Diagnosing SAH, are we ready to move forward?

Clinical Topic Review

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Disclosure: nothing to disclose, no conflict of interest.

I confirm this is my own work and there has been no plagiarism.
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Contents

Background & Clinical Dilemma

One of my junior FY2 doctors approached me for advice regarding a patient he was seeing. The patient presented with a sudden onset of severe headache associated with vomiting. He suspected Subarachnoid Haemorrhage (SAH) and requested a CT scan of his head, which turned out to be negative for any intracranial bleeding. His question was, "Do I need to admit this patient for Lumbar Puncture (LP) to rule out SAH or is a negative result from a high resolution CT is good enough to send this patient home?" I wondered if there was any evidence about the sensitivity of CT head scans in the diagnosis of SAH and that prompted me to explore the literature to find out what is recommended.

Introduction

Sudden onset of a sharp headache is one of the most common (1—2%) emergency presentations. One of the most sinister differentials of this symptom is subarachnoid haemorrhage, which is most commonly investigated and fortunately, least commonly found. SAH, defined as the presence of blood in the subarachnoid space, is diagnosed initially with a computed tomography (CT) scan or by the presence of blood cells or their breakdown products in cerebrospinal fluid and confirmed and by CT angiography.

The standardised incidence rate (adjusted for age) of SAH is 6-7 patients per 100,000 per year, in most populations.[1] Sudden onset acute headache and 'thunderclap' headache, described by the patient as if they were hit in the head with a baseball bat, is a classic presenting symptom of SAH or most commonly described as 'the worst headache of their life'. Clinically, the sudden onset is more important for diagnosis. Most patients are alert, awake and have no focal abnormal neurology, which could be

deceiving for including SAH as a differential. Red flags in history include nausea, occipital location, neck pain or stiffness and loss of consciousness. The onset during exertion in patients aged 40 or older, with or without past medical history of cystic lesions (e.g. polycystic ovary or multiple renal cysts) had a sensitivity of 98.5% and a specificity of 27.5% for SAH. Adding 'thunderclap headache' (i.e., an instantly peaking pain) and 'limited neck flexion on examination' resulted in the *Ottawa SAH Rule*, with a sensitivity of 100% and a specificity of 15.3%.

Though the *World Federation of Neurological Societies classification* and *Hunt-Hess risk stratification system* are available to predict the outcome and *Ottawa SAH Rule* been mentioned as Clinical Decision Rule but there is no nationally or internationally agreed pre-test probability score system available which could guide towards the application of CT Head and after that a further work up could be chosen on the basis of post-test probability.

A major cause of spontaneous SAH is a ruptured aneurysm; an intracranial Saccular or berry aneurysm being the cause in approximately 85% of patients. Non-aneurysmal perimesencephalic haemorrhage accounts for 10% of cases and the remaining 5% are derived from uncommon causes, including mycotic aneurysms, arteriovenous malformations and bleeding disorders. An aneurysmal hemorrhage occurs most commonly in 40-65 year olds, although it may occur at any age.

Current RCEM guideline (2009) on SAH, recommends non-contrast CT head as the first line investigation. If CT head is negative, sub-optimal, or inconclusive for any reason, CSF analysis should be performed. If CSF is positive for blood or bilirubin, the next line of investigation is CT angiography.

Objective

This clinical topic review aims to assimilate the current evidence of the diagnostic ability of modern, multi-detector CT to confirm the diagnosis of intra-cranial bleeds and need of lumbar puncture to rule out SAH.

Methodology

The search strategy was carried out using the following established method:

Step 1 – formulating a three-part, answerable question on the basis of a hypothesis

Step 2 – conducting the search

Step 3 – finding evidence

Step 4 – appraising evidence

Step 1: Three-part question

This study was designed to investigate the hypothesis that the latest multi-detector CT imaging can exclude SAH in patients with a sudden onset headache. Therefore, a three-part question was formulated:

"(In patients presenting with acute lone headache) is (modern CT sensitive enough to rule out) (Subarachnoid Haemorrhage)".

Step 2: Conducting the search

A literature search was conducted using:

1) Medline 1950 – May 2015, via NHS Evidence Health Information Resources

2) CINAHL, 1981–present, via NHS Evidence Health Information Resources

3) EMBASE, 1980–present, via NHS Evidence Health Information Resources

4) Cochrane Database – 'subarachnoid hemorrhage', 'CT Head', 'CSF Analysis'.

5) Google Scholar – 'subarachnoid hemorrhage', 'CT Head', 'CSF Analysis'.

6) References of selected papers were searched for any other relevant articles.

7) Manual searching of key journals (EMJ, Neurosurgery, Stroke, Radiology)

8) BestBets website (www.bestbets.org)

9) International Clinical Trials Registry Platform (http://www.who.int/ictrp/en/),

The Meta registers of clinical trials, (http://www.controlled-trials.com/mrct/) and (http://www.clinicaltrials.gov), were searched for unpublished and incomplete trials.

A combination of medical subject headings (MeSH), headings and title and abstract key words were used for a literature search using the resources above:

1) Subarachnoid He*morrhage, intracranial Haemorrhage NOT trauma$, acute headache, Sudden onset headache, Thunderclap headache.

2) Head CT Scan, high resolution CT, High definition CT, Multi detector CT.

3) Lumbar Puncture, spinal tap, and spinal fluid analysis, CSF Analysis.

Step 3: Finding the evidence (Appendix 2)

After excluding duplicates and limiting results to humans and those in English, results were as follows.

Table 1: Summary of literature search

No	Key Words	Medline	Embase	CINHAL
1	SAH	79040	234174	15542
2	Multidetector CT/CT Head	158725	202096	12244
3	CSF Analysis	6335	19090	979
4	Combined 1,2,3	91	66	30

Selection of relevant papers

Inclusion criteria

- Studies looking at non-traumatic SAH were included
- Studies looking at CT results and/or comparing those with LP results were included
- Studies looking at safety and efficacy of CT scans were included.

Exclusion Criteria

- Studies of subjects with any neurological deficits.
- Studies looking at other aspects of SAH diagnosis e.g. angiography.
- Studies involving healthy volunteers as subjects.
- Case reports

Checking & Validation of searches

These searches have been checked & reproduced by

- Mr Imran Zakria (Consultant ED).

Step 4: Appraising the evidence

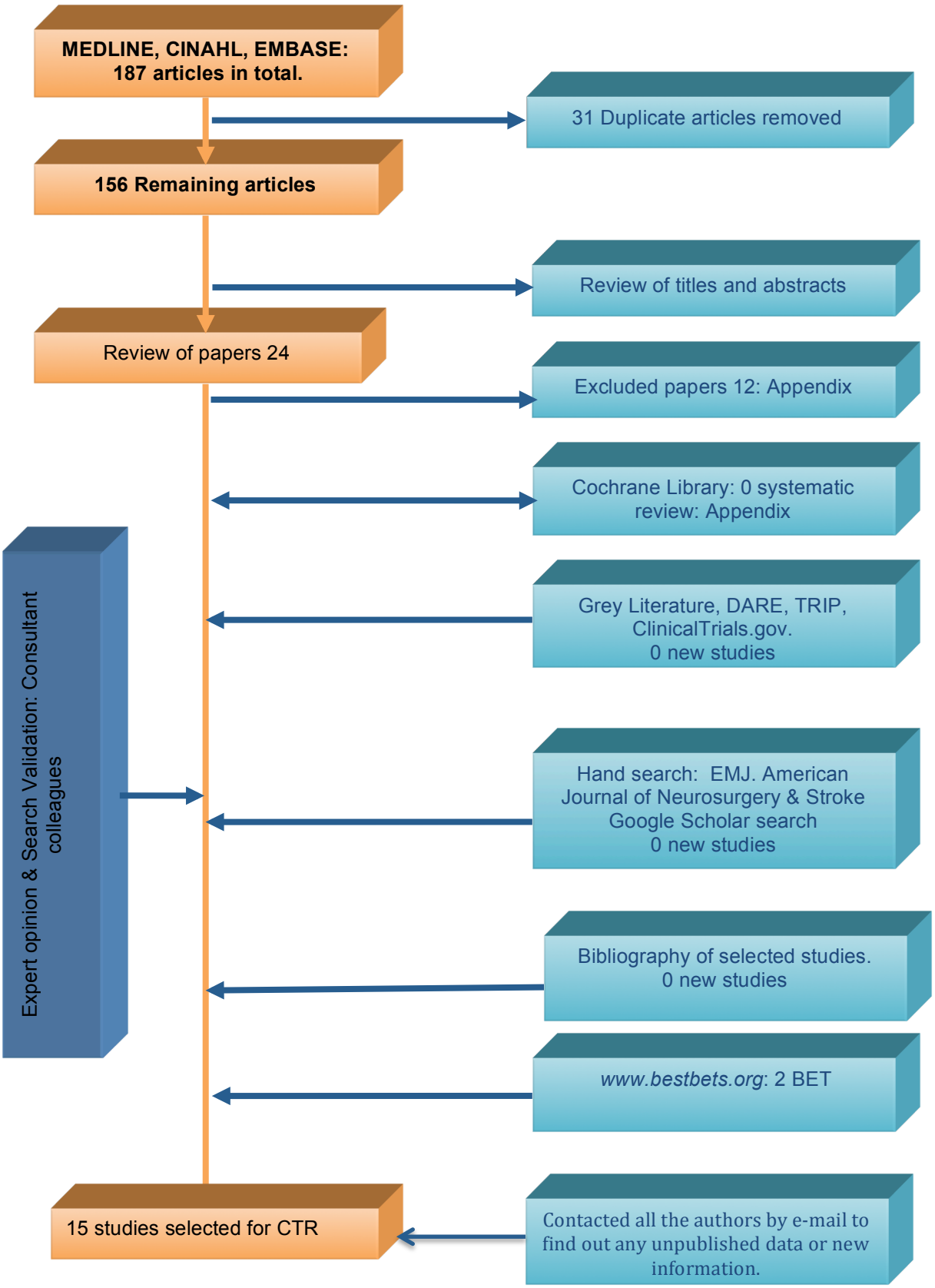


Table 2: Appraisal of the evidence in the literature.

<table>
<tr><th>Author, Country & Date</th><th>Patient Group</th><th>Study Type</th><th>Key Results</th><th>Outcome</th><th>Comments</th></tr>
<tr><td>1) Sayer D et al
UK
2015</td><td>Total of 2248 patients presented with acute onset headaches included in a study conducted in 6 urban Type 1 EDs.</td><td>Retrospective, multicenter observational cohort study.
OCEBM—Level of evidence 2B</td><td><table><tr><td>Total LP performed</td><td>2248</td></tr><tr><td>Total Positive</td><td>4% (92)</td></tr><tr><td>True Positive</td><td>0.4% (9)</td></tr><tr><td>Negative</td><td>1507 (67%)</td></tr><tr><td>Inconclusive & Un-interpretable</td><td>13% & 16%</td></tr></table>NNT= Number Needed to Tap(LP) to find one true positive result = 250</td><td>0.4% LP found true positive, very low diagnostic yield.
3.6 % False Positive, 9 times higher than TPs.</td><td>Retrospective review of charts.
Huge number of inconclusive & un-interpretable samples, which were not investigated further.
All patients went through CT first and then LP.</td></tr>
<tr><td>2) Blok MK et al
Netherland
2015</td><td>760 patients presented between January 2007 and January 2013 with spontaneous acute headache were reviewed.</td><td>Retrospective, multicenter Cohort study
OCEBM—Level of Evidence 2B.</td><td>760 patients’ head CT <6hrs of onset of symptoms, followed by LP >12hrs.
NPV for detection of SAH= 99.9%(95%CI 99.3—100%)</td><td>High NPV of CT studied by Staff Radiologist.
Change in practice is proposed to withhold LP if CT has been done within 6hrs of onset of symptoms.</td><td>Retrospective study design.
Large sample size & blinding of neuroradiolgists for Final out come.</td></tr>
<tr><td>3) Backes D et al
Netherland
April 2012</td><td>1039 Adult patients admitted b/w Jan 2005 & Jan 2012, two databases, one confirmed with CT Head & other confirmed with CSF analysis were compared.</td><td>Tertiary Care Hospital Retrospective Study
OCEBM—Level of Evidence 2B.</td><td><table><tr><td colspan="4">Sensitivity of CT Head for entire population=95.4%</td></tr><tr><td colspan="2">CT <6hrs
137 pts.</td><td colspan="2">CT>6hrs
113 pts.</td></tr><tr><td rowspan="2">Confirmed by CT= 68</td><td>Negative CT=69</td><td rowspan="2">CT Confirmed 37</td><td>Negative CT=76</td></tr><tr><td>CSF+ 1 CSF- 68</td><td>CSF+ 5 CSF- 71</td></tr><tr><td colspan="2">Sensitivity 98.5%
(95% CI=92.1—100)</td><td colspan="2">Sensitivity 90.0%
(95% CI=76.3—97.2)</td></tr></table></td><td>CT performed within 6hours after Acute Headache onset is a perfect tool to diagnose SAH, while patients presenting after 6hrs of symptoms onset CSF Analysis could be necessary if CT Head is negative.</td><td>Retrospective design, selection Bias,
Inability to generalize to low volume hospitals or where radiologists are not specialist neuro-radiologists.</td></tr>
</table>

4) Gee C et al Utah, USA 2011	134 Patients referred with diagnosis of SAH to an urban referral center, b/w Jan 2005 to Dec 2008.	Retrospective study OCEBM—Level of Evidence 2C.	Bayesian Analysis & Beta probability distributions were used. 131/134 had Positive CT Head by 16-slice or better scanner. Posterior probability distribution with a median sensitivity of 97.3% (95%CI 91.3—99.6%) was found.	High sensitivity of 16-slice or greater non-contrast CT of the head for SAH Very small False-Negative rate of these scanners.	Retrospective nature, single center study, small number of patients, who were already diagnosed with SAH. No Blinding used.
5) Perry JJ et al ON, Canada 2011	3132 adult patients enrolled over the period of 9 years (2000—2009) with worst headache ever, 240 had subarachnoid haemorrhage.	Prospective, multicenter, cohort study OCEBM—Level of Evidence 1B.	<table><tr><td></td><td>CT< 6</td><td>CT>6</td><td>All Patients</td></tr><tr><td>Sens. %</td><td>100</td><td>85.7</td><td>92.9</td></tr><tr><td>Spec. %</td><td>100</td><td>100</td><td>100</td></tr><tr><td>NPV %</td><td>100</td><td>99.2</td><td>99.4</td></tr><tr><td>PPV %</td><td>100</td><td>100</td><td>100</td></tr></table>	Modern multi-row detector 3rd generation CT is highly sensitive for SAH, if performed with thin slices within six hours of onset of symptoms, and interpreted by a qualified radiologist.	Good sample size, multicenter, blinding was used. Absence of single standard criterion for SAH.
6) Cortnum S et al Denmark 2009	510 patients admitted from Jan. 2000 to Dec. 2005, with suspected & verified SAH	Retrospective, university Hospital level study. OCEBM—Level of Evidence 2B.	<table><tr><td colspan="3">499 patients met the inclusion criteria</td></tr><tr><td>203/499 had CT-/LP- 296/499 had SAH+ 295/295 proven by CT</td><td>Up to 5 Days</td><td>Sensitivity 100%</td></tr><tr><td>1/296 proven by LP+</td><td>On 6th day</td><td></td></tr></table>Sensitivity 100% up to 5 days Overall CT scanning Sensitivity 99.7% (95% CI 98.1–99.9%) Specificity 100% (95% CI 98.2–100%).	CT scanning is an excellent evaluating Tool for diagnosis of SAH. This study has shown that CT has a sensitivity of 100% from day 1 to day 5.	Good sample size Testing techniques not mentioned clearly.
7) Byyny RL et al USA 2008	149 Patients presented to the ED in b/w August 2001 to Dec. 2004 with the diagnosis of SAH	Retrospective review of charts, Academic tertiary care hospital, Cohort Study OCEBM—Level of Evidence 2B.	149 patients diagnosed with CT & LP. 139/149 diagnosed by CT only with Sensitivity of 93% (95%CI 88—97%)	Non-Contrast CT has inadequate sensitivity to serve as a sole diagnostic modality for the detection of SAH.	Retrospective study design. No preformed set data to record patient's details. CT interpretation by inexperienced radiologist resulting in false negatives.
8) Carley S UK 2008 (last modified)	Literature review & critical appraisal. Medline engine searched for studies from 1966 till 2008, using Ovid interface.	Retrospective Systematic r/v in the form of Best Bet. OCEBM—Level of Evidence 2A.	Sensitivity of CT found as high as 91—98%. This goes further down with increasing duration to CT from onset of headache. Sensitivity depends upon the concentration of blood in CSF.	Sensitivity is high, but need to be up to 100% considering the mortality & morbidity of the condition. CT alone not enough to rule out SAH.	Thorough search of current evidence available up to that time. Good critical appraisal of literature.

<table>
<tr>
<td>9) Lourenco AP et al
USA
2007</td>
<td>61 Patients admitted with S/S suggestive of SAH, in b/w sep.2003 & Dec.2004.</td>
<td>Retrospective
Academic Tertiary Center
Cohort Study
OCEBM—Level of Evidence 2B.</td>
<td>60/61 had SAH on CT scan of head
01/61 had SAH on CSF analysis but not on CT.
Overall sensitivity of CT=97% (95%CI 84—100%)</td>
<td>16-Detector CT Scanner results compared with Single detector CT. No significant difference found.</td>
<td>Retrospective design
Single center study
Small sample size</td>
</tr>
<tr>
<td>10) Boesiger BM et al
North Carolina
USA
2005</td>
<td>177 Adult patients presented to the ED with a complaint of acute headache, from January1, 2002 to December 31, 2002</td>
<td>Retrospective
Academic Level 1 Trauma Center
Cohort Study
OCEBM—Level of Evidence 2B.</td>
<td>177 patients enrolled according to inclusion criteria.
<table><tr><td></td><td>SAH$^+$</td><td>SAH$^-$</td></tr><tr><td>CT$^+$</td><td>6</td><td>1</td></tr><tr><td>CT$^-$</td><td>0</td><td>170</td></tr></table>
Sensitivity of CT=100% (95%CI 61—100%)
Specificity of CT=99.4% (95%CI 96.8—99.9%)
Pre-test probability for SAH=3.4%</td>
<td>Study suggests a sensitivity of 100% for fifth generation CT scanners with wide 95%CI of 61.0–100%.
Low pre-test probability, Higher Specificity</td>
<td>Retrospective chart review, missing few cases in enrolling right patients, Non-compliance for LP or LP not considered necessary for low probability cases.</td>
</tr>
<tr>
<td>11) Coates TJ et al
UK
2005</td>
<td>A literature review & critical appraisal performed to estimate the likelihood ratios to detect SAH.</td>
<td>Bayesian Analysis of Data
OCEBM—Level of Evidence 1B.</td>
<td><table><tr><td>Time</td><td>LR-</td></tr><tr><td><12hrs</td><td>0.02</td></tr><tr><td><24hrs</td><td>0.07</td></tr><tr><td>>24hrs</td><td>0.18</td></tr></table>Likelihood ratio of Negative CT scan decreases with time.</td>
<td>Risk/benefit ratio of LP is unclear in patients with low pre-test probability & early CT Scan. Need of Stratification rule is emphasized.</td>
<td>Retrospective review of data.
Difficult statistical calculations.
NNI analogue to NNT calculated, showing interesting facts</td>
</tr>
<tr>
<td>12) Morgenstern, LB
TX, USA
1998</td>
<td>455 Patients attended ED from March 1995 through June 1996 with worst headache or severity of 10/10.</td>
<td>Prospective study
Large academic hospital
OCEBM—Level of Evidence 1B.</td>
<td><table><tr><td colspan="4">Patient fulfilled the inclusion criteria= 107</td></tr><tr><td colspan="2"><24hrs of onset
51/107</td><td colspan="2">>24hrs of onset
56/107</td></tr><tr><td>CT$^+$
14/51</td><td>CT$^-$
37/51</td><td>CT$^+$
4/56</td><td>CT$^-$
52/56</td></tr><tr><td colspan="2">CT$^-$/LP$^-$=77/79</td><td colspan="2">CT$^-$/LP$^+$=2/79</td></tr><tr><td colspan="4">CT$^+$=18/107 (95%CI=10—25%)</td></tr><tr><td colspan="4">Sensitivity = 97%</td></tr></table></td>
<td>2/107 CT$^-$/LP$^+$= (95%CI 0.3 to 8.8%)

Which is lower than with early generation CT Scanners. But author suggested that patient should under go CSF analysis in case of negative CT.</td>
<td>Prospective study design
Complete blindness of radiologist
Two separate radiologists interpreted the scans
Comprehensive CSF analysis</td>
</tr>
</table>

<table>
<tr>
<td>13) Sames TA et al
TX, USA
1996</td>
<td>A retrospective chart review of 349 patients with confirmed SAH diagnosis, admitted between March 1988 and July1994.</td>
<td>Retrospective, Single center, cohort study
OCEBM—Level of Evidence 2B.</td>
<td>Of 181/349 met inclusion criteria
Patients divided in two groups
<table>
<tr><td>Group I<24hrs (n=144)</td><td>Group II>24hrs (n=37)</td></tr>
<tr><td>Sensitivity=93.1%</td><td>Sensitivity=83.8%</td></tr>
<tr><td colspan="2">Overall sensitivity=91.2%</td></tr>
</table>
</td>
<td>New Generation CTs do not perform 100% yet, and its efficiency even drops with time elapsed from the onset of symptoms. Therefore, Value of LP could not be ignored.</td>
<td>Inherent limitations of retrospective design, lack of available records, and level of radiologist interpreting CT scans not observed in study.</td>
</tr>
<tr>
<td>14) Sidman R et al
USA
1996</td>
<td>Charts reviewed retrospectively of 140 Patients, who attended ED, from Jan 1991 to Sep.1994, who were coded non-traumatic SAH as their final diagnosis.</td>
<td>Retrospective study
Tertiary care hospital
OCEBM—Level of Evidence 2B.</td>
<td>
<table>
<tr><td colspan="2">140 patients charts were reviewed</td></tr>
<tr><td>CT^{+}=129/140</td><td>LP^{+}=11/140</td></tr>
<tr><td><12hr presentation</td><td>>12hr presentation</td></tr>
<tr><td>80/140 CT^{+}=80/80
Sensitivity=100%
(95%CI 95—100%)</td><td>60/140
CT^{+}=49/60
Sensitivity=81.7%
(95%CI 69.5—90.4%)</td></tr>
<tr><td colspan="2">Fisher’s exact test; p<0.0001</td></tr>
</table>
</td>
<td>Use of 3rd generation CT Scanner.
100% sensitivity for CT scans within 12hrs of symptoms.
It lowers down to 69.5 – 90.4 % if scan is done more than 12hrs after the onset of symptoms.</td>
<td>Retrospective, small sample size, unauthentic CT report issued by duty radiologist regardless of experience.</td>
</tr>
<tr>
<td>15) Wee NV et al
Netherland
1994</td>
<td>175 Patients admitted between Jan. 1989 and Jan. 1993 with the main complains of Acute headache but without any abnormal neurology. They all had CT Head done in 12 hrs.</td>
<td>Prospective study
University Hospital level Cohort Study
OCEBM—Level of Evidence 1B.</td>
<td>175 patients were investigated within 12 hours.
117/175 found positive for SAH on CT head.
2/58 found positive for SAH on CSF analysis with normal CT (3%; 95%CI 0-4-12%). Thus CT was False Negative in 2/119 patients with SAH (2%; 95% CI 0.2-6%).</td>
<td>This study showed 98% sensitivity of CT Head in the diagnosis of SAH.</td>
<td>Technical deficiencies & lack of proper statistical analysis</td>
</tr>
</table>

Synthesis of Evidence

The studies appraised above mainly investigated the following questions,

1) How sensitive is CT head in the diagnosis of SAH?
2) Is LP necessary and safe?

Though most of these studies (10/15) are retrospective chart review, they are very relevant to the starting hypothesis. With respect to the sensitivity of CT scans, time between symptom onset and scanning seems to be most important. Most of the studies divided the time to head CT scan into 6, 12 and 24 hours periods, and assessed the sensitivity of scans within those time limits.

The majority of studies concluded that CT scans were effective. Backes *et al.* (2012) suggested that scans performed within 6 hours of acute headache onset were the perfect tool for diagnosing SAH. Gee *et al.* (2011) found a 16-slice contrast CT of the head for SAH to have high sensitivity, with a very small false negative rate for these scanners. Similarly, Perry *et al.* (2011) indicated that modern multi-row detector 3rd generation CT is highly sensitive for SAH, if performed with thin slices within 6 hours of symptom onset. Cortnum *et al.* (2009) agreed, stating that CT scanning is an excellent evaluation tool for SAH diagnosis, with a sensitivity of 100% found up to 5 days of symptom onset, which is the longest duration for blood to be detected in the CSF. A very high level of sensitivity was also indicated using a 16-detector CT scanner, estimating sensitivity in SAH diagnosis of 97% (Lourenco *et al.*, 2007). Similarly, Boesiger *et al.* (2005) indicated 100% sensitivity for 5th generation CT scanners, although with a broad 95% confidence interval from 61.0% to 100.0%. High specificity at 99.4% was also indicated within this study, with a 95% confidence interval ranging from 96.8% to 99.9%. Similar results were found by Morgenstern (1998). Sidman *et al.* (1996) reported excellent results, with a sensitivity of 100%

found if a CT scan was done within 12 hours of symptom onset; the figure decreased to 69.5%-90.4% if scanning was done later than at 12 hours. Finally, Wee *et al.* reported a CT head scan sensitivity of 98% for SAH diagnosis.

In conclusion, the vast majority of the studies included found high specificity and sensitivity and indicated CT to be efficacious and appropriate. Table 3 summarises the findings described above.

Table 3: Summary of synthesis of evidence

Study	Time to CT (hours)	Sensitivity	95% CI
Backes *et al*	< 6	98.5%	92.1—100
Perry *et al*	< 6	100%	97—100
Cortnum *et al*	Up to 5 days	99.7%	98.1—99.9
Byyny *et al*	--	93%	88—97
Lourenco *et al*	--	97%	84—100
Boesiger *et al*	< 6	100%	61—100
Sidman *et al*	< 12	100%	95—100
Wee *et al*	< 12	98%	

Out of these 9 studies, GEM NET has considered the last 6 studies in RCEM SAH guidelines in 2009. Two of these studies do show 100% sensitivity of CT head, however their 95% CI were very wide making them less useful. The first 3 studies here in Table 3 have come up more recently. These are showing 100% sensitivity of CT head scan in first 6 hours of onset of headache with quite narrow 95% Confidence Interval while the Cortnum et al mentioned 99.7% Sensitivity with 95% CI (98.1—99.9) for CT heads done up to 5 days.

As far as CSF analysis is concerned, the question remains of whether LP, an invasive procedure with its inherent complications and high false positive rate, is safe? A recent study by Sayer et al (2015) shows some very interesting facts. The study looked at 2248 patients, of which 67% were negative, 13% inconclusive, 16% were un-interpretable, while 4% were positive for blood. Of these 4%(92), only 0.4% (9) were true positive while a large section (3.6—83%) of these blood-positive LPs were false positive. Therefore, NNT—numbers needed to tap calculated at 250, i.e., 250 taps(LPs) needed to be done for one positive result. Similarly, Coates *et al.* (2005) calculated the negative likelihood ratio of CT scans at 12(0.02), 24(0.07) and more than 24(0.18) hours duration. They calculated a very interesting parameter—'number needed to investigate (NNI)' an analogue to 'number needed to treat'. According to their negative likelihood ratio (LR-) of 0.02 at 12 hours, with the pre-test probability of 5%—more than 1000 LPs would be required to detect one SAH.

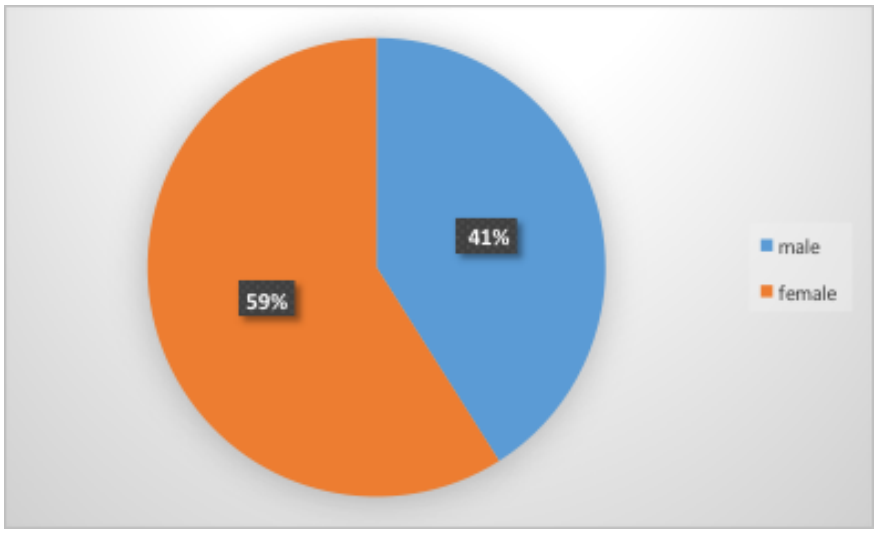
Furthermore, it is found that most false negative CTs were from patients who had a pre-mesencephalic type of SAH[1, 8], which is usually a non-aneurysmal leak. It is not considered as serious as an aneurysmal rupture and is usually treated conservatively; although this could happen in 1 out of 20 patients. Therefore, Blok *et al*. presented good statistics on these false negative CTs, and stated that this type of SAH will be missed in 1 out of 15,200 (760x20) patients, with 760 being his sample size. He also mentioned that 15,200 LPs would be carried out to find one SAH, which is actually not even serious enough for emergency treatment.

Personal Work

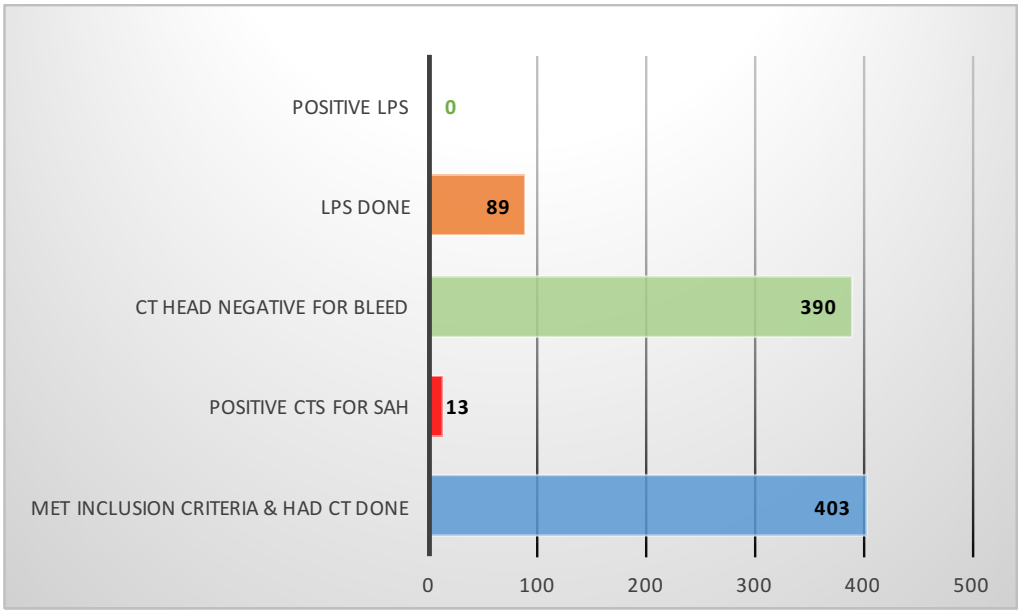
A) Audit (Appendix 3)

A study was designed and executed with departmental approval, to assess the sensitivity of a multi-detector CT scanner in the diagnosis of SAH, at our district general hospital with an annual patient turnover of approximately 85,000. The Emergency Department (ED) electronic medical records and radiology information system were queried to identify all patients who presented with acute headache, from 1st January 2014 to 31st December 2014, and had a CT scan of their head for SAH detection. Patients' records were retrospectively reviewed for those who had non-traumatic headache of a sudden onset nature, and did not have any abnormal focal neurology.

A total of 771 patients attended our Emergency Department with the major complaint being headache, which was significant enough for a CT head scan being performed in order to diagnose suspected intracranial bleeding. Out of the 771 patients, 403 (52%) had non-traumatic, sudden onset, 'thunderclap' type headache. Of these 403, only 13 patients' CTs were positive for SAH. The mean age of the patients who presented with sudden onset headache was 51 years old (with a range of 31-69 years), with 59% being female.



CTs of 309 patients did not indicate any acute bleeding, although some CTs were positive for other pathologies, e.g. meningioma, old infarcts and other space occupying lesions, which are not relevant to the present study.



The charts of the 403 patients who met all the inclusion criteria were examined retrospectively. As the exact time of symptom onset was not indicated in 189 patients, the length of time they had a headache before the CT scan of their head could not be accurately determined. However, for the 13 patients who had a positive CT for bleeding, the mean elapsed time between the symptom onset and the CT scan was 16.8 hours (ranging from 3-38 hours).

The remainder of the patients (390/403) had a negative CT for bleeding, with 89 of the 390 being admitted for LP. The mean time of carrying out LP from the onset of symptoms was 56 hours (ranging from 16 hours to 2 weeks). It was found that all 89 patients who had LP were negative for blood cells or xanthochromia (confirmed by spectrophotometry). This finding indicated that CT had diagnosed SAH in all 13 patients with 100% sensitivity, and among patients whose CT was negative, their LPs

were negative as well. Unfortunately, it is not possible to comment on the outcomes of those 13 patients who were SAH positive on their CT scans, as they were referred to a tertiary care neurosurgical unit and followed up there. Further information on these patients could not be found. However, we attempted to randomly contact those patients who had LPs to find out if any had experienced a serious complication post-procedure. We could only contact 30 out of the 89 patients who did not mention any major complaints other than a headache for a few weeks before it settled completely, but none had to be re-admitted for this reason or any other complications. We also randomly contacted those whose CTs were negative, but they did not go for or were not offered LPs (40 patients), and we found that none had any serious problems afterwards up until 11-18 months post ictus. As mentioned above, we found 100% sensitivity for CT scans of the head in the diagnosis of SAH in our limited retrospective cohort study. Our findings can be summarised in the following table.

Table 4: Summary of personal work results

		Subarachnoid Haemorrhage		
		Positive	Negative	
CT	Positive	True Positive (TP) 13	False Positive (FP) 0	PPV=TP/(TP+FP) 100%
	Negative	False Negative (FN) 0	True Negative (TN) 390	NPV=TN/(FN+TN) 100%
		Sensitivity =TP/(TP+FN) 100%	Specificity =TN/(FP+TN) 100%	

B. Abstract (Appendix 5)

An abstract submitted based on this study & another from other end of the globe (New Zealand) on the same topic, for Scientific ICEM conference 2016 in Cape Town; has been accepted for poster presentation.

C. Guideline Review (Appendix 6)

We proposed to change the guidelines in our Trust, based on the current work done, to discharge the patients after negative CT Head if it has been done within 6 hours and there is no abnormal focal neurology. It has to go through the local Trust governance processes.

D. Presentation at RCEM Annual Conference

I presented my study at RCEM Clinical Studies Group in January 2016. The conclusion was appreciated and the panel encouraged extending our work to the next level more formally at an RCEM platform.

E. Cochrane Collaboration (Appendix 7)

We have requested Cochrane collaboration, for other professionals from medical community to share their views and experiences on "Role of CT in the diagnosis of SAH".

Discussion

Misdiagnosis of SAH is a nightmare for an emergency physician. It usually happens because of the failure to appreciate the spectrum of clinical presentations, and interpretation of CT and CSF analysis results. Unfortunately, misdiagnosis mostly affects those who have the greatest likelihood of benefitting from early surgery. Up until the 1990s there was a 50% misdiagnosis rate for SAH[9], which has improved a lot since the improvement in the design and efficacy of CT scanners, and because of improved awareness of the condition and its related morbidity and mortality. Our study to determine the sensitivity of CT scans of the head in the diagnosis of SAH is principally a part of the improved awareness and care in the NHS.

SAH usually presents as a 'sentinel bleeding' or 'warning leak' in up to 40% of patients[7]. This usually occurs about 24 hours to 2 weeks before the major catastrophic calamity and may provide an opportunity for early intervention. Thunderclap headache could be regarded as a blessing symptom for this premonitory condition because most of the time this is the only presenting complaint for this dire condition. In the majority of cases there is no abnormal focal neurology of any kind and vital signs are within the normal range. Therefore, this is the only warning symptom for the emergency physician to embark upon and start a work up for suspected SAH.

CT scans of brains remain the standard criteria for SAH detection. The sensitivity of such CT scans has been of interest since the inception of CT scanners in 1973. The first study was carried out in 1974 by Scott *et al*[15] who found a 50% sensitivity for the detection of SAH. Scooti *et al*[16] in 1977, reviewed the technique again with a small sample size, and although he had no solid data for backup, he assumed that CT scans of the head were 100% sensitive for the diagnosis of SAH and concluded that LPs are obsolete.

As CT technology has grown from 1st to 8th generation (Appendix 4), better hardware and faster software, thinner slices and an ability to differentiate the attenuation coefficients of blood vs brain parenchyma is at its best, its accuracy is still challenged for SAH detection. Low contrast resolution (LCR) describes the ability to discriminate between tissues with slight differences in attenuation properties. Values of LCR have been gradually decreasing in different generations from >1.2 to < 0.75, and hence sensitivity has increased. The reliability of increase is the main question, and hence still has to win the full confidence. Therefore, when CT does not detect an intracranial bleed, an LP has to be performed, and although it is considered a gold standard test for the diagnosis of SAH, it has been questioned as well for its complications, compliance and false positive values. There are so many issues regarding the complications of LP and a patient's compliance that even if it is considered, patients usually do not agree. This is why it has been evaluated time and again to see if it is really needed or whether we have reached a point with CT head scans where SAH can comfortably be excluded with 100% confidence. As what is apparent from the synthesis of our evidence and our personal work, is that CT head scans seem to have greatest sensitivity if performed as soon as possible after the onset of symptoms. The studies discussed above have shown up to 100% sensitivity within 6 hours to 24 hours, although one study[5] is over 5 days.

SAH has been a widely debated topic on social media globally. It could be seen on different blogs on social media like FOAMed, on twitter @stemlyns, Life in the fast lane etc., that it is already in practice not to LP everybody after negative CT. Rather it is guided by the "red flags" and an informed patient discussion about 'risks/benefits', because if that is positive it leads to a more invasive procedure with even more complications.

Conclusion

We have come to the following conclusions:

1) CT scans of the head have 100% sensitivity, if performed within 6 hours of symptom onset.
2) CT scans have a fair sensitivity if performed within 12-24 hours of symptom onset, but has not yet reached 100%. Therefore, it has to be complemented with LP in cases where results are negative.
3) A well-calculated, evidence-based Clinical Decision Rule for pre-test probability criteria is much needed.

Recommendations

We have recommended this as a policy guideline (Appendix 6) for our Emergency Department to:

1) Use 6-hour criterions as a cut off point for no admission following a negative CT head scan and admission for LP if the CT head was done more than 6 hours after the onset of symptoms.
2) We recommend a prospective, multicenter, observational study to validate the results in our ED population.
3) Latest available evidence needs to be incorporated in RCEM SAH guidelines, which are due to be renewed imminently. This could hugely affect NHS costs and also the quality of patient experience.

Bottom Line

Recent literature is revealing a growing body of promising evidence suggesting that the CT scanners of 3rd generation and beyond have sensitivity high enough to exclude a diagnosis of SAH and avoid the need for an LP. A 'window of opportunity' (CT imaging done within 6 hours of onset of headache) seems to be

associated with 100% sensitivity while CSF analysis has proved to be a low yield test with high false positive rate. This might be an indication to move on to the next step in the diagnosis of SAH.

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Appendices

Appendix 1: Search Strategy

Search History
1. Medline; exp INTRACRANIAL HEMORRHAGES/; 57126 results.
2. Medline; exp SUBARACHNOID HEMORRHAGE/; 16886 results.
3. Medline; exp HEADACHE/; 22814 results.
4. Medline; "Sudden onset headache".ti,ab; 60 results.
5. Medline; "Acute Headache".ti,ab; 349 results.
6. Medline; "Thunder Clap Headache".ti,ab; 1 results.
7. Medline; 1 OR 2 OR 3 OR 4 OR 5 OR 6; 79040 results.
8. Medline; exp MULTIDETECTOR COMPUTED TOMOGRAPHY/; 2922 results.
9. Medline; "High resolution CT".ti,ab; 2738 results.
10. Medline; "High Definition CT".ti,ab; 25 results.
11. Medline; "CT Head".ti,ab; 323 results.
12. Medline; "Head Scan".ti,ab; 150 results.
13. Medline; "Computed Tomography".ti,ab; 155296 results.
14. Medline; "Brain Computed Tomography".ti,ab; 879 results.
15. Medline; "CT Scan Head".ti,ab; 23 results.
16. Medline; 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15; 158725 results.
17. Medline; exp SPINAL PUNCTURE/; 5239 results.
18. Medline; "Spinal Tap".ti,ab; 217 results.
19. Medline; "Lumber Puncture".ti,ab; 52 results.
20. Medline; "CSF Analysis".ti,ab; 928 results.
21. Medline; 17 OR 18 OR 19 OR 20; 6335 results.
22. Medline; 7 AND 16 AND 21; 91 results.
23. EMBASE; exp INTRACRANIAL HEMORRHAGES/; 92932 results.
24. EMBASE; exp SUBARACHNOID HEMORRHAGE/; 30463 results.
25. EMBASE; exp HEADACHE/; 146890 results.
26. EMBASE; "Sudden onset headache".ti,ab; 102 results.
27. EMBASE; "Acute Headache".ti,ab; 529 results.
28. EMBASE; "Thunder Clap Headache".ti,ab; 4 results.
29. EMBASE; 23 OR 24 OR 25 OR 26 OR 27 OR 28; 234174 results.
30. EMBASE; exp MULTIDETECTOR COMPUTED TOMOGRAPHY/; 22354 results.
31. EMBASE; "High resolution CT".ti,ab; 3676 results.
32. EMBASE; "High Definition CT".ti,ab; 42 results.
33. EMBASE; "CT Head".ti,ab; 944 results.
34. EMBASE; "Head Scan".ti,ab; 228 results.
35. EMBASE; "Computed Tomography".ti,ab; 186731 results.
36. EMBASE; "Brain Computed Tomography".ti,ab; 1117 results.
37. EMBASE; "CT Scan Head".ti,ab; 48 results.
38. EMBASE; 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37; 202096 results.
39. EMBASE; exp SPINAL PUNCTURE/; 16981 results.
40. EMBASE; "Spinal Tap".ti,ab; 349 results.
41. EMBASE; "Lumber Puncture".ti,ab; 102 results.
42. EMBASE; "CSF Analysis".ti,ab; 1884 results.
43. EMBASE; 39 OR 40 OR 41 OR 42; 19090 results.
44. EMBASE; 29 AND 38 AND 43; 66 results.
45. CINAHL; exp INTRACRANIAL HEMORRHAGES/; 0 results.
46. CINAHL; exp SUBARACHNOID HEMORRHAGE/; 1817 results.
47. CINAHL; exp HEADACHE/; 13870 results.
48. CINAHL; "Sudden onset headache".ti,ab; 1 results.
49. CINAHL; "Acute Headache".ti,ab; 87 results.
50. CINAHL; "Thunder Clap Headache".ti,ab; 1 results.
51. CINAHL; 45 OR 46 OR 47 OR 48 OR 49 OR 50; 15542 results.
52. CINAHL; exp MULTIDETECTOR COMPUTED TOMOGRAPHY/; 136 results.
53. CINAHL; "High resolution CT".ti,ab; 224 results.
54. CINAHL; "High Definition CT".ti,ab; 0 results.
55. CINAHL; "CT Head".ti,ab; 76 results.
56. CINAHL; "Head Scan".ti,ab; 20 results.

57. CINAHL; "Computed Tomography".ti,ab; 11917 results.
58. CINAHL; "Brain Computed Tomography".ti,ab; 86 results.
59. CINAHL; "CT Scan Head".ti,ab; 3 results.

60. CINAHL; 52 OR 53 OR 54 OR 55 OR 56 OR 57 OR 58 OR 59; 12244 results.
61. CINAHL; exp SPINAL PUNCTURE/; 909 results.
62. CINAHL; "Spinal Tap".ti,ab; 21 results.
63. CINAHL; "Lumber Puncture".ti,ab; 3 results.
64. CINAHL; "CSF Analysis".ti,ab; 62 results.
65. CINAHL; 61 OR 62 OR 63 OR 64; 979 results.
66. CINAHL; 51 AND 60 AND 65; 30 results.
67. Medline, EMBASE, CINAHL; Duplicate filtered: [7 AND 16 AND 21], [29 AND 38 AND 43], [51 AND 60 AND 65]; 187 results.

Appendix 2: Level of Evidence

Level	Therapy / Prevention, Aetiology / Harm	Prognosis	Diagnosis	Differential diagnosis / symptom prevalence study	Economic and decision analyses
1a	SR (with homogeneity*) of RCTs	SR (with homogeneity*) of inception cohort studies; CDR" validated in different populations	SR (with homogeneity*) of Level 1 diagnostic studies; CDR" with 1b studies from different clinical centres	SR (with homogeneity*) of prospective cohort studies	SR (with homogeneity*) of Level 1 economic studies
1b	Individual RCT (with narrow Confidence Interval"¡)	Individual inception cohort study with > 80% follow-up; CDR" validated in a single population	Validating** cohort study with good" " " reference standards; or CDR" tested within one clinical centre	Prospective cohort study with good follow-up****	Analysis based on clinically sensible costs or alternatives; systematic review(s) of the evidence; and including multi-way sensitivity analyses
1c	All or none§	All or none case-series	Absolute SpPins and SnNouts" "	All or none case-series	Absolute better-value or worse-value analyses " " " "
2a	SR (with homogeneity*) of cohort studies	SR (with homogeneity*) of either retrospective cohort studies or untreated control groups in RCTs	SR (with homogeneity*) of Level >2 diagnostic studies	SR (with homogeneity*) of 2b and better studies	SR (with homogeneity*) of Level >2 economic studies
2b	Individual cohort study (including low quality RCT; e.g., <80% follow-up)	Retrospective cohort study or follow-up of untreated control patients in an RCT; Derivation of CDR" or validated on split-sample§§§ only	Exploratory** cohort study with good" " " reference standards; CDR" after derivation, or validated only on split-sample§§§ or databases	Retrospective cohort study, or poor follow-up	Analysis based on clinically sensible costs or alternatives; limited review(s) of the evidence, or single studies; and including multi-way sensitivity analyses
2c	"Outcomes" Research; Ecological studies	"Outcomes" Research		Ecological studies	Audit or outcomes research
3a	SR (with homogeneity*) of case-control studies		SR (with homogeneity*) of 3b and better studies	SR (with homogeneity*) of 3b and better studies	SR (with homogeneity*) of 3b and better studies
3b	Individual Case-Control Study		Non-consecutive study; or without consistently applied reference standards	Non-consecutive cohort study, or very limited population	Analysis based on limited alternatives or costs, poor quality estimates of data, but including sensitivity analyses incorporating clinically sensible variations.
4	Case-series (and poor quality cohort and case-control studies§§)	Case-series (and poor quality prognostic cohort studies***)	Case-control study, poor or non-independent reference standard	Case-series or superseded reference standards	Analysis with no sensitivity analysis
5	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Expert opinion without explicit critical appraisal, or based on economic theory or "first principles"

Appendix 3: Audit Proforma

Audit for CTR

Age		
Sex		
Presenting Complain		
Headache	Bad (severe)	
	Worst	
	Thunderclap	
	Severity Score (0-10)	
Onset of symptoms	<12hrs	Exact
	>12hrs	Estimated
Any focal neurology	Photophobia	
	Weakness	
	Speech	
	Fast +/-	
	Others	
PMHx/Risk Fxs	H/T	
	DM-ID/NID	
	IHD	
	Others	
Smoker		
Alcohol use		
CT done/not done		
Admitted or D/C		
LP done	Result +ive	
	Result -ive	

Appendix 4: CT development through generations

Generations	source	Source collimation	detector	Detector collimation	Source-Detector movement	Advantages	Disadvantages
1st Gen.	single	Pencil beam	single	no	Trans.+ Rotates	No scatter	slow
2nd Gen.	single	Fan-beamlet	multiple	yes	Trans.+ Rotates	Faster than 1G	Low efficiency
3rd Gen.	single	Fan-beam	many	no	Rotates together	Faster than 2G	High cost and Low efficiency
4th Gen.	single	Fan-beam	Stationary ring	no	Source Rotates only	Higher efficiency than 3G	high scatter
5th Gen.	multiple	Fan-beam	Stationary ring	no	No movement	Ultrafast for cardiac	high cost
6th Gen.	single	Fan-beam	many	yes	3rdGen.+ bed trans.	faster 3D imaging	higher cost
7th Gen.	single	Narrow cone- beam	Multiple arrays	yes	3rdGen.+ bed trans.	faster 3D imaging	higher cost
8th Gen.	single	wide cone- beam	FPD	no	3rd Gen.	Large 3D	Relatively slow

Appendix 5: ICEM Letter & Poster

ICEM
CAPE TOWN 2016
EM NOW: KNOWLEDGE, ACTION & ACCOUNTABILITY
18-21 April 2016 • Cape Town International Convention Centre

January 2016

Mr Nadeem Khan,

I am delighted to inform you that your abstract '**A tale of two cities: Do we need to do a lumbar puncture to rule out subarachnoid hemorrhage in neurologically intact CT head negative adult patients?**' has been chosen for a **POSTER PRESENTATION** at the ICEM Conference on 18-21 April 2016 in Cape Town.

Your poster will be displayed on '**4/19/2016**' in the Exhibition Hall.
Poster number: **5**
Poster boards will be numbered. Please ensure that you place your poster on the correct board.

Please be present at your poster at the tea and lunch breaks to discuss your poster with delegates and moderators.

Please ensure that your poster is set up by 10:00 and removed by latest 18:00. All posters not removed by 18:00 will be taken down by the CTICC staff.
The CTICC and ICEM staff unfortunately cannot take responsibility for posters not taken down by 18:00 on the day of your poster presentation.

Please see the poster guidelines below:

- Posters should be constructed from light-weight material – heavy posters will not affix to the boards.
- Posters should not measure more than 90 cm wide x 1.5m high.
- Posters should include:
- The title (not less than 3cm in size)
- The text (readable from 1m away).
- The authors names, name of institution and country of origin
- Please bring a double sided tape to attach your poster to a poster board

Once again, congratulations! We look forward to welcoming you at the Conference!

Yours sincerely

Jolandi Ackermann

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A TALE OF TWO CITIES

Do we need to do a lumbar puncture to rule out subarachnoid haemorrhage in neurologically intact CT head negative adult patients?

N. Khan[1], I. Zakraia[1], T. Cheri[2], S. Mukerji[2], G. Marchant[2]
[1]Emergency Department, Tameside General Hospital, UK
[2]Emergency Department, Palmerston North Hospital, New Zealand

Introduction

Subarachnoid haemorrhage (SAH) is a diagnosis that no clinician wants to miss. Most international guidelines recommend the use of computed tomography (CT) and lumbar puncture (LP) as initial investigations for the diagnosis of subarachnoid haemorrhage. Some authors quote that in patients who are computed tomography negative for subarachnoid haemorrhage, around 2–10% of them would be lumbar puncture positive for SAH.

Objective

The objective of this study was to review the pickup rate of SAH by LP in patients who were computed tomography negative and neurologically intact.

Methods

A retrospective review of all patients who were investigated for a suspected SAH and had a normal head CT and normal neurology was reviewed with their LP results. The study was done from 2011 to 2013 (two year period) at an Emergency Department (ED) in New Zealand (ED volume of 40,000 per year) and 2014 in a UK ED (ED volume of 85,000 per year).

Results

A total of 491 neurologically intact patients suspected to have subarachnoid haemorrhage underwent computed tomography head. None of the CT scans showed any evidence of SAH. Of these only one patient ended up having an LP which was positive for xanthochromia which was confirmed by angiogram.

Conclusion

The results of our study show that in our practice we have 0.2% pick up rate of subarachnoid haemorrhage by LP if the initial CT was negative in a neurologically intact patient.

Tameside Hospital NHS

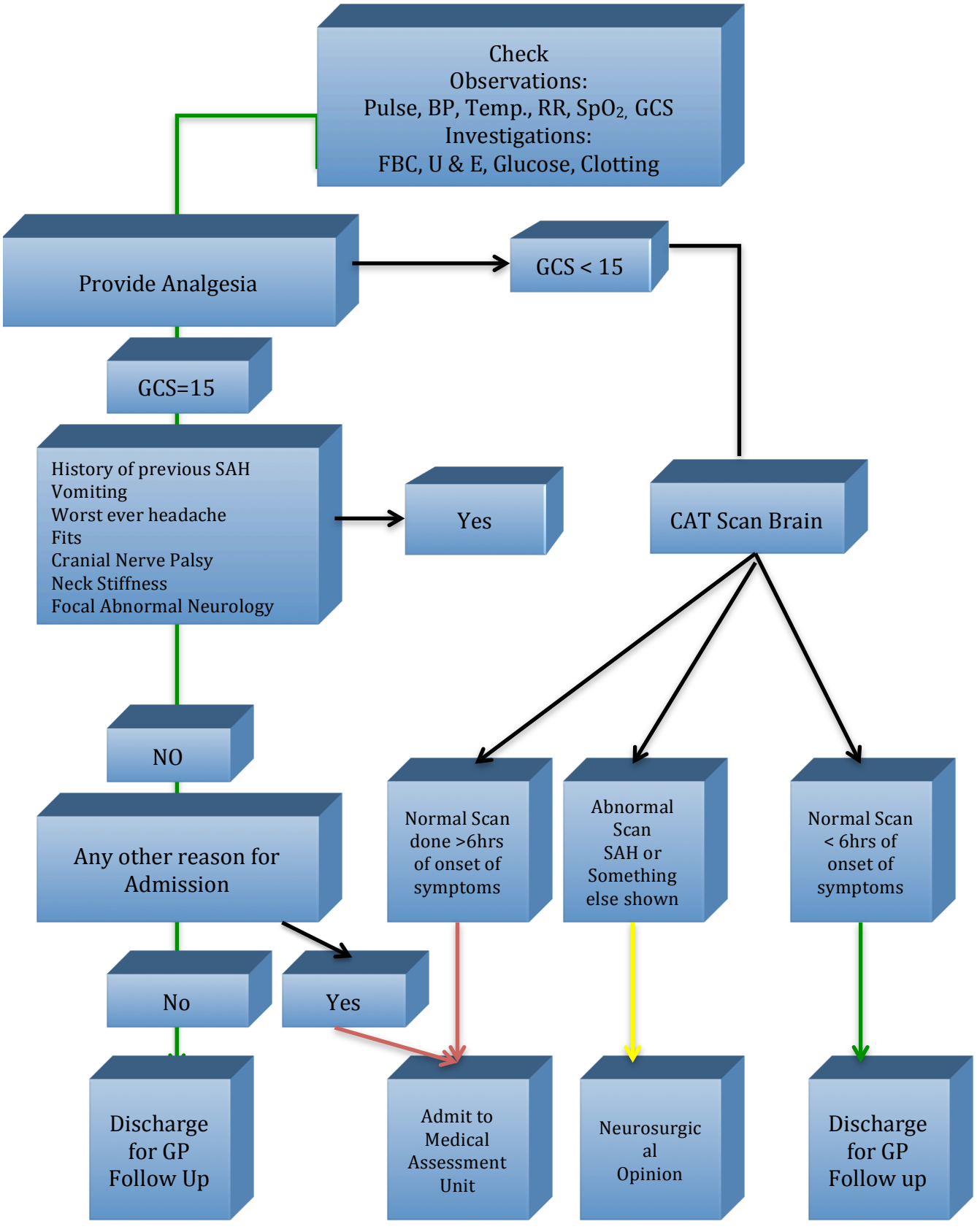
Appendix 6: Changes to trust policy Guidelines

Tameside Hospital NHS

NHS Foundation Trust

Acute Lone Headache

(Sudden onset, not previously diagnosed by neurologist)



Appendix 7: Request for Cochrane Collaboration

Subject:	Cochrane review Group
From:	Nadeem Khan (nak65@yahoo.co.uk)
To:	editorial-unit@cochrane.org;
Cc:	tcracknell@cochrane.org;
Date:	Wednesday, 1 July 2015, 15:15

Dear Ms Simmonds,
I am writing to you to request an addition of a new group in "Cochrane Review Group". I have done a literature review on the topic of " Role of CT in Subarachnoid Haemorrhage". I would like to set up collaboration on this topic and invite wider medical community to speak out their experiences which may pave a path towards collaboration of high quality work leading to new recommendations and change in current practice.
Please find attached my work herewith. I would like this to be part of Cochrane database of systematic reviews.
Thanks
Mr N Khan
Locum Consultant ED
Tameside general Hospital NHS Trust