Managing uncertainty: Physicians' decision-making for stroke prevention for patients with atrial fibrillation and intracerebral haemorrhage.

Running Title: Physicians' decision-making for stroke prevention

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Essentials

Background

 Stroke prevention in high-risk patients with atrial fibrillation is an area of clinical equipoise

Setting

• Acute stroke care in five European countries

Results

- Physicians rely on personal experience to make decisions in complex atrial fibrillation patients.
- Communicating uncertainty is challenging for physicians in the absence of high-quality evidence.

Abstract

Background Stroke prevention in patients with atrial fibrillation (AF) post-intracerebral haemorrhage (ICH) is an area of clinical equipoise. Little is known about the tools and processes that physicians use to make decisions regarding anticoagulation in this high-risk patient population.

Objective To explore physicians' decision-making process regarding stroke prevention in patients with AF and a recent history of ICH.

Method Qualitative study, utilising semi-structured interviews and analysed using Framework analysis.

Results Twenty physicians from five European countries (Austria, France, Germany, Spain, United Kingdom) participated. The over-arching theme 'Managing uncertainty', addressed the process of making high-risk clinical decisions in the context of little available robust clinical evidence for best practice. Three sub-themes were identified under the umbrella theme: (1) 'Computing the Risks', captured the challenge of balancing the risks of ischaemic stroke with the risk of recurrent ICH in a complex patient population; (2) 'Patient Factors' highlighted the influence that patients' beliefs and previous experience of stroke had on physicians' decisions; and (3) 'Making a Decision' explored the process of reaching a final decision regarding initiation of OAC therapy or not.

Conclusion Physicians described the process of deciding on stroke prevention in patients with AF post-ICH as 'challenging' due to considerable 'clinical equipoise'. Key factors that affected decision-making was patient comorbidities, functional status, and patient willingness to engage with oral anticoagulation therapy. Shared

decision-making was believed to be beneficial, but physicians believed that the ultimate responsibility to decide on stroke prevention lay with the clinician.

Introduction

Clinical guidelines for atrial fibrillation (AF) recommend life-long oral anticoagulation (OAC) for patients with a CHA₂DS₂-VASc score ≥1 in men and ≥2 in women) [1]. However, OAC is associated with an increased risk of bleeding [2]. Non-vitamin K antagonist OAC (NOACs, sometimes referred to as direct oral anticoagulants, DOACs) are associated with a reduced risk of intracranial haemorrhage compared to warfarin in patients with AF (Relative Risk 0.48, 95% CI 0.39–0.59) [3] but existing randomised controlled trial data in the AF and ICH population are limited and the results are inconsistent. Intracerebral haemorrhage (ICH) is a potentially life-threatening complication of OAC [4], associated with increased mortality and morbidity [5, 6]. In patients with AF who have sustained an ICH, stroke prevention poses a clinical dilemma because of risk of ischaemic stroke and concurrent increased risk of recurrent major bleeding, including ICH.

Clinical decisions as regard stroke prevention in patients with AF and ICH are complicated by a lack of high-quality evidence and differences in physician and patient perceptions of the risks and benefits of OAC therapy [7, 8]. Contemporary guidelines on stroke prevention fall short of making direct recommendations regarding patients with AF post-ICH [9, 10] in the relative absence of RCT-evidence. To date, no qualitative research has attempted to understand what tools and processes physicians use to decide on stroke prevention in patients with AF and ICH.

The aim of this study was to explore physicians' decision-making process regarding stroke prevention in patients with AF and a recent history of ICH.

Methods

This project is a sub-study of the PREvention of Stroke in Intracerebral
HaemorrhaGE survivors with Atrial Fibrillation (PRESTIGE-AF) trial (NCT03996772)
[11], which is comparing the efficacy and safety of NOAC versus antiplatelets or no therapy in patients with AF and ICH. This study received ethical approval from South
Central – Oxford A Research Ethics Committee (REC reference 19/SC/0435)

Participant selection

Criterion sampling was utilised to recruit participants. The main criterion was that participants must have experience of decision-making about antithrombotic therapy for cardioembolic stroke prevention in patients with ICH. Physicians from five European countries were eligible to participate providing they could complete the interview in English.

In-line with standard practice in qualitative research, recruitment continued until data saturation was achieved [12].

Data collection and analysis

Semi-structured interviews were undertaken, using an interview schedule to guide questioning [13] (Supplementary Materials Box S1). Interviews were undertaken online or via telephone, audio-recorded, and transcribed verbatim to facilitate data analysis.

Data were analysed using framework analysis [14], with NVivo (version 12) to facilitate data management. Framework analysis is performed in five stages [14]. First, familiarisation involves reading the transcripts, then the data were separated into manageable sections [15] and re-read with the thematic framework in mind. The

next stage is charting, which is the population of the framework matrix and finally mapping identifies the over-arching themes.

A reflexive diary was kept as part of this project and the researcher had access to debrief sessions, which helped address any personal bias and uphold trustworthiness [16].

Results

Participants

Twenty stroke physicians from five European countries (UK, Austria, France, Germany, Spain) participated in the study. Participants were experienced clinicians, including six heads of a stroke department, ten consultant stroke physicians, two consultant geriatricians working in stroke, and two residents in stroke (Table 1).

Most participants saw 100-200 patients with an ICH per year and fewer than 50 patients with ICH and AF per year. All participants worked with to a multidisciplinary team (MDT) (which included allied health professionals and physicians from other medical specialties) and had regular meetings with fellow stroke physicians. Some participants had access to local guidelines that addressed the issue of stroke prevention in patients post-ICH with concomitant AF.

Themes

'Managing uncertainty' was the over-arching theme evident in the data. This theme reflected participants' decision-making journey and contained three sub-themes: 'Computing the risks – evidence and experience'; 'Patient factors – patient beliefs and engagement with OAC'; and 'Making a decision – conversation or information' (Figure 1).

Computing the risks – evidence and experience

The sub-theme 'computing the risks' addressed the challenging nature of decision-making arising from the lack of high-quality evidence. Reliance on existing knowledge, personal clinical experience, and awareness of patients' co-morbidities and clinical risks of stroke affected physicians' decision-making.

A challenging decision

Participants referred to the decision of prescribing long-term OAC in patients with AF and ICH as 'complex' or 'challenging' due to the risks associated with both prescribing and withholding long-term OAC. The decision was therefore reliant on balancing the risk and benefit, where it was difficult to quantify either, resulting in high levels of uncertainty.

"Whether it's worth accepting that risk of side effects and something going wrong in order to achieve a benefit, and how much... that benefit might help the patient" [008]. Decision-making was driven by the 'First, Do No Harm approach'.

"I think, for me, personally, and anecdotally speaking, to lump in my colleagues, the hardest thing to get over in your head is the... is to get away from the First, Do No Harm approach" [008]

Physicians were cautious of prescribing OAC to ICH patients due to a professional and personal sense of responsibility for any negative consequences associated with their decision-making.

"It's our own decision as a clinician, while we have the life of the patients in our hands, you know" [017]

This meant that many physicians avoided the use of OACs in patients with AF after an ICH, instead adopting a cautionary approach.

"We're really strict not to treat atrial fibrillation after cerebral bleeding" [004].

Relying on knowledge and experience

A lack of high-quality evidence from RCTs added to physicians' sense of uncertainty. Participants described the clinical question as to whether an ICH survivor with AF ought to receive long-term OAC as an area of 'clinical equipoise' [Participant 006], where the existing literature fails to adequately direct and support decision-making "The science, the level of scientific evidence that's available is far from being solid"

[005]

Lack of clear guidelines led to a reliance on personal clinical experience and expertise at the time of OAC decision-making

"...I've been slightly more reliant on my anecdotal experiences in this situation is because this... is a situation which is a total equipoise, we don't know what the right answer is" [006].

This was explained as a reliance on 'rationalisation' of data [Participant 008], where patients with AF and ICH tend to be 'on the margins' [Participant 009] of available RCT data.

It was felt that having access to RCT-level evidence would reassure physicians in their decision-making and alleviate any divisions in clinicians' approach to stroke prevention in patients with AF and ICH.

"I think something needs to be out there, just to support everyone else doing the same thing" [010].

Patient comorbidities and functional status

With a lack of best practice evidence, physicians relied on what quantitative data they could garner. This meant aspects such as patients' comorbidities were primary considerations in the decision-making process. The pathophysiology of a patient's ICH affected physicians' perception of a patient's clinical risk of either ischaemic or haemorrhagic stroke and influenced the choice to offer stroke prevention therapy (and the specific medication that could be offered) or to consider alternative non-pharmacological treatments.

"You should really think about why he had the bleeding. Because they don't bleed because they have NOAC... So, there was another cause for the bleeding, and you have to look for this cause" [001]

In situations where the ICH was likely caused by modifiable risk factors, such as poorly controlled or uncontrolled hypertension, physicians prioritised risk reduction.

"If the patient has had intracerebral haemorrhage due to hypertension or not controlled hypertension, I put the focus on the control of hypertension" [015].

Patients' functional status and level of disability post-ICH also guided decisionmaking as to OAC therapy post-ICH.

"But the patients that we would do nothing, would probably be severely... severely disabled at first place, because of their ICH" [019].

As a result, there was greater likelihood of prescribing long-term OAC to younger patients.

"I'm more prompt to start an anticoagulant in someone who is younger, with less...

comorbidities" [007].

Similarly, the decision making was influenced by perceptions of the patients' quality of life.

"What do we think how long will the patient [live]... in which quality of life?" [004].

Summary

Overall, stroke prevention in patients with AF post-ICH was described as an area of "clinical equipoise" given the lack of available clinical evidence. Practitioners were guided by the First, Do No Harm approach and often relied on their personal clinical experience when deciding if a patient ought to receive OAC post-ICH. Decision—making was also influenced by the pathophysiology of a patient's ICH and the patient's comorbidities, as these dictated the perceived risk of stroke.

Patient factors – patient beliefs and engagement with OAC

The sub-theme 'Patient factors –patient beliefs and engagement with OAC' addressed physicians' understanding of patients' individual beliefs and attitudes towards OAC therapy. This included patients' previous experience of stroke, health beliefs, and social and lifestyle factors.

Previous experience of stroke

Physicians understood that patients' previous experience of stroke affected their willingness to accept particular treatments

"If you've had such... such a terrible event already and if this happens again, you might be dead. So, there are reasons that I can understand" [005]

Patients who had previously sustained an ischaemic stroke appeared to be more aware of the risk of thromboembolism and the risk of recurrent ischaemic events, in

spite of a recent ICH. In such cases, discussions around anticoagulation were often initiated by the patient or family.

"The patient but also the family, were very, very aware about the risk of embolic stroke and ask many times about the anticoagulation" [015].

However, patients who had only experienced an ICH appeared to focus on the risk of recurrent haemorrhage potentially associated with OAC, which affected their willingness to receive stroke prevention therapy.

"Some of them also are really afraid about restarting anticoagulation because they had their intracerebral haemorrhage while they were... under this treatment" [017] In individuals who accepted OAC, clinicians suggested that minor side-effects could reverse patients' decision to accept the medication.

"We will prescribe the anticoagulant and... have convinced the patient ... but then three weeks later there's a small... haematoma... and then they ... find a way to... not take it anymore" [020].

Health beliefs

Patients' perception of health treatments and healthcare were also reported as impacting on physicians' decision-making. For example, patients understanding of the vitamin-K antagonist, warfarin, as 'rat poison' negatively impacted on their acceptance of the drug.

"The vast majority of time it's not anticoagulation as such that they have an issue with, it's the idea of warfarin" [008].

Where physicians felt that patients were reluctant to engage with long-term OAC because of long-standing personal beliefs, these beliefs were seldom challenged

"Well, people have their preferences and I think it's often difficult to change preferences, especially in health settings" [020].

In situations where patients declined OAC therapy, physicians felt that this was an expression of patients' freedom of choice, even if their choice did not align with the physician's advice.

"You get a strong sense of some patients that they... wouldn't want anything done at all and they'd rather take their chances with nature, as it were" [009]

Social and lifestyle factors

Patients' willingness to receive long-term OAC therapy was also influenced the experiences of close family members and the wider community around them.

"Especially men, are very influenced by their women. So, it doesn't make sense to discuss this with the patient himself, you have also to include the relatives" [001].

This meant that physicians often involved a patient's next-of-kin or family in discussions about long-term OAC.

"...The patient is better cared for, if the family is on board with the decision making"
[019].

Families were viewed as helpful because they could be engaged in promoting the benefits of OAC to patients.

"The children, you know... they can understand, and they can convince their parents, mother or father, to go and take the treatment if we advise them" [011].

Access to social support networks was perceived as a further important consideration prior to commencing patients on long-term OAC, because long-term OAC therapy required commitment from the patient.

"If the patient can... can deal by itself with this kind of very important medication or be there for example support from community or the family" [007].

Conversely, lack of social support networks was perceived as significant limitation to adherence and persistence with treatment.

"And the patients cannot care for themselves so nobody cares, and they will never restart [OAC]" [003].

Finally, patients' lifestyle was instrumental in the decision-making process, as both patients and physicians perceived it to be a significant factor in willingness to accept OAC treatment.

"One patient, ... he has a lot of work to do in the woods and he decided against the medication. Because he was afraid that if something happens in the woods and he's alone, and he's scared that he would bleed to death" [019]

Summary

The decision to prescribe OAC to a patient with AF post ICH was universally described as being personalised to each patient. Physicians considered patients' social support networks when deciding if a patient was a candidate for long-term OAC. Health-beliefs, previous experience of stroke, and the opinions of family members influenced patients' willingness to receive OAC, which also affected physicians' decision-making.

Making a decision – conversation or information

The third sub-theme addressed how the final decision about OAC therapy is made. Physicians identified that joint working with fellow clinicians aided decision-making, as did the involvement of patients in the final stages of the decision-making process. There was a perception that the ultimate decision to prescribe or withhold OAC was the responsibility of the physician, although the patient had the right to decline or accept this decision.

Multidisciplinary working

Successful multi-disciplinary team working eased the decision-making process for physicians because discussing complex cases with fellow stroke clinicians was perceived as a useful way of overcoming clinical uncertainty

"Because it's something that we are less familiar with, we tend to discuss those patients ... in our monthly consultant meeting" [008].

Working as a team was viewed as a helpful 'reality check' for physicians, and an opportunity to share responsibility

"It's better still to accept this is shared decision when the patient has problem after, we're not alone to decide" [017].

However, discussing patients with other specialties could be complicated by the fact that different specialties viewed the subject of stroke prevention in high-risk AF patients differently

"I think we see more of a cautious approach from elderly care or gastroenterology fields compared to probably pure stroke or pure cardiology teams" [012]. The lack of consensus among clinicians also influenced patients' willingness to accept OAC, because it meant that patients received mixed messages from different physicians

"[Patients] tell us that the cardiologist or their own physician... told them that the best treatment **is**... anticoagulation or left appendage occlusion. They heard from someone that there is a treatment and there is no question" [017].

Engaging patients in decision-making

Participants referred to the decision-making process as being shared between the patient and the physician.

"You feel that you... jointly made that decision and that was something the patient was very involved in" [009]

In situations where a patient lacks capacity, the family's wishes influenced decisionmaking.

"I always think that the family has the last word. We are to be able to convince them but we can't go over their decision" [017].

Some physicians described themselves as advisors, whose role was to make suggestions instead of deciding on the patients' behalf.

"We are there to help, at the end, that's their decision whether they want to take it or not" [011].

Physicians engaged with certain patient' preferences, such as medication regimes, to support patient participation

"For someone who's involved [in decision-making] I would say, would you prefer a drug that is taken twice a day or once a day?" [007]

Participants engaged patients by personalising the decision-making process to the patient's individual circumstances. For some patients, this was achieved by focusing on the wish to preserve quality of life

"I explain them so what happens if you don't get [OAC], whatever your quality of life is, if you have an ischaemic stroke, you will lose this" [011].

For other patients, there was a focus on the individual's clinical risk of ischaemic stroke.

"We inform them about the risks again, what would happen... what could happen. I think it's very important in these cases that... that one explains directly the consequences of what could happen to them" [019].

The feeling of clinical uncertainty described by physicians in the sub-theme 'Computing the risks' had some influence over physicians' engagement of patients in the decision-making process. For some clinicians, the patient had a right to be aware of the uncertainty that exists around evidence for OAC post-ICH and part of the physician's role was to explain the lack of clear clinical evidence to patients. This meant that patients were made aware of the consequences of either accepting or declining OAC therapy.

"I like to lay it out to people that there are no... low risk options here, in the sense that... that we are walking a tightrope so that they're aware of that" [009].

However, other physicians were uncomfortable to admit their uncertainty to patients, partly because of concerns that patients mistrust clinicians who cannot give them a clear treatment recommendation.

"Some patients might be disturbed and more, even more if you say that you don't know what to do" [004].

"You are the doctor"

While participants discussed shared decision-making and their willingness to involve patients in the decision-making process, there was also a sense that the ultimate decision to prescribe or withhold OAC therapy lay with the physician.

"...You have to know what you want to give [the patient]... Have an idea of what would be a solution for your patient" [001].

Some physicians said that patients preferred doctors to make the final decision.

"In most of the cases it comes to ...saying of the patient that they say, you are the doctor, I do what you think is best" [002].

Physicians said that they decide whether a patient ought to be prescribed OAC therapy before they speak with the patient in question, which appears to contradict previous descriptions of a shared approach to decision-making.

"We explain our decision to him, but we normally have already decided what we think would be best" [004].

There was a view that patients can find it difficult to effectively consider all of the factors that contribute to a decision about stroke prevention, meaning that physicians are better able to be the final decision makers.

"I think the subtleties of that decision-making process can be challenging to convey to patients" [008]

Similarly, there was a perception that not all patients wished to engage with clinical uncertainty, preferring instead clear guidance and instructions from the medical team.

"Patients want to have strict recommendation and explanation why this is the correct and the only correct way" [001]

For many participants, good communication meant an explanation that patients could 'follow' and that led to patients taking the physician's advice, rather than a conversation between the physician and the patient.

"Most of the times, I feel if we explain to them well, communicate with them well, they tend to leave... leave it to us to make a decision for them" [011].

In such situations, patients' main involvement in decision-making was their ability to refuse treatment.

"My attitude is to say, Ok, this patient doesn't want anticoagulants then I will... try to convince him but if he still doesn't want any medication, then I will not hurt him to do it" [018].

Summary

Overall, there was a sense that the ultimate decision as to stroke prevention in patients with AF and ICH lay with the physician. The final decision-making process was aided by input from fellow clinicians and consultation with patients and families, which some participants described as 'shared decision-making'.

Discussion

The over-arching theme in this study - 'Managing uncertainty' - highlights the need for physicians to address clinical unknowns to reach a concordant decision between the patient and doctor regarding stroke prevention in patients with ICH and concomitant AF. Physicians' decision-making is influenced by the First, Do No Harm approach and a focus on patients' clinical factors. Joint working between clinicians aided decision-making and physicians were willing to engage patients in the decision-making process. However, the overall decision to prescribe or withhold OAC therapy in patients with AF and ICH was perceived to lie with the physician.

Uncertainty in medical decision-making

There are two basic types of medical uncertainty: the limitations of medical knowledge and the incomplete mastery of available knowledge, which are connected by therapeutic limitations [17]. Participants in this study spoke of having to confront an area of 'clinical equipoise', where no clear 'right' answer was evident. Although some clinical guidelines make suggestions as to possible stroke prevention therapy in patients with AF and ICH, such as long-term NOAC in eligible patients [18] and left atrial appendage occlusion (LAAO) procedure [19], the level of available evidence is low. Physicians described how the lack of high-level evidence leads to a multiplicity of opinions among clinicians, which results in increased uncertainty and disjointed decision-making.

One way of coping with high levels of uncertainty is to engage in medical research. Participants in this study believed that better evidence would help overcome some of their uncertainty. A survey of European Heart Rhythm Association (EHRA) members found that nearly 50% of respondents believed that better clinical knowledge would aid decision-making as regard stroke prevention in patients with AF and ICH [20]. On

an individual level, the structure and logic of research may counter-balance some of the stresses that physicians experience when working in fields where there is considerable uncertainty [17].

'Team membership' was a way in which physicians can cope with uncertainty because having access to colleagues dealing with similar issues can help physicians engage in meaningful discussions that facilitates the sharing of ideas [17]. In this study, joint decision-making with the stroke team or within the MDT was seen as an important part of the critical thinking process that ensured a more satisfactory decision. Acknowledging different individuals' views during decision-making is part of information gathering, a way of facilitating the decision-making process [21] and may be a way of overcoming the limitations of knowledge [17]. Furthermore, communal decision-making minimises the psychological burden experienced by individuals by reducing feelings of stress and regret associated with the risk of making a 'wrong' decision [22].

Shared decision-making

The degree to which patients wish to actively participate in decision-making differs between individuals. While patients express a desire to have their healthcare wishes acknowledged by physicians [23], some patients ultimately prefer the physician to make decisions as regard the most appropriate treatment [24, 25]. This issue was also raised by several participants in this study, who stated that patients often deferred to physicians' experience and knowledge. An international survey of AF patients' preference for involvement in treatment choice reported that 19-40% of respondents preferred shared physician-patient decision-making [26], with patient preference affected both by their previous experience of ischaemic stroke and their nationality.

However, shared decision making was described by some participants as beneficial because it led to patient participation in the decision-making process. The 2020 European Society of Cardiology guidelines on the management of AF advise physicians to promote patient involvement in decision-making as part of integrated AF care [18]. Patient involvement in clinical decision-making is presented as the cornerstone of patient-centred care, since it is said to ensure that the offered therapy aligns with the patient's health beliefs and treatment goals [27]. Patient participation may also promote improved adherence to treatment [28], especially if patients' preference for easy-to-administer therapy is taken into account [29]. It is therefore prudent for physicians to elicit their patients' desire for involvement in decision-making prior to arriving at a final decision as regard stroke prevention therapy [26].

Communicating uncertainty

Physicians' willingness to communicate uncertainty to patients is influenced by physicians' internal assessment of patients' perceived tolerance of ambiguity; patients who were perceived to be less tolerant of ambiguity were less likely to be offered treatments associated with greater uncertainty [30]. Some physicians in this study expressed unease at communicating uncertainty for fear of being perceived as less knowledgeable or competent by patients. Participants also expressed concern that the multiple uncertainties involved in choosing stroke prevention treatment for an individual with AF and ICH may be overwhelming for patients. There is some evidence that increased uncertainty over treatment options is associated with reduced decision satisfaction [31] and increased disease-related worry [32] in some patients.

Acknowledgement of the risks associated with any treatment are required for true patient autonomy [33] although the degree to which different patients and physicians

may be willing to engage with medical uncertainty differs [34]. Nonetheless, embracing uncertainty may allow clinicians and patients the opportunity to consider a greater spectrum of treatment options. Open communication may encourage trust between clinician and patient, and support patient participation in decision-making [35]. When dealing with unclear diagnoses or prognoses, a physician's willingness to be open as to their lack of clarity with patients can help normalise the sense of uncertainty [36]. To promote successful communication of uncertainty, clinicians can also rely on the following four domains: ascertain a patient's preference for communication, identify risk communication strategies, provide emotional support, and identify contingency plans [37].

Suggestions for future research and clinical education

This study has highlighted the impact that medical uncertainty has on physicians' decision-making process, which is an area that is receiving increasing attention in medical education. Future research ought to consider how future and existing physicians can be best prepared to cope with the negative personal and professional effects of perceived or real uncertainty. Clinical trials may wish to explore how physicians can best communicate medical uncertainty to patients.

Conclusions

The uncertainties involved in deciding on stroke prevention in patients with AF post-ICH led physicians to rely as much on their personal experience and on joint decision-making with fellow physicians as on available clinical evidence. Physicians' decision to prescribe or withhold OAC for stroke prevention was largely guided by a patient's functional status, perceived quality of life, and willingness to engage with long-term OAC therapy. Physicians believed in the benefits of shared decision-making but there was also a perception that the final decision as to stroke prevention

in patients with AF post-ICH lay with the physician. Future research ought to explore how physicians can best communicate uncertainty in clinical decision-making to patients.

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Conflicts of interest

RL: None to declare

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References

- 1. Chao, T.-F., et al., 2021 Focused Update Consensus Guidelines of the Asia Pacific Heart Rhythm Society on Stroke Prevention in Atrial Fibrillation: Executive Summary. Thrombosis and haemostasis, 2021.
- 2. Eikelboom, J. and G. Merli, *Bleeding with Direct Oral Anticoagulants vs Warfarin: Clinical Experience*. The American Journal of Medicine, 2016. **129**(11): p. S33-S40.
- 3. Ruff, C.T., et al., Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised trials. The Lancet, 2014. **383**(9921): p. 955-962.
- 4. Hart, R.G., B.S. Boop, and D.C. Anderson, *Oral anticoagulants and intracranial hemorrhage*. Stroke, 1995. **26**(8): p. 1471-1477.
- 5. Delcourt, C., et al., Associations with health-related quality of life after intracerebral haemorrhage: pooled analysis of INTERACT studies. Journal of Neurology, Neurosurgery & Psychiatry, 2017. **88**(1): p. 70-75.
- 6. Poon, M.T.C., A.F. Fonville, and R.A.-S. Salman, *Long-term prognosis after intracerebral haemorrhage: systematic review and meta-analysis.* Journal of Neurology, Neurosurgery & Psychiatry, 2014. **85**: p. 660-667.
- 7. Borg Xuereb, C., R.L. Shaw, and D.A. Lane, *Patients' and health professionals' views and experiences of atrial fibrillation and oral-anticoagulant therapy: A qualitative meta-synthesis.*Patient Education and Counselling, 2020. **88**: p. 330-337.
- 8. Pritchett, R.V., et al., *Clinicians' views and experiences of prescribing oral anticoagulants for stroke prevention in atrial fibrillation: A qualitative meta-synthesis.* PLoS One, 2020. **15**(5): p. e0232484.
- 9. Klijn, C.J.M., et al., Antithrombotic treatment for secondary prevention of stroke and other thromboembolic events in patients with stroke or transient ischemic attack and non-valvular atrial fibrillation: A European Stroke Organisation guideline. European Stroke Journal, 2019. **4**(3): p. 198-223.
- 10. NICE, *Atrial fibrillation: diagnosis and management.*, N.I.f.H.a.C. Excellence, Editor. 2021, NICE: London.
- 11. ClinicalTrials.gov. *NCT03996772*. *PREvention of STroke in Intracerebral haemorrhaGE Survivors With Atrial Fibrillation (PRESTIGE-AF)*. 2019 [cited 2021 13 July].
- 12. Cresswell, J.W., *Qualitative Inquiry & Research Design: Choosing among Five Approaches*. 3rd Edition ed. 2013, Thousand Oaks, CA: SAGE.
- 13. Hardon, A., C. Hodgkin, and D. Fresle, *How to investigate the use of medicines by consumers.* 2004, Geneva: World Health Organization.
- 14. Ritchie, J. and L. Spencer, *Qualitative Data Analysis for Applied Policy Research.*, in *Analyzing Qualitative Data*, A. Bryman and B. Burgess, Editors. 1994, Routledge: London. p. 173-194.
- 15. Pope, C., S. Ziebland, and N. Mays, *Analysing qualitative data*. British Medical Journal, 2000. **320**(114).
- 16. Barber, J.P. and K.K. Walzcak, *Conscience and critic: peer debriefing strategies in grounded theory research*, in *Annual Meeting of the American Educational Research Association*. 2009: San Diego, CA.
- 17. Fox, R.C., *Experiment Perilous: Physicians and Patients Facing the Unknown*. 1st Edition ed. 1997, New Brunswick, New Jersey: Taylor and Francis.
- 18. Hindricks, G., et al., 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS). European Heart Journal, 2020. ehaa612.
- 19. Kleindorfer, D.O., et al., 2021 Guideline for the Prevention of Stroke in Patients With Stroke and Transient Ischemic Attack. A Guideline From the American Heart Association/American Stroke Association. Stroke, 2021. **52**: p. e364-e467.

- 20. Ivany, E., et al., Antithrombotic therapy for stroke prevention in patients with atrial fibrillation who survive an intracerebral haemorrhage: results of an EHRA survey. EP Europace, 2021. euaa423: p. 1-9.
- 21. Helou, M.A., et al., *Uncertainty in Decision-Making in Medicine: A Scoping Review and Thematic Analysis of Conceptual Models.* Academic Medicine: Journal of the Association of American Medical Colleges, 2020. **95**(1): p. 157-165.
- 22. El Zein, M., B. Bahrami, and R. Hertwig, *Shared responsibility in collective decisions*. Nature Human Behaviour, 2019. **3**: p. 554-559.
- 23. Entwistle, V., et al., *Involvement in treatment decision-making: its meaning to people with diabetes and implications for conceptualisation.* Social Science & Medicine, 2008. **66**(2): p. 362-375.
- 24. Chewning, B., et al., *Patient preferences for shared decisions: A systematic review.* Counselling, 2012. **86**(1): p. 9-18.
- 25. Lindsay, S.E., et al., *Patient Preferences for Shared Decision Making: Not All Decisions Should Be Shared.* Journal of the American Academy of Orthopaedic Surgeons, 2020. **28**(10): p. 419-426.
- 26. Lane, D.A., et al., *Patients' Perceptions of Atrial Fibrillation, Stroke Risk, and Oral Anticoagulation Treatment: An International Survey.* TH Open, 2018. **2**(3): p. e233-e241.
- 27. NICE, *Shared decision making.*, N.C.G.C. UK, Editor. 2021, NICE: London.
- 28. Loh, A., et al., *The impact of patient participation on adherence and clinical outcome in primary care of depression.* Patient Education and Counselling, 2007. **65**(1): p. 69-78.
- 29. Wilke, T., et al., *Patient Preferences for Oral Anticoagulation Therapy in Atrial Fibrillation: A Systematic Literature Review.* The Patient, 2017. **10**(1): p. 17-37.
- 30. Portnoy, D.B., et al., *Physicians' attitudes about communicating and managing scientific uncertainty differ by perceived ambiguity aversion of their patients.* Health Expectations, 2013. **16**(4): p. 362-372.
- 31. Politi, M.C., et al., Communicating uncertainty can lead to less decision satisfaction: a necessary cost of involving patients in shared decision making? Health Expectations, 2011. **14**(1): p. 84-91.
- 32. Han, P.K.J., et al., *Communication of uncertainty regarding individualized cancer risk estimates: effects and influential factors.* Medical Decision Making, 2011. **31**(2): p. 354-366.
- 33. GMC, Guidance on professional standards and ethics for doctors. Decision making and consent. 2020, General Medical Council: Manchester, England.
- 34. Politi, M.C., P.K.J. Han, and N.F. Col, *Communicating the uncertainty of harms and benefits of medical interventions.* Medical Decision Making, 2007. **27**(5): p. 681-695.
- 35. Braddock, C.H., *Supporting shared decision making when clinical evidence is low.* Medical Care Research and Review, 2013. **70**: p. 129S-140S.
- 36. Than, M.P. and D.F. Flaws, *Communicating diagnostic uncertainties to patients: The problems of explaining unclear diagnosis and risk.* Evidence-Based Medicine, 2009. **14**(3).
- 37. Simpkin, A.L. and K.A. Armstrong, *Communicating Uncertainty: a Narrative Review and Framework for Future Research.* Journal of General Internal Medicine, 2019. **34**: p. 2586-2591.

List of Tables and Figures

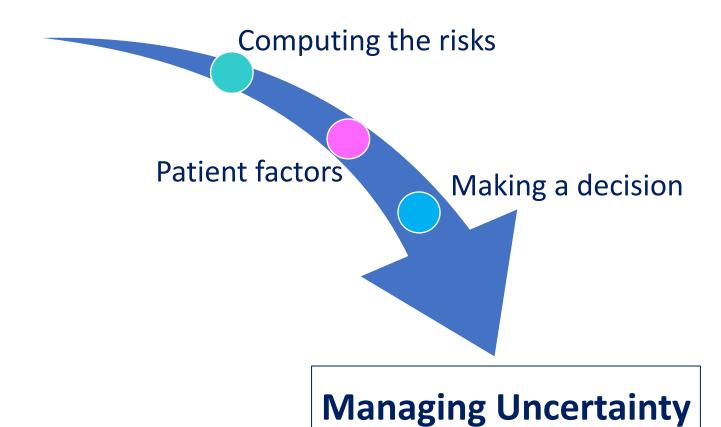
Table 1: Participant baseline characteristics

Figure 1: Three sub-themes ('Computing the risks', 'Patient factors', and 'Making a decision'), which make up the over-arching theme 'Managing uncertainty'.

Table 1. Participant baseline characteristics

Gender	Country of practice	Clinical role	Patients (n) with ICH seen per year
Male = 14	United Kingdom = 8	Consultant in stroke = 10	<50 = 2
Female = 6	Germany = 5	Head of stroke unit = 6	50-100 = 6
	Spain = 3	Consultant geriatrician = 2	101-200 = 8
	France = 2	Resident in stroke = 2	>200 = 2
	Austria = 2		>600 = 2

Figure 1: Three sub-themes ('Computing the risks', 'Patient factors', and 'Making a decision'), which make up the over-arching theme 'Managing uncertainty'.



Supplementary Materials

Supplementary Box S1: Physician Interview Guide

What is your current clinical role?

How long have you been in post?

Tell me about your experience with prescribing antithrombotic therapy for patients with AF and ICH.

Could you talk me through the process of deciding if a patient should be prescribed antithrombotic therapy?

How do you decide if oral anticoagulation is appropriate for a patient?

Could you talk me through how you discuss the topic of antithrombotic therapy with your patients?

In your experience, do some patients decline oral anticoagulants?

Can you tell me how you involve the patient in the treatment decision?