NIHR | National Institute for Health and Care Research

Health Technology Assessment

Check for updates

Synopsis

Stopping anticoagulation for isolated or incidental subsegmental pulmonary embolism: the challenges and lessons from the STOPAPE RCT

Daniel Lasserson[1*] Pooja Gaddu[2] Samir Mehta[2] Agnieszka Ignatowicz[3] Sheila Greenfield[3] Clare Prince,[4] Carole Cummins[3] Graham Robinson[5] Jonathan Rodrigues[5] Simon Noble[6] Susan Jowett[3] Mark Toshner[7] Michael Newnham[3] and Alice Turner[3]

[1]Health Sciences Division, University of Warwick, Coventry, UK
[2]Clinical Trials Unit, University of Birmingham, Edgbaston, Birmingham, UK
[3]Institute of Applied Health Research University of Birmingham, Edgbaston, Birmingham, UK
[4]Thrombosis UK, Llanwrda, Wales, UK
[5]Royal United Hospitals Bath NHS Trust, Bath, UK
[6]University of Cardiff, Cardiff, UK
[7]University of Cambridge, Cambridge, UK

[*]Corresponding author Daniel.Lasserson@warwick.ac.uk

Published April 2025
DOI: 10.3310/UGHF6892

Abstract

Background: The increasing use of computed tomography pulmonary angiography to investigate patients with suspected pulmonary embolism has led to an increase in diagnosis of small subsegmental pulmonary embolism, which is rarely detectable with nuclear medicine-based imaging, the standard imaging modality prior to the development of computed tomography pulmonary angiography. The case fatality of pulmonary embolism has fallen in line with the increase in subsegmental pulmonary embolism diagnoses from computed tomography pulmonary angiography suggesting that we may be over-diagnosing pulmonary embolism (i.e. we may be diagnosing mild forms of pulmonary embolism which may not need any treatment). Given that full anticoagulation has significant side effects of bleeding and subsegmental pulmonary embolism was not commonly diagnosed previously with nuclear medicine imaging (and therefore left predominantly untreated prior to computed tomography pulmonary angiography scanning), there is growing equipoise about the value of full anticoagulation for patients with subsegmental pulmonary embolism.

Methods: We tried to undertake an open randomised trial with blinded end-point adjudication that recruited patients diagnosed with subsegmental pulmonary embolism without evidence of thrombus in the leg veins, termed 'isolated subsegmental pulmonary embolism'. We allocated patients with isolated subsegmental pulmonary embolism to either continuing with at least 3 months of full-dose anticoagulation (standard care) or stopping anticoagulation completely, unless they had a temporary hospital admission where prophylactic (i.e. preventative doses) of anticoagulation is standard practice. In addition, we interviewed patients and clinicians about their views on stopping anticoagulation for isolated subsegmental pulmonary embolism which would be a substantial change from current practice. We planned to assess the accuracy of isolated subsegmental pulmonary embolism diagnoses from computed tomography pulmonary angiographies.

Results: The trial was stopped prematurely due to low recruitment. This was due to a combination of insufficient trial sites, problems with identifying patients who were suitable to be recruited at the time of acute assessment in hospital, the impact of COVID-19 on research infrastructure and a lower prevalence than had been predicted based on published studies. Our interview study showed that the intervention (i.e. changing practice to stopping

This synopsis should be referenced as follows:
Lasserson D, Gaddu P, Mehta S, Ignatowicz A, Greenfield S, Prince C, *et al.* Stopping anticoagulation for isolated or incidental subsegmental pulmonary embolism: the challenges and lessons from the STOPAPE RCT [published online ahead of print April 9 2025]. *Health Technol Assess* 2025. https://doi.org/10.3310/UGHF6892

treatment) is feasible, although there were concerns raised about safety, which a trial would be needed to address. We did not have sufficient trial participants to determine accuracy of initial isolated subsegmental pulmonary embolism diagnoses.
Conclusion: Although we were not able to answer the question of whether it is clinically effective and cost-effective to stop anticoagulating patients with isolated subsegmental pulmonary embolism, we developed a protocol which can be used by future trialists who can successfully attract funding to address this research question, which remains important and an ongoing uncertainty for clinicians and patients.
Future work: Trialists attempting to answer this research question should plan for longer recruitment times and ensure there is sufficient resource for a large number of recruiting centres.
Limitations: There were insufficient recruits to progress from the pilot phase to the full STOPAPE trial.
Funding: This synopsis presents independent research funded by the National Institute for Health and Care Research (NIHR) Health Technology Assessment programme as award number NIHR128073.
A plain language summary of this synopsis is available on the NIHR Journals Library Website https://doi.org/10.3310/UGHF6892.

Introduction

This synopsis paper describes the difficulties that the STOPAPE trial team had in setting up and recruiting to a trial comparing different treatment strategies for patients with isolated or incidental subsegmental pulmonary embolism (ISSPE). STOPAPE aimed to test whether a strategy of withholding oral anticoagulation for ISSPE was clinically effective and cost-effective, compared with the standard care of at least 3 months of full anticoagulation.[1] The trial design was a pragmatic open-label blinded end-point study, where patients would be randomised predominantly from acute assessment settings (Emergency Departments, Acute Medical Units and Same Day Emergency Care units) once the diagnosis of ISSPE had been confirmed at the local site.

There are two linked papers to this synopsis in the National Institute for Health and Care Research (NIHR) Library – the protocol, which represents the final trial protocol version agreed by the Trial Management Group (TMG)[2], and the qualitative study exploring the views of patients and clinicians on the feasibility of withholding anticoagulation in ISSPE which is a marked change from standard practice (ref Protocol).

The rationale for the trial is presented in the Protocol and is not repeated here (ref Protocol). Similarly, the qualitative study (ref Qualitative study) report details findings which are concentrated on the challenges involved in changing a very established practice for both patients and clinicians and are not reprised in this synopsis.

In this report, we detail the challenges and reasons why the STOPAPE trial was halted prematurely in the hope that future trialists who address the question of whether it is clinically effective and cost-effective to withhold anticoagulation in ISSPE can benefit from our experiences and successfully deliver such a trial. At the time of writing, there is only one trial that is actively recruiting patients with ISSPE and randomising to withholding anticoagulation, the Surveillance versus Anticoagulation For low-risk patiEnts with isolated SubSegmental Pulmonary Embolism trial[3] led from Switzerland, although personal communication from their Chief Investigator has confirmed a lower than anticipated recruitment rate. The impact of large-scale research efforts to complete COVID trials and address the key challenges of the recent and ongoing pandemic are likely to be affecting a broader research portfolio in many countries.

Below, we report on the main challenges related to delivering STOPAPE which include the impact of the COVID-19 pandemic on research infrastructure, the difficulties in identifying patients with ISSPE and a lower prevalence of ISSPE in acute medical patients than predicted from our pre-trial database analyses.

Patient and public involvement

We worked with patient partners with lived experience of thrombosis as we designed and delivered the trial, including one funding co-applicant with lived experience of thrombosis. Patients were members of our TMG and have advised us throughout on trial set-up, patient leaflet design and wording, mechanisms to increase recruitment, interpretation of our qualitative data and ultimately supported the decision of premature cessation of the trial.

Challenges in trial delivery

Trial set-up

The initial planned date for regulatory submission was 1 April 2020 with a projected patient recruitment start date for 1 June 2020. During these months of preparation, the COVID-19 pandemic was established[4] and the medical co-applicants in STOPAPE were increasingly diverted to acute medical care service

provision, supporting the rapid development of COVID-related trials and other studies which reduced capacity to keep STOPAPE on track.

Regulatory approval from the Health Research Authority was given in September 2020 and the first patient was randomised in May 2021, 12 months later than our initial planned date.

Trial sites

We had identified acute trusts to approach at the time of submission for funding to reach our planned 50 sites. As the COVID pandemic became established, there was an initial restriction on Clinical Research Network teams to recruit to studies given Urgent Public Health (UPH) status – as STOPAPE was not a specific COVID trial it was not included in this national portfolio. However, as this restriction was loosened, acute trusts continued to focus on UPH studies and many declined to include STOPAPE in their local hospital research portfolios, citing the ongoing demand of COVID studies on their research support teams. The impact that this had on our actual site recruitment compared with our projected recruitment is shown in the *Figure 1*.

At the point when we were requested to cease recruiting in April 2022, we had 11 active sites with a further 2 sites preparing to open, 8 sites undergoing set up with their research and development departments finalising contracts, and another 26 sites completing feasibility assessment. It took an average of 393 days from initial contact to site activation.

In addition to the pandemic, there were other issues that prevented sites from signing up for STOPAPE. In order to determine whether subsegmental pulmonary embolism (SSPE) is truly isolated, that is thrombus occurs in the subsegmental arteries and not also in the proximal deep leg veins, a lower limb ultrasound study should be undertaken to detect lower limb venous thrombus. This is because the presence of proximal limb venous thrombus poses a risk for a subsequent large pulmonary embolism (PE) in addition to the small emboli resting in the subsegmental pulmonary arteries, and, as such, patients would not be suitable for a trial which has a 'no-treatment' intervention arm.

Feedback from some trusts showed that the requirement to undertake a separate ultrasound scan on both legs was a barrier to joining the trial. Under partition of research costs, this scan cost is not provided by NIHR as, if the trial were to be shown to be positive and change practice, the ultrasound scan would become part of standard care for patients with SSPE if they appropriately matched the trial inclusion and exclusion criteria. As such, even though this ultrasound would only be undertaken in the context of the research study for patients recruited into the trial, it would need to be paid for by the NHS trusts. Although the NHS and NIHR have agreed these principles of partition of research and NHS costs, individual trusts are able to

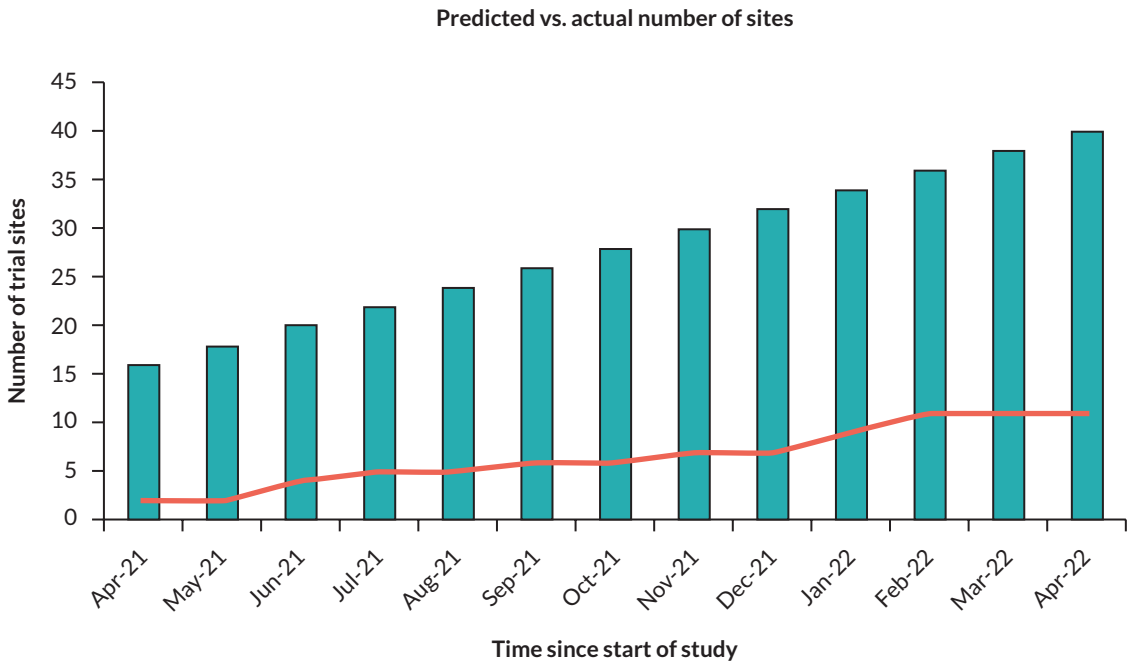

FIGURE 1 Predicted vs. recruited research sites.

This synopsis should be referenced as follows:
Lasserson D, Gaddu P, Mehta S, Ignatowicz A, Greenfield S, Prince C, *et al.* Stopping anticoagulation for isolated or incidental subsegmental pulmonary embolism: the challenges and lessons from the STOPAPE RCT [published online ahead of print April 9 2025]. *Health Technol Assess* 2025. https://doi.org/10.3310/UGHF6892

make their own judgements, and did so in the case of STOPAPE, thereby further reducing the pool of trusts that could support the trial.

As *Figure 1* shows, the inability to recruit trial sites was a major barrier to delivering STOPAPE and although major pushes through professional networks were made by members of the TMG via British Thoracic Society, Society for Acute Medicine, Thrombosis UK and the NIHR Clinical Research Networks, there was little impact and no other interventions could have increased the recruitment of trial sites.

Recruitment of patients with isolated subsegmental pulmonary embolism and feedback from trial sites

For trial sites that were open for recruitment in STOPAPE, the recruitment rate was lower than anticipated. Based on analyses undertaken by co-applicants using local data, we calculated an initial projection of 1.5 patients per recruiting centre per month. During the recruitment window however, trial sites averaged between 0 and 0.3 patients per month, and as such there was only a very small recruitment to the trial, with *Figure 2* demonstrating the substantial shortfall in patients recruited.

We instigated a monthly 'drop in' video clinic where any members of the active site research teams could join and share challenges and any successes as well as ask the Chief Investigator questions about the trial including open discussion around potential solutions to support deliverability of STOPAPE.

From these regular discussions, we learnt that trial sites took different approaches to patient identification, depending primarily on the engagement of the local

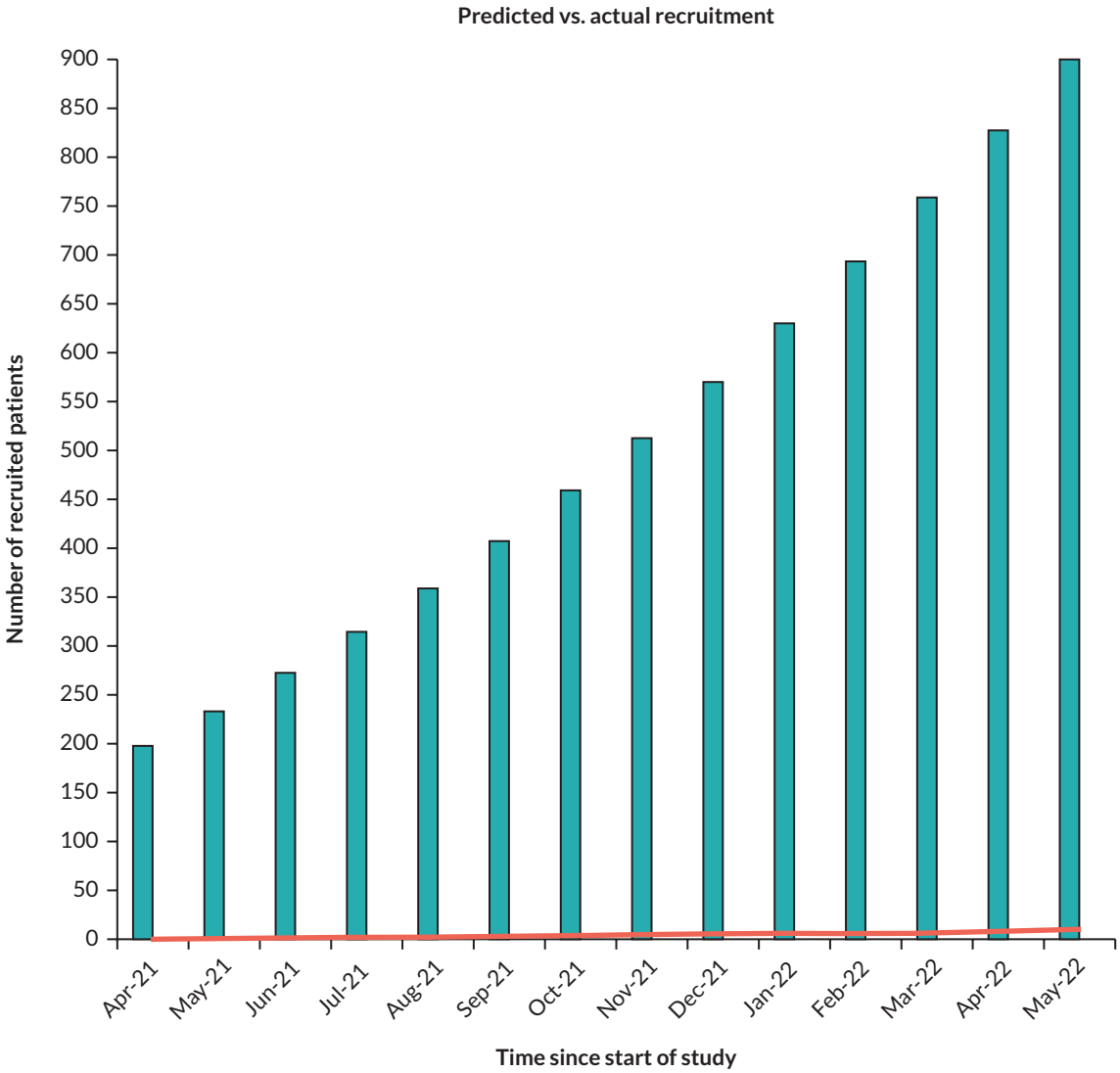

FIGURE 2 Cumulative recruitment of patients to STOPAPE.

radiology department with some radiology departments proactively providing lists of patients with diagnoses of PE or SSPE for further assessment by research teams to determine eligibility, although this would not always be a 'real time' activity as such lists were created to cover the previous 24–48 hours of new diagnoses. Other sites had a more clinically led recruitment strategy which was more reliant on awareness of the trial by clinicians on acute assessment units, identifying potential patients to discuss the trial as they were given the computed tomography results. However, as recruitment rates were very low, no particular strategy for identification seemed more successful than others.

We regularly reviewed reasons for exclusion to determine if there were any areas where an initial potentially cautious approach in our protocol may be inappropriately reducing recruitment. Included within the 'other' category in *Figure 3* are patients where there is an indication for hospital admission not related to treatment of PE, that is where the ISSPE is not directly contributing to the reason for admission, but has been diagnosed in addition to the main diagnosis that has led to admission.

Initially the TMG had developed the protocol to exclude patients admitted to hospital, on the grounds that a 'no-treatment' group would still receive some anticoagulation as prophylactic low-molecular-weight heparin is a standard of care for the majority of inpatients to reduce the chance of hospital-acquired venous thromboembolism (VTE).[1] However, further discussion at TMG meetings resulted in a consensus view that over the course of 3 months of observation, a short course of prophylactic rather than treatment dose anticoagulation would not have a clinical impact on recurrent VTE and, as such, patients who are being admitted, or who are already inpatients should also be eligible for recruitment, provided that the ISSPE has no significant physiological impact as per the standard exclusion criteria. In some centres, this could remove over 20% of exclusions and could therefore contribute to an increase in trial recruits.

At the time of cessation of recruitment, this change to the protocol was prepared for submission (protocol version 3.1) but on the grounds of futility, given that no remediable action could result in meeting recruitment targets, the formal submission to the funder and Research Ethics Committee was not made. However, as the TMG felt that this would be an important step in the general delivery of the trial, we included this in the protocol paper (ref to Protocol paper) to represent the strongest chance for future trialists to successfully deliver a trial in this area and benefit from our experience of attempting to deliver this trial.

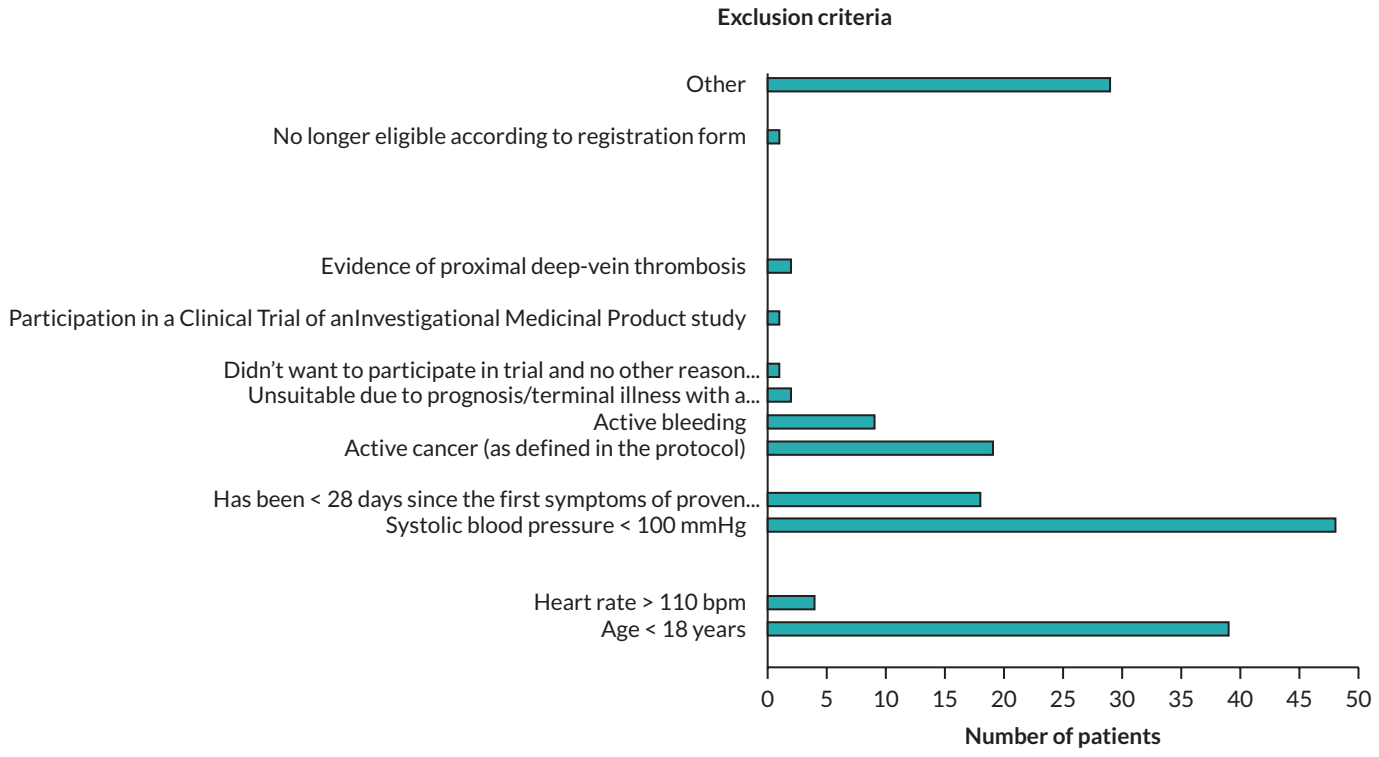

FIGURE 3 Patients meeting exclusion criteria.

Recruited patients

In *Tables 1* and *2*, we report the data collected on the patients recruited to STOPAPE. Of 176 patients screened, 11 patients were registered into the initial consent for an ultrasound of the lower limbs and subsequently 10 patients were randomised.

As *Figure 4* demonstrates in the Consolidated Standards of Reporting Trials diagram, our central expert radiology review showed that not all patients had a confirmed diagnosis of SSPE after expert assessment and also one patient had a PE that was larger than a SSPE and would require anticoagulation (in this case they were already on appropriate treatment as randomised to continuing anticoagulation, i.e. standard care arm).

One patient in the intervention arm of stopping anticoagulation was withdrawn on the advice of an endocrinologist where a pre-existing endocrine condition was deemed an additional risk factor for VTE.

Equality, diversity and inclusion

Due to very low recruitment, we were unable to assess how well participants recruited to the STOPAPE trial represented the populations served at trial sites.

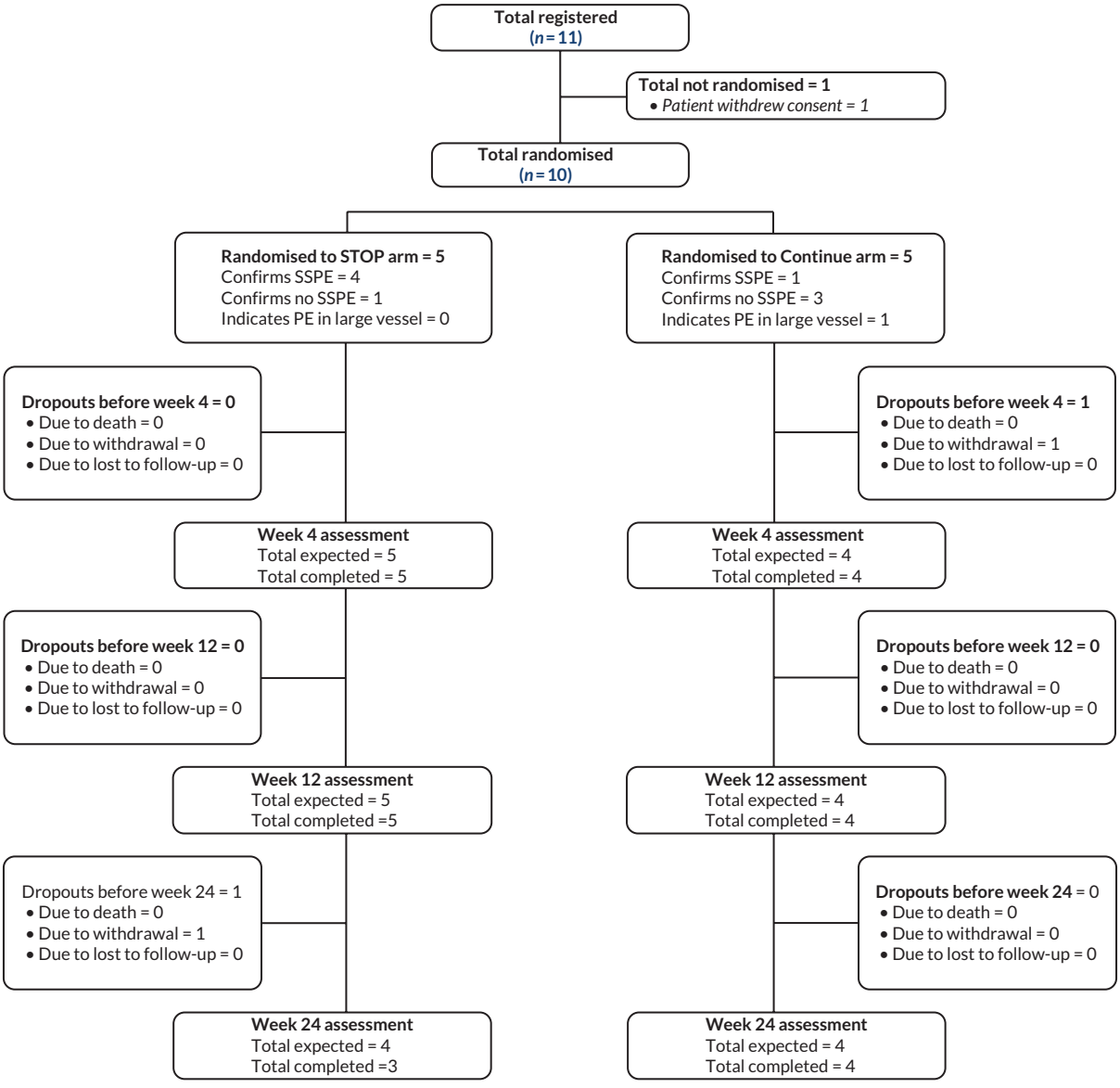

FIGURE 4 Consolidated Standards of Reporting Trials diagram.

TABLE 1 Baseline data

Baseline data	STOP (*N* = 5)	Continue (*N* = 5)	Total (*N* = 10)
Minimisation variables			
Age (years)			
< 50	1 (20%)	1 (20%)	2 (20%)
50–70	2 (40%)	2 (40%)	4 (40%)
> 70	2 (40%)	2 (40%)	4 (40%)
Mean (SD)	59.2 (16.5)	68 (13.4)	63.6 (14.9)
Minimum–maximum	43–79	47–82	43–82
History of cancer			
No	5 (100%)	5 (100%)	10 (100%)
Yes	0 (0%)	0 (0%)	0 (0%)
Type of SSPE			
Symptomatic	5 (100%)	3 (60%)	8 (80%)
Incidental	0 (0%)	2 (40%)	2 (20%)
Previous clinically relevant bleeding as defined by ISTH			
No	5 (100%)	5 (100%)	10 (100%)
Yes	0 (0%)	0 (0%)	0 (0%)
Clinically suspected or confirmed COVID-19			
No	5 (100%)	5 (100%)	10 (100%)
Yes	0 (0%)	0 (0%)	0 (0%)
Demographic and examination data			
Gender			
Male	0 (0%)	2 (40%)	2 (20%)
Female	5 (100%)	3 (60%)	8 (80%)
Smoking status			
Never smoker	1 (20%)	2 (40%)	3 (30%)
Ex-smoker	3 (60%)	3 (60%)	6 (60%)
Current smoker	1 (20%)	0 (0%)	1 (10%)
Ethnicity			
White	5 (100%)	5 (100%)	10 (100%)
Type of scan performed			
Doppler ultrasound	5 (100%)	1 (20%)	6 (60%)
Point-of-care ultrasound	0 (0%)	4 (80%)	4 (40%)
Modified Medical Research Council dyspnoea scale			
Grade 0	3 (60%)	2 (40%)	5 (50%)
Grade 1	0 (0%)	1 (20%)	1 (10%)
Grade 2	2 (40%)	2 (40%)	4 (40%)

continued

TABLE 1 Baseline data (*continued*)

Baseline data	STOP (*N* = 5)	Continue (*N* = 5)	Total (*N* = 10)
Height (metres)			
N	3	3	6
Mean (SD)	160.7 (7.8)	181.3 (15.2)	171 (15.6)
Minimum–maximum	152–167	165–195	152–195
Weight (kg)			
N	4	3	7
Mean (SD)	93.3 (24.6)	90.7 (9.5)	92.2 (18.3)
Minimum–maximum	71.2–115	81–100	71.2–115
Heart rate (bpm)			
N	5	4	9
Mean (SD)	82.8 (16.2)	83.3 (12.3)	83 (13.7)
Minimum–maximum	66–105	68–97	66–105
Systolic blood pressure (mmHg)			
N	5	4	9
Mean (SD)	144.8 (20.1)	138.3 (12.5)	141.9 (16.5)
Minimum–maximum	128–176	121–151	121–176
Respiratory rate (per minute)			
N	5	5	10
Mean (SD)	17.4 (1.1)	27.4 (13.5)	22.4 (10.4)
Minimum–maximum	16–19	16–49	16–49
Oxygen saturation (%)			
N	5	4	9
Mean (SD)	96.2 (0.8)	96 (3.4)	96.1 (2.1)
Minimum–maximum	95–97	91–98	91–98
Past medical history			
Diabetes			
Yes	1 (20%)	0 (0%)	1 (10%)
Varicose veins			
Yes	0 (0%)	2 (40%)	2 (20%)
Ischaemic heart disease			
Yes	0 (0%)	1 (20%)	1 (10%)
Chronic lung disease			
Yes	2 (40%)	0 (0%)	2 (20%)

TABLE 1 Baseline data (*continued*)

Baseline data	STOP (*N* = 5)	Continue (*N* = 5)	Total (*N* = 10)
Peripheral arterial disease			
Yes	0 (0%)	1 (20%)	1 (10%)
Chronic liver disease			
Yes	0 (0%)	1 (20%)	1 (10%)
Blood tests			
Haemoglobin (g/l)			
N	5	5	10
Mean (SD)	127.8 (6.4)	149.2 (12.5)	138.5 (14.6)
Minimum–maximum	117–132	139–169	117–169
Platelet count (× 10^9/l)			
N	5	5	10
Mean (SD)	270.2 (54.2)	249 (71.9)	259.6 (61)
Minimum–maximum	212–359	170–321	170–359
Creatinine (µmol/l)			
N	5	5	10
Mean (SD)	69.8 (15)	96.4 (20.8)	83.1 (22.1)
Minimum–maximum	45–82	70–118	45–118
Estimated glomerular filtration rate			
N	5	4	9
Mean (SD)	73 (15.7)	62.3 (16.7)	68.2 (16.1)
Minimum–maximum	60–90	39–77	39–90

ISTH, International Society on Thrombosis and Haemostasis; SD, standard deviation.

TABLE 2 Adherence

Time point	Adherence	STOP	Continue
Week 4	Number of patients completed week 4 follow-up	*N* = 5	*N* = 4
	N (%) that remained adherent up to week 4	4 (80%)	0 (0%)
	N (%) that were non-adherent by week 4	1 (20%)[a]	4 (100%)
Week 12	Number of patients completed week 12 follow-up	*N* = 5	*N* = 4
	N (%) that remained adherent up to week 12	5 (100%)	4 (100%)
	N (%) that were non-adherent by week 12	0 (0%)	0 (0%)
Week 24	Number of patients completed week 24 follow-up	*N* = 3	*N* = 4
	N (%) that remained adherent up to week 24	3 (100%)	4 (100%)
	N (%) that were non-adherent by week 24	0 (0%)	0 (0%)

a Reason for non-adherence:
- Endocrinology consultant decision.
- Patient felt Cushing's and presented a high risk for VTE and so the endocrinologist did not feel comfortable patient being involved in the trial and switched patient back to continuing long-term anticoagulation.

Interpretation and lessons for future trialists

Poor recruitment of trial sites and very low site recruitment contributed to the inability to deliver the STOPAPE trial. It is clear that had we managed to meet our trial site recruitment projections, we would still not have been able to reach power as the per site recruitment was too low. Thus, while the impact of the COVID-19 pandemic was the greatest barrier to trial site recruitment and delays in getting sites open, more fundamental issues of lower than anticipated prevalence of ISSPE would still have hampered delivery of the trial, independent of the pandemic. While this can be partially mitigated with more pragmatic exclusion criteria, a much longer study duration is likely to be needed to reach power. It is interesting to note that an observational study of outcomes comparing patients with ISSPE treated with an observation-only strategy (equivalent to the STOPAPE intervention arm) with a standard treatment strategy of full-dose anticoagulation took 10 years to collect data from 18 trial centres on 292 patients prior to reporting.[5]

No conclusions can be drawn from our empirical data related to the primary research question, but the disagreements between the expert radiology panel and the local reporting radiologists in this small sample may indicate that this is an important future area of study, possibly outside of a randomised trial so that a formal diagnostic accuracy study can be conducted in a sufficiently large sample, comparing general radiologist reporting of SSPE and expert thoracic radiologist reporting.

Any future trialists should therefore anticipate a low recruitment rate based on a genuine low prevalence of ISSPE with the consequent impact on trial duration and costs, identify funding mechanisms for all trial-related procedures and seek to maximise inclusion criteria based on pragmatic assessment of the impact of short hospital admissions for unrelated conditions and ensure expert thoracic radiological assessment is embedded.

Our qualitative data[6] indicate that the optimal treatment of ISSPE remains an important question for clinicians and patients and data from randomised trials are needed to determine the balance of benefits and harms of anticoagulation.

Additional information

CRediT contribution statement

Daniel Lasserson (https://orcid.org/0000-0001-8274-5580): Conceptualisation, Methodology, Writing – original draft, review and editing, Supervision, Funding acquisition.

Pooja Gaddu (https://orcid.org/0009-0009-4980-1689): Project administration, Investigation, Resources, Writing – review and editing.

Samir Mehta (https://orcid.org/0000-0001-7096-513X): Methodology, Formal analysis, Resources, Writing – review and editing.

Agnieszka Ignatowicz (https://orcid.org/0000-0002-5863-0828): Methodology, Formal analysis, Investigation, Resources, Data curation, Writing – review and editing.

Sheila Greenfield (https://orcid.org/0000-0002-8796-4114): Methodology, Supervision, Formal analysis, Writing – review and editing.

Clare Prince: Resources, Writing – review and editing.

Carole Cummins (https://orcid.org/0000-0001-5464-1944): Methodology, Formal analysis, Resources, Writing – review and editing.

Graham Robinson (https://orcid.org/0000-0001-5191-1451): Methodology, Investigation, Resources, Writing – review and editing.

Jonathan Rodrigues (https://orcid.org/0000-0003-2744-3509): Methodology, Investigation, Resources, Writing – review and editing.

Simon Noble (https://orcid.org/0000-0001-5425-2383): Conceptualisation, Methodology, Writing – review and editing.

Susan Jowett (https://orcid.org/0000-0001-8936-3745): Methodology, Resources, Writing – review and editing.

Mark Toshner (https://orcid.org/0000-0002-3969-6143): Conceptualisation, Methodology, Writing – review and editing, Funding acquisition.

Michael Newnham (https://orcid.org/0000-0002-2972-6249): Methodology, Writing – review and editing, Funding acquisition.

Alice Turner (https://orcid.org/0000-0002-5947-3254): Conceptualisation, Methodology, Writing – review and editing, Funding acquisition.

Data-sharing statement

Due to the very small number of patients recruited and closure of the trial, all relevant data are presented here and there are no data that can be shared. There are no additional data to share for this synopsis of the STOPAPE trial.

Ethics statement

Research ethics approval was given on 18 September 2020 by Wales Research Ethics Committee 6. REC Reference: 20/WA/026.

Wales REC 6, Reference: 20/WA/0256, approved 30 September 2020.

Information governance statement

The University of Birmingham is committed to handling all personal information in line with the UK Data Protection Act (2018) and the General Data Protection Regulation (EU GDPR) 2016/679. Under the Data Protection legislation the University of Birmingham is the Data Controller, and you can find out more about how we handle personal data, including how to exercise your individual rights and the contact details for our Data Protection Officer here: The Data Protection Office, Legal Services, University of Birmingham, Edgbaston, Birmingham, B15 2TT. E-mail: dataprotection@contacts.bham.ac.uk Telephone: 0121 414 3916.

Disclosure of interests

Full disclosure of interests: Completed ICMJE forms for all authors, including all related interests, are available in the toolkit on the NIHR Journals Library report publication page at https://doi.org/10.3310/UGHF6892.

Primary conflicts of interest: Daniel Lasserson is funded by the NIHR Applied Research Collaboration (ARC) West Midlands, the NIHR Community Healthcare MedTech and In Vitro Diagnostics Cooperative (MIC) and the NIHR Oxford Biomedical Research Centre (BRC) and has received funding from the NIHR Policy Research Programme. He was on the NIHR HTA CET Committee 2016–22. He reports institutional funding from Vifor Pharma Ltd and Butterfly Net Inc for research projects outside this study.

Agnieszka Ignatowicz has received grants from NIHR Genomic Medicine Service Alliance (GMSA) and NIHR Global Health Research (GHR).

Jonathan Rodrigues has received funding from the NIHR Research for Patient Benefit Programme and reports consulting fees from NHS X and Heartflow, speaker fees from Sanofi and Aidence, is the Director of Clinical Quality at Heart and Lung Imaging Limited, and declares shares in Radnet.

Simon Noble has received honoraria from Leo Pharma and Pfizer. He is Chair of MePFAC Trial Steering Committee, Database Safety and Monitoring committee member for Prepare Kidney and Medical Director of Thrombosis UK.

Susan Jowett was a member of the NIHR NTA CET 2016–20 and HTA Funding Committee 2019–21.

Mark Toshner is funded by the NIHR Cambridge BRC and reports consulting fees from Jansen and MorphogenIX, and support for attending meetings from Glaxo Smith Kline and Jansen. He participates on boards for FluCov and ComCov.

Alice Turner is a member of the NIHR HTA prioritisation committee (2020–25). Outside this work/subject area, she has received research funds and/or honoraria from Vertex, AstraZeneca, CSL Behring, Grifols Biotherapeutics, GSK, Chiesi, Phillips, ResMed and Boehringer within the last 3 years.

Department of Health and Social Care disclaimer

This publication presents independent research commissioned by the National Institute for Health and Care Research (NIHR). The views and opinions expressed by authors in this publication are those of the authors and do not necessarily reflect those of the NHS, the NIHR, MRC, NIHR Coordinating Centre, the Health Technology Assessment programme or the Department of Health and Social Care.

This synopsis was published based on current knowledge at the time and date of publication. NIHR is committed to being inclusive and will continually monitor best practice and guidance in relation to terminology and language to ensure that we remain relevant to our stakeholders.

Trial registration

This trial is registered as ISRCTN15645679.

Funding

This synopsis presents independent research funded by the National Institute for Health and Care Research (NIHR) Health Technology Assessment programme as award number NIHR128073.

This synopsis provided an overview of the research award Stopping anticoagulation for isolated or incidental sub-segmental pulmonary embolism (STOPAPE). For more information about this research please view the award page (www.fundingawards.nihr.ac.uk/award/NIHR128073).

About this synopsis

The contractual start date for this research was in December 2019. This article began editorial review in September 2023 and was accepted for publication in July 2024. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The Health Technology Assessment editors and publisher have tried to ensure the accuracy of the authors' article and would like to thank the reviewers for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this article.

Copyright

Copyright © 2025 Lasserson *et al*. This work was produced by Lasserson *et al*. under the terms of a commissioning contract issued by the Secretary of State for Health and Social Care. This is an Open Access publication distributed under the terms of the Creative Commons Attribution CC BY 4.0 licence, which permits unrestricted use, distribution, reproduction and adaptation in any medium and for any purpose provided that it is properly attributed. See: https://creativecommons.org/licenses/by/4.0/. For attribution the title, original author(s), the publication source – NIHR Journals Library, and the DOI of the publication must be cited.

List of abbreviations

ISSPE	incidental subsegmental pulmonary embolism
NIHR	National Institute for Health and Care Research
PE	pulmonary embolism
SSPE	subsegmental pulmonary embolism
TMG	Trial Management Group
UPH	Urgent Public Health
VTE	venous thromboembolism

References

1. National Institute for Health and Care Excellence. *Venous Thromboembolic Diseases: Diagnosis, Management and Thrombophilia Testing*. London: NICE; 2020.
2. Lasserson D, Gaddu P, Mehta S, Ignatowicz A, Greenfield S, Prince C, *et al.* Stopping anticoagulation for isolated or incidental pulmonary embolism: the STOPAPE RCT protocol. *Health Technol Assess* 2024;26:1–17. https://doi.org/10.3310/HRCW7937
3. Baumgartner C, Klok F, Carrier M, Limacher A, Moor J, Righini M, *et al*. Clinical Surveillance vs. Anticoagulation For low-risk patiEnts with isolated SubSegmental Pulmonary Embolism: protocol for a multicentre randomised placebo-controlled non-inferiority trial (SAFE-SSPE). *BMJ Open* 2020;**10**:e040151. https://doi.org/10.1136/bmjopen-2020-040151
4. ISARIC. International Severe Acute Respiratory and Emerging Infections Consortium (ISARIC): COVID 19 Report; 2020. URL: https://isaric.org/wp-content/uploads/2020/10/ISARIC_Data_Platform_COVID-19_Report_04.10.2020.pdf
5. Le Gal G, Kovacs MJ, Bertoletti L, Couturaud F, Dennie C, Hirsch AM, *et al*.; SSPE Investigators. Risk for recurrent venous thromboembolism in patients with subsegmental pulmonary embolism managed without anticoagulation: a multicenter prospective cohort study. *Ann Intern Med* 2022;**175**:29–35. https://doi.org/10.7326/M21-2981
6. Ignatowicz A, Greenfield S, Gaddu P, Prince C, Toshner M, Robinson G, *et al*. Interventions that challenge established and accepted clinical practice: lessons learnt from a process evaluation of the STOP-APE trial [published online ahead of print February 26 2025]. *Health Technol Assess* 2025. https://doi.org/10.3310/PSDG7298