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Incidence and course of head injury and risk factors for complications.
Subtitle: Head injury in primary care; spectrum bias in current guidelines?

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Abstract

Objectives

To assess the incidence of head injury and predictors of complication across the care continuum.

Design

Combined retrospective cohort study using data from a research network. We calculated the incidence of overall head injury in a longitudinal cohort covering 1 year interval (31,369 patient years), and the incidence of complicated head injury in a longitudinal cohort covering 10 years interval (220,352 patient years). Incidence rates were calculated per 1000 patient-years with 95% CI using the Mid-P exact test. We calculated Odds ratios to assess potential risk factors for a complicated head injury.

Setting

A practice-based research network covering a population of >30,000 patients.

Participants

All patients listed in practices within the research network during the years 2005-2014.

Main outcome measures

Incidence of (complicated) head injury and predictors for clinical complications.

Results

The incidence of overall head injury was 22.1 per 1000 person years and the incidence of a complicated course following head injury was 0.16 per 1000 person years. The following determinants were risk factors for a complicated course: high energy trauma, bicycle accident, traffic accident in general, use of anticoagulants, alcohol intoxication, age above 60 years and low Glasgow Coma Scale at initial presentation. A complicated course was very unlikely when the first patients' first encounter with a healthcare professional was in primary care (OR 0.03, 95%CI 0.01-0.07).

Conclusions

Complication after head injury are rarely seen in general practice. Patients who do experience complications are often easily identifiable as requiring specialist care. A more conservative referral policy for general practice may be desirable, suggesting that current guidelines are too defensive.

Trial registration

None.

Strengths and limitations of this study

A particular strength of our study is that we were able to use a robust, comprehensive data base including all encounters of individual patients with healthcare professionals both from primary and secondary care. This was possible because all patients in the Netherlands are registered with one particular general practitioner, who collects all patient related health data.

A limitation of this study is its retrospective design. Most of the patients only had minor head injuries which do not necessitate full reporting in daily practice. Therefore, signs and symptoms of head injuries were not fully and structurally registered in the health records, limiting the interpretation of predictive values of signs and symptoms.

Introduction

Patients presenting with head injury in primary care challenge general practitioners to differentiate between those who may be reassured, and those who are at risk of serious intracranial injury. Intracranial injuries such as epidural and subdural hematoma or skull fractures may lead to death or permanent damage if left untreated (1-4).

High quality clinical management of head injury takes the small chance of intracranial injury into account. Safe and cost-effective practice guidelines for primary care must therefore be based on a reliable risk calculation, for which precise data are needed on the incidence of both head injury and serious intracranial injury or complicated head injury. In Europe, the annual incidence of head injury presenting in hospital emergency departments is 2.3 per 1000 person-years (5) (6). In general practice, this incidence is expected to be higher because only a subset of patients are referred to hospital. Robust data about incidence rates in primary care are lacking. For example, a New Zealand study in a primary care population found an incidence rate of 7.5 per 1000 person-years (7), whereas, in a small pilot study in the Netherlands, we found the incidence of (mild and severe) head injury to be as high as 22.3 per 1000 person-years (8).

The incidence of severe damage after a head injury is also unclear. In the UK, head injury accounts for 3.4% of all emergency department attendances. About 90% of head injuries in clinical setting are considered to be mild (6, 7). Incidence of moderate to severe head injury was 40 per 100.000 persons – a figure which may in reality be slightly higher because it does not include patients who die before admittance to the hospital (9). This makes the identification of patients at risk challenging.

Currently, guidelines for the identification, referral and management of patients with head injury at risk for intracranial damage are based on epidemiological studies from secondary or tertiary care (10, 11). It is likely that this case-mix of head injury patients is essentially different from that in primary care (12, 13). The risk for a complicated course may therefore be exaggerated, resulting in spectrum bias in current guidelines (12-16).

In this study, we aim to assess the incidence of head injury in primary care and to identify risk factors for intracranial injury. Our research questions were: (1) what is the incidence of head injury and complicated head injury, and (2) what predicts a complicated course?

Methods

Study Setting

We performed a retrospective cohort study in the practice based research network Family Medicine Network (FaMe-net) of the Department of Primary and Community Care (ELG) at the Radboud University Medical Centre. FaMe-net consists of nine Dutch general practices in 3 geographical regions (approximately 31.000 listed patients). FaMe-net physicians systematically and prospectively register data on the reason for encounter, diagnostic procedures, diagnoses, interventions, and referrals. The network uses the ICPC-2 and ICD-10 classification systems to code procedures and diagnosis. All data can be linked to demographic information (age, gender, geographic location, family composition). In the Netherlands, all patients are listed in one general practice to which all encounters in secondary care are reported. Reports from other care-providers are coded and linked to a new or existing episode (17). Participating doctors in FaMe-net meet on a regular basis to discuss registration issues and improve the uniformity of registration.

Definitions

We defined head injury as any trauma to the head other than superficial injuries to the face (18). A complicated head injury was defined as a head injury for which treatment and surveillance in secondary care was deemed necessary: a need for surgical intervention (defined as any neurosurgical procedure including drainage and placement of ICD), seizures in the acute posttraumatic phase, resulting neurological deficits within 12 months after trauma, and death. Neurological deficits were defined as any neurological abnormalities, including facial fracture associated nerve lesions.

Study Population and data collection

We selected patients in two stages: first we performed a sensitive electronic search based on the list of ICPC labels indicating head injury (Appendix; table I). Next, we manually scrutinized all retrieved patient records for final inclusion. In this way we created two (retrospective) cohorts:

Cohort1: *patients with (all types of) head injury*; we expected the incidence of all head injury to be high and therefore limited the inclusion period to one year (between 1 January 2014 and 31

December 2014). Through a pilot study we constructed an inclusive list of 23 diagnostic ICPC labels that (might) refer to a head injury or traumatic brain injury. For example, to refer to a head injury the code 'concussion' (N79) could be selected, but also 'bruise/contusion' (S16) referring to skin involvement of the trauma (Appendix). Next, all available clinical data from these preselected patients were manually screened for a match to our inclusion criteria of head injury. Additionally, we screened all files of deceased patients in 2014 for the cause of death to verify if head injury occurred up to 4 weeks before time of death.

Cohort 2: *patients with a complicated course*; we expected complicated head injury to be rare and therefore included patients from a 10-year time interval (between 1 January 2005 and 31 December 2014). To identify patients with a complicated head injury we used different ICPC codes that (might) refer to (consequences of) severe and complicated head injury. We also searched for specialist letters and hospital admission in the field of neurology, neurosurgery or rehabilitation medicine. All specialist letters from these preselected patients were then manually screened for occurrence of head injury. In addition to specialist letters, we used GP documentation to identify known risk factors for complicated course (19-22).

We reviewed all available clinical data, including general notes, hospital (including emergency department) correspondence, radiological imaging findings, surgical records and autopsy records. We extracted data using a predefined form (Appendix) and excluded patients with severe multi-trauma injury.

Statistical analysis

We calculated the incidence of head injury and complicated head injury per 1000 person years with 95% Confidence Intervals, using the Mid-P exact test (Open source calculator OpenEpi, version 3). Age and sex structures of the mid-time population were used as denominators.
The incidence of head injury was defined as any new case of head injury during the study period. Some patients had more than one isolated case of head injury. To determine the proportion of patients with complicated head injury, their incidence was compared to incidence of all head injuries as identified during the one-year study period. We evaluated all included cases for demographic and trauma characteristics.

In order to assess potential risk factors for a complicated course of head injury, we calculated Odds ratios on trauma mechanism, trauma setting, type-of-contact (hospital/GP/telephonically) after trauma and patient characteristics. Odds ratios were calculated using SPSS (IBM SPSS Statistics, Version 22.0. Armonk, NY). A p-value of <0,05 was considered statistically significant. Multivariate regression analysis was performed on the variables gender, age and high-energy trauma (HET) as the most relevant trauma mechanism. Factors predicting a complicated head injury were calculated by multivariate analysis with logistic regression models. Variables were age, gender, trauma mechanism, symptoms for fracture and use of anti-coagulant. Moderate and severe head injury was combined during analysis due to small sample sizes. Clinical findings and data are presented using frequencies as well as percentages.

Results

(1) Incidence of all head injury.

During one year follow up (31.369 patient years), we identified 694 patients with head injury (figure 1), resulting in an overall incidence rate of 22.1 per 1000 person years (20.5-23.8; 95% CI). The incidence rate was 123.0 per 1000 person years (95%CI 101.1-148.2) for children aged 0-1 years and 34% of all patients were under 15 years old. Patient characteristics are shown in table 1. Two of 694 patients (0.3%) died during the study period; one was a 101-year old male patient who injured his head when falling from bed and died 28 days later and the other was a 94-year old male patient who fell against a radiator and died one day later. In both cases the GP decided to renounce referral, with informed consent from patient and family, because of age and co-morbidity.

Patients presenting themselves to the GP were managed without referral in 90.0% of cases [n=546]. 21.3% [n=148] of all head injury patients attended the hospital emergency department (ED). Only 39.2% [n=58] were referred by the GP, with the remainder coming directly by ambulance or their own transport. Patients visiting the ED underwent CT-scanning in 50.6% [n=75] of cases and were hospitalized for at least 24 hours in 29.7% [n=44] of cases. Intra-cerebral lesion was seen in 6.8% [n=10] of patients undergoing a CT-scan; four of these patients underwent a neurosurgical intervention.

(2) Incidence of complicated head injury.

Over an observation period of ten years we identified 36 patients with complicated head injury (220.352 patient years), resulting in an incidence rate of 0.16 per 1000 person-years (0.12-0.22; 95%CI). Incidence rates are shown in table 2. In 97.2% of cases it was possible to assess the severity of traumatic brain injury from specialist correspondence. 25% [n=9] of patients, all over 60 years old, received anticoagulant therapy at time of head injury. No patients had a history of coagulopathies or other bleeding disorders. Most patients with a complicated head injury (72.2% [n=26]) were referred directly to the hospital without involvement of a GP. If the initial contact was in primary care, all complicated patients presented with severe symptoms such as neurological deficits, loss of consciousness and epilepsy. A total of eight patients (1.7%) died during study period; two were not sent to a hospital and died without an autopsy, these were the

same patients as found in cohort 1. We found out-of-hospital delay in two patients, leading to delayed neurosurgical intervention. One patient consulted his GP due to a headache without reporting that he suffered head injury two weeks earlier: when the headache worsened the GP referred the patient to the hospital where a subdural hematoma was diagnosed. The second patient was residing in a care home and suffering from dementia. Following a fall from bed and non-response to pain medication he was referred to hospital, where a subarachnoid haemorrhage was diagnosed.

(3) Predictors for complicated course.

Univariate regression analysis showed that a High Energy Trauma (HET) was related to a significantly higher risk of developing a complicated head injury (OR 3.93, 95%CI 1.97-7.84) (Table 3). Traffic and isolated bicycle accidents were also associated with a higher risk of complicated head injury (OR 2.88, 95%CI 1.04-7.02) respectively (OR 2.70, 95%CI 1.24- 5.61). The risk of a complicated head injury was significantly reduced if the first encounter was in primary care (OR 0.03, 95%CI 0.01-0.07), and conversely much higher when an ambulance was the first responder (OR 22.14, 95%CI 10.6- 48.05). Hospital admission without previous GP contact was related to a higher risk of complicated head injury (OR 18.04, 95%CI 8.54-40.41). A complicated course was also seen more often with oral anticoagulants (OAC) (OR 4.10, 95%CI 1.75-9.03), alcohol-intoxication (OR 4.30, 95%CI 1.38-11.53), lowering of Glasgow Coma Scale (OR 41.2, 95%CI 16.43-105.00) and age above 60 years (OR 6.60, 95%CI 3.30-13.36).

Gender, age, trauma-mechanism assault and usage of anti-coagulation were included in the multivariate analysis (limited sample size precluded inclusion of further variables). We found a significantly higher risk of hospital admittance, as well a complicated course after head injury, for age 60 years and older (OR 12.6, 95%CI 5.0-31.9) and the presence of symptoms that could indicate a fracture (above clavicle) (OR 2.4, 95%CI 1.4-4.1). When compared to the trauma mechanism ‘fall’, high energetic trauma was associated with a higher risk for hospital; admission (OR 2.8, 95% CI 1.5-5.2). Male gender was not found to be a predictor of a complicated course (p=0.233).

Discussion

This is the first study to investigate the full spectrum of traumatic head injury in both primary and secondary care. We found much higher incidence rates than previously reported: 22 per 1000 patients per year, with a peak incidence in babies (0-1 years) of 123/1000. The incidence of a complicated head injury, on the other hand, is very low (0.16 per 1000 person-years) and much more in line with previous research. The vast majority of head injury patients (78.7%) were treated in primary care without referral, whereas the majority of patients with complicated head injury (72%) were directly admitted to secondary care without involvement of a primary care professional. Patients with complicated injury who initially presented in primary care seemed to be easily identified and referred to secondary care, except for two patients of 94 and 101 years old in which a palliative approach was chosen. Known risk factors for a complicated course such as oral anticoagulants and age above 60 years were confirmed in this study (20-22).

A particular strength of our study is its setting in the Dutch health-care system, in which all patients are registered with one particular primary care provider and all encounters with healthcare professionals reported back. This means that the primary care doctor holds an overview of all encounters with health care of a particular patient (17). We used the FaMe-network database, which is linked to electronic patient files in which all encounters are registered and coded. In this system, new data (encounters, letters, reports) cannot be entered without linking to a new or existing diagnosis code – making it impossible to miss even the simplest case of head injury. Moreover, it is not possible to miss cases that started in primary care but were followed up elsewhere because these encounters would be reported back, registered and coded in the same file. Because the registration network has a focus on diagnosis and medical processes (e.g. referrals, prescription), signs and symptoms of head injuries are registered in the same way as in any other practice. Most of the patients seen by the GP's involved simple head injuries, with no need for detailed reporting.

We found substantially higher incidence of head injury compared to existing reports. A recent systematic review on the incidence of all types of traumatic brain injury found a pooled incident rate of only 3.49 per 1000 patients per year, whereas our finding was 22 per 1000 patients per

year (5). In contrast with this review, we conclude that most head injuries occur amongst young children – identifying incidence more than a hundred times higher in children. This difference might be explained by variable classification, especially since the systematic review's authors point out the problem of non-standardized reporting among neuro-epidemiological studies on incidence of (particularly mild) head injury. One particular study claimed to assess the full spectrum of head injury by including data from general practice, resulting in an incidence of 7.90 per 1000 patients per year. Unfortunately, this study limited inclusion to patients with head injury and "physiological disruption of brain function" (7).

Variation in definition of head injury is an ongoing problem in current literature, resulting in a wide range of incidence figures of traumatic head injury (5, 23-25). One particular review stated that the term 'silent epidemic' could be used to characterize the incidence of head injury, because many cases are not recognized and therefore excluded from official statistics (25). Our study captures the full spectrum of head injury as presented in the entire health-care system (in and out of hospital) with inclusion based on any trauma of the head excluding injuries of the face. This is in line with current guidelines for primary care that apply a similar broad definition of head trauma. We fully endorse this broad definition for future diagnostic and prognostic research aimed at primary care populations. The nature of primary care is that it is easily and rapidly accessible for every patient with no pre-selection or other thresholds. Even in primary care it is difficult to rule out a complicated course. After all, the condition was (per definition) sufficiently severe for patient, parents or bystanders to seek professional help. Moreover, neurological indications may not develop in this early stage so a definition based on signs of 'disruption of brain function' - as has previously been advocated - is not feasible (25). We are furthermore convinced that identifying patients with mild trauma (including those not seen in a hospital setting) is relevant because, as demonstrated, uncomplicated head injury may be associated with significant on-going cost in terms of disability, lost work or neuropsychiatric complications (29, 30).

Although existing guidelines are based on a broad definition of head injury, the underlying evidence is based almost exclusively on clinical populations. In clinical populations a (self-) selection for complicated head injury has already taken place and a narrow definition of head

injury is used (10, 11, 18, 26, 27), leading to a higher estimated risk for complications and over-treatment of patients with head injury (27, 28).

We conclude that head injury as seen in primary care comprises an essentially different case-mix as compared to secondary care. Moreover, complicated cases appear to be easily identified and readily presented to secondary care either by self-selection of the patient (or bystanders) or by the primary care professional. Our study requires confirmation in other settings using other databases, but we are convinced that current guidelines are based on limited evidence of true incidence rates. This makes them prone to spectrum bias. A more reserved management of head injury in primary care should be considered, leading to more cost-effective use of costly hospital diagnostic resources. This study also calls for an internationally accepted definition (coupled with a universal diagnostic algorithm) of head injury and (mild) traumatic brain injury.

Statements concerning this study

Contributor ship:

- Gerritsen, H (MD); was involved and made contributions in the design of the study, acquisition, analysis and interpretation of the data. Drafted the work and revised it critically for important intellectual content. Gave final approval of the version published and made agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
- Samim, M (Msc); was involved and made contributions in the design of the study, acquisition, analysis and interpretation of the data. Revised the work critically for important intellectual content. Gave final approval of the version published and made agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
- Peters, H (Bsc); was involved and made contributions in the design of the study, acquisition, analysis and interpretation of the data. Revised the work critically for important intellectual content. Gave final approval of the version published and made agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
- Schers, H (MD, PhD); was involved and made contributions in the design of the study, acquisition, analysis and interpretation of the data. Revised the work critically for important intellectual content. Gave final approval of the version published and made agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
- Laar, F vd. (MD, PhD); was involved and made contributions in the design of the study, acquisition, analysis and interpretation of the data. Revised the work critically for important intellectual content. Gave final approval of the version published and made agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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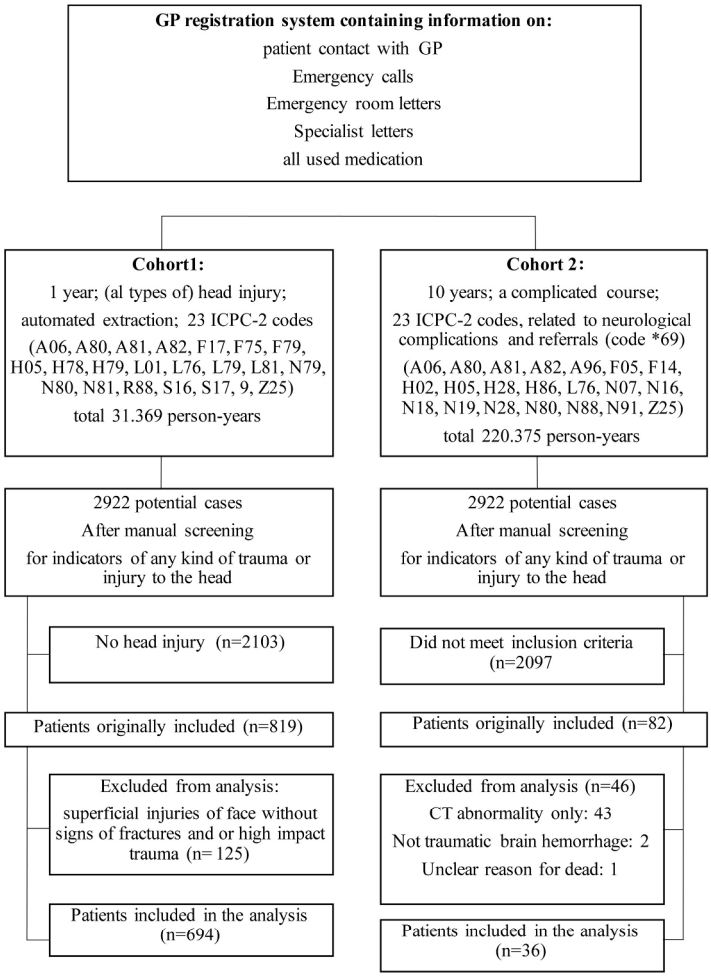

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Table 1. Characteristics of patient and trauma

Patient Characteristics	Cohort 1. All head injury	Cohort 2. Complicated head injury
Variables	No.(%) of patients	No. (%) of clinical complications
Gender		
Male	371 (53.5)	16 (44.4)
Female	323 (46.5)	20 (55.6)
Mean age		
All	25.8 ; SD 27.7	58.0; SD 29
- Male	20.2 ; SD 23.6	48.9; SD 30
- Female	32.2 ; SD 30.5	65.3; SD 27
Presence of indicators of cHI †		
Multiple cHI indicators	-	12 (33.3)
Death	2 (0.3)	8 (22.2)
Neurosurgical intervention	4 (0.6)	12 (33.3)
Seizure	1 (0.1)	6 (16.7)
Neurological deficit	4 (0.6)	24 (66.7)
Current anticoagulant therapy		
No	642 (92.5)	27 (75.0)
Yes	52 (7.5) **	9 (25.0) **
Trauma TBI-classification *		
Mild	-	26 (72.2)
Moderate	3 (0.4)	2 (5.6)
Severe	2 (0.3)	7 (19.4)
Not reported	689 (99.3)	1 (2.8)
Trauma setting		
Home	272 (39.2)	12 (33.3)
Work	-	2 (5.6)
School/daycare	47 (6.8)	2 (5.6)
Recreation/sport	137 (19.7)	3 (8.3)
Traffic	45 (6.5)	6 (16.7)
Bicycle/motor bike	97 (13.9)	11 (30.6)
Not reported	96 (13.8)	-
Trauma mechanism		
Fall >1m	449 (64.7)	20 (55.6)
HET	52 (7.5)	12 (33.3)
Blunt trauma	151 (21.8)	2 (5.6)
acceleration/deceleration	-	-
Assault	25 (3.6)	2 (5.6)
Not reported	15 (2.2)	-
Contacts		
GP only	546 (78.7)	2 (5.6)
Hospital only	90 (12.9)	26 (72.2)
GP and hospital	58 (8.4)	8 (22.2)
Vomiting		
No	320 (46.1)	10 (27.8)

Yes	54 (7.8)	9 (25.0)
Not reported	320 (46.1)	17 (47.2)
Neurological deficit in acute phase		
No	308 (44.4)	10 (27.8)
Yes	51 (7.3)	21 (58.3)
Not reported	335 (48.3)	5 (13.9)
Change in mental functioning		
No	308 (44.4)	10 (27.8)
Yes	107 (15.4)	18 (50.0)
Not reported	279 (40.2)	8 (22.2)
External injury		
No	165 (23.8)	7 (19.4)
Yes	424 (61.1)	23 (63.9)
Not reported	105 (15.1)	6 (16.7)
Intracranial lesions		
No (lesions on CT scan)	75 (10,8)	9 (25.0)
Yes (lesions on CT scan)	10 (1.4)	22 (61.1)
Not reported/ or no CT scan	609 (87.8)	5 (13.8)
If intracranial lesions on CT scan		
- neurosur. intervention	4 (0.6)	12 (33.3)
- no neurosur. intervention	6 (0.9)	10 (27.8)

† cHI= complicated Head Injury; indicators of occurrence of complicated head injury.
* Traumatic Brain Injury
** All in age group >60years

Table 2. Incidence rates of (complicated) head injury

Patient age & sex	All head injuries (n=694)			Complicated head injury (n=36)			
	Midtime population*	HI (n)	Incidence rate per 1000 person years (95% CI)	Midtime population*	cHI (n)	Incidence rate per 1000 person years (95% CI)	Proportion complicated cHI of all HI (in %)
Male							
0 - 1 year	418	54	129.2 (98.0 - 167.3)	3741	1	0.27 (0.01-1.31)	0.21
2 - 5 years	1001	93	92.9 (75.4 - 113.3)	6708	1	0.15(0.007-0.74)	0.16
6 - 15 years	2309	89	38.5 (31.1 - 47.2)	15135	1	0.07 (0.003- 0.33)	0.18
16 - 40 years	4678	53	11.3 (8.6 - 14.7)	32484	4	0.12 (0.04-0.30)	1.06
41 - 60 years	4606	48	10.4 (7.8 - 13.7)	32375	3	0.09 (0.02-0.25)	0.87
> 60 years	2482	34	13.7 (9.6 - 18.9)	17694	6	0.34 (0.14-0.71)	2.48
Total	15494	371	23.9 (21.6 - 26.5)	108137	16	0.15 (0.09-0.24)	0.63
Female							
0 - 1 year	436	51	117.0 (88.0 - 152.6)	3650	0	0 (-)	0
2 - 5 years	949	41	43.2 (31.4 - 58.1)	6119	1	0.16 (0.008- 0.81)	0.37
6 - 15 years	2104	45	21.4 (15.8 - 28.4)	14127	2	0.14 (0.024-0.047)	0.65
16 - 40 years	5010	70	14.0 (11.0 - 17.6)	34546	0	0 (-)	0
41 - 60 years	4550	37	8.1 (5.8 - 11.1)	32265	3	0.09 (0.024-0.25)	1.11
> 60 years	2826	79	28.0 (22.3- 34.7)	21531	14	0.65 (0.37-1.07)	2.32
Total	15875	323	20.4 (18.2 - 22.7)	112238	20	0.18 (0.11-0.27)	0.88
Male and Female							
0 - 1 year	854	105	123.0 (101.1 - 148.2)	7391	1	0.14 (0.006-0.67)	0.11
2 - 5 years	1950	134	68.7 (57.8 - 81.1)	12827	2	0.16 (0.026- 0.52)	0.23
6 - 15 years	4413	134	30.4 (25.5 - 35.9)	29262	3	0.10 (0.03-0.28)	0.33

16 – 40 years	9688	123	12.7	(10.6 - 15.1)	67030	4	0.06 (0.02-0.14)	0.47
41 - 60 years	9156	85	9.3	(7.5 - 11.4)	64640	6	0.09 (0.038-0.19)	0.97
> 60 years	5308	113	21.3	(17.6 - 25.5)	39225	20	0.51 (0.32-0.77)	2.39
Total	31369	694	22.1	(20.5 - 23.8)	220375	36	0.16 (0.12-0.22)	0.72

* Midtime population is calculated by means of total patient population on 1st of January and 31th of December.

Table 3. Univariate regression analysis for complicated head injury

Variable	OR*	95%CI (Mid P exact)	p Value (two-tailed. Mid P exact)
Trauma mechanism			
HET	3.93	1.97-7.84	<0.000
Car vs. pedestrian/bicycle	1.709	0.24- 7.90	0.5134
Fall >1m	1.029	0.35- 2.69	0.9307
High impact	1.285	0.47- 3.24	0.5935
Fall	0.68	0.35-1.37	0.2767
Trauma setting			
Home	0.78	0.37-1.57	0.493
Work	1.301	0.20- 4.91	0.682
School	0.81	0.13- 2.98	0.846
Rec/sport	0.37	0.09-1.11	0.080
Traffic	2.88	1.04- 7.02	0.042
Bicycle	2.70	1.24- 5.61	0.014
Contacts			
First encounter GP	0.03	0.01-0.07	<0.000
First encounter Ambulance	22.14	10.60-48.05	<0.000
GP only	0.02	0.00-0.06	<0.000
Hospital only	18.04	8.54-40.41	<0.000
GP/hospital	3.15	1.29-7.07	0.0138
Patient characteristics			
Use of OAC	4.10	1.75-9.03	0.002
Alcoholintoxication	4.30	1.38-11.53	0.015
GCS <12 (excl. not reported)	41.2	16.43-105.00	<0.000
Male gender	0.69	0.35-1.37	0.292
Age >60	6.60	3.30-13.36	<0.000
*Agegroups***			<0.000
0-1 yr (reference group)	-	-	-
2-5 yr	1.58	0.14- 17.65	0.711
6-15 yr	2.37	0.24- 23.10	0.458
16-40 yr	3.42	0.38- 31.02	0.275
41-60yr	7.50	0.89- 63.51	0.065
>60 yr	19.27	2.5- 146.13	0.004

* Odds ratios are based on Conditional maximum likelihood estimate
** Glasgow Coma Scale
*** Significances of Odds ratios calculated are in relation to youngest age group

Appendix; definition of initial variables for data extraction.

Data collection was performed based on information from specialist correspondence and GP documentation. There-fore selected ICPC codes were used (Table I). Data was systematically screened on several variables (Table II).

The Glasgow Coma Scale (GCS), Initial GCS documented at first medical contact, was documented only if it was reported in the data without calculating scores afterwards.

Based on the standardised Traumatic Brain Injury classification, head injury was classified into mild, moderate or severe brain injury based on initial GCS, PTA and duration of loss of consciousness. If classification was not possible due to lack of data but classification was documented in the specialist letter, this classification was used for analysis. To assess the trauma characteristics, trauma setting and mechanism was documented. We considered a patient to have a head injury at home, work, school and day-care when documented as such or when indicated by context. Recreation and sport was chosen as trauma setting if the accident happened in recreational time not related to traffic. Traffic was chosen as trauma setting if the patient sustained head injury in a traffic setting (car vs. pedestrian/bicycle/car). Falling off a bicycle as cause of trauma was documented apart if no other traffic members were affected in the accident.

Trauma mechanism was divided into several subcategories with high energy trauma defined as fall from elevation, traffic accidents with high velocity and high impact, including acceleration/deceleration trauma.

We defined neurological deficit in the acute phase as any abnormality documented on routine clinical neurological examination that indicated a focal cerebral lesion. Mental state was scored as any documented change in behaviour or deviation of compos mentis. Symptoms of dementia and changed behaviour due to intoxication were scored as “other”. Signs of basal skull fracture were Battle’s sign, Raccoon eyes and/or liquor leakage/bleeding from nose and ear. External injury was defined as any documented discontinuity of the facial skin or head. Intoxication was scored as ‘yes’ if explicit reported. If overall documentation was limited than intoxication was scored as “not reported”; in all other patients intoxication was score as “no”.

Within ‘contacts’ information about all contacts in the acute posttraumatic period were scored. ‘GP’ indicates that patients were seen by a GP only, ‘GP/hospital’ indicates that patient was referred to the hospital after being seen by a GP, ‘hospital’ indicates that patients

are not seen by a GP before. Variables which are not mentioned here but are only displayed in the table were scored as indicated in the table.

Table I. ICPC Codes* indicating Head Injury

A06	Fainting/syncope
A80	Trauma/injury NOS
A81	Multiple trauma/injuries
A82	Secondary effect of trauma
A96	Death
H05	Bleeding ear
L76	Fracture: other
N07	Convulsion/seizure
N79	Concussion
N80	Head injury other
N88	Epilepsy
Z25	Assault/harmful event problem

ICPC Codes indicating a Complicated Course

*** 67**	Referral to Physician/Specialist/ Clinic/Hospital
A96	Death
F05	Visual disturbance other
F14	Eye movements abnormal
H02	Hearing complaint
H28	Limited function/disability ear
H86	Deafness
N07	Convulsion/seizure
N16	Disturbance of smell/taste
N18	Paralysis/weakness
N19	Speech disorder
N28	Limited function/disability (n)
N88	Epilepsy
N91	Facial paralysis/bell's palsy

* ICPC-2 – English International Classification of Primary Care – 2nd Edition, Wonca International Classification Committee (WICC)

Table II. Variables used for Data Extraction

Variable	Categories
Glasgow Coma Scale	1= 15, 2= 14, 3= 13, 4= 9-12, 5= 8 or lower, 9= not reported
Loss of consciousness	0= no, 1= <5min, 2= 5-30min, 3= >30min, 4= duration unclear, 5= Unclear if LOC, 9= not reported
Posttraumatic amnesia	0= no, 1= <24h, 2= 1-7 days, 3= >7 days, 4= unclear if PTA, 9= not documented
TBI classification	1= mild, 2= moderate, 3= severe, 9= no classification possible
Trauma setting	0= not reported 1= home, 2= work, 3= school/daycare 4= recreation/sport, 5= traffic 6= bicycle
Trauma mechanism	0= not reported, 1= fall, 2=HET, 3= blunt trauma, 4= acceleration/deceleration, 5= assault, 6= other 7= not sure
Nausea	0= no, 1= yes, 2= not applicable, 9= not reported
Vomiting	0= no, 1= yes, 9= not reported
Neurological deficit in acute phase	0= no, 1= weakness, 2= loss of balance, 3= change in vision, 4= change in speech, 5= change in motor function, 6= change in sensory function, 7= multiple, 9= not reported
Mental state	0= no change, 1= confusion 2= disorientation, 3= slowed thinking, 4= other, 9= not reported
External injury	0= no, 1= laceration/cut, 2= hematoma, 3= edema, 4= graze/superficial, 5= multiple, 9= not reported
Suspected skull fracture	0= no, 1= yes, 9= not reported
Signs of basal skull fracture	0= no, 1= yes, 9= not reported
Alcohol/drug intoxication	0= no, 1= alcohol, 2= drugs, 3= combined, 9= not reported
First encounter	1= General practitioner, 2= Emergency department, 3= ambulance, 9= not reported
Contacts	1= General practitioner only, 2= General practitioner/hospital, 3= Hospital only
Gender	0= male, 1= female
Age	-
Current anticoagulant therapy	0= no, 1= VitK antagonist, 2= anti platelet, 3= NOAC, 4= multiple
Risk medication:	0= no 1= yes
Sedatives	
Anti-diabetics	0= no, 1= yes
	0= no, 2= metformine, 2= sulfonylureas, 3= insulin, 4= multiple
Anti-epileptics	0= no, 1= yes

STROBE (Strengthening The Reporting of OBservational Studies in Epidemiology) Checklist

A checklist of items that should be included in reports of observational studies. You must report the page number in your manuscript where you consider each of the items listed in this checklist. If you have not included this information, either revise your manuscript accordingly before submitting or note N/A.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

Section and Item	Item No.	Recommendation	Reported on Page No.
Title and Abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/Rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study Design	4	Present key elements of study design early in the paper	7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7 & 8
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	7
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7

Section and Item	Item No.	Recommendation	Reported on Page No.
Data Sources/ Measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7
Bias	9	Describe any efforts to address potential sources of bias	8
Study Size	10	Explain how the study size was arrived at	7 & 8
Quantitative Variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8 & 9
Statistical Methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8 & 9
		(*b*) Describe any methods used to examine subgroups and interactions	8 & 9
		(*c*) Explain how missing data were addressed	9
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	8 & 9
		(*e*) Describe any sensitivity analyses	9
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	10 & 11
		(b) Give reasons for non-participation at each stage	Fig. 1
		(c) Consider use of a flow diagram	Fig. 1
Descriptive Data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10 & 11
		(b) Indicate number of participants with missing data for each variable of interest	10 & 11 Tab. 1
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	10 & 11
Outcome Data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	10 & 11 Tab. 2
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	

Section and Item	Item No.	Recommendation	Reported on Page No.
Main Results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10 & 11
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	11
Other Analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key Results	18	Summarise key results with reference to study objectives	12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12 & 13
Generalisability	21	Discuss the generalisability (external validity) of the study results	13 & 14
Other Information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

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BMJ Open

Incidence, course and risk factors of head injury in The Netherlands.

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Title: Incidence, course and risk factors of head injury in The Netherlands.

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Abstract

Objectives

To assess the incidence of head injury and predictors of complication across the care continuum.

Design

Retrospective cohort study using data from a research network. We calculated the incidence of overall head injury in a longitudinal cohort covering 1 year interval (31,369 patient years), and the incidence of complicated head injury in a longitudinal cohort covering 10 years interval (220,352 patient years). Incidence rates were calculated per 1000 patient-years with 95% CI using the Mid-P exact test. We calculated Odds ratios to assess potential risk factors for a complicated head injury.

Setting

A practice-based research network covering a population of >30,000 patients.

Participants

All patients listed in practices within the research network during the years 2005-2014.

Main outcome measures

Incidence of (complicated) head injury and predictors for clinical complications.

Results

The incidence of overall head injury was 22.1 per 1000 person years and the incidence of a complicated course following head injury was 0.16 per 1000 person years. The following determinants were risk factors for a complicated course: high energy trauma, bicycle accident, traffic accident in general, use of anticoagulants, alcohol intoxication, age above 60 years and low Glasgow Coma Scale at initial presentation. A complicated course was very unlikely when the first patients' first encounter with a healthcare professional was in primary care (OR 0.03, 95%CI 0.01-0.07).

Conclusions

Complication after head injury are rarely seen in general practice. Patients who do experience complications are often easily identifiable as requiring specialist care. A more reserved referral policy for general practice may be desirable, suggesting that current guidelines are too defensive.

Trial registration

None.

Strengths and limitations

Strengths of study:

- Based on robust, comprehensive data set including all encounters of individual patients with healthcare professionals both from primary and secondary care.
- Scrutinous manual screening of all patients.

Limitation of this study:

- Incomplete data set; use of routine data from general practice

Ethical approval

No formal ethical approval was needed for this study. Patients in the participating practices are informed about the continuous data collection. The data set is anonymized and encrypted before transfer to the researchers.

Patient and Public Involvement statement

No patients where involved during development of research question, outcome measures and design of this study.

Introduction

Patients presenting with head injury in primary care challenge general practitioners to differentiate between those who may be reassured, and those who are at risk of serious intracranial injury. Intracranial injuries such as epidural and subdural hematoma or skull fractures may lead to death or permanent damage if left untreated (1-4).

High quality clinical management of head injury takes the small chance of intracranial injury into account. Safe and cost-effective practice guidelines for primary care must therefore be based on a reliable risk calculation, for which precise data are needed on the incidence of both head injury and serious intracranial injury or complicated head injury. In Europe, the annual incidence of head injury presenting in hospital emergency departments is 2.3 per 1000 person-years (5) (6). In general practice, this incidence is expected to be higher because only a subset of patients are referred to hospital. Robust data about incidence rates in primary care are lacking. For example, a New Zealand study in a primary care population found an incidence rate of 7.5 per 1000 person-years (7), whereas, in a small pilot study in the Netherlands, we found the incidence of (mild and severe) head injury to be as high as 22.3 per 1000 person-years (8).

The incidence of severe damage after a head injury is also unclear. In the UK, head injury accounts for 3.4% of all emergency department attendances. About 90% of head injuries in clinical setting are considered to be mild (6, 7). Incidence of moderate to severe head injury was 40 per 100.000 persons – a figure which may in reality be slightly higher because it does not include patients who die before admittance to the hospital (9). This makes the identification of patients at risk challenging.

Currently, guidelines for the identification, referral and management of patients with head injury at risk for intracranial damage are based on epidemiological studies from secondary or tertiary care (10, 11). Currently two different guidelines are used in the Netherlands, both have strong resemblance with the NICE guideline as used in the UK (12-14). It is likely that this case-mix of head injury patients is essentially different from that in primary care (15, 16). The risk for a

complicated course may therefore be exaggerated, resulting in spectrum bias in current guidelines (15-19).

In this study, we aim to assess the incidence of head injury in primary care and to identify risk factors for intracranial injury. Our research questions were: (1) what is the incidence of head injury and complicated head injury, and (2) what predicts a complicated course?

Methods

Study Setting

We performed a retrospective cohort study in the practice based research network Family Medicine Network (FaMe-net) of the Department of Primary and Community Care (ELG) at the Radboud University Medical Centre. FaMe-net consists of nine Dutch general practices in 3 geographical regions (approximately 31.000 listed patients). FaMe-net physicians systematically and prospectively register data on the reason for encounter, diagnostic procedures, diagnoses, interventions, and referrals. The network uses the ICPC-2 and ICD-10 classification systems to code procedures and diagnosis. All data can be linked to demographic information (age, gender, geographic location, family composition). In the Netherlands, all patients are listed in one general practice to which all encounters in secondary care are reported. Reports from other care-providers are coded and linked to a new or existing episode (20). Participating doctors in FaMe-net meet on a regular basis to discuss registration issues and improve the uniformity of registration.

Definitions

We defined head injury as any trauma to the head other than superficial injuries to the face (14). A complicated head injury was defined as a head injury for which treatment and surveillance in secondary care was deemed necessary: a need for surgical intervention (defined as any neurosurgical procedure including drainage and placement of ICD), seizures in the acute posttraumatic phase, resulting neurological deficits within 12 months after trauma, and death. Neurological deficits were defined as any neurological abnormalities, including facial fracture associated nerve lesions.

Study Population and data collection

We selected patients in two stages: first we performed a sensitive electronic search based on the list of ICPC labels indicating head injury (Appendix; table I). Next, we manually scrutinized all retrieved patient records for final inclusion. In this way, we created two (retrospective) cohorts:

Cohort1: *patients with (all types of) head injury*; we expected the incidence of all head injury to be high and therefore limited the inclusion period to one year (between 1 January 2014 and 31

December 2014). Through a pilot study we constructed an inclusive list of 23 diagnostic ICPC labels that (might) refer to a head injury or traumatic brain injury. For example, to refer to a head injury the code 'concussion' (N79) could be selected, but also 'bruise/contusion' (S16) referring to skin involvement of the trauma (Appendix). Next, all available clinical data from these preselected patients were manually screened for a match to our inclusion criteria of head injury. Additionally, we screened all files of deceased patients in 2014 for the cause of death to verify if head injury occurred up to 4 weeks before time of death.

Cohort 2: *patients with a complicated course*; we expected complicated head injury to be rare and therefore included patients from a 10-year time interval (between 1 January 2005 and 31 December 2014). To identify patients with a complicated head injury we used different ICPC codes that (might) refer to (consequences of) severe and complicated head injury. We also searched for specialist letters and hospital admission in the field of neurology, neurosurgery or rehabilitation medicine. All specialist letters from these preselected patients were then manually screened for a match to our inclusion criteria of head injury. In addition to specialist letters, we used GP documentation to identify known risk factors for complicated course (21-24).

We reviewed all available clinical data, including general notes, hospital (including emergency department) correspondence, radiological imaging findings, surgical records and autopsy records. We extracted data using a predefined form (Appendix) and excluded patients with severe multi-trauma injury.

Statistical analysis

We calculated the incidence of head injury and complicated head injury per 1000 person years with 95% Confidence Intervals, using the Mid-P exact test (Open source calculator OpenEpi, version 3). Age and sex structures of the mid-time population were used as denominators.
The incidence of head injury was defined as any new case of head injury during the study period. Some patients had more than one isolated case of head injury. To determine the proportion of patients with complicated head injury, their incidence was compared to incidence of all head injuries as identified during the one-year study period. We evaluated all included cases for demographic and trauma characteristics.

In order to assess potential risk factors for a complicated course of head injury, we calculated Odds ratios on trauma mechanism, trauma setting, type-of-contact (hospital/GP/telephonically) after trauma and patient characteristics. Odds ratios were calculated using SPSS (IBM SPSS Statistics, Version 22.0. Armonk, NY). A p-value of <0,05 was considered statistically significant. Multivariate regression analysis was performed on the variables gender, age and high-energy transfer – during trauma (HET) as the most relevant trauma mechanism. Factors predicting a complicated head injury were calculated by multivariate analysis with logistic regression models. Variables were age, gender, trauma mechanism, symptoms for fracture and use of anti-coagulant. Moderate and severe head injury was combined during analysis due to small sample sizes. Clinical findings and data are presented using frequencies as well as percentages.

Results

(1) Incidence of all head injury.

During one year follow up (31.369 patient years), we identified 694 patients with head injury (figure 1), resulting in an overall incidence rate of 22.1 per 1000 person years (20.5-23.8; 95% CI). The incidence rate was 123.0 per 1000 person years (95%CI 101.1-148.2) for children aged 0-1 years. Out of all the patients with a head injury, 34% were under 15 years old. Patient characteristics are shown in table 1.

Table 1. Characteristics of patient and trauma

Patient Characteristics	Cohort 1. All head injury	Cohort 2. Complicated head injury
Variables	No.(%) of patients	No. (%) of clinical complications
Gender		
Male	371 (53.5)	16 (44.4)
Female	323 (46.5)	20 (55.6)
Mean age		
All	25.8 ; SD 27.7	58.0; SD 29
- Male	20.2 ; SD 23.6	48.9; SD 30
- Female	32.2 ; SD 30.5	65.3; SD 27
Presence of indicators of cHI †		
Multiple cHI indicators	-	12 (33.3)
Death	2 (0.3)	8 (22.2)
Neurosurgical intervention	4 (0.6)	12 (33.3)
Seizure	1 (0.1)	6 (16.7)
Neurological deficit	4 (0.6)	24 (66.7)
Current anticoagulant therapy		
No	642 (92.5)	27 (75.0)
Yes	52 (7.5) **	9 (25.0) **
Trauma TBI-classification *		
Mild	-	26 (72.2)
Moderate	3 (0.4)	2 (5.6)
Severe	2 (0.3)	7 (19.4)
Not reported	689 (99.3)	1 (2.8)
Trauma setting		
Home	272 (39.2)	12 (33.3)
Work	-	2 (5.6)
School/daycare	47 (6.8)	2 (5.6)
Recreation/sport	137 (19.7)	3 (8.3)
Traffic	45 (6.5)	6 (16.7)
Bicycle/motor bike	97 (13.9)	11 (30.6)

Not reported	96 (13.8)	-
Trauma mechanism		
Fall >1m	449 (64.7)	20 (55.6)
HET	52 (7.5)	12 (33.3)
Blunt trauma	151 (21.8)	2 (5.6)
acceleration/deceleration	-	-
Assault	25 (3.6)	2 (5.6)
Not reported	15 (2.2)	-
Contacts		
GP only	546 (78.7)	2 (5.6)
Hospital only	90 (12.9)	26 (72.2)
GP and hospital	58 (8.4)	8 (22.2)
Vomiting		
No	320 (46.1)	10 (27.8)
Yes	54 (7.8)	9 (25.0)
Not reported	320 (46.1)	17 (47.2)
Neurological deficit in acute phase		
No	308 (44.4)	10 (27.8)
Yes	51 (7.3)	21 (58.3)
Not reported	335 (48.3)	5 (13.9)
Change in mental functioning		
No	308 (44.4)	10 (27.8)
Yes	107 (15.4)	18 (50.0)
Not reported	279 (40.2)	8 (22.2)
External injury		
No	165 (23.8)	7 (19.4)
Yes	424 (61.1)	23 (63.9)
Not reported	105 (15.1)	6 (16.7)
Intracranial lesions		
No (lesions on CT scan)	75 (10,8)	9 (25.0)
Yes (lesions on CT scan)	10 (1.4)	22 (61.1)
Not reported/ or no CT scan	609 (87.8)	5 (13.8)
If intracranial lesions on CT scan		
- neurosur. intervention	4 (0.6)	12 (33.3)
- no neurosur. intervention	6 (0.9)	10 (27.8)

† cHI= complicated Head Injury; indicators of occurrence of complicated head injury.
* Traumatic Brain Injury
** All in age group >60years

Two of 694 patients (0.3%) died during the study period; one was a > 90-year old patient who injured his head when falling from bed and died 28 days later and the other was a > 90-year old patient who fell against a radiator and died one day later. In both cases the GP decided to

renounce referral, with informed consent from patient and family, because of age and co-

Patient age & sex	All head injuries (n=694)	Complicated head injury (n=36)

morbidity.

Patients presenting themselves to the GP were managed without referral in 90.0% of cases [n=546]. 21.3% [n=148] of all head injury patients attended the hospital emergency department (ED). Only 39.2% [n=58] were referred by the GP, with the remainder coming directly by ambulance or their own transport. Patients visiting the ED underwent CT-scanning in 50.6% [n=75] of cases and were hospitalized for at least 24 hours in 29.7% [n=44] of cases. Intra-cerebral lesion was seen in 6.8% [n=10] of patients undergoing a CT-scan; four of these patients underwent a neurosurgical intervention.

(2) Incidence of complicated head injury.

Over an observation period of ten years we identified 36 patients with complicated head injury (220.352 patient years), resulting in an incidence rate of 0.16 per 1000 person-years (0.12-0.22; 95%CI). Incidence rates are shown in table 2.

Table 2. Incidence rates of (complicated) head injury

	Midtime population*	HI (n)	Incidence rate per 1000 person years (95% CI)	Midtime population*	cHI (n)	Incidence rate per 1000 person years (95% CI)
Male						
0 - 1 year	418	54	129.2 (98.0 - 167.3)	3741	1	0.27 (0.01-1.31)
2 - 5 years	1001	93	92.9 (75.4 - 113.3)	6708	1	0.15(0.007-0.74)
6 - 15 years	2309	89	38.5 (31.1 - 47.2)	15135	1	0.07 (0.003- 0.33)
16 - 40 years	4678	53	11.3 (8.6 - 14.7)	32484	4	0.12 (0.04-0.30)
41 - 60 years	4606	48	10.4 (7.8 - 13.7)	32375	3	0.09 (0.02-0.25)
> 60 years	2482	34	13.7 (9.6 - 18.9)	17694	6	0.34 (0.14-0.71)
Total	15494	371	23.9 (21.6 - 26.5)	108137	16	0.15 (0.09-0.24)
Female						
0 - 1 year	436	51	117.0 (88.0 - 152.6)	3650	0	0 (-)
2 - 5 years	949	41	43.2 (31.4 - 58.1)	6119	1	0.16 (0.008- 0.81)
6 - 15 years	2104	45	21.4 (15.8 - 28.4)	14127	2	0.14 (0.024-0.047)
16 - 40 years	5010	70	14.0 (11.0 - 17.6)	34546	0	0 (-)
41 - 60 years	4550	37	8.1 (5.8 - 11.1)	32265	3	0.09 (0.024-0.25)
> 60 years	2826	79	28.0 (22.3- 34.7)	21531	14	0.65 (0.37-1.07)
Total	15875	323	20.4 (18.2 - 22.7)	112238	20	0.18 (0.11-0.27)
Male and Female						
0 - 1 year	854	105	123.0 (101.1 - 148.2)	7391	1	0.14 (0.006-0.67)
2 - 5 years	1950	134	68.7 (57.8 - 81.1)	12827	2	0.16 (0.026- 0.52)
6 - 15 years	4413	134	30.4 (25.5 - 35.9)	29262	3	0.10 (0.03-0.28)
16 – 40 years	9688	123	12.7 (10.6 - 15.1)	67030	4	0.06 (0.02-0.14)
41 - 60 years	9156	85	9.3 (7.5 - 11.4)	64640	6	0.09 (0.038-0.19)
> 60 years	5308	113	21.3 (17.6 - 25.5)	39225	20	0.51 (0.32-0.77)
Total	31369	694	22.1 (20.5 - 23.8)	220375	36	0.16 (0.12-0.22)

* Midtime population is calculated by means of total patient population on 1st of January and 31th of December.

In 97.2% of cases it was possible to assess the severity of traumatic brain injury from specialist correspondence. 25% [n=9] of patients, all over 60 years old, received anticoagulant therapy at time of head injury. No patients had a history of coagulopathies or other bleeding disorders. Most patients with a complicated head injury (72.2% [n=26]) were referred directly to the hospital without involvement of a GP. If the initial contact was in primary care (22.2% [n=8), all complicated patients presented with severe symptoms such as neurological deficits, loss of consciousness and epilepsy. A total of eight patients (1.7%) died during study period; two were

not sent to a hospital and died without an autopsy, these were the same patients as found in cohort 1. We found out-of-hospital delay in two patients, leading to delayed neurosurgical intervention. One patient consulted his GP due to a headache without reporting that he suffered head injury two weeks earlier: when the headache worsened the GP referred the patient to the hospital where a subdural hematoma was diagnosed. The second patient was residing in a care home and suffering from dementia. Following a fall from bed and non-response to pain medication he was referred to hospital, where a subarachnoid haemorrhage was diagnosed.

(3) Predictors for complicated course.

Univariate regression analysis showed that a High Energy Transfer was related to a significantly higher risk of developing a complicated head injury (OR 3.93, 95%CI 1.97-7.84) (Table 3).

Table 3. Univariate regression analysis for complicated head injury

Variable	OR*	95%CI (Mid P exact)	p Value (two-tailed. Mid P exact)
Trauma mechanism			
HET	3.93	1.97-7.84	<0.000
Car vs. pedestrian/bicycle	1.709	0.24- 7.90	0.5134
Fall >1m	1.029	0.35- 2.69	0.9307
High impact	1.285	0.47- 3.24	0.5935
Fall	0.68	0.35-1.37	0.2767
Trauma setting			
Home	0.78	0.37-1.57	0.493
Work	1.301	0.20- 4.91	0.682
School	0.81	0.13- 2.98	0.846
Rec/sport	0.37	0.09-1.11	0.080
Traffic	2.88	1.04- 7.02	0.042
Bicycle	2.70	1.24- 5.61	0.014
Contacts			
First encounter GP	0.03	0.01-0.07	<0.000
First encounter Ambulance	22.14	10.60-48.05	<0.000
GP only	0.02	0.00-0.06	<0.000
Hospital only	18.04	8.54-40.41	<0.000
GP/hospital	3.15	1.29-7.07	0.0138
Patient characteristics			
Use of OAC	4.10	1.75-9.03	0.002

Alcoholintoxication	4.30	1.38-11.53	0.015
GCS <12 (excl. not reported)	41.2	16.43-105.00	<0.000
Male gender	0.69	0.35-1.37	0.292
Age >60	6.60	3.30-13.36	<0.000
*Agegroups***			<0.000
0-1 yr (reference group)	-	-	-
2-5 yr	1.58	0.14- 17.65	0.711
6-15 yr	2.37	0.24- 23.10	0.458
16-40 yr	3.42	0.38- 31.02	0.275
41-60yr	7.50	0.89- 63.51	0.065
>60 yr	19.27	2.5- 146.13	0.004

* Odds ratios are based on Conditional maximum likelihood estimate
** Glasgow Coma Scale
*** Significances of Odds ratios calculated are in relation to youngest age group

Traffic and isolated bicycle accidents were also associated with a higher risk of complicated head injury (OR 2.88, 95%CI 1.04-7.02) respectively (OR 2.70, 95%CI 1.24- 5.61). The risk of a complicated head injury was significantly reduced if the first encounter was in primary care (OR 0.03, 95%CI 0.01-0.07), and conversely much higher when an ambulance was the first responder (OR 22.14, 95%CI 10.6- 48.05). Hospital admission without previous GP contact was related to a higher risk of complicated head injury (OR 18.04, 95%CI 8.54-40.41). A complicated course was also seen more often with oral anticoagulants (OAC) (OR 4.10, 95%CI 1.75-9.03), alcohol-intoxication (OR 4.30, 95%CI 1.38-11.53), lowering of Glasgow Coma Scale (OR 41.2, 95%CI 16.43-105.00) and age above 60 years (OR 6.60, 95%CI 3.30-13.36).

Gender, age, trauma-mechanism assault and usage of anti-coagulation were included in the multivariate analysis (limited sample size precluded inclusion of further variables). We found a significantly higher risk of hospital admittance, as well a complicated course after head injury, for age 60 years and older (OR 12.6, 95%CI 5.0-31.9) and the presence of symptoms that could indicate a fracture (above clavicle) (OR 2.4, 95%CI 1.4-4.1). When compared to the trauma mechanism 'fall', high energetic trauma was associated with a higher risk for hospital; admission (OR 2.8, 95% CI 1.5-5.2). Male gender was not found to be a predictor of a complicated course (p=0.233).

Discussion

This is the first study to investigate the full spectrum of traumatic head injury in both primary and secondary care. We found much higher incidence rates than previously reported: 22 per 1000 patients per year, with a peak incidence in babies (0-1 years) of 123/1000. The incidence of a complicated head injury, on the other hand, is very low (0.16 per 1000 person-years) and much more in line with previous research. The vast majority of head injury patients (78.7%) were treated in primary care without referral, whereas the majority of patients with complicated head injury (72%) were directly admitted to secondary care without involvement of a primary care professional. Patients with complicated injury who initially presented in primary care seemed to be easily identified and referred to secondary care, except for two patients both > 90 years old in which a palliative approach was chosen. Known risk factors for a complicated course such as oral anticoagulants and age above 60 years were confirmed in this study (22-24).

A particular strength of our study is its setting in the Dutch health-care system, in which all patients are registered with one particular primary care provider and all encounters with healthcare professionals reported back. This means that the primary care doctor holds an overview of all encounters with health care of a particular patient (20). We used the FaMe-network database, which is linked to electronic patient files in which all encounters are registered and coded. In this system, new data (encounters, letters, reports) cannot be entered without linking to a new or existing diagnosis code – making it hard to miss even the simplest case of head injury. Moreover, it is not possible to miss cases that started in primary care but were followed up elsewhere because these encounters would be reported back, registered and coded in the same file. Because the registration network has a focus on diagnosis and medical processes (e.g. referrals, prescription), signs and symptoms of head injuries are registered in the same way as in any other practice. Most of the patients seen by the GP's involved simple head injuries, with no need for detailed reporting.

We found substantially higher incidence of head injury compared to existing reports. A recent systematic review on the incidence of all types of traumatic brain injury found a pooled incident rate of only 3.49 per 1000 patients per year, whereas our finding was 22 per 1000 patients per

year (5). In contrast with this review, we conclude that most head injuries occur amongst young children – identifying incidence more than a hundred times higher in children. This difference might be explained by variable classification, especially since the systematic review's authors point out the problem of non-standardized reporting among neuro-epidemiological studies on incidence of (particularly mild) head injury. One particular study claimed to assess the full spectrum of head injury by including data from general practice, resulting in an incidence of 7.90 per 1000 patients per year. Unfortunately, this study limited inclusion to patients with head injury and "physiological disruption of brain function" (7).

Variation in definition of head injury is an ongoing problem in current literature, resulting in a wide range of incidence figures of traumatic head injury (5, 25-27). One particular review stated that the term 'silent epidemic' could be used to characterize the incidence of head injury, because many cases are not recognized and therefore excluded from official statistics (27). Our study captures the full spectrum of head injury as presented in the entire health-care system (in and out of hospital) with inclusion based on any trauma of the head excluding injuries of the face. This is in line with current guidelines for primary care that apply a similar broad definition of head trauma. We fully endorse this broad definition for future diagnostic and prognostic research aimed at primary care populations. The nature of primary care is that it is easily and rapidly accessible for every patient with no pre-selection or other thresholds. Even in primary care it is difficult to rule out a complicated course. After all, the condition was (per definition) sufficiently severe for patient, parents or bystanders to seek professional help. Moreover, neurological indications may not develop in this early stage so a definition based on signs of 'disruption of brain function' - as has previously been advocated - is not feasible (27). We are furthermore convinced that identifying patients with mild trauma (including those not seen in a hospital setting) is relevant because (un-)complicated head injury may still be associated with significant cost in terms of disability, lost work or neuropsychiatric complications (28, 29).

Although existing guidelines are based on a broad definition of head injury, the underlying evidence is based almost exclusively on clinical populations. In clinical populations a (self-) selection for complicated head injury has already taken place and a narrow definition of head injury is used (10, 11, 14, 30, 31), leading to a higher estimated risk for complications and over-treatment of patients with head injury (31, 32).

We conclude that head injury as seen in primary care comprises an essentially different case-mix as compared to secondary care. Moreover, complicated cases appear to be easily identified and readily presented to secondary care. Our study requires confirmation in other settings using other databases, but we are convinced that current guidelines are based on limited evidence of true incidence rates. This makes them prone to spectrum bias. A more reserved management of head injury in primary care should be considered, leading to more cost-effective use of costly hospital diagnostic resources. This study also calls for an internationally accepted definition (coupled with a universal diagnostic algorithm) of head injury and (mild) traumatic brain injury.

Figure and tables

Statements concerning this study

Contributor ship:

- Gerritsen, H (MD); was involved and made contributions in the design of the study, acquisition, analysis and interpretation of the data. Drafted the work and revised it critically for important intellectual content. Gave final approval of the version published and made agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
- Samim, M (Msc); was involved and made contributions in the design of the study, acquisition, analysis and interpretation of the data. Revised the work critically for important intellectual content. Gave final approval of the version published and made agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
- Peters, H.J.G. (Bsc); was involved and made contributions in the design of the study, acquisition, analysis and interpretation of the data. Revised the work critically for important intellectual content. Gave final approval of the version published and made agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
- Schers, H (MD, PhD); was involved and made contributions in the design of the study, acquisition, analysis and interpretation of the data. Revised the work critically for important intellectual content. Gave final approval of the version published and made agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
- Laar, F.A. vd. (MD, PhD); was involved and made contributions in the design of the study, acquisition, analysis and interpretation of the data. Revised the work critically for important intellectual content. Gave final approval of the version published and made agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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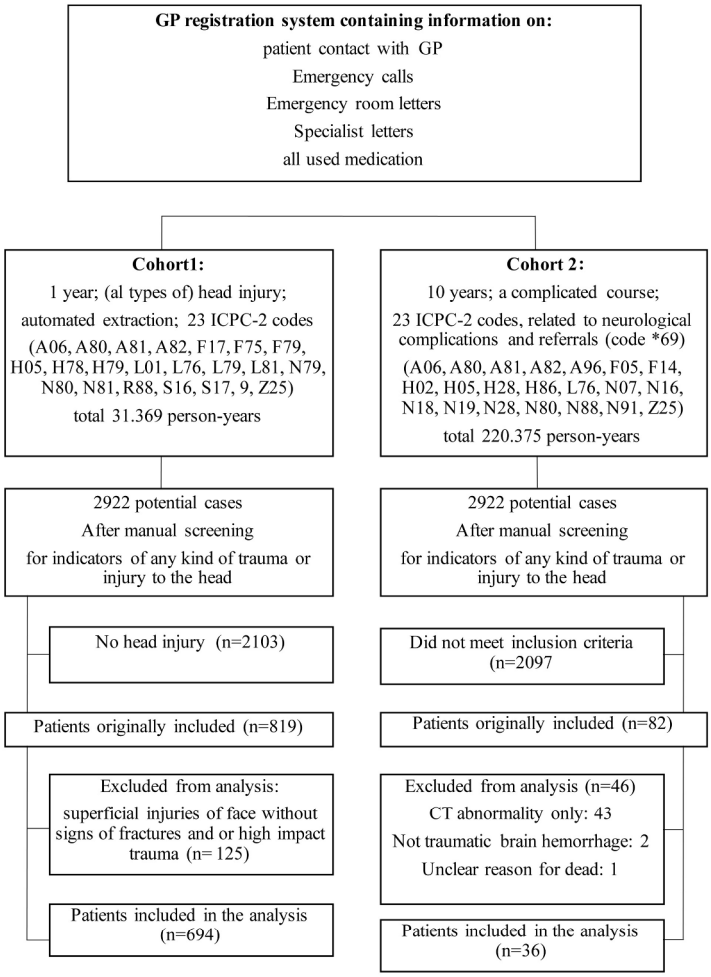

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Appendix; definition of initial variables for data extraction.

Data collection was performed based on information from specialist correspondence and GP documentation. There-fore selected ICPC codes were used (Table I). Data was systematically screened on several variables:

Variable	Categories
Glasgow Coma Scale	1= 15, 2= 14, 3= 13, 4= 9-12, 5= 8 or lower, 9= not reported
Loss of consciousness	0= no, 1= <5min, 2= 5-30min, 3= >30min, 4= duration unclear, 5= Unclear if LOC, 9= not reported
Posttraumatic amnesia	0= no, 1= <24h, 2= 1-7 days, 3= >7 days, 4= unclear if PTA, 9= not documented
TBI classification	1= mild, 2= moderate, 3= severe, 9= no classification possible
Trauma setting	0= not reported 1= home, 2= work, 3= school/daycare 4= recreation/sport, 5= traffic 6= bicycle
Trauma mechanism	0= not reported, 1= fall, 2=HET, 3= blunt trauma, 4= acceleration/deceleration, 5= assault, 6= other 7= not sure
Nausea	0= no, 1= yes, 2= not applicable, 9= not reported
Vomiting	0= no, 1= yes, 9= not reported
Neurological deficit in acute phase	0= no, 1= weakness, 2= loss of balance, 3= change in vision, 4= change in speech, 5= change in motor function, 6= change in sensory function, 7= multiple, 9= not reported
Mental state	0= no change, 1= confusion 2= disorientation, 3= slowed thinking, 4= other, 9= not reported
External injury	0= no, 1= laceration/cut, 2= hematoma, 3= edema, 4= graze/superficial, 5= multiple, 9= not reported
Suspected skull fracture	0= no, 1= yes, 9= not reported
Signs of basal skull fracture	0= no, 1= yes, 9= not reported
Alcohol/drug intoxication	0= no, 1= alcohol, 2= drugs, 3= combined, 9= not reported
First encounter	1= General practitioner, 2= Emergency department, 3= ambulance, 9= not reported

Contacts	1= General practitioner only, 2= General practitioner/hospital, 3= Hospital only
Gender	0= male, 1= female
Age	-
Current anticoagulant therapy	0= no, 1= VitK antagonist, 2= anti platelet, 3= NOAC, 4= multiple
Risk medication:	0= no 1= yes
Sedatives	
Anti-diabetics	0= no, 1= yes
	0= no, 2= metformine, 2= sulfonylureas, 3= insulin, 4= multiple
Anti-epileptics	0= no, 1= yes

The Glasgow Coma Scale (GCS), Initial GCS documented at first medical contact, was documented only if it was reported in the data without calculating scores afterwards.
Based on the standardised Traumatic Brain Injury classification, head injury was classified into mild, moderate or severe brain injury based on initial GCS, PTA and duration of loss of consciousness. If classification was not possible due to lack of data but classification was documented in the specialist letter, this classification was used for analysis. To assess the trauma characteristics, trauma setting and mechanism was documented. We considered a patient to have a head injury at home, work, school and day-care when documented as such or when indicated by context. Recreation and sport was chosen as trauma setting if the accident happened in recreational time not related to traffic. Traffic was chosen as trauma setting if the patient sustained head injury in a traffic setting (car vs. pedestrian/bicycle/car). Falling off a bicycle as cause of trauma was documented apart if no other traffic members were affected in the accident.
Trauma mechanism was divided into several subcategories with high energy trauma defined as fall from elevation, traffic accidents with high velocity and high impact, including acceleration/deceleration trauma.
We defined neurological deficit in the acute phase as any abnormality documented on routine clinical neurological examination that indicated a focal cerebral lesion. Mental state was scored as any documented change in behaviour or deviation of compos mentis. Symptoms of dementia and changed behaviour due to intoxication were scored as “other”. Signs of basal skull fracture were Battle’s sign, Raccoon eyes and/or liquor leakage/bleeding from nose and ear. External injury was defined as any documented discontinuity of the facial skin or head.

Intoxication was scored as ‘yes’ if explicit reported. If overall documentation was limited than intoxication was scored as “not reported”; in all other patients intoxication was score as “no”.

Within ‘contacts’ information about all contacts in the acute posttraumatic period were scored. ‘GP’ indicates that patients were seen by a GP only, ‘GP/hospital’ indicates that patient was referred to the hospital after being seen by a GP, ‘hospital’ indicates that patients are not seen by a GP before. Variables which are not mentioned here but are only displayed in the table were scored as indicated in the table.

Table I. ICPC Codes* indicating Head Injury	
A06	Fainting/syncope
A80	Trauma/injury NOS
A81	Multiple trauma/injuries
A82	Secondary effect of trauma
A96	Death
H05	Bleeding ear
L76	Fracture: other
N07	Convulsion/seizure
N79	Concussion
N80	Head injury other
N88	Epilepsy
Z25	Assault/harmful event problem

ICPC Codes indicating a Complicated Course	
*** 67**	Referral to Physician/Specialist/ Clinic/Hospital
A96	Death
F05	Visual disturbance other
F14	Eye movements abnormal
H02	Hearing complaint
H28	Limited function/disability ear
H86	Deafness
N07	Convulsion/seizure
N16	Disturbance of smell/taste
N18	Paralysis/weakness
N19	Speech disorder
N28	Limited function/disability (n)
N88	Epilepsy
N91	Facial paralysis/bell's palsy

* ICPC-2 – English International Classification of Primary Care – 2nd Edition, Wonca International Classification Committee (WICC)

STROBE (Strengthening The Reporting of OBservational Studies in Epidemiology) Checklist

A checklist of items that should be included in reports of observational studies. You must report the page number in your manuscript where you consider each of the items listed in this checklist. If you have not included this information, either revise your manuscript accordingly before submitting or note N/A.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

Section and Item	Item No.	Recommendation	Reported on Page No.
Title and Abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/Rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study Design	4	Present key elements of study design early in the paper	7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7 & 8
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	7
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7

Section and Item	Item No.	Recommendation	Reported on Page No.
Data Sources/ Measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7
Bias	9	Describe any efforts to address potential sources of bias	8
Study Size	10	Explain how the study size was arrived at	7 & 8
Quantitative Variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8 & 9
Statistical Methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8 & 9
		(*b*) Describe any methods used to examine subgroups and interactions	8 & 9
		(*c*) Explain how missing data were addressed	9
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	8 & 9
		(*e*) Describe any sensitivity analyses	9
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	10 & 11
		(b) Give reasons for non-participation at each stage	Fig. 1
		(c) Consider use of a flow diagram	Fig. 1
Descriptive Data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10 & 11
		(b) Indicate number of participants with missing data for each variable of interest	10 & 11 Tab. 1
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	10 & 11
Outcome Data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	10 & 11 Tab. 2
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	

Section and Item	Item No.	Recommendation	Reported on Page No.
Main Results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10 & 11
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	11
Other Analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key Results	18	Summarise key results with reference to study objectives	12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12 & 13
Generalisability	21	Discuss the generalisability (external validity) of the study results	13 & 14
Other Information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Once you have completed this checklist, please save a copy and upload it as part of your submission. DO NOT include this checklist as part of the main manuscript document. It must be uploaded as a separate file.

BMJ Open

Incidence, course and risk factors of head injury in The Netherlands.

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Title: Incidence, course and risk factors of head injury in The Netherlands.

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Word count: 2941

Abstract

Objectives

To assess the incidence of head injury and predictors of complication across the care continuum.

Design

Retrospective cohort study using data from a research network. We calculated the incidence of overall head injury in a longitudinal cohort covering 1 year interval (31,369 patient years), and the incidence of complicated head injury in a longitudinal cohort covering 10 years interval (220,352 patient years). Incidence rates were calculated per 1000 patient-years with 95% CI using the Mid-P exact test. We calculated Odds ratios to assess potential risk factors for a complicated head injury.

Setting

A practice-based research network covering a population of >30,000 patients.

Participants

All patients listed in practices within the research network during the years 2005-2014.

Main outcome measures

Incidence of (complicated) head injury and predictors for clinical complications.

Results

The incidence of overall head injury was 22.1 per 1000 person years and the incidence of a complicated course following head injury was 0.16 per 1000 person years. The following determinants were risk factors for a complicated course: high energy trauma, bicycle accident, traffic accident in general, use of anticoagulants, alcohol intoxication, age above 60 years and low Glasgow Coma Scale at initial presentation. A complicated course was very unlikely when the first patients' first encounter with a healthcare professional was in primary care (OR 0.03, 95%CI 0.01-0.07).

Conclusions

Complication after head injury are rarely seen in general practice. Patients who do experience complications are often easily identifiable as requiring specialist care. A more reserved referral policy for general practice may be desirable, suggesting that current guidelines are too defensive.

Trial registration

None.

Strengths and limitations

Strengths of study:

- Based on robust, comprehensive data set including all encounters of individual patients with healthcare professionals both from primary and secondary care.
- Scrutinous manual screening of all patients.

Limitation of this study:

- Incomplete data set; use of routine data from general practice

Ethical approval

No formal ethical approval was needed for this study. Patients in the participating practices are informed about the continuous data collection. The data set is anonymized and encrypted before transfer to the researchers.

Patient and Public Involvement statement

No patients where involved during development of research question, outcome measures and design of this study.

Introduction

Patients presenting with head injury in primary care challenge general practitioners to differentiate between those who may be reassured, and those who are at risk of serious intracranial injury. Intracranial injuries such as epidural and subdural hematoma or skull fractures may lead to death or permanent damage if left untreated (1-4).

High quality clinical management of head injury takes the small chance of intracranial injury into account. Safe and cost-effective practice guidelines for primary care must therefore be based on a reliable risk calculation, for which precise data are needed on the incidence of both head injury and serious intracranial injury or complicated head injury. In Europe, the annual incidence of head injury presenting in hospital emergency departments is 2.3 per 1000 person-years (5) (6). In general practice, this incidence is expected to be higher because only a subset of patients are referred to hospital. Robust data about incidence rates in primary care are lacking. For example, a New Zealand study in a primary care population found an incidence rate of 7.5 per 1000 person-years (7), whereas, in a small pilot study in the Netherlands, we found the incidence of (mild and severe) head injury to be as high as 22.3 per 1000 person-years (8).

The incidence of severe damage after a head injury is also unclear. In the UK, head injury accounts for 3.4% of all emergency department attendances. About 90% of head injuries in hospital setting are considered to be mild (6, 7). Incidence of moderate to severe head injury was 40 per 100.000 persons – a figure which may in reality be slightly higher because it does not include patients who die before admittance to the hospital (9). This makes the identification of patients at risk challenging.

Currently, guidelines for the identification, referral and management of patients with head injury at risk for intracranial damage are based on epidemiological studies from secondary or tertiary care (10, 11). Currently two different guidelines are used in the Netherlands, both have strong resemblance with the NICE guideline as used in the UK (12-14). It is likely that this case-mix of head injury patients is essentially different from that in primary care (15, 16). The risk for a

complicated course may therefore be exaggerated, resulting in spectrum bias in current guidelines (15-19).

In this study, we aim to assess the incidence of head injury across the care continuum, and to identify risk factors for intracranial injury. Our research questions were: (1) what is the incidence of head injury and complicated head injury, and (2) what predicts a complicated course?

Methods

Study Setting

We performed a retrospective cohort study in the practice based research network Family Medicine Network (FaMe-net) of the Department of Primary and Community Care (ELG) at the Radboud University Medical Centre. FaMe-net consists of nine Dutch general practices in 3 geographical regions (approximately 31.000 listed patients). FaMe-net physicians systematically and prospectively register data on the reason for encounter, diagnostic procedures, diagnoses, interventions, and referrals. The network uses the ICPC-2 and ICD-10 classification systems to code procedures and diagnosis. All data can be linked to demographic information (age, gender, geographic location, family composition). In the Netherlands, all patients are listed in one general practice to which all encounters in secondary care are reported. Reports from other care-providers are coded and linked to a new or existing episode (20). Participating doctors in FaMe-net meet on a regular basis to discuss registration issues and improve the uniformity of registration.

Definitions

We defined head injury as any trauma to the head other than superficial injuries to the face (14). A complicated head injury was defined as a head injury for which treatment and surveillance in secondary care was deemed necessary: a need for surgical intervention (defined as any neurosurgical procedure including drainage and placement of ICD), seizures in the acute posttraumatic phase, resulting neurological deficits within 12 months after trauma, and death. Neurological deficits were defined as any neurological abnormalities, including facial fracture associated nerve lesions.

Study Population and data collection

We selected patients in two stages: first we performed a sensitive electronic search based on the list of ICPC labels indicating head injury (Appendix; table I). Next, we manually scrutinized all retrieved patient records for final inclusion. In this way, we created two (retrospective) cohorts:

Cohort1: *patients with (all types of) head injury*; we expected the incidence of all head injury to be high and therefore limited the inclusion period to one year (between 1 January 2014 and 31

December 2014). Through a pilot study we constructed an inclusive list of 23 diagnostic ICPC labels that (might) refer to a head injury or traumatic brain injury. For example, to refer to a head injury the code 'concussion' (N79) could be selected, but also 'bruise/contusion' (S16) referring to skin involvement of the trauma (Appendix). Next, all available clinical data from these preselected patients were manually screened for a match to our inclusion criteria of head injury. Additionally, we screened all files of deceased patients in 2014 for the cause of death to verify if head injury occurred up to 4 weeks before time of death.

Cohort 2: *patients with a complicated course*; we expected complicated head injury to be rare and therefore included patients from a 10-year time interval (between 1 January 2005 and 31 December 2014). To identify patients with a complicated head injury we used different ICPC codes that (might) refer to (consequences of) severe and complicated head injury. We also searched for specialist letters and hospital admission in the field of neurology, neurosurgery or rehabilitation medicine. All specialist letters from these preselected patients were then manually screened for a match to our inclusion criteria of head injury. In addition to specialist letters, we used GP documentation to identify known risk factors for complicated course (21-24).

We reviewed all available clinical data, including general notes, hospital (including emergency department) correspondence, radiological imaging findings, surgical records and autopsy records. We extracted data using a predefined form (Appendix) and excluded patients with severe multi-trauma injury.

Statistical analysis

We calculated the incidence of head injury and complicated head injury per 1000 years with 95% Confidence Intervals, using the Mid-P exact test (Open source calculator OpenEpi, version 3). Age and sex structures of the mid-time population were used as denominators.

The incidence of head injury was defined as any new case of head injury during the study period. Some patients had more than one isolated case of head injury, each case was scored as a new finding. To determine the proportion of patients with complicated head injury, their incidence was compared to incidence of all head injuries as identified during the one-year study period. We evaluated all included cases for demographic and trauma characteristics.

In order to assess potential risk factors for a complicated course of head injury, we calculated Odds ratios on trauma mechanism, trauma setting, type-of-contact (hospital/GP/telephonically) after trauma and patient characteristics. Odds ratios were calculated using SPSS (IBM SPSS Statistics, Version 22.0. Armonk, NY). A p-value of <0,05 was considered statistically significant. Multivariate regression analysis was performed on the variables gender, age and high-energy transfer – during trauma (HET) as the most relevant trauma mechanism. Factors predicting a complicated head injury were calculated by multivariate analysis with logistic regression models. Variables were age, gender, trauma mechanism, symptoms for fracture and use of anti-coagulant. Moderate and severe head injury was combined during analysis due to small sample sizes. Clinical findings and data are presented using frequencies as well as percentages.

Results

(1) Incidence of all head injury.

During one year follow up (31.369 patient years), we identified 694 patients with head injury (figure 1), resulting in an overall incidence rate of 22.1 per 1000 person years (20.5-23.8; 95% CI). The incidence rate was 123.0 per 1000 person years (95%CI 101.1-148.2) for children aged 0-1 years. Out of all the patients with a head injury, 34% were under 15 years old. Patient characteristics are shown in table 1.

Table 1. Characteristics of patient and trauma

Patient Characteristics	Cohort 1. All head injury	Cohort 2. Complicated head injury
Variables	No.(%) of patients	No. (%) of clinical complications
Gender		
Male	371 (53.5)	16 (44.4)
Female	323 (46.5)	20 (55.6)
Mean age		
All	25.8 ; SD 27.7	58.0; SD 29
- Male	20.2 ; SD 23.6	48.9; SD 30
- Female	32.2 ; SD 30.5	65.3; SD 27
Presence of indicators of cHI †		
Multiple cHI indicators	-	12 (33.3)
Death	2 (0.3)	8 (22.2)
Neurosurgical intervention	4 (0.6)	12 (33.3)
Seizure	1 (0.1)	6 (16.7)
Neurological deficit	4 (0.6)	24 (66.7)
Current anticoagulant therapy		
No	642 (92.5)	27 (75.0)
Yes	52 (7.5) **	9 (25.0) **
Trauma TBI-classification *		
Mild	-	26 (72.2)
Moderate	3 (0.4)	2 (5.6)
Severe	2 (0.3)	7 (19.4)
Not reported	689 (99.3)	1 (2.8)
Trauma setting		
Home	272 (39.2)	12 (33.3)
Work	-	2 (5.6)
School/daycare	47 (6.8)	2 (5.6)
Recreation/sport	137 (19.7)	3 (8.3)
Traffic	45 (6.5)	6 (16.7)
Bicycle/motor bike	97 (13.9)	11 (30.6)

Not reported	96 (13.8)	-
Trauma mechanism		
Fall >1m	449 (64.7)	20 (55.6)
HET	52 (7.5)	12 (33.3)
Blunt trauma	151 (21.8)	2 (5.6)
acceleration/deceleration	-	-
Assault	25 (3.6)	2 (5.6)
Not reported	15 (2.2)	-
Contacts		
GP only	546 (78.7)	2 (5.6)
Hospital only	90 (12.9)	26 (72.2)
GP and hospital	58 (8.4)	8 (22.2)
Vomiting		
No	320 (46.1)	10 (27.8)
Yes	54 (7.8)	9 (25.0)
Not reported	320 (46.1)	17 (47.2)
Neurological deficit in acute phase		
No	308 (44.4)	10 (27.8)
Yes	51 (7.3)	21 (58.3)
Not reported	335 (48.3)	5 (13.9)
Change in mental functioning		
No	308 (44.4)	10 (27.8)
Yes	107 (15.4)	18 (50.0)
Not reported	279 (40.2)	8 (22.2)
External injury		
No	165 (23.8)	7 (19.4)
Yes	424 (61.1)	23 (63.9)
Not reported	105 (15.1)	6 (16.7)
Intracranial lesions		
No (lesions on CT scan)	75 (10,8)	9 (25.0)
Yes (lesions on CT scan)	10 (1.4)	22 (61.1)
Not reported/ or no CT scan	609 (87.8)	5 (13.8)
If intracranial lesions on CT scan		
- neurosur. intervention	4 (0.6)	12 (33.3)
- no neurosur. intervention	6 (0.9)	10 (27.8)

† cHI= complicated Head Injury; indicators of occurrence of complicated head injury.
* Traumatic Brain Injury
** All in age group >60years

Two of 694 patients (0.3%) died during the study period; one was a > 90-year old patient who injured his head when falling from bed and died 28 days later and the other was a > 90-year old patient who fell against a radiator and died one day later. In both cases the GP decided to

renounce referral, with informed consent from patient and family, because of age and co-

Patient age & sex	All head injuries (n=694)	Complicated head injury (n=36)

morbidity.

Patients presenting themselves to the GP were managed without referral in 90.0% of cases [n=546]. 21.3% [n=148] of all head injury patients attended the hospital emergency department (ED). Only 39.2% [n=58] were referred by the GP, with the remainder coming directly by ambulance or their own transport. Patients visiting the ED underwent CT-scanning in 50.6% [n=75] of cases and were hospitalized for at least 24 hours in 29.7% [n=44] of cases. Intra-cerebral lesion was seen in 6.8% [n=10] of patients undergoing a CT-scan; four of these patients underwent a neurosurgical intervention.

(2) Incidence of complicated head injury.

Over an observation period of ten years we identified 36 patients with complicated head injury (220.352 patient years), resulting in an incidence rate of 0.16 per 1000 person-years (0.12-0.22; 95%CI). Incidence rates are shown in table 2.

Table 2. Incidence rates of (complicated) head injury

	Midtime population*	HI (n)	Incidence rate per 1000 person years (95% CI)	Midtime population*	cHI (n)	Incidence rate per 1000 person years (95% CI)
Male						
0 - 1 year	418	54	129.2 (98.0 - 167.3)	3741	1	0.27 (0.01-1.31)
2 - 5 years	1001	93	92.9 (75.4 - 113.3)	6708	1	0.15(0.007-0.74)
6 - 15 years	2309	89	38.5 (31.1 - 47.2)	15135	1	0.07 (0.003- 0.33)
16 - 40 years	4678	53	11.3 (8.6 - 14.7)	32484	4	0.12 (0.04-0.30)
41 - 60 years	4606	48	10.4 (7.8 - 13.7)	32375	3	0.09 (0.02-0.25)
> 60 years	2482	34	13.7 (9.6 - 18.9)	17694	6	0.34 (0.14-0.71)
Total	15494	371	23.9 (21.6 - 26.5)	108137	16	0.15 (0.09-0.24)
Female						
0 - 1 year	436	51	117.0 (88.0 - 152.6)	3650	0	0 (-)
2 - 5 years	949	41	43.2 (31.4 - 58.1)	6119	1	0.16 (0.008- 0.81)
6 - 15 years	2104	45	21.4 (15.8 - 28.4)	14127	2	0.14 (0.024-0.047)
16 - 40 years	5010	70	14.0 (11.0 - 17.6)	34546	0	0 (-)
41 - 60 years	4550	37	8.1 (5.8 - 11.1)	32265	3	0.09 (0.024-0.25)
> 60 years	2826	79	28.0 (22.3- 34.7)	21531	14	0.65 (0.37-1.07)
Total	15875	323	20.4 (18.2 - 22.7)	112238	20	0.18 (0.11-0.27)
Male and Female						
0 - 1 year	854	105	123.0 (101.1 - 148.2)	7391	1	0.14 (0.006-0.67)
2 - 5 years	1950	134	68.7 (57.8 - 81.1)	12827	2	0.16 (0.026- 0.52)
6 - 15 years	4413	134	30.4 (25.5 - 35.9)	29262	3	0.10 (0.03-0.28)
16 – 40 years	9688	123	12.7 (10.6 - 15.1)	67030	4	0.06 (0.02-0.14)
41 - 60 years	9156	85	9.3 (7.5 - 11.4)	64640	6	0.09 (0.038-0.19)
> 60 years	5308	113	21.3 (17.6 - 25.5)	39225	20	0.51 (0.32-0.77)
Total	31369	694	22.1 (20.5 - 23.8)	220375	36	0.16 (0.12-0.22)

* Midtime population is calculated by means of total patient population on 1st of January and 31th of December.

In 97.2% of cases it was possible to assess the severity of traumatic brain injury from specialist correspondence. 25% [n=9] of patients, all over 60 years old, received anticoagulant therapy at time of head injury. No patients had a history of coagulopathies or other bleeding disorders. Most patients with a complicated head injury (72.2% [n=26]) were referred directly to the hospital without involvement of a GP. If the initial contact of a complicated course was in primary care (22.2% [n=8), patients presented with severe symptoms such as neurological deficits, loss of consciousness and epilepsy. A total of eight patients (1.7%) died during study

period; two were not sent to a hospital and died without an autopsy, these were the same patients as found in cohort 1. We found out-of-hospital delay in two patients, leading to delayed neurosurgical intervention. One patient consulted his GP due to a headache without reporting that he suffered head injury two weeks earlier: when the headache worsened the GP referred the patient to the hospital where a subdural hematoma was diagnosed. The second patient was residing in a care home and suffering from dementia. Following a fall from bed and non-response to pain medication he was referred to hospital, where a subarachnoid haemorrhage was diagnosed.

(3) Predictors for complicated course.

Univariate regression analysis showed that a High Energy Transfer was related to a significantly higher risk of developing a complicated head injury (OR 3.93, 95%CI 1.97-7.84) (Table 3).

Table 3. Univariate regression analysis for complicated head injury

Variable	OR*	95%CI (Mid P exact)	p Value (two-tailed. Mid P exact)
Trauma mechanism			
HET	3.93	1.97-7.84	<0.000
Car vs. pedestrian/bicycle	1.709	0.24- 7.90	0.5134
Fall >1m	1.029	0.35- 2.69	0.9307
High impact	1.285	0.47- 3.24	0.5935
Fall	0.68	0.35-1.37	0.2767
Trauma setting			
Home	0.78	0.37-1.57	0.493
Work	1.301	0.20- 4.91	0.682
School	0.81	0.13- 2.98	0.846
Rec/sport	0.37	0.09-1.11	0.080
Traffic	2.88	1.04- 7.02	0.042
Bicycle	2.70	1.24- 5.61	0.014
Contacts			
First encounter GP	0.03	0.01-0.07	<0.000
First encounter Ambulance	22.14	10.60-48.05	<0.000
GP only	0.02	0.00-0.06	<0.000
Hospital only	18.04	8.54-40.41	<0.000
GP/hospital	3.15	1.29-7.07	0.0138
Patient characteristics			

Use of OAC	4.10	1.75-9.03	0.002
Alcoholintoxication	4.30	1.38-11.53	0.015
GCS <12 (excl. not reported)	41.2	16.43-105.00	<0.000
Male gender	0.69	0.35-1.37	0.292
Age >60	6.60	3.30-13.36	<0.000
*Agegroups***			<0.000
0-1 yr (reference group)	-	-	-
2-5 yr	1.58	0.14- 17.65	0.711
6-15 yr	2.37	0.24- 23.10	0.458
16-40 yr	3.42	0.38- 31.02	0.275
41-60yr	7.50	0.89- 63.51	0.065
>60 yr	19.27	2.5- 146.13	0.004

* Odds ratios are based on Conditional maximum likelihood estimate
** Glasgow Coma Scale
*** Significances of Odds ratios calculated are in relation to youngest age group

Traffic and isolated bicycle accidents were also associated with a higher risk of complicated head injury (OR 2.88, 95%CI 1.04-7.02) respectively (OR 2.70, 95%CI 1.24- 5.61). The risk of a complicated head injury was significantly reduced if the first encounter was in primary care (OR 0.03, 95%CI 0.01-0.07), and conversely much higher when an ambulance was the first responder (OR 22.14, 95%CI 10.6- 48.05). Hospital admission without previous GP contact was related to a higher risk of complicated head injury (OR 18.04, 95%CI 8.54-40.41). A complicated course was also seen more often with oral anticoagulants (OAC) (OR 4.10, 95%CI 1.75-9.03), alcohol-intoxication (OR 4.30, 95%CI 1.38-11.53), lowering of Glasgow Coma Scale (OR 41.2, 95%CI 16.43-105.00) and age above 60 years (OR 6.60, 95%CI 3.30-13.36).

Gender, age, trauma-mechanism assault and usage of anti-coagulation were included in the multivariate analysis (limited sample size precluded inclusion of further variables). We found a significantly higher risk of hospital admittance, as well a complicated course after head injury, for age 60 years and older (OR 12.6, 95%CI 5.0-31.9) and the presence of symptoms that could indicate a fracture (above clavicle) (OR 2.4, 95%CI 1.4-4.1). When compared to the trauma mechanism 'fall', high energetic trauma was associated with a higher risk for hospital; admission

(OR 2.8, 95% CI 1.5-5.2). Male gender was not found to be a predictor of a complicated course (p=0.233).

Discussion

This is the first study to investigate the full spectrum of traumatic head injury in both primary and secondary care. We found much higher incidence rates than previously reported: 22 per 1000 patients per year, with a peak incidence in babies (0-1 years) of 123/1000. The incidence of a complicated head injury, on the other hand, is very low (0.16 per 1000 person-years) and much more in line with previous research. The vast majority of head injury patients (78.7%) were treated in primary care without referral, whereas the majority of patients with complicated head injury (72%) were directly admitted to secondary care without involvement of a primary care professional. Patients with complicated injury who initially presented in primary care seemed to be easily identified and referred to secondary care, except for two patients both > 90 years old in which a palliative approach was chosen. Known risk factors for a complicated course such as oral anticoagulants and age above 60 years were confirmed in this study (22-24).

A particular strength of our study is its setting in the Dutch health-care system, in which all patients are registered with one particular primary care provider and all encounters with healthcare professionals reported back. This means that the primary care doctor holds an overview of all encounters with health care of a particular patient (20). We used the FaMe-network database, which is linked to electronic patient files in which all encounters are registered and coded. In this system, new data (encounters, letters, reports) cannot be entered without linking to a new or existing diagnosis code – making it hard to miss even the simplest case of head injury. Moreover, it is not possible to miss cases that started in primary care but were followed up elsewhere because these encounters would be reported back, registered and coded in the same file. Because the registration network has a focus on diagnosis and medical processes (e.g. referrals, prescription), signs and symptoms of head injuries are registered in the same way as in any other practice. Most of the patients seen by the GP's involved simple head injuries, with no need for detailed reporting.

We found substantially higher incidence of head injury compared to existing reports. A recent systematic review on the incidence of all types of traumatic brain injury found a pooled incident rate of only 3.49 per 1000 patients per year, whereas our finding was 22 per 1000 patients per

year (5). In contrast with this review, we conclude that most head injuries occur amongst young children – identifying incidence more than a hundred times higher in children. This difference might be explained by variable classification, especially since the systematic review's authors point out the problem of non-standardized reporting among neuro-epidemiological studies on incidence of (particularly mild) head injury. One particular study claimed to assess the full spectrum of head injury by including data from general practice, resulting in an incidence of 7.90 per 1000 patients per year. Unfortunately, this study limited inclusion to patients with head injury and "physiological disruption of brain function" (7).

Variation in definition of head injury is an ongoing problem in current literature, resulting in a wide range of incidence figures of traumatic head injury (5, 25-27). One particular review stated that the term 'silent epidemic' could be used to characterize the incidence of head injury, because many cases are not recognized and therefore excluded from official statistics (27). Our study captures the full spectrum of head injury as presented in the entire health-care system (in and out of hospital) with inclusion based on any trauma of the head excluding injuries of the face. This is in line with current guidelines for primary care that apply a similar broad definition of head trauma. We fully endorse this broad definition for future diagnostic and prognostic research aimed at primary care populations. The nature of primary care is that it is easily and rapidly accessible for every patient with no pre-selection or other thresholds. Even in primary care it is difficult to rule out a complicated course. After all, the condition was (per definition) sufficiently severe for patient, parents or bystanders to seek professional help. Moreover, neurological indications may not develop in this early stage so a definition based on signs of 'disruption of brain function' - as has previously been advocated - is not feasible (27). We are furthermore convinced that identifying patients with mild trauma (including those not seen in a hospital setting) is relevant because (un-)complicated head injury may still be associated with significant cost in terms of disability, lost work or neuropsychiatric complications (28, 29).

Although existing guidelines are based on a broad definition of head injury, the underlying evidence is based almost exclusively on clinical populations. In clinical populations a (self-) selection for complicated head injury has already taken place and a narrow definition of head injury is used (10, 11, 14, 30, 31), leading to a higher estimated risk for complications and over-treatment of patients with head injury (31, 32).

We conclude that head injury as seen in primary care comprises an essentially different case-mix as compared to secondary care. Moreover, complicated cases appear to be easily identified and readily presented to secondary care. Our study requires confirmation in other settings using other databases, but we are convinced that current guidelines are based on limited evidence of true incidence rates. This makes them prone to spectrum bias. A more reserved management of head injury in primary care should be considered, leading to more cost-effective use of costly hospital diagnostic resources. This study also calls for an internationally accepted definition (coupled with a universal diagnostic algorithm) of head injury and (mild) traumatic brain injury.

Figure and tables

Statements concerning this study

Contributor ship:

- Gerritsen, H (MD); was involved and made contributions in the design of the study, acquisition, analysis and interpretation of the data. Drafted the work and revised it critically for important intellectual content. Gave final approval of the version published and made agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
- Samim, M (Msc); was involved and made contributions in the design of the study, acquisition, analysis and interpretation of the data. Revised the work critically for important intellectual content. Gave final approval of the version published and made agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
- Peters, H.J.G. (Bsc); was involved and made contributions in the design of the study, acquisition, analysis and interpretation of the data. Revised the work critically for important intellectual content. Gave final approval of the version published and made agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
- Schers, H (MD, PhD); was involved and made contributions in the design of the study, acquisition, analysis and interpretation of the data. Revised the work critically for important intellectual content. Gave final approval of the version published and made agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
- Laar, F.A. vd. (MD, PhD); was involved and made contributions in the design of the study, acquisition, analysis and interpretation of the data. Revised the work critically for important intellectual content. Gave final approval of the version published and made agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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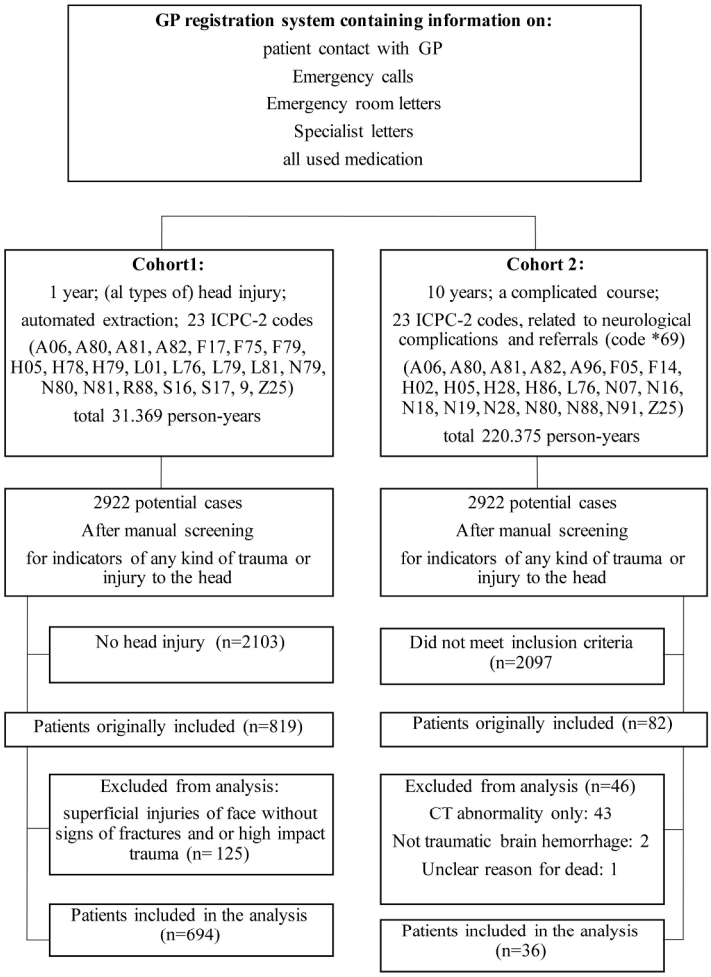

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Appendix; definition of initial variables for data extraction.

Data collection was performed based on information from specialist correspondence and GP documentation. There-fore selected ICPC codes were used (Table I). Data was systematically screened on several variables:

Variable	Categories
Glasgow Coma Scale	1= 15, 2= 14, 3= 13, 4= 9-12, 5= 8 or lower, 9= not reported
Loss of consciousness	0= no, 1= <5min, 2= 5-30min, 3= >30min, 4= duration unclear, 5= Unclear if LOC, 9= not reported
Posttraumatic amnesia	0= no, 1= <24h, 2= 1-7 days, 3= >7 days, 4= unclear if PTA, 9= not documented
TBI classification	1= mild, 2= moderate, 3= severe, 9= no classification possible
Trauma setting	0= not reported 1= home, 2= work, 3= school/daycare 4= recreation/sport, 5= traffic 6= bicycle
Trauma mechanism	0= not reported, 1= fall, 2=HET, 3= blunt trauma, 4= acceleration/deceleration, 5= assault, 6= other 7= not sure
Nausea	0= no, 1= yes, 2= not applicable, 9= not reported
Vomiting	0= no, 1= yes, 9= not reported
Neurological deficit in acute phase	0= no, 1= weakness, 2= loss of balance, 3= change in vision, 4= change in speech, 5= change in motor function, 6= change in sensory function, 7= multiple, 9= not reported
Mental state	0= no change, 1= confusion 2= disorientation, 3= slowed thinking, 4= other, 9= not reported
External injury	0= no, 1= laceration/cut, 2= hematoma, 3= edema, 4= graze/superficial, 5= multiple, 9= not reported
Suspected skull fracture	0= no, 1= yes, 9= not reported
Signs of basal skull fracture	0= no, 1= yes, 9= not reported
Alcohol/drug intoxication	0= no, 1= alcohol, 2= drugs, 3= combined, 9= not reported
First encounter	1= General practitioner, 2= Emergency department, 3= ambulance, 9= not reported

Contacts	1= General practitioner only, 2= General practitioner/hospital, 3= Hospital only
Gender	0= male, 1= female
Age	-
Current anticoagulant therapy	0= no, 1= VitK antagonist, 2= anti platelet, 3= NOAC, 4= multiple
Risk medication:	0= no 1= yes
Sedatives	
Anti-diabetics	0= no, 1= yes
	0= no, 2= metformine, 2= sulfonylureas, 3= insulin, 4= multiple
Anti-epileptics	0= no, 1= yes

The Glasgow Coma Scale (GCS), Initial GCS documented at first medical contact, was documented only if it was reported in the data without calculating scores afterwards.
Based on the standardised Traumatic Brain Injury classification, head injury was classified into mild, moderate or severe brain injury based on initial GCS, PTA and duration of loss of consciousness. If classification was not possible due to lack of data but classification was documented in the specialist letter, this classification was used for analysis. To assess the trauma characteristics, trauma setting and mechanism was documented. We considered a patient to have a head injury at home, work, school and day-care when documented as such or when indicated by context. Recreation and sport was chosen as trauma setting if the accident happened in recreational time not related to traffic. Traffic was chosen as trauma setting if the patient sustained head injury in a traffic setting (car vs. pedestrian/bicycle/car). Falling off a bicycle as cause of trauma was documented apart if no other traffic members were affected in the accident.
Trauma mechanism was divided into several subcategories with high energy trauma defined as fall from elevation, traffic accidents with high velocity and high impact, including acceleration/deceleration trauma.
We defined neurological deficit in the acute phase as any abnormality documented on routine clinical neurological examination that indicated a focal cerebral lesion. Mental state was scored as any documented change in behaviour or deviation of compos mentis. Symptoms of dementia and changed behaviour due to intoxication were scored as “other”. Signs of basal skull fracture were Battle’s sign, Raccoon eyes and/or liquor leakage/bleeding from nose and ear. External injury was defined as any documented discontinuity of the facial skin or head.

Intoxication was scored as ‘yes’ if explicit reported. If overall documentation was limited than intoxication was scored as “not reported”; in all other patients intoxication was score as “no”.

Within ‘contacts’ information about all contacts in the acute posttraumatic period were scored. ‘GP’ indicates that patients were seen by a GP only, ‘GP/hospital’ indicates that patient was referred to the hospital after being seen by a GP, ‘hospital’ indicates that patients are not seen by a GP before. Variables which are not mentioned here but are only displayed in the table were scored as indicated in the table.

Table I. ICPC Codes* indicating Head Injury	
A06	Fainting/syncope
A80	Trauma/injury NOS
A81	Multiple trauma/injuries
A82	Secondary effect of trauma
A96	Death
H05	Bleeding ear
L76	Fracture: other
N07	Convulsion/seizure
N79	Concussion
N80	Head injury other
N88	Epilepsy
Z25	Assault/harmful event problem

ICPC Codes indicating a Complicated Course	
*** 67**	Referral to Physician/Specialist/ Clinic/Hospital
A96	Death
F05	Visual disturbance other
F14	Eye movements abnormal
H02	Hearing complaint
H28	Limited function/disability ear
H86	Deafness
N07	Convulsion/seizure
N16	Disturbance of smell/taste
N18	Paralysis/weakness
N19	Speech disorder
N28	Limited function/disability (n)
N88	Epilepsy
N91	Facial paralysis/bell's palsy

* ICPC-2 – English International Classification of Primary Care – 2nd Edition, Wonca International Classification Committee (WICC)

STROBE (Strengthening The Reporting of OBservational Studies in Epidemiology) Checklist

A checklist of items that should be included in reports of observational studies. You must report the page number in your manuscript where you consider each of the items listed in this checklist. If you have not included this information, either revise your manuscript accordingly before submitting or note N/A.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

Section and Item	Item No.	Recommendation	Reported on Page No.
Title and Abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/Rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study Design	4	Present key elements of study design early in the paper	7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7 & 8
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	7
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7

Section and Item	Item No.	Recommendation	Reported on Page No.
Data Sources/ Measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7
Bias	9	Describe any efforts to address potential sources of bias	8
Study Size	10	Explain how the study size was arrived at	7 & 8
Quantitative Variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8 & 9
Statistical Methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8 & 9
		(*b*) Describe any methods used to examine subgroups and interactions	8 & 9
		(*c*) Explain how missing data were addressed	9
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	8 & 9
		(*e*) Describe any sensitivity analyses	9
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	10 & 11
		(b) Give reasons for non-participation at each stage	Fig. 1
		(c) Consider use of a flow diagram	Fig. 1
Descriptive Data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10 & 11
		(b) Indicate number of participants with missing data for each variable of interest	10 & 11 Tab. 1
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	10 & 11
Outcome Data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	10 & 11 Tab. 2
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	

Section and Item	Item No.	Recommendation	Reported on Page No.
Main Results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10 & 11
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	11
Other Analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key Results	18	Summarise key results with reference to study objectives	12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12 & 13
Generalisability	21	Discuss the generalisability (external validity) of the study results	13 & 14
Other Information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Once you have completed this checklist, please save a copy and upload it as part of your submission. DO NOT include this checklist as part of the main manuscript document. It must be uploaded as a separate file.

BMJ Open

Incidence, course and risk factors of head injury in The Netherlands: a retrospective cohort study.

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Title: Incidence, course and risk factors of head injury in The Netherlands: a retrospective cohort study.

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Abstract

Objectives

To assess the incidence of head injury and predictors of complication across the care continuum.

Design

Retrospective cohort study using data from a research network. We calculated the incidence of overall head injury in a longitudinal cohort covering 1 year interval (31,369 patient years), and the incidence of complicated head injury in a longitudinal cohort covering 10 years interval (220,352 patient years). Incidence rates were calculated per 1000 patient-years with 95% CI using the Mid-P exact test. We calculated Odds ratios to assess potential risk factors for a complicated head injury.

Setting

A practice-based research network covering a population of >30,000 patients.

Participants

All patients listed in practices within the research network during the years 2005-2014.

Main outcome measures

Incidence of (complicated) head injury and predictors for clinical complications.

Results

The incidence of overall head injury was 22.1 per 1000 person years and the incidence of a complicated course following head injury was 0.16 per 1000 person years. The following determinants were risk factors for a complicated course: high energy trauma, bicycle accident, traffic accident in general, use of anticoagulants, alcohol intoxication, age above 60 years and low Glasgow Coma Scale at initial presentation. A complicated course was very unlikely when the first patients' first encounter with a healthcare professional was in primary care (OR 0.03, 95%CI 0.01-0.07).

Conclusions

Complication after head injury are rarely seen in general practice. Patients who do experience complications are often easily identifiable as requiring specialist care. A more reserved referral policy for general practice may be desirable, suggesting that current guidelines are too defensive.

Trial registration

None.

Strengths and limitations

Strengths of study:

- Based on robust, comprehensive data set including all encounters of individual patients with healthcare professionals both from primary and secondary care.
- Scrutinous manual screening of all patients.

Limitation of this study:

- Incomplete data set; use of routine data from general practice

Ethical approval

No formal ethical approval was needed for this study. Patients in the participating practices are informed about the continuous data collection. The data set is anonymized and encrypted before transfer to the researchers.

Patient and Public Involvement statement

No patients where involved during development of research question, outcome measures and design of this study.

Introduction

Patients presenting with head injury in primary care challenge general practitioners to differentiate between those who may be reassured, and those who are at risk of serious intracranial injury. Intracranial injuries such as epidural and subdural hematoma or skull fractures may lead to death or permanent damage if left untreated (1-4).

High quality clinical management of head injury takes the small chance of intracranial injury into account. Safe and cost-effective practice guidelines for primary care must therefore be based on a reliable risk calculation, for which precise data are needed on the incidence of both head injury and serious intracranial injury or complicated head injury. In Europe, the annual incidence of head injury presenting in hospital emergency departments is 2.3 per 1000 person-years (5) (6). In general practice, this incidence is expected to be higher because only a subset of patients are referred to hospital. Robust data about incidence rates in primary care are lacking. For example, a New Zealand study in a primary care population found an incidence rate of 7.5 per 1000 person-years (7), whereas, in a small pilot study in the Netherlands, we found the incidence of (mild and severe) head injury to be as high as 22.3 per 1000 person-years (8).

The incidence of severe damage after a head injury is also unclear. In the UK, head injury accounts for 3.4% of all emergency department attendances. About 90% of head injuries in hospital setting are considered to be mild (6, 7). Incidence of moderate to severe head injury was 40 per 100.000 persons – a figure which may in reality be slightly higher because it does not include patients who die before admittance to the hospital (9). This makes the identification of patients at risk challenging.

Currently, guidelines for the identification, referral and management of patients with head injury at risk for intracranial damage are based on epidemiological studies from secondary or tertiary care (10, 11). Currently two different guidelines are used in the Netherlands, both have strong resemblance with the NICE guideline as used in the UK (12-14). It is likely that this case-mix of head injury patients is essentially different from that in primary care (15, 16). The risk for a

complicated course may therefore be exaggerated, resulting in spectrum bias in current guidelines (15-19).

In this study, we aim to assess the incidence of head injury across the care continuum, and to identify risk factors for intracranial injury. Our research questions were: (1) what is the incidence of head injury and complicated head injury, and (2) what predicts a complicated course?

Methods

Study Setting

We performed a retrospective cohort study in the practice based research network Family Medicine Network (FaMe-net) of the Department of Primary and Community Care (ELG) at the Radboud University Medical Centre. FaMe-net consists of nine Dutch general practices in 3 geographical regions (approximately 31.000 listed patients). FaMe-net physicians systematically and prospectively register data on the reason for encounter, diagnostic procedures, diagnoses, interventions, and referrals. The network uses the ICPC-2 and ICD-10 classification systems to code procedures and diagnosis. All data can be linked to demographic information (age, gender, geographic location, family composition). In the Netherlands, all patients are listed in one general practice to which all encounters in secondary care are reported. Reports from other care-providers are coded and linked to a new or existing episode (20). Participating doctors in FaMe-net meet on a regular basis to discuss registration issues and improve the uniformity of registration.

Definitions

We defined head injury as any trauma to the head other than superficial injuries to the face (14). A complicated head injury was defined as a head injury for which treatment and surveillance in secondary care was deemed necessary: a need for surgical intervention (defined as any neurosurgical procedure including drainage and placement of ICD), seizures in the acute posttraumatic phase, resulting neurological deficits within 12 months after trauma, and death. Neurological deficits were defined as any neurological abnormalities, including facial fracture associated nerve lesions.

Study Population and data collection

We selected patients in two stages: first we performed a sensitive electronic search based on the list of ICPC labels indicating head injury (Appendix; table I). Next, we manually scrutinized all retrieved patient records for final inclusion. In this way, we created two (retrospective) cohorts:

Cohort1: *patients with (all types of) head injury*; we expected the incidence of all head injury to be high and therefore limited the inclusion period to one year (between 1 January 2014 and 31

December 2014). Through a pilot study we constructed an inclusive list of 23 diagnostic ICPC labels that (might) refer to a head injury or traumatic brain injury. For example, to refer to a head injury the code 'concussion' (N79) could be selected, but also 'bruise/contusion' (S16) referring to skin involvement of the trauma (Appendix). Next, all available clinical data from these preselected patients were manually screened for a match to our inclusion criteria of head injury. Additionally, we screened all files of deceased patients in 2014 for the cause of death to verify if head injury occurred up to 4 weeks before time of death.

Cohort 2: *patients with a complicated course*; we expected complicated head injury to be rare and therefore included patients from a 10-year time interval (between 1 January 2005 and 31 December 2014). To identify patients with a complicated head injury we used different ICPC codes that (might) refer to (consequences of) severe and complicated head injury. We also searched for specialist letters and hospital admission in the field of neurology, neurosurgery or rehabilitation medicine. All specialist letters from these preselected patients were then manually screened for a match to our inclusion criteria of head injury. In addition to specialist letters, we used GP documentation to identify known risk factors for complicated course (21-24).

We reviewed all available clinical data, including general notes, hospital (including emergency department) correspondence, radiological imaging findings, surgical records and autopsy records. We extracted data using a predefined form (Appendix) and excluded patients with severe multi-trauma injury.

Statistical analysis

We calculated the incidence of head injury and complicated head injury per 1000 years with 95% Confidence Intervals, using the Mid-P exact test (Open source calculator OpenEpi, version 3). Age and sex structures of the mid-time population were used as denominators.

The incidence of head injury was defined as any new case of head injury during the study period. Some patients had more than one isolated case of head injury, each case was scored as a new finding. To determine the proportion of patients with complicated head injury, their incidence was compared to incidence of all head injuries as identified during the one-year study period. We evaluated all included cases for demographic and trauma characteristics.

In order to assess potential risk factors for a complicated course of head injury, we calculated Odds ratios on trauma mechanism, trauma setting, type-of-contact (hospital/GP/telephonically) after trauma and patient characteristics. Odds ratios were calculated using SPSS (IBM SPSS Statistics, Version 22.0. Armonk, NY). A p-value of <0,05 was considered statistically significant. Multivariate regression analysis was performed on the variables gender, age and high-energy transfer – during trauma (HET) as the most relevant trauma mechanism. Factors predicting a complicated head injury were calculated by multivariate analysis with logistic regression models. Variables were age, gender, trauma mechanism, symptoms for fracture and use of anti-coagulant. Moderate and severe head injury was combined during analysis due to small sample sizes. Clinical findings and data are presented using frequencies as well as percentages.

Results

(1) Incidence of all head injury.

During one year follow up (31.369 patient years), we identified 694 patients with head injury (figure 1), resulting in an overall incidence rate of 22.1 per 1000 person years (20.5-23.8; 95% CI). The incidence rate was 123.0 per 1000 person years (95%CI 101.1-148.2) for children aged 0-1 years. Out of all the patients with a head injury, 34% were under 15 years old. Patient characteristics are shown in table 1.

Table 1. Characteristics of patient and trauma

Patient Characteristics	Cohort 1. All head injury	Cohort 2. Complicated head injury
Variables	No.(%) of patients	No. (%) of clinical complications
Gender		
Male	371 (53.5)	16 (44.4)
Female	323 (46.5)	20 (55.6)
Mean age		
All	25.8 ; SD 27.7	58.0; SD 29
- Male	20.2 ; SD 23.6	48.9; SD 30
- Female	32.2 ; SD 30.5	65.3; SD 27
Presence of indicators of cHI †		
Multiple cHI indicators	-	12 (33.3)
Death	2 (0.3)	8 (22.2)
Neurosurgical intervention	4 (0.6)	12 (33.3)
Seizure	1 (0.1)	6 (16.7)
Neurological deficit	4 (0.6)	24 (66.7)
Current anticoagulant therapy		
No	642 (92.5)	27 (75.0)
Yes	52 (7.5) **	9 (25.0) **
Trauma TBI-classification *		
Mild	-	26 (72.2)
Moderate	3 (0.4)	2 (5.6)
Severe	2 (0.3)	7 (19.4)
Not reported	689 (99.3)	1 (2.8)
Trauma setting		
Home	272 (39.2)	12 (33.3)
Work	-	2 (5.6)
School/daycare	47 (6.8)	2 (5.6)
Recreation/sport	137 (19.7)	3 (8.3)
Traffic	45 (6.5)	6 (16.7)
Bicycle/motor bike	97 (13.9)	11 (30.6)

Not reported	96 (13.8)	-
Trauma mechanism		
Fall >1m	449 (64.7)	20 (55.6)
HET	52 (7.5)	12 (33.3)
Blunt trauma	151 (21.8)	2 (5.6)
acceleration/deceleration	-	-
Assault	25 (3.6)	2 (5.6)
Not reported	15 (2.2)	-
Contacts		
GP only	546 (78.7)	2 (5.6)
Hospital only	90 (12.9)	26 (72.2)
GP and hospital	58 (8.4)	8 (22.2)
Vomiting		
No	320 (46.1)	10 (27.8)
Yes	54 (7.8)	9 (25.0)
Not reported	320 (46.1)	17 (47.2)
Neurological deficit in acute phase		
No	308 (44.4)	10 (27.8)
Yes	51 (7.3)	21 (58.3)
Not reported	335 (48.3)	5 (13.9)
Change in mental functioning		
No	308 (44.4)	10 (27.8)
Yes	107 (15.4)	18 (50.0)
Not reported	279 (40.2)	8 (22.2)
External injury		
No	165 (23.8)	7 (19.4)
Yes	424 (61.1)	23 (63.9)
Not reported	105 (15.1)	6 (16.7)
Intracranial lesions		
No (lesions on CT scan)	75 (10,8)	9 (25.0)
Yes (lesions on CT scan)	10 (1.4)	22 (61.1)
Not reported/ or no CT scan	609 (87.8)	5 (13.8)
If intracranial lesions on CT scan		
- neurosur. intervention	4 (0.6)	12 (33.3)
- no neurosur. intervention	6 (0.9)	10 (27.8)

† cHI= complicated Head Injury; indicators of occurrence of complicated head injury.
* Traumatic Brain Injury
** All in age group >60years

Two of 694 patients (0.3%) died during the study period; one was a > 90-year old patient who injured his head when falling from bed and died 28 days later and the other was a > 90-year old patient who fell against a radiator and died one day later. In both cases the GP decided to

renounce referral, with informed consent from patient and family, because of age and co-

Patient age & sex	All head injuries (n=694)	Complicated head injury (n=36)

morbidity.

Patients presenting themselves to the GP were managed without referral in 90.0% of cases [n=546]. 21.3% [n=148] of all head injury patients attended the hospital emergency department (ED). Only 39.2% [n=58] were referred by the GP, with the remainder coming directly by ambulance or their own transport. Patients visiting the ED underwent CT-scanning in 50.6% [n=75] of cases and were hospitalized for at least 24 hours in 29.7% [n=44] of cases. Intra-cerebral lesion was seen in 6.8% [n=10] of patients undergoing a CT-scan; four of these patients underwent a neurosurgical intervention.

(2) Incidence of complicated head injury.

Over an observation period of ten years we identified 36 patients with complicated head injury (220.352 patient years), resulting in an incidence rate of 0.16 per 1000 person-years (0.12-0.22; 95%CI). Incidence rates are shown in table 2.

Table 2. Incidence rates of (complicated) head injury

	Midtime population*	HI (n)	Incidence rate per 1000 person years (95% CI)	Midtime population*	cHI (n)	Incidence rate per 1000 person years (95% CI)
Male						
0 - 1 year	418	54	129.2 (98.0 - 167.3)	3741	1	0.27 (0.01-1.31)
2 - 5 years	1001	93	92.9 (75.4 - 113.3)	6708	1	0.15(0.007-0.74)
6 - 15 years	2309	89	38.5 (31.1 - 47.2)	15135	1	0.07 (0.003- 0.33)
16 - 40 years	4678	53	11.3 (8.6 - 14.7)	32484	4	0.12 (0.04-0.30)
41 - 60 years	4606	48	10.4 (7.8 - 13.7)	32375	3	0.09 (0.02-0.25)
> 60 years	2482	34	13.7 (9.6 - 18.9)	17694	6	0.34 (0.14-0.71)
Total	15494	371	23.9 (21.6 - 26.5)	108137	16	0.15 (0.09-0.24)
Female						
0 - 1 year	436	51	117.0 (88.0 - 152.6)	3650	0	0 (-)
2 - 5 years	949	41	43.2 (31.4 - 58.1)	6119	1	0.16 (0.008- 0.81)
6 - 15 years	2104	45	21.4 (15.8 - 28.4)	14127	2	0.14 (0.024-0.047)
16 - 40 years	5010	70	14.0 (11.0 - 17.6)	34546	0	0 (-)
41 - 60 years	4550	37	8.1 (5.8 - 11.1)	32265	3	0.09 (0.024-0.25)
> 60 years	2826	79	28.0 (22.3- 34.7)	21531	14	0.65 (0.37-1.07)
Total	15875	323	20.4 (18.2 - 22.7)	112238	20	0.18 (0.11-0.27)
Male and Female						
0 - 1 year	854	105	123.0 (101.1 - 148.2)	7391	1	0.14 (0.006-0.67)
2 - 5 years	1950	134	68.7 (57.8 - 81.1)	12827	2	0.16 (0.026- 0.52)
6 - 15 years	4413	134	30.4 (25.5 - 35.9)	29262	3	0.10 (0.03-0.28)
16 – 40 years	9688	123	12.7 (10.6 - 15.1)	67030	4	0.06 (0.02-0.14)
41 - 60 years	9156	85	9.3 (7.5 - 11.4)	64640	6	0.09 (0.038-0.19)
> 60 years	5308	113	21.3 (17.6 - 25.5)	39225	20	0.51 (0.32-0.77)
Total	31369	694	22.1 (20.5 - 23.8)	220375	36	0.16 (0.12-0.22)

* Midtime population is calculated by means of total patient population on 1st of January and 31th of December.

In 97.2% of cases it was possible to assess the severity of traumatic brain injury from specialist correspondence. 25% [n=9] of patients, all over 60 years old, received anticoagulant therapy at time of head injury. No patients had a history of coagulopathies or other bleeding disorders. Most patients with a complicated head injury (72.2% [n=26]) were referred directly to the hospital without involvement of a GP. If the initial contact of a complicated course was in primary care (22.2% [n=8), patients presented with severe symptoms such as neurological deficits, loss of consciousness and epilepsy. A total of eight patients (1.7%) died during study

period; two were not sent to a hospital and died without an autopsy, these were the same patients as found in cohort 1. We found out-of-hospital delay in two patients, leading to delayed neurosurgical intervention. One patient consulted his GP due to a headache without reporting that he suffered head injury two weeks earlier: when the headache worsened the GP referred the patient to the hospital where a subdural hematoma was diagnosed. The second patient was residing in a care home and suffering from dementia. Following a fall from bed and non-response to pain medication he was referred to hospital, where a subarachnoid haemorrhage was diagnosed.

(3) Predictors for complicated course.

Univariate regression analysis showed that a High Energy Transfer was related to a significantly higher risk of developing a complicated head injury (OR 3.93, 95%CI 1.97-7.84) (Table 3).

Table 3. Univariate regression analysis for complicated head injury

Variable	OR*	95%CI (Mid P exact)	p Value (two-tailed. Mid P exact)
Trauma mechanism			
HET	3.93	1.97-7.84	<0.000
Car vs. pedestrian/bicycle	1.709	0.24- 7.90	0.5134
Fall >1m	1.029	0.35- 2.69	0.9307
High impact	1.285	0.47- 3.24	0.5935
Fall	0.68	0.35-1.37	0.2767
Trauma setting			
Home	0.78	0.37-1.57	0.493
Work	1.301	0.20- 4.91	0.682
School	0.81	0.13- 2.98	0.846
Rec/sport	0.37	0.09-1.11	0.080
Traffic	2.88	1.04- 7.02	0.042
Bicycle	2.70	1.24- 5.61	0.014
Contacts			
First encounter GP	0.03	0.01-0.07	<0.000
First encounter Ambulance	22.14	10.60-48.05	<0.000
GP only	0.02	0.00-0.06	<0.000
Hospital only	18.04	8.54-40.41	<0.000
GP/hospital	3.15	1.29-7.07	0.0138
Patient characteristics			

Use of OAC	4.10	1.75-9.03	0.002
Alcoholintoxication	4.30	1.38-11.53	0.015
GCS <12 (excl. not reported)	41.2	16.43-105.00	<0.000
Male gender	0.69	0.35-1.37	0.292
Age >60	6.60	3.30-13.36	<0.000
*Agegroups***			<0.000
0-1 yr (reference group)	-	-	-
2-5 yr	1.58	0.14- 17.65	0.711
6-15 yr	2.37	0.24- 23.10	0.458
16-40 yr	3.42	0.38- 31.02	0.275
41-60yr	7.50	0.89- 63.51	0.065
>60 yr	19.27	2.5- 146.13	0.004

* Odds ratios are based on Conditional maximum likelihood estimate
** Glasgow Coma Scale
*** Significances of Odds ratios calculated are in relation to youngest age group

Traffic and isolated bicycle accidents were also associated with a higher risk of complicated head injury (OR 2.88, 95%CI 1.04-7.02) respectively (OR 2.70, 95%CI 1.24- 5.61). The risk of a complicated head injury was significantly reduced if the first encounter was in primary care (OR 0.03, 95%CI 0.01-0.07), and conversely much higher when an ambulance was the first responder (OR 22.14, 95%CI 10.6- 48.05). Hospital admission without previous GP contact was related to a higher risk of complicated head injury (OR 18.04, 95%CI 8.54-40.41). A complicated course was also seen more often with oral anticoagulants (OAC) (OR 4.10, 95%CI 1.75-9.03), alcohol-intoxication (OR 4.30, 95%CI 1.38-11.53), lowering of Glasgow Coma Scale (OR 41.2, 95%CI 16.43-105.00) and age above 60 years (OR 6.60, 95%CI 3.30-13.36).

Gender, age, trauma-mechanism assault and usage of anti-coagulation were included in the multivariate analysis (limited sample size precluded inclusion of further variables). We found a significantly higher risk of hospital admittance, as well a complicated course after head injury, for age 60 years and older (OR 12.6, 95%CI 5.0-31.9) and the presence of symptoms that could indicate a fracture (above clavicle) (OR 2.4, 95%CI 1.4-4.1). When compared to the trauma mechanism 'fall', high energetic trauma was associated with a higher risk for hospital; admission

(OR 2.8, 95% CI 1.5-5.2). Male gender was not found to be a predictor of a complicated course (p=0.233).

Discussion

This is the first study to investigate the full spectrum of traumatic head injury in both primary and secondary care. We found much higher incidence rates than previously reported: 22 per 1000 patients per year, with a peak incidence in babies (0-1 years) of 123/1000. The incidence of a complicated head injury, on the other hand, is very low (0.16 per 1000 person-years) and much more in line with previous research. The vast majority of head injury patients (78.7%) were treated in primary care without referral, whereas the majority of patients with complicated head injury (72%) were directly admitted to secondary care without involvement of a primary care professional. Patients with complicated injury who initially presented in primary care seemed to be easily identified and referred to secondary care, except for two patients both > 90 years old in which a palliative approach was chosen. Known risk factors for a complicated course such as oral anticoagulants and age above 60 years were confirmed in this study (22-24).

A particular strength of our study is its setting in the Dutch health-care system, in which all patients are registered with one particular primary care provider and all encounters with healthcare professionals reported back. This means that the primary care doctor holds an overview of all encounters with health care of a particular patient (20). We used the FaMe-network database, which is linked to electronic patient files in which all encounters are registered and coded. In this system, new data (encounters, letters, reports) cannot be entered without linking to a new or existing diagnosis code – making it hard to miss even the simplest case of head injury. Moreover, it is not possible to miss cases that started in primary care but were followed up elsewhere because these encounters would be reported back, registered and coded in the same file. Because the registration network has a focus on diagnosis and medical processes (e.g. referrals, prescription), signs and symptoms of head injuries are registered in the same way as in any other practice. Most of the patients seen by the GP's involved simple head injuries, with no need for detailed reporting.

We found substantially higher incidence of head injury compared to existing reports. A recent systematic review on the incidence of all types of traumatic brain injury found a pooled incident rate of only 3.49 per 1000 patients per year, whereas our finding was 22 per 1000 patients per

year (5). In contrast with this review, we conclude that most head injuries occur amongst young children – identifying incidence more than a hundred times higher in children. This difference might be explained by variable classification, especially since the systematic review's authors point out the problem of non-standardized reporting among neuro-epidemiological studies on incidence of (particularly mild) head injury. One particular study claimed to assess the full spectrum of head injury by including data from general practice, resulting in an incidence of 7.90 per 1000 patients per year. Unfortunately, this study limited inclusion to patients with head injury and "physiological disruption of brain function" (7).

Variation in definition of head injury is an ongoing problem in current literature, resulting in a wide range of incidence figures of traumatic head injury (5, 25-27). One particular review stated that the term 'silent epidemic' could be used to characterize the incidence of head injury, because many cases are not recognized and therefore excluded from official statistics (27). Our study captures the full spectrum of head injury as presented in the entire health-care system (in and out of hospital) with inclusion based on any trauma of the head excluding injuries of the face. This is in line with current guidelines for primary care that apply a similar broad definition of head trauma. We fully endorse this broad definition for future diagnostic and prognostic research aimed at primary care populations. The nature of primary care is that it is easily and rapidly accessible for every patient with no pre-selection or other thresholds. Even in primary care it is difficult to rule out a complicated course. After all, the condition was (per definition) sufficiently severe for patient, parents or bystanders to seek professional help. Moreover, neurological indications may not develop in this early stage so a definition based on signs of 'disruption of brain function' - as has previously been advocated - is not feasible (27). We are furthermore convinced that identifying patients with mild trauma (including those not seen in a hospital setting) is relevant because (un-)complicated head injury may still be associated with significant cost in terms of disability, lost work or neuropsychiatric complications (28, 29).

Although existing guidelines are based on a broad definition of head injury, the underlying evidence is based almost exclusively on clinical populations. In clinical populations a (self-) selection for complicated head injury has already taken place and a narrow definition of head injury is used (10, 11, 14, 30, 31), leading to a higher estimated risk for complications and over-treatment of patients with head injury (31, 32).

We conclude that head injury as seen in primary care comprises an essentially different case-mix as compared to secondary care. Moreover, complicated cases appear to be easily identified and readily presented to secondary care. Our study requires confirmation in other settings using other databases, but we are convinced that current guidelines are based on limited evidence of true incidence rates. This makes them prone to spectrum bias. A more reserved management of head injury in primary care should be considered, leading to more cost-effective use of costly hospital diagnostic resources. This study also calls for an internationally accepted definition (coupled with a universal diagnostic algorithm) of head injury and (mild) traumatic brain injury.

Figure and tables

Statements concerning this study

Contributor ship:

- Gerritsen, H (MD); was involved and made contributions in the design of the study, acquisition, analysis and interpretation of the data. Drafted the work and revised it critically for important intellectual content. Gave final approval of the version published and made agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
- Samim, M (Msc); was involved and made contributions in the design of the study, acquisition, analysis and interpretation of the data. Revised the work critically for important intellectual content. Gave final approval of the version published and made agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
- Peters, H.J.G. (Bsc); was involved and made contributions in the design of the study, acquisition, analysis and interpretation of the data. Revised the work critically for important intellectual content. Gave final approval of the version published and made agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
- Schers, H (MD, PhD); was involved and made contributions in the design of the study, acquisition, analysis and interpretation of the data. Revised the work critically for important intellectual content. Gave final approval of the version published and made agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
- Laar, F.A. vd. (MD, PhD); was involved and made contributions in the design of the study, acquisition, analysis and interpretation of the data. Revised the work critically for important intellectual content. Gave final approval of the version published and made agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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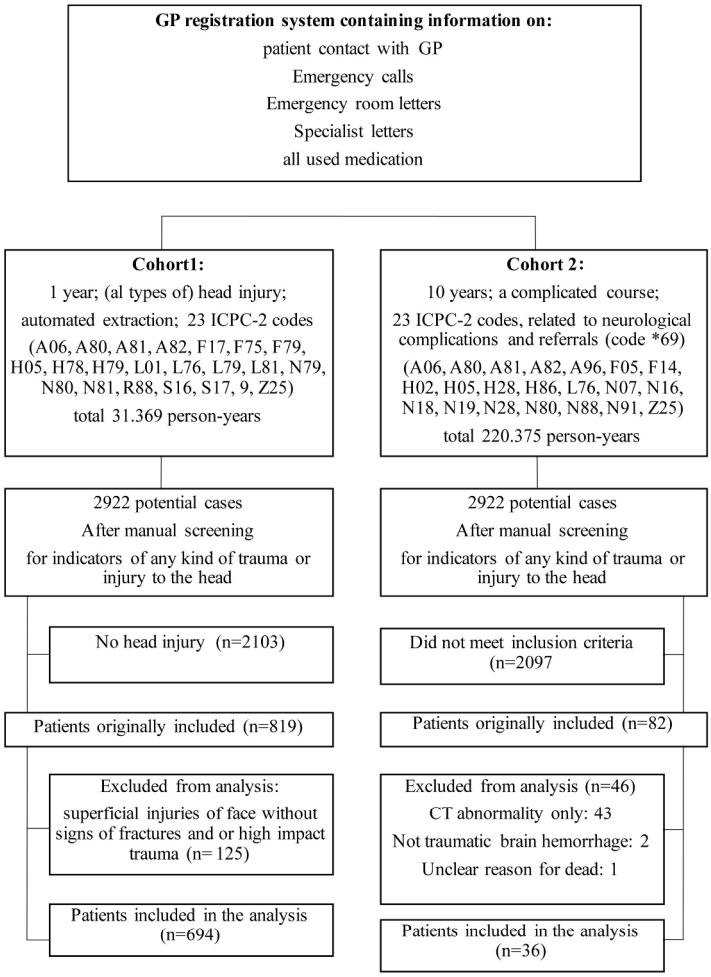

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Appendix; definition of initial variables for data extraction.

Data collection was performed based on information from specialist correspondence and GP documentation. There-fore selected ICPC codes were used (Table I). Data was systematically screened on several variables:

Variable	Categories
Glasgow Coma Scale	1= 15, 2= 14, 3= 13, 4= 9-12, 5= 8 or lower, 9= not reported
Loss of consciousness	0= no, 1= <5min, 2= 5-30min, 3= >30min, 4= duration unclear, 5= Unclear if LOC, 9= not reported
Posttraumatic amnesia	0= no, 1= <24h, 2= 1-7 days, 3= >7 days, 4= unclear if PTA, 9= not documented
TBI classification	1= mild, 2= moderate, 3= severe, 9= no classification possible
Trauma setting	0= not reported 1= home, 2= work, 3= school/daycare 4= recreation/sport, 5= traffic 6= bicycle
Trauma mechanism	0= not reported, 1= fall, 2=HET, 3= blunt trauma, 4= acceleration/deceleration, 5= assault, 6= other 7= not sure
Nausea	0= no, 1= yes, 2= not applicable, 9= not reported
Vomiting	0= no, 1= yes, 9= not reported
Neurological deficit in acute phase	0= no, 1= weakness, 2= loss of balance, 3= change in vision, 4= change in speech, 5= change in motor function, 6= change in sensory function, 7= multiple, 9= not reported
Mental state	0= no change, 1= confusion 2= disorientation, 3= slowed thinking, 4= other, 9= not reported
External injury	0= no, 1= laceration/cut, 2= hematoma, 3= edema, 4= graze/superficial, 5= multiple, 9= not reported
Suspected skull fracture	0= no, 1= yes, 9= not reported
Signs of basal skull fracture	0= no, 1= yes, 9= not reported
Alcohol/drug intoxication	0= no, 1= alcohol, 2= drugs, 3= combined, 9= not reported
First encounter	1= General practitioner, 2= Emergency department, 3= ambulance, 9= not reported

Contacts	1= General practitioner only, 2= General practitioner/hospital, 3= Hospital only
Gender	0= male, 1= female
Age	-
Current anticoagulant therapy	0= no, 1= VitK antagonist, 2= anti platelet, 3= NOAC, 4= multiple
Risk medication:	0= no 1= yes
Sedatives	
Anti-diabetics	0= no, 1= yes
	0= no, 2= metformine, 2= sulfonylureas, 3= insulin, 4= multiple
Anti-epileptics	0= no, 1= yes

The Glasgow Coma Scale (GCS), Initial GCS documented at first medical contact, was documented only if it was reported in the data without calculating scores afterwards.
Based on the standardised Traumatic Brain Injury classification, head injury was classified into mild, moderate or severe brain injury based on initial GCS, PTA and duration of loss of consciousness. If classification was not possible due to lack of data but classification was documented in the specialist letter, this classification was used for analysis. To assess the trauma characteristics, trauma setting and mechanism was documented. We considered a patient to have a head injury at home, work, school and day-care when documented as such or when indicated by context. Recreation and sport was chosen as trauma setting if the accident happened in recreational time not related to traffic. Traffic was chosen as trauma setting if the patient sustained head injury in a traffic setting (car vs. pedestrian/bicycle/car). Falling off a bicycle as cause of trauma was documented apart if no other traffic members were affected in the accident.
Trauma mechanism was divided into several subcategories with high energy trauma defined as fall from elevation, traffic accidents with high velocity and high impact, including acceleration/deceleration trauma.
We defined neurological deficit in the acute phase as any abnormality documented on routine clinical neurological examination that indicated a focal cerebral lesion. Mental state was scored as any documented change in behaviour or deviation of compos mentis. Symptoms of dementia and changed behaviour due to intoxication were scored as “other”. Signs of basal skull fracture were Battle’s sign, Raccoon eyes and/or liquor leakage/bleeding from nose and ear. External injury was defined as any documented discontinuity of the facial skin or head.

Intoxication was scored as ‘yes’ if explicit reported. If overall documentation was limited than intoxication was scored as “not reported”; in all other patients intoxication was score as “no”.

Within ‘contacts’ information about all contacts in the acute posttraumatic period were scored. ‘GP’ indicates that patients were seen by a GP only, ‘GP/hospital’ indicates that patient was referred to the hospital after being seen by a GP, ‘hospital’ indicates that patients are not seen by a GP before. Variables which are not mentioned here but are only displayed in the table were scored as indicated in the table.

Table I. ICPC Codes* indicating Head Injury	
A06	Fainting/syncope
A80	Trauma/injury NOS
A81	Multiple trauma/injuries
A82	Secondary effect of trauma
A96	Death
H05	Bleeding ear
L76	Fracture: other
N07	Convulsion/seizure
N79	Concussion
N80	Head injury other
N88	Epilepsy
Z25	Assault/harmful event problem

ICPC Codes indicating a Complicated Course	
*** 67**	Referral to Physician/Specialist/ Clinic/Hospital
A96	Death
F05	Visual disturbance other
F14	Eye movements abnormal
H02	Hearing complaint
H28	Limited function/disability ear
H86	Deafness
N07	Convulsion/seizure
N16	Disturbance of smell/taste
N18	Paralysis/weakness
N19	Speech disorder
N28	Limited function/disability (n)
N88	Epilepsy
N91	Facial paralysis/bell's palsy

* ICPC-2 – English International Classification of Primary Care – 2nd Edition, Wonca International Classification Committee (WICC)

STROBE (Strengthening The Reporting of OBservational Studies in Epidemiology) Checklist

A checklist of items that should be included in reports of observational studies. You must report the page number in your manuscript where you consider each of the items listed in this checklist. If you have not included this information, either revise your manuscript accordingly before submitting or note N/A.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

Section and Item	Item No.	Recommendation	Reported on Page No.
Title and Abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/Rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study Design	4	Present key elements of study design early in the paper	7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7 & 8
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	7
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7

Section and Item	Item No.	Recommendation	Reported on Page No.
Data Sources/ Measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7
Bias	9	Describe any efforts to address potential sources of bias	8
Study Size	10	Explain how the study size was arrived at	7 & 8
Quantitative Variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8 & 9
Statistical Methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8 & 9
		(*b*) Describe any methods used to examine subgroups and interactions	8 & 9
		(*c*) Explain how missing data were addressed	9
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	8 & 9
		(*e*) Describe any sensitivity analyses	9
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	10 & 11
		(b) Give reasons for non-participation at each stage	Fig. 1
		(c) Consider use of a flow diagram	Fig. 1
Descriptive Data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10 & 11
		(b) Indicate number of participants with missing data for each variable of interest	10 & 11 Tab. 1
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	10 & 11
Outcome Data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	10 & 11 Tab. 2
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	

Section and Item	Item No.	Recommendation	Reported on Page No.
Main Results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10 & 11
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	11
Other Analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key Results	18	Summarise key results with reference to study objectives	12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12 & 13
Generalisability	21	Discuss the generalisability (external validity) of the study results	13 & 14
Other Information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Once you have completed this checklist, please save a copy and upload it as part of your submission. DO NOT include this checklist as part of the main manuscript document. It must be uploaded as a separate file.