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Research Article

Interventions that challenge established and accepted clinical practice: lessons learnt from a process evaluation of the STOP-APE trial

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Abstract

Background: Developing and implementing interventions that change clinical practice can be challenging and complex. Such interventions can be particularly difficult when attempting to change established behaviours and practices. While extensive literature on implementation of interventions that focus on changing clinical practice exists, understanding of the difficulties involved in implementing interventions that go against accepted clinical practice is limited.

Objectives: To describe the challenges involved in delivering a complex intervention that goes against established clinical practice, using a clinical trial assessing the balance of benefits and risks of withholding anticoagulation for subsegmental pulmonary embolism as an example.

Design and methods: This study draws from a process evaluation conducted as part of a clinical trial. The evaluation utilised semistructured interviews with patients and clinicians during the trial's internal pilot phase to investigate the acceptability of withholding anticoagulant medication and participants' experiences within the trial. The data were analysed using the framework method.

Setting and participants: Eight patients with subsegmental pulmonary embolism (six females and two males) and three acute care clinicians (two males and one female) from five trial sites were interviewed.

Results: Our findings indicated that factors such as clinician equipoise, discomfort with certain patient characteristics, and effective patient communication are closely connected and significantly impact both the process of changing clinical practice and the conduct of the trial. Clinicians faced difficulties in approaching eligible patients for trial participation, especially when a diagnosis and treatment plan had already been provided by another clinician. The tension between maintaining clinical equipoise and addressing the needs of unwell patients further complicated decisions, particularly when withholding anticoagulation in those with severe symptoms or multiple comorbidities. Communication about the risks and benefits of non-medication strategies for pulmonary embolism was also challenging, with concerns about undermining patient trust. Patients, on the other hand, expressed considerable anxiety about not receiving anticoagulants, with their perspectives on study participation and treatment heavily influenced by their prior health experiences and ongoing medical conditions. The active involvement of clinicians in the consent process had a positive effect on patients' perceptions and experiences, with many feeling reassured in knowing they could contact clinical staff if needed.

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Limitations: Small sample size of patients and clinicians across limited study sites; single method of data collection.
Conclusions: Our results highlight the multifaceted challenges when attempting to conduct studies that challenge accepted practices and norms. These complexities are deeply intertwined, influencing both clinical decision-making and patient recruitment for those studies.
Future work: Future research should focus on developing strategies to help clinicians maintain equipoise and communicate the risks and benefits of interventions, while also deepening the understanding of patients' experiences and perceptions to enhance recruitment strategies.
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Background

Developing and implementing interventions that change clinical practice can be complex and challenging.[1] Such interventions are particularly difficult when attempting to change behaviours and practices since they necessitate clinicians learning new behaviours while unlearning old ones.[2,3] Other factors can add to this inherent difficulty, such as clinicians' beliefs about the appropriateness of the intervention, and time and resources needed to implement the change.[4,5] While there exists extensive literature on drivers and barriers to implementation of interventions that focus on changing clinical practice,[6–8] understanding of the difficulties involved in implementing interventions that go against established and accepted clinical practice is limited.[9] The clinicians not only have a difficult time adopting new behaviours and practices but also struggle with the social and ethical implications associated with these new practices.[10,11] Patient preferences and the dynamics of the professional–patient relationship can also play a role.

In this article, we use the example of a trial testing the balance of benefits and risks of withholding anticoagulation for isolated or incidental subsegmental pulmonary embolism (PE), a treatment that otherwise is accepted as standard care. We describe the challenges experienced when implementing such an intervention. Lessons learnt presented here are drawn from a qualitative process evaluation undertaken as part of the STOP-APE trial.[12] The evaluation investigated, during the internal pilot phase of the trial, the acceptability of not providing anticoagulant medication and clinician and patient experiences in the study.

Context of the current study

Pulmonary embolism is a potentially serious condition, whereby blood clots cause a blockage of the blood supply to the lungs.[13] The symptoms of a PE depend on the size and location of the blood clot. The established treatment for PE includes anticoagulant medications that are taken over at least 3 months. As the scanning technology for PE has become more sensitive, smaller clots are being diagnosed.[14] However, small PEs may not cause any symptoms and may be found incidentally on scans performed for other reasons. In these situations, it is unclear whether treatment is required as these clots in smaller blood vessels away from the centre of the lungs (called subsegmental PE) may be removed by the body's own mechanisms without needing medications. At the same time, anticoagulant medication can cause side effects in some patients, such as bleeding and severe bruising, which, if severe, may need hospital treatment.[15]

The STOP-APE trial was designed to test how a strategy of withholding anticoagulation in subsegmental PE compares to standard care which is full anticoagulation for at least 3 months. It aimed to recruit 1466 consenting adult patients with subsegmental PE from approximately 50 trial sites in secondary care clinical settings of emergency departments, ambulatory care and acute medical units within NHS hospitals in the UK. The internal pilot study begun in 2020, with a nested process evaluation to evaluate the acceptability of the intervention. However, due to restrictions imposed by the COVID-19 pandemic, the trial could not recruit for 7 months. When the recruitment restarted, we encountered various difficulties that generated uncertainty about the trial progress. Subsequently, with the advice from the funder, the trial was closed prematurely in December 2022.

There are two linked papers to this study in the National Institute for Health and Care Research (NIHR) Library: the protocol[12] and the synopsis that details the challenges and reasons why the STOP-APE trial was halted prematurely.[12] This qualitative article draws on our learning from the interviews with patients and clinicians and explores difficulties involved in implementing intervention (withholding anticoagulation in subsegmental PE) that is a marked change from standard practice.

Methods

Details of the main study design, sampling, data collection and analysis are published in the protocol.[12] The embedded process evaluation employed semistructured interviews and aimed to interview up to 30 patients and 30 healthcare professionals taking part in the trial to allow for data saturation.[16] Within our samples, we aimed for maximum variation to include the range of characteristics of eligible participants (e.g. site and symptomatic/incidental patients).

Data collection took place at five NHS sites throughout the UK between April and September 2021. All interviews were conducted by an experienced qualitative researcher (AI, female and social scientist) and were audio-recorded. The interviews lasted between 24 and 55 minutes and were undertaken via Zoom (Zoom Video Communications, San Jose, CA, USA) or telephone.[17] The topic guide explored attitudes and practical issues surrounding patient understanding of PE and its management, tolerance of risk by patients and clinicians, preferences for content and delivery of information and any potential concerns. Verbal informed consent was obtained from all study participants.

Data collection and analysis were undertaken concurrently. Gale *et al.*'s framework method[18] was adopted to analyse the data with the aid of the NVivo program (QSR International, Warrington, UK) for data management. First, AI read three interview transcripts to identify examples of participants' perceptions of and experiences in the study; views on acceptability of a no anticoagulation treatment strategy for isolated subsegmental PE; understanding of risk and incidental diagnosis; and any potential concerns. The codes were developed both 'horizontally' (by coding each interview as a standalone source of data) and 'vertically' (by scanning across the interviews for the specific areas described above). This created an initial set of codes and categories, and all the remaining transcripts were coded against that coding framework. The initial results of the analysis were then discussed during a study meeting with three members of the analysis team (AI, SG and DS). Following agreement on the initial themes, as our final analytic step, AI mapped the themes that emerged from the coding process to two broader themes that were related to practical and methodological challenges experienced by the team when designing and implementing the trial.

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 Trial Management Group 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.

Results

Eight patients (six females and two males) and three acute care clinicians (two males and one female) were interviewed due to the trial stopping prematurely (*Table 1*). All of the participants approached for an interview accepted the invitation.

The results were synthesised under three inter-related themes, which were presented separately for clarity: (1) approaching patients to take part in the trial; (2) recruiting and treating patients who are unwell; and (3) navigating communication about non-medication and patient preference for the trial arm.

Approaching patients to take part in the trial

Clinicians talked about instances where eligible patients were not approached to take part in the study because other clinicians who saw patients first believed they needed anticoagulants. Such instances led the clinicians to reflect on the broader challenges of changing current

TABLE 1 Participant characteristics

Participant group	Variables	Categories	Count
Patients	Gender	Female	6
		Male	2
	Trial recruitment site	Site 1	2
		Site 2	3
		Site 3	2
		Site 4	1
	Randomised clinical trial arm	Anticoagulants	5
		No anticoagulants	3
Clinicians	Gender	Female	1
		Male	2
	Trial recruitment site	Site 1	1
		Site 3	1
		Site 5	1

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practice and the perceived appropriateness of approaching patients who were already diagnosed and informed about the treatment. For example, one clinician recalled a situation where the patient ended up feeling conflicted because the initial treatment plan was challenged during a conversation about taking part in the study:

> *Someone clearly told them [the patient] that this is what they need, and now you're saying that maybe that's not the case, and certainly [with] one patient it felt a little bit like if I carried on the conversation for too long, there was going to introduce the trust issue. That they would be like: well, hang about, you're telling me this isn't clear cut but, you know, it was absolutely clear cut in their mind. And they [the patient] started to get a little bit nervous and confused. And I didn't push, you know, I thought they would lose trust in us as doctors.*
>
> *Clinician*

These decisions were often influenced by whether the patient had already received information about their diagnosis from another clinician. One clinician reflected:

> *I honestly think that the key thing was that, it was the fact that they their first conversation after the diagnosis was with someone who knew about the trial and was interested in enrolling them versus someone who believes that the treatment was absolute and there were no other options, and I think … I mean this gentleman [the patient], he was gonna say no … the fact he had, I thought, there were a number of co-morbidities and because this patient maybe was relatively well … I didn't bother approaching him.*
>
> *Clinician 2*

Another clinician echoed this sentiment, noting that patients were sometimes not put forward for the trial because the treating clinician was convinced that anticoagulation was necessary:

> *We've had one patient whose clinician didn't want them to be treated, they didn't want them treated regardless, and so they didn't. I wanted to put them forward for the trial but they weren't prepared for them to be anticoagulated.*
>
> *Clinician 3*

Adding to these challenges, clinicians highlighted a general lack of awareness about the trial among their colleagues, which further hindered patient identification and recruitment:

> *There are very few people in this [NHS] trust, who are trying to recruit and enrol, we're trying to work on that, but it's not happening at the moment. And the vast majority of other people just don't have any idea what's happening or aren't aware enough and so their standard presentation of a blood clot is the same as it's always been, which is you've got a blood clot gone to your lungs that serious, you need treatment and you need at least three months of treatment and so here's the tablet and off you go.*
>
> *Clinician 1*

Recruiting and treating patients who are unwell

Clinicians described a tension between the need to balance the risks and benefits of treating with anticoagulants for patients who were visibly unwell. Although clinicians acknowledged the clinical equipoise around the idea of treating or not treating subsegmental PE with anticoagulants, they generally held a view that there may be some patients who will still require medication and therefore may not be the best candidate for the trial. For instance, one clinician expressed the difficulty in withholding anticoagulants for a recruited patient who was unwell:

> *The only thing is symptomatic patients. Though the one patient I have recruited if he wasn't in the placebo group, I would have treated him. Later down the line when I actually met him because he was bizarrely symptomatic, acutely breathless when his sub-segmental PE was identified. And so it's harder to not treat that population, normally sub-segmentals you treat are, it was never a PE in the first place and they weren't symptomatic from it. Whereas his story was actually, he seemed to be very symptomatic from what was only a subsegmental PE. But luckily, he was put in the treatment arm.*
>
> *Clinician 1*

Another clinician shared a similar concern, highlighting specific cases where withholding treatment might not be appropriate:

> *I wouldn't do it with someone with a DVT, cancer. I mean I suppose the only thing is if they had limited reserve so if they had already for whatever reason cardio respiratory reasons that a small pulmonary vascular event could cause significant harm, that would be a reason that I would not want to not treat*
>
> *Clinician 3*

In contrast, another clinician noted that in many cases, the subsegmental PE was an incidental finding and not

associated with significant symptoms, which made the decision to not being anticoagulated more straightforward:

> *In terms of the sub-segmental PE, symptoms have not been an issue because they're often, they're normally an incidental sub-segmental finding.*
>
> *Clinician 2*

However, the challenge intensified when patients had multiple comorbidities or were generally unwell, making the decision to withhold anticoagulation even more complex:

> *The patient we didn't enrol had quite a lot of co-morbidities and had quite a lot of other health issues and a lot of contact with medic medical teams … So, you know, this gentlemen was, he was unwell, really unwell.*
>
> *Clinician 3*

Navigating communication about non-medication and patient preference for the trial arm.

Clinicians reported that they frequently had to take a different approach when discussing non-medication with prospective trial participants. They emphasised the importance of clear communication to ensure patients understood that, in some cases, not medicating might be the appropriate course of action:

> *I tend to ask them [the patient] what they know about what they've come in with and what they've been diagnosed with or what you know, what they're in ambulatory care with. And then obviously you get a feel for whether they have a good understanding or not, and then I tend to talk to them about blood clots in general. This idea that we know that smaller blood clots that are, you know, potentially the edge of the lungs we don't really know what the right form of treatment is. And we use, you know historically, when you have a clot, but we don't know that's the right thing to do.*
>
> *Clinician 1*

For patients, the diagnosis of PE – especially when symptoms were not obvious – often brought significant anxiety, particularly around the possibility of not receiving anticoagulants. Many viewed participation in the trial as potentially withholding treatment, which heightened their concerns about taking part in the trial:

> *I guess it is worrying, obviously a doctor has just told you that you have blood clots on your lungs, regardless as to what size they might be. Obviously, I hadn't been selected at that point and at that point, you think, 'If I don't have medication, could I get worse?' Can't they not give me treatment? Being a human, you automatically think, 'Oh my gosh! I could die. I might not be able to breathe. It might affect something else. The blood clot might move.'*
>
> *Patient 1, female*

> *I had mixed emotions. I'm not going to lie … anxiety-wise and as a human, you think, "Have I done the right thing? Should I have drugs or not?" Obviously, it's a worrying thing to have clots in your lungs.*
>
> *Patient 6, female*

Patients appeared to have opinions about the study arms they were allocated to, often because of their previous health experiences and other ongoing health issues. For example, patients' views on taking medication when they already had other health conditions and/or took medication influenced whether they thought being in the no anticoagulant therapy study arm was acceptable or not:

> *I wanted to be without the drugs completely (…) I'd had two years on quite high dose infusions for my disease. I'd been on really heavy drugs, and I just wanted to drug-free. For me, you know, I just didn't want to be given anymore drugs. I just didn't want to take anything else.*
>
> *Patient 4, female*

> *I think because I'm not someone who's ever very fortunately had to take any medication, I was particularly sort of hoping that I was going to end up in the side of the trial that was not [taking medication]. I think I was rather upset when I got allocated to the medication group. I wanted to get well quickly; you know.*
>
> *Patient 8, male*

> *I was selected to not have them [anticoagulants] this time and I was so thankful that I didn't have to. I remember weeks previously having the injections when I came out of surgery and just feeling so sore to thinking my body could potentially get rid of it and be healthier without the injections than with them, if I'm honest.*
>
> *Patient 3, female*

Despite these challenges, the involvement of clinicians in the consent and management process had a positive impact on how patients perceived and experienced study participation. Many patients reported feeling reassured by knowing they could contact clinical staff if they had concerns:

> *I did feel like I could go back to the hospital at any point and say, 'I don't feel well', or 'I don't feel that this is right for me. It's too much for me to handle', and I could have gone off the program, so I felt safe.*
>
> *Patient 7, male*

However, there were instances where conflicting medical advice added complexity to patients' experiences. One patient, who was initially assigned to the non-medication group, had their allocation overturned by another consultant due to concerns related to their existing condition:

> *I was randomised not to have medication. But then my other doctor consultant who deals with my [disease] overturned it because she felt that I needed to have the medication because of the blood clots, but also with the medication I'm on, there's a possibility I could produce more clots so she was more concerned about that. I was only concerned because of what the other consultant had told me originally about my [disease], I was only concerned about that. I was willing to do it without the medication but because of the concerns of my other doctor, they decided to put me on the medication anyhow.*

Trust in clinicians and their decision-making was recognised as a crucial factor that likely influenced patients' decisions to participate in and continue with the trial, especially for those who were ultimately assigned to the no-anticoagulant group.

Discussion

The interview data with clinicians and patients, albeit limited by a small participant sample, emphasise the complex and overlapping challenges involved in changing established clinical practice, particularly in the context of managing PE and conducting research that impacts accepted clinical norms. Our findings reveal that issues such as clinician equipoise, clinician discomfort with certain patient characteristics, the need to reframe information provision and patient communication are intricately connected and relevant to both the challenge of changing clinical practice and the conduct of the trial. In this section, we integrate insights from related studies to offer a broader context for understanding these challenges. We emphasise the importance of nuanced approaches to implementing complex interventions that challenge established practices and recruiting for trials with varying intervention arms.

One of the key issues identified in our analysis is the role of clinician equipoise – or the lack thereof – in shaping decisions about patient care and recruitment. Our findings suggest that it was often challenging for clinicians to 'unwind' the information about PE that patients had received from other clinical staff and therefore convince them that anticoagulation may not be required. They often refrained from approaching eligible patients for study participation, especially when patients had already received a diagnosis and treatment plan from another clinician who believed anticoagulation was necessary. They also felt more uncomfortable recruiting particular groups of patients, such as those who were symptomatic. The findings also reflected broader difficulties in clinical practice, such as the challenge of communicating the potential risks and benefits of non-medication strategies for incidental subsegmental PE. Clinicians expressed discomfort when discussing these options with patients, largely due to concerns about potentially undermining the patient's trust in their care. Explaining the concept of equipoise to patients can be challenging,[11] as our findings indicated. Yet, patients can decide not to join a trial based on how they perceive their clinicians' treatment preferences.[19]

A number of other studies have reported similar findings, reinforcing the challenges we observed in our research. For instance, a lack of equipoise among clinicians has previously been recognised as a significant factor contributing to the low recruitment for trials.[9,19–21] Studies found that clinicians face many practical and emotional challenges as they work to reconcile the conflicts that arise between their clinical responsibilities and their research roles.[10,11] The concept of 'compulsion for diagnosis'[22] reflects the deep-rooted tendency among clinicians to adhere to established diagnostic and treatment protocols. This need appears to be driven by a desire to provide patients with a sense of certainty and security, but it can also hinder the adoption of new practices that challenge the status quo.

Research on clinical decision-making has further highlighted the difficulty in balancing the need for clear evidence-based communication with the complexities of individual patient cases.[23,24] The decision to administer or withhold anticoagulation involves substantial changes in care delivery, which can be challenging for clinicians to navigate, especially in the context of inherent uncertainty that accompanies such decisions.[25] Psychological mechanisms tied to the role of diagnosis further complicate these situations as patients often have strong expectations for clinicians to provide a diagnosis and treatment for their condition. These expectations can

influence clinical decision-making and present obstacles to recruiting patients for research trials.

Our findings underscore the complex interplay between patient perceptions, clinical decision-making and the management of PE, building on previous research that has highlighted patients' concerns about unknown side effects and uncertain treatment effectiveness in trial participation.[26,27] In this study, patients diagnosed with PE, particularly those without overt symptoms, often experienced significant anxiety about the possibility of not receiving anticoagulants. This anxiety appeared to stem from a fear that the absence of medication could worsen their condition, reflecting the common concern that withholding treatment equates to increased risk. The role of clinicians in managing these anxieties proved crucial. In contrast to the clinicians who feared that such conversations might undermine patient trust or cause confusion, patients saw discussion of treatment as valuable as it allowed to express their concerns and reach an informed decision.[28]

Research on recruitment to randomised trials has shown that when recruiters are actively involved in the consent process and maintain clear communication, patients tend to feel more secure and confident in their participation.[29–31] This reassurance is particularly important for those who are initially apprehensive about the trial,[32] as it helps alleviate fears about being placed in less conventional treatment groups, such as the no-anticoagulant arm.

In conclusion, our analysis highlights the multifaceted challenges when attempting to conduct research that challenges accepted norms. The complexities of clinician equipoise, patient communication and the dynamics involved in diagnosis are deeply intertwined, influencing both clinical decision-making and patient recruitment for trials. These findings emphasise the need for nuanced approaches that address the overlapping concerns of clinicians and patients.

Implications for future research

Many of the challenges highlighted in the study are not unique but rather indicative of broader issues faced in delivering complex interventions that challenge established clinical practices and studies recruiting for trials with varying intervention arms. Below, we explore the key lessons learnt.

First, the difficulties related to clinicians' equipoise and obtaining consent for the study warrant further exploration. Our findings suggest that clinicians' decisions to approach and recruit patients were influenced by whether the PE diagnosis had been communicated by another member of the clinical team. This highlights the need to anticipate and address sources of uncertainty that may arise during the recruitment process. Providing additional support and training for clinicians to maintain equipoise and effectively communicate the risks and benefits of new clinical practices is essential for successful patient recruitment and trial participation.[10,11] Future research should focus on strategies to support clinicians in navigating these challenges.[11]

Second, recruitment issues are likely to remain a significant consideration in this type of research. Despite concerns that the no-anticoagulation arm might hinder patient recruitment, most patients found this aspect acceptable, even though they had distinct preferences for their assigned trial arm. Understanding patients' experiences of being approached and recruited is critical for improving recruitment strategies.[28] Future research should explore the factors that influence patients' perceptions specifically for such interventions and trials to better tailor communication approaches and support recruitment efforts. Current recruitment and research processes may need to be adapted to meet the specific needs of trials that challenge accepted practices and where there is a lack of clinical equipoise.[11,33]

Third, the practicalities of implementing the intervention must be carefully considered. Factors such as the timing of the trial and the challenges of restarting research after the COVID-19 pandemic likely impacted our recruitment rates. The complexity of the intervention itself may have influenced both patient and clinician experiences, contributing to the challenges reported. Future studies should carefully evaluate and address these practical challenges to ensure successful recruitment and implementation.

Finally, although the trial ceased prematurely, our findings suggest the need for further research into the long-term effects of the no-anticoagulant therapy. If patients, aware of their PE diagnosis, are not treated, this may alter their response to transient symptoms (e.g. leg or chest pain), potentially leading to increased healthcare utilisation, such as excess scans and emergency presentations. Future research should explore the psychological impact of not medicating and assess the potential 'harm' associated with repeated diagnostic imaging in this context.

Limitations

This study has several important limitations that should be noted. Our findings are based on the experiences

of a limited number of patients and clinicians across a small number of study sites. As a result, the challenges reported may not be encountered or applicable outside the acute care setting. Additionally, our ability to gather more data and achieve thematic saturation was constrained by the premature termination of the trial. However, the challenges we identified are those that were most significant to the study participants and research team.

Furthermore, this study employed interviews with patients and clinicians as methods of data collection. Other methods, such as direct observations of clinical interactions and focus groups, could have provided additional perspectives and a more nuanced understanding of the challenges faced during trial recruitment and implementation.

Equality, diversity and inclusion

The STOP-APE randomised clinical trial was stopped prematurely due to very low recruitment, and we were unable to assess how well subjects recruited to this qualitative study represented the populations served at trial sites.

Conclusions

This study highlights the complex and overlapping challenges involved in changing established clinical practices, particularly in the context of managing PE and recruiting to trials that impact accepted clinical norms. The complexities surrounding clinician equipoise, patient communication and clinician discomfort with certain patient characteristics are intricately connected, significantly influencing both clinical decision-making and patient recruitment for trials. Future research should focus on developing strategies to help clinicians maintain equipoise and communicate the risks and benefits of these interventions effectively. Moreover, gaining a deeper understanding of patients' experiences and perceptions is vital for enhancing recruitment strategies and boosting trial participation.

Additional information

CRediT contribution statement

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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.

Alice Turner is a member of the NIHR HTA prioritisation committee (2020–5). 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.

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Data-sharing statement

There are no additional data to share for this analysis of the STOP-APE trial. 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.

Ethics statement

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

Information governance statement

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About this article

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List of abbreviations

NIHR	National Institute for Health and Care Research
PE	pulmonary embolism

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