BMJ Open

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Journal:	*BMJ Open*
Manuscript ID	bmjopen-2016-013742
Article Type:	Research
Date Submitted by the Author:	03-Aug-2016
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Primary Subject Heading:	Emergency medicine
Secondary Subject Heading:	Health economics, Health policy, Radiology and imaging, Neurology
Keywords:	Anticoagulation < HAEMATOLOGY, Head & neck imaging < RADIOLOGY & IMAGING, TRAUMA MANAGEMENT, Warfarin

Should all anticoagulated patients with head injury receive a CT scan? Decision-analysis modelling of an observational cohort

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Word count: 2680 (excluding title page, abstract, references, tables and figures)

ABSTRACT

Objectives: It is not currently clear whether all anticoagulated patients with a head injury should receive CT scanning or only those with evidence of traumatic brain injury (e.g. loss of consciousness or amnesia). We aimed to determine the cost-effectiveness of CT for all compared to selective CT use for anticoagulated patients with a head injury.

Design: Decision-analysis modelling of data from a multi-centre observational study.

Setting: 33 Emergency Departments in England and Scotland.

Participants: 3566 adults (aged ≥16 years) who had suffered blunt head injury, were taking warfarin and underwent selective CT scanning.

Main outcome measures: Estimated expected benefits in terms of quality-adjusted life years (QALYs) were the entire cohort to receive a CT scan; estimated increased costs of CT and also the potential cost implications associated with patient survival and improved health. These values were used to estimate the cost per QALY of implementing a strategy of CT for all patients compared to observed practice based on guidelines recommending selective CT use.

Results: Of the 1420/3534 patients (40%) who did not receive a CT scan, 7 (0.5%) suffered a potentially avoidable head injury related adverse outcome. If CT scanning had been performed in all patients, appropriate treatment could have gained 3.41 additional quality-adjusted life years (QALYs) but would have incurred £193,149 additional treatment costs and £130,683 additional CT costs. The incremental cost-effectiveness ratio of £94,895/QALY gained for unselective compared to selective CT use is markedly above the threshold of £20-30,000/QALY used by the UK National Institute for Care Excellence to determine cost-effectiveness.

Conclusions: CT scanning for all anticoagulated patients with head injury is not cost-effective compared with selective use of CT scanning based on guidelines recommending scanning only for those with evidence of traumatic brain injury.

Trial registration ClinicalTrials.gov NCT 02461498.

ARTICLE SUMMARY

Strengths and limitations of this study

- This is the largest study to model options for the clinical management of anticoagulated patients taking warfarin with a head injury.
- The methods used to estimate health gain from treating additional cases detected by universal CT scanning are transparent and reproducible, and were robust to the sensitivity analyses undertaken.
- Some patients who suffered adverse outcome may not have been identified on follow-up potentially being a limitation of the study, leading to underestimation of the potential benefit of CT scan for all patients.

BACKGROUND

It is estimated that at least 1% of the United Kingdom (UK) population are taking an anticoagulant, such as warfarin, increasing to 8% in those aged 80 years and over[1, 2]. People taking an anticoagulant who experience a head injury are at an increased risk of intracranial haemorrhage[3,4] with rates of mortality reported between 45-70%.[3,5–7] Liberal use of CT scanning is therefore required to identify intracranial haemorrhage in these patients. However, it is not clear whether all anticoagulated patients with head injury should receive a CT scan or whether CT should be used selectively and limited to those with evidence of traumatic brain injury, such as those with loss of consciousness or amnesia.[8]

Management of head injury in the UK follows guidance from the National Institute for Health and Care Excellence (NICE). NICE guidance issued in 2007[9] recommended that patients with coagulopathy (including those currently treated with warfarin) should undergo CT scanning only if they report amnesia or loss of consciousness following injury. Updated guidance issued in 2014[10] recommended that all patients having warfarin treatment should undergo CT scanning regardless of whether they reported amnesia or loss of consciousness (Figure 1). The new guidance should increase the number of scans performed and intracranial injuries identified but it is not clear whether the benefits of this approach justify the costs of additional CT scanning.

The AHEAD study was an observational cohort study of patients with head injury who were taking warfarin and presented to a hospital emergency department (ED).[11] It was undertaken when NICE 2007 guidance was in operation but before NICE 2014 guidance was issued. We aimed to use data from the AHEAD study and decision analysis modelling to determine the cost-effectiveness of CT for all compared to observed practice based on guidelines recommending selective CT for those with evidence of traumatic brain injury.

Figure 1: NICE guidance 2007 versus 2014

NICE Guidance CG56, 2007

- CT head scan patients with any of the following risk factors within 1 hour:
  - GCS<13
  - GCS<15 at 2 hours
  - Open or depressed skull fracture
  - Sign of fracture at base of skull
  - Post-traumatic seizure
  - Focal neurological deficit
  - >1 episode of vomiting
  - Amnesia >30minutes before impact
- CT head scan patients that have experienced **Loss of consciousness** or **amnesia** AND any of the following risk factors:
  Within 8 hours
  - Aged 65 years or over
  - Dangerous mechanism of injury

  Within 1 hour
  - Coagulopathy

NICE Guidance CG176, 2014

- CT head scan with any of the following risk factors within 1 hour:
  - GCS<13
  - GCS<15 at 2 hours
  - Open or depressed skull fracture
  - Any sign of basal skull fracture
  - Post-traumatic seizure
  - Focal neurological deficit
  - >1 episode of vomiting
- CT head scan patients that have experienced **Loss of consciousness** or **amnesia** AND any of the following risk factors:
  Within 8 hours
  - Aged 65 years or over
  - History of bleeding or clotting disorders
  - Dangerous mechanism of injury
  - >30 minutes retrograde amnesia of events
- CT head scan patients with no other indications for CT head scan AND having warfarin treatment, within 8 hours

METHODS

The methods for the AHEAD study are described in detail elsewhere (Mason S, Kuczawski M, Teare MD, et al. The AHEAD Study: An observational study of anticoagulated patients who suffer head injury. UK; 2016. Unpublished). Briefly, 3566 adults who were taking warfarin and attended the ED of 33 hospitals in England and Scotland between September 2011 and March 2013 following head injury were recruited. Research staff in hospital sites recorded basic demographic information, attendance details, injury mechanism, clinical examination findings and CT results. Patients were then followed up to 10 weeks after presentation using hospital record review and postal questionnaire.

We identified all patients with an adverse outcome who had not received a CT scan at their initial hospital attendance. It is this group of patients who would be expected to receive clinical benefit from a policy of CT scanning all patients. An adverse outcome was defined as: death; neurosurgery; positive CT scan finding; or re-attendance to the hospital with a significant head injury-related complication up to 10-weeks after the original attendance. These re-attendances were confirmed following the review of hospital records and CT scan results, where undertaken.

Decision analysis modelling was used to estimate the quality adjusted life years (QALY) and cost implications had those patients with an adverse outcome that were not CT scanned received a CT scan on initial hospital attendance. Different assumptions were required for patients conditional on whether they survived the adverse event. For patients who died, assumptions were required regarding: the probability of survival if a CT scan had been performed; the Glasgow Outcome Scale (GOS) state to which the patient would be categorised if they survived;[11] and the cost of neurosurgery. For patients who survived, an assumption was required relating to the probability of GOS increase if a CT scan had been performed. Regardless of survival outcome, assumptions were required on: the life expectancy of a person with the same gender and age profile; the costs and utility associated with each GOS state; and the cost of a CT scan. The assumptions used within the model are detailed below. The results presented take an English and Scottish perspective and use direct healthcare and personal social services costs.

Model Assumptions

For patients who did not survive the adverse event:

The probability of survival if a CT scan had been performed

Two clinicians provided estimates of the probability of survival had the patient received a CT scan. In the main analysis an average value was used, although sensitivity analyses were undertaken assuming that each clinician was correct.

The GOS state to which the patient would be categorised if they survived

A single clinician provided an estimate of the GOS of the patient if they had survived. In a sensitivity analysis the impact of the GOS state being one level higher (that is, more favourable to the patient) was explored.

The costs of neurosurgery

The cost of neurosurgery was assumed to be that associated with the weighted average of NHS Reference Cost Codes AA50A – AA57B, excluding codes relating to patients aged 18 years and under, which was £3994.[12] It was assumed that all patients who died without having a CT scan would undergo neurosurgery.

For patients who survived the adverse event:

The probability of GOS increase if a CT scan had been performed

Two clinicians provided estimates of the probability of an increase in the GOS level, (i.e. a better patient outcome) if a CT scan had been performed. In the main analysis an average value was used, although sensitivity analyses were undertaken assuming that each clinician was correct.

For all patients:

The life expectancy of the person

These data were taken from UK Life Tables[13] and it was assumed that these were not affected by an adverse event that had been survived.

The costs and utility associated with each GOS state

The data for GOS states 2-4 were taken from Pandor et al[14] with costs inflated from 2008/2009 values to 2014/15 prices using hospital and community health services indices reported in Curtis and Burns.[15] The resultant values are provided in Table 1. For GOS state 5 it was assumed that the UK general population utility conditional on age and sex was appropriate which was taken from Ara and Brazier.[16]

Table 1: Assumed costs and utility associated with each GOS state, and assumed cost of neurosurgery.

GOS state	One-off Cost (£)	Annual Costs (£)	Utility value	Source
2	47,674	46,595	0.00	Pandor et al[14] with costs inflated using Curtis and Burns[15]
3	0	37,214	0.15	
4	18,837	0	0.51	
5	0	0	Population Value†	Assumption

† The utility in GOS state 5 were estimated from Ara and Brazier[16] conditional on age and sex.

The cost of a CT scan

The cost of a CT scan was assumed to be that associated with NHS Reference Cost Code RD20A, which was £92.

The mathematical model

The model calculated the expected difference in costs and QALYs of moving from observed practice to a strategy of CT scanning all patients. The following formulae were used in calculating the cost and quality adjusted life years (QALY) impacts associated with provided CT scans to patients with adverse events who did not receive a CT scan. All values were discounted at 3.5% per annum in accordance with NICE guidelines.[17] A lifetime horizon was assumed due to potential mortality benefits of the CT all strategy.

For patients who did not survive:

Change in costs: Average probability of survival if CT scan performed x (Life Expectancy x Cost per year in estimated GOS state + cost of neurosurgery)

Change in QALYs: Average probability of survival if CT scan performed x (Life Expectancy x utility per year in estimated GOS state)

For patients who did survive

Change in costs: Average probability of GOS increase if CT scan performed x Life Expectancy x (Cost per year in higher GOS state – Cost per year in lower GOS state)

Change in QALYs: Average probability of GOS increase if CT scan performed x (Life Expectancy x utility per year in higher GOS state – utility per year in lower GOS state)

RESULTS

Follow-up data were available for 3534/3566 patients (99%) in the AHEAD cohort. Details of the cohort are published elsewhere (Mason S, Kuczawski M, Teare MD, et al. The AHEAD Study: Managing anticoagulated patients who suffer head injury. UK; 2016. Unpublished). Glasgow Outcome Scale and diagnosis was available for 91.4% (n=3229) and 99.9% (n=3530) patients respectively. Overall 2114/3534 patients (60%) received a CT scan. Of the 1420 patients without a CT scan, 728 (51%) were admitted to hospital, 20 (1.4%) had subsequent head injury related hospital attendances, and 74 (5.2%) died during follow-up. Cause of death was head injury related in four (0.3%), unrelated in 52 (3.7%) and unknown in 19 (1.3%). Adverse outcomes were identified in 7/1420 (0.5%) patients who did not have CT scan: four deaths and three with a related further hospital attendance and significant finding on CT scan at re-attendance.

The estimated changes in costs and QALYs per individual patient are provided in Table 2. The summarised analyses including the increased costs of CT scans are provided in Table 3.

Table 2: Estimated outcomes for patients with adverse events who were not CT scanned if they had been CT scanned on admission to hospital and modelled implications for costs and QALYs

Patient	Outcomes								Modelling				
	Age	Sex	Admitted	Observed CT head scan	Reversal therapy	Neurosurgery	Further hospital attendance	HI Death	Probability of survival (%)		Estimated GOS if survived	Change in costs	Change in QALYs
									Clinician 1	Clinician 2			
1	81	M	×	×	×	×	✓	✓	75	75	3	£169,279	0.67
2	74	M	×	×	×	×	×	✓	25	15	2	£13,528	0.00
3	90	M	×	×	×	×	×	✓	0	0	2	£3,994	0.00
4	88	M	×	×	×	×	✓	✓	75	75	4	£18,122	1.45
									Probability of GOS increase (+1, %)		Lower GOS score	Δ C	Δ Q
									Clinician 1	Clinician 2			
5	76	M	×	×	×	×	✓	×	25	50	4	-£7,064	0.86
6	77	F	×	×	×	×	✓	×	25	0	4	-£2,355	0.27
7	82	M	×	×	×	×	✓	×	25	0	4	-£2,355	0.17

Table 3: The comparison of CT all with observed practice.

	Change in costs from CT scanning (£)	Change in QALYs from CT scanning	ICER (Cost per QALY gained (£))
Changes in individual patient values	193,149	3.41	
Additional CT scanning costs	130,683		
Net Values	323,832	3.41	94,895

It is estimated that the cost per QALY gained through providing a CT scan is in excess of £90,000 per QALY which is markedly greater than the £20,000 to £30,000 per QALY gained threshold reported by NICE.[17] This conclusion did not alter within the sensitivity analyses performed. Using the estimates from the individual expert clinicians which produced values of £90,659 and £99,547 per QALY gained or if the cost of neurosurgery was not included for the patient who neither expert clinician believed would have survived even with a CT scan (£93,725 per QALY gained). When it was assumed that all patients survived at one GOS state better than estimated in the base case the cost per QALY gained reduced to £36,864 (an additional £213,139 to obtain 5.78 QALYs) but still did not fall below NICE thresholds.

DISCUSSION

Follow-up of 1420 patients who did not have a CT scan in the AHEAD cohort identified seven cases (four deaths, three delayed diagnoses) that might have been identified by CT scanning at initial hospital attendance. Decision analytic modelling showed that appropriate treatment of these cases could have gained 3.41 QALYs but would have incurred £193,149 additional treatment costs and £130,683 additional costs for CT scanning. This produces an incremental cost of £94,895 per QALY gained, which is greatly above the usual threshold of £20-30,000/QALY that NICE uses to determine cost-effectiveness. Our analysis therefore suggests that CT for all anticoagulated patients with head injury, as recommended in NICE 2014 guidance, is not cost-effective compared to the selective use of CT scanning observed in practice when NICE 2007 guidance was in operation.

Our analysis has a number of strengths and weaknesses. It was based upon a large representative cohort of patients who presented to a wide range of hospitals. The methods used to estimate health gain from treating additional cases detected by universal CT scanning are transparent and reproducible, and were robust to the sensitivity analyses undertaken. A potential limitation is that some patients who suffered adverse outcome may not have been identified on follow-up leading to underestimation of the potential benefit of CT scan for all patients. However, it is worth noting that 10.79 QALYs would be required to reach the NICE threshold of £30,000/QALY for cost-effectiveness, so our conclusion regarding the lack of cost-effectiveness of unselective CT scanning would only be undermined if follow-up had identified less than 1 in 3 patients with adverse events. This seems extremely unlikely. Other limitations may have underestimated the additional costs of unselective CT scanning, for example we did not include knock-on costs from additional CT scanning, such as those generated by incidental findings.

Most international guidance, including the National Emergency X-Radiology Utilisation Study (NEXUS II), CT in Head Injury Patients (CHIP), American College of Emergency Physicians (ACEP) head CT and the European Federation of Neurological Societies (EFNS)[18-21] advocate that all patients taking warfarin should have an immediate CT scan irrespective of injury severity, GCS or neurological symptoms. The UK guidelines (NICE) are based on the Canadian CT Head Rule(CCHR)[22] which excluded patients taking warfarin and up until January 2014, stated that a CT scan should be performed on patients taking warfarin if the patient presented with loss of consciousness or amnesia. These guidelines have now been updated to recommend all anticoagulated patients receive a CT scan but no new evidence appears to have been published to support this recommended change in practice. Our analysis suggests that the 2014 revision to NICE guidance has resulted in less cost-effective care.

Previous literature investigating the patient outcomes and costs associated with diagnosing and treating head injured patients who are taking anticoagulants are limited and difficult to compare to our analysis. Several recent studies have used decision analysis modelling to estimate the costs and benefits of CT scanning in the general (i.e. non-anticoagulated) head injured population[23-25] and have generally shown that using a clinical decision rule to select patients for CT scanning is more cost-effective than unselective CT scanning. The only study identified that focused solely on anticoagulated patients was undertaken by Li in 2012.[26] Li questioned how this cohort of patients should be managed due to the nature of delayed complications associated with anticoagulant use, whilst also considering the costs attached to CT imaging and admittance to hospital. The analyses were based on data taken from other studies and included repeated CT scans (2) and 24-hour admission per patient. The costs per year of a life saved in the US, Spain and Canada were estimated as $1 million, $158,000 and $105,000 respectively.

CONCLUSION

CT scanning for all anticoagulated patients with head injury is not cost-effective compared with selective use of CT scanning based on guidelines recommending scanning only for those with evidence of traumatic brain injury. A move (or return to) selective use of CT scanning would substantially reduce health care costs with only a small increase in potentially avoidable adverse outcomes.

Acknowledgements: We thank Rosemary Harper for her contribution as a patient representative throughout the duration of the study; all the clinicians and research staff in the participating hospital sites who identified patients in this study, without whose hard work this study would not have been possible.

Contributors: All authors provided substantial contributions to the conception, design, acquisition of the data, or analysis and interpretation of the study data. MK drafted the article and all authors contributed to its revision for important intellectual content. All authors approved the final version. SM is guarantor. All authors agree to be accountable for all aspects of the work ensuring that questions related to accuracy or integrity of any party of the work are appropriately investigated and resolved.

Transparency: SM affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Funding: This paper presents independent research commissioned by the National Institute for Health Research (NIHR) under its Research for Patient Benefit (RfPB) Programme grant reference number PB-PG-0808-17148. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

Competing interests: All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Ethical approval: NRES Committee Yorkshire and The Humber – Sheffield: 11/H1308/13.

Sponsor: Sheffield Teaching Hospitals NHS Foundation Trust – Ref.: STH15705.

Provenance and peer review: Not commissioned; externally peer reviewed.

Data Sharing Statement: No additional data are available.

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CHEERS checklist - Items to include when reporting economic evaluations of health interventions

Should all anticoagulated patients with head injury receive a CT scan? Decision-analysis modelling of an observational cohort

Section/item	Item No	Recommendation	Reported on page No/ line No
Title and abstract			
Title	1	Identify the study as an economic evaluation or use more specific terms such as "cost-effectiveness analysis", and describe the interventions compared.	1
Abstract	2	Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions.	2
Introduction			
Background and objectives	3	Provide an explicit statement of the broader context for the study.	4
		Present the study question and its relevance for health policy or practice decisions.	4
Methods			
Target population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	5
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	5
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	6
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	4
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	8
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	8
Choice of health outcomes	10	Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.	6,10
Measurement of effectiveness	11a	*Single study-based estimates:* Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	*4*

	11b	*Synthesis-based estimates:* Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.	*N/A*
Measurement and valuation of preference based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	N/A
Estimating resources and costs	13a	*Single study-based economic evaluation:* Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	*N/A*
	13b	*Model-based economic evaluation:* Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	*7-8*
Currency, price date, and conversion	14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.	7
Choice of model	15	Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended.	8
Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytical model.	5-8
Analytical methods	17	Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.	5-8
Results			
Study parameters	18	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.	6-8
Incremental costs and outcomes	19	For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.	10

Characterising uncertainty	20a	*Single study-based economic evaluation:* Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact of methodological assumptions (such as discount rate, study perspective).	
	20b	*Model-based economic evaluation:* Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	10
Characterising heterogeneity	21	If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.	N/A
Discussion			
Study findings, limitations, generalisability, and current knowledge	22	Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.	10-12
Other			
Source of funding	23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.	13
Conflicts of interest	24	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.	13

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Journal:	*BMJ Open*
Manuscript ID	bmjopen-2016-013742.R1
Article Type:	Research
Date Submitted by the Author:	24-Oct-2016

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Primary Subject Heading:	Emergency medicine
Secondary Subject Heading:	Health economics, Health policy, Radiology and imaging, Neurology
Keywords:	Anticoagulation < HAEMATOLOGY, Head & neck imaging < RADIOLOGY & IMAGING, TRAUMA MANAGEMENT, Warfarin

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Should all anticoagulated patients with head injury receive a CT scan? Decision-analysis modelling of an observational cohort

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Word count: 2911 (excluding title page, abstract, references, tables and figures)

ABSTRACT

Objectives: It is not currently clear whether all anticoagulated patients with a head injury should receive CT scanning or only those with evidence of traumatic brain injury (e.g. loss of consciousness or amnesia). We aimed to determine the cost-effectiveness of CT for all compared to selective CT use for anticoagulated patients with a head injury.

Design: Decision-analysis modelling of data from a multi-centre observational study.

Setting: 33 Emergency Departments in England and Scotland.

Participants: 3566 adults (aged ≥16 years) who had suffered blunt head injury, were taking warfarin and underwent selective CT scanning.

Main outcome measures: Estimated expected benefits in terms of quality-adjusted life years (QALYs) were the entire cohort to receive a CT scan; estimated increased costs of CT and also the potential cost implications associated with patient survival and improved health. These values were used to estimate the cost per QALY of implementing a strategy of CT for all patients compared to observed practice based on guidelines recommending selective CT use.

Results: Of the 1420/3534 patients (40%) who did not receive a CT scan, 7 (0.5%) suffered a potentially avoidable head injury related adverse outcome. If CT scanning had been performed in all patients, appropriate treatment could have gained 3.41 additional quality-adjusted life years (QALYs) but would have incurred £193,149 additional treatment costs and £130,683 additional CT costs. The incremental cost-effectiveness ratio of £94,895/QALY gained for unselective compared to selective CT use is markedly above the threshold of £20-30,000/QALY used by the UK National Institute for Care Excellence to determine cost-effectiveness.

Conclusions: CT scanning for all anticoagulated patients with head injury is not cost-effective compared with selective use of CT scanning based on guidelines recommending scanning only for those with evidence of traumatic brain injury.

Trial registration ClinicalTrials.gov NCT 02461498.

ARTICLE SUMMARY

Strengths and limitations of this study

- This is the largest study to model options for the clinical management of anticoagulated patients taking warfarin with a head injury.
- The methods used to estimate health gain from treating additional cases detected by universal CT scanning are transparent and reproducible, and were robust to the sensitivity analyses undertaken.
- Some patients who suffered adverse outcome may not have been identified on follow-up potentially being a limitation of the study, leading to underestimation of the potential benefit of CT scan for all patients.

BACKGROUND

It is estimated that at least 1% of the United Kingdom (UK) population are taking an anticoagulant, such as warfarin, increasing to 8% in those aged 80 years and over[1, 2]. People taking an anticoagulant who experience a head injury are at an increased risk of intracranial haemorrhage[3,4] with rates of mortality reported between 45-70%.[3,5–7] Liberal use of CT scanning is therefore required to identify intracranial haemorrhage in these patients. However, it is not clear whether all anticoagulated patients with head injury should receive a CT scan or whether CT should be used selectively and limited to those with evidence of traumatic brain injury, such as those with loss of consciousness or amnesia.[8]

Management of head injury in the UK follows guidance from the National Institute for Health and Care Excellence (NICE). NICE guidance issued in 2007[9] recommended that patients with coagulopathy (including those currently treated with warfarin) should undergo CT scanning only if they report amnesia or loss of consciousness following injury. Updated guidance issued in 2014[10] recommended that all patients having warfarin treatment should undergo CT scanning regardless of whether they reported amnesia or loss of consciousness (Figure 1). The new guidance should increase the number of scans performed and intracranial injuries identified but it is not clear whether the benefits of this approach justify the costs of additional CT scanning.

The AHEAD study was an observational cohort study of patients with head injury who were taking warfarin and presented to a hospital emergency department (ED).[11] It was undertaken when NICE 2007 guidance was in operation but before NICE 2014 guidance was issued. We aimed to use data from the AHEAD study and decision analysis modelling to determine the cost-effectiveness of CT for all compared to observed practice based on guidelines recommending selective CT for those with evidence of traumatic brain injury.

METHODS

The methods for the AHEAD study are described in detail elsewhere.[11] Briefly, 3566 adults who were taking warfarin and attended the ED of 33 hospitals in England and Scotland between September 2011 and March 2013 following head injury were recruited. Research staff in hospital sites recorded basic demographic information, attendance details, injury mechanism, clinical examination findings and CT results. Patients were then followed up to 10 weeks after presentation using hospital record review and postal questionnaire.

We identified all patients with an adverse outcome who had not received a CT scan at their initial hospital attendance. The patients that did receive a CT scan (under a selective CT scanning policy) would receive the same treatment if a CT scan all policy was in place, therefore it is the former group of patients who would be expected to receive clinical benefit from a policy of CT scanning all patients. However, a threshold analysis was conducted to estimate the proportion of inpatient attendances of less than 48 hours that would need to be avoided for the CT scan all policy to have a cost per quality adjusted life year (QALY) below £30,000, assuming the cost of such an inpatient stay to be that associated with a non-elective inpatient stay (£615)[12]. An adverse outcome was defined as: death; neurosurgery; positive CT scan finding; or re-attendance to the hospital with a significant head injury-related complication up to 10-weeks after the original attendance. These re-attendances were confirmed following the review of hospital records and CT scan results, where undertaken.

Decision analysis modelling was used to estimate the incremental QALYs and costs had those patients with an adverse outcome that were not CT scanned received a CT scan on initial hospital attendance. Different assumptions were required for patients conditional on whether they survived the adverse event. For patients who died, assumptions were required regarding: the probability of survival if a CT scan had been performed; the Glasgow Outcome Scale (GOS) state to which the patient would be categorised if they survived;[13] and the cost of neurosurgery. For patients who survived, an assumption was required relating to the probability of GOS increase if a CT scan had been performed. Regardless of survival outcome, assumptions were required on: the life expectancy of a person with the same gender and age profile; the costs and utility associated with each GOS state; and the cost of a CT scan. The assumptions used within the model are detailed below. The results presented take an English and Scottish perspective and use direct healthcare and personal social services costs.

Model Assumptions

For patients who did not survive the adverse event:

The probability of survival if a CT scan had been performed

Two clinicians provided estimates of the probability of survival had the patient received a CT scan. In the main analysis an average value was used, although sensitivity analyses were undertaken assuming that each clinician was correct.

The GOS state to which the patient would be categorised if they survived

A single clinician provided an estimate of the GOS of the patient if they had survived. In a sensitivity analysis the impact of the GOS state being one level higher (that is, more favourable to the patient) was explored.

The costs of neurosurgery

The cost of neurosurgery was assumed to be that associated with the weighted average of NHS Reference Cost Codes AA50A – AA57B, excluding codes relating to patients aged 18 years and under, which was £3994.[14] It was assumed that all patients who died without having a CT scan would undergo neurosurgery.

For patients who survived the adverse event:

The probability of GOS increase if a CT scan had been performed

Two clinicians provided estimates of the probability of an increase in the GOS level, (i.e. a better patient outcome) if a CT scan had been performed. In the main analysis an average value was used, although sensitivity analyses were undertaken assuming that each clinician was correct.

For all patients:

The life expectancy of the person

These data were taken from UK Life Tables[15] and it was assumed that these were not affected by an adverse event that had been survived.

The costs and utility associated with each GOS state

The data for GOS states 2-4 were taken from Pandor et al[16] with costs inflated from 2008/2009 values to 2014/15 prices using hospital and community health services indices reported in Curtis and Burns.[12] The resultant values are provided in Table 1. For GOS state 5 it was assumed that the UK general population utility conditional on age and sex was appropriate which was taken from Ara and Brazier.[17]

Table 1: Assumed costs and utility associated with each GOS state, and assumed cost of neurosurgery.

GOS state	One-off Cost (£)	Annual Costs (£)	Utility value	Source
2	47,674	46,595	0.00	Pandor et al[16] with costs inflated using Curtis and Burns[12]
3	0	37,214	0.15	
4	18,837	0	0.51	
5	0	0	Population Value†	Assumption

† The utility in GOS state 5 were estimated from Ara and Brazier[17] conditional on age and sex.

The cost of a CT scan

The cost of a CT scan was assumed to be that associated with NHS Reference Cost Code RD20A, which was £92.

The mathematical model

The model calculated the expected difference in costs and QALYs of moving from observed practice to a strategy of CT scanning all patients. The following formulae were used in calculating the cost and quality adjusted life years (QALY) impacts associated with provided CT scans to patients with adverse events who did not receive a CT scan. All values were discounted at 3.5% per annum in accordance with NICE guidelines.[18] A lifetime horizon was assumed due to potential mortality benefits of the CT all strategy.

For patients who did not survive:

Change in costs: Average probability of survival if CT scan performed x (Life Expectancy x Cost per year in estimated GOS state + cost of neurosurgery)

Change in QALYs: Average probability of survival if CT scan performed x (Life Expectancy x utility per year in estimated GOS state)

For patients who did survive

Change in costs: Average probability of GOS increase if CT scan performed x Life Expectancy x (Cost per year in higher GOS state – Cost per year in lower GOS state)

Change in QALYs: Average probability of GOS increase if CT scan performed x (Life Expectancy x utility per year in higher GOS state – utility per year in lower GOS state)

RESULTS

Follow-up data were available for 3534/3566 patients (99%) in the AHEAD cohort. Details of the cohort are published.[11] Glasgow Outcome Scale and diagnosis was available for 91.4% (n=3229) and 99.9% (n=3530) patients respectively. Overall 2114/3534 patients (60%) received a CT scan. Of the 1420 patients without a CT scan, 728 (51%) were admitted to hospital, 20 (1.4%) had subsequent head injury related hospital attendances, and 74 (5.2%) died during follow-up. Cause of death was head injury related in four (0.3%), unrelated in 52 (3.7%) and unknown in 19 (1.3%). Adverse outcomes were identified in 7/1420 (0.5%) patients who did not have CT scan: four deaths and three with a related further hospital attendance and significant finding on CT scan at re-attendance.

The estimated changes in costs and QALYs per individual patient are provided in Table 2. The summarised analyses including the increased costs of CT scans are provided in Table 3.

Table 2: Estimated outcomes for patients with adverse events who were not CT scanned if they had been CT scanned on admission to hospital and modelled implications for costs and QALYs.

Patient	Outcomes									Modelling				
	Age	Sex	Admitted	INR	Observed CT head scan	Reversal therapy	Neurosurgery	Further hospital attendance	HI Death	Probability of survival (%)		Estimated GOS if survived	Change in costs	Change in QALYs
										Clinician 1	Clinician 2			
1	81	M	×	NP	×	×	×	✓	✓	75	75	3	£169,279	0.67
2	74	M	×	NP	×	×	×	×	✓	25	15	2	£13,528	0.00
3	90	M	×	4.4	×	×	×	×	✓	0	0	2	£3,994	0.00
4	88	M	×	NP	×	×	×	✓	✓	75	75	4	£18,122	1.45
										Probability of GOS increase (+1, %)		Lower GOS score	Δ C	Δ Q
										Clinician 1	Clinician 2			
5	76	M	×	2.0	×	×	×	✓	×	25	50	4	-£7,064	0.86
6	77	F	×	3.0	×	×	×	✓	×	25	0	4	-£2,355	0.27
7	82	M	×	3.5	×	×	×	✓	×	25	0	4	-£2,355	0.17

NP= Not performed.

Table 3: The comparison of CT all with observed practice.

	Change in costs from CT scanning (£)	Change in QALYs from CT scanning	ICER (Cost per QALY gained (£))
Changes in individual patient values	193,149	3.41	
Additional CT scanning costs	130,683		
Net Values	323,832	3.41	94,895

It is estimated that the cost per QALY gained through providing a CT scan is in excess of £90,000 per QALY which is markedly greater than the £20,000 to £30,000 per QALY gained threshold reported by NICE.[18] This conclusion did not alter within the sensitivity analyses performed. Using the estimates from the individual expert clinicians which produced values of £90,659 and £99,547 per QALY gained or if the cost of neurosurgery was not included for the patient who neither expert clinician believed would have survived even with a CT scan (£93,725 per QALY gained). When it was assumed that all patients survived at one GOS state better than estimated in the base case the cost per QALY gained reduced to £36,864 (an additional £213,139 to obtain 5.78 QALYs) but still did not fall below NICE thresholds.

It was estimated that over 67% of the 537 inpatient stays of less than 48 hours observed would need to be avoided in order for the CT scan all policy to have a cost per QALY of less than £30,000.

DISCUSSION

Follow-up of 1420 patients who did not have a CT scan in the AHEAD cohort identified seven cases (four deaths, three delayed diagnoses) that might have been identified by CT scanning at initial hospital attendance. Decision analytic modelling showed that appropriate treatment of these cases could have gained 3.41 QALYs but would have incurred £193,149 additional treatment costs and £130,683 additional costs for CT scanning. This produces an incremental cost of £94,895 per QALY gained, which is greatly above the usual threshold of £20-30,000/QALY that NICE uses to determine cost-effectiveness. Our analysis therefore suggests that CT for all anticoagulated patients with head injury, as recommended in NICE 2014 guidance, is not cost-effective compared to the selective use of CT scanning observed in practice when NICE 2007 guidance was in operation.

Our analysis has a number of strengths and weaknesses. It was based upon a large representative cohort of patients who presented to a wide range of hospitals. The methods used to estimate health gain from treating additional cases detected by universal CT scanning are transparent and reproducible, and were robust to the sensitivity analyses undertaken. A potential limitation is that some patients who suffered adverse outcome may not have been identified on follow-up leading to underestimation of the potential benefit of CT scan for all patients. However, it is worth noting that 10.79 QALYs would be required to reach the NICE threshold of £30,000/QALY for cost-effectiveness, so our conclusion regarding the lack of cost-effectiveness of unselective CT scanning would only be undermined if follow-up had identified less than 1 in 3 patients with adverse events. This seems extremely unlikely.

It is not believed that the threshold level for avoiding inpatient admissions of less than 48 hours would be plausible. Due to the age and comorbidities of this cohort of patients there will be many reasons for patients being admitted irrespective of whether a CT scan was performed. These reasons may be head injury-related such as observation, but are also likely to include other reasons such as intercurrent infections, injuries relating to attendance (other than the head injury) and for social reasons. Additionally, one could also postulate that by detecting incidental findings the additional CT scans could result in additional admissions. If so, the incremental costs of the CT all strategy would increase and it would become less cost-effective. We have no data to determine whether additional CT scans result in more or fewer admissions.

Most international guidance, including the National Emergency X-Radiology Utilisation Study (NEXUS II), CT in Head Injury Patients (CHIP), American College of Emergency Physicians (ACEP) head CT and the European Federation of Neurological Societies (EFNS)[19-22] advocate that all patients taking warfarin should have an immediate CT scan irrespective of injury severity, GCS or neurological symptoms. The UK guidelines (NICE) are based on the Canadian CT Head Rule(CCHR)[23] which excluded patients taking warfarin and up until January 2014, stated that a CT scan should be performed on patients taking warfarin if the patient presented with loss of consciousness or amnesia. These guidelines have now been updated to recommend all anticoagulated patients receive a CT scan but no new evidence appears to have been published to support this recommended change in practice. Our analysis suggests that the 2014 revision to NICE guidance has resulted in less cost-effective care.

Previous literature investigating the patient outcomes and costs associated with diagnosing and treating head injured patients who are taking anticoagulants are limited and difficult to compare to our analysis. Several recent studies have used decision analysis modelling to estimate the costs and benefits of CT scanning in the general (i.e. non-anticoagulated) head injured population[24-26] and have generally shown that using a clinical decision rule to select patients for CT scanning is more cost-effective than unselective CT scanning. The only study identified that focused solely on anticoagulated patients was undertaken by Li in 2012.[27] Li questioned how this cohort of patients should be managed due to the nature of delayed complications associated with anticoagulant use, whilst also considering the costs attached to CT imaging and admittance to hospital. The analyses were based on data taken from other studies and included repeated CT scans (2) and 24-hour admission per patient. The costs per year of a life saved in the US, Spain and Canada were estimated as $1 million, $158,000 and $105,000 respectively.

Future research is needed to validate our findings on the potential benefits, harms and costs of CT scanning since the introduction of NICE 2014, in addition to further work on the criteria used for deciding whether a CT scan is appropriate such as the use of serum protein biomarkers.

CONCLUSION

CT scanning for all anticoagulated patients with head injury is not cost-effective compared with selective use of CT scanning based on guidelines recommending scanning only for those with evidence of traumatic brain injury. A move (or return to) selective use of CT scanning would substantially reduce health care costs with only a small increase in potentially avoidable adverse outcomes.

Acknowledgements: We thank Rosemary Harper for her contribution as a patient representative throughout the duration of the study; all the clinicians and research staff in the participating hospital sites who identified patients in this study, without whose hard work this study would not have been possible.

Contributors: All authors provided substantial contributions to the conception, design, acquisition of the data, or analysis and interpretation of the study data. MK drafted the article and all authors contributed to its revision for important intellectual content. All authors approved the final version. SM is guarantor. All authors agree to be accountable for all aspects of the work ensuring that questions related to accuracy or integrity of any party of the work are appropriately investigated and resolved.

Transparency: SM affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Funding: This paper presents independent research commissioned by the National Institute for Health Research (NIHR) under its Research for Patient Benefit (RfPB) Programme grant reference number PB-PG-0808-17148. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

Competing interests: All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Ethical approval: NRES Committee Yorkshire and The Humber – Sheffield: 11/H1308/13.

Sponsor: Sheffield Teaching Hospitals NHS Foundation Trust – Ref.: STH15705.

Provenance and peer review: Not commissioned; externally peer reviewed.

Data Sharing Statement: No additional data are available.

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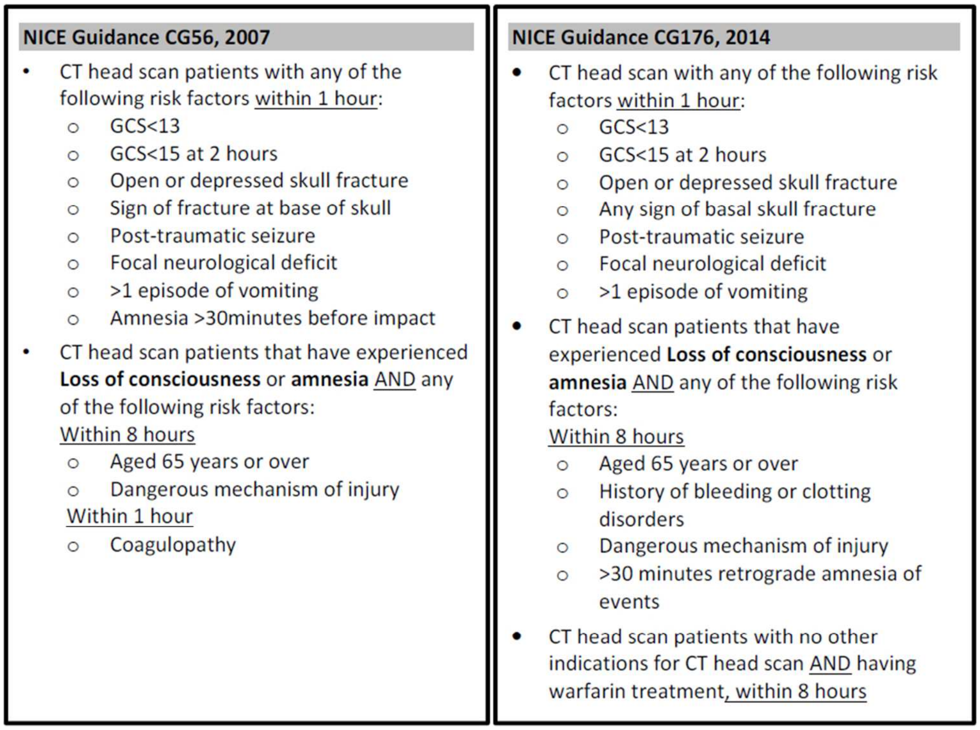

NICE Guidance CG56, 2007

- CT head scan patients with any of the following risk factors within 1 hour:
  - GCS<13
  - GCS<15 at 2 hours
  - Open or depressed skull fracture
  - Sign of fracture at base of skull
  - Post-traumatic seizure
  - Focal neurological deficit
  - >1 episode of vomiting
  - Amnesia >30minutes before impact
- CT head scan patients that have experienced **Loss of consciousness** or **amnesia** AND any of the following risk factors:
  Within 8 hours
  - Aged 65 years or over
  - Dangerous mechanism of injury

  Within 1 hour
  - Coagulopathy

NICE Guidance CG176, 2014

- CT head scan with any of the following risk factors within 1 hour:
  - GCS<13
  - GCS<15 at 2 hours
  - Open or depressed skull fracture
  - Any sign of basal skull fracture
  - Post-traumatic seizure
  - Focal neurological deficit
  - >1 episode of vomiting
- CT head scan patients that have experienced **Loss of consciousness** or **amnesia** AND any of the following risk factors:
  Within 8 hours
  - Aged 65 years or over
  - History of bleeding or clotting disorders
  - Dangerous mechanism of injury
  - >30 minutes retrograde amnesia of events
- CT head scan patients with no other indications for CT head scan AND having warfarin treatment, within 8 hours

Figure 1: NICE guidance 2007 versus 2014
Figure 1
79x59mm (300 x 300 DPI)

CHEERS checklist - Items to include when reporting economic evaluations of health interventions

Should all anticoagulated patients with head injury receive a CT scan? Decision-analysis modelling of an observational cohort

Section/item	Item No	Recommendation	Reported on page No/ line No
Title and abstract			
Title	1	Identify the study as an economic evaluation or use more specific terms such as "cost-effectiveness analysis", and describe the interventions compared.	1
Abstract	2	Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions.	2
Introduction			
Background and objectives	3	Provide an explicit statement of the broader context for the study.	4
		Present the study question and its relevance for health policy or practice decisions.	4
Methods			
Target population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	5
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	5
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	6
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	4
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	8
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	8
Choice of health outcomes	10	Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.	6,10
Measurement of effectiveness	11a	*Single study-based estimates:* Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	*4*

	11b	*Synthesis-based estimates:* Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.	*N/A*
Measurement and valuation of preference based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	N/A
Estimating resources and costs	13a	*Single study-based economic evaluation:* Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	*N/A*
	13b	*Model-based economic evaluation:* Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	*7-8*
Currency, price date, and conversion	14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.	7
Choice of model	15	Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended.	8
Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytical model.	5-8
Analytical methods	17	Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.	5-8
Results			
Study parameters	18	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.	6-8
Incremental costs and outcomes	19	For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.	10

Characterising uncertainty	20a	*Single study-based economic evaluation:* Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact of methodological assumptions (such as discount rate, study perspective).	
	20b	*Model-based economic evaluation:* Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	10
Characterising heterogeneity	21	If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.	N/A
Discussion			
Study findings, limitations, generalisability, and current knowledge	22	Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.	10-12
Other			
Source of funding	23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.	13
Conflicts of interest	24	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.	13