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AHEAD Study

The AHEAD Study: Managing anticoagulated patients who suffer head injury

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The problem

- Head injury is a common problem in emergency departments, worldwide
- ~1% UK population receives anticoagulation therapy
- Most commonly prescribed oral anticoagulant, Warfarin
- Anticoagulated patients who suffer head injury:-
  - Increased risk of suffering serious complications ……. But how big?
  - Lack of evidence on how patients should be managed
- Prospective research needed to gain understanding of complications and develop management strategies

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NICE Guidance: old & new

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 **LOC** or **amnesia** AND any of the following risk factors:

LoC

- 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 **LoC** 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

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Current Evidence

Study	No. of patients in study	% of patients anticoagulated	Incidence of ICH in anticoagulated patients
Li, 2001	144	100% (144)	6.2%
Lavoie, 2004	384	9% (35)	incidence of ICH not measured - mortality only
Fabbri, 2004	501	13% (66)	24%
Reynolds, 2003	32	100% (32)	25%
Gittleman, 2005	89	100% (89)	30.4% if GCS ≤ 14, 0% if GCS =15
Menditto, 2011	97	100% (97)	27.6%
Nishiijima, 2012	1064	72.2% (768)	5.1%

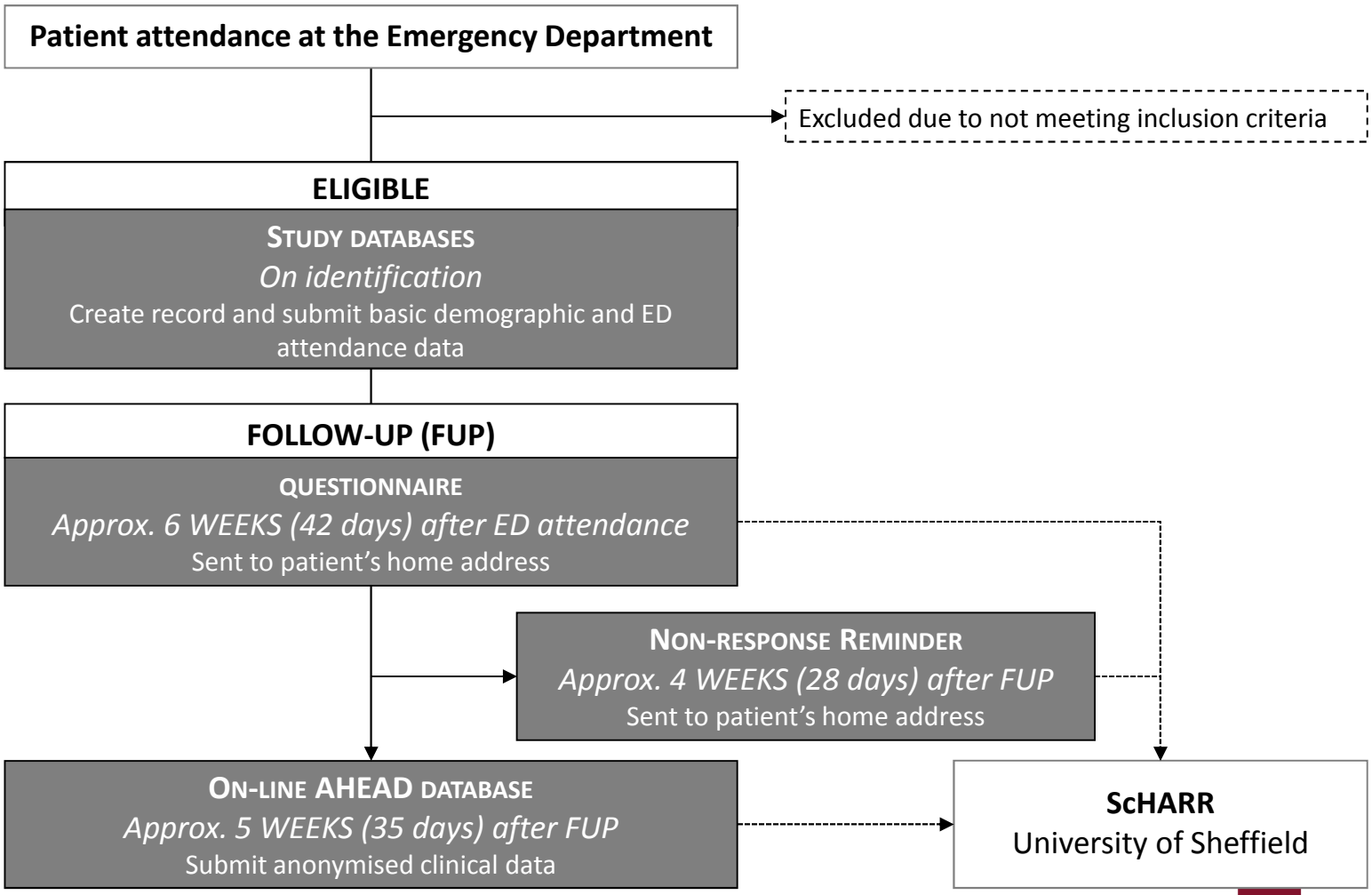
Study aims

- Identify and determine incidence of clinically significant outcomes
- Identify predictors of adverse outcomes
- Identify cost-effectiveness of different models of care
- Develop robust clinical guidance to reduce risk of complication and death

Setting & participants

- 33 acute hospital trusts with Type 1 Emergency Departments (EDs) throughout the UK
- Patient inclusion criteria:-
  - Aged 16 years and older
  - Anticoagulated, prescribed Warfarin only
  - Presenting with a head injury (defined as a clinically apparent injury to the head – including facial trauma) within the preceding 48 hours of ED attendance.
- Study sample size 3,000 patients – based on 5% estimated complication rate

Study process



Outcomes

- **Primary outcome** – Incidence of clinically significant brain injury defined by:-
  - Head injury-related death
  - Neurosurgery resulting from the initial injury
  - Clinically-significant CT head scan
  - Re-attendance to the ED with related significant complication (up to 10 weeks after the original attendance)
- **Secondary outcomes :-**
  - Identification of predictors of adverse clinical outcome
  - Costs per patient of the head injury as managed in the participating centres and when applied to a derived 'ideal' model

Recruitment

- Total sites (England & Scotland) = **33**
- Total number of patients = **3,566**
  - Figure excludes withdrawals (154)
- Clinical records (anonymised) = **3,534 (99%)**

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Patients

	N (3534)	%
Male	**1738**	**49.2**
Age (Mean (SD))	78.5 (11.6)	
16-29	17	0.5
30-39	36	1.0
40-49	65	1.8
50-59	133	3.8
60-69	**313**	**8.9**
70-79	**925**	**26.2**
80-89	**1674**	**47.4**
90+	**371**	**10.5**
INR (mean(SD))	2.67 (1.34)	
INR <2	741	21.0
INR 2-4	1941	54.9
INR>4	252	7.1
GCS 13-15	**3169**	**89.7**
GCS 8-12	33	1.0
GCS <8	27	0.76
Cause of injury: Fall	**3238**	**91.6**

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Outcomes

	n (3534)	%
Admission	**2216**	**62.7**
CT grading (n=2114)	**1979**	**56.0**
Significant intracranial abnormality likely to be due to injury	***192***	***9.1***
Other abnormality likely to be due to injury (e.g. scalp haematoma, uncomplicated fracture)	*417*	*19.7*
Other abnormality unlikely to be due to injury	*909*	*43.0*
Normal CT head scan	*461*	*21.8*
Reversal therapy	**189**	**5.3**
Prothrombin complex concentrate	*29*	*15.3*
Intravenous Vitamin K	*97*	*51.3*
Oral Vitamin K	*16*	*8.5*
Other	*46*	*24.3*
Neurosurgical procedures	**18**	**0.5**
Further hospital attendances	**557**	**14.2**
Head-injury related to original attendance	***37***	***1.0***
Other	*520*	*13.2*
Died	**249**	**7.0**
Head-injury related	***41***	***1.2***
Other	*158*	*4.5*
OVERALL COMPLICATION RATE	**208**	**5.9**

Basic data

- Adverse outcomes = **208 (5.9%)**
  - 41 (1.1%) deaths, 16 (0.5%) neurosurgery, 145 (4.1%) CT scans grade 1
  - Further Hospital Attendances (n=37, HI-related): 4 CT scans grade 1, 0 deaths, 2 neurosurgery (**overall 0.16% delayed complication**)
- Aim to identify variables (measured at presentation) which may predict the adverse outcome.
- Variables considered: age, gender, INR, GCS, symptoms: vomiting, amnesia, headache, loss of consciousness

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Univariate analyses

Univariate analysis	OR	Lower limit 95% CI	Upper limit 95%CI	No. of records
Age(70 -79)	1.534	0.939	2.506	**3534**
Age(80+)	1.558	0.995	2.440	
Age (70+)	**1.550**	**1.001**	**2.402**	**3534**
Gender (female)	0.793	0.600	1.049	**3534**
GCS(3-12)	**15.907**	**9.254**	**27.342**	**3229**
INR (2-3.9)	1.010	0.712	1.431	**2934**
INR(4+)	1.724	1.055	2.816	
INR(4+)	**1.712**	**1.124**	**2.607**	**2934**
Vomiting	**4.276**	**2.693**	**6.792**	**2634**
Loss of consciousness	**4.444**	**3.156**	**6.258**	**2914**
Headache	**2.046**	**1.354**	**3.092**	**2023**
Amnesia	**4.698**	**3.150**	**7.008**	**2070**

Logistic regression with adverse outcome as ‘outcome’ and hospital site treated as a random effect

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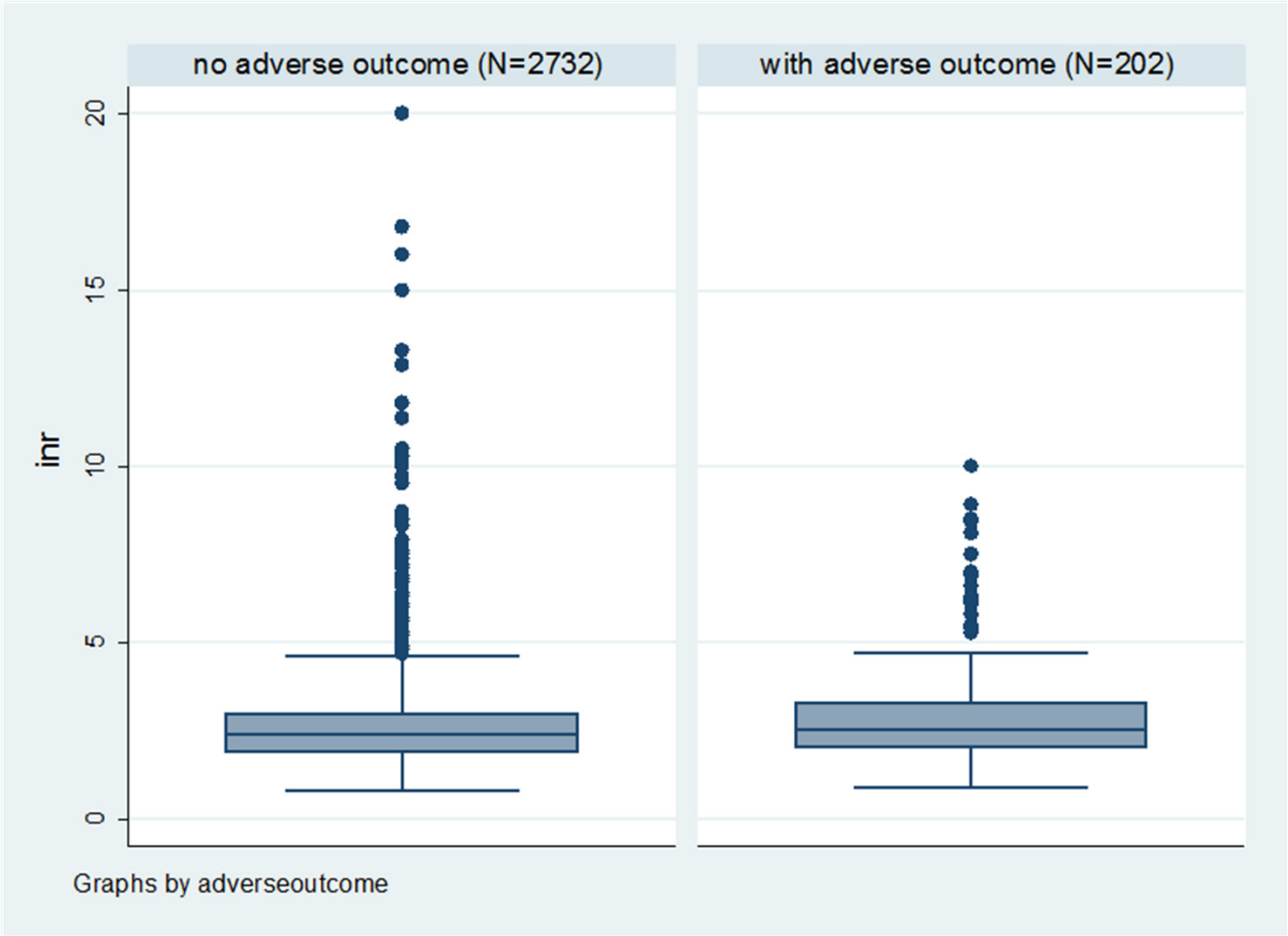
Distribution of INR by adverse outcome



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GCS below 13

- 60 patients have a GCS below 13 and 29 of these have an adverse outcome.
- The absolute risk for this group is 48% (95% CI 35.69% to 60.97%).
- Compared to those with GCS 13 and above, the relative risk is 8.7 (95%CI 6.46-11.73).
- As the risk in this small group is very high we removed these from the analysis to try to predict risk for those with GCS of 13 and above.

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Univariate analysis (GCS≥13)

Univariate analysis	OR	Lower limit 95% CI	Upper limit 95%CI	No. of records
Age(70-79)	1.496	0.877	2.551	**3169**
Age(80+)	1.459	0.894	2.382	
Age (70 plus)	1.471	0.912	2.371	**3169**
Gender (female)	0.871	0.642	1.182	**3169**
INR (2-4)	1.044	0.718	1.519	**2667**
INR(>4)	1.150	0.629	2.103	
INR(>4)	1.115	0.651	1.908	**2667**
Vomiting	**3.836**	**2.314**	**6.359**	**2434**
Loss of consciousness	**3.348**	**2.279**	**4.920**	**2654**
Headache	**1.990**	**1.299**	**3.049**	**1874**
Amnesia	**4.487**	**2.967**	**6.785**	**1928**

So when limiting the analysis to those with ≥GCS 13 only the four symptoms above are significant.

Relative Risk of Adverse Outcome

Risk level	Patients, n	Adverse events, n (%)	RR	95%CI	p-value
GCS=15 and no neurological symptoms	1838 (52.0%)	52 (2.8%)	--		
GCS=15 and at least one neurological symptom	828 (23.4%)	70 (8.5%)	2.76	1.88 – 4.06	<0.001
GCS below 15	358 (10.1%)	75(20.9%)	7.38	5.28 – 10.31	<0.001

Excludes records with missing data

NICE 2007

- **756** patients eligible for a CT scan, 70% identified due to risk factors other than warfarin
- In real practice, of these 756 patients:
  - **82.4%** [623] patients had a CT scan performed
  - **14.2 %** [107] significant intracranial abnormality identified
  - Average time to scan **4 hrs 42 mins**, **75%** scanned within 4hrs
- **133** patients eligible for a CT scan (according to NICE) but no CT scan performed

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NICE 2007: eligible patients

Patient outcomes	CT scan (n=623)		No CT scan (n=133)	
	n	%	n	%
Admitted	*501*	*80.4*	95	*71.4*
Length of stay, mean	*9.2 days*		4.5 days	
Reversal therapy	*106*	*17.0*	2	*1.5*
Neurosurgery	*12*	*1.9*	0	-
HI-related deaths	*25*	*4.0*	1*	*0.8*
Re-attended ED due to HI	*9*	*1.4*	1	*0.8*

* RTA, patient died in ED before CT could be done

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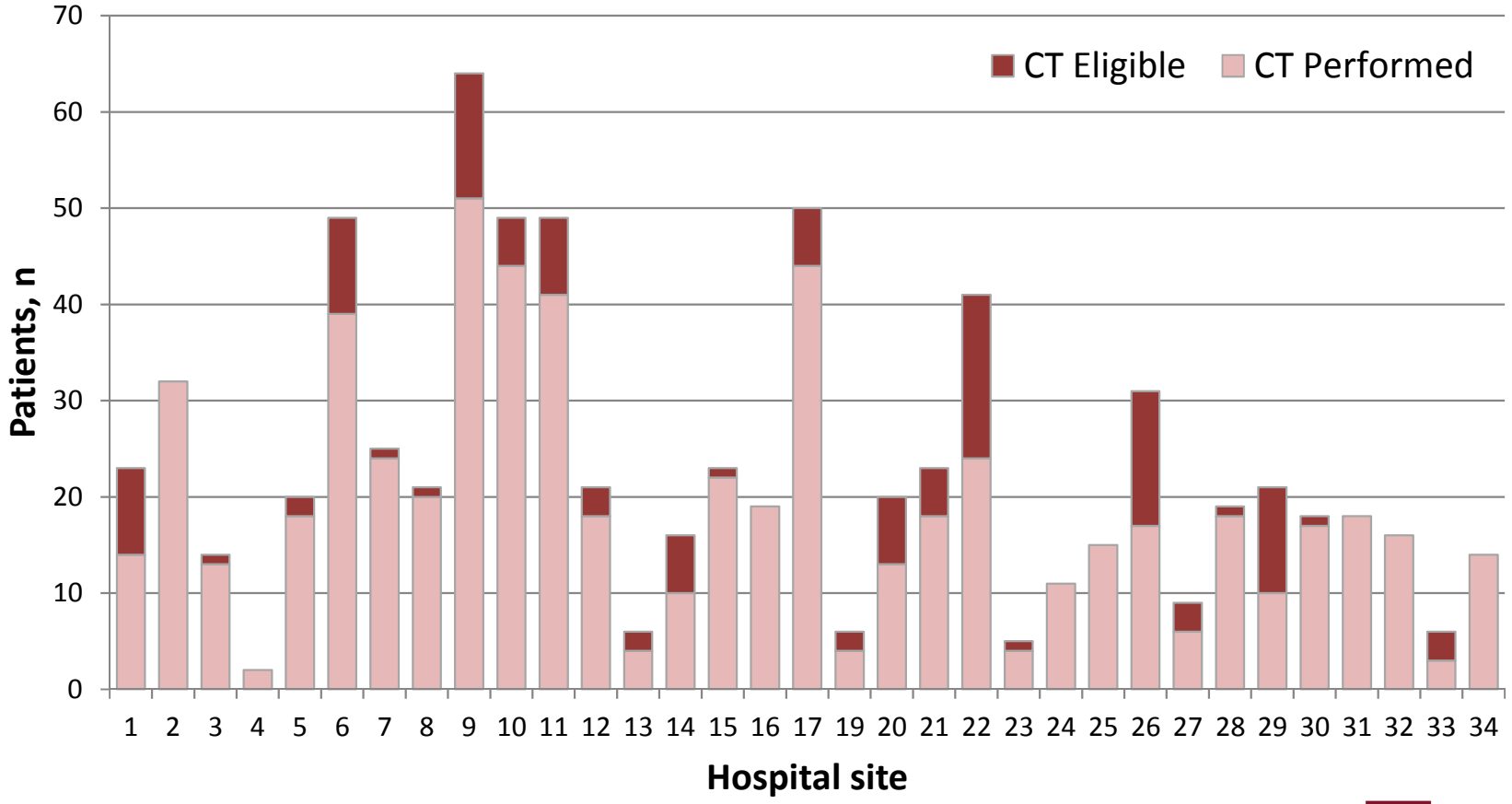
NICE 2007: site variability



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CT scanning 'Real World'

- According to NICE 2007 criteria, **20.4%** [756] AHEAD patients should have had a CT scan
- In practice, **60%** [2,114] patients actually had a CT scan
  - Significant intracranial abnormality identified in **9.2%** [195]
  - Average time to scan **6.3 hours**
- Outcomes for all anticoagulated patient cohort
  - HI-related deaths **1.2%** [42], no CT scan for 4 patients
  - Re-attended ED due to HI **1.0%** [37], no CT scan for 20 patients initially. 4 CT scans grade 1, 0 deaths, 2 neurosurgery (overall 0.16% delayed complication)
- Lots of variability across sites in use of CT scans

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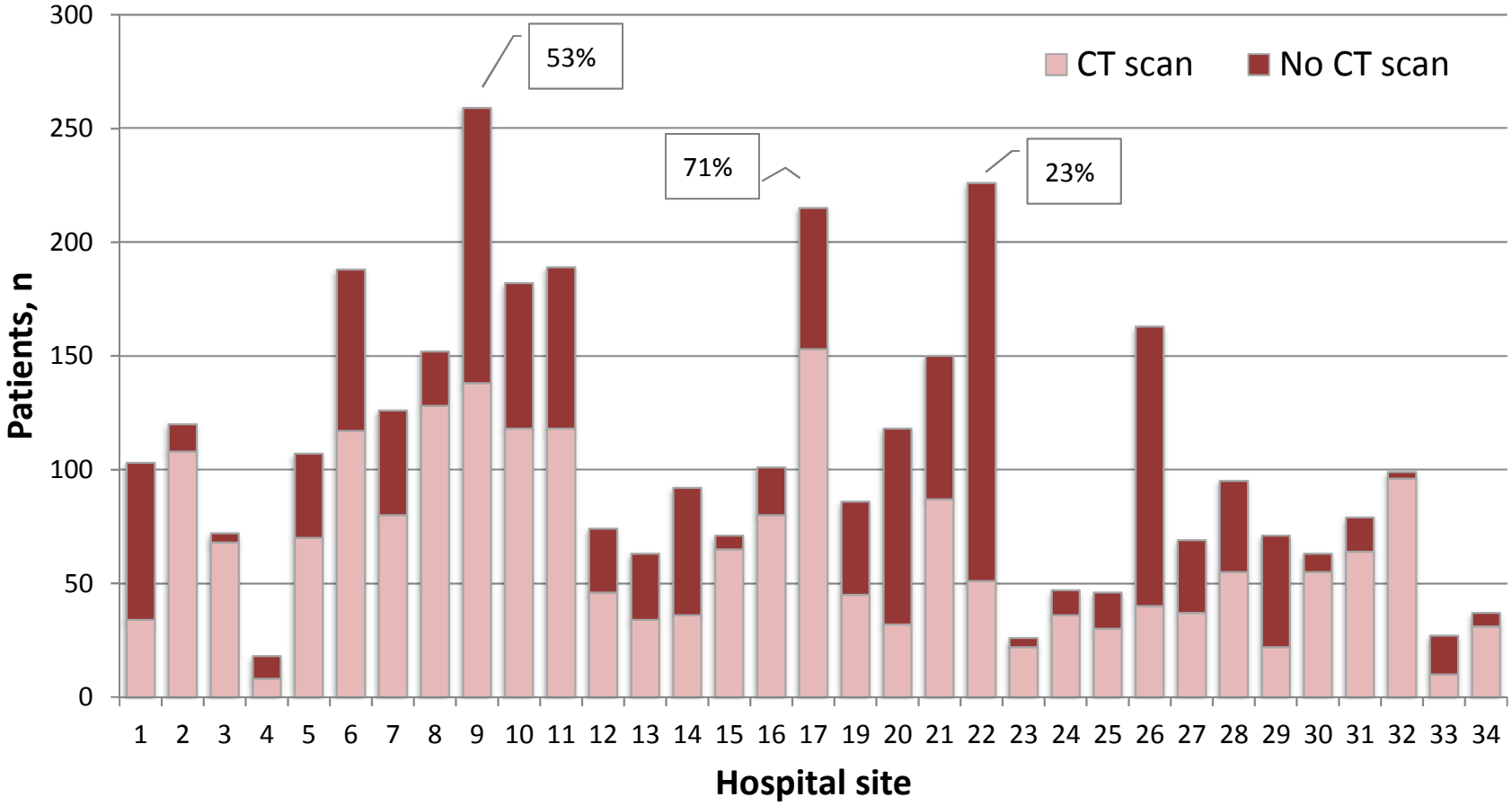
CT scanning: site variability



NICE 2014

- All patients taking warfarin that experience a head injury should receive a CT scan
- Based on this cohort, additional **40%** [1,420] patients
- Additional costs, time, resources
- Burden may not be felt the same across all hospital sites, impact some sites significantly more than others

Cost-effectiveness

- Various scenarios modelled to explore cost-effectiveness including:-

  CT scan no patients

  CT scan patients with significant risk factors (vomiting; LoC)

  CT scan all patients (NICE 14)

  CT scan 'Real World'

- Impact/ yearly costs and utility costs assigned to GOS level
- Considerable uncertainty i.e. observed data only, estimation of GOS score, assessment of the counterfactual

Take Home message

- Largest cohort of anticoagulated head injury patients reported
- Complication rate low @5.9% in all, 4.3% in GCS=15
- Delayed bleeds very low @0.16%
- Risk of complication significantly increased in alert patients who present with **amnesia, vomiting, loss of consciousness, headache**

- Majority of patients that fulfilled the NICE 2007 criteria did have a CT scan (82%), but significant inter-site variation
- A significant number of patients that did not fulfill the NICE 2007 criteria also had a CT scan
- Require a significant increase in CT scans performed to adhere to NICE 2014
- Modelling suggests 'Real World' CT scanning practice most cost-effective strategy…… go with your gut!!
- **Further studies include validation of these findings**

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With thanks to all our study sites for their participation

Barts Health NHS Trust	Nottingham University Hospitals NHS Trust
Blackpool Teaching Hospitals NHS Foundation Trust	Plymouth Hospitals NHS Trust
Cambridge University Hospitals NHS Foundation Trust	Poole Hospital NHS Foundation Trust
County Durham and Darlington NHS Foundation Trust	Portsmouth Hospitals NHS Trust
Gateshead Health NHS Trust	Royal Berkshire NHS Foundation Trust
Heatherwood and Wexham Park Hospitals NHS Foundation Trust	Royal United Hospital Bath NHS Trust
Hull and East Yorkshire Hospitals NHS Trust	Sheffield Teaching Hospitals NHS Foundation Trust
King's College Hospital NHS Foundation Trust	South Tees Hospitals NHS Foundation Trust
Mid Essex Health Services NHS Trust	The Queen Elizabeth Hospital King's Lynn NHS Foundation Trust
Milton Keynes Hospital NHS Foundation Trust	University Hospitals Bristol NHS Foundation Trust
Newcastle Upon Tyne Hospitals NHS Foundation Trust	University Hospitals of Leicester NHS Trust
NHS Lothian	University Hospitals Of Morecambe Bay NHS Foundation Trust
North Bristol NHS Trust	Western Sussex Hospitals NHS Trust
North Tees And Hartlepool NHS Foundation Trust	York Teaching Hospital NHS Foundation Trust
Northampton General Hospital NHS Trust	

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