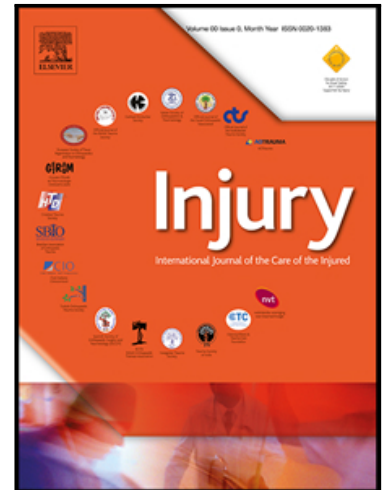


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Incidence of intracranial bleeding in seniors presenting to the emergency department after a fall: a systematic review.

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HIGHLIGHTS

- Falling on level-ground is the most common cause of traumatic intracranial bleeding.
- The number of seniors who present to emergency departments after a fall increases each year.
- Our systematic review found sparse, heterogeneous and generally low-quality research in this patient group.
- Our meta-analysis found that 1 in 20 seniors who present to an emergency department after a fall are diagnosed with intracranial bleeding.

Journal Pre-proof

**Incidence of intracranial bleeding in seniors presenting to the
emergency department after a fall:
a systematic review.**

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ABSTRACT**INTRODUCTION**

Seniors who fall are an increasing proportion of the patients who are treated in emergency departments (ED). Falling on level-ground is the most common cause of traumatic intracranial bleeding. We aimed to determine the incidence of intracranial bleeding among all senior patients who present to ED after a fall.

METHOD

We performed a systematic review. Medline, EMBASE, Cochrane, and Database of Abstracts of Reviews of Effects databases, Google Scholar, bibliographies and conference abstracts were searched for articles relevant to senior ED patients who presented after a ground-level fall. Studies were included if they reported on patients aged 65 or older who had fallen. At least 80% of the population had to have suffered a ground-level fall. There were no language restrictions. We performed a meta-analysis (using the random effects model) to report the pooled incidence of intracranial bleeding within 6 weeks of the fall.

RESULTS

We identified eleven studies (including 11,102 patients) addressing this clinical question. Only three studies were prospective in design. The studies varied in their inclusion criteria, with two requiring evidence of head injury and four requiring the emergency physician to have ordered a head computed tomography (CT). One study excluded patients on therapeutic anticoagulation. Overall, there was a high risk of bias for eight out of eleven studies. The pooled incidence of intracranial bleeding was 5.2% (95% CI 3.2-8.2%). A sensitivity analysis excluding studies with a high risk of bias gave a pooled estimate of 5.1% (95% CI 3.6-7.2%).

CONCLUSION

We found a lack of high-quality evidence on senior ED patients who have fallen. The available literature suggests there is around a 5% incidence of intracranial bleeding in seniors who present to the ED after a fall.

INTRODUCTION

Each year, one in three adults over the age of 65 (seniors) fall and half of these seniors seek treatment at a hospital emergency department (ED) [1]. Unintentional injuries are the 5th leading cause of death [2] and seniors who fall make up 20% of all these deaths [3]. Falling on level ground is now the most common cause of traumatic intracranial bleeding world-wide, accounting for up to 80% of cases [4-8].

There are several reasons why seniors are at particular risk of intracranial bleeding following a fall. Population level data suggests that prescription of anticoagulation increases the risk of intracranial bleeding [9] and antithrombotic therapy is becoming increasingly prevalent among seniors [10, 11]. Falling in itself is associated with frailty [12]. Vulnerable seniors in poorer health states are most likely to fall and may have a higher risk of intracranial bleeding.

The traditional signs of traumatic brain injury may not be evident among seniors and clinical assessment can be hampered by dementia, delirium, lack of information about the fall and other neurological comorbidities. This makes selective CT scanning challenging for the emergency physician. The Canadian CT head rule [13] may be applied for patients with head injury followed by loss of consciousness, amnesia or disorientation, however there may not be a clear history of these symptoms and only a minority of patients hit their head when they fall [14, 15]. One approach to this clinical problem is to order head CT scans on every senior who has fallen. However 24-hour CT access is not always available, and CT could also result in a prolonged ED stay which increases the risk of risk of delirium among seniors [18]. A more discriminative approach to CT scanning is also increasingly relevant in the current cost and resource conscious healthcare setting.

Better evidence is needed to establish which of these patients is at risk of intracranial bleeding. However, to ensure adequately powered research, it is important to establish the incidence of intracranial bleeding amongst seniors who present to the ED after a fall. We aimed to determine the incidence of intracranial bleeding in seniors who present to the ED after a fall by performing a systematic review and meta-analysis of all previous literature.

METHODS

We followed the Meta-analysis of Observational Studies in Epidemiology (MOOSE) methodological approach [14]. The protocol was registered with PROSPERO (CRD42018086134).

Search Strategy

Medline, EMBASE (via OVID 1946 until 21st July 2019), Cochrane, and Database of Abstracts of Reviews of Effects databases were searched for articles relevant to senior ED patients who presented after a ground-level fall. The bibliographies of full papers and reviews were examined for additional relevant references that may have been missed in the electronic search. The Medline and EMBASE search strategies are shown in Appendix 1. An additional search was conducted on Google Scholar in July 2019. Researchers in the field were contacted for information on any unpublished data. Conference abstracts from academic emergency medicine research conferences were hand searched.

The database search results were independently reviewed by KdW and EM. Potentially eligible papers were identified, and the full texts reviewed. The authors met to agree on inclusion or exclusion of each full text by consensus.

Inclusion and Exclusion

We identified studies including consecutive senior ED patients who presented after a fall on level-ground. We followed strict inclusion and exclusion criteria. Included studies had to report on ED patients aged 65 or older who had fallen. At a minimum, included studies had to report the incidence of intracranial bleeding on ED assessment. Ideally, the study also reported the incidence of intracranial

bleeding during 4 to 6-week follow up, although this was not required to be included in our analysis. We included conference abstracts, unpublished and published studies. There were no language restrictions. Papers in a language other than English were forwarded to a colleague who was fluent in the language for translation.

To avoid inclusion of anomalous results, studies reporting on less than 20 patients were excluded. We decided *a priori* to exclude studies where less than 80% of the population were over the age of 65, or had experienced a ground-level fall. Studies restricted to subgroups of senior ED patients who had fallen were excluded as these studies would not reflect the true incidence of intracranial bleeding found in ED patients and may introduce spectrum bias. Examples were cohorts restricted to patients admitted onto hospital wards, patients managed by the neurosurgical service or trauma service, and patients prescribed anticoagulants or antiplatelet medications. Studies on patients who fell during a hospital admission were excluded because in-patients are frequently prescribed anticoagulation thromboprophylaxis and are likely to have greater co-morbidity than those who present to ED. We excluded cohort studies reporting only the incidence of delayed bleeding and not intracranial bleeding on initial ED assessment.

Where it was unclear from the manuscript, we contacted the authors to confirm whether the study met inclusion criteria. We used a systematic approach for contact by email. An email letter was sent to the corresponding author, followed two weeks later by a letter to both the first and last authors. If there was still no response, then a third and final email was sent.

Data extraction

Four reviewers (KdW, EM, ZM and YK) independently abstracted data from the eligible studies. Any discrepancy was resolved by consensus review. The primary outcome was the proportion of seniors presenting to the ED after a fall who were diagnosed with intracranial bleeding at index ED presentation or during follow up. We accepted each study's definition of intracranial bleeding.

Assessment of study quality

A risk of bias assessment was completed independently by ZM, YK and KdW. Discrepancies were resolved by consensus. The “Tool to Assess Risk of Bias in Longitudinal Symptom Research Studies Aimed at the General Population”, created by the Clarity group at McMaster University was used [18]. The tool reviews whether the sampling frame is representative of the general population, if the assessment of the outcome is accurate, and the proportion of missing data.

Statistical Analysis

The data were reviewed for statistical heterogeneity with I^2 . Meta-analysis was performed using the random effects model. We did not construct funnel plots to assess for publication bias as these have been shown to be inaccurate for studies addressing proportions and may cross the 0% or 100% boundaries [16]. A sensitivity analysis was performed including only the studies with low/intermediate risk of bias. To explore reasons for heterogeneity, additional pooled estimates were calculated using the random effects model for studies restricted to patients who had sustained a head injury and studies where all patients had head CT scanning. Statistical analysis was performed using MedCalc.net, Belgium.

RESULTS

OID Medline and EMBASE identified 7,240 unique publications. In total, 181 full text papers and abstracts from this search were reviewed, along with another four papers identified in Google Scholar (Figure 1). A total of 11 studies [20-30] (and 11,102 patients), from the USA, Japan, Italy, Canada, Finland, France and Australia were included in our meta-analysis (Table 1).

There was considerable clinical heterogeneity among the included studies. Eight of the 11 studies identified patients in retrospect [19-23], either by head CT scan request [22, 27-29] or ICD coding [21]. Two of these retrospective studies also required the patient to have sustained a head injury [24, 29]. Three studies identified patients prospectively at the time of assessment and management in the ED [21, 23, 25]. None of the three prospective studies required the patient to have sustained a head injury.

The studies also differed in their exclusion criteria: four studies excluded patients with an abnormal neurological examination [22, 23, 25, 29], one study excluded patients found to have chronic subdural bleeds [22] and one study excluded patients on therapeutic anticoagulation [29]. The study with the broadest inclusion criteria was de Wit *et al.* [21] (N=1753, any patient who fell on level-ground, out of bed or off a chair). The study with the most restrictive inclusion/exclusion criteria was Riccardi *et al.* [29] (N=2149, sustained a head injury and had a head CT, with absence of neurological symptoms, neurological deficit, prior neurological disease and anticoagulant therapy). Only four studies followed each patient to identify delayed diagnoses of intracranial bleeding [20, 21, 23, 25], including all prospective studies. Assessment of bias identified a high risk of bias in the sampling frame among all retrospective studies. No study combined head CT with clinical follow up in all patients (thereby capturing both immediate and delayed intracranial bleeding).

The incidence of traumatic intracranial bleeding following a fall ranged from 1.7% to 12.2% in the included studies. The pooled estimate for the incidence of intracranial bleeding among seniors who present to the ED after a fall was 5.2% (95% CI 3.2-8.2%), I^2 95%. (Figure 2). The sensitivity analysis including three studies with the lowest risk of bias [21, 23, 25] showed a pooled estimate of 5.1% (95% CI 3.4-7.3%), I^2 83%. Analysis of studies reporting on similar patient groups did not reduce the statistical heterogeneity: the pooled estimate for studies restricted to patients who had a head CT scan [22, 27-29] was 5.9% (95% CI 2.2-11.3%), I^2 95%, for studies restricted to patients who sustained a head injury [24, 29], 6.3% (95% CI 0.2-19.5%), I^2 99% and for studies including patients with both normal and abnormal neurological examination [20, 21, 24, 26-28, 30], 5.1% (95% CI 3.2%-7.3%), I^2 93%.

DISCUSSION

We performed a systematic review and meta-analysis to determine the proportion of senior patients presenting to the ED after a fall who develop intracranial bleeding. We found heterogeneous and generally low-quality research to answer this question. We found a 5% incidence of intracranial bleeding, although individual study reports ranged from 2% to 12%. Our sensitivity analysis including studies with lower risk of bias found a 5% incidence of intracranial bleeding.

The proportion of the world's population who is aged over 65 is currently estimated at 13% and is projected to rise to 25% by 2050 [31]. EDs are experiencing yearly increases in the number of seniors who present with falls [32] and it is important that physicians have access to sufficient medical evidence to guide management of this population. We have identified an area which is lacking in evidence for senior emergency patients. Our findings suggest there is a 1 in 20 risk of being diagnosed with intracranial bleeding.

This is the first meta-analysis on traumatic brain injury in senior emergency patients who have fallen. We included all studies addressing our question and there is little to compare our findings to. Carpenter *et al.* encountered a similar lack of quality emergency research in a meta-analysis on prediction of adverse outcomes in senior emergency patients [33], and Lowthian *et al.* for effective discharge of senior emergency patients [34]. In contrast, there has been much research focusing on how to prevent falls in the community [35] [36]. It appears that emergency medicine research lags behind with little on the assessment and treatment of seniors who fall.

There are guidelines for diagnosis of traumatic brain injury in the ED such as the Canadian CT head rule [13] and the New Orleans Criteria [37]. However, these guidelines may not always apply to seniors who fall because they were developed on patients with a history of head injury and either loss of consciousness or amnesia of the event. Seniors who fall do not always sustain a head injury and intracranial bleeding has been reported even in the absence of any direct or facial impact. At times, establishing a clear history is challenging if the fall was unwitnessed or the patient has dementia. We have demonstrated that this patient group has a clear risk of intracranial bleeding which justifies investigation. However, around 95% of these patients do not develop intracranial bleeding which poses the question of whether a selective head CT scan approach might be feasible in the future.

The strengths of this study are that we included all available research on this topic, in any language, whether published or unpublished. We also reported the incidence of intracranial bleeding up to 6-weeks after the fall. The main weakness of our analysis is that many of the included studies had a high risk of bias from the sampling frame, given the retrospective nature of the studies. This highlights

the need for high quality, prospective research on diagnosis of traumatic brain injury in seniors. Although the included studies defined intracranial bleeding in a similar way, we do not know whether there were small differences in their definitions. We are unable to draw a causal relationship between falling and the diagnosis of intracranial bleeding because pre-existing intracranial bleeding might cause a fall.

Additionally, there is evidence that even a minor head injury is associated with long-term disability in seniors (as measured by the extended Glasgow outcome scale) [38], and it is possible that intracranial bleeding is not the most patient oriented outcome. At the time of writing, there has been insufficient research on this topic to recommend changing focus to another outcome such as independent living, disability or quality of life. Finally, intracranial bleeding is not the only concern among seniors who fall. Hip, pubic rami, wrist and shoulder fractures all have a negative impact on seniors, and can precipitate a decompensation in general health state [39].

CONCLUSION

We found a lack of high-quality evidence on senior ED patients who have fallen. The available literature suggests there is around a 5% incidence of intracranial bleeding in seniors who present to the ED after a fall.

Conflict of interest statement

The authors have no conflicts of interest.

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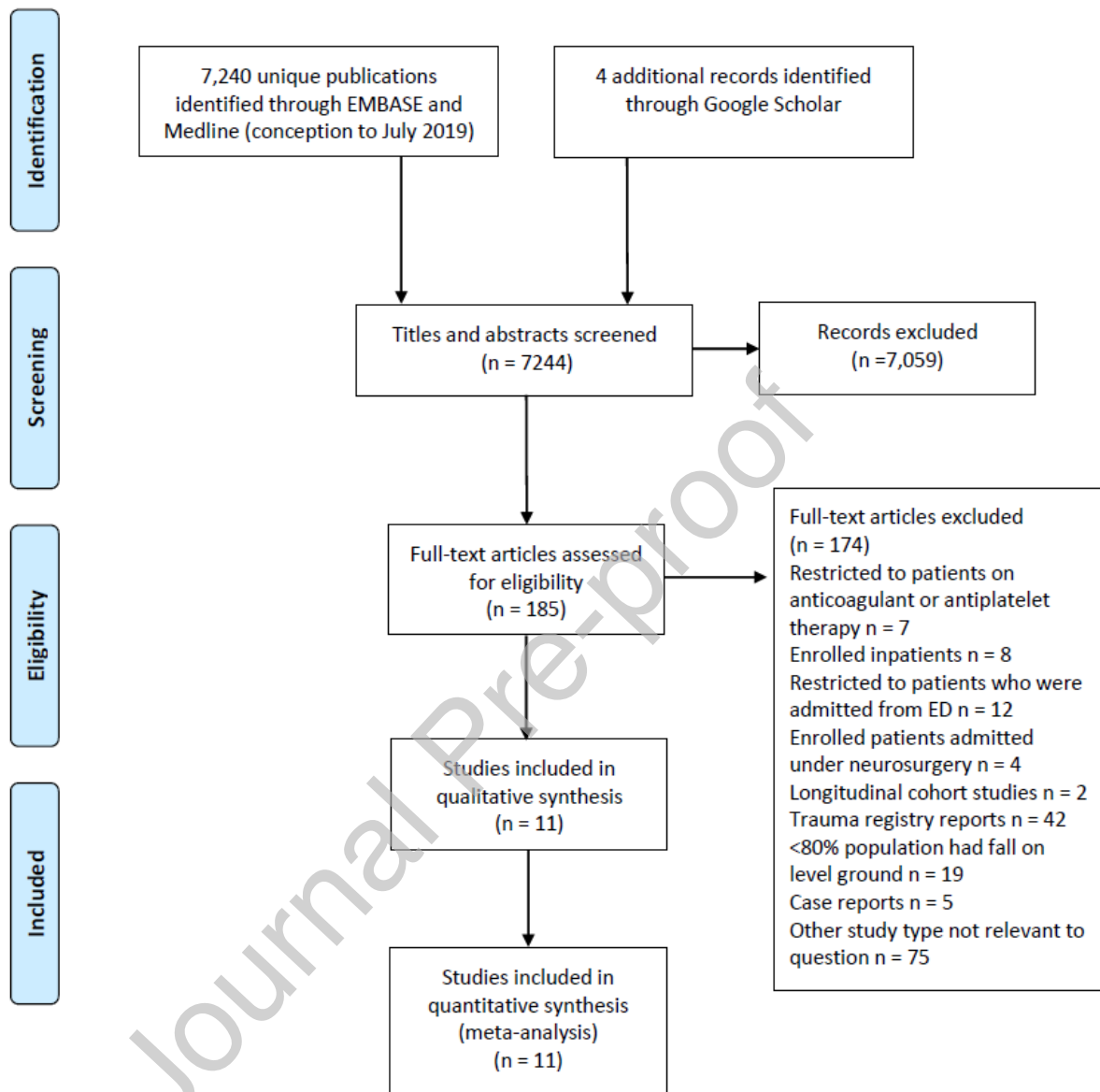
Figure 1. PRISMA flow diagram for selection of studies

Figure 2: Forest plot for incidence of intracranial bleeding among emergency department seniors presenting after a fall

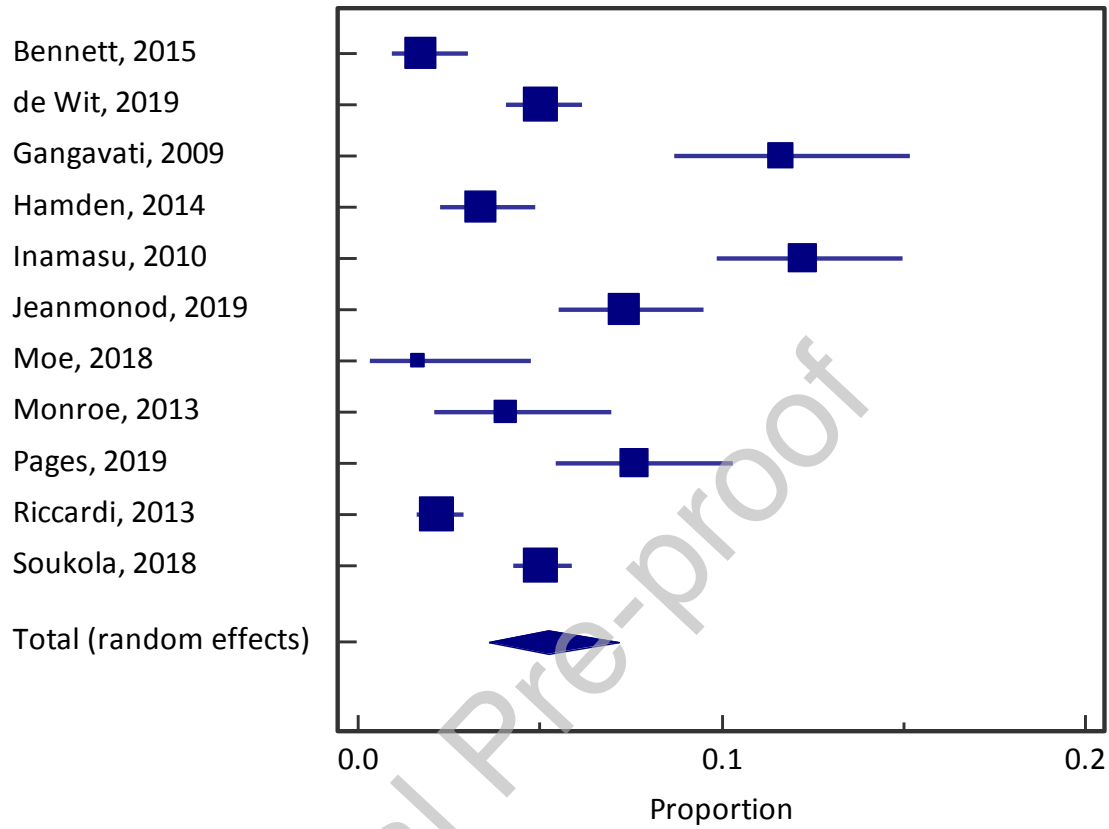


Table 1: Description of included studies

| Author, year of study, country | Type of Study | N | Age* % | % female | Inclusion /exclusion | N (%) head CT in ED | Was there patient follow up? | In-hospital death | Neurosurgical intervention | ICB | Proportion with ICB (%) |
|--------------------------------------|---------------|------|-----------|-------------|---|---------------------------|--|----------------------|-------------------------------|-----|----------------------------|
| Bennett, 2008 USA [20] | Retrospective | 687 | 81 | 79% | ICD-9 code 'fall' or 'traumatic injury' Excluded transfers from another hospital and multisystem trauma | 321 (46%) | 30-day chart review | 2 | 0 | 12 | 12/687 (1.7%) |
| de Wit, 2016-17 Canada [21] | Prospective | 1753 | 82 | 61% | Fall on level ground/bed/ chair/ a step. Excluded transfers from another hospital. | 994 (57%) | 42-day chart review and telephone contact | 14 | 5 | 88 | 88/1753 (5.0%) |
| Gangavati, dates NR USA [22] | Retrospective | 404 | 83 | 65% | Fall and CT head scan. Excluded chronic subdural bleeds, bleed within brain tumour, abnormal neurological exam, motor vehicle accidents. | 404 (100%) | None | NR | 7 | 47 | 47/404 (11.6%) |
| Hamden, 2011-12 | Prospective | 799 | 85 | 67% | Fall, baseline neurological status. Excluded if major trauma, | 632 (79%) | 30-day chart review and telephone contact | 1 | 2 | 27 | 27/799 (3.4%) |

| | | | | | | | | | | | |
|-----------------------------------|---------------|------|----|-----|---|----------------|---|----|----|----|-------------------|
| USA [23] | | | | | treated in trauma bay. | | | | | | |
| Inamasu, 2003-08 Japan [24] | Retrospective | 670 | NR | NR | Head injury from ground level fall. No exclusions. | NR | None | 21 | 7 | 82 | 82/670 (12.2%) |
| Jeanmonod, 2013-15 USA [25] | Prospective | 711 | 83 | 66% | Fall, baseline neurological status. Excluded if major trauma, treated in trauma bay. | 568 (80%) | 30-day chart review and telephone contact | 1 | 0 | 52 | 52/711 (7.3%) |
| Moe, 2015 Australia [26] | Retrospective | 182 | 81 | 58% | Fall. Exclusions not stated. | NR | None | NR | NR | 3 | 3/182 (1.6%) |
| Monroe, 2008 USA [27] | Retrospective | 296 | 81 | NR | Fall and CT head scan. No exclusions. | 296 (100%) | None | NR | 0 | 12 | 12/296 (4.1%) |
| Pages, 2017-18 France [28] | Retrospective | 500 | 85 | 60% | Fall from standing and CT head scan. No exclusions. | 500 (100%) | None | 2 | 3 | 38 | 38/500 (7.6%) |
| Riccardi, | Retrospective | 2149 | 81 | 55% | Minor head injury and CT head scan. | 2149 (100%) | None | NR | 3 | 47 | 47/2149 |

| | | | | | | | | | | | | |
|--|---------------|------|----|-----|---|----|------|----|----|-----|----------|--------|
| 2004-10 Italy [29] | | | | | Excluded if abnormal neurological exam, coagulopathy, dementia, neurological disorder, deep wounds, neurological symptoms, intoxicated. | | | | | | (2.2%) | |
| Soukola, 2015-16, Finland [30] | Retrospective | 2951 | 87 | 73% | Patients \geq 80 years with a fall No exclusions | NR | None | NR | NR | 148 | 148/2951 | (5.0%) |
| NR = not reported, ICB = intracranial bleed | | | | | | | | | | | | |
| * Either median or mean as reported by authors | | | | | | | | | | | | |

Table 2: Risk of bias for included studies

| Study | Sampling Frame | Outcome Assessment | Missing Data |
|-----------------|-----------------------|---------------------------|---------------------|
| Bennett, 2015 | High | Intermediate | Low |
| de Wit, 2019 | Low | Intermediate | Low |
| Gangavati, 2009 | High | Intermediate | Low |
| Hamden, 2014 | Low | Intermediate | Low |
| Inamasu, 2010 | High | High | Low |
| Jeanmonod, 2019 | Low | Intermediate | Low |
| Moe, 2018 | High | High | Low |
| Monroe, 2013 | High | Intermediate | Low |
| Pages, 2019 | High | Intermediate | Low |
| Riccardi, 2013 | High | Intermediate | Low |
| Soukola, 2018 | High | High | Low |

APPENDIX 1

Medline and EMBASE via the OVID interphase

1. fall.mp. or exp Accidental Falls/ or level ground.mp. or ground level.mp. or falls.mp. or trip.mp. or stumble.mp. or minor head injuries.mp. or mild head injuries.mp. or minor head injury.mp. or mild head injury.mp.

2. elderly.mp. or exp Aged/ or seniors.mp. or older adults.mp. or "65".mp. or retired.mp. or exp Retirement/

3. exp Tomography, X-Ray Computed/ or CT.mp. or computer tomography.mp. or exp Craniocerebral Trauma/ or exp Head Injuries, Closed/ or Hematoma, Epidural, Cranial/ or epidural.mp. or extradural.mp. or subdural.mp. or exp Hematoma, Subdural/ or exp Hematoma, Subdural, Intracranial/ or exp Hematoma, Subdural, Chronic/ or exp Hematoma, Subdural, Acute/ or exp Subarachnoid Hemorrhage, Traumatic/ or subarachnoid.mp. or exp Subarachnoid Hemorrhage/ or exp Intracranial Hemorrhages/ or exp Cerebral Hemorrhage/ or exp Brain Injuries/ or intracerebral.mp. or intraventricular.mp. or cerebral contusion.mp. or exp Brain Contusion/ or brain contusion.mp. or traumatic brain injury.mp. or exp Brain Injuries, Traumatic/ or exp Intracranial Hemorrhages/ or exp Intracranial Hemorrhage, Traumatic/ or intracranial.mp.

4. 1 and 2 and 3