) after ICH.



These studies are difficult to do, but the researchers will not be defeated!

So Rustam called

the collaboration **COCROACH**, which stands for Collaboration Of Controlled Randomised trials Of long-term oral Antithrombotic agents after spontaneous intraCranial Haemorrhage.

The team combined data from 4 randomised studies and found that oral anticoagulation reduced the risk of stroke due to clotting. But the studies were too small to be conclusive about safety and overall 'net' effects: to do that we must complete ongoing studies.

You can listen to Rustam discussing the findings in a short podcast, which is accessible via: <https://thelancetneurology.buzzsprout.com/>.



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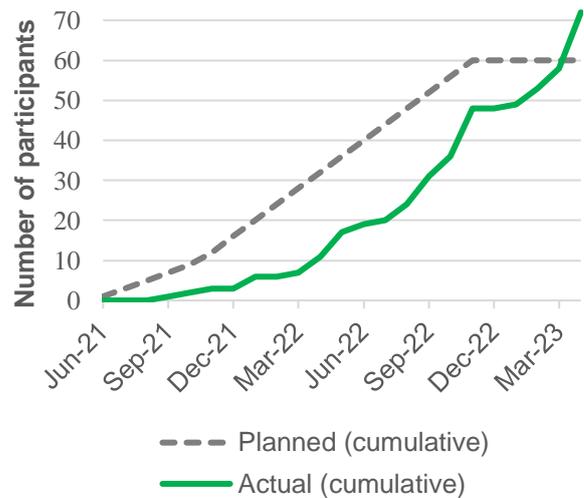
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CARE completes and hopes to continue...

The Cavernomas: A Randomised Effectiveness (CARE) study began in August 2020. It's the first randomised study to compare surgery with medical management for people with brain cavernomas. Randomised studies are the fairest tests of treatment. But not everyone takes part in these studies and cavernomas are rare.

line) throughout, until the final month of a 5-month extension when we overshot!



So the CARE pilot study was a first attempt to see if it might be feasible to do a large study that would answer the question.

We are so grateful to the many investigators at the 28 hospitals that took part, and to the 72 participants. We're writing up the papers that will report the final results to present to the team in January and to the Society of British Neurosurgeons in April...

We started the study during the COVID-19 pandemic, so the process of getting hospitals on board was slow. Recruiting people to the study (green line) was behind our target (dashed



Most people with brain cavernomas who don't have surgery or decided not to take part in the CARE study would prefer to take a drug to prevent bleeding from their cavernoma. However, specific drugs aren't known to be effective.

So, we got an Acceleration Award from the NIHR for a project called **CARE PREP**. It brought together patients, doctors, and researchers to design a randomised study of drugs for brain cavernomas. We completed this project in 2023, which culminated in the design of a 3-arm randomised study comparing two drugs (aspirin or propranolol) with standard care for people with brain cavernoma. This is called CARE MAP, and we've submitted a funding application for it to the NIHR.

We hope for good news about this in 2024, when we'll also consider whether it could run alongside a main phase of the CARE study of surgery.

PLINTH begins

Our new study this year is called a PPlatform study for INTracerebral Haemorrhage (or PLINTH, for short).



PLINTH

Standard care for people with brain haemorrhage involves doing things that can help them. For example, brain scans can show the cause and care in a hospital Stroke Unit helps people to recover. Randomised studies showed us what helps people with brain haemorrhage, which is what constitutes standard care.

We want to improve recovery after brain haemorrhage by doing more research. Some studies might investigate things that we already do for some people because we're still not sure if they help: like reducing blood pressure as soon as possible. Other studies might investigate

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new tests or treatments, like drugs to reduce brain swelling.

Because many different things may help, in future we want to be able to investigate all of them in one study, called a 'platform study'. A platform study of several treatments gets results quicker than doing lots of separate studies and could make treatments available to people with brain haemorrhage faster.

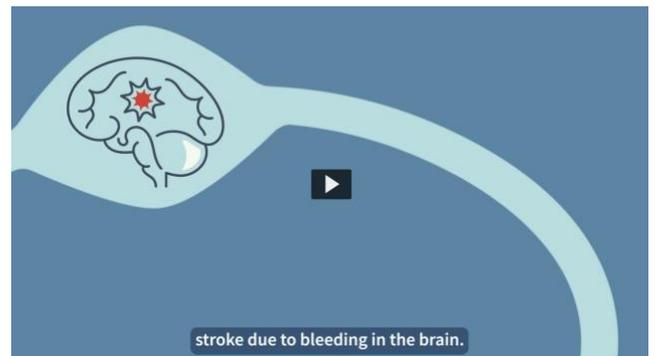
PLINTH is a small-scale study to see if a bigger, definitive platform study would be feasible.



CHIEF SCIENTIST OFFICE

Our funding from the Chief Scientist Office of the Scottish Government began in April, and recruitment was underway in Lothian in October and in Lanarkshire by November. You can watch a short video about

the study, narrated by Allan, via www.ed.ac.uk/plinth:



Now we're **ASPIRING**

The Antiplatelet Secondary Prevention International Randomised study after INtracerebral haemorrhage (ASPIRING) aims to determine if aspirin (or similar drugs) reduce all major clotting and bleeding problems compared to avoiding these drugs for adults with a history of brain haemorrhage.

ASPIRING

Antiplatelet Secondary Prevention International Randomised study after INtracerebral haemorrhage



ASPIRING is the definitive main phase trial following RESTART (www.RESTARTtrial.org), which

we completed in 2021. Since then, we have won funding in the UK, Canada, The Netherlands, and Australia from a variety of government and charity funders via the [Global Cardiovascular Research Funders Forum Multinational Clinical Trials Initiative](#). We plan to recruit 4,148 brain haemorrhage survivors over 4 years, starting in the UK in late 2024.

Arthur Fonville Award for Stroke Research

We held the annual award ceremony with the Fonville family and friends via Zoom on 24th November 2023. We had attendees from The Netherlands, France, Belgium and the UK to hear the three prize-winning presentations followed by the customary gentle inquisition from Joost and Rustam. This year, the winners were: **Abel Sandmann (Amsterdam, pictured right)** for his dissertation, “Natural history of cerebral cavernous malformations: a retrospective



single-centre cohort study”, **Carlos Rangkuti (Amsterdam, pictured left)** for his dissertation, “Effects of intravenous Alteplase in patients with

carotid tandem lesions undergoing endovascular treatment for proximal anterior circulation stroke – a post-hoc



analysis of the MR CLEAN – NO IV Trial”, and **Liza Chong (Edinburgh, pictured right, receiving her certificate from**

Rustam, left) for her dissertation, “Retinal vascular changes in relation to brain changes in Mild Stroke Study 3 patients: a one-year follow-up study.”

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Congratulations to all three winners! Each of them received an Arthur Stone, a £100 cash prize, and the opportunity to receive a bursary of up to £750 towards presenting their research at a stroke conference.



The Fonville family and friends fundraise for this award in inspiring ways. The photograph above shows the grandchildren of friends of the Fonville family, Catherine and Christian De Berail, who organised a pancake party in Toulon to raise funds with friends and family. The children prepared and served pancakes in this beautiful setting: something that the weather wouldn't allow in Scotland!

We celebrate 10 years of Arthur's award next year, when we hope to plan a special event in The Netherlands...

Patient Reference Group

We continue to be indebted to the 8-person strong RUSH [Patient Reference Group](#) (PRG), who help to identify, design, develop, oversee, deliver, and disseminate our research studies. They have helped Nesh, Alice, Rustam and Tom this year, and supported ASPIRING and PLINTH.

If you are a brain haemorrhage survivor or carer interested in joining our PRG, please contact us. We are looking for women, people with disability, and people from black and minority ethnic groups in particular.

World Stroke Day



Raising money for RUSH

We are extraordinarily grateful to those who donate to our research programme.

Members of the RUSH team (Tom Moullaali, Alice Hosking, Allan MacRaid, and Mark Rodrigues) joined other colleagues (Marja Main and Ellen Backhouse) to form a team for the half marathon in May at the Edinburgh Marathon Festival (below). They raised a whopping £883 for The Stroke Association!



If you want to fundraise for us or make a donation, you can find out how to do so via the 'Donate or Fundraise' section of our website: www.RUSH.ed.ac.uk.

Season's greetings from the RUSH team!



Left-to-right: Allan MacRaid, Alice Hosking, Elaine Lord, Nesh Samarasekera, Rustam Al-Shahi Salman, Rosemary Anderson, and Tom Moullaali.

Contact us

Feel free to contact us using any of the methods described below:

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Twitter [@BleedingStroke](https://twitter.com/BleedingStroke)

Facebook www.facebook.com/bleedingstroke



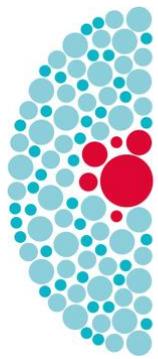
Publications in 2023 that involved the RUSH team:

1. Vacek A, Mair G, White P, Bath PM, Muir KW, Al-Shahi Salman R, Martin C, Dye D, Chappell FM, von Kummer R, Macleod M, Sprigg N, Wardlaw JM. Evaluating artificial intelligence software for delineating hemorrhage extent on CT brain imaging in stroke. *J Stroke Cerebrovasc Dis* 2023 (in press)
2. Kirby C, Barrington J, Sondag L, Loan JJM, Schreuder FHBM, McColl BW, Klijn CJM, Al-Shahi Salman R, Samarasekera N. Association between circulating inflammatory biomarkers and functional outcome or perihematomal oedema after ICH: a systematic review & meta-analysis. *Wellcome Open Research* 2023;8:239
3. Askew KE, Beverley J, Sigfridsson E, Szymkowiak S, Emelianova K, Dando O, Hardingham GE, Duncombe J, Hennessy E, Koudelka J, Samarasekera N, Al-Shahi Salman R, Smith C, Tavares AAS, Gomez-Nicola D, Kalara RN, McColl BW, Horsburgh K. Inhibiting CSF1R alleviates cerebrovascular white matter disease and cognitive impairment. *Glia* 2023 (in press)
4. Syed M, Martin H, Sena E, Williamson PR, Al-Shahi Salman R. Selective outcome reporting in randomised controlled trials including participants with stroke or transient ischaemic attack: a systematic review. *Eur J Stroke* 2023;8:923-931
5. Best JG ... 14 authors ... Al-Shahi Salman R ... 33 authors ... Werring DJ. Clinical associations and prognostic value of MRI-visible perivascular spaces in patients with ischaemic stroke or TIA: a pooled analysis. *Neurology* 2023 (in press)
6. Al-Shahi Salman Ret al. for the Collaboration Of Controlled Randomised trials of long-term Oral Antithrombotic agents after



spontaneous intraCranial Haemorrhage (COCROACH). Effects of oral anticoagulation for atrial fibrillation after spontaneous intracranial haemorrhage: prospective individual participant data meta-analysis of randomised trials. *Lancet Neurol* 2023;22:1140-49

7. Moullaali TJ, Walters R, Rodrigues M, Samarasekera N, Bernal J, Wang X, Humphreys C, Wardlaw JM, Farrall A, Smith C, Anderson CS, Al-Shahi Salman R, McKinstry B. Association between systolic blood pressure variability and severity of cerebral amyloid angiopathy in incident intracerebral haemorrhage. *Frontiers in Stroke* 2023;2: doi:10.3389/fstro.2023.1278610
8. Eilertsen H, Menon CS, Law ZK, Chen C, Bath PM, Steiner T, Desborough MJR, Sandset EC, Sprigg N, Al-Shahi Salman R. Haemostatic therapies for stroke due to acute, spontaneous intracerebral haemorrhage. *Cochrane Database of Systematic Reviews* 2023, Issue 10. Art. No.: CD005951.
9. Jensen M, Al-Shahi Salman R, Ng GA, van der Worp HB, Loh P, Campbell B, Kalman JM, Hill MD, Sposato L, Andrade JG, Metzner A, Kirchhof P, Thomalla G. Current practice and attitudes of stroke physicians towards early rhythm-control therapy for stroke prevention: results of an international survey. *Neurological Research and Practice* 2023;5:29
10. Soo Y ... 43 authors ... Al-Shahi Salman R ... 63 authors on behalf of the Microbleeds International Collaborative Network. Impact of Cerebral Microbleeds in Stroke Patients with Atrial Fibrillation. *Ann Neurol* 2023;94:61-74
11. Desborough MJR, Al-Shahi Salman R, Stanworth SJ, Havard D, Woodhouse LJ, Craig J, Krishnan K, Brennan PM, Dineen RA, Coats TJ, Hepburn T, Bath PM, Sprigg N for DASH trial investigators. Desmopressin for patients with spontaneous intracerebral



haemorrhage taking antiplatelet drugs (DASH): a UK-based, phase 2, randomised, placebo-controlled, multicentre feasibility trial. *Lancet Neurology* 2023;22:557-67

12. Cliteur MP, Sondag L, Cunningham L, Al-Shahi Salman R, Samarasekera N, Klijn CJM, Schreuder FHBM. The association between perihæmatomal oedema and functional outcome after spontaneous intracerebral haemorrhage: a systematic review and meta-analysis. *Eur J Stroke* 2023;8:423-33
13. Appleton JP, Law ZK, Woodhouse LJ, Al-Shahi Salman R, Beridze M, Christensen H, Collins R, Dineen RA, Egea-Guerrero JJ, England TJ, Karlinski M, Krishnan K, Laska AC, Lyrer PA, Ozturk S, Roffe C, Roberts I, Robinson TG, Scutt P, Werring DJ, Bath PM, Sprigg N. Effects of blood pressure and tranexamic acid in spontaneous intracerebral haemorrhage: a secondary analysis of a large randomised controlled trial. *BMJ Neurology Open* 2023;14:1125038
14. Martí-Fàbregas J ... 44 authors ... Al-Shahi Salman R ... 25 authors ... Prats-Sanchez L. Stroke risk and antithrombotic treatment during follow-up of patients with ischemic stroke and cortical superficial siderosis. *Neurology* 2023;100:e1267-81
15. Boe NJ, Hald SM, Jensen MM, Bojsen JA, Elhakim MT, Florisson S, Saleh A, Clausen A, Möller S, Harbo FSG, Graumann O, Hallas J, Rodríguez LAG, Al-Shahi Salman R, Goldstein LB, Gaist D. Association between statin use and intracerebral hemorrhage location. A nested case-control registry study. *Neurology* 2023;100:e1048-61
16. Cochrane A, Chen C, Stephen J, Rønning OM, Anderson CS, Hankey GJ, Al-Shahi Salman R. Antithrombotic treatment after stroke due to intracerebral haemorrhage. *Cochrane Database of Systematic Reviews* 2023;1(1):CD012144