

IDENTIFICATION OF APPROPRIATE STROKE EVENT AND MANAGEMENT COSTS IN ATRIAL FIBRILLATION

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BACKGROUND

- ▶ Non-vitamin K antagonist oral anticoagulants, also known as direct acting oral anticoagulants (DOACs), are a well established treatment option for the prevention of stroke and other thromboembolic events in non-valvular atrial fibrillation (NVAF) patients
- ▶ A review of a study investigating the cost-effectiveness of DOACs for the prevention of stroke in patients (Thom *et al.*, 2019) found that cost-effectiveness results were particularly sensitive to acute and post-event management costs, in particular those of ischaemic stroke (IS) and intracranial haemorrhage (ICH)
- ▶ IS and ICH costs feature in economic analyses conducted for NICE guidance development, including the recent NG196 clinical guideline ‘Atrial Fibrillation: Diagnosis and Management’, published 27 April 2021, (NICE NG196, 2021) and NICE Single Technology Appraisals (STAs) (TA249, 2012; TA256, 2012; TA275, 2013; TA355, 2015)
- ▶ The NG196 guideline consultation period highlighted various aspects of interest relating to the use of costs for IS and ICH
 - The sourced costs from Luengo-Fernandez *et al.* (2013) in NG196 are outdated (studied prior to DOACs becoming available) so may not be generalisable to current clinical practice
 - NHS reference costs are not available for post-event management costs, therefore, it becomes necessary to seek costs from alternative sources
 - Inclusion of NHS reference costs for acute event costs in economic models may lead to double counting when alternative costs are sourced for longer-term costs but overlap with the acute period of care
- ▶ In light of these complexities, questions arise as to what IS and ICH costs are available and suitable for use in economic evaluation in an NVAF population

OBJECTIVE

- ▶ To systematically identify and review the costs associated with managing IS and ICH in patients with NVAF in the UK in order to understand what cost sources are available and most suitable for economic evaluation

METHODS

- ▶ A targeted literature review was conducted to identify UK costs for acute and post-event IS and ICH

Population, intervention, comparators and outcomes (PICO)

- ▶ The population for this literature review was the UK adult patient with AF
 - Although it is understood that the impact of IS (in terms of severity and effect on disability/quality of life) is higher for NVAF patients than in other patient populations, this review focused on the broader population of AF to aid in the retrieval of relevant articles that may be omitted by a narrower NVAF search
- ▶ The relevant intervention and comparators were routine care and management of acute and post-acute IS and ICH
- ▶ The outcomes of interest were UK costs (for acute and post-event IS and ICH) and/or healthcare resource utilisation (HRU). Studies had to be UK based and report on UK specific costs (in Great British Pounds)

Search strategy and databases

- ▶ A search strategy was developed in line with current economic evaluation guidance
- ▶ Searches were conducted in standard, recommended search engines/sites and databases – including Medline, Cochrane and NICE website
- ▶ Targeted searches were also cascaded where appropriate by searching the references of key reviews or publications to investigate whether there were other key studies of relevance. *De novo* cost studies were also identified from secondary studies citing these publications

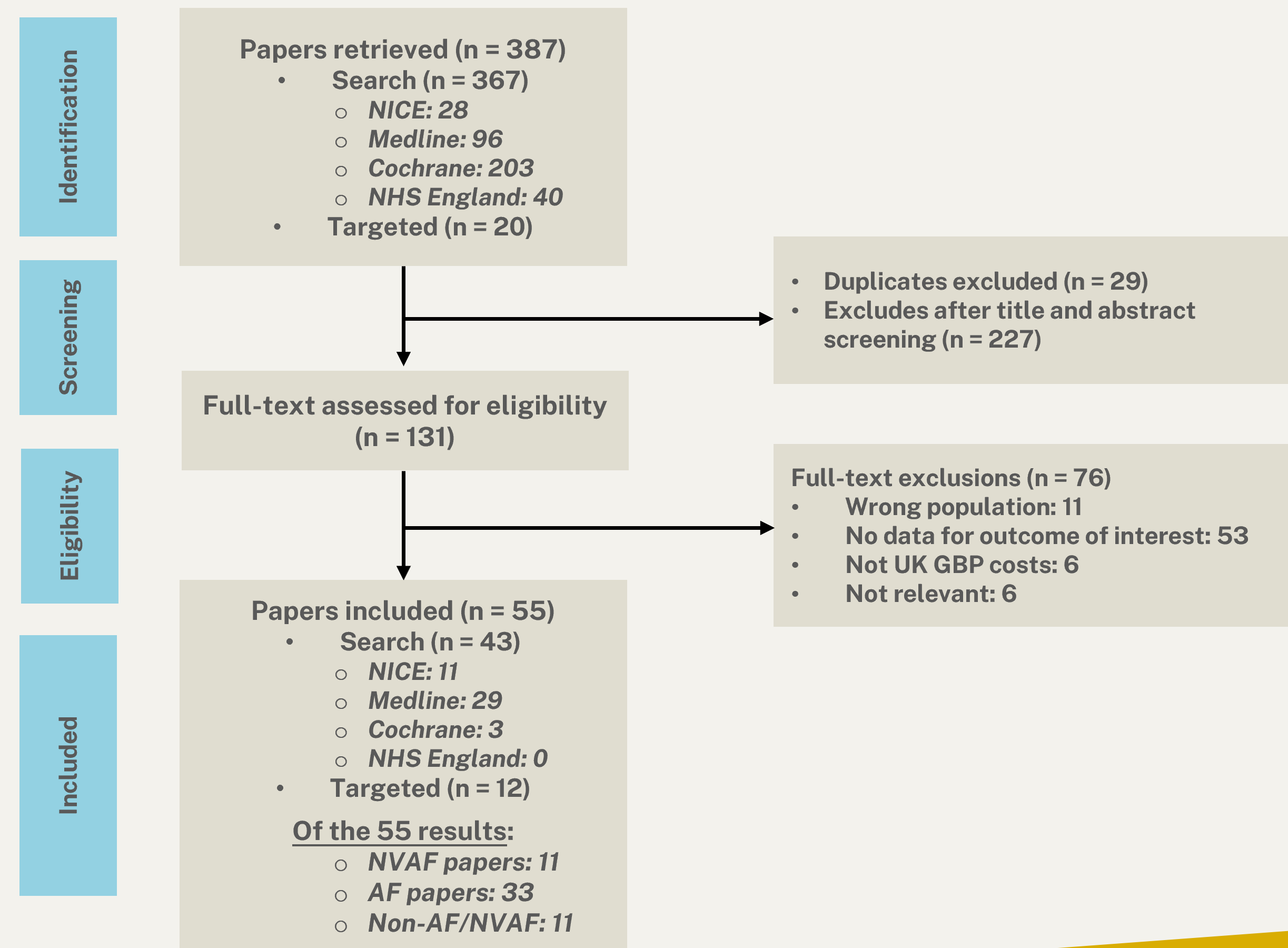
RESULTS

- ▶ 55 relevant studies were identified in total reporting on acute and post-event costs for IS and ICH (**Figure 1**)
 - Only 4 were *de novo* cost or HRU studies (1 NVAF and 3 AF) (**Table 1**)
 - Of the 4 *de novo* cost or HRU studies found in the AF/NVAF population, only 2 reported post-event management costs
 - 40 AF/NVAF studies (10 NVAF and 30 AF) utilised the results from these 4 *de novo* studies or other *de novo* studies conducted in non-AF/non-NVAF populations
 - Although the PICO was originally restricted to AF/NVAF populations, due to the low number of *de novo* studies identified above, non-AF/non-NVAF studies were also included if they were cited by AF/NVAF studies as IS and ICH cost sources
 - Thus, 11 studies were identified in the non-AF/non-NVAF populations of which 7 were *de novo* cost or HRU studies
 - The remaining 4 studies utilised the results from these 7 *de novo* studies
- ▶ The cost range reported in the literature for both acute and post-event management costs is broad (**Table 1 & Supplement information**)
 - When inflated to the 2020 price year, acute event costs range from £7,758 to £17,000
 - Post-event management costs reported in the literature range from £5,568 to £31,988, however disparity in these figures is largely due to wide range of follow-up time amongst studies (ranging from 1 to 10 years)
- ▶ Acute event costs reported in the literature were typically higher than the NHS reference costs for stroke events (**Supplement Figure 2**)
- ▶ Key critiques of the identified studies (when using in decision modelling)
 - The majority of the studies were conducted before DOAC use became established in the UK
 - Acute event costs were typically not disaggregated from post-event costs
 - Costs were typically not disaggregated by AF or stroke subtype

Table 1 List of 4 identified AF/NVAF *de novo* cost or HRU studies

STUDY	SAMPLE SIZE, FOLLOW UP DURATION, COST YEAR	COST CATEGORIES	ACUTE EVENT COSTS	LONG-TERM COSTS	KEY LIMITATION IN USE IN DECISION MODELLING
Luengo-Fernandez <i>et al.</i> (2006)	n=346 Mean: 394 days (S.D. 209) 2004/05	Hospitalisation (general ward, stroke unit, rehabilitation, long-term NHS care), diagnostics tests, primary care	Total acute care cost per patient: £6607 (95% CI, £5597–£7882)	Not reported	. Old study (prior to established DOAC usage) . Only 21% of patients reported a history of AF at baseline & the study does not distinguish between AF subtypes . Population sample limited to Oxfordshire . Primary care costs only relate to GP visits . No post-event costs
Luengo-Fernandez <i>et al.</i> (2013)	n=153 Mean: 731 days (S.D. 725) 2008/09	A&E visits, emergency transport, outpatient care, day cases & hospitalisations, incl. community hospitals. Primary care resource use included home, surgery & nurse/GP telephone consultations	IS: £10,844 (S.D. £15,733) HS: £10,683 (S.D. £12,885) For strokes of unknown subtypes: £4,206 (S.D. £5,650)	Non-disabling: £2,135 (S.D. £3,675) Moderately disabling: £4,165 (S.D. £7,668) Totally disabling: £6,324 (S.D. £14,898)	. Study conducted prior to established DOAC usage . Significant comorbidity prior to stroke in patient demographic – large proportion at high risk of stroke . Does not distinguish AF subtypes
Yiin <i>et al.</i> (2014)	n=468 2008/09	Hospital care - inpatient, outpatient & emergency visits	AF-related IS: £12,417 hospital care costs over 1-year post-stroke	Long-term institutionalisation (residential care) over 5 years after IS: £10,007	. Study conducted prior to established DOAC usage . No post-event HRU costs . Hospital care costs were not disaggregated by initial hospital care treatment for IS and any subsequent hospital-related HRU . HRU categories captured quite restrictive . Costs not disaggregated by AF subtype
Bakhai <i>et al.</i> (2020)	n=42,966 2015/16	GP visits, specialist referrals, laboratory tests, prescriptions, A&E visits & investigations, outpatient visits & hospitalisations	Mean total NHS costs in NVAF patients with IS up to 1-year post-index NVAF diagnosis: £9204 compared to £7318 in patients who experienced no event.	Not reported	. Study does not disaggregate acute and post event costs . Costs are not disaggregated by event type

Figure 1 PRISMA



CONCLUSIONS

- ▶ The evidence base for UK cost studies of IS and ICH management in patients with NVAF (and AF) is limited
- ▶ The bulk of the *de novo* cost studies are non-generalisable to current clinical practice as they were published prior to 2013, before UK DOAC use became established
 - These studies are likely to produce overestimates of the true cost of stroke in this population since DOAC use has been shown to reduce the incidence and morbidity of stroke in NVAF patients (Van Ganse *et al.*, 2020)
- ▶ NHS reference costs and Personal Social Services Research Unit (PSSRU) unit costs are the gold standard source of acute event costs in UK economic evaluations appraised by NICE
 - However, the NHS reference costs identified were lower than those identified as ‘acute’ costs in the *de novo* studies reviewed, even with higher CC scores
- ▶ A challenge for economic models is to ensure that the source of event costs remains up to date while capturing all relevant follow-on costs
 - Double counting of HRU could also be an issue for any model that ‘counts’ IS or ICH events, given that no studies stratify costs of repeat-events from those of the initial index event
- ▶ Further research is warranted in this area

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