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DEAR WRITER, PLEASE READ THE AUTHOR GUIDELINES

Welcome to the fifth issue of The British Student Doctor, and the first of 2019. This is our third year of proudly publishing this journal, with the ethos of providing a platform to medical students to develop their critical appraisal and academic publishing skills through practical experience. The breadth and quality of the articles featured in this issue are a strong testament to our success in achieving this goal, and the ability of medical students to produce high quality outcomes in research and academic discourse.

The past three years have been a steep learning curve for the whole editorial team at The British Student Doctor, and a key component of that learning curve has been developing the way in which we deliver clear and constructive feedback to authors. A repeated issue that we have faced, however, is that often submissions are made to the journal without reference to our author guidelines. These guidelines, which are available on our website at the link below, are crucial reading for all writers wishing to publish in The BSDJ. More broadly, all academic journals will have published guidelines detailing their focus and scope, alongside suggested word counts and manuscript structure.

We wrote our author guidelines with clarity in mind, given that many writers who publish their work in The BSDJ are first time authors. The guidelines detail: the focus and scope of The British Student Doctor, the articles types that we publish alongside the section specific word, reference and figure limits and requirements for abstracts, our standard requirements for all sections which covers manuscript formatting, referencing, required cover page details including conflict of interest statements, and our requirements for copyright. Lastly, instructions on how to use our electronic article submission platform are described.

Before beginning to write your next article for *The British Student Doctor,* please read the guidelines and use them to structure your writing. In particular, the majority of articles submitted to the journal do not follow our required formatting for references (we have a detailed referencing guide to help you with this) and many are not uploaded with a completed copyright assignment form, which is necessary for all manuscripts before they can enter the peer review process. Ensuring that you follow the author guidelines, alongside the referencing and copyright instructions, will allow us to ensure that your manuscript is expedited swiftly through the peer review process, and hence that there is no delay in publication. Crucially, it will also save your editor's sanity!

As we progress into an increasingly complex health system, the focus on developing good medical leadership is one of the top priorities for the NHS. As such, we are pleased to feature a guest editorial by Peter Homa and Claire Lodge from the NHS Leadership Academy, on the importance of medical leadership. We also feature an article by Dr Samuel Tretheway and his colleagues on the challenges of identifying high quality complementary and alternative treatments, as they are often categorised into one broad category. Elliott Sharp and Keegan Curlewis, two medical students

from Brighton and Sussex Medical School, explore a similar challenge with assigning appropriate names within the specialty of general surgery.

We hope that you enjoy this issue of *The British Student Doctor*, and we look forward to publishing your work in our next issue in June.

The author guidelines for all submissions to The British Student Doctor can be found at: https://www.bsdj.org.uk/author-guidelines.

The referencing guide and the copyright form are available to download at: https://www.bsdj.org.uk/downloads.

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Guest Editorial

Guest Editorial

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LEARN ABOUT LEADERSHIP AND NEVER STOP

The NHS is not one organisation; it's made up of hundreds of individual organisations, each with their own unique culture - and often sub or 'micro' cultures. Consider all of the teams and departments that are working together for patients and their loved ones; where would they be without effective leadership? And for those not well-led, consider where they would be if they were. Peter Homa and Claire Lodge, from the NHS Leadership Academy, explore why learning about leadership is one of the wisest investments you can make.

When it comes to leadership rather than management - influencing and motivating rather than directing and controlling - hierarchies and positional power only get us so far. In high-pressure settings, good leadership can be the difference between life and death. In high stress environments, communication needs to be seamless and everyone needs to trust their team and feel trusted. Good leaders create the environments in which these conditions flourish.

Doctors and fellow clinicians are uniquely-placed to take on leadership roles; who better to decide how care should be arranged and resourced than the staff at the heart of delivering it? Increasingly, clinicians are taking leadership roles across the NHS. The Leadership Academy supports leaders across the arc of their working lives.

As a student doctor, you use your leadership skills every day. You may not be using them consciously, but you're still using them. In his paper: *"Are you an unconscious or conscious leader"*, John Wood sets out the differences and beliefs between the two approaches, some of which are included below:

- **Appearing fearless**: Although they experience fear, as all people do, they are not governed by it and simply use it to channel their energy and effort.
- **Being extraordinary, active listeners**: They are curious about and listen deeply to others. They encourage those who have a different reality to express their views, fully and frankly. They are not threatened by that difference.
- **They are vanguards** – champions for the advancement of their colleagues for the greater good. They are courageous yet humble in sponsoring what they see will assist those they serve.
- **Not blindly following**: They don't *'tow the party line,'* making independent decisions, maintaining their integrity even when pressured to vote with the in-crowd, while relying for guidance on accumulated wisdom and common sense.
- **Personifying loyalty**. Even when practical realities demand they make difficult decisions, including personnel decisions, they do so from integrity and conscience.

All of the above are manifested as innate self-confidence, regardless of seniority. This will be recognised as credible and compelling leadership.

The Leadership Academy programmes draws on these insights and supports leaders to be themselves more skillfully. Sometimes the way we behave as leaders and the way we view ourselves as leaders are very different things – it's a blind spot for some of us. We aim to help our participants close that gap, increasing self-awareness and knowing how to harness our skills. Learning to understand your impact on others is a key leadership skill.

Leadership is not simply about being told what to do by someone more senior. Effective leadership requires humanity, humility, compassion and diversity in which difference is treasured to enrich achievement of shared goals. Great leadership encourages these qualities in others. As one of our leadership programme participants recently said: *"I'm confident that I'm doing things that are right for the NHS, not just because someone has said they need to be done."*

Evidence shows that compassionate leadership leads to improved staff engagement and better patient outcomes and care. The Leadership Academy involves patients and carers at every stage of leaders' development to ensure that leaders understand how they can have a positive impact on patient care. We recently worked with the parent of an eight-year-old patient, Tommy, who has developmental delay of his gross motor skills. Tommy's mum told us how every NHS appointment feels like starting all over again. That the way Tommy is greeted – such a small thing to many – can have a profound impact on his wellbeing. The way we conduct ourselves at work impacts on people's health and their wellbeing. Many clinical teams now practice *"Schwartz Rounds".* These rounds create a safe environment in which teams can share concerns and insights that help build high trust and highly performing teams. As Gandhi said: *"Be the change you want to see in the world".*

Be a great teacher, and have one

Great leaders are, in part, the product of those who led them. We all have people in our lives that shape our life story. They have an enduring impact. Who are yours? And whose life stories will you help to shape?

Regardless of hierarchy, leaders are looked to as teachers, and will find themselves being asked for their input and counsel. But it's equally critical that we too have someone to approach for wisdom and advice. The Academy's coaching and mentoring service caters for staff at all levels, and tellingly, there's considerable resource for chief executives, who are offered membership to our development network in the first two years of their role and are then offered the opportunity to impart their wisdom to existing and aspiring chief executives.

Leadership is a lifelong journey, so not only is being a great teacher important – having them is too.

Exceptional leaders are often great teachers and great learners. When teaching, they elicit learning from their personal and professional lives, sharing their experience and teaching with authenticity. Great leaders encourage others' continuous professional and personal development. Many of the NHS Leadership Academy's alumni have relationships with the Academy that span many years and will stretch into the future. An NHS chief executive recently said: *"The impact of the NHS Leadership Academy's development work on me has been two-fold; to listen and understand other examples that I've used in my thinking and planning, and to listen to examples of how other chief executives work, and different styles, which has also been useful. I've also been able to offer my experience to others and in return gain extra knowledge from other parts of the country"*.

Our invitation to you is to consider the NHS Leadership Academy as a resource and one of your spiritual homes in which you can learn how to become even more effective as you write your clinical and leadership story.

Go boldly, go well.

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Original Research

Risk of stroke in the periprocedural period: a literature review comparing carotid endarterectomy and stenting

ORIGINAL RESEARCH

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ABSTRACT

Background: Atherosclerosis of the carotid arteries is a pathophysiological process increasing the risk of stroke. Carotid endarterectomy (CEA) and carotid artery stenting (CAS) are two recognised procedures indicated by the National Institute of Clinical Excellence (NICE) guidelines aiming to reduce the risk of stroke. However, both are associated with periprocedural complications (defined as within 30 days), particularly stroke. This review aims to identify which treatment, CAS or CEA, has a lower risk of periprocedural stroke in patients with symptomatic or asymptomatic carotid artery stenosis.

Methods: NICE Evidence Search identified relevant UK guidelines. Search strategies combining free-text terms searched the Cochrane Database of Systematic Reviews, MEDLINE, PubMed, CINAHL, and EMBASE for systematic reviews post-2011, and RCTs from 2015 onwards. Studies were included if they contained a comparison of CEA vs CAS with regards to periprocedural risk of stroke, and if they contained novel studies not seen in the NICE guidance. English language and full-text limits were applied.

Results: Searches identified 202 articles. Two reviewers performed independent screening identifying 3 guidelines, 7 systematic reviews, and 1 randomised control trial eligible for inclusion. Guidelines currently advocate usage of both procedures, unlike Scottish Guidelines (SIGN) who only support CEA. Four appraised systematic reviews found a statistically significant increase in stroke probability with CAS ($p<0.05$). The remaining reviews and RCT did not show a significantly increased risk with CAS ($p>0.05$).

Discussion: This review's findings suggest that CAS is associated with an increased risk of periprocedural stroke when compared to CEA. Current UK guidelines by NICE and SIGN may require revisiting and take into account the new evidence not included in the original guidelines. There is a need for ongoing research as stenting technology improves over time.

BACKGROUND

Atherosclerosis is the pathophysiological process of lipid and fibrous tissue deposition within the tunica intima of arteries, leading to plaque formation. These plaques cause luminal narrowing and may rupture, becoming a site for thrombus formation. (1) Plaque formation and subsequent rupture in the carotid arteries can form emboli that migrate to the cerebral vasculature, potentially causing occlusion leading to ischaemia. (2,3) Ischaemic stroke, caused by such an occlusion, is defined as a sudden onset of neurological symptoms lasting more than 24 hours. (4) This form of stroke accounts for 85% of all strokes; the remaining 15% are haemorrhagic. (5)

Stroke is a major cause of morbidity and mortality, responsible for over 40,000 deaths in 2015, making it the 4th largest cause of death that year. (5) Non-lethal strokes have numerous long-term consequences such as loss of movement, speech problems, and life-changing impacts on the patient's relatives, especially if long-term care is required following the incident. (6)

Carotid artery stenosis is responsible for approximately 20% of all strokes in the UK. (7) There is a recognised need to manage the disease process of carotid atherosclerosis, to prevent adverse events such as stroke. Conservative measures are crucial in targeting modifiable risk factors, particularly in an ageing population where atherosclerosis is of increasing incidence. (8) Table 1 shows the modifiable and non-modifiable risk factors for carotid atherosclerosis.

Table 1 - Modifiable and non-modifiable risk factors for carotid atherosclerosis (8)

Modifiable	Non-Modifiable
Smoking	Age
Blood Cholesterol	Family History
Hypertension	Gender
Obesity	Genetics
Immobility	
Diabetes	

Treatment of established carotid artery stenosis is divided into medical and surgical therapies. (9) Medical therapies aim to reduce the risk of clot formation through agents such as aspirin and clopidogrel. There are two major surgical options: carotid endarterectomy (CEA) and carotid artery stenting (CAS). CEA is an open procedure performed by vascular surgeons, whereby the carotid artery is opened, and the plaque physically removed. Stenting is a minimally invasive procedure performed by interventional radiologists who feed a catheter through a distant artery, for instance the femoral, and placing a mesh to maintain the patency of the carotid artery lumen. Currently, NICE guidelines acknowledge a lack of evidence to support early stenting. (10) However, it can be performed at the surgeon and patient's discretion. (11,12) Indications for carotid surgery as mentioned in the NICE TIA and Stroke Guideline CG68 can be found in Table 2. (10)

Table 2 - NICE CG68 Indications for operating (10)

1.	Individuals who have a suspected TIA/non-disabling stroke should undergo a clinical assessment and relevant Radiology with surgery potentially to follow.
2.	Recognised stable neurological symptoms with associated luminal narrowing of >50% according to the North American Symptomatic Carotid Endarterectomy Trial (NASCET) criteria or >70% according to the European Carotid Surgery Trialists' Collaborative Group (ECST) criteria.
3.	Surgery within 2 weeks of TIA/Stroke symptoms.

RATIONALE

Interventional radiology has emerged as a field involving minimally invasive surgery associated with lower rates of periprocedural complications, quicker recovery times and smaller scars compared to open surgery. (13) Therefore, it is perhaps expected that CAS could be a safer procedure with fewer complications compared to CEA. Scoping searches identified stroke to be a complication associated with both interventions.

This review was performed to ascertain the relative safety of the two surgical procedures, focussing on periprocedural stroke as the measure of safety, as stroke is the major adverse event that the surgeries are aiming to prevent. Similarly, periprocedural outcomes give a more accurate reflection of the surgery itself than longer-term outcomes which are more likely to be confounded by other factors contributing to the patient's health.

Patients with symptomatic and asymptomatic carotid stenosis represent the population most likely to receive surgery, therefore representing the population of interest. Symptomatic is defined as patients who have suffered neurological symptoms due to stenosis and asymptomatic as patients picked up incidentally. All author definitions of stenosis were accepted as this review compared periprocedural outcomes, not successful treatment of the stenosis itself. The intervention was CAS; the newer method to treat stenosis. For the comparator, the current established method, endarterectomy, was chosen. With regards to outcome, periprocedural stroke (stroke within 30 days post-procedure) was selected as it is a known complication of both procedures and reflects operational safety.

The Population Intervention Comparator Outcome (PICO) for this review is therefore:

- **Population:** Patients with symptomatic/asymptomatic carotid artery stenosis requiring surgical intervention
- **Intervention:** Carotid artery stenting
- **Comparator:** Carotid endarterectomy
- **Outcome:** Periprocedural stroke (defined as stroke within 30 days post-procedure)
- R**eview Question:** Which treatment, CAS or CEA, has a lower risk of periprocedural stroke in patients with symptomatic or asymptomatic carotid artery stenosis?

METHODOLOGY

A literature review was designed following a pre-defined protocol outlined below:

1. Creation of a PICO question
2. Development of inclusion and exclusion criteria
3. Formation of a search strategy for the databases NICE Evidence Search, MEDLINE, EMBASE, CINAHL, Cochrane Database of Systematic Reviews, and PubMed
4. Article selection and appraisal
5. Discussion and conclusion of findings

Search Strategy

UK guidelines were identified using NICE Evidence Search. The electronic databases NICE Evidence Search, MEDLINE, EMBASE, CINAHL, Cochrane Database of Systematic Reviews, and PubMed were searched in parallel for eligible systematic reviews. All the aforementioned databases except NICE Evidence Search were used to identify RCTs. Search terms used for each database were similar, generally including "Carotid stenosis AND stent AND endarterectomy" (Table 3). Variations in search terms were due to differences in the terminology accepted by the individual databases.

Article Selection and Management

Date limits were pre-specified for systematic reviews to identify reviews and RCTs not seen in guidelines. RCTs were limited to find novel trials not in any reviews or guidelines. English language and full-text limits were applied for all searches. Two authors performed independent title and abstract screening against pre-defined inclusion and exclusion criteria. Disagreements were resolved through consensus agreement with a third reviewer.

Included papers compared carotid endarterectomy and stenting to treat stenosis, with assessment of periprocedural stroke as an outcome. Excluded papers did not compare the procedures, did not feature periprocedural stroke as an outcome, or were reviews/RCTs found in guidelines. EndNote x7 (Clarivate Analytics, USA) managed study records throughout the review process.

Data Extraction

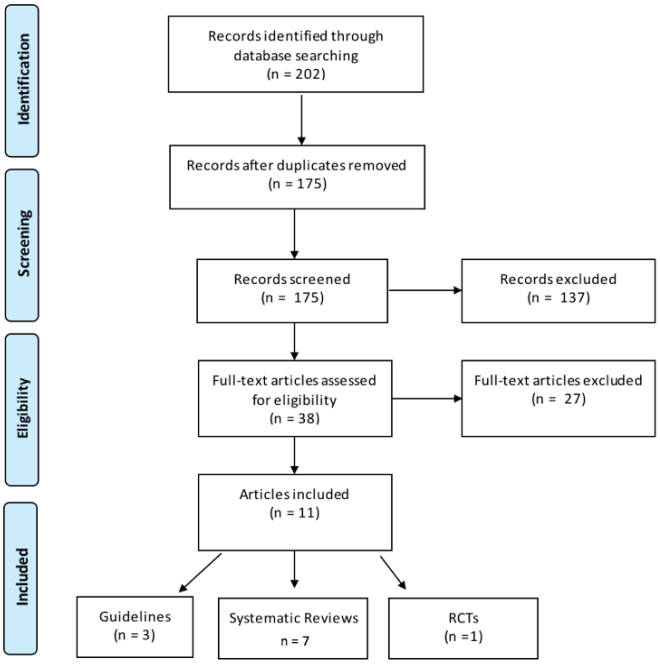
Two authors performed extraction of results comparing the two procedures and their risk of stroke in the periprocedural period. Appraisal of guidelines used the Appraisal of Guidelines for Research and Evaluation (AGREE) II tool. (14) Two authors independently appraised the Systematic reviews and the RCT using the appropriate Critical Appraisal Skills Programme (CASP) checklists. (15)

Table 3 - Search terms

Search	Database	Search Terms	Limits applied
Guidelines	NICE Evidence Search	Carotid stenosis AND stent AND endarterectomy	NICE Accredited Guidance
Systematic reviews	Cochrane	Carotid stenosis AND Stents AND Carotid Endarterectomy AND Stroke	Systematic Reviews Year 2011 – current
	MEDLINE	Carotid stenosis AND Stents AND Endarterectomy, Carotid AND Stroke	Systematic Reviews Year 2011 – current English Language
	CINAHL	Carotid endarterectomy AND carotid stenting AND stroke AND periprocedural	Year 2011 – current Systematic review
	PubMed	Carotid stenosis AND Stents AND Endarterectomy, Carotid AND Stroke	Systematic Reviews Year 2011 – current English Language
	EMBASE	Carotid Artery Obstruction AND Stent AND carotid endarterectomy AND cerebrovascular accident	Systematic Reviews Year 2011 – current

Randomised Controlled Trials	MEDLINE	Carotid stenosis AND Stents AND Endarterectomy, Carotid AND Strokee	Randomised Controlled Trials Year 2015 - current
	EMBASE	Carotid Artery Obstruction AND Stent AND carotid endarterectomy AND cerebrovascular accident	Randomised Controlled Trials Year 2015 - current
	PubMed	Carotid stenosis AND Stents AND Endarterectomy, Carotid AND Stroke	Randomised Controlled Trials Year 2015 - current
	CINAHL	Carotid endarterectomy AND carotid stenting AND stroke AND periprocedural	Randomised Controlled Trials Year 2015 - current
	Cochrane	Carotid stenosis AND Stents AND Carotid Endarterectomy AND Stroke	Trials 2015 - current

Figure 1 - Adapted PRISMA flowchart showing review process (16)



Results

From 202 search results a total of eleven eligible papers were found. These included three guidelines, seven systematic reviews and one RCT (Figure 1).

All three guidelines concluded that there is inadequate evidence to assess the efficacy and safety of early CAS (Table 4). (11,12,17) CEA remains the first-line intervention for both scenarios. NICE recommends performing CAS only if a skilled clinician is available and in certain situations (e.g. for research purposes) after patients have consented and been made aware of endarterectomy as an alternative. (11,12) The results of the systematic reviews and RCT are shown in Table 5.

Table 4 - Summary of guidelines

Guideline	Date of publication	Evidence base	Conclusion
Carotid artery stent placement for asymptomatic extracranial carotid stenosis (IPG388) (11) **Author: NICE**	April 2011 however evidence overview was performed in 2010	2 meta-analyses 2 randomised controlled trials 2 non-randomised controlled studies 3 case series 3 case reports	Stenting for asymptomatic stenosis can be performed by skilled clinicians under special arrangements, such as research, but CEA remains first line
Carotid artery stent placement for symptomatic extracranial carotid stenosis (IPG389) (12) **Author: NICE**	April 2011 however evidence overview was performed in 2010	2 meta-analyses 4 randomised controlled trials 2 non-randomised controlled studies 5 case series 4 case reports	CEA is first line. Evidence accepts usage of stenting if the specialist and patient choose.
Management of patients with stroke or TIA: assessment, investigation, immediate management and secondary prevention (17) **Author: SIGN**	December 2008	1 systematic review	Carotid angioplasty and stenting is not recommended without further evidence of its safety and efficacy above CEA.

Table 5 - Systematic review and RCT results (18-25)

Name of Study	Study Design	Number of trials	Total number of patients	Main results (CAS vs CEA)
Bonati LH et al. (2012) (18)	Systematic review	16 RCTs	7,527	OR 1.81, 95% CI: 1.40 to 2.34, P<0.00001 I^2 = 12%
Gahramenpour A et al. (2012) (19)	Systenatic review	14 RCTs 15 meta-analyses 1 data registry	74,003	No meta-analysis performed.
Paraskevas KI et al. (2016) (20)	Systematic review	21 data registries	Over 1.5 million procedures assessed	No meta-analysis performed.
Raman G et al. (2013) (21)	Systematic review	3 RCTs 7 NRCS	377,361	NRCS RR 1.74 (95% CI: 1.41-2.16)
Zhang L et al. (2015) (22)	Systematic review	12 RCTs 3 Prospective Controlled Studies 20 Retrospective comparative studies	27,525	Studies in 2011-2015 RR 1.50 (95% CI 1.14-1.98 p=0.004) I2 = 0% Studies in 2006-2010 RR was 1.61 (95% CI 1.35-1.91 p< 0.001) I2 = 45% Studies in 2001-2005 RR 1.01 (95% CI 0.64-1.60 p=0.95) I2 = 10%
Ouyang Y et al. (2015) (23)	Systematic review	9 RCTs	6,984	RR=1.62 (95% CI: 1.31–2.00, P<0.0001, I2 =37%)
Vincent S et al. (2015) (24)	Systematic review	8 RCTs	7,091	RR=1.49 (95% CI: 1.11-2.01, P value not stated, I2=42.2%)
Rosenfield K et al. (2016) (25)	RCT	1 RCT	1,453	CAS 2.8% vs CEA 1.4%, p=0.23)

DISCUSSION

This literature review identified 3 guidelines and 7 systematic reviews and 1 RCT comparing CEA vs CAS and the development of stroke in the periprocedural period. (11,12,17-25) All provided evidence to suggest CEA is associated with a lower risk of periprocedural stroke, some with statistical significance. (11,12,17-25)

Guideline Appraisal

The three eligible guidelines identified were the NICE IPG388 (asymptomatic stenosis) (12) and IPG389 (symptomatic stenosis) (13) along with SIGN 108. (17) NICE IPG388/389 were produced in 2011 and clearly state the PICO and the outcomes to be assessed. (11,12) Outcomes compared patients that had either procedure performed, categorised as 'efficacy' (stroke, mortality, and arterial patency) and 'safety' (mortality, stroke, myocardial infarction, and other). (11,12) Searches of MEDLINE, CINAHL, EMBASE, Cochrane Database and other specified databases were

performed. (11,12) Searches yielded eligible meta-analyses, RCTs, non-randomised controlled studies (NRCS), case series, and case reports. Due to heterogeneity, NICE did not perform a meta-analysis. (11,12) No mention of inclusion or exclusion criteria was made, and whilst the search strategy for MEDLINE was shown, other databases strategies were not included. (11,12)

Results for the studies used were given as relative risks (RR) and hazard ratios (HR), and significance was defined as a $p<0.05$. Three of the studies in IPG388 (asymptomatic stenosis) (1 meta-analysis, 1 RCT and 1 NRCS) showed that CEA had a significantly lower rate of periprocedural stroke. (11) IPG389 demonstrated a similar picture in symptomatic patients, with CAS significantly increasing periprocedural stroke in five (2 meta-analyses, 3 RCTS) of the 17 studies, although most studies found no statistically significant difference. (12) Both guidelines acknowledged the use of *'low quality'* evidence, concluding endarterectomy remains first-line, but this does not represent a contraindication for stenting to occur. (11,12)

SIGN Guideline 108 was produced in 2008 which recommends against using stenting to treat both symptomatic and asymptomatic stenosis. (17) The basis of this recommendation is entirely from the meta-analysis by Ederle et al. (26) This analysis is also appraised by NICE and it is interesting to note that the conclusion by SIGN differs to NICE despite both using the same meta-analysis. The SIGN guideline, however, lacked the methodological rigour of the NICE guidelines, with no defined search strategy and no explanation of how the evidence was sourced.

Systematic Reviews Appraisal

A total of seven systematic reviews were included (18-24); these vary in the study types featured, but all suggest CAS to be associated with increased risk of periprocedural stroke compared to CEA. (18-24) Three limited their reviews to only RCTs. (18, 23,24) Another three included RCTs along with other study designs such as meta-analyses and retrospective studies. (19,21,22) One review looked at dataset registries in isolation. (20) Due to variation in studies included, only five performed meta-analyses of the data that they collected. (18, 21-24) None of the systematic reviews looked solely at UK populations and were mainly North American in origin. Given the variation in international healthcare systems, there may be questionable applicability to UK populations. Those looking at only RCTs contained the smallest numbers of patients (ranging from 6988 to 7527 patients), while the study looking at dataset registries contained a pool of over 1.5 million procedures. Six out of seven reviews (except Raman et al.) (21) looked at both asymptomatic and symptomatic patients.

Search strategy quality varied across the reviews, with the most comprehensive search strategy performed by Bonati et al. (18) They searched for RCTs in CENTRAL, MEDLINE, EMBASE, Science Citation Index, and Cochrane Stroke Group Trials Register. Additionally, they searched three registries for ongoing trials, searched reference lists for relevant studies, and contacted experts in the field. Only Bonati et al. (18) and Paraskevas et al. (20) had two independent reviewers perform a title screen of each database. Most of the reviews limited their inclusion criteria to English language only, with two exceptions: Vincent et al. (24) accepted English and French languages, while Bonati et al. (18) did not apply any language limits.

Additionally, Paraskevas et al. (20) was the only study to apply a date limit to their search by excluding pre-2008 studies. They justified this by wanting to exclude historical studies, however, no justification was made as to why 2008 was seen as a cut off. All reviews performed quality assessments of their studies and reviewed for bias, except for Gahramenpour et al. (19) Furthermore, only Bonati et al. supported each of their judgements of bias using quotes from the original trials. (18) Use of a consistent tool allows a reader to critique the authors' bias assessments and ensure that the authors were not biased themselves.

All but Gahramenpour et al. (19) or Paraskevas et al. (20) performed a meta-analysis of the data. Only Paraskevas et al. justified their lack of meta-analysis, stating that baseline patient characteristics and outcomes were reported variably, and there was substantial heterogeneity in the registries used. (20) The five meta-analyses measured heterogeneity using I^2 statistics. The I^2 values varied between 0 and 45% when analysing RCTs, indicating low to moderate heterogeneity as per Cochrane definitions. (27,28)

In reviews where RCTs were used, the most common RCTs were CREST, (29) EVA-3S, (30) SAPPHIRE, (31) SPACE, (32) and ICSS. (33) These were large-scale RCTs with the smallest including 334 patients (SAPPHIRE (31)) and the largest 2522 (CREST (29)). These five in particular were all considered to have low bias when assessed by two independent reviewers in Bonati et al. (18) Three of the aforementioned RCTs used in the meta-analyses by Bonati et al. (20) and Zhang et al. (22) found a statistically significant difference in our primary outcome of stroke (EVA-3S, (30) ICSS, (33) CREST (29)) and 2 (SAPPHIRE (31) and SPACE (32)) did not, however, the cumulative data did point to a significant difference.

Bonati et al. presented their results as odds ratios, finding that in symptomatic patients, CAS had statistically significant increased odds of stroke (OR 1.81, 95% CI: 1.40 to 2.34, $P<0.00001$). (18) Four studies presented their findings in the form of relative risks (Vincent et al., Ouyang et al., Raman et al. and Zhang et al.). (21-24) Their findings varied between RR=1.49 (95% CI: 1.11-2.01) (Vincent et al. (24)) and RR=1.74 (95% CI: 1.41–2.16) (Raman et al. (21)). A notable abnormality with Ouyang et al. (23) was the lack of correlation of results in the abstract and results sections of

the article.

Interestingly, not all of the studies in Zhang et al. support this conclusion. (22) The authors performed a chronological analysis and found that studies from 2001-2005 showed no statistically significant difference between the procedures. (22) In their discussion, they attribute this to the novelty of the procedure at that time, thus CAS was only used in simple cases. (22)

RCT Appraisal

The ACT-1 trial had a clearly focused PICO, with the aims being well defined. (25) The sample size was large, with 1453 patients randomised at a ratio of 3:1 to receive CAS or CEA. Randomisation was performed with use of a web-based system. (25) Blinding was not possible due to the nature of the interventions; this increases the possibility of bias. A baseline characteristics table is included in the study and shows similar characteristics between the two study arms. Important possible confounders such as age, gender, cigarette smoking, diabetes and previous cardiovascular disease were considered. The presence of two similar groups indicates successful randomisation. Moreover, the study mentions that analysis was by intention to treat (ITT). This refers to analysis with respect to the groups to which participants were originally randomised. The inclusion criteria for ACT-1 was specific; it focused on patients aged 79 years or younger, with severe carotid stenosis who were asymptomatic and not considered to be at high risk of stroke. (25) This specificity may limit applicability to the wider population.

Review Findings

This review identified literature suggesting CAS is associated with increased periprocedural stroke relative to CEA. Given Interventional Radiology and Endovascular Surgery are modern and rapidly advancing fields, it is possible that periprocedural outcomes will change over time as technology improves. Previous evidence has shown that improved operator skill is associated with superior outcomes (34-36) and that the use of different stenting technology has been associated with variations in safety outcomes. (37) Relevant RCTs were included, published after the most recent systematic review to see if contemporary evidence supports the trend seen up until now.

Currently, NICE guidelines withhold from offering any definitive recommendation regarding the use of CAS over CEA. (11,12) They appreciate that CAS is an expanding field and recommend the use of stenting for research purposes. On the other hand, SIGN concluded that stenting was not recommended without further evidence. The SIGN guidelines were published in 2008, before the results of many important large-scale trials were released. This guideline is in need of an update. (17)

As previously alluded to, our review seems to indicate that the NICE guidelines need updating regarding the safety of carotid stenting versus endarterectomy, however, this review focused on a single outcome. Many of the studies we analysed considered a number of important safety and efficacy outcomes, such as periprocedural myocardial infarction. In order to make a conclusive recommendation, a multitude of periprocedural complications should be looked at to gauge the overall picture of CAS vs CEA. Similarly, factors such as patient preference, specialist availability, and cost effectiveness play a role in national decision-making.

Limitations

A limitation of our review was our exclusion of studies which we were unable to access in full or those which were non-English language. Where information was absent or unclear, a future review could contact study authors to obtain information. Furthermore, we did not search for ongoing or unpublished trials, which could provide relevant up-to-date results reflecting current practice.

CONCLUSION

This review aimed to compare the safety of two procedures, endarterectomy and stenting, to ascertain which is associated with a greater risk of periprocedural stroke. The conclusion, based on available research, suggests stenting is associated with an increased risk of periprocedural stroke in asymptomatic and symptomatic patients when compared to carotid endarterectomy. This may change as surgical practice continues to evolve. Based on the probability of periprocedural stroke, endarterectomy may remain preferable to stenting, until adequate high-impact research can argue to the contrary.

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Original Research

Exploring barriers to hospital delivery in Sub-Saharan Africa: a review of the literature

ORIGINAL RESEARCH

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ABSTRACT

Background: The maternal mortality ratio (MMR) in sub-Saharan Africa is more than 60 times that in the UK. Both the Millennium Development Goals and the Sustainable Development Goals set out by the United Nations include a focus on reducing worldwide MMR. One way in which to achieve this is to encourage mothers in the developing world to deliver their babies in healthcare facilities. This review aims to identify the barriers to hospital delivery in sub-Saharan Africa.

Methods: Two databases were searched for relevant studies published within the last five years. All articles included in the review were critically appraised using CASP checklists and the STROBE statement to assess for bias. Barriers to hospital delivery were identified in each study and organised into categories according to the three delays model.

Results: Thirteen barriers to facility delivery were identified. Fear of maltreatment by healthcare staff, perceived low quality of care, distance and lack of transport to facilities, and cost of delivery were identified as the barriers for which there was the highest level of evidence.

Discussion: Successful interventions to tackle lack of transport and cost of delivery have been identified. It appears more difficult to find a solution to the barriers created by societal norms, however, as it would be culturally insensitive to impose Western beliefs on those with different traditional and religious views. This review provides suggestions for future research and potential interventions to reduce maternal mortality in sub-Saharan Africa.

BACKGROUND

Every day there are approximately 830 preventable deaths of women relating to pregnancy worldwide, with more than half of these occurring in sub-Saharan Africa. (1) The most common causes of death include haemorrhage, sepsis, hypertensive disorders, pulmonary embolism, unsafe abortion and delivery complications. (2) Maternal death has huge societal impact in low- and middle-income countries due to the economic roles of women. (3, 4) Children of mothers who die have increased rates of mortality, (4-6) poverty, (3, 4, 7) psychological problems, (8) early pregnancy, (9) malnutrition (7, 9) and poor educational attainment. (4, 7-9)

The United Nations Millennium Development Goals (MDGs) are eight goals that were set in 2000 to be achieved by 2015. (10) MDG5 aimed to improve maternal health by reducing the worldwide maternal mortality ratio (MMR) by 75%. (10) MMR is measured in maternal deaths per 100,000 live births. Significant progress has been made, with worldwide MMR decreasing by 37% between 2000 and 2015. (11) However, geographical inequalities still exist: in 2015, the MMR in sub-Saharan Africa was estimated at 546, compared to just nine in the UK. (11)

In 2015, the United Nations (UN) adopted the Development Agenda *"Transforming our World"*, containing 17 Sustainable Development Goals (SDGs) for review in 2030. (12) SDG3 aims to improve health at all ages, again focusing on reducing worldwide MMR. (12)

Skilled attendance at delivery was recognised as a key factor in the reduction of maternal mortality by the Safe Motherhood Initiative in 1987. (13) As part of progress towards achieving MDG5 and SDG3, interventions have been introduced to encourage mothers in the developing world to deliver in healthcare facilities. (10, 12) However, rates of facility delivery in this setting remain low. (14) This review will explore the barriers towards facility delivery in sub-Saharan Africa.

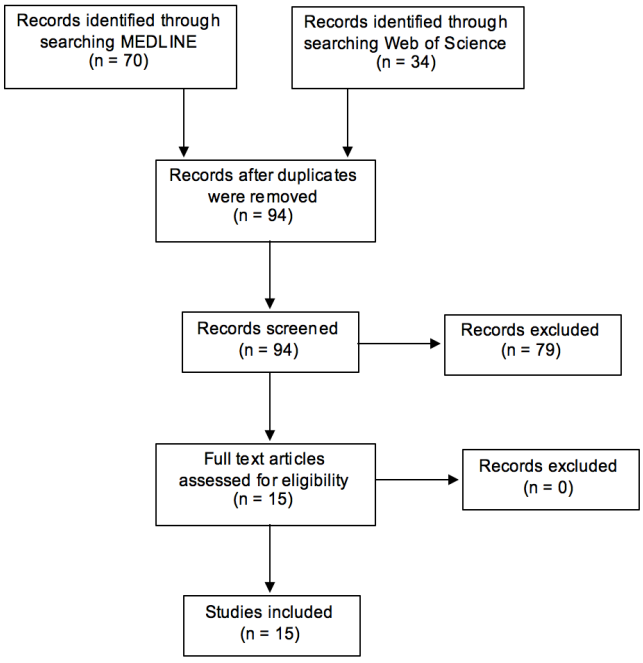
Maternal mortality is an important global health issue that UK medical students should be aware of. An appreciation of the barriers towards facility delivery in developing countries is essential in understanding why maternal healthcare inequalities exist globally and to identify successful interventions to improve maternal mortality in these countries in the future. This review is of particular interest to students with an interest in global health, international obstetrics or those undertaking a medical elective in sub-Saharan Africa.

METHODS

A comprehensive literature search was conducted using two databases: MEDLINE and Web of Science. MEDLINE was chosen for its wide range of medical literature whilst Web of Science was chosen to reflect a multi-disciplinary approach. Three key themes of the research question were identified: hospital delivery, barrier, and sub-Saharan Africa. Variations of these themes were used to conduct the searches. Search filters included English language and 'published since 2012'. The literature search was limited to papers published between 1st January 2012 and 17th February 2017 (the date on which the searches were conducted) in order to ensure that all of the identified barriers were relevant to the present day.

104 papers were identified in total, ten of which were duplicates. The titles and abstracts of the remaining 94 papers were read and papers were excluded from the review if they did not specifically focus on barriers to hospital birth in sub-Saharan Africa. 15 papers remained at the end of this process, all of which were included in the review. Articles were reviewed by one researcher (R Best).

Figure 1 - PRISMA flow diagram



The resulting articles were critically appraised in order to assess risk of bias and quality of evidence. The Critical Appraisal Skills Programme (CASP) Qualitative Research checklist (15) was used to critically appraise the qualitative studies; CASP Systematic Review checklist (16) was used for the systematic reviews; and the STROBE Statement Cross-Sectional Study checklist (17) was used to assess the cross-sectional studies.

The proposed barriers to hospital delivery were identified in each paper and collated into a spreadsheet. These barriers were then organised into three categories according to the three delays model proposed by Thaddeus and Maine in 1994. This model identifies three points at which delays prevent mothers from delivering at hospital: 1) delays in decisions to seek care; 2) delays to arrival at a healthcare facility; and 3) delays in care provision. (18) Considering the barriers to facility delivery using this framework allows interventions to be targeted to these three stages in seeking and receiving care.

The barriers are discussed below with consideration of the scientific rigour of the papers in which they were identified. Ethical approval was not required for this literature review.

RESULTS

Summary of studies

Twelve studies explored barriers to hospital delivery in individual communities within sub-Saharan Africa, (19-30) whilst three focused on wider populations. (31-33) A systematic review by Brighton et al. explored perceptions across sub-Saharan Africa, (31) whilst Tey and Lai and Bohren et al. reviewed barriers in low- and middle-income countries. (32, 33)

Seven studies focused on women who were pregnant or who had recently delivered; (19, 20, 23-25, 28, 32) two focused on women of childbearing age regardless of gravidity; (26, 30) two explored healthcare workers' perceptions of barriers; (21, 22) and the remainder looked more broadly at populations, including healthcare workers, pregnant women and communities. (27, 29, 31, 33)

Critical appraisal

Six of the studies were deemed to be of high quality, with low risk of bias and high confidence in the findings. (21, 24, 26, 28, 30, 33) Five studies were assessed as being of moderate quality, (19, 22, 23, 25, 32) whilst the remaining four were deemed to have low confidence in the study findings. (20, 27, 29, 31) Full details of the critical appraisal findings for each study are given in Table 2.

Barriers identified

Thirteen barriers to facility delivery were identified: community influence, cost of treatment, cultural beliefs, fear of HIV testing, lack of autonomy and confidentiality, lack of knowledge, lack of a support person, lack of transport, perceived low quality of care, fear of maltreatment, medicalisation of childbirth, precipitous labour, and poor facility equipment. These barriers are further discussed in terms of the three delays model below. (18)

Delays in decisions to seek care

Community influence

Five papers identified family or community influence as a barrier to facility delivery due to the pregnant woman's lack of autonomy within her community. (21, 30-33) In the settings described, the decision to receive hospital care is made either by the woman's husband or community elders, (21, 30-33) particularly when there are costs associated with delivery. (31)

Cultural beliefs

Four papers identified women's cultural beliefs as a barrier. (21, 28, 31, 33) Bohren et al. highlight the belief that complications of childbirth, particularly eclamptic seizures, are spiritual in nature rather than physical and therefore could not be treated by healthcare professionals. (33) Similarly, Brighton et al. describe the belief that complications during pregnancy are caused by women's bad behaviour and the only curative treatment is the confession of sins. (31) In Tigray, Ethiopia, women value traditional practices during childbirth such as rituals to summon the support of Saint Mary, which are infeasible to replicate in a healthcare setting. (21)

Fear of HIV testing

Two studies found fear of HIV testing to be a barrier to facility delivery in pregnant women. (26, 33) Bohren et al. highlight how women in low- and middle-income countries fear the discrimination associated with a positive HIV test result. (33) Mason et al. noted a similar fear in Kenyan women, with many participants not wishing to know their own result as well as being fearful of others discovering that they tested positive. (26)

Lack of autonomy and confidentiality

O'Donnell et al. identified lack of autonomy as a major barrier to facility delivery in Malawi, with women reporting that they often did not understand why a treatment had been given in hospital and had not been asked for consent for procedures. (29) Also in Malawi, Kumbani et al. found lack of confidentiality to be a reason to avoid delivering at a facility. (25)

Lack of knowledge

Echoka et al. describe women's lack of knowledge about pregnancy as a barrier to seeking a facility delivery in the Malindi district of Kenya. Many women stated that they thought the pregnancy complications they were experiencing were part of a normal labour and delivery and therefore did not know to seek help. (20) This

barrier was also identified by women in Coast Province, Kenya (27) and healthcare workers in Rwanda. (22)

Lack of support person

Crissman et al. identified lack of a support person as a barrier to hospital delivery in rural Ghana, (19) as the presence of a birth partner is a prerequisite for healthcare worker delivery in this area.

Low quality of care

Six papers identified a perception of poor-quality care at facilities as a barrier to hospital delivery. (24-26, 28, 32, 33) In the study by Bohren et al., women reported healthcare workers to be undertrained, incompetent and inexperienced. (33) Other perceptions of low quality care included lack of pain relief and unavailability of delivery attendants; (24) long waiting times for antenatal care appointments; (25, 26) and unprofessional attitudes from staff. (26)

Maltreatment

The most commonly identified barrier in this review was women's fear of maltreatment by hospital staff, with more than two thirds of the reviewed papers highlighting this issue. (19, 23-29, 31, 33) Maltreatment experienced by women included neglect, (23, 24, 27, 29, 33) verbal, (19, 23-29, 31, 33) physical (23, 27, 33) and sexual (23) abuse. Bohren et al. describe pregnant women being slapped, hit and forcefully restrained by medical staff. (33) Brighton et al. highlight how women are not allowed to express pain or make noise during labour. (31)

Medicalisation of childbirth

One theme identified by five papers was the perception of childbirth as a natural process that should not require medical treatment. (20-22, 30, 32) Echoka et al. discuss the fact that despite high levels of birth preparedness, mothers in Kenya choose to deliver at home because they do not associate pregnancy with ill-health. (20) Similarly, Gebrehiwot et al. found that women living in rural Ethiopia are reluctant to visit hospital for delivery unless they perceive themselves to be sick. (21) This finding is reflected in studies in Rwanda (22) and Nigeria (30) as well as in Tey and Lai's quantitative study in sub-Saharan African and South Asia. (32)

Poor facility equipment

Poor-quality facility equipment was identified as a barrier by Gebrehiwot et al. in Ethiopia. (21) In this study, healthcare workers describe an absence of infection prevention equipment such as masks and goggles as well as shortage of clean water and electricity, which acts as a barrier to women seeking healthcare at the facilities. (21)

Delays in arrival at facility

Distance and lack of transport

Nine studies identified distance or lack of transport to a healthcare provider as a barrier to facility delivery. (19, 20, 27, 28, 30-33) More specific barriers within this theme included high cost of transportation, (19, 27, 33) limited availability of transportation, (19, 27, 28, 32, 33) inability to travel at night, (19, 33) poor roads (19, 20, 27, 33) and distance to facility. (28, 30-32)

Precipitous labour

Three studies described precipitous labour as a barrier to facility delivery, whereby women had intended on attending the hospital to give birth but were unable to make it to the hospital in time. (19, 25, 28)

Delays after reaching hospital

Cost of delivery

Cost of facility delivery was identified as a barrier in eight studies. (19, 22, 26-28, 30, 32, 33) In many settings, patients are denied medical treatment unless they pay for the service beforehand, (33-35) limiting the number of hospital deliveries even when mothers are able to reach the facility in time. Even in countries where there is no fee for delivery, studies describe the 'hidden costs' of childbirth, which include transportation, (27, 33) registration, (26) laboratory tests (26) and items such as sheets and antiseptics that women are expected to bring with them to hospital. (19)

DISCUSSION

Thirteen barriers to facility delivery were identified by this review. An important link that can be made between several of these barriers is societal norms. Cultural beliefs, community influence, maltreatment in hospital facilities and childbirth as a natural process are barriers that result from what is perceived as normal in sub-Saharan African communities. It can therefore be difficult to implement effective interventions to tackle these barriers, as it would be culturally insensitive to try to impose Western beliefs on

those with different traditional and religious views.

Barriers that may be tackled more readily are cost of delivery and lack of transport to facilities. Free and heavily subsidised obstetric care programmes have already been introduced in many countries in sub-Saharan Africa, which have been shown to increase the number of facility deliveries and reduce maternal mortality. (34, 36-38) Similarly, a free emergency transport service implemented in central India, which is also a developing country with a high maternal mortality ratio, has been found to increase the number of hospital deliveries. (39)

Interestingly, Mason et al. identified HIV testing as both a barrier and facilitator to hospital delivery, as some women recognised the value of being tested and appreciated the free service whilst others feared the stigma of a positive result. (26) A suggested intervention here might be to highlight the importance of a woman's right to choose whether or not she receives the test, though this does raise potential ethical issues surrounding unknown vertical transmission of HIV.

The three most commonly identified barriers to facility delivery were fear of maltreatment by healthcare staff; (19, 23-29, 31, 33) distance and lack of transport to facilities; (19-21, 25, 27, 28, 30, 32, 33) and cost of delivery. (19, 22, 26-28, 30, 32, 33) Each of these barriers were identified by four papers that were assessed to be of high quality as well as a number of papers that were assessed to be of moderate or low quality. Perceived poor quality of care was another barrier identified by four high quality studies, (24-26, 28, 32, 33) though it was identified as a barrier in fewer total papers than the other three common barriers.

On the other hand, three barriers to hospital delivery were only identified by papers that were assessed to be of moderate or low quality: lack of a support person; (19) lack of knowledge; (20, 22, 27) and lack of autonomy and confidentiality. (25, 29) The evidence for these barriers is therefore weaker than the evidence for the other barriers identified.

Strengths of this review include the recent nature of all of the articles included. This suggests that all of the barriers identified are current issues, as it is recognised that barriers to hospital delivery may change over time. The included studies also represent the views of healthcare workers and communities as well as pregnant women themselves. Finally, validated scoring systems have been used to critically appraise the literature.

Limitations of the review include the relatively small sample size and the fact that several of the included studies were assessed as having low confidence in the quality of evidence. The qualitative study by Mwangome et al (27) in particular was found to be poorly conducted with reference to the CASP criteria. Another limitation is that different scoring systems were used to critically appraise the papers, due to differences in study design, and each paper was only appraised by one researcher (R Best).

This review has identified the main barriers to hospital delivery in sub-Saharan Africa, which enables organisations such as the World Health Organisation and the United Nations to target their interventions towards the relevant barriers in order to improve maternal mortality.

CONCLUSION

The barriers identified by the most papers with the highest quality evidence in this review were fear of maltreatment by healthcare staff; perceived low quality of care at facilities; distance and lack of transport; and cost of delivery. Successful interventions to tackle lack of transport and cost of delivery have been identified, though it appears more difficult to find a solution to the barriers created by societal norms.

Future research should focus on the implementation of effective interventions to target transport and cost as well as investigating the reasons behind maltreatment of pregnant women by hospital staff. Investment should also be made in hospitals where there is lack of equipment and utilities such as running water and electricity in order to improve standards and encourage women to deliver in hospital.

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APPENDIX

Table 1: Summary of studies

Paper	Study Design	Setting and Population	Barriers Identified	Intervention(s) Identified
Bohren et al 2014 (33)	Systematic review of qualitative studies using thematic analysis	Women, partners and healthcare professionals in 17 low- and middle-income countries worldwide	Traditional and family influences Distance to facility Cost of delivery Low perceived quality of care Fear of discrimination	Reduction of abuse and disrespect of women during childbirth
Brighton et al 2013 (31)	Systematic review of qualitative studies using thematic analysis	Men, women and communities in sub-Saharan Africa	Abuse from healthcare staff Inability to express pain during childbirth Cultural beliefs about pathophysiology of childbirth Community influence	Promotion of behavioural change amongst healthcare workers Incorporation of traditional birth attendants into the hospital setting

Table 1: Summary of studies (Continued)

Paper	Study Design	Setting and Population	Barriers Identified	Intervention(s) Identified
Crissman et al 2013 (19)	Qualitative study using semi-structured interviews and grounded theory analysis	85 pregnant women attending an antenatal clinic in Akwatia, Ghana	Maltreatment by midwives Cost of delivery Lack of a support person Difficulties in transportation Precipitous labour	Reduction or removal of delivery fees Introduction of tractor / bicycle / donkey ambulances Introduction of a "red card" transport system
Echoka et al 2014 (20)	Qualitative study using in-depth interviews and thematic analysis	30 women in Malindi District, Kenya who had experienced near-death obstetric complications	Lack of transportation Lack of knowledge of dangers Childbirth viewed as natural	Development of better roads and access to emergency transport
Gebrehiwot et al 2014 (21)	Qualitative study using in-depth interviews and thematic analysis	4 midwives and 12 health extension workers in Tigray, Ethiopia	Delivery is a natural event Cultural traditions and rituals Inaccessible transport Unmet community expectation Shortage of water and electricity	Humanisation of the delivery process
Hagey et al 2014 (22)	Qualitative study using semi-structured interviews and content analysis	17 healthcare professionals working in Kigali, Rwanda	Lack of knowledge Experience of previous births Lack of support from partners Cost of delivery Antenatal care cultural beliefs	Improvement of maternal education Introduction of HIV testing as an incentive Improved tracking of antenatal visits
Kujawski et al 2015 (23)	Quantitative study using structured questionnaires and multivariate logistic regression	1388 women who delivered at hospital in the Tanga region, Tanzania	Abuse from healthcare professionals	Reduction of abuse and disrespect of women during childbirth
Kumbani et al 2012 (24)	Qualitative study using in-depth interviews and thematic analysis	14 women who had delivered in Chiradzulu District Hospital in the Chiradzulu district, Malawi	Poor communication Poor attitudes from staff Discrimination from staff Delays in care	Improved antenatal information Improved maternal education on danger signs Improved attitudes of healthcare workers
Kumbani et al 2013 (25)	Qualitative study using in-depth interviews and thematic analysis	12 women who had delivered at home in the Chiradzulu district, Malawi	Abuse from healthcare workers Delays in antenatal care Difficulty getting to facility Precipitous labour No guarantee of confidentiality	Improved maternal education Improved staffing levels

Table 1: Summary of studies (Continued)

Paper	Study Design	Setting and Population	Barriers Identified	Intervention(s) Identified
Mwangome et al 2012 (27)	Qualitative study using structured interviews, focus groups and thematic analysis	90 hospital staff and general public and 26 mothers who delivered outside of hospital in Coast Province, Kenya	Cost of care Lack of transport Poor patient-staff relationship Lack of knowledge	Improved links between the hospital and community Development of individual birth plans Improved staff training Development of introductory visits for expectant mothers to healthcare facilities
Nakua et al 2015 (28)	Quantitative cross-sectional study analysed with weighted multivariate logistic regression	400 mothers aged between 15 and 49 with a child less than 12 months old in Amansie West District, Ghana	Insults from healthcare workers Unavailability of transport Lack of birth preparedness Lack of knowledge Lack of partner involvement	Improved staff training Improved maternal education about the benefits of hospital delivery Introduction of an incentive
O'Donnell et al 2014 (29)	Qualitative study using in-depth interviews, focus groups and thematic analysis	33 postnatal mothers aged between 16 and 36 who had delivered in the last 7 days, and 10 healthcare providers in Mangochi district, Malawi	Lack of autonomy Strained relationships and poor communication with staff	Improved communication between mothers and healthcare providers
Tey and Lai 2013 (32)	Quantitative cross-sectional study analysed with logistic regression	Currently married women aged 15-49 who had given birth within 5 years of the survey in Bangladesh, India, Pakistan, Kenya, Nigeria or Tanzania	Preference for traditional birth Lack of transport Cost of delivery Objection from partner Lack of trust in facility	Improved maternal education on the risks of childbirth and the benefits of institutional delivery
Yar'Zever and Said 2013 (30)	Quantitative cross-sectional study analysed with Chi-square tests	1,000 married women aged between 14 and 49 from the Hausa clan, Nigeria	Husband's refusal Lack of illness Distance to healthcare facility Lack of money	Improved education of husbands / partners Improved antenatal care

Table 2: Critical appraisal of studies

Paper	Critical Appraisal Tool	Confidence in Evidence	Comments
Bohren et al 2014	CASP systematic review checklist	High confidence	Comprehensive literature search. Clear assessment of the quality of included studies. Results of all included studies clearly displayed and combination of results appropriate. Overall findings clearly and appropriately expressed and applicable to the population studied. All important outcomes considered.
Brighton et al 2013	CASP systematic review checklist	Low confidence	It is not clear whether grey literature and non-English language literature was searched or whether key experts in the field were contacted as part of the search strategy. There is no evidence of critical appraisal of the included literature. Results of individual studies have not been clearly displayed and it is therefore unclear whether combination of results is appropriate. Overall results are clearly and appropriately expressed and are relevant to the study population. All important outcomes have been considered.
Crissman et al 2013	CASP qualitative research checklist	Moderate confidence	Limited justification for methods used or recruitment method, though convenience sampling is appropriate. Reasons stated for participant refusal. Detailed description of data collection methods, data form and data saturation with limited justification for methods used. Reflexivity explored in terms of translation but not in formulation of research questions, sample recruitment or data analysis. Ethics not considered and no mention of ethical approval. Comprehensive description of data analysis methods with clear themes. Findings clearly stated and research deemed valuable.
Echoka et al 2014	CASP qualitative research checklist	Low confidence	No justification of research design and limited discussion of recruitment process. Clear description of data collection method and data form. Limited justification of data collection methods and data saturation not discussed. Reflexivity not discussed. Ethical approval granted but limited exploration of potential ethical issues. Limited description of data analysis methods. Findings are clearly stated according to the three delays model, and relate back to the original research question. Research deemed valuable.
Gebrehiwot et al 2014	CASP qualitative research checklist	High confidence	Limited justification of research design. Appropriate recruitment strategy with justification of methods. Appropriate and well explored data collection methods with justification for setting. No discussion of data saturation. Reflexivity adequately explored. Ethical approval granted but limited exploration of potential ethical issues. Detailed description of data analysis methods. Overall findings are clearly stated. Research deemed valuable.

Table 2: Critical appraisal of studies (Continued)

Paper	Critical Appraisal Tool	Confidence in Evidence	Comments
Hagey et al 2014	CASP qualitative research checklist	Moderate confidence	No justification of research design. Appropriate recruitment strategy and data collection method, though neither justified. Clear explanation of data collection method and data form. No discussion of data saturation. Reflexivity discussed in terms of data collection. Ethical approval granted but limited exploration of potential ethical issues. Limited discussion of data analysis methodology. Clear statement of findings. Research deemed valuable.
Kujawski et al 2015	STROBE statement cross-sectional study checklist	Moderate confidence	Clear scientific basis, rationale and aims. Comprehensive description of study design, setting, participants, variables and measures. No mention of potential biases or sample size calculations. Brief description of statistical methods. Data provided on study participant demographics and results reported clearly using odds ratios and confidence intervals. Key results presented clearly. Limitations discussed but no mention of generalizability of results.
Kumbani et al 2012	CASP qualitative research checklist	High confidence	Limited justification of research design. Clear explanation of recruitment method with justification. Clear explanation of data collection methods, data form, setting and saturation. Comprehensive exploration of reflexivity. Ethical approval obtained but limited exploration of potential ethical issues. Some explanation of data analysis methodology. Clear statement of overall findings. Research deemed valuable.
Kumbani et al 2013	CASP qualitative research checklist	Moderate confidence	Some justification of research design. Detailed explanation and justification of recruitment strategy. Clear explanation of data collection methodology, data form and data saturation without justification. Limited consideration of reflexivity. Ethical approval obtained but limited exploration of potential ethical issues. Some exploration of data analysis methods. Unclear how themes were derived from data. Clear overall statement of findings. Research deemed valuable.
Mason et al 2015	CASP qualitative research checklist	High confidence	Good justification of research design. Recruitment strategy appropriate and justified. Detailed description of data collection methods, data form and setting. No discussion of data saturation. Limited consideration of reflexivity. Ethical approval obtained but no exploration of potential ethical issues. Comprehensive description of data analysis methodology. Clear statement of findings. Research deemed valuable.

Table 2: Critical appraisal of studies (Continued)

Paper	Critical Appraisal Tool	Confidence in Evidence	Comments
Mwangome et al 2012	CASP qualitative research checklist	Low confidence	Limited justification of research design. Unclear recruitment strategy due to involvement with another study. Data collection setting and data saturation not described. No consideration of reflexivity. Ethical approval obtained but no exploration of potential ethical issues. Some description of data analysis methods. Statement of findings could be clearer. Research deemed valuable.
Nakua et al 2015	STROBE statement cross-sectional study checklist	High confidence	Clear scientific basis, rationale and aims. Comprehensive description of setting, participant recruitment, study design and sample size calculation. No mention of potential biases. Comprehensive description of statistical methods. Data provided on study participant demographics and results reported clearly using appropriate statistics as well as graphs and charts. Key results presented clearly and comprehensive discussion of limitations. No discussion of generalizability of results.
O'Donnell et al 2014	CASP qualitative research checklist	Low confidence	Limited justification of research design. Description of purposive sampling of facilities but limited description of recruitment strategy within clusters. Clear description of methods of data collection and data form but no mention of data saturation. Limited exploration of reflexivity. Ethical approval obtained but no exploration of potential ethical issues. Poor description of analysis methods. Clear statement of findings and suggestions for future research.
Tey and Lai 2013	STROBE statement cross-sectional study checklist	Moderate confidence	Clear scientific basis, rationale and stated objective. Brief description of participants and setting. Comprehensive description of variables and measures. No mention of potential biases or sample size calculations. Comprehensive description of statistical methods. Data provided on study participant demographics and results reported clearly using odds ratios, percentages and confidence intervals. Key results presented clearly. No discussion of limitations or generalizability of results.

Table 2: Critical appraisal of studies (Continued)

Paper	Critical Appraisal Tool	Confidence in Evidence	Comments
Yar'zever and Said 2013	STROBE statement cross-sectional study checklist	High confidence	Clear scientific basis, rationale and stated objectives, including comprehensive use of a theoretical framework. Comprehensive description of participants, setting, study design, sample size calculations, variables and measures. No mention of potential biases. Limited description of statistical methods. Data provided on study participant demographics and results reported clearly using frequency tables. Key results presented clearly. Consideration of limitations and future areas for research.

Table 3: Summary of identified barriers. Green = high confidence; yellow = moderate confidence; red = low confidence

Barrier		Papers identifying barrier
Delays in decisions to seek care	Community influence	Bohren et al, 2014 Gebrehiwot et al, 2014 Tey and Lai, 2013 Yar'zever and Said, 2013 Brighton et al, 2013
	Cultural beliefs	Bohren et al, 2014 Gebrehiwot et al, 2014 Brighton et al, 2013 Nakua et al, 2015
	Fear of HIV testing	Mason et al, 2015 Bohren et al, 2014
	Lack of autonomy and confidentiality	Kumbani et al, 2013 O'Donnell et al, 2014
	Lack of knowledge	Echoka et al, 2014 Hagey et al, 2014 Mwangome et al, 2012
	Lack of support person	Crissman et al, 2013
	Low quality of care	Bohren et al, 2014 Kumbani et al, 2013 Kumbani et al, 2012 Mason et al, 2015 Tey and Lai, 2013 Nakua et al, 2015

Table 3: Summary of identified barriers. Green = high confidence; yellow = moderate confidence; red = low confidence (Continued)

Barrier		Papers identifying barrier
Delays in decisions to seek care	Maltreatment	Bohren et al, 2014 Crissman et al, 2013 Kujawski et al, 2015 Kumbani et al, 2013 Kumbani et al, 2012 Mason et al, 2015 Mwangome et al, 2012 Nakua et al, 2015 O'Donnell et al, 2014 Brighton et al, 2013
	Medicalisation of childbirth	Echoka et al, 2014 Gebrehiwot et al, 2014 Hagey et al, 2014 Tey and Lai, 2013 Yar'zever and Said, 2013
	Poor facility equipment	Gebrehiwot et al, 2014
Delays in arrival at facility	Distance and lack of transport	Bohren et al, 2014 Crissman et al, 2013 Echoka et al, 2014 Gebrehiwot et al, 2014 Kumbani et al, 2013 Mwangome et al, 2012 Tey and Lai, 2013 Yar'zever and Said, 2013 Nakua et al, 2015
	Precipitous labour	Crissman et al, 2013 Kumbani et al, 2013 Nakua et al, 2015
Delays after reaching hospital	Cost of delivery	Bohren et al, 2014 Crissman et al, 2013 Hagey et al, 2014 Mason et al, 2015 Mwangome et al, 2012 Tey and Lai, 2013 Yar'zever and Said, 2013 Nakua et al, 2015

Table 4: Details of literature searches

Database	Search Date	Search Type	Search Strategy	Papers Identified
MEDLINE via Ovid	17/02/2017	Advanced – some terms mapped to subject heading with an exploded search (identified in search strategy with 'Exp.'). All search terms limited to English language and timeframe '2012 – current'.	[barrier OR limit* OR "limiting factor"] **AND** ["hospital birth" OR "attended delivery" OR "hospital delivery" OR Obstetrics (Exp.) OR "obstetric care"] **AND** [Africa South of the Sahara (Exp.) OR "sub-Saharan Africa"]	70
Web of Science	17/02/2017	Basic, searching in 'Topic', excluding items published before January 2012.	barrier **AND** hospital delivery **AND** Africa	34

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Discussion

General Surgery: Is it time for a name change in an era of unprecedented sub specialisation?

DISCUSSION

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ABSTRACT

In an era of increasing medical sub-specialisation, is the title of 'general surgery' still fit for purpose? The practicalities of a name change are considered alongside the potential benefits. We argue that traditional dogma should not mean ambiguous or inaccurate specialty titles are kept.

If you were to ask a member of the public which medical conditions they visit their general practitioner for, the answer would be almost any. What about a general surgeon? Some individuals may be surprised to hear that general surgeons in the UK do not perform all procedures, as their name might imply, and appear instead to be becoming increasingly specialised.

Historically, general surgeons in the United Kingdom operated on multiple body systems and their title therefore reflected this role – as is still true in some countries. There is no universally accepted list of general surgery's many sub-specialities, though colorectal, upper gastrointestinal and hepatobiliary all fall within its realm. Having previously been a subspecialty of general surgery, vascular surgery became a speciality in its own right in the UK in 2012. (1) Currently, there is debate as to whether breast surgery should follow suit. (2) Fiona MacNeill, President of the Association of Breast Surgery, notes that breast surgeons have wanted to break away from general surgery over the past decade, hoping to improve the skills of trainees by establishing a separate curriculum. (2)

Misnomers are rife throughout medicine, so why should general surgery be any different? A pyogenic granuloma is neither pyogenic nor a granuloma, so why take issue with this nomenclatorial inaccuracy? A title is a useful insight for the patient into a doctor's role during introductions – the importance of which is highlighted by Dr Kate Granger's #hellomynameis Twitter campaign. (3) Building a strong rapport from introductions is integral to patient-centred care. (4) Any improvement in accuracy when sharing the summary of a surgeon's role will strengthen the patient-surgeon relationship.

In 1999, The Royal College of Surgeons of England discussed ambiguous titles in relation to patients' understanding of theatre staff, stating that *"the patient must be aware of the role of the person treating them"*. (5) A patient should know the area of expertise of a general surgeon when consenting to an operation to make an informed decision, which may not be the case if the word general is present in a title as this is not reflective of a surgeon's area of practice. (6) For example, it is possible that patient rapport and trust in a general surgeon may be affected if it is unclear in what field the surgeon has trained and what their subspecialty is. Their area of expertise needs to be stated in order for informed consent to be given.

So why has the title not changed?

An inevitable consequence of a name change would be the formation of multiple subspecialties. The GMC has a temporary suspension on the addition of new subspecialties following the Shape of Training report in 2013. (7) Authors of the report felt that patients should be treated by generalists who can care for their needs holistically. The report also suggests that patients' needs would be better met by doctors who have received broader training as they may flexibly adapt their roles to meet local requirements. (7) If the aim is to keep the scope of surgical training broad, keeping the title of general surgeon would help towards this.

If new specialities were allowed to form, this would not be straightforward, with economic and political barriers to be overcome; not everyone will necessarily see the potential impact that a change of name of general surgery could have on everyday practice. On a practical level, if general surgery were to subspecialise, new curricula may need to be developed for each sub-speciality, a process which would be both costly and laborious. (8) There may also be resistance from individuals who feel that the title of general surgeon remains accurate. There is no proof beyond anecdotal evidence that the title of general surgeon is confusing and negatively affects patients' experiences in hospital. Those critical of a name change might argue that many patients do accurately understand the scope of general surgeons' work and would merely need to ask the surgeon to clarify their areas of expertise, were there to be any doubt.

General surgery is not the only surgical speciality to encompass a wide range of disciplines. If general surgery were to change its name, it could be suggested that ENT ought to sub-specialise to more accurately reflect the disciplines encompassed within it; paediatric otolaryngology is considerably different to rhinology. (9) However, the word *"general"* in the title of general surgeons is the source of ambiguity. The title carries historical connotations, implying that the surgeon operates across multiple surgical specialties, which is not the case with ENT.

There will remain a need for surgeons who can act as generalists during an emergency. This is currently covered by a range of general surgical sub-disciplines whose surgeons receive training in emergency general surgery. A 2017 statement by the Association of Surgeons of Great Britain and Ireland suggested a title change to *"consultant surgeon with specialist interest in acute surgical practice"* to highlight those who perform emergency work. (7) This would provide a clearer distinction between a truly specialist surgeon and one who performs generalist emergency work.

Unofficial sub-disciplines (e.g. breast surgery, transplant surgery, etc.) within general surgery have already formed and will have potential to become official in the future. When this time comes, there should be a name change for general surgery – but now does not seem to be the appropriate time.

If you were tasked with reclassifying surgical specialties based on which operations they perform, how would you do it?

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Discussion

Prescribing pills or people: the perplexity of social prescriptions

DISCUSSION

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ABSTRACT

Social prescriptions are increasingly being integrated into the medical curriculum – whether that be prescribing physical exercise for heart disease or a book group for depression. This is unknown territory for many medical students (and indeed doctors) with the risks and benefits being largely uncharted. Medical schools today adopt a holistic approach to medicine, teaching students to consider the whole patient rather than just their disease and encouraging shared decision making between doctor and patient. Social prescribing goes hand in hand with this, and so will undoubtedly become increasingly popular in the future despite conflicting evidence. For these reasons, it is important for medical students to understand exactly what social prescribing is and how it can potentially benefit their future patients.

Everybody knows that one of a doctor's main roles is to prescribe, whether that be pain medication for a joint problem, antibiotics for an infection or chemotherapy for cancer. The possibilities are endless. Receiving a prescription could be a patient's main expectation following a GP consultation, with many expecting a prescription involving a trip to the pharmacy and physical medication. Recent movements, however, is diverging from this 'traditional' route and encouraging the prescription of a wider range of therapies, such as exercise or an art class. Initially, this may seem slightly odd to patients and convincing them of the benefits could potentially be a consultation in itself. Despite this, emerging evidence suggests that it could make a real difference to their health and wellbeing.

What is social prescribing?

Social prescribing refers to a non-clinical recommendation, often to local services, which can improve the health of a patient in some way. The options available vary widely but some examples include support groups which help with pain and fatigue management, language support for those with learning disability, and respite care for carers. (1) Rather than fixing a problem in the short-term, this enables doctors to tackle the root of a problem with the aim of preventing the patient from presenting again in the future with a similar problem. Not only could this drastically change our patients' lives for the better, but it could change the approach to many conditions, and ultimately healthcare. The World Health Organisation places an emphasis on preventing disease and allowing patients to take control of their own health; (2) furthermore, the Secretary of State for Health has expressed his view that the government should not "stand in the way of" what a GP thinks is necessary to improve a person's health. (3) Social prescribing is a unique, holistic way to empower both doctors and patients to make decisions regarding care.

The importance of holism

Holism within healthcare has been encouraged for a long time; it promotes self-reliance and breaks down the paternalistic walls which were historically placed within the doctor-patient relationship. (4) It emphasises prevention rather than cure, and accounts for entire communities rather than just the individual. (5) Not only does social prescribing do this, but it could also be the cure. The World Health Organisation defines health as a state of not just physical, but also mental and social wellbeing (6) and many patients may consult their GP due to concerns regarding their social situation rather than a 'traditional' health problem. Interestingly, studies have shown that patients from more socially-deprived backgrounds rate consultations based on whether their doctor takes a holistic approach to care as opposed to the quality of care given. (7) Moreover, doctors who socially prescribe tend to take a more holistic approach in general and believe that encouraging a patient to take control of their own health is at the core of general practice. (8) With the current fragile state of the NHS and the increasing burden of an ageing population, it is important now, more than ever, that the public have trust in their doctors. By prescribing socially, not only could it benefit the patient's health, but it could also improve their satisfaction with the system.

The evidence

Although social prescribing is being promoted as revolutionising general practice, (9) the evidence is conflicting. In fact, several systematic reviews have found little evidence to suggest that social prescribing is cost-effective or successful. (10) One particular outcome that has been measured many times is physical activity following the social prescription of exercise. In their meta-analysis, Pavey et al. found no significant difference in the amount of physical activity per week, cardiorespiratory fitness at follow-up, systolic and diastolic blood pressure and depression and anxiety in patients who were in the exercise referral scheme compared to those who were not. (11) However, the quality of the evidence is low in that many of the primary studies have a high risk of bias and are only small, given that they are pilot studies. In order to determine whether such an intervention is worthwhile, further research is required such that higher quality studies can be included in a systematic review and meta-analysis.

However, the amount of evidence which favours drug-based therapies is overwhelming and is not as difficult to promote as social prescribing. For example, informal diet and lifestyle advice is the first-line treatment for a patient presenting with high blood pressure, closely followed by a drug prescription. The evidence to support this is vast (12) and many may argue that adding a social prescription to this list has the potential to waste time, especially due to the existence of evidence which shows that a patient is no more likely to experience any benefit from it. (11) If a patient would benefit from a drug, then it could be viewed as detrimental to instead prescribe something else which has not been found to be successful.

To determine the feasibility and effectiveness of social prescribing, it is true that further studies and analyses are needed. However, social prescribing varies from gardening to poetry, and can be prescribed for multiple problems. Consequently, it would be almost impossible to commission such a large-scale study, and the number of singular studies needed to incorporate everything would be endless. Instead of hoping for this unlikely definitive evidence, it is more realistic to place a focus on the patients themselves, especially given that they are the group who would be most affected by the formal introduction of social prescribing in general practice. Studies have found that, in terms of mental health, patients benefit enormously. For example, when addressing specific mental health issues, such as depression and anxiety, the social prescription of a self-help computer program is beneficial and is recommended by the National Institute for Health and Care Excellence, following several randomised-controlled trials. (13) Furthermore, several meta-analyses have found that the prescription of bibliotherapy improves the mental health of those who suffer from depression. (14) A review which evaluated 35 of the UK's social prescribing schemes using 42 papers found not only an increase in confidence and self-esteem, but also physical health, amongst patients who fulfilled their social prescriptions. (15) This can be translated into quantitative evidence, for example in the Rotherham 'Social Prescribing' pilot, which found that hospital admissions and outpatient appointments reduced by half in selected patients following the implementation of a social prescribing scheme. (15) Despite there being an overall lack of evidence for social prescribing, the pooling of results from current schemes undeniably show the potential advantages to patients.

The future

As more and more studies gradually emerge, it is inevitable that social prescribing will become increasingly integrated into general practice. The impact of this is currently unknown. It is hoped that it will help to reduce the number of consultations for those who see their GP often and as a result reduce the burden on general practice, which was observed amongst a group of socially isolated patients in London. (16) Furthermore, increases in mental wellness and patient satisfaction may be observed, which is driven by the behavioural changes encouraged by social prescribing. (17) 'Heartsink patients' will no longer be a source of anxiety and stress, clinic lists will no longer consistently be behind schedule, and consultations for social problems will reduce. Although optimistic, this future is one that is desired amongst many general practitioners. (18) Social prescribing, although perhaps not the answer, could be the first baby-step in this direction. Although currently unclear as to how drastic these changes may be, the benefits clearly outweigh any potential damage and current schemes suggest that the future looks promising.

Conclusions

This promising future lies in the hands of current students, which is an exhilarating prospect. In order to truly make changes, the patient must always come first, a fact which both students and current doctors must always remember. Social prescribing, which may involve venturing into unknown territory for many, puts patients in charge and allows them to drive their own healthcare forward. This contrasts with the passive role a patient adopts when handed a drug prescription. This shift away from paternalism is still occurring and promoting patient autonomy and empowerment is at the heart of the future of medicine. As medical students, it is especially important to adapt to this movement and take the lead. This way, we can truly make a difference – even if it is just seeing your patient smile.

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Discussion

Defining 'complementary and alternative medicine'

DISCUSSION

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ABSTRACT

The topic of complementary and alternative medicine (CAM) is controversial. CAM is a confusing term used to encapsulate a broad range of health-related practices. In this article we explore several CAM practices including homeopathy and manipulation therapies such as osteopathy and chiropractic. We examine the difficulty in understanding the meaning of the term CAM and argue that the term is unhelpful and should be avoided in the education of healthcare professionals. Medical educators should be careful to highlight the heterogeneity of health-related practices and treat each practice as an individual entity without the need for the umbrella term CAM.

The topic of complementary and alternative medicine (CAM) is controversial. Debate surrounding CAM is largely driven by the unclear efficacy of many practices, a perceived potential risk of harm and a perception that financial motivations of CAM practitioners may influence their treatment recommendations. But what exactly is CAM? The term CAM is often used to describe a broad range of health-related practices which are thought to lie outside the realm of 'conventional' medicine. (1) In 2005, a national survey of the general population in England found that approximately 1 in 4 adults had used some form of CAM and around 1 in 8 adults had consulted a CAM practitioner during the previous 12 months. (2) Given the significant proportion of adults accessing CAM, it is important that healthcare professionals are able to discuss CAM with patients. To do this we must first have a clear understanding of what CAM is and its role, or lack of, in treating patients.

There are many health-related practices typically described as CAM, including acupuncture, aromatherapy, manipulation therapies (osteopathy and chiropractic) and homeopathy. (1) Professional opinion of these practices is varied. For example, homeopathy draws extensive criticism due to the pseudoscientific concepts underpinning it and the weak evidence of efficacy. (3-5) In the UK, Chief Medical Officer Dame Sally Davies and Chief Scientific Advisor Sir Mark Walport have both made their opinions of homeopathy clear, describing homeopathy as *"rubbish"* and *"nonsense"* respectively. (6,7) Osteopathy and chiropractic, on the other hand, are both regulated at a government level, and the National Institute for Health and Care Excellence (NICE) recommends manual therapy (including spinal manipulation, mobilisation and soft tissue massage) for the management of low back pain. (8) The clear heterogeneity of these practices raises the question of whether it is appropriate to group them together under the umbrella term 'CAM'. Evidence suggests that certain treatments offered by chiropractors and osteopaths can be useful for the treatment of low back pain, (8) therefore surely these treatments can simply be defined as 'medicine'?

The National Center for Complementary and Integrative Health (NCCIH) makes a distinction between the terms 'complementary' and 'alternative'. (1) They state that *"if a non-mainstream practice is used together with conventional medicine, it's considered 'complementary'"* and *"if a non-mainstream practice is used in place of conventional medicine, it's considered 'alternative'"*. This distinction is also found on the Cancer Research UK website. (9) These definitions are vague and therefore open to interpretation. What is 'mainstream' or 'conventional' in one region of the world may be very different in another region. Assuming that for a health-related practice to become 'conventional' in the UK it should have demonstrated efficacy in the face of rigorous scientific investigation, it could be suggested that 'conventional' has been substituted for 'evidence-based'. One might therefore infer that 'non-conventional' has been substituted for 'non-evidence based'. However, this relies heavily on the assumption that all 'conventional 'or 'mainstream' medicine in the UK is evidence-based. This may be an un-wise assumption to make given the shortfalls of the evidence-based medicine movement. In a BMJ editorial, Greenhalgh et al. described evidence-based medicine as *"a movement in crisis"* due to various factors including *"evidence biases and the hidden hand of vested interests"*. (10) Pharmaceutical companies play an important role in funding medical research, however the influence of pharmaceutical companies on healthcare practices and public health policy is a concern. (11) Examples of

financial conflicts of interest include consultant fees and honoraria related to new medicinal products or technologies. These conflicts of interest have the potential to influence medical research and individual clinical practice, undermining evidence-based medicine. (12)

Despite randomised controlled trials (RCTs) being regarded as the highest level of evidence in the hierarchical 'evidence pyramid', they are not without their limitations. RCTs may produce misleading results due to various forms of statistical bias inherent in their design. RCTs may also not be representative of 'real life' patients in that participants may be highly selected in terms of characteristics such as age and comorbidity. It is also critical to differentiate between statistical and clinical significance. An RCT of a new treatment that shows a highly statistically significant difference in outcome, but a small treatment effect size, is unlikely to affect clinical practice. Publication bias also influences dissemination of evidence; a clinical trial which shows a statistically significant treatment benefit is more likely to be published than a 'negative' trial, despite the scientific value of both. (13) A notable proponent of evidence-based medicine, Ben Goldacre, recently published a study highlighting that over half of all clinical trials registered on the EU Clinical Trials Register (EUCTR) did not comply with the European Commission's requirement that all trials must publish trial results to the EUCTR within 12 months of completion. (14) Despite the delays in publishing clinical trial data, the volume of new evidence published daily in peer-reviewed journals is overwhelming. (15) As clinicians, we therefore rely on reputable organisations such as NICE and other national societies to evaluate the evidence-base for a particular treatment and provide guidance on how this treatment should or should not be integrated into clinical practice. Complicating the matter further, the assessment of evidence performed by NICE (in the context of the 'free at the point of delivery' healthcare system that is the NHS) considers treatment cost and the relative benefit in terms of quality of life years (QALY) gained. Whilst critiquing the strength of evidence for CAM, it is important to keep in mind the shortcomings that exist even within mainstream, 'evidence-based' medicine.

A further issue with the term CAM is that defining something as an 'alternative medicine' implies that it is indeed a 'medicine', and therefore has proven efficacy above and beyond the placebo effect. Given the weak evidence base of many CAM practices, (16) the use of the term 'medicine' may be misleading for patients and healthcare professionals. It could be argued that the potential placebo effect conferred by a treatment of unclear efficacy may warrant the use of the term 'medicine'. (17) However, this is problematic, as we would therefore have to accept that any health-related practice intended to treat, or perceived to have efficacy by the patient,' is 'medicine'. This seems unsatisfactory and contradicts the mantra of evidence-based medicine.

An essential component of undergraduate medical education is teaching medical students to critically appraise literature to determine the evidence-base for treatments and guide clinical practice. However, teaching of the evidence-base of health-related practices that are currently described as CAM may be subject to several barriers. For example, medical educators may dismiss certain treatments due to personal biases, inadequate understanding of the evidence-base or a perception that teaching about

specific treatments gives these treatments 'undeserved credibility'. (18) The contrary can be true, teaching medical students about pseudoscience is important and may improve their ability to identify health-related practices with weak evidence bases. By confronting specific health-related practices and examining the evidence, educators can help to 'dispel pseudoscience and promote scientific scepticism, while avoiding the unhealthy extremes of either uncritical acceptance or cynicism.' (19)

In conclusion, the ambiguity of the term CAM is unhelpful and oversimplifies a highly heterogeneous group of health-related practices with significantly different evidence bases. There is a risk that these practices are perceived by healthcare professionals as having a shared illegitimacy. As a result, evidence-based treatments may be dismissed or underutilised. Every health-related practice should be treated as an individual entity and evaluated as such, without the need for a blanket term. Medical educators should be careful to highlight the heterogeneity of health-related practices and avoid using the term CAM in the teaching of healthcare professionals.

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Education

Novichok: An overview of the world's deadliest nerve agent

EDUCATION

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ABSTRACT

Relevance

The Novichok class of nerve agents are noxious chemical-weaponized organophosphates. Though its use is prohibited under the 1997 Chemical Weapons Convention, the attempted murder of an ex-Russian spy and his daughter has turned a spotlight on one of the world's deadliest poisons.

Summary

Novichok was developed by the Soviet Union in the 1970s and is reportedly ten times more lethal than VX, the nerve agent used to assassinate the half-brother of North Korean leader Kim Jong-un. Novichok produces its toxic effect by irreversibly inhibiting acetylcholinesterase. Unlike other nerve agents, it is thought to target both the central and peripheral nervous systems. Exposure to Novichok invariably leads to death.

Take Home Messages

With an increase in worldwide chemical weapons usage, including recent use in the United Kingdom, clinicians should know how to rapidly recognize symptoms of nerve agent poisoning, lend their expertise in the education and treatment of such attacks and administer life-saving antidotes.

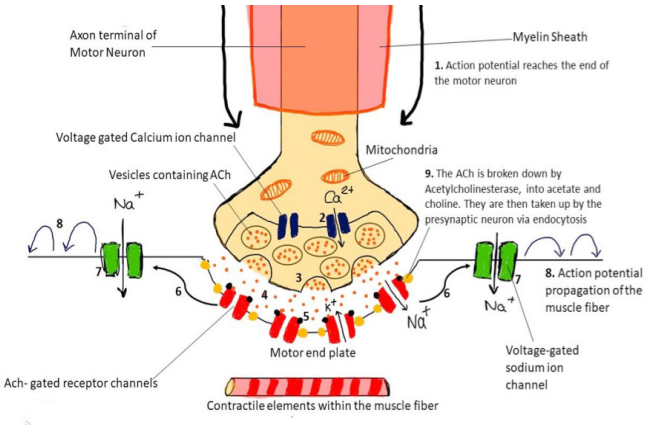
In March 2018, the United Kingdom, along with the rest of the world, were shocked by news of the poisoning of an ex-Russian spy. Less than three months later, paramedics were called to a flat in Amesbury, England, after a local couple were exposed to the very same agent used earlier in the year. (1) Subsequent confirmation that the substance used in these attacks belonged to the Novichok class of nerve agents has turned a spotlight on what are considered amongst the world's deadliest chemical weapons. This article aims to explore Novichok and its effects on the human body, given the high likelihood of future usage of these agents.

The name Novichok means *"newcomer"* in Russian, highlighting the fact that its development marked a breakthrough in chemical weapons. (2) Novichok is a series of organophosphate nerve agents. Nerve agents are organic substances which disrupt the body's normal nervous communication to muscles and organs. (1)

Novichok was developed as part of the Russian classified nerve agent program named FOLIANT over a period of two decades from 1971. (3) It has never been used on the battlefield as its use is forbidden under the terms of the Chemical Weapons Convention of 1993. It is believed that Novichok was developed as the Soviet Union's response to false information that the USA was producing its own nerve agents during the Cold War. (2,4)

The effects of Novichok, like all nerve agents, are due to the blocking of acetylcholinesterase (AChE) which catalyses the breakdown of acetylcholine (ACh). (4) ACh is a neurotransmitter found in vesicles of pre-synaptic neurons at neuromuscular junctions. As an action potential passes down a neuron, the depolarisation causes an influx of calcium ions, triggering exocytosis of ACh from the pre-synaptic neuron and diffusion across the synaptic cleft. ACh then binds onto nicotinic ACh receptors (nAChRs) on the post-synaptic membrane, causing sodium ion channels to open. An influx of sodium ions through the post-synaptic membrane causes depolarisation. The subsequent action potential results in contraction of a muscle or release of a hormone. Once the action has been produced, the enzyme AChE catabolises the neurotransmitter to allow the muscle or organ to relax. (See Figure 1)

Figure 1 - Events at a neuromuscular junction



Novichok is a non-competitive inhibitor of AChE, accounting for its irreversible inactivation. (5) The nerve agent causes a build-up of ACh, preventing further re-depolarisation of the post-synaptic membrane, so that impulse transmission ceases. This results in muscles remaining in their contracted states. Symptoms of poisoning appear within seconds of exposure and death occurs rapidly by asphyxiation or cardiac arrest due to failure of contraction of the diaphragm and heart. Whilst most nerve agents affect the central nervous system exclusively, Novichok also affects the peripheral nervous system, leading to peripheral weakness and paraesthesia. (6)

Exposure to Novichok is generally by inhalation, although absorption may also occur percutaneously. (7) Early symptoms include rhinorrhea, chest tightness, and miosis. Later stages involve involuntary salivation, loss of continence and abdominal pain. This is followed by myoclonic jerks and status epilepticus. (6) If treatment is not initiated timely, death will ensue. Most of the literature on Novichok is based on testimonies from the scientists involved in developing the agent. As it is still a relatively new chemical which few people have been exposed to, our understanding of the symptomology and treatment are limited. Andrei Zheleznyakov, a scientist involved in the Novichok's development, was accidentally exposed to the agent in 1987. He was unconscious for 10 days post-exposure. Zheleznyakov then began to suffer from *"chronic weakness in his arms, a toxic hepatitis that gave rise to cirrhosis of the liver, epilepsy, spells of severe depression, and an inability to read or concentrate that left him totally disabled and unable to work"*. (8) Five years following exposure, Zheleznyakov died.

"Circles appeared before my eyes: red and orange. A ringing in my ears, I caught my breath. And a sense of fear: like something was about to happen. I sat down on a chair and told the guys: it's got me!" – Andrei Zheleznyakov, Russian military researcher after he was exposed to Novichok from a malfunctioning fume hood (1987). (8)

Initial management of Novichok poisoning includes removal of contaminated clothing and contact lenses. This should be followed by thorough rinsing of the skin with soap and water to prevent further exposure. Patients will then require basic life support and oxygen should be administered. (9) The mainstay treatment of Novichok poisoning is with anticholinergic drugs. (5) Atropine, an ACh receptor antagonist, blocks receptors to prevent poisoning.

Other antidotes include pralidoxime and diazepam. Pralidoxime binds to AChE causing the phosphate group of the nerve agent to be displaced. The poison/antidote complex then unbinds from the active site, thus regenerating the fully functional AChE enzyme. (10) It is possible to survive a Novichok attack; however, victims may be left with permanent disabilities such as chronic muscle weakness and reduced cognitive ability.

Since its creation, seven people are known to have been exposed

by Novichok; of which three have died. Today, news of such chemical attacks is rapidly circulated and information about the poison and the risk of exposure can become misconstrued by the public. Therefore, it is increasingly important that clinicians can be called upon to lend their expertise in the education and treatment of attacks caused by dangerous chemical weapons.

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Education

The radiology of the complications of Warfarin therapy - a pictorial review

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ABSTRACT

Summary

This article aims to teach about the complications of warfarin therapy through radiological imaging and highlight the importance of radiology in diagnosing challenging cases.

Relevance

Warfarin is the most widely used anticoagulant worldwide and is vital in the treatment of many conditions. However, the use of warfarin increases one's risk of bleeding which can have potentially fatal consequences. It is vital that the complications of warfarin use are considered as part of the differential diagnosis when a patient presents with unexplained symptoms, as quickly diagnosing an acute bleed will improve outcomes.

Take Home Messages

Complications of warfarin therapy can present in a variety of ways, not always associated with trauma, with potentially dangerous consequences. Radiological investigations are one of the best ways to confirm the diagnosis and so should always be considered to aid diagnosis and treatment.

INTRODUCTION

Warfarin is the most widely used oral anticoagulant in the world. (1) In the UK alone, it is thought that around 1% of the total population and 8% of those over 80 are taking warfarin. (2) Originally developed as a rat poison, it is now recommended by the National Institute for Health and Care Excellence (NICE) in the treatment of conditions such as atrial fibrillation (AF), deep vein thrombosis (DVT) and stroke prophylaxis. More rarely, it is given to those who have had a myocardial infarction. (3-6) These conditions primarily affect the elderly population and with the average age increasing in the UK, anticoagulant use is likely to increase.

Warfarin blocks vitamin K reductase which normally activates vitamin K and, consequently, the clotting ability of factors II, VII, IX and X are reduced. (7) It usually takes a few days, depending on the patient's physiology, for warfarin to start having a therapeutic effect, therefore concurrent heparin therapy is needed until warfarin is effective. Warfarin has a narrow therapeutic range and, once started on warfarin, the patient must be closely monitored to ensure the dose is correct. Too low and the patient will be at risk of blood clots forming, too high and the patient is at risk of bleeding complications. (8) Monitoring is done via regular blood testing measuring the patient's international normalised ratio (INR). Due to warfarin's therapeutic range and differing physiology between patients it can be difficult to get a patient stabilised on a regular dose. Indeed, one study of over 6000 patients taking warfarin for AF showed that for nearly 50% of the time, the INR was outside the target range. (9) Warfarin has many potential drug interactions which can destabilise the INR (e.g. alcohol can increase the INR putting the patient at risk of bleeding).

A major drawback with warfarin therapy is its side effects, including the increased risk of bleeding. These bleeds can range from something as insignificant as a simple cut on the hand taking longer to clot to an uncontrollable, potentially fatal, haemorrhage in the brain. In terms of hospital admissions related to drug therapy, warfarin ranks 3rd on the list, with the clear majority of these admissions being due to a bleeding event. (10)

One of the issues with warfarin related bleeding is that it may be of insidious onset, or not immediately apparent that bleeding is the cause of the patient's symptoms, and it can also mimic other conditions. In these cases, after taking a full history and examination, further investigation is needed including radiological input. It is often here that the bleeding is identified or confirmed. Other rare but serious complications of warfarin treatment such as osteoporosis or calcification of blood vessels may also be identified by radiological investigation.

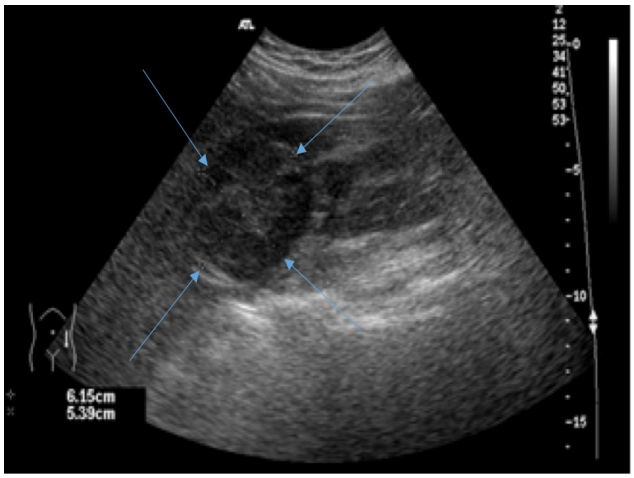
This review will demonstrate warfarin related haemorrhage in all parts of the body using different imaging modalities, and it will demonstrate how some difficulties in clinical diagnosis were aided by radiological investigation.

Cases – Diagnostic Challenges

The first section of this pictorial review will focus on those cases which presented a diagnostic challenge and the diagnosis was assisted greatly with radiological investigation. The first three images are all from different patients. However, all had a similar presentation.

Image one shows an example of a haematoma located in the psoas muscle. The patient presented with an acutely painful abdomen. The pain had started acutely that day and had been growing worse in severity. The patient was otherwise well and had no other symptoms. On examination the abdomen was soft but tender in the left flank, particularly when balloting for the kidneys, and rectal examination was normal. Acute abdomen has a broad differential diagnosis. Infection, bowel or ureteric obstruction, renal stones and ectopic pregnancy must all be considered. However, the patient was not of child bearing age, had no urinary or bowel symptoms and had been otherwise well making these causes less likely and further investigation was needed.

Figure 1 - Left psoas haematoma



An abdominal radiograph did not show any acute pathology, so an ultrasound was requested, given the tenderness over the left kidney. The bleed was spontaneous and difficult to diagnose through history and examination alone. In this case, it was only through using ultrasound that the cause and source of the pain could be identified.

Similar scenarios are shown in images two and three, with the patients suffering from an intramuscular bleed and presenting with

acute pain and no history of trauma. Ultrasound investigation was again needed in aiding diagnosis and treatment.

Figure 2 - Left sided retroperitoneal haematoma, possibly in psoas muscle

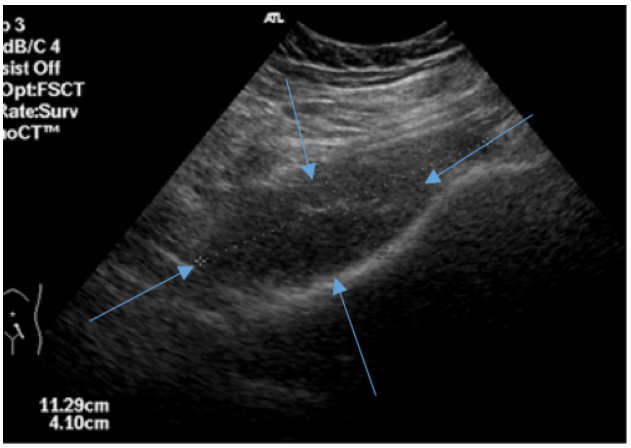
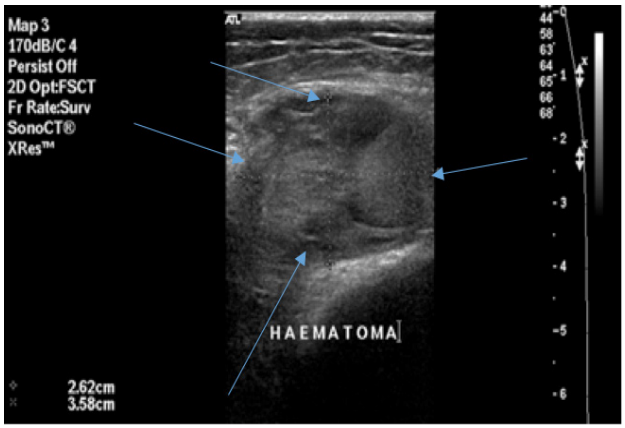


Figure 3 - Quadriceps haematoma



Both images four and five show examples of a spontaneous haemothorax in the absence of significant trauma. Both patients presented with gradually increasing breathlessness over several hours. Examination revealed reduced breath sounds and dullness to percussion of the affected areas. A pleural effusion was suspected, and a chest radiograph confirmed this but did not show a likely cause. CT thorax was requested which revealed a haemothorax. Chest drains were required in both cases.

Figure 4 - Chest wall haematoma with haemothorax. The denser area indicates a fresher bleed

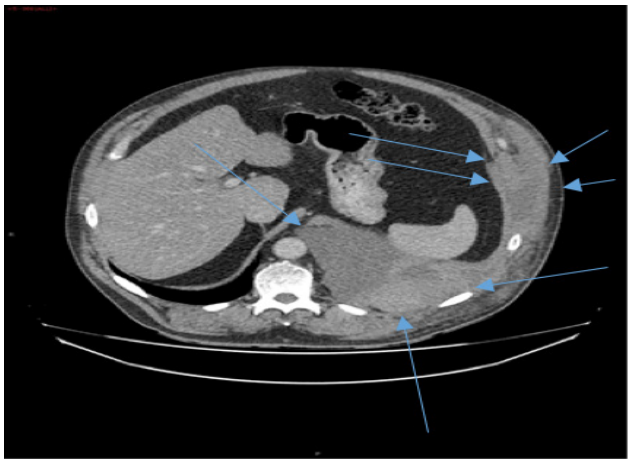


Figure 5 - Left sided haemothorax. In this case the denser area within the fluid is collapsed

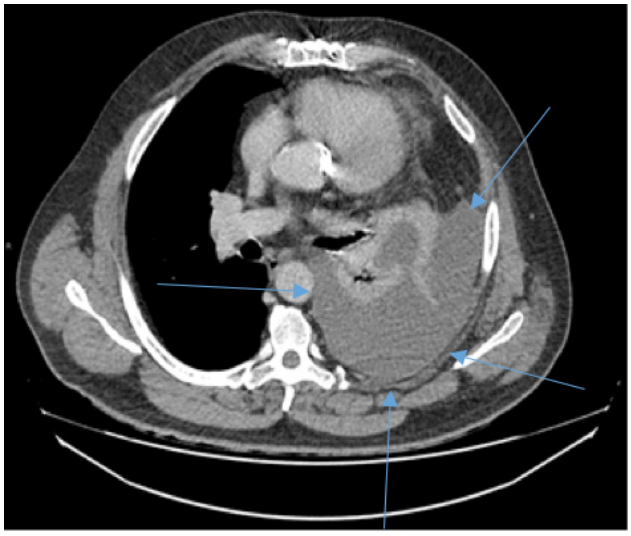
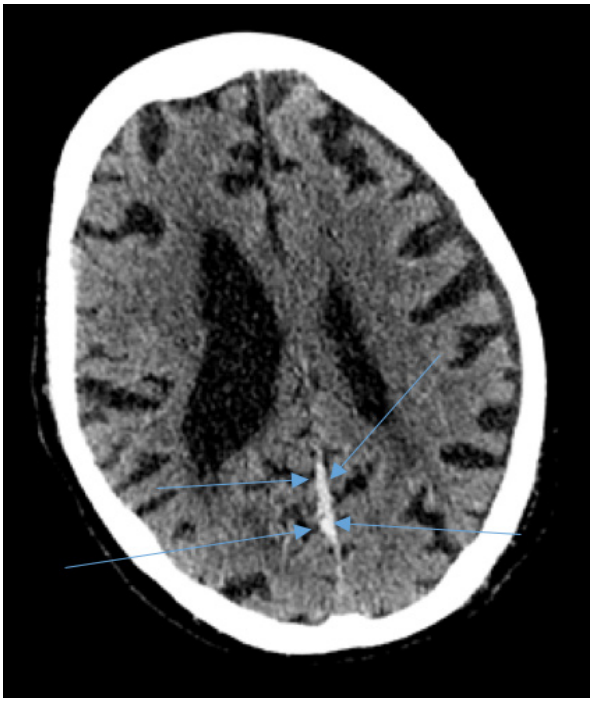


Image six shows a subtle subdural haemorrhage. The elderly patient presented with confusion which had been getting gradually worse over several days. This is a very non-specific yet common presentation.

Figure 6 - Subdural haemorrhage visible in the falx



Confusion in the in the elderly is often caused by infection (classically a urinary tract infection, UTI), dementia or injury to the brain such as a stroke or bleed.

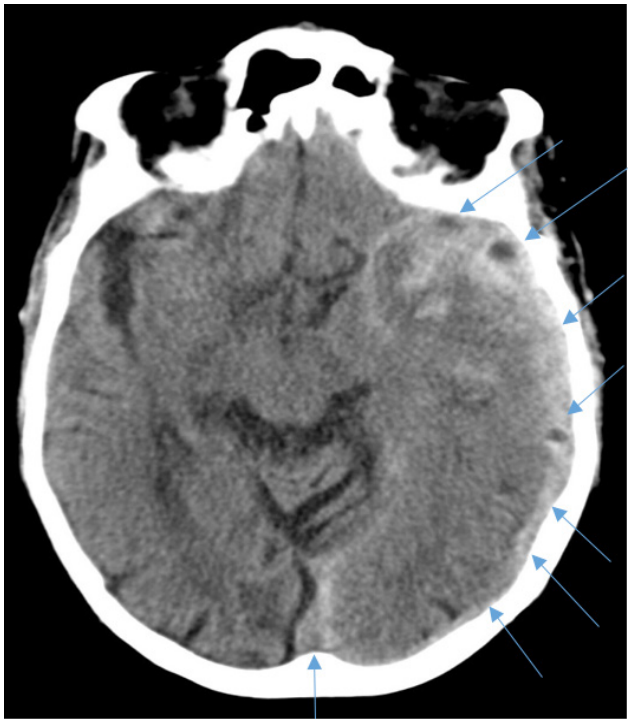
The urine dipstick was negative, and the short duration of the symptoms made dementia unlikely. It is vital to always consider the possibility of a spontaneous bleed in the brain in patients on warfarin therapy, and CT head is needed to rule this out even in the absence of trauma. In this patient's case, the CT head revealed a small subdural haemorrhage in the falx. Due to its small size, treatment was conservative, and the patient recovered.

Cases- Fatalities and Emergencies

This section will focus on the more serious, life-threatening complications of warfarin therapy. In all cases, there was no history of a significant trauma.

Image seven shows an acute left sided subdural haemorrhage. When a patient is on anticoagulant medication and presents with an acute drop in conscious level, intercranial haemorrhage must always be considered. Differential diagnosis in this case include infections such as meningitis or an ischaemic event. Due to their anticoagulation status the patient was sent for a CT head to enable a quick diagnosis.

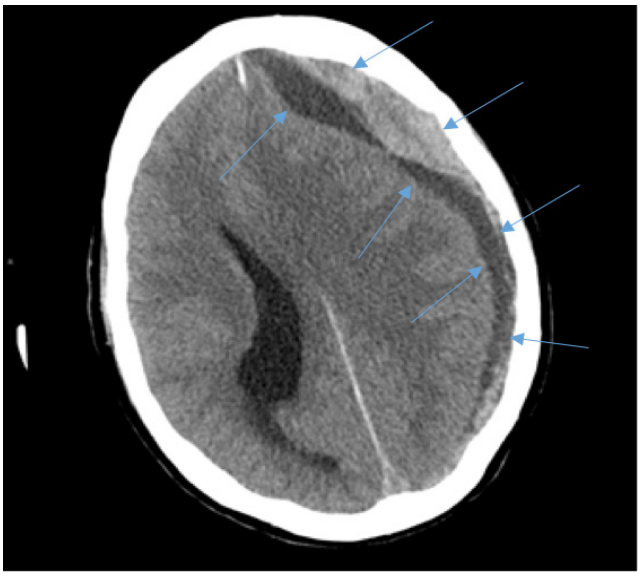
Figure 7 - Subdural haemorrhage with fresh blood visible in the sylvian fissure



There is mass effect visible as a shift of the midline of the brain to the right is present, and there is blood visible in the sylvian fissure. In this case, the bleed is still in the acute stage and may resolve spontaneously, therefore depending on the condition of the patient treatment may be conservative.

Image eight shows an acute-on-chronic left sided subdural haemorrhage. The patient presented similarly to the patient in image seven, however, in this case there has been a long-term bleed, which is the low-density area between the brain and the skull, then on top of this there has been a fresh bleed which is the high-density area lying more superficially. If the rate of bleeding is slow, it is not uncommon for it to go unnoticed for a long time and only present when the patient acutely decompensates. Unfortunately, this is what happened in this case. A CT head showed that there is a huge mass effect visible and the loss of sulci suggests a very tight, oedematous brain. In this case, due to the swelling, the patient coned and did not survive.

Figure 8 - Acute on chronic subdural haemorrhage



Haemorrhage within the abdomen: Image nine shows a large haematoma with active haemorrhage in the liver which has ruptured into the peritoneum. The patient did not survive. Image ten shows a large retroperitoneal bleed in front of the aortic bifurcation, again fatal.

Figure 9 - Liver haematoma with retroperitoneal haemorrhage

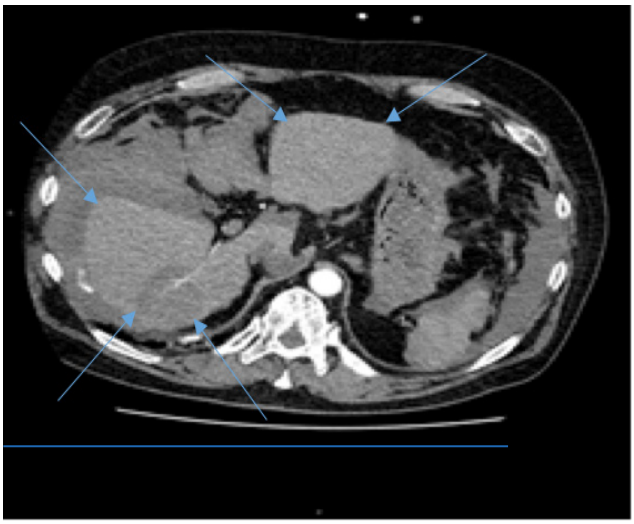
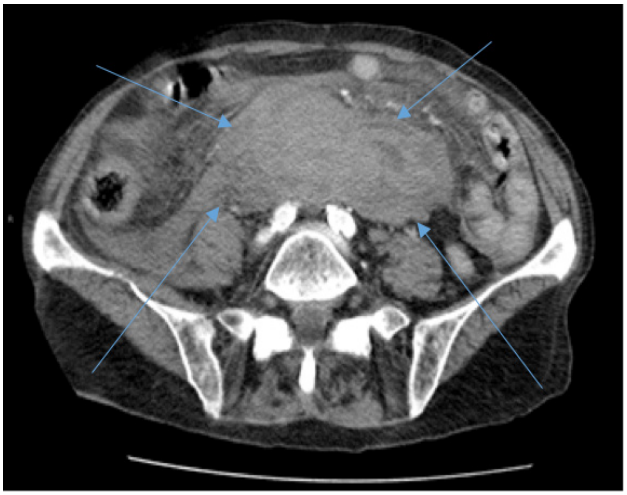


Figure 10 - Retroperitoneal haemorrhage



SUMMARY AND THE FUTURE

Warfarin has been an incredibly reliable and effective medication for the past fifty years. However, as has been previously discussed, the combination of constant monitoring and side effects means it has never been the perfect treatment. Direct oral anticoagulation (DOAC) drugs such as Rivaroxaban, Edoxaban and Dabigatran have all been shown to work as well as, if not better, than warfarin whilst having fewer side effects and no need for constant monitoring. (11-13) As time and medical research advances, warfarin may be coming to the end of its domination of anticoagulation.

This review aims to highlight the potential dangers of using warfarin. The images included are just examples of a larger number of cases which unfortunately are not uncommon in clinical practice.

Note: All the images in this report were taken at York Teaching Hospital in Scarborough. All identifying factors have been removed from the images to preserve patient confidentiality and were used with permission from the responsible consultant radiologist at the hospital. Further details such as warfarin dose and concurrent medications at the time were unavailable.

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