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Epidemiology of Traumatic Brain Injury in Europe: A Living Systematic Review

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Abstract

This systematic review provides a comprehensive, up-to-date summary of traumatic brain injury (TBI) epidemiology in Europe, describing incidence, mortality, age, and sex distribution, plus severity, mechanism of injury, and time trends. PubMed, CINAHL, EMBASE, and Web of Science were searched in January 2015 for observational, descriptive, English language studies reporting incidence, mortality, or case fatality of TBI in Europe. There were no limitations according to date, age, or TBI severity. Methodological quality was assessed using the Methodological Evaluation of Observational Research checklist. Data were presented narratively. Sixty-six studies were included in the review. Country-level data were provided in 22 studies, regional population or treatment center catchment area data were reported by 44 studies. Crude incidence rates varied widely. For all ages and TBI severities, crude incidence rates ranged from 47.3 per 100,000, to 694 per 100,000 population per year (country-level studies) and 83.3 per 100,000, to 849 per 100,000 population per year (regional-level studies). Crude mortality rates ranged from 9 to 28.10 per 100,000 population per year (country-level studies), and 3.3 to 24.4 per 100,000 population per year (regional-level studies.) The most common mechanisms of injury were traffic accidents and falls. Over time, the contribution of traffic accidents to total TBI events may be reducing. Case ascertainment and definitions of TBI are variable. Improved standardization would enable more accurate comparisons.

Key words: epidemiology; living systematic review; traumatic brain injury

Editor's Note: This article is published as a Living Systematic Review. All Living Systematic Reviews will be updated at approximately three-six month intervals, with these updates published as supplementary material in the online version of the Journal of Neurotrauma (see Update 5).

Introduction

Traumatic brain injury (TBI) is among the most severe types of injury in terms of both case fatality[1] and long-term implications for survivors.[2] Treatment of TBI can be complex and expensive.[3] Upon clinical examination, TBI is most commonly sub-divided into mild, moderate, and severe, according to the Glasgow Coma Scale (GCS).[4,5] Such categories have been found to be predictive of a patient's long-term outcome,[6] although other measures and models also have been tested.[7,8]

A previous review of the epidemiology of TBI in Europe concluded that the leading causes of TBI were road traffic collisions, and falls.[3] Consequently, in a densely populated and economically advanced area such as the European Union (EU), the potential for prevention of morbidity and mortality is great. The variability in incidence and mechanism of TBI, which may be observed on this mainly contiguous land-mass with a well-developed road network, is also of scientific interest, as it may lead to better prevention of TBI. Countries within the EU adhere to certain multi-national laws and agreements, but nonetheless retain their own law-making and

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enforcement responsibilities.[9] This may add further complexity to the understanding of TBI epidemiology, for example, in the contributions of varying road speed limits or the legal restrictions on the availability of firearms. More generally, the issues relating to the contemporary demographic and lifestyle characteristics of the similar countries or regions suggest that epidemiological trends from EU countries also may be applicable to other high income countries.

Considerable variability has been observed between national rates, largely attributable to significant variability in data collection, case ascertainment, and case definition. This has led to calls for standardized definitions and data collection in population-based studies, and an associated paradigm shift in studying TBI and its impact.[10–12]

In order to improve the understanding of causes of TBI and the scale of the problem, it is important to analyze the current situation and time trends, using good quality comparable observational studies. One comprehensive systematic review of the epidemiology of TBI in Europe was published nearly ten years ago.[3] A recent systematic review,[13] published as a follow-up to Tagliaferri (2006),[3] addresses similar issues but was more restrictive in dates of publication (1990–2014) and has not been set up as a ''living'' systematic review (i.e., it is not expected that it will be kept up-to-date as new research is published).[13]

The overall objective of this systematic review was to provide a comprehensive, up-to-date summary of TBI epidemiology in Europe by reviewing all relevant observational studies. Specific aims were to determine the incidence, mortality, age, and sex distribution of TBI in Europe, along with the severity and mechanism of injury and time trends.

Methods

This review was conducted and reported in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement.[14] Details of the protocol for this systematic review were registered on PROSPERO (registration number 2014: CRD42014015517) and can be accessed at www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42014015517.

This review was prepared as a ''living systematic review'' as part of the Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury (CENTER-TBI) project. CENTER-TBI is a European project aiming to improve outcomes for people with TBI through better classification, characterization, and management of this injury.[15] A living systematic review is a high quality, up-to-date online summary of health research that is updated as data from new relevant research that meets study inclusion criteria becomes available.[16] In practice, this means that the searches will be re-run frequently, any new studies incorporated into the review, and updates will be regularly published.[17]

Information sources

The following databases were searched: PubMed, Web of Science, CINAHL, and EMBASE from 1960 up to January 15, 2015. For each of these, searches were performed in March and April 2014 with a combination of key words and subject headings (Appendix 1). The same searches were re-run in January 2015. To reduce the risk of publication bias, searches also were undertaken in gray literature and references of included studies.

Study selection/inclusion criteria

Retrospective and prospective descriptive studies that reported on the epidemiology of TBI in Europe were included. To be eligible for the review, studies must have been an original study (i.e., not a review or duplicate of previously published data) that measured and reported incidence, mortality, or case fatality of TBI in Europe, and was published in English. Study size was not restricted and data collected from hospitals or official statistics were eligible. There were no limitations regarding the dates of data collection, study performance or publication, participant age, or TBI severity.

For some of these terms, such as TBI, incidence, mortality, and case fatality, the definition used by authors can vary. For the purposes of this review, these terms were defined in the following ways:

- TBI: Defined as an injury to the head, by either blunt force or penetrative means, which causes sufficient damage that the patient suffers a change in brain function; or more recently, as an alteration in brain function, or other evidence of brain pathology, caused by an external force.[11] Ascertainment of a TBI case could be by any of the following: *International Classification of Diseases* (ICD) in its 8th, 9th and 10th revision codes, Abbreviated Injury Score for head injuries (AIS_{Head} or HAIS), the Glasgow Coma Scale (GCS), or clinical signs (such as loss of consciousness, post-traumatic amnesia, or pathologies found in computed tomography/magnetic resonance imaging scan).
- Incidence: Rate of TBIs recorded per 100,000 population per year. These were usually first-time events.
- Mortality: Total number of fatal TBIs in a given population per 100,000 population per year.
- Case fatality: Proportion of people with TBI who subsequently died due to a cause related to the TBI at certain time-points.
- TBI severity: Categories of severity (severe, moderate, mild), as defined by the GCS (e.g., 3–8 [mild], 9–12 [moderate], and 13–15 [severe],[5] or other classification system used by the authors.

Two authors (WP, VB) independently screened citations on titles and abstracts, excluding any obviously irrelevant or duplicate citations. Results were compared and disagreements discussed with a third author and/or with members of an expert panel. Agreed citations were retrieved in full text and screened independently by two authors (AB, VB, MM, VR, MT) using the same process. Screening was undertaken using Covidence, a not-for-profit web-based tool designed to assist in conducting systematic reviews.[18]

Data collection and assessment of methodological quality

Two authors (AB, VB, MM, VR, or MT) independently extracted data and assessed methodological quality of selected studies. Any discrepancies were resolved by discussion.

The following items were extracted from each study: study authors, year of publication, study time period, type of data source, method and completeness of case ascertainment, criteria for identifying TBI, source population, number of TBI cases reported, reported data on TBI incidence, mortality, and case fatality, broken down by sex, age, severity, and mechanism of injury.

Methodological quality was assessed using the Methodological Evaluation of Observational Research (MORE) checklist, as previously used in reviews of non-therapeutic studies.[19,20] The following domains of bias or quality are assessed with the MORE checklist: funding of study, conflict of interest, study design, sampling, definition of cases, source of data, and reliability of estimates. Each domain was judged according to specific criteria and scored as ''OK, Minor Flaw, Major Flaw, and Poor reporting'' (Appendix 2) No studies were excluded from the review based on methodological quality.

Data synthesis

To facilitate appropriate comparisons, studies were first grouped according to whether they reported country-level data (derived from national hospital or mortality registries) or regional-level

data, denoting smaller populations within studies (derived from regional/country or hospital catchment areas). Other stratifications–for example, by study design and retrospective/prospective data collection–were considered, but the strata generated by this means were too small to make meaningful comparisons.

Findings are described overall, and also broken down according to age, sex, severity of TBI, and mechanism of injury. Time trends of incidence and mortality of TBI also are described.

Statistical analysis

Data are presented in tables and figures. Meta-analysis of incidence and mortality rates was not possible, as too few studies reported age-adjusted data and it was not possible to obtain the raw data from study authors to perform standardization. A funnel plot was generated to consider small study effects in regional-level studies; the country-level studies were not plotted as there were too few studies (fewer than 10).

Results

Description of studies

A total of 4289 citations were identified. After removing duplicates, 4232 were screened on citation and abstract and 4011 were excluded. As such, 221 papers were screened for eligibility, with 66 included as full-text (Fig. 1).

Characteristics of included studies

Of the 66 included studies, 22 provided country-level data from Finland ($n=4$); Austria ($n=4$); Denmark ($n=3$); the Netherlands ($n=2$); Norway ($n=2$); Sweden ($n=2$); and Scotland, Germany, Great Britain, Spain, Portugal, Switzerland, and the Republic of San Marino, ($n=1$, each). A further 44 reported on either a regional population (one or more country regions, counties or provinces) or the catchment area of one or more treatment centers. All studies together represented 23 European countries–those mentioned above and Italy, France, Iceland, Ireland, United Kingdom, Bosnia, Croatia, Macedonia, Slovak Republic, Estonia, and Greece.

The majority of studies ($n=25$) had study periods of 1 or 2 years, with a further 17 reporting data over 10 years or more. The remaining studies reported a time period of 3 – 10 years. The number of included cases ranged from 101[21] (included severe TBI only) to 208,195.[22] Tables 1 and 2 present the characteristics of included studies.

Inclusion criteria, case ascertainment, and case definition varied markedly across studies. Most had data from hospital registries, either

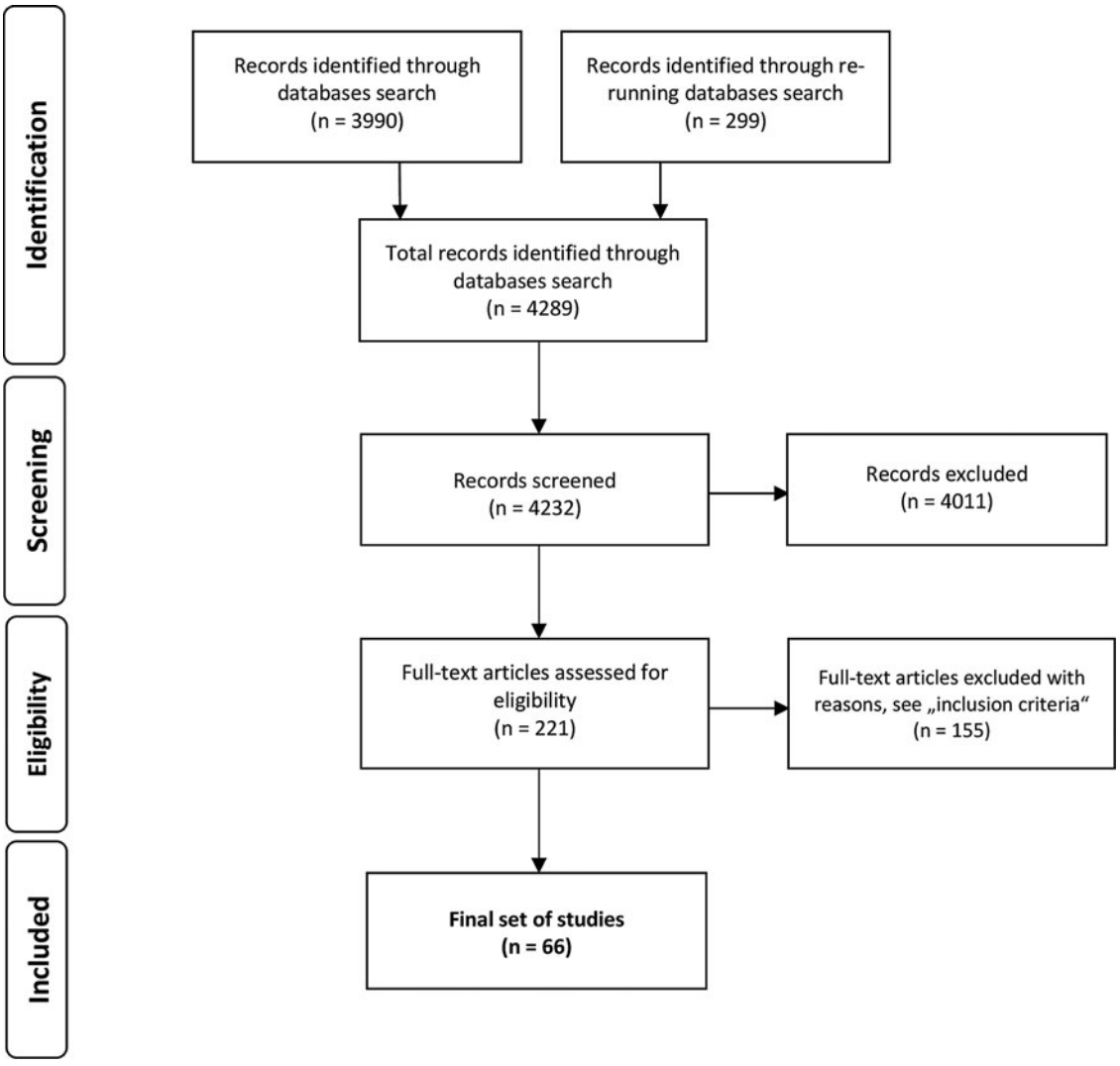

FIG. 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart of the study selection process.

Table 1. Characteristics of Studies With Country-Level Population

	Study author(s) (year) reference number	*Source population*	*Study period*	*Data source*	*Case ascertainment*	*Type of severity*	*Number of cases*	*Average age*	*% of males/ M:F ratio*	*Mechanism of TBI injury (up to 3 most frequent in % *)*
1	Kannus and colleagues (1999)[48]	Finland (≥ 60 years; fall-induced only)	1970–1995	National hospital discharge registry	ICD 8, ICD 9	Severe	554 in 1970 1393 in 1995	69.6 in 1970 75 in 1995	NR	F only
2	Steudel and colleagues (2005)[31]	Germany	1972–1998	Hospital admissions registry; mortality registry	ICD 9, ICD 10	All	279,029 (in 1996)	NR	NR	NR
3	Jennett and MacMillan (1981)[49]	Scotland, England, Wales	1974–1975	Hospital admissions report; Registrar's general report	Clinical definition	All	Unclear	NR	NR	Unclear
4	Engberg, and Teasdale (1998)[23]	Denmark (0–14 years)	1979–1993	Danish hospital registry	ICD 8	All	47,794	NR	58	NR
5	Engberg and colleagues (2001)[50]	Denmark	1979–1996	Danish hospital registry	ICD 8, ICD 10	All	166,443	NR	2.12:1	NR
6	Mauritz and colleagues (2014)[51]	Austria	1980–2012	Statistik Austria (national statistical office)	ICD 9, ICD 10	Fatal	47,827	NR	2.2:1	T F Su
7	Brazinova and colleagues (2014)[52]	Austria (≥ 65 years)	1980–2012	Statistik Austria (national statistical office)	ICD 9, ICD 10	Fatal	16,204	NR	61	F 48 T 22 Su 17
8	Majdan and colleagues (2014)[53]	Austria (0–19 years)	1980–2012	Statistik Austria (national statistical office)	ICD 9, ICD 10	Fatal	5319	NR	75	T 78 F 8
9	Servadei and colleagues (1985)[28]	Republic of San Marino	1981 and 1982	Hospital records	Clinical definition	All	207	26.7	67.2	NR
10	Williamson and colleagues (2002)[54]	Scotland (0–14 years)	1986–1995	Registrar General's report	Clinical definition; ICD 9	Fatal	290	NR	64/1.7:1	T 72 F 11
11	Hartholt and colleagues (2011)[46]	Netherlands (≥ 65 years; fall-induced only)	1986–2008	National medical registration	ICD 9	Severe	32,133	NR	40	F only
12	Sundstrøm and colleagues (2007)[55]	Denmark, Finland Norway, Sweden	1987–2001	National statistical offices	ICD 8; ICD 9; ICD 10	Fatal	NR	1987: Denmark M 41.8, F 50.1 Finland M 44.2, F 56.3 Norway M 44.5, F 54.8 Sweden M 48.1, F 53.6	NR	NR

(*continued*)

Table 1. (Continued)

Study author(s) (year) reference number	Source population	Study period	Data source	Case ascertainment	Type of severity	Number of cases	Average age	% of males/ M:F ratio	Mechanism of TBI injury (up to 3 most frequent in % *)
							2001: Denmark M 49.8, F 60.1 Finland M 52.1, F 62.3 Norway M 52.3, F 66.3 Sweden M 56.8, F 69.3		
13 Kleiven and colleagues (2003)[56]	Sweden	1987–2000	Swedish Hospital Discharge Registry	ICD 9; ICD 10	All	≈22,000/year	NR	2:1	F T
14 Alaranta and colleagues (2000)[57]	Finland	1991–1995	National hospital discharge registry	ICD 9	All	24,497	NR	58.7	F 61 T 26
15 Koskinen and Alaranta (2008)[58]	Finland	1991–2005	National hospital discharge registry; cause of death registry	ICD 9; ICD 10	All	77,959	NR	59.2	F 51.8 T 16.6 V 2.9
16 Shivaji and colleagues (2014)[22]	Scotland	1998–2009	Scottish Morbidity Record	ICD 10	All	208,195	NR	70	F 47 V 18
17 Pérez and colleagues (2012)[27]	Spain	2000–2009	National hospital discharge registry	ICD 9; ISS; Barell matrix	All	206,503	NR	2.7:1	T
18 Dias and colleagues (2014)[59]	Portugal (≥ 18 years)	2000–2010	National diagnosis-related groups database	ICD 9	All	72,865	57.9 ± 21.8	64.1/1.8:1	F 57 T 29
19 Walder and colleagues (2013)[24]	Switzerland (≥ 16 years)	2007–2010	Hospital records (all hospitals)	HAIS	Severe	921	Median, 55	74.2	F 52.6 T 31.6
20 Mauritz and colleagues (2014)[32]	Austria	2009–2011	Statistik Austria (national statistical office); AUVA hospital discharges database	ICD 10	All	73,622	44.5 ± 29.2	58.3	T 6.8 (81% unknown)
21 Andelic and colleagues (2012)[60]	Norway (≥ 16 years)	2009–2010	Norwegian trauma referral centers	ICD 10, GCS	Severe	359	46.7 ± 21.6	77	F 50 T 40
22 Scholten and colleagues (2014)[61]	Netherlands	2010–2012	Dutch Injury Surveillance System; national hospital discharge registry	ICD 9	All	3762/year (DIS), 34,681/year (natlional estimate)	NR	NR	H 48 T 33.4 S 8.2

*% if clearly stated.

M, males; F, females; TBI, traumatic brain injury; *ICD, International Classification of Diseases;* NR, not reported; T, traffic related; F, falls; Su, suicide; ISS, Injury Severity Score; HAIS, Head Abbreviated Injury Scale; GCS, Glasgow Coma Scale.

Table 2. Characteristics of Studies With Regional-Level Population

Study author(s) (year) reference number	*Source population*	*Study period*	*Data source*	*Case ascertainment*	*Type of severity*	*Number of cases*	*Average age*	*% of males/ M:F ratio*	*Mechanism of TBI injury (up to 3 most frequent in % *)*
23 Winqvist and colleagues (2007)[62]	Finland (≤34 years; birth cohort)	1966–2000	Finnish Hospital Discharge Registry; Causes and Death Register	ICD 8; ICD 9; ICD 10	All	457	NR	66.5	T 41.7 F 25.8
24 Berney and colleagues (1995)[63]	Switzerland (0–15 years)	1969–1991	Children's Hospital of Geneva records	Clinical definition	All	4003	NR	NR	1969: T 56.5 F 26.5 1990: T 46 F 32
25 Berney and colleagues (1994)[64]	Switzerland (0–15 years)	1975–1983	Children's Hospital of Geneva records	Clinical definition	All	1835	NR	63	F 46 T 43
26 Nestvold and colleagues (1988)[65]	Norway	1975	Hospital. records of four hospital of Akershus county	Clinical definition	All	488	29.75	1.9:1	T 57.6 H 7.8
27 Edna and Cappelen (1984)[66]	Norway	1979–1980	Hospital records of four hospital of Trøndelag county	Clinical definition	All	1124	NR	69.7	T 44.8 S 13.9 H 12.5
28 Edna and Cappelen (1985)[67]	Norway (traffic-induced only)	1979–1980	Hospital records of four hospitals of Trøndelag county	Clinical definition	All	503	NR	2.0:1	T only
29 Alvarez and colleagues (2011)[68]	Spain (1 m.–14 years)	1983–2009	Pediatric ICU of The Canary Islands provincial hospital	Clinical definition; GCS	Severe	389	67.9 ± 41.6 m.	67	T 56 F 24
30 Johansson and colleagues (1991)[69]	Sweden (16–60 years)	1984–1985	Hospital records of regional hospitals of Umeå district	ICD 9	All	242	NR	64.5	NR
31 Servadei and colleagues (1988)[30]	Italy	1984–1985	Ravenna City hospital records	Clinical definition	All	1468	NR	NR	T 66.4 F 27.7
32 Tiret and colleagues (1990)[70]	France	1986	Hospital records of referral teaching hospitals in Aquitaine registry	Clinical definition	All	8940	NR	2.1:1	T 59.6 F 32.5
33 Emanuelson and Wendt (1997)[71]	Sweden (0–17 years)	1987–1991	Hospital records of hospital of southwestern Sweden	Clinical definition; ICD 9	All	210	9.44 ± 4.96	64.3	T 60 F 22 S 7

(*continued*)

TABLE 2. (CONTINUED)

Study author(s) (year) reference number	*Source population*	*Study period*	*Data source*	*Case ascertainment*	*Type of severity*	*Number of cases*	*Average age*	*% of males/ M:F ratio*	*Mechanism of TBI injury (up to 3 most frequent in % *)*
34 Arnarson and colleagues (1995)[72]	Iceland (0–14 years)	1987–1991	Reykjavík City hospital records	Clinical definition; ICD 9	All	359	NR	62.4	F 62 T 19
35 Boto and colleagues (2009)[25]	Spain (>14 years)	1987–1999	Department of Neurosurgery of the Hospital ''12 de Octubre,'' Madrid	GCS	Severe	895	35.2 ± 17.8	78.2	T 64.6 F 30.9
36 Vazquez-Barquero and colleagues (1992)[26]	Spain	1988	Hospital records of University Hospital ''Marqués de Valdecilla''	Clinical definition	All	477	NR	73.4	T 60 F 24 W 8
37 Bouillon and colleagues (1999)[73]	Germany	1990–1996	Prehospital and hospital records of Cologne region	GCS or AIS_{Head}	Severe	650	39	71	T 56 F 31
38 Maegele and colleagues (2007)[74]	Germany	1990–1999	Pre-hospital and hospital records of Cologne region	GCS or AIS_{Head}	Severe	731	40.3	73	T 55.3 F 35
39 Andersson and colleagues (2003)[75]	Sweden	1992–1993	Central Hospital Borås records	ICD 9; ACRM categories	All	753	27	59	F 58 T 16
40 Hawley and colleagues (2003)[37]	United Kingdom (0–15 years)	1992–1998	North Staffordshire health district hospitals records	GCS; British Society of Rehabilitation Medicine Classification	All	1,553	6.76 ± 4.6	64.3	F 45.1 T 21.1
41 Ingebrigtsen and colleagues (1998)[76]	Norway	1993	University Hospital of Tromsø records	Clinical definition; HISS	All	247	NR	63.6/1.7:1	F 62 T 21 V 7
42 Javouhey and colleagues (2006)[77]	France (traffic-induced only)	1996–2001	Road Trauma Registry in Rhône region	Clinical definition; AIS	All	64,298	NR	severe 74.7	T only
43 Baldo and colleagues (2003)[78]	Italy	1996–2000	Hospital records of Veneto Region; Regional Statistics Office	ICD 9; AIS	All	55,368	M 37.7 ± 24.7 F 45.6 ± 29.7	61.1	T 48.5 H 12.2 W 8.8
44 Masson and colleagues (2001)[79]	France	1996	Hospital records in Aquitaine region	HAIS; GCS	Severe	497	HAIS4 median, 44 HAIS5 median, 45	71.4/2.5:1	T 48.3 F 41.8

(*continued*)

TABLE 2. (CONTINUED)

Study author(s) (year) reference number	*Source population*	*Study period*	*Data source*	*Case ascertainment*	*Type of severity*	*Number of cases*	*Average age*	*% of males/ M:F ratio*	*Mechanism of TBI injury (up to 3 most frequent in % *)*
45 Puljula and colleagues (2013)[47]	Finland	1999 and 2007	Oulu University Hospital records, Northern Ostrobothnia region	GCS	Moderate; severe	126 in 1999 135 in 2007	44 in 1999 48 in 2007	72.2 in 1999 76.3 in 2007	1999: F 33 V 30 T 29 2007: F 50 T 22 V 20
46 Servadei and colleagues (2002)[80]	Italy	1998	Ospedale Maurizio Bufalini records, Romagna region	ICD 9	All	2,430	NR	61.5	T 47.9 F 32.6 W 7.8
47 Di Bartolomeo and colleagues (2001)[81]	Italy	1998–1999	regional trauma data bank of Friuli Venezia Giulia Region	ISS; AIS; TRISS; GCS	Severe	184	44.5	77.2	NR
48 Servadei and colleagues (2002)[82]	Italy	1998	hosp. records of Romagna and Trention regions	ICD 9	All	4,442	NR	61.5 Romagna 63.7 Trentino	Romagna: T 48.2 Trentino: T 23, H 19.6
49 Dahl and colleagues (2006)[83]	Sweden (0–17 years)	1999 and 2000	Central Hosp.of Borås records, south-western Sweden	Clinical definition; GCS	Mild	192	7.5 ± 4.8	57.3	F 61 S 16 T 13
50 Rusnak and colleagues (2007)[45]	Austria	1999–2004	Hospital records of five participating hospitals	GCS	Severe	492	47.5 (95% CI, 45.7 – 49.3)	71.9	NR
51 Rickels and colleagues (2010)[33]	Germany	2000–2001	Hospital records, Hannover region, Münster county	ICD 10	All	6783	NR	58.4	F 52,5 T 26,3 V 14,2
52 Ventsel and colleagues (2008)[84]	Estonia (0–14 years)	2001–2005	Tartu University Hospital records, Tartu county	ICD 10	All	478	6.2 (95% CI, 5.80 – 6.64)	57	F 63.6 T 16.9
53 Styrke and colleagues (2007)[34]	Sweden	2001	Hospital records of regional hospital of Umeå district	ICD 10	All	449	median, M 23 median, F 22	55	F 55 T 30
54 Rosso and colleagues (2007)[85]	Austria	1999–2004	hosp. records of 5 participating hosp.	GCS	Severe	492	48.2 ± 21.1	72	T 44 F 41 S 5
55 Mauritz and colleagues (2008)[86]	Austria, Bosnia, Croatia, Macedonia and Slovak Republic	2001–2005	Hospital records of 13 participating hospital	GCS	Severe	1172	41	77.3	T 44.3 F 36

(*continued*)

Table 2. (Continued)

Study author(s) (year) reference number	Source population	Study period	Data source	Case ascertainment	Type of severity	Number of cases	Average age	% of males/ M:F ratio	Mechanism of TBI injury (up to 3 most frequent in % *)
56 Numminen (2011)[87]	Finland (>14 years)	2002–2004	Hospital records from three municipalities in South East Finland	ICD 10, GCS	All	370	M 50.6 F 55.7	54	F 58.4 T 17.8
57 Falk (2007)[88]	Sweden (<16 years)	2002–2003	Astrid Lindgren Children's Hospital records, Stockholm region	Clinical definition	All	3168	5.5	NR	F 68 T 8
58 Heskestad and colleagues (2009)[89]	Norway	2003	University Hospital of Stavanger records, Stavanger region	Clinical definition; GCS; Scandinavian guidelines	All	585	NR	1.7:1	F 51 T 21 V 14
59 Andelic and colleagues (2008)[29]	Norway	2005–2006	Ulleval University hospital records, Oslo City	Clinical definition; ICD 10; GSC	All	445	median, 29	63.8	F 51 T 29.7 V 12.8
60 Von Elm and colleagues (2008)[21]	Switzerland	2005 (6 months)	Hospital records of three trauma centers	GCS and AIS_{Head}	Severe	101	median, 41	74.2	T 40 F 31
61 Frohlich and colleagues (2011)[35]	Ireland	2005–2007	One university teaching hospital ICU records	Clinical definition	All	46	NR	80	V 37 T 33 F 24
62 Van Pelt and colleagues (2011)[38]	Netherlands (1m.-24 years)	2007–2008	Sophia Children's Hospital records	Clinical definition	All	472	12±7.5	67.2	T 40.7 H 18.9 S 7.4
63 Andriessen and colleagues (2011)[90]	Netherlands (≥ 16 years)	2008–2009	Hospital records of five trauma centers	GCS	Moderate; severe	508	47.3	70.1	T 50.6 F 38
64 Roe and colleagues (2013)[91]	Norway (≥16 years)	2009–2011	Hospital records of five university hospitals	ICD 10; GCS	Severe	271	NR	77.5	F 57.2 T 32.5
65 Hawley and colleagues (2013)[36]	United Kingdom (0–14 years)	2011 (6 months)	Children's ED at University Hospital Coventry and Warwickshire records	Clinical definition; GCS	Mild	1,747	5.5±4.8	63.9	F 62.2 V 6.3 T 3.2
66 Katsaragakis and colleagues (2010)[92]	Greece	12 months, year unclear	Hospital records of 30 participating hospitals	Clinical definition	All	3,383	NR	72.5	T 54.1 F 27.7

*% if clearly stated.

M, males; F, females; TBI, traumatic brain injury; ICD, *International Classification of Diseases;* NR, not reported; T, traffic related; F, falls; H, accidents at home; ICU, intensive care unit; GCS, Glasgow Coma Scale; S, sport; W, accidents at work/industrial accidents; AIS_{Head}, Abbreviated Injury Score for head injuries; ACRM, American Congress of Rehabilitation Medicine; HISS, Head Injury Severity Scale; V, violence; HAIS, Head Abbreviated Injury Scale; TRISS, Trauma and Injury Severity Score.

Table 3. Case Ascertainment in Studies With Country-Level Population

Study author(s) (year) reference number		Study period	Case ascertainment		
			*Inclusion criteria**	*TBI classification***	*Clinical definition***
1	Kannus and colleagues (1999)[48]	1970–1995	People ≥60 years old in Finland with a fall-induced severe TBI as a consequence of a fall from standing height (1 m) or less and that results in hospitalization of the victim	ICD 8: 80000 - 80410, 85000 - 85100, 85200 - 85411 ICD 9: 8000A - 8033A, 8500A - 8519X, and 8520A - 8541X	-
2	Steudel and colleagues (2005)[31]	1972–1998	People in Germany who were hospitalized with and those who died due to TBI	ICD 9: 800 - 804, 850 - 854 ICD 10: S02.0 - S02.9, S06.0 - S06.9	-
3	Jennett and MacMillan (1981)[49]	1974–1975	People of Scotland, England, and Wales who were hospitalized with head injury	-	Patients with a history of a blow to the head or with altered consciousness after a relevant injury, or with a scalp or forehead laceration, or who had had a skull x-ray examination
4	Engberg, and Teasdale (1998)[23]	1979–1993	People of Denmark 0–14 years old who were hospitalized with TBI	ICD 8: 800,801, 803, 850 - 854	-
5	Engberg and colleagues (2001)[50]	1979–1996	People of Denmark who were hospitalized with and those who died due to TBI	ICD 8: 800,801, 803, 851 - 854 ICD 10: S01.0 - S09.9	-
6	Mauritz and colleagues (2014)[51]	1980–2012	People of Austria who died due to TBI	ICD 9: 800, 801, 803, 804, 850 - 854, 873, 905, 907 ICD10: S01.0 - S01.9, S02.0 - S02.3, S02.7 - S02.9, S04.0, S06.0 - S06.9, S07.0 -S07.9, S09.7 - S09.9, T01.0, T02.0, T04.0, T06.0, T90.1, T90.2, T90.4, T90.5, T90.8, T90.9	-
7	Brazinova and colleagues (2014)[52]	1980–2012	People of Austria ≥65 years old who died due to TBI	ICD 9: 800, 801, 803, 804, 850 - 854, 873, 905, 907 ICD10: S01.0-S01.9, S02.0-S02.3, S02.7-S02.9, S04.0, S06.0-S06.9, S07.0-S07.9, S09.7-S09.9, T01.0, T02.0, T04.0, T06.0, T90.1, T90.2, T90.4, T90.5, T90.8, T90.9	-
8	Majdan and colleagues (2014)[53]	1980–2012	People of Austria 0–19 years old who died due to TBI	ICD 9: 800, 801, 803, 804, 850 - 854, 873, 905, 907 ICD10: S01.0 - S01.9, S02.0 - S02.3, S02.7 - S02.9, S04.0, S06.0 - S06.9, S07.0 -S07.9, S09.7 - S09.9, T01.0, T02.0, T04.0, T06.0, T90.1, T90.2, T90.4, T90.5, T90.8, T90.9	-
9	Servadei and colleagues (1985)[28]	1981 and 1982	People of the Republic of San Marino who were hospitalized with TBI	-	All patients with a head injury (scalp lacerations were considered separately), those having a skull fracture and/or loss of consciousness (no matter how brief)

(*continued*)

Table 3. (Continued)

Study author(s) (year) reference number		Study period	Case ascertainment		
			*Inclusion criteria**	*TBI classification***	*Clinical definition***
10	Williamson and colleagues (2002)[54]	1986–1995	People of Scotland 0–14 years old who died due to TBI	ICD 9	ICD 9 injury code of either skull fracture or intracranial injury
11	Hartholt and colleagues (2011)[46]	1986–2008	People of Netherlands ≥65 years who were hospitalized with a fall-induced severe TBI	ICD 9: 800, 801, 803, 804, 850 - 854	-
12	Sundstrøm and colleagues (2007)[55]	1987–2001	People of Denmark, Finland, Norway, Sweden who died due to head injury	ICD 8: 800, 801, 803, 851 - 854 ICD 9: 800 - 804, 850 - 854 ICD 10: S00, S02 - S04, S06 - S09	-
13	Kleiven and colleagues (2003)[56]	1987–2000	People of Sweden who were hospitalized due to head injury	ICD 9: 800 - 804; 850 - 854 ICD 10: S2.0 - S2.9; S6.0 - S6.9	-
14	Alaranta and colleagues (2000)[57]	1991–1995	People of Finland who were hospitalized with TBI	ICD 9: 800, 801, 803, 850-854	-
15	Koskinen and Alaranta (2008)[58]	1991–2005	People of Finland who were hospitalized with TBI	ICD 9: 800, 801, 803, 850, 851 - 854 ICD 10: S02.0, S02.00, S02.01, S02.1, S02.10, S02.11, S02.7, S02.70, S02.71, S02.8, S02.80, S02.81, S02.9, S02.90, S02.91, T020, S06.0, S06.1 - 9	-
16	Shivaji and colleagues (2014)[22]	1998–2009	People of Scotland who were hospitalized with TBI	ICD 10: S01.0, S01.9, S02.0,S02.1, S02.3, S02.7, S02.9, S04.0, S06.0, S06.9, S07.0, S07.1, S07.8, S07.9, S09.7, S09.9, T01.0, T02.0, T04.0, T06.0, T90.1, T90.2, T90.4, T90.5, T90.8, T90.9	An occurrence of an injury to the head with one or more of the following attributable to the head injury: decreased level of consciousness, amnesia, skull fracture, a neurological, neurophysiological or intracranial lesion, or an occurrence of death from trauma with head injury listed in the sequence of conditions leading to death
17	Pérez and colleagues (2012)[27]	2000–2009	People of Spain who were hospitalized with TBI	ICD 9: 800,801; 803,804, 850, 851, 852, 853, 854	-
18	Dias and colleagues (2014)[59]	2000–2010	People of Portugal ≥18 years who were hospitalized with TBI	ICD 9: 800-804, 850 - 854	-
19	Walder and colleagues (2013)[24]	2007–2010	People of Switzerland ≥16 years who were hospitalized with severe TBI	all admissions with head trauma and HAIS >3	-
20	Mauritz and colleagues (2014)[32]	2009–2011	People of Austria who were hospitalized with and those who died due to TBI	ICD 10: S01.0 - S01.9, S02.0, S02.1, S02.7, S06.0 - S06.9,T01.0, T02.0, T04.0, T06.0, T90.1, T90.2, or T90.4 - T90.9	-
21	Andelic and colleagues (2012)[60]	2009–2010	People of Norway ≥16 years who were hospitalized with severe TBI	ICD 10:S06.0 - S06.9	-
22	Scholten and colleagues (2014)[61]	2010–2012	People of Netherlands who were hospitalized with TBI	ICD 9: 850, 800 - 801, 803, 804, 851 - 854, 905, 907, 950, 959	-

*all ages and all severity if not specified otherwise; **presented terminology is the same as in the original study.
TBI, traumatic brain injury; ICD, *International Classification of Diseases.*

Table 4. Case Ascertainment in Studies With Regional-Level Population

Study author(s) (year) (reference number		Study period	Case ascertainment		
			Inclusion criteria*	TBI classification**	Clinical definition**
23	Winqvist and colleagues (2007)[62]	1966–2000	Members of Northern Finland Birth Cohort ≤34 years who were hospitalized with TBI and those who died due to TBI	ICD 8 and ICD 9: 800, 801, 803, 850, 851 - 854 ICD 10: S02.0 - S02.11, S06.0 - S06.9, S07.1	-
24	Berney and colleagues (1995)[63]	1969–1991	People of Geneva region, Switzerland 0–15 years who were hospitalized with TBI	-	Alteration of consciousness (primary or secondary), neurological deficit, or early epileptic seizures, with or without confirmation by CT scan or operation
25	Berney and colleagues (1994)[64]	1975–1983	People of Geneva region, Switzerland 0–15 years who were hospitalized with TBI	-	Severe trauma contained the categories extradural haematoma, subdural haematoma, open brain laceration and brain contusion. Contusion was defined on clinical grounds, with or without CT, angiography, operation or EEG.
26	Nestvold and colleagues (1988)[65]	1975	People of Akershus county, Norway who were hospitalized with and those who died due to head injury	-	Trauma to face, head or neck with one or more of the following symptoms: unconsciousness, retrograde amnesia, posttraumatic amnesia, scull or neck fracture, or trauma combined with headache, nausea or vomiting during the first day after the accident
27	Edna and Cappelen (1984)[66]	1979–1980	People of Trøndelag county, Norway who were hospitalized with head injury	-	Loss of consciousness following the head trauma, a skull fracture, and development of intracranial hematoma
28	Edna and Cappelen (1985)[67]	1979–1980	People of Trøndelag county, Norway who were hospitalized with traffic-induced head injury	-	Loss of consciousness following the head trauma, a skull fracture, and development of intracranial hematoma
29	Alvarez and colleagues (2011)[68]	1983–2009	People of the Canary Islands, Spain 1 m.-14 years who were hospitalized with severe head injury	Classification of the Trauma Coma Data Bank[93]	-
30	Johansson and colleagues (1991)[69]	1984–1985	People of Umeå district, Sweden 16–60 years who were hospitalized with TBI	ICD 9: 850.00 - 854.00	-
31	Servadei and colleagues (1988)[30]	1984–1985	People of Ravenna region, Italy who were hospitalized with and those who died due to TBI	-	Loss of consciousness, clinical, radiological or EEG findings
32	Tiret and colleagues (1990)[70]	1986	People of Aquitaine region, France who were hospitalized with and those who died due to head trauma	-	Contusions, lacerations, skull fractures or brain injuries, and/or loss of consciousness after a relevant injury

(*continued*)

TABLE 4. (CONTINUED)

Study author(s) (year) (reference number		Study period	Case ascertainment		
			Inclusion criteria*	TBI classification**	Clinical definition**
33	Emanuelson and Wendt (1997)[71]	1987–1991	People of south-western Sweden 0–17 years who were hospitalized with and those who died due to TBI	ICD 9: 800 - 801, 803 - 804, 851 - 854	TBI was defined as the presence of unconsciousness lasting ≥60 min and/or clinical signs of brain contusion and/or radiological and/or neurophysiological signs of brain contusion
34	Arnarson and colleagues (1995)[72]	1987–1991	People of Reykjavík area, Iceland 0–14 years who were hospitalized with head trauma	ICD 9: 850, 851 - 854	Head trauma requiring at least 1 night in hospital
35	Boto and colleagues (2009)[25]	1987–1999	People of Madrid area, Spain >14 years who were hospitalized with severe head injury	Head injury with GCS score ≤8	-
36	Vazquez-Barquero and colleagues (1992)[26]	1988	People of Autonomous Region of Cantabria, Spain who were hospitalized with head injury	-	Head injury with loss of consciousness, skull fracture, objective neurologic findings which could be reasonably attributed to the head injury
37	Bouillon and colleagues (1999)[73]	1990–1996	People of Cologne region, Germany who were hospitalized with and those who died due to severe brain trauma	Brain trauma with GCS ≤8 or AIS_{Head} ≥3	-
38	Maegele and colleagues (2007)[74]	1990–1999	People of Cologne region, Germany who were hospitalized with and those who died due to severe TBI	TBI with GCS ≤8 or AIS_{Head} ≥2	-
39	Andersson and colleagues (2003)[75]	1992–1993	People of Borås region, Sweden who were hospitalized with TBI	ICD 9: 800 - 804 and 850 - 854	-
40	Hawley and colleagues (2003)[37]	1992–1998	People of North Staffordshire region, United Kingdom 0–15 years who were hospitalized with TBI	TBI with period of unconsciousness, GCS	-
41	Ingebrigtsen and colleagues (1998)[76]	1993	People of Tromsø region, Norway who were hospitalized with head injury	-	Head injury was defined as physical damage to the brain or skull caused by external force
42	Javouhey and colleagues (2006)[77]	1996–2001	People of Rhône region, France who were hospitalized with and those who died due to traffic-induced TBI	-	Injury to the brain or the skull
43	Baldo and colleagues (2003)[78]	1996–2000	People of Veneto region, Italy who were hospitalized with or died due to TBI	ICD9:800.0 - 801.9, 803.0 - 804.9, 850.0 - 854.1	-
44	Masson and colleagues (2001)[79]	1996	People of Aquitaine region, France who were hospitalized with severe TBI	Severe TBI with HAIS ≥4, GCS ≤8	-
45	Puljula and colleagues (2013)[47]	1999 and 2007	People of Northern Ostrobothnia region, Finland who were hospitalized with or died due to moderate to severe TBI	Moderate-to-severe TBI GCS ≤12 on admission to ED	-
46	Servadei and colleagues (2002)[80]	1998	People of Romagna region, Italy who were hospitalized with and those who died due to TBI	ICD 9: 800.0 - 800.3, 801.0 - 801.3, 803.0 - 804.3, 850, 851, 851.1, 852.0, 852.1, 853.0, 853.1, 854.0, 854.1	-

(*continued*)

TABLE 4. (CONTINUED)

Study author(s) (year) (reference number		Study period	Case ascertainment		
			Inclusion criteria*	TBI classification**	Clinical definition**
47	Di Bartolomeo and colleagues (2001)[81]	1998–1999	People of Friuli Venezia Giulia region, Italy who were hospitalized with or died due to severe head injury	Severe head injury with ISS >16, AIS of the head ≥4	-
48	Servadei and colleagues (2002)[82]	1998	People of Romagna and Trentino regions, Italy who were hospitalized with head injury	ICD 9: 800.0 - 854.1	-
49	Dahl and colleagues (2006)[83]	1999 and 2000	People of Borås region, south-western Sweden 0–17 years hospitalized with mild TBI	-	Loss of consciousness, loss of memory of events immediately before or after the accident, any alteration in mental state at the time of the accident, focal neurological deficit
50	Rusnak and colleagues (2007)[45]	1999–2004	Patients of 5 treatment centers in Austria who were hospitalized with severe TBI	Severe TBI with GCS ≤8	-
51	Rickels and colleagues (2010)[33]	2000–2001	People of Hannover and Münster regions, Germany who were hospitalized with TBI	ICD 10: S02, S04, S06, S07, S09	Nausea or vomiting, headache, loss of consciousness with anterograde/ retrograde amnesia, impaired consciousness or impaired vigilance, fracture of face and/or scull, focal neurological symptom
52	Ventsel and colleagues (2008)[84]	2001–2005	People of Tartu county, Estonia 0–14 years who were hospitalized with and those who died due to TBI	ICD 10: S02.0, S02.1, S02.7, S06, S07, S09.7	-
53	Styrke and colleagues (2007)[34]	2001	People of Umeå district, Sweden who were hospitalized with TBI	ICD 10: S06	-
54	Rosso and colleagues (2007)[85]	1999–2004	Patients of 5 treatment centers in Austria who were hospitalized with severe TBI	Severe TBI with GCS ≤8	-
55	Mauritz and colleagues (2008)[86]	2001–2005	Patients of thirteen participating hospitals in Austria, Bosnia, Croatia, Macedonia and Slovak Republic who were hospitalized with severe TBI	Severe TBI with GCS ≤8	-
56	Numminen (2011)[87]	2002–2004	People of 3 municipalities in South East Finland >14 years who were hospitalized with and died due to TBI	ICD 10: S06, S07	Patients who had experienced loss of consciousness or had a headache, nausea or dizziness after head trauma
57	Falk (2007)[88]	2002–2003	People of Stockholm region, Sweden <16 years who were hospitalized with TBI	-	Head injury was defined as any physical damage to the brain or scull caused by external force
58	Heskestad and colleagues (2009)[89]	2003	People of Stavanger region, Norway who were hospitalized with head injury	-	Head injury was defined as physical damage to the brain or skull caused by external force
59	Andelic and colleagues (2008)[29]	2005–2006	People of Oslo City, Norway who were hospitalized with TBI	ICD 10: S02.0 - S02.9, S06.0 - S06.9, S07.0, S07.1, S07.8, S07.9, S09.7 - S09.9, T04, T06	TBI was defined as damage to brain tissue caused by external mechanical force as evidenced by: loss of consciousness due to brain trauma, or posttraumatic amnesia, or skull fracture

(*continued*)

TABLE 4. (CONTINUED)

Study author(s) (year) (reference number		Study period	Case ascertainment		
			*Inclusion criteria**	*TBI classification***	*Clinical definition***
60	Von Elm and colleagues (2008)[21]	2005 (6 m.)	Patients of three trauma centers, Switzerland hospitalized with and those who died due to severe TBI	Severe TBI with GCS <9 and AIS_{Head} >3	-
61	Frohlich and colleagues (2011)[35]	2005–2007	Patients of one university teaching hospital, Ireland hospitalized with TBI	-	Patients who were admitted to ICU due to TBI
62	Van Pelt and colleagues (2011)[38]	2007–2008	Patients of one children's hospital in Netherlands 1 month.-24 years hospitalized with TBI	-	History or observed loss of consciousness after head trauma, and/or posttraumatic amnesia, and/or abnormalities at neurological examination, and/or acute traumatic abnormalities on scan images of brain
63	Andriessen and colleagues (2011)[90]	2008–2009	Patients of five trauma centres in Netherlands ≥16 years hospitalized with moderate and severe TBI	TBI with GCS ≤13	-
64	Roe and colleagues (2013)[91]	2009–2011	Patients of five university hospitals, Norway ≥16 years hospitalized with severe TBI	ICD 10: S06.1- S06.9 and TBI with GCS ≤8 within first 24 hours after injury	-
65	Hawley and colleagues (2013)[36]	2011 (6 m.)	People of Coventry and Warwickshire, United Kingdom 0–14 years hospitalized with minor head injury	Minor child head injury with GCS of 13–15	Head injury defined as any trauma to the head, other than superficial injuries to the face
66	Katsaragakis and colleagues (2010)[92]	12 m., year unclear	Patients of 30 hospitals in Greece hospitalized with TBI	-	All patients that had at least one brain injury as assessed in the receiving hospital

*all ages and all severity if not specified otherwise; **presented terminology is the same as in the original study.

TBI, traumatic brain injury; ICD, *International Classification of Diseases;* CT, computed tomography; EEG, electroencephalogram; GCS, Glasgow Coma Scale; AIS_{Head}, Abbreviated Injury Score for head injuries; HAIS, Head Abbreviated Injury Scale; ED, emergency department; ISS, Injury Severity Score; ICU, intensive care unit.

directly from participating centers or from regional/national registries to which the hospitals reported. Some studies also used mortality registries, either hospital-based or regional/national mortality databases. Our review found a wide variety of definitions of the injury itself. A summary of the inclusion criteria, case ascertainment, and classification of TBI in individual studies is presented in Tables 3 and 4.

More recent studies commonly, although not exclusively, use the ICD 9 and ICD 10 coding systems. Some early studies used ICD 8 (e.g., Engberg and Teasdale [1998]).[23] Other standardized coding schemes, such as the Abbreviated Injury Score for head injuries (AIS_{Head} or HAIS) as in Walder and colleagues (2013),[24] and the Glasgow Coma Scale (GCS) as in Boto and colleagues (2009),[25] also were used occasionally. In summary, 31 studies used ICD (8th, 9th, or 10th revision), and 20 studies used GCS or GCS and/or other criteria (usually AIS).

Older studies (from the 1980s and 1990s) tended to use definitions of TBI based on clinical signs, such as ''[Head/brain injury with] a) loss of consciousness; b) skull fracture; c) objective neurologic findings which could be reasonably attributed to the head injury,'' as in Vazquez-Barquero and colleagues (1992).[26]

Severity of TBI was measured mainly by GCS, although other scales such as AIS_{Head} also were seen, along with non-standardized clinical definitions, for example, based on duration of lost consciousness.

Of the 66 included studies, 15 presented information on severe TBI only, two on moderate and severe, and two on mild TBI only. The rest of the studies presented information on all TBI severities.

Methodological quality

General markers of study rigor, such as a clearly specified research design and the reporting of ethical clearance, funding sources, or potential conflicts of interest were more complete in more recent papers, but rarely found in older papers (see Table 5 for summary assessment).

The quality of reporting in the final set of studies was found to be mixed. Some items were generally well reported, for example, the criteria used to define TBI and the data source use of either hospital records or national statistics to calculate incidence.

Incidence

Fifty-one studies reported a measure of TBI incidence, albeit with significant variation around the definition of case ascertainment and case definition (Tables 3, 4, 6, 7). Only eight studies reported the use of age-standardization of incidence rates or confidence intervals around these figures.

Of the 22 country-level studies (Table 6), 12 reported on the incidence of TBI across all severities and of these, 11 included subjects of all ages. Two studies reported on fall-related TBIs only, while the majority of studies reported two or more types of mechanism of injury.

In the group of country-level studies, the range of reported crude incidence rates is as follows: the lowest reported incidence rate is by Pérez and colleagues (2012) in Spain (study period 2000–2009; 47.3 per 100,000 population per year)[27]; the highest is reported by Servadei and colleagues (1985) for the Republic of San Marino (study period 1981–1982; 694 per 100,000 population per year).[28] Crude incidence and mortality rates of all country-level studies that include all ages and all severities of injury are presented in Figure 2 in chronological order by study period.

Of 44 regional-level area studies (Table 7), 14 reported incidence rates for all ages and all severities. Two studies reported on only one mechanism of injury–traffic accidents. Figure 3 shows the crude incidence and mortality rates of these studies that include all ages and all TBI severity in chronological order by study period. The range is even larger here than in the group of country-level studies (Fig. 2): the lowest is reported by Andelic and colleagues (2008) for Norway (83.3 per 100,000 population per year)[29]; and the largest is reported by Servadei and colleagues (1988) for Italy (849 per 100,000 population per year).[30]

The range of crude incidence rates with confidence intervals in two sets of studies – nine country-level studies and 14 regional-

Table 5. Quality Assessment of Included Studies Using MORE Checklist–Summary Results

	OK n (%)	*Minor flaws* n (%)	*Major flaws* n (%)	*Poor reporting* n (%)
General descriptive elements				
Aim of study	46 (67.6)	7 (10.3)	8 (11.8)	5 (7.4)
Funding of study	38 (55.9)	0	0	29 (42.6)
Conflict of interest	31 (45.6)	0	0	36 (52.9)
Ethical approval	24 (35.3)	0	0	38 (55.9)
Study design	42 (61.8)	0	0	24 (35.3)
External validity				
Sampling	25 (36.8)	40 (58.8)	0	2 (2.9)
Definition of cases				
• Validation	42 (61.8)	20 (29.4)	3 (4.4)	2 (2.9)
• Severity of TBI	37 (54.4)	12 (17.6)	8 (11.8)	1 (1.5)
Address bias	5 (7.4)	36 (52.9)	19 (27.9)	6 (8.8)
Subject flow	58 (85.3)	7 (10.3)	2 (2.9)	0
Internal validity				
Reporting of methods				
• Source of data	32 (47.1)	35 (51.5)	0	0
• Reliability of estimates	50 (73.5)	13 (19.1)	4 (5.9)	0
Reporting of estimates				
• Incidence	38 (55.9)	11 (16.2)	11 (16.2)	1 (1.5)
• Mortality	22 (32.4)	3 (4.4)	24 (35.3)	0

MORE, Methodological Evaluation of Observational Research checklist; TBI, traumatic brain injury.

Table 6. Outcomes in Studies With Country-Level Population

	Study author(s) (year) reference number	*Source population**	*Incidence** per 100,000*	*Mortality** per 100,000*	*Case fatality rate*** %*
1	Kannus and colleagues (1999)[48]	Finland (≥60 years, fall-induced only)	Severe: 85 in 1970 Severe:144 in 1995	NR	NR
2	Steudel and colleagues (2005)[31]	Germany	337 Severe: 33.50	27.20 in 1972 9 in 2000	NR
3	Jennett and MacMillan (1981)[49]	Scotland, England, Wales	270 (En and W) 313 (Scot)	10.50 in 1972 (En and W), 9.20 in 1976 (En and W), 10.90 in 1972 (Scot), 9.30 1976 (Scot)	NR
4	Engberg, and Teasdale (1998)[23]	Denmark (0–14 years)	430 in 1979 240 in 1993	M 7.40 and F 4.20 in 1979–1981 M 4.40 and F 3.10 in 1991–1993	1.40
5	Engberg and colleagues (2001)[50]	Denmark	265[st.] in 1979–1981 157[st.] in 1991–1993	14.68 in 1979–1981 10.67 1991–1993	30
6	Mauritz and colleagues (2014)[51]	Austria	NR	28.10 in 1980–1984 11.80 in 2010 – 2012	NR
7	Brazinova and colleagues (2014)[52]	Austria (≥65 years)	NR	40	NR
8	Majdan and colleagues (2014)[53]	Austria (0–19 years)	NR	76 in 1980 5 in 2012	NR
9	Servadei and colleagues (1985)[28]	Republic of San Marino	694	NR	NR
10	Williamson and colleagues (2002)[53]	Scotland (0–14years)	NR	4.10 - 1.80	NR
11	Hartholt and colleagues (2011)[46]	Netherlands (≥65 years, fall-induced only)	Severe: 53.10[st.] in 1986 Severe: 119.30[st.] in 2008	NR	NR
12	Sundstrøm and colleagues (2007)[55]	Denmark, Finland Norway, Sweden	NR	12.6[a] 11.50 DE, 21.20 FI, 10.40 NO, 9.50 SE	NR
13	Kleiven and colleagues (2003)[56]	Sweden	259	NR	NR
14	Alaranta and colleagues (2000)[57]	Finland	99.50 in 1991 99 in 1995	NR	NR
15	Koskinen and Alaranta (2008)[58]	Finland	101[b]	18.30[b]	5.10 in 2001 – 2005
16	Shivaji and colleagues (2014)[22]	Scotland	M 446.4 in 2009 F 194,80 in 2009	NR	NR
17	Pérez and colleagues (2012)[27]	Spain	47.26	NR	NR
18	Dias and colleagues (2014)[59]	Portugal (≥18 years)	NR	NR	8.70 Mild: 1.10 Moderate - severe: 12.90
19	Walder and colleagues (2013)[24]	Switzerland (≥16 years)	Severe: 10.58	NR	30.20 (at 14 days)
20	Mauritz and colleagues (2014)[32]	Austria	303	11	3.60
21	Andelic and colleagues (2012)[60]	Norway (≥16 years)	Severe: 5.20[st.] in 2009 Severe: 4.10[st.] in 2010	NR	29.00
22	Scholten and colleagues (2014)[61]	Netherlands	213.60	NR	NR

*All ages, if not specified otherwise; **crude rates, if not specified otherwise; ***hospital, if not specified otherwise; [st.]standardized; [a]median for all countries; [b]average during 15 years.
NR, not reported; En, England; W, Wales; Scot, Scotland; M, males; F, females; DE, Denmark; FI, Finland; NO, Norway; SE, Sweden.

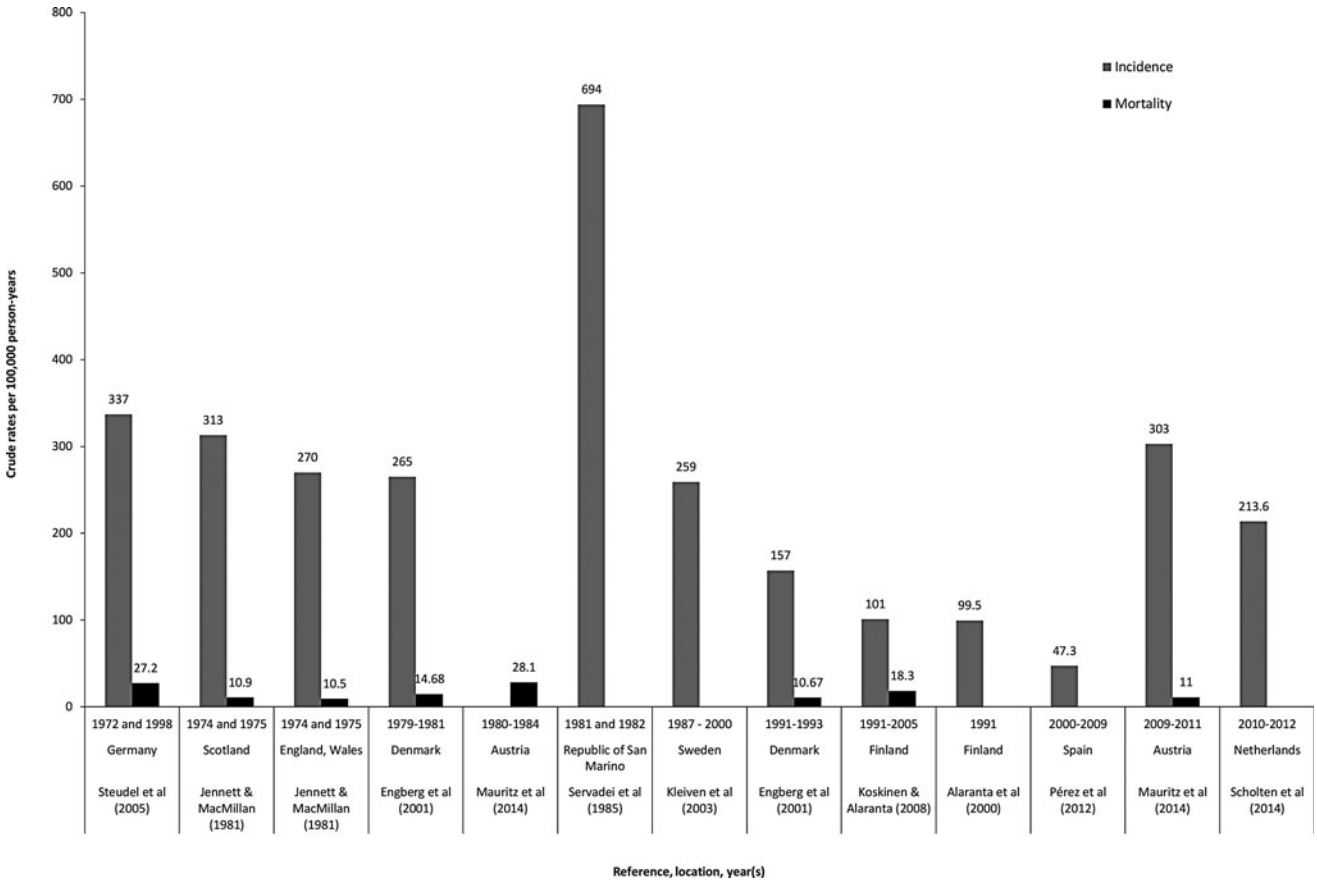

FIG. 2. Traumatic brain injury incidence and mortality rates (crude) per 100,000 population per year in country-level studies.

level studies is shown in Figure 4 and 5, respectively. In order to make the fairest assessment, the figures include only studies reporting on all ages and all TBI severities.

The funnel plot of incidence rates of regional-level studies, shown in Figure 6, suggests there is little indication of missing or selectively unpublished data. The plot shows a wider variability in incidence estimates in smaller studies, with a more stable incidence rate in larger studies, close to the mean value of 258 per 100,000 population per year. There were insufficient studies at national level reporting enough detail to produce a funnel plot for country-level studies.

Mortality and case fatality rates

Of the 27 studies reporting mortality rates, 14 reported mortality across ages and severities (Tables 6 and 7). Mortality rates of studies including all ages and all severities are presented together, with incidence rates in Figure 2 for country-level studies, and Figure 3 for regional-level area studies. As with incidence, range of reported crude mortality rates is quite large–from 9 per 100,000 population per year (Steudel and colleagues [2005])[37] to 28.10 per 100,000 population per year (Mauritz and colleagues [2014])[38] in country-level studies, and from 3.3 per 100,000 population per year (Rickels and colleagues [2010])[39] to 24.4 per 100,000 population per year (Servadei and colleagues [1988])[36] in regional-level studies.

Age and sex

Age and sex breakdown was reported in the majority of studies. It is difficult to compare distribution of TBI across populations, as many studies report only on part of the population (children or older adults, or adults only, etc.). Mean (or median) age was stated in 32 studies. In studies of all ages, all TBI severities, and all mechanisms, the lowest reported mean age was 26.7 in the Republic of San Marino (Servadei and colleagues [1985]),[28] the highest was 44.5 in Austria in 2009–2011.[32] The reported proportion of males was always greater than that of females (irrespective of age, severity and mechanism of injury), ranging from 55% in Sweden in 2001[34] to 80% in Ireland in 2005–2007.[35]

Mechanism of injury

A total of 57 studies recorded the mechanisms of injury; of these, 16 were studies that reported on TBI across country-level populations and a further 41 studies reported on specific mechanisms of injury from regional-level populations. Across ages and severities, the three most common mechanisms (or two if only two mechanisms were reported) of injury for each sample are presented in the Figures 7 and 8.

These seven distinct injury mechanisms include traffic-related, falls, violence, sports-related, accidents in the home or at work, and suicides or suicide attempts. Some studies also reported ''struck by object'' as a separate mechanism[36,37]; however, this is not reported in the graphs as it was felt that it may overlap with other more specific causes, such as violence, sports, or domestic accident. One study noted that the mechanism of ''accidents in the home'' may include instances of domestic violence.[38]

Time trends

Although no formal test or meta-analysis has been carried out, it is possible to observe an apparent slight downwards trend in

Table 7. Outcomes in Studies With Regional-Level Population

	Study author(s) (year) reference number	*Source population**	*Incidence** per 100,000*	*Mortality** per 100,000*	*Case fatality rate*** %*
23	Winqvist and colleagues (2007)[62]	Finland (≤ 34 years; birth cohort)	118 (95% CI,108 – 130)	14 (95% CI, 11 – 18)	12
24	Berney and colleagues (1995)[63]	Switzerland (0–15 years)	291 in 1969–1973 368 in 1986–1990	10.40 in 1969–1973 3.50 in 1986–1990	29.4 in 1975–1978 15.2 in 1986–1990
25	Berney and colleagues (1994)[64]	Switzerland (0–15 years)	334	NR	NR
26	Nestvold and colleagues (1988)[65]	Norway	236	NR	4.50
27	Edna and Cappelen (1984)[66]	Norway	200	NR	2.76
28	Edna and Cappelen (1985)[67]	Norway (traffic-induced only)	89	NR	3.60
29	Alvarez and colleagues (2011)[68]	Spain (1 months–14 years)	11 Severe: 5	NR	24.70
30	Johansson and colleagues (1991)[69]	Sweden (16–60 years)	249	NR	NR
31	Servadei and colleagues (1988)[30]	Italy	849	24.40	NR
32	Tiret and colleagues (1990)[70]	France	281	22	6.4
33	Emanuelson and Wendt (1997)[71]	Sweden (0–17 years)	12	2.60	NR
34	Arnarson and colleagues (1995)[72]	Iceland (0–14 years)	170	3	NR
35	Boto and colleagues (2009)[25]	Spain (>14 years)	NR	NR	Severe: 46.80
36	Vazquez-Barquero and colleagues (1992)[26]	Spain	91	19.70	1.70
37	Bouillon and colleagues (1999)[73]	Germany	Severe: 10	NR	46.60
38	Maegele and colleagues (2007)[74]	Germany	Severe: 7.30	NR	Severe: 45.80
39	Andersson and colleagues (2003)[75]	Sweden	546	NR	NR
40	Hawley and colleagues (2003)[37]	United Kingdom (0–15 years)	280 Mild: 232 Moderate: 25 Severe: 17	2	NR
41	Ingebrigtsen and colleagues (1998)[76]	Norway	229	NR	NR
42	Javouhey and colleagues (2006)[77]	France (traffic-induced only)	Mild: 74.7 Moderate: 47.5 Severe: 13.7	5.30	38.10
43	Baldo and colleagues (2003)[78]	Italy	301 in 1996 212.40 in 2000	7.40 in 1996 6.10 in 2000	NR
44	Masson and colleagues (2001)[79]	France	Severe:17.30 (95% CI, 15.80 – 18.80)	Severe: 5.20 (95% CI, 4.29 – 6)	Severe: 30
45	Puljula and colleagues (2013)[47]	Finland	Moderate-severe:34 in 1999 Moderate-severe:35 in 2007	NR	60
46	Servadei and colleagues (2002)[80]	Italy	250	18.3	2.8
47	Di Bartolomeo and colleagues (2001)[81]	Italy	NR	NR	Severe: 27
48	Servadei and colleagues (2002)[82]	Italy	314	NR	NR
49	Dahl and colleagues (2006)[83]	Sweden (0–17 years)	Mild: 468	0	0
50	Rusnak and colleagues (2007)[45]	Austria	NR	NR	38
51	Rickels and colleagues (2010)[33]	Germany	332 Mild: 302, moderate: 13, s: 17	3.3	NR
52	Ventsel and colleagues (2008)[84]	Estonia (0–14 years)	369 (95% CI, 337 – 403) Mild: 303 (95% CI, 274 – 334) Moderate: 30 (95% CI, 21 – 40) Severe: 36 (95% CI, 27 – 47)	3.10	NR

(*continued*)

TABLE 7. (CONTINUED)

	Study author(s) (year) reference number	*Source population**	*Incidence** per 100,000*	*Mortality** per 100,000*	*Case fatality rate*** %*
53	Styrke and colleagues (2007)[34]	Sweden	354	NR	NR
54	Rosso and colleagues (2007)[85]	Austria	NR	NR	Severe: 34 (at 3 months)
55	Mauritz and colleagues (2008)[86]	Austria, Bosnia, Croatia, Macedonia and Slovak Republic	NR	NR	42 in HI 48 in UMI 55 in LMI (at 3 months)
56	Numminen (2011)[87]	Finland (>14 years)	221 (95% CI, 176–265)	NR	7.60 (at 1 month)
57	Falk (2007)[88]	Sweden (<16 years)	865 (95% CI, 835–895)	NR	NR
58	Heskestad and colleagues (2009)[89]	Norway	207	NR	NR
59	Andelic and colleagues (2008)[29]	Norway	83.30	5.00	2 Severe: 18.5 Moderate: 5.7 Mild: 0.5
60	Von Elm and colleagues (2008)[21]	Switzerland	Severe: 8.20	NR	70
61	Frohlich and colleagues (2011)[35]	Ireland	NR	NR	37
62	Van Pelt and colleagues (2011)[38]	Netherlands (1m.–24 years)	113.90	1.50	NR
63	Andriessen and colleagues (2011)[90]	Netherlands (≥16 years)	NR	NR	Severe: 46 Moderate: 21 (at 6 months)
64	Roe and colleagues (2013)[91]	Norway (≥16 years)	NR	NR	Severe: 34.00 (at 3 months)
65	Hawley and colleagues (2013)[36]	United Kingdom (0–14 years)	Mild: 3419	NR	NR
66	Katsaragakis and colleagues (2010)[92]	Greece	NR	NR	11.50

*All ages, if not specified otherwise; **crude rates, if not specified otherwise; ***hospital, if not specified otherwise; [st]standardized; [a]median for all countries; [b]average during 15 years.
NR, not reported; CI, confidence interval; HI, high income; UMI, upper middle income; LMI, lower middle income.

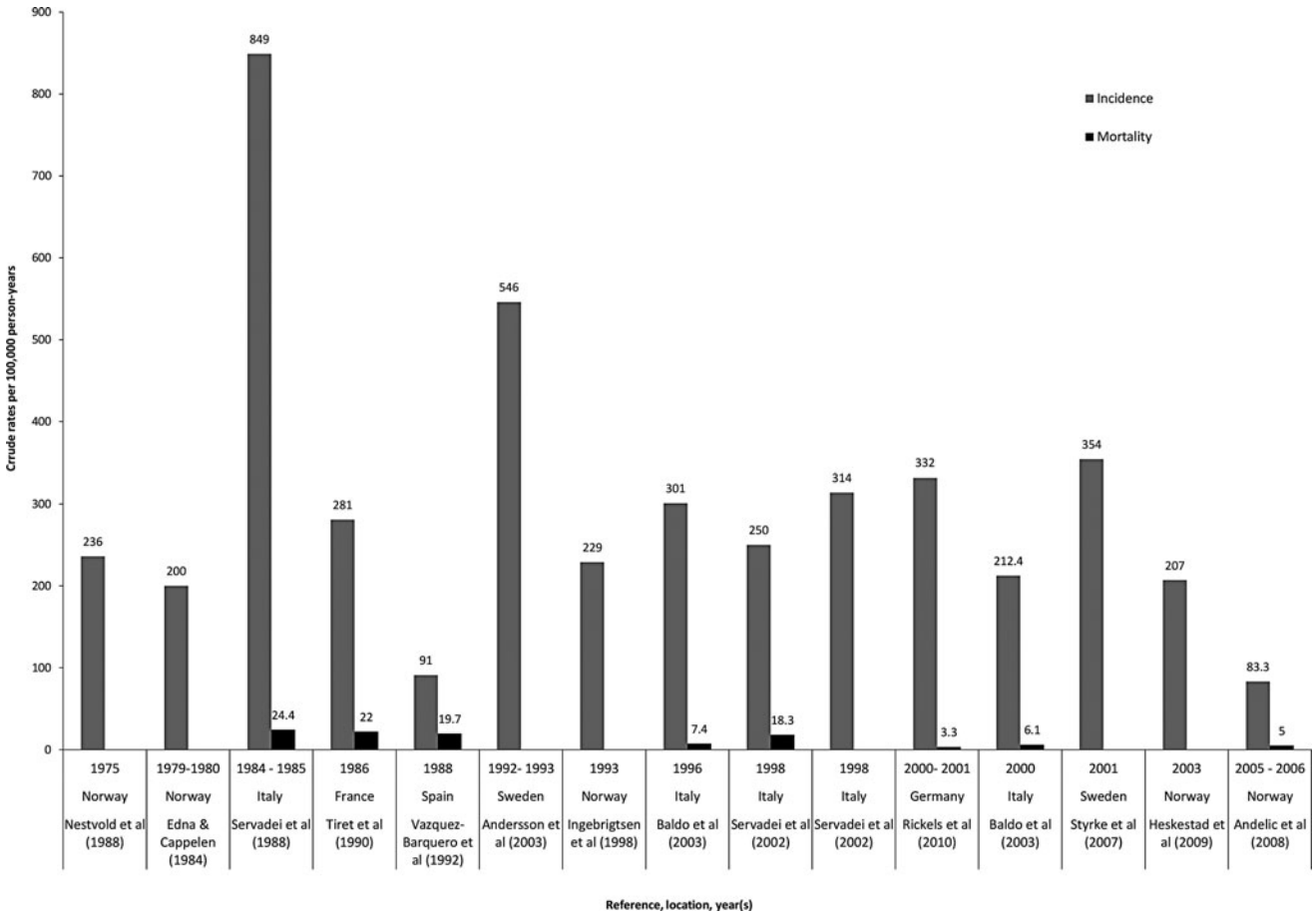

FIG. 3. Traumatic brain injury incidence and mortality (crude) rates per 100,000 population per year in regional-level studies.

incidence of TBI over time, in both country-level (Fig. 2) and regional-level graphs (Fig. 3). However, if the highest outliers on each graph are ignored (Servadei and colleagues [1985][28] and Servadei and colleagues [1988],[30] respectively), the reduction over time is much less apparent. There is little or no indication of a change over time in the mortality rates at either country- or regional-level.

When examining mechanisms, the proportion of TBIs caused by traffic collisions has been lower in recent years, and correspondingly there is an increase in the proportion of cases attributed to falls. This pattern appears in the studies of mechanisms of injury at a regional level. Country-level studies–which included all severities of injury and all age groups, and reported on mechanism of injury–number only four, and three of these describe overlapping

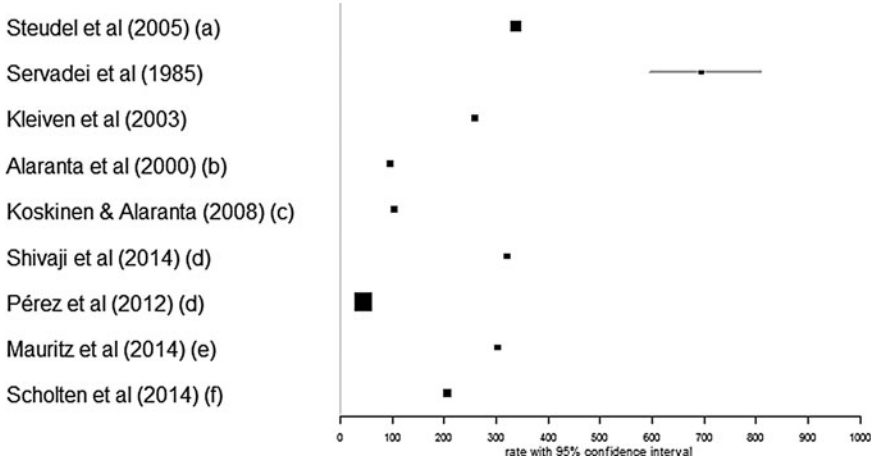

FIG. 4. Traumatic brain injury (TBI) incidence rates (crude) per 100,000 population per year in country-level studies. Studies reporting on all ages and all TBI severity were used. The size of the boxes depicts the weight (relative to other studies in the analysis) that the study has in relation to the summary measure of the meta-analysis; larger boxes depict higher weight. (a), 1998 data; (b), average for 5-year period (1991–1995); (c), 2001–2005 data; (d), 2009 data; (e), average for 2009–2011; (f), average for 2010–2012.

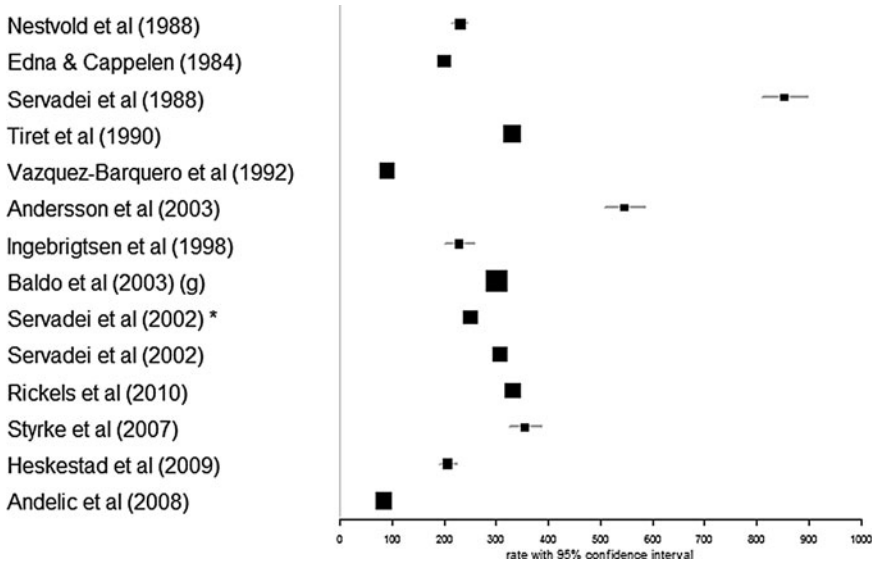

FIG. 5. Traumatic brain injury (TBI) incidence rates (crude) per 100,000 population per year in regional-level studies. Studies reporting on all ages and all TBI severity were used. The size of the boxes depicts the weight (relative to other studies in the analysis) that the study has in relation to the summary measure of the meta-analysis; larger boxes depict higher weight. *ref. no. 80; (g), 1996 data.

time periods; it is not possible to make any inferences regarding time trends among this small sub-group.

Discussion

The aim of this work was to produce a comprehensive and up-to-date review of incidence, mortality, and mechanisms of TBI across Europe. In accordance with the geographical scope of the overarching CENTER-TBI project, the aim of this study was to review TBI patterns in Europe. A wide range of rates of incidence and mortality were reported. For all ages, all TBI severity studies, the lowest reported crude incidence rate was 47.3 per 100,000 population per year; the highest was 849 per 100,000 population per year. The reported crude mortality rates ranged from 3.3 to 28.10 per 100,000 population per year. These rates are broadly similar to those seen in the 2006 review.[3] The most common mechanism of injury in studies within our review appears to be shifting in Europe from road traffic incidents to falls in more recent studies (Fig. 7 and Fig. 8).

Distribution of TBI in European populations is widely researched and presented in numerous published studies. However, it is difficult to produce informative comparisons of these presented data, as the studies vary greatly in TBI definition and case

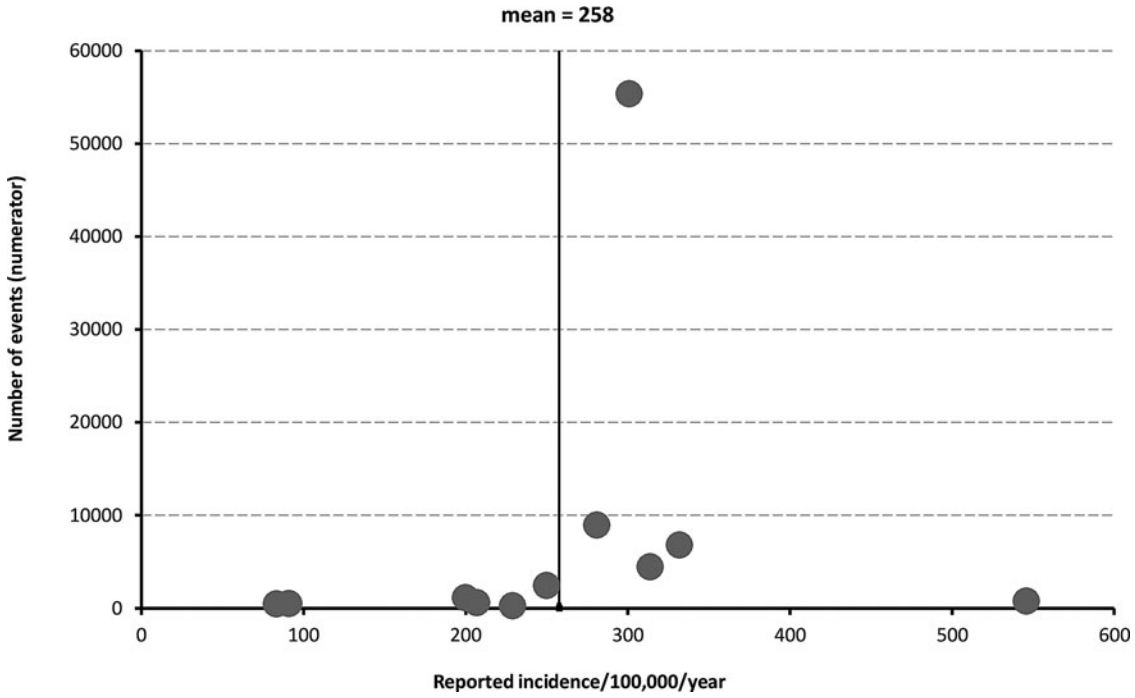

FIG. 6. Funnel plot of traumatic brain injury incidence in regional-level studies.

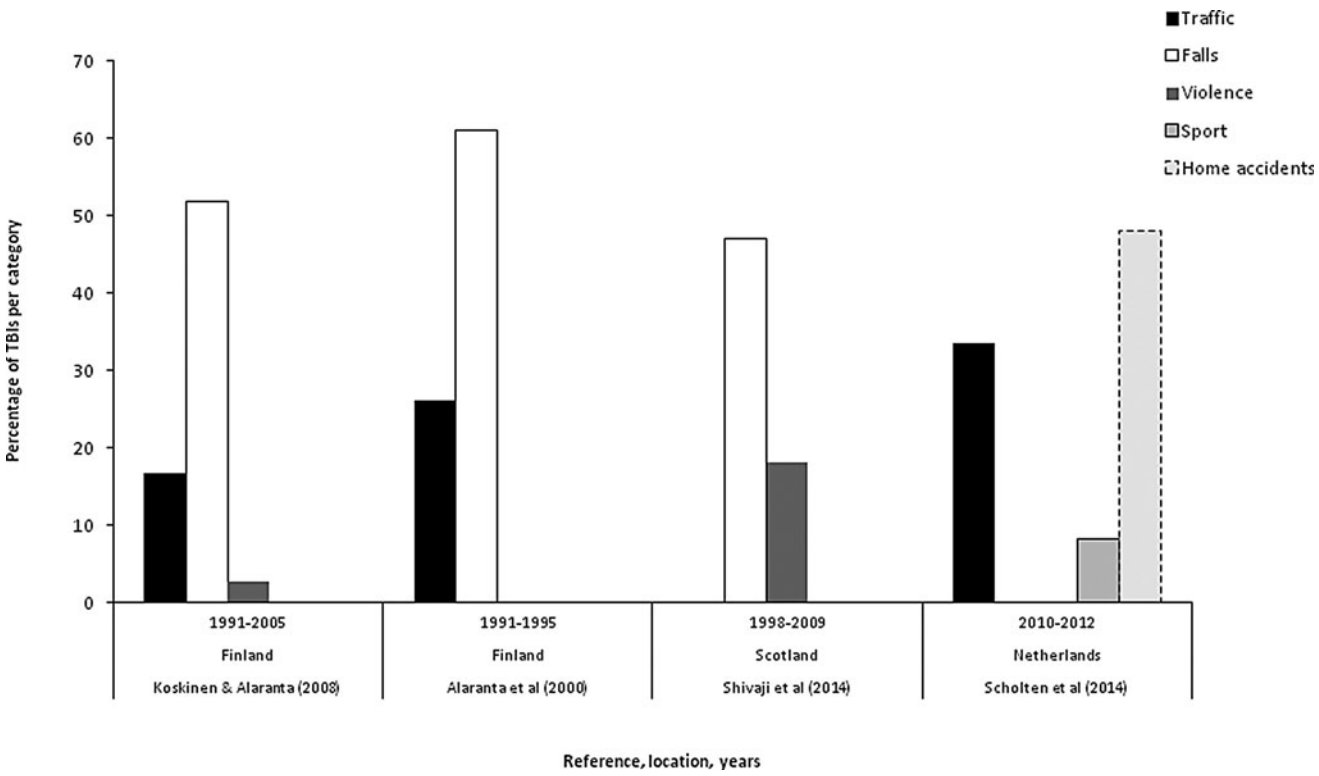

FIG. 7. The most common mechanisms of injury in country-level studies.

ascertainment methods. Comparison is also difficult due to the fact the reviewed data were not standardized. This should be improved in the future by standardized data collection and coding.[10] For the time being, it is important to make the best use the existing data, and we believe the systematic review presented here provides the most useful opportunity to compare results with those of Tagliaferri and colleagues published a decade ago[53] and Peeters and colleagues published recently.[13] The incidence is changing only slightly over time and it may be contributed by the reporting variations during the period under investigation..

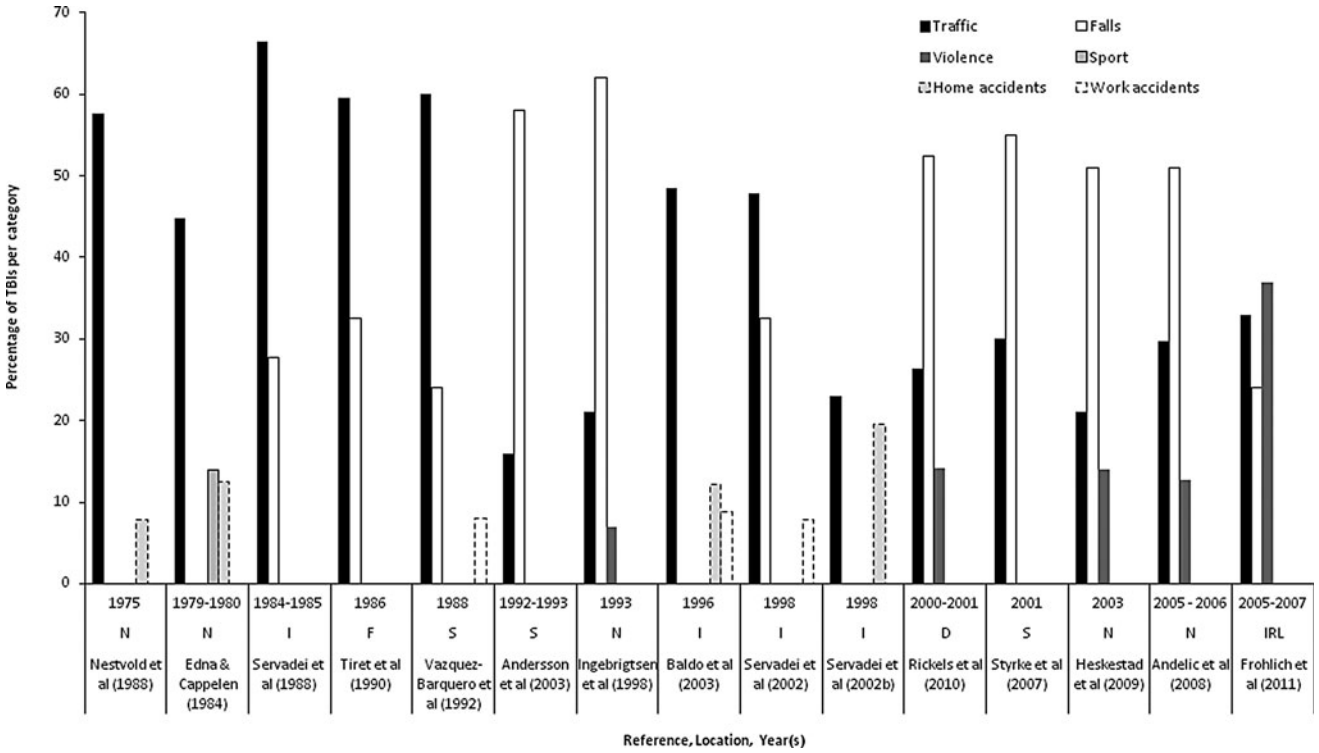

FIG. 8. The most common mechanisms of injury in regional-level studies.

The recently-published systematic review of traumatic brain injury in Europe–set up as an update to Tagliaferri and colleagues' 2006 review,[3] presenting data for the period 1990-2014–had broadly similar findings and conclusions to our review, (i.e., no decreasing trend of TBI incidence in Europe). This review, like ours, found large variations in inclusion criteria, case ascertainment and case definitions. The incidence of TBI is thus difficult to compare between included studies, as well as between this and other reviews. In Peeters and colleagues' report, the incidence of TBI ranged between 47.3 and 546 per 100,000 population per year.[13] Given our broader time scale (no time limit), we found an even larger range–the incidence range in combined country- and regional-level studies was 47.3 to 849 per 100,000 population per year.

While some countries may be seeing a reduction in TBI (or a subgroup of TBI) incidence,[39–41] our review suggests that across the continent of Europe, mean incidence rates remain broadly the same as in the 2006 review.[3] These findings from Europe are similar to the incidence rates in the United States (180 to 250 per 100,000 population per year),[42] but considerably lower than in a recent study in New Zealand, which found an incidence in excess of 700 per 100,000 person-years.[43]

Worldwide, TBI incidence may be increasing still due to the wider use of motor vehicles in low-middle income countries and an increase in falls among older people in high-income countries.[41,44]

The main methodological weaknesses observed in studies included in our review concerned poor reporting of funding, ethical approval, and study design. Very few studies were performed well according to the MORE assessment criteria. This may be in part because of the differing objectives of the included studies (some set out to study incidence and/or mortality, but others focused on mechanisms). However, it might have been expected that more of the studies focusing on incidence would perform well on this checklist. This again highlights the need for standardization of definitions and reporting if published studies are to be more comparable and informative.

It is also important to note that in this systematic review, which set out to review the available studies from all of Europe, suitable nationally-representative data were only found for 13 countries. These countries were principally members of the EU, plus Switzerland and Norway. Given that the EU currently comprises 28 countries and Europe as a whole includes almost 50 countries, it is apparent that there is a lack of good quality data collection and publication in many states. This limits the completeness of any attempt to describe European TBI incidence and mortality.

The reported crude incidence rates in regional populations or hospital catchment areas were found to be slightly higher than national surveys. It may be that studies of smaller regions or in a few nominated hospitals were conducted there because that region or hospital contains a specialist center, to which TBI cases are more frequently referred. International transfers of patients are assumed to be rarer, so national incidence data may be more complete.

When regional data were examined in a funnel plot, publication bias appeared unlikely.

There was some variability in the way relevant scientific terms have been used in different studies. In this review, incidence is defined as the rate of TBIs recorded in the original studies per 100,000 population per year. Using this measure, the majority of included studies reported actual hospital admission rate of participating treatment centers (or all hospitals in case of country-level studies). This is a slightly different measure to population incidence, in which all cases would have been traced, rather than just those arriving in a hospital. Again this limits the completeness of this review and implies that true population incidences are likely to be higher than the rates reported here.

Although the lack of age-adjusted figures make it difficult to draw direct comparisons, certain trends can be observed. Mortality rates in studies, including TBIs of all severities, vary many-fold; however, there was little indication of a trend towards increase or decrease over time. Some studies stated that they excluded patients who were dead on arrival at hospital (e.g., Rusnak and colleagues [2007], Vazquez-Barquero and colleagues [1992]).[26,45] As such, mortality rates shown in national data, rather than hospital records, may present a more complete picture.

In every study reporting sex ratios, there are more male patients recorded as having TBI than female patients. This may reflect the fact that some of the major causes of TBI, such as traffic incidents, violence, and sporting injuries, are related to more male-dominated activities. But the proportion of men in TBI studies decreased with age. In studies of older patients, with more women, the prevailing mechanism of TBI in older cases is falls.[46] However, a lack of age-adjusted results makes it impossible to draw firm conclusions about any difference in sex distributions of TBI.

There appears to be a changing pattern of mechanisms of injury over time, as the number of TBIs occurring in traffic incidents reduces, and conversely the contribution of falls becomes relatively greater in recent studies. This trend already has been described in studies in high-income countries.[44] This may relate to improved road infrastructure and traffic discipline and therefore declining traffic-related TBI incidence, as well as demographic trend of population aging. Few studies have attempted to look at epidemiological causes ''upstream'' of the immediate injury event; however, alcohol is considered a possible risk factor contributing to traffic or personal violence incidents.[47] This topic warrants further investigation.

Strengths and limitations

This review follows contemporary best practice in systematic review methods, with a comprehensive search strategy specified *a priori,* and a clear indication of why studies were included or excluded. It is likely that this search strategy, which was re-run as close as possible to the time of publication, has captured the vast majority of relevant published results.

It is likely that the figures shown here represent a relatively complete picture of the existing research on the burden of TBI in Europe. It is possible that mild TBIs may be under-diagnosed when a patient is admitted with multiple trauma or other injuries in addition to TBI. However, it seems unlikely that many TBI sufferers would be treated at home without the attention of medical professionals. The legal requirements for recording of fatal traumatic injuries vary across Europe but are usually strict. The gradual acceptance of systematic classification of injuries, such as ICD 10, means that, especially in more recent studies, data can be easily sorted to analyze events such as TBI.

Many studies stated that their incidence rates excluded non-residents who suffered TBI in the area. Hence, it is possible that some cases may not have been normally resident in the population used as the denominator in incidence calculations, leading to a small bias toward increased rates in places such as holiday destinations.

In summarizing the studies of TBI here, all papers that include an incidence, mortality or case-fatality rate for TBI are presented, regardless of how the authors defined the actual injury. In recent studies the ICD 9 or 10 coding systems were widely used and

specifically described; however, in older papers, there were several different non-standard descriptions used based on external signs of injury and/or assessment of brain function. Thus, it is possible that there will be some variability in those deemed eligible, which may reduce the relevance of comparisons between different papers. The same can be said for classifications according to severity, where GCS is now a widely-accepted standard but alternative classifications, such as duration of lost consciousness, have been used at times.

No attempts were made to identify or translate non-English language publications. This is a weakness and it is possible that some relevant studies have been omitted due to this.

No attempt was made to verify the methods used by different research groups to ascertain mechanism of injury. Whereas some events may be unlikely to be misclassified (e.g., a traffic accident will often be associated with police reports of the event), others may possibly be confused, such falls and (attempted) suicides. One paper mentioned the likelihood that some acts of inter-personal violence (i.e., domestic abuse) are sometimes recorded as home accidents.[38] Further, the different countries included at different time-points may also exhibit other characteristics that would affect the likelihood of a particular mechanism of injury (e.g., variation in the laws or conventions of driving certain classes of vehicle). Hence, no causal conclusions are drawn about changing mechanisms, but the general trend of reduction in the proportion of traffic-related injury is consistent with the findings of other recent research.

Conclusions and Recommendations

This review found that large variations of TBI incidence and mortality rates exist between different countries and populations. There is some evidence of a changing pattern of mechanisms over time, which may indicate success of previous public health initiatives to reduce traffic-related injuries, but also highlight the contemporary need to understand fall-related injuries, especially among the elderly. The higher rates observed in these studies present opportunities for public health policy and evidence-based clinical guidelines to reduce the suffering caused by this serious injury.

We have highlighted above the variable nature of the definitions of TBI, and the thresholds applied to classify such injuries as mild, moderate, or severe. We concur with other research groups (Maas and colleagues; Feigin and colleagues)[10,43] who have argued that the comparability of research outputs and the opportunities to exploit collaborative research can only benefit from improved levels of standardization of case ascertainment and definitions of grades of injury.

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Author Disclosure Statement

No competing financial interests exist.

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(Appendices follows →)

Appendix 1. Database Search Algorithms and Key Words

PubMed search algorithm

(((((((((epidemiology[Title/Abstract]) OR case fatality[Title/Abstract]) OR incidence[Title/Abstract]) OR prevalence[Title/Abstract]) OR mortality[Title/Abstract])) AND ((europe[MeSH Terms]) OR europ*)) AND ((((((craniocerebral injuries[MeSH Terms]) OR brain injuries[MeSH Terms]) OR head injur*[Title/Abstract]) OR brain injur*[Title/Abstract]) OR head trauma[Title/Abstract]) OR brain trauma[Title/Abstract])))

Web of Science search algorithm

((TS = (''brain injur*'')) OR (TS = (''head injur*'')) OR (TS = (''brain trauma'')) OR (TS = (''head trauma''))) AND ((TS = (epidemiology)) OR (TS = (incidence)) OR (TI = (prevalence)) OR (TI = (mortality))) Refined by: *[excluding]:* *DOCUMENT TYPES:* (REVIEW) AND *COUNTRIES/TERRITORIES:* (CROATIA OR ENGLAND OR WALES OR GERMANY OR CZECH REPUBLIC OR ITALY OR SLOVAKIA OR MACEDONIA OR FRANCE OR SPAIN OR NORTH IRELAND OR SWEDEN OR NETHERLANDS OR SCOTLAND OR SWITZERLAND OR ALBANIA OR HUNGARY OR AZERBAIJAN OR NORWAY OR AUSTRIA OR SERBIA OR SLOVENIA OR BYELARUS OR ESTONIA OR DENMARK OR FINLAND OR IRELAND OR ICELAND OR LITHUANIA OR BELGIUM OR ROMANIA OR GREECE OR YUGOSLAVIA OR POLAND)

CINAHL search

S1 TI epidemiology OR AB epidemiology
S2 TI case fatality OR AB case fatality
S3 TI incidence OR AB incidence
S4 TI prevalence OR AB prevalence
S5 TI mortality OR AB mortality
S6 S1 OR S2 OR S3 OR S4 OR S5
S7 (MH ''Europe'')
S8 TI europe*
S9 S7 OR S8
S10 (MH ''Brain Injuries'')
S11 (MH ''Head Injuries'')
S12 TI head injur* OR AB head injur*
S13 TI brain injur* OR AB brain injur*
S14 TI head trauma OR AB head trauma
S15 TI brain trauma OR AB brain trauma
S16 S10 OR S11 OR S12 OR S13 OR S14 OR S15
S17 S6 AND S9 AND S16

EMBASE Search

1. epidemiology.mp.
2. case fatality.mp.
3. incidence.mp.
4. prevalence.mp.
5. mortality.mp.
6. exp head injury/
7. head*.mp.
8. brain*.mp.
9. 7 or 8
10. (injur* or trauma*).mp
11. ((head* or brain*) adj2 (injur* or trauma*)).mp.
12. exp Europe/
13. europ*.mp.
14. 12 or 13
15. 6 or 11
16. or/1–5
17. 14 and 15 and 16

APPENDIX 2. METHODOLOGICAL EVALUATION OF OBSERVATIONAL RESEARCH (MORE) CHECKLIST FOR QUALITY ASSESSMENT OF INCLUDED STUDIES

Type	*Criteria*		*Conditions*	*Assessment*
General descriptive	Aim of study		a) Included incidence/prevalence estimation with clear target population	OK
			b) Included incidence/prevalence estimation without clear target population	Minor flaw
			c) Aim of study was not stated	Major flaw
			d) Unclear due to poor reporting	Poor reporting
	Funding of study		Reported	OK
			Not reported	Poor reporting
	Conflict of interest		Reported	OK
			Not reported	Poor reporting
	Ethical approval		Reported	OK
			Not reported	Poor reporting
	Study design		Reported	OK
			Not reported	Poor reporting
External validity	Sampling	Sampling frame	a) Not applicable for study design	NA
			b) Sampling within nationally representative registries or databases	OK
			c) Medical records	Minor flaw
			d) Insurance claims	Minor flaw
			e) Outpatients contacts	Major flaw
			f) Unclear due to poor reporting	Poor reporting
	Definition of cases	Validation	a) Criteria of TBI were stated according to the guidelines	OK
			b) TBI were defined by ICD codes	OK
			c) Criteria of TBI were not stated according to the guidelines	Minor flaw
			d) Criteria of TBI were not stated	Major flaw
			e) Unclear due to poor reporting	Poor reporting
		Severity of TBI	a) Stated in the study with scales	OK
			b) Stated in the study without scales	Minor flaw
			c) Not stated in the study	Major flaw
			d) Unclear due to poor reporting	poor reporting
	Address bias	Sampling bias is addressed in the analysis *(can by mentioned in recommendations)*	a) Not applicable for study design	NA
			b) Weighting of the estimates by probability of selection	OK
			c) Weighting of the estimates by non-response adjustment within sampling subgroups	OK
			d) Post-stratification by age	OK
			e) Post-stratification by sex	OK
			f) Mentioned, but not addressed in analysis	Minor flaw
			g) Not mentioned and not addressed in analysis	Major flaw
			h) Unclear due to poor reporting	Poor reporting
		Subject flow	a) Not applicable for study design	NA
			b) Number of enrolled stated clearly	OK
			c) Number of enrolled not stated clearly	Minor flaw
			d) Number of enrolled not stated	Major flaw
			e) Unclear due to poor reporting	Poor reporting
Internal validity	Reporting of methods	Source of data	a) Objectively measured with diagnostic methods for the purpose of the study (independent on health care)	OK
			b) Measured by interviewers for the study	OK
			c) Obtained during clinical examination for the purpose of the study	OK
			d) Obtained from registries or administrative databases (collected for epidemiologic evaluation independent of health care)	OK
			e) Obtained from medical records (mining of the data collected for health care purposes)	Minor flaw
			f) Obtained from administrative database (mining of the data collected for health care purposes)	Minor flaw

(*continued*)

Table A2. (Continued)

Type	*Criteria*		*Conditions*	*Assessment*
			g) Source of data is not stated in the study	Major flaw
			h) Unclear due to poor reporting	Poor reporting
		Reliability of the estimates	a) Methods of data analysis (nominators/denominators) are stated clearly	OK
			b) Methods of data analysis (nominators/denominators) are stated, but not clearly	Minor flaw
			c) Methods of data analysis (nominators/denominators) are not stated	Major flaw
			d) Unclear due to poor reporting	Poor reporting
	Reporting of estimates	Incidence	a) Incidence type (cumulative incidence, incidence rate) stated and counted clearly	OK
			b) Incidence type (cumulative incidence, incidence rate) stated and counted not clearly	Minor flaw
			c) Incidence type (cumulative incidence, incidence rate) not stated and not counted	Major flaw
			d) Unclear due to poor reporting	Poor reporting
			a) Precision of estimation (error, 95% CI) reported in all	OK
			b) Precision of estimation (error, 95% CI) reported not in all	Minor flaw
			c) Precision of estimation (error, 95% CI) omitted	Major flaw
			d) Unclear due to poor reporting	Poor reporting
			a) Age adjusted incidence in total sample	OK
			b) Crude incidence in total sample	Minor flaw
			c) The incidence is not stated as age adjusted or crude	Major flaw
			d) Unclear due to poor reporting	Poor reporting
			a) Age adjusted incidences in all population subgroups	OK
			b) Age adjusted incidences not in all population subgroups	Minor flaw
			c) Crude incidences in subgroups	Minor flaw
			d) Incidences are not stated as age adjusted or crude	Major flaw
			e) Unclear due to poor reporting	Poor reporting
		Mortality	a) Mortality in all population is counted from all population	OK
			b) Mortality in all population is counted not clearly	Minor flaw
			c) Mortality in all population is counted as case fatality rate (only from the cases not from all population)	Major flaw
			d) Unclear due to poor reporting	Poor reporting
			a) Precision of estimation (error, 95% CI) reported in all	OK
			b) Precision of estimation (error, 95% CI) reported not in all	Minor flaw
			c) Precision of estimation (error, 95% CI) omitted	Major flaw
			d) Unclear due to poor reporting	Poor reporting
			a) Age adjusted mortality in total sample	OK
			b) Crude mortality in total sample	Minor flaw
			c) The mortality is not stated as age adjusted or crude	Major flaw
			d) Unclear due to poor reporting	Poor reporting
			a) Age adjusted mortalities in all population subgroups	OK
			b) Age adjusted mortalities not in all population subgroups	Minor flaw
			c) Crude mortalities in subgroups	Minor flaw
			d) Mortalities are not stated as age adjusted or crude	Major flaw
			e) Unclear due to poor reporting	Poor reporting

TBI, traumatic brain injury; ICD, *International Classification of Diseases;* NA, not applicable.