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Validity of algorithms for identifying mild traumatic brain injury in the French national Emergency department database OSCOUR®: a validation study protocol

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Abstract

Introduction:

The French emergency department (ED) surveillance network OSCOUR® transmits data on ED visits to Santé publique France (the national public health agency). As these data are collected daily and are almost exhaustive at a national level, it would seem relevant to use them for national epidemiological surveillance of mild traumatic brain injury (mTBI). This article presents the protocol of a planned study to validate algorithms for identifying mTBI in the OSCOUR® database. Algorithms to be tested will combine ICD-10 codes and keywords found in a free text variable describing the chief complaint for visiting ED.

Methods and analysis

We will perform a multicentre validation study of algorithms for identifying mTBI in OSCOUR®. Different combinations of ICD-10 codes and keywords found in free text descriptions of the chief complaint for ED visits will be used to identify cases of mTBI in the OSCOUR® database. A random sample of mTBI cases and non-cases will be selected from six ED. Medical charts will serve as the reference standard to validate the algorithms. The sensitivity, specificity, positive and negative predictive values of the different algorithms, as well as their 95% confidence intervals, will be calculated and compared.

Ethics and dissemination

The ethics committee of the French National Data Protection Authority (CNIL) approved this study (n° 921152, 1 August 2021). Results will be submitted to national and international peer-reviewed journals and presented at conferences dedicated to trauma and to methodologies for the construction and validation of algorithms.

Article Summary

Strengths and limitations of this study

- **This is a multicentre study conducted in six ED in France; it will be the first in France to develop algorithms to identify cases of mTBI at a national level.**
- **The review of patients' medical charts will be used as the reference standard to validate the accuracy of the algorithms.**
- **A wide variety of algorithms will be evaluated, combining not only ICD-10 codes but also keywords found in free text descriptions of complaints for ED visits from the national OSCOUR® database.**
- **In some cases, difficulties in diagnosing mTBI may complicate case identification in patient charts.**

Introduction

Between 50 and 60 million new cases of traumatic brain injury (TBI) of all levels of severity are recorded worldwide each year [1]. Of these, over 90% are mild traumatic brain injury (mTBI) [2], defined as "an acute brain injury resulting from mechanical energy to the head from external physical forces". Operational criteria for clinical identification include: (1) one or more of the following: confusion or disorientation, loss of consciousness for 30 minutes or less, post-traumatic amnesia for less than 24 hours, and/or other transient neurological abnormalities such as focal signs, seizure, and intracranial lesions not requiring surgery; (2) Glasgow Coma Scale score of 13–15 after 30 minutes post-injury or later upon presentation for healthcare [3].

An increase in mTBI incidence has been described in several recent international studies [4-7]. These very common traumas mainly affect men. All age groups are concerned but particularly young children under five years of age, people aged 15-24 years old, and those aged 75 years and over. The most common causes are falls and road accidents [8]. Although mTBI are classified as mild, they are not benign. While rarely life-threatening, the literature shows that a significant proportion of patients (20-36%) continue to have symptoms months and even years after the trauma occurs [9]. These symptoms, which are not specific to mTBI, are physical (headaches, fatigue, balance or hearing disorders, neck pain, etc.) and intellectual (attention, concentration, memory disorders, etc.) in nature; some patients have mood and behavioural disorders (impatience, anxiety, irritability, depression, guilt, etc.). All these symptoms cause personal and family suffering and can lead to situations of social withdrawal. They sometimes also affect employment or schooling opportunities in younger people. Moreover, several studies have shown that mTBI may be a risk factor for several neurodegenerative diseases [10].

In France, despite the severity of this issue, no recent epidemiological data exist to quantify and characterise the victims of mTBI at the national level. However, such data are essential to estimate the burden of mTBI, with a view to better adapting the offer of care - in particular for patients suffering from complications - and to implementing prevention measures. Using data from the French emergency department (ED) visits database (OSCOUR® network data) could be relevant for national epidemiological surveillance of mTBI, since these data are collected daily and are almost exhaustive at the national level. Moreover, a significant proportion of patients with mTBI who seek medical care are diagnosed and managed in ED [6]. However, the accuracy of potential algorithms which could be used in OSCOUR® is not as yet known.

A study conducted in the United States which evaluated the accuracy of a proposed algorithm based on the ICD-9 (ICD, International Classification of Diseases) codes proposed by the Centers for Disease Control and Prevention (CDC) to detect mTBI cases from medical and administrative databases [11], and which used the clinical examination of ED patients as the reference standard, showed that the algorithm had low sensitivity (45.9%) but high specificity (97.8%). While these results are informative, they do not predict the accuracy of algorithms based on ICD-10 codes that could be used to detect cases of mTBI in the OSCOUR® database, as each database has specific features and coding practices vary within and between countries. Accordingly, before OSCOUR® data can be used to monitor mTBI in France, a multicentre validation study of potential algorithms is essential.

The study protocol presented here aims to measure the accuracy of potential algorithms in the OSCOUR® database, which combine ICD-10 codes and free text reasons for visiting ED to identify visits for mTBI in France.

Methods and analysis

Study population selection

The validation study we will conduct is a retrospective multicentre study. Initially, six ED will be randomly selected from the OSCOUR® network.

In each selected ED, a sample of visits (all ages) among all-cause visits occurring between 01/01/2019 and 31/12/2019 will be selected. This period reflects the most recent year before the COVID-19 pandemic for which we have consolidated data on ED visits which are representative of ED activity before the pandemic started).

Setting and data source

Administrative database

In France, data on ED visits are collected on a daily basis by ED participating in the OSCOUR® network.

In 2019, the network included 680 ED and covered 93% of all ED visits, including French overseas regions (except Martinique). An average of 56,700 ED visits per day were recorded in the OSCOUR® database.

For each ED visit, an Emergency Visit Report (EVR) is systematically produced. EVR contain medical information such the primary diagnosis (PD), up to 10 associated diagnoses (AD) coded according to the ICD-10 [12] (in 2019, the PD was recorded in 77% of EVR while AD were recorded in less than 10%), and chief complaints. EVR also contain demographic (sex, age, residence area code) and administrative (ED structural information, release date and time from ED, and orientation on discharge from ED (i.e., home, hospital ward, etc.)) data. Data for each visit in the OSCOUR® database are anonymized; accordingly individual patients cannot be distinguished.

Case and non-case identification in OSCOUR®

The EVR from the six selected ED will be classified as mTBI 'cases' and 'non-cases' by the different algorithms tested.

Two main types of algorithms will be tested to identify cases of mTBI: algorithms based only on ICD-10 codes, and algorithms combining ICD-10 codes with keywords used in free text describing the chief complaint for the ED visit. For the latter, several combinations will be tested to identify cases.

The list of ICD-10 codes used will include ICD-10 codes (or ICD-9 translated into ICD-10 codes) identified in the literature [13-16], and codes recommended by expert physicians in mTBI participating in the project, as they reference lesions frequently associated with mTBI. As we are only looking to identify occurrences of mTBI (i.e., acute phase), codes referring to mTBI sequelae are not included in our list. Table 1 presents the list of ICD-10 codes.

Table 1: List of ICD-10 codes used to select cases of mTBI in OSCOUR®

The list of free text keywords used to identify mTBI cases is presented in Table 2. This list includes three keyword categories that meet the three WHO mTBI diagnostic criteria.

Table 2: List of keywords used to select cases of mTBI in OSCOUR®

EVR with at least one medical diagnosis (PD or AD) ICD-10 code included in the algorithm or/and with a keyword describing an mTBI in the free text chief complaints variable, will be considered 'cases' in OSCOUR®. EVR containing no ICD-10 codes included in the algorithm in diagnostic variables or keywords in the free text chief complaints variable will be considered 'non-cases'.

Medical Chart abstraction and case ascertainment

The computerized medical charts produced for each ED visit and stored on the hospital servers which the ED use, will be used as the reference standard to validate the mTBI case identification algorithms in the OSCOUR® database. To identify medical charts which correspond to selected EVR, we will cross-link various variables (sex, residential postal code, date of birth, date and time of entry to ED, ED exit date and time, and orientation upon discharge from ED).

First, an automatic search of keywords specific to the medical charts will be performed on all selected charts to identify potential cases of mTBI. These will include "TBI with loss of consciousness", "concussion", "Glasgow 15", among others. Medical charts where no mTBI keyword is found will be considered non-cases. A pilot study will determine the specific list of keywords to be used (see below).

Second, all the medical charts of potential cases will be read by an epidemiologist who will then categorise the patient as an mTBI 'certain case', 'possible case' or 'non-case' using the validation criteria presented below. File classification will be blinded. The epidemiologist will not know the ICD-10 codes in the EVR corresponding to the medical chart analysed. Problems with classifying potential cases will be resolved through telephone exchanges between the epidemiologist and expert physicians in the field.

Criteria for the classification of medical charts:

No biological or radiological examination exists to help definitively diagnose an mTBI. Diagnosis of an mTBI is based solely on the search for symptoms and clinical signs reported by the patient or his/her family and on the physician's clinical examination. Accordingly, the diagnosis of mTBI is sometimes uncertain. In order to take into account this uncertainty, we will distinguish 'certain' cases of mTBI from 'possible' cases based on the elements found in the medical charts.

Certain (i.e., conclusive) cases of mTBI will be defined according to the most widely accepted criteria established by the WHO [3]:

(1) An explicit statement of head trauma:

- A direct or indirect blow to the head

Or

-A whiplash-like mechanism involving a violent head acceleration/deceleration movement.

AND

(2) A Glasgow score between 13 and 15 minutes, 30 minutes post-injury or later upon presentation for healthcare

AND

(3) At least one of the following: post-traumatic amnesia of less than 24 hours, confusion or disorientation, loss of consciousness for 30 minutes or less, and/or other transient neurological abnormalities such as focal neurological deficits, seizures and intracranial lesions found by CT scans that do not require neurosurgical intervention.

Possible cases of mTBI will be defined based on the first two WHO criteria only**:**

(1) An explicit statement of head trauma:

- A direct or indirect blow to the head

Or

-A whiplash-like mechanism involving a violent head acceleration/deceleration movement.

AND

(2) A Glasgow score between 13 and 15 minutes, 30 minutes post-injury or later upon presentation for healthcare.

Medical chart not classified in certain cases (no criteria of certain cases) or possible cases (no criteria of possible cases) will be considered as “non-cases”.

The various steps leading to file classification in the event of certain cases, possible cases, and non-mTBI cases are summarised in Figure 1.

Figure 1: Diagram of the presentation of the various steps leading to classification in medical charts (i.e., reference standard) of certain, possible, and non-mTBI cases.

Pilot study

A pilot study will be conducted before the validation study at one of the study's six participating sites on a sample of 1,000 medical records of ED visits that will be linked to the OSCOUR® database. This pilot study will help refine the list of specific keywords to use to identify potential cases from medical charts. All medical charts classified as non-cases will be read again to ensure they are in reality non-cases. The pilot study will also be useful to refine the criteria to categorize potential cases from medical records as 'certain', 'possible', and 'non-case', and to determine the length of time needed to review the charts. The lessons from this pilot study will ensure the validation study to be implemented effectively.

Statistical analysis

Sample size

We estimate that a minimum sample size of 100 confirmed mTBI cases in patients' medical charts is needed to achieve a sensitivity and specificity of the algorithms of 50% (worst case scenario knowing that we do not know, *a priori*, the sensitivity and specificity of our algorithms applied to data in the OSCOUR® database) with a precision of 10% and a 5% α risk. Accordingly, assuming that mTBI cases account for 1% of ED visits [17], we would need a sample of at least 10,000 patients for our validation study. As is may not be possible to link or analyse some files (because of a lack of information to classify the patient) 12,000 files will be selected. An equal number of files will be randomly selected in each of the six ED sites (i.e., 2,000 cases per site).

Accuracy of algorithms

Patients with medical charts that are not linkable or not analysable will be excluded from the analysis.

The sensitivity, specificity, PPV, and NPV of the different algorithms tested in the OSCOUR® database will be calculated, respectively, for 'certain' cases and for 'total' cases (ie., certain and possible cases combined). The calculation formulas used to calculate these different indicators are presented in Table 3. Ninety-five percent confidence intervals will be calculated for each of these four metrological qualities. All four qualities of the various algorithms will be measured globally (i.e., for all six ED) in the study . Statistical analyses will be performed using SAS Enterprise Guide 7.4.

Table 3: Formulas for Calculating Sensitivity, Specificity, PPV, and NPV of mTBI case selection algorithms in OSCOUR®

Patient and public involvement

No patients were involved in the design, or conduct, or reporting, or dissemination plans of the research.

Reporting

We will ensure that we present the methodology and results of our study in a transparent and accurate manner. We will follow guidelines proposed by Benchimol et al. in 2011 regarding the presentation of the methodology and results of validation studies [18].

Discussion

This protocol outlines the approach we will follow to study the accuracy of potential algorithms for identifying mTBI in the OSCOUR® database . The method we will use is based on the methodological framework and recommendations proposed by Widdifield et al. regarding the implementation of validation studies [19].

ED data (OSCOUR® database) are a particularly relevant source of data for national-level mTBI surveillance in France, and can be used to produce regularly updated information, for victims of all ages. More generally, the use of the OSCOUR® database for national surveillance of mTBI could help highlight this importance of this public health issue in France.

Before this database can be used for epidemiological monitoring of mTBI, it is essential to conduct a validation study to ensure that cases can be accurately defined using algorithms based on ICD-10 codes and ED visit chief complaint descriptions (free text, keywords). We will seek to identify which of the algorithms tested has the highest sensitivity and specificity. If no algorithm is found to be effective in identifying mTBI cases, the results of the validation study will nevertheless be useful in making recommendations to improve the coding of mTBI in OSCOUR®.

Ethics and dissemination

The ethics committee of the French National Data Protection Authority (CNIL) approved this study (n° 921152, 1 August 2021). Results will be submitted to national and international peer-reviewed journals and presented at conferences dedicated to trauma and to methodologies for the construction and validation of algorithms.

Footnotes

Author Contributions:
LMP, AG, NB, FL, NA, MR and CF designed the study. LMP performed the review of literature. LMP drafted the first version of the manuscript. LMP, AG, NB, FL, NA, MR and CF critically revised the manuscript. All authors approved the final version.

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Competing interests: Dr Fleur Lorton has a scientific expert contract without grants with the LABORATOIRE GLAXOSMITHKLINE. The authors report no other conflict of interest in this work.

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Data sharing statement: Not relevant

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Table 1: List of ICD-10 codes used to select cases of mTBI in OSCOUR®

ICD-10 codes: Code title
S01.0: Open scalp wound
S01.7: Multiple open head wounds
S01.8: Open wound from other parts of the head
S01.9: Open wound of unspecified part of head
S02.0: Fracture of vault of skull
S02.1: Fracture of base of skull
S06.0: Concussion
S06.9: Unspecified intracranial injury
S09.9: Unspecified traumatic head injury

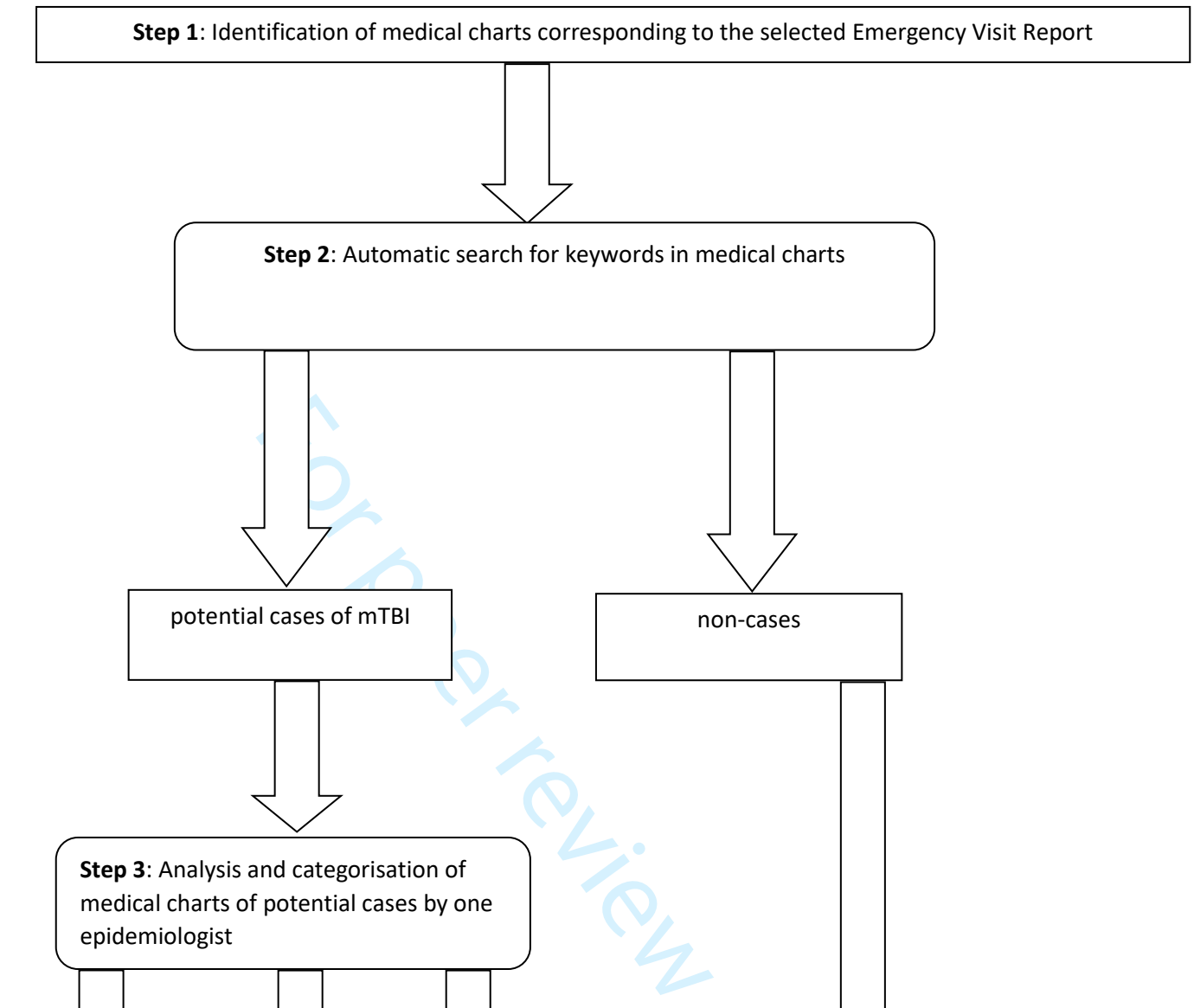
“TBI” and “Mechanisms that are indicative of TBI” keywords
“BI”
“Brain injury”
“Brain injury”
“Concussion”
“Fall”
“Fell”
“Blow”
“Impact”
“Shock”
“Knocked”
“Harm”
“RA”
“WA”
“Glasgow score” keywords
“GCS 13”
“GCS 14”
“GCS 15”
“Glasgow 13”
“Glasgow 14”
“Glasgow 15”
“mTBI symptoms/signs” keywords:
“Loss of consciousness”
“Became unconscious”
“LOC”
“ILOC”
“Amnesia”
“Disorientation”
“Disoriented”
“Confusion”
“Confused”

Table 2: List of keywords used to select cases of mTBI in OSCOUR®

TBI, Traumatic Brain Injury; BI, Brain Injury; RA, Roadway Accident; WA, Work Accident; GCS, Glasgow Coma Scale; LOC, Loss of Consciousness; ILOC, Initial Loss of Consciousness;

Table 3: Formulas for Calculating Sensitivity, Specificity, PPV, and NPV of mTBI case selection algorithms in OSCOUR®

		Medical chart: Reference standard		
		Case	**Non-case**	
OSCOUR® database	**Case**	True Positives (TP)	False Positives (FP)	PPV=TP/ (TP+FP)
	Non-case	False-negative (FN)	True-negative (TN)	NPV=TN/ (TN+FN)
		Sensitivity=TP/ (TP+FN)	Specificity=TN/ (TN+FP)	



Section & Topic	No	Item	Reported on page #
TITLE OR ABSTRACT			
	1	Identification as a study of diagnostic accuracy using at least one measure of accuracy (such as sensitivity, specificity, predictive values, or AUC)	1
ABSTRACT			
	2	Structured summary of study design, methods, results, and conclusions (for specific guidance, see STARD for Abstracts)	Not applicable : Protocol
INTRODUCTION			
	3	Scientific and clinical background, including the intended use and clinical role of the index test	3
	4	Study objectives and hypotheses	3
METHODS			
Study design	**5**	Whether data collection was planned before the index test and reference standard were performed (prospective study) or after (retrospective study)	4
Participants	**6**	Eligibility criteria	4
	7	On what basis potentially eligible participants were identified (such as symptoms, results from previous tests, inclusion in registry)	4
	8	Where and when potentially eligible participants were identified (setting, location and dates)	4
	9	Whether participants formed a consecutive, random or convenience series	4
Test methods	**10a**	Index test, in sufficient detail to allow replication	5
	10b	Reference standard, in sufficient detail to allow replication	6
	11	Rationale for choosing the reference standard (if alternatives exist)	Not applicable
	12a	Definition of and rationale for test positivity cut-offs or result categories of the index test, distinguishing pre-specified from exploratory	5
	12b	Definition of and rationale for test positivity cut-offs or result categories of the reference standard, distinguishing pre-specified from exploratory	6-7
	13a	Whether clinical information and reference standard results were available to the performers/readers of the index test	Not applicable
	13b	Whether clinical information and index test results were available to the assessors of the reference standard	6
Analysis	**14**	Methods for estimating or comparing measures of diagnostic accuracy	8
	15	How indeterminate index test or reference standard results were handled	6
	16	How missing data on the index test and reference standard were handled	8
	17	Any analyses of variability in diagnostic accuracy, distinguishing pre-specified from exploratory	Not applicable
	18	Intended sample size and how it was determined	8
RESULTS			
Participants	**19**	Flow of participants, using a diagram	Not applicable : Protocol
	20	Baseline demographic and clinical characteristics of participants	Not applicable : Protocol
	21a	Distribution of severity of disease in those with the target condition	Not applicable : Protocol
	21b	Distribution of alternative diagnoses in those without the target condition	Not applicable : Protocol
	22	Time interval and any clinical interventions between index test and reference standard	Not applicable : Protocol
Test results	**23**	Cross tabulation of the index test results (or their distribution) by the results of the reference standard	Not applicable : Protocol
	24	Estimates of diagnostic accuracy and their precision (such as 95% confidence intervals)	Not applicable : Protocol
	25	Any adverse events from performing the index test or the reference standard	Not applicable : Protocol
DISCUSSION			
	26	Study limitations, including sources of potential bias, statistical uncertainty, and generalisability	Not applicable : Protocol
	27	Implications for practice, including the intended use and clinical role of the index test	9

OTHER INFORMATION			
	28	Registration number and name of registry	1 et 10
	29	Where the full study protocol can be accessed	Not applicable : Protocol
	30	Sources of funding and other support; role of funders	Not applicable

STARD 2015

AIM

STARD stands for "Standards for Reporting Diagnostic accuracy studies". This list of items was developed to contribute to the completeness and transparency of reporting of diagnostic accuracy studies. Authors can use the list to write informative study reports. Editors and peer-reviewers can use it to evaluate whether the information has been included in manuscripts submitted for publication.

EXPLANATION

A **diagnostic accuracy study** evaluates the ability of one or more medical tests to correctly classify study participants as having a **target condition.** This can be a disease, a disease stage, response or benefit from therapy, or an event or condition in the future. A medical test can be an imaging procedure, a laboratory test, elements from history and physical examination, a combination of these, or any other method for collecting information about the current health status of a patient.

The test whose accuracy is evaluated is called **index test.** A study can evaluate the accuracy of one or more index tests. Evaluating the ability of a medical test to correctly classify patients is typically done by comparing the distribution of the index test results with those of the **reference standard**. The reference standard is the best available method for establishing the presence or absence of the target condition. An accuracy study can rely on one or more reference standards.

If test results are categorized as either positive or negative, the cross tabulation of the index test results against those of the reference standard can be used to estimate the **sensitivity** of the index test (the proportion of participants *with* the target condition who have a positive index test), and its **specificity** (the proportion *without* the target condition who have a negative index test). From this cross tabulation (sometimes referred to as the contingency or "2x2" table), several other accuracy statistics can be estimated, such as the positive and negative **predictive values** of the test. Confidence intervals around estimates of accuracy can then be calculated to quantify the statistical **precision** of the measurements.

If the index test results can take more than two values, categorization of test results as positive or negative requires a **test positivity cut-off**. When multiple such cut-offs can be defined, authors can report a receiver operating characteristic (ROC) curve which graphically represents the combination of sensitivity and specificity for each possible test positivity cut-off. The **area under the ROC curve** informs in a single numerical value about the overall diagnostic accuracy of the index test.

The **intended use** of a medical test can be diagnosis, screening, staging, monitoring, surveillance, prediction or prognosis. The **clinical role** of a test explains its position relative to existing tests in the clinical pathway. A replacement test, for example, replaces an existing test. A triage test is used before an existing test; an add-on test is used after an existing test.

Besides diagnostic accuracy, several other outcomes and statistics may be relevant in the evaluation of medical tests. Medical tests can also be used to classify patients for purposes other than diagnosis, such as staging or prognosis. The STARD list was not explicitly developed for these other outcomes, statistics, and study types, although most STARD items would still apply.

DEVELOPMENT

This STARD list was released in 2015. The 30 items were identified by an international expert group of methodologists, researchers, and editors. The guiding principle in the development of STARD was to select items that, when reported, would help readers to judge the potential for bias in the study, to appraise the applicability of the study findings and the validity of conclusions and recommendations. The list represents an update of the first version, which was published in 2003.

More information can be found on http://www.equator-network.org/reporting-guidelines/stard.

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Validity of algorithms for identifying mild traumatic brain injury in the French national Emergency department database OSCOUR®: a retrospective multicentre validation study protocol

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Validity of algorithms for identifying mild traumatic brain injury in the French national Emergency department database OSCOUR®: a retrospective multicentre validation study protocol

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Abstract

Introduction:

The French emergency department (ED) surveillance network OSCOUR® transmits data on ED visits to Santé publique France (the national public health agency). As these data are collected daily and are almost exhaustive at a national level, it would seem relevant to use them for national epidemiological surveillance of mild traumatic brain injury (mTBI). This article presents the protocol of a planned study to validate algorithms for identifying mTBI in the OSCOUR® database. Algorithms to be tested will be based on ICD-10 codes.

Methods and analysis

We will perform a multicentre validation study of algorithms for identifying mTBI in OSCOUR®. Different combinations of ICD-10 codes will be used to identify cases of mTBI in the OSCOUR® database. A random sample of mTBI cases and non-cases will be selected from four ED. Medical charts will serve as the reference standard to validate the algorithms. The sensitivity, specificity, positive and negative predictive values of the different algorithms, as well as their 95% confidence intervals, will be calculated and compared.

Ethics and dissemination

The ethics committee of the French National Data Protection Authority (CNIL) approved this study (n° 921152, 1 August 2021). Results will be submitted to national and international peer-reviewed journals and presented at conferences dedicated to trauma and to methodologies for the construction and validation of algorithms.

Article Summary

Strengths and limitations of this study

- **This is a multicentre study conducted in four ED in France; it will be the first in France to develop algorithms to identify cases of mTBI at a national level.**
- **The review of patients' medical charts will be used as the reference standard to validate the accuracy of the algorithms.**
- **A wide variety of algorithms will be evaluated, combining ICD-10 codes.**
- **In some cases, difficulties in diagnosing mTBI may complicate case identification in patient charts.**

Introduction

Between 50 and 60 million new cases of traumatic brain injury (TBI) of all levels of severity are recorded worldwide each year [1]. Of these, over 90% are mild traumatic brain injury (mTBI) [2], defined as "an acute brain injury resulting from mechanical energy to the head from external physical forces". Operational criteria for clinical identification include: (1) one or more of the following: confusion or disorientation, loss of consciousness for 30 minutes or less, post-traumatic amnesia for less than 24 hours, and/or other transient neurological abnormalities such as focal signs, seizure, and intracranial lesions not requiring surgery; (2) Glasgow Coma Scale score of 13–15 after 30 minutes post-injury or later upon presentation for healthcare [3].

An increase in mTBI incidence has been described in several recent international studies [4-7]. These very common traumas mainly affect men. All age groups are concerned but particularly young children under five years of age, people aged 15-24 years old, and those aged 75 years and over. The most common causes are falls and road accidents [8]. Although mTBI are classified as mild, they are not benign. While rarely life-threatening, the literature shows that a significant proportion of patients (20-36%) continue to have symptoms months and even years after the trauma occurs [9]. These symptoms, which are not specific to mTBI, are physical (headaches, fatigue, balance or hearing disorders, neck pain, etc.) and intellectual (attention, concentration, memory disorders, etc.) in nature; some patients have mood and behavioural disorders (impatience, anxiety, irritability, depression, guilt, etc.). All these symptoms cause personal and family suffering and can lead to situations of social withdrawal. They sometimes also affect employment or schooling opportunities in younger people. Moreover, several studies have shown that mTBI may be a risk factor for several neurodegenerative diseases [10].

In France, despite the severity of this issue, no recent epidemiological data exist to quantify and characterise the victims of mTBI at the national level. However, such data are essential to estimate the burden of mTBI, with a view to better adapting the offer of care - in particular for patients suffering from complications - and to implementing prevention measures. Using data from the French emergency department (ED) visits database (OSCOUR® network data) could be relevant for national epidemiological surveillance of mTBI, since these data are collected daily and are almost exhaustive at the national level. Moreover, a significant proportion of patients with mTBI who seek medical care are diagnosed and managed in ED [6]. However, the accuracy of potential algorithms which could be used in OSCOUR® is not as yet known.

A study conducted in the United States which evaluated the accuracy of a proposed algorithm based on the ICD-9 (ICD, International Classification of Diseases) codes proposed by the Centers for Disease Control and Prevention (CDC) to detect mTBI cases from medical and administrative databases [11], and which used the clinical examination of ED patients as the reference standard, showed that the algorithm had low sensitivity (45.9%) but high specificity (97.8%). While these results are informative, they do not predict the accuracy of algorithms based on ICD codes that could be used to detect cases of mTBI in the OSCOUR® database as each database has specific features and coding practices vary within and between countries. Accordingly, before OSCOUR® data can be used to monitor mTBI in France, a multicentre validation study of potential algorithms is essential.

The study protocol presented here aims to measure the accuracy of potential algorithms in the OSCOUR® database, which combine ICD-10 codes to identify visits for mTBI in France.

Methods and analysis

Study population selection

The validation study we will conduct is a retrospective multicentre study. Initially, three ED have been randomly selected from the OSCOUR® network and in addition, we also included the ED in which we conducted a pilot study. Of the 4 centers included for this study, 2 were teaching hospitals and 2 were non-teaching hospitals. These centers were located in different regions in France: Auvergne-Rhône-Alpes region, Centre-Val de Loire region, Grand-Est region, Ile-de France region (Paris region).
In each selected ED, a sample of visits (all ages) among all-cause visits occurring between 01/01/2019 and 31/12/2019 will be selected. This period reflects the most recent year before the COVID-19 pandemic for which we have consolidated data on ED visits which are representative of ED activity before the pandemic started.

Setting and data source

Administrative database

In France, data on ED visits are collected on a daily basis by ED participating in the OSCOUR® network.

In 2019, the network included 680 ED and covered 93% of all ED visits, including French overseas regions (except Martinique). An average of 56,700 ED visits per day were recorded in the OSCOUR® database.

For each ED visit, an Emergency Visit Report (EVR) is systematically produced. EVR contain medical information such the primary diagnosis (PD), up to 10 associated diagnoses (AD) coded according to the ICD-10 [12] (in 2019, the PD was recorded in 77% of EVR while AD were recorded in less than 10%), and chief complaints. EVR also contain demographic (sex, age, residence area code) and administrative (ED structural information, release date and time from ED, and orientation on discharge from ED (i.e., home, hospital ward, etc.)) data. Data for each visit are in the OSCOUR® database pseudonymized; accordingly individual patients cannot be directly identified.

Case and non-case identification in OSCOUR®

The EVR from the four selected ED will be classified as mTBI 'cases' and 'non-cases' by the different algorithms tested based on ICD-10. In our article, the term algorithm is used simply to refer to a list of ICD-10 codes.

The first algorithm we plan to test is based on the S06.0 "concussion" ICD-10 code alone. This is the only code which specifically describes mTBI in ICD-10 classification. In addition, a literature review we conducted earlier pointed out that the most frequently found mTBI identification algorithm included only the code of concussion.

Next, we plan to develop other algorithms in order to explore the feasibility of better accuracy in identifying mTBI cases compared to the algorithm based on the S06.0 code. We will use a list of ICD-10 codes which will include the S06.0 and all clinically relevant ICD-10 codes found in EVR which correspond to medical charts of cases that we will have identified during the review of the medical charts we will carry out in the 4 centers. From this list, different algorithms (i.e. combinations of ICD-10 codes) will be developed. Table 1 shows, for information purposes, the list of all clinically relevant ICD-10 codes identified during the pilot study. This list includes most of the codes identified in the literature previously [13-16] but also other codes never used such as open wound codes.

Table 1: List of ICD-10 codes of mTBI cases identified during the pilot study

EVR with at least one medical diagnosis (PD or AD) ICD-10 code included in the algorithm will be considered 'cases' in OSCOUR®. EVR containing no ICD-10 codes included in the algorithm in diagnostic will be considered 'non-cases'.

Medical Chart abstraction and case ascertainment

The computerized medical charts produced for each ED visit and stored on the hospital servers which the ED use, will be used as the reference standard to validate the mTBI case identification algorithms in the OSCOUR® database. We will identify the medical charts through the computerized medical charting systems (DMU, Cristal-Net, DxCare, and Crossway) of the ED selected for the study.

To identify medical charts which correspond to selected EVR, we will cross-link various variables (sex, residential postal code, date of birth, date and time of entry to ED, ED exit date and time, and orientation upon discharge from ED).

For feasibility reasons, we will not review all medical charts. We will use an approach that allows to select all medical charts of mTBI cases while minimizing the number of medical charts of non-case.

First a part of the medical charts randomly selected in the 4 centers will be read. These medical charts will be read by an epidemiologist who will then categorise medical charts as an mTBI 'certain case','probable case', 'possible case' or 'non-case' using the validation criteria presented below. File classification will be blinded. The epidemiologist will not know the ICD-10 codes in the EVR corresponding to the medical chart analysed. Problems with classifying medical charts will be resolved through telephone exchanges between the epidemiologist and expert physicians in the field.

Then, after classifying the medical charts into cases ('certain' cases, 'probable' cases, 'possible' cases) and non-cases we will be able to identify the ICD-10 codes found in the EVR corresponding to medical charts of cases. All ICD-10 codes associated with mTBI cases medical charts will be considered as potential ICD-10 codes for mTBI. In addition, in order to reduce the risk of missing medical charts of mTBI cases, for each potential ICD-10 code initially identified, we will also take into account all codes of the ICD-10 subchapter to which this code belongs. We will also select other codes that are likely to be used to code mTBI cases either because they describe a consequence of mTBI or because they describe lesions possibly associated with mTBI or because they describe the circumstances in which mTBI occurs. Thus, the potential codes of mTBI will include not only all the ICD-10 codes identified following the analysis of the files but also other codes: all codes of signs and symptoms possibly associated to mTBI [17], all codes of the chapter XIX (Injury, poisoning and certain other consequences of external causes) of the ICD-10 classification as well as all codes of the chapter XX (External causes of morbidity and mortality) and any other codes previously used in the literature to identify cases of mTBI [13, 15, 18].

Medical charts corresponding to EVR with no potential mTBI codes will automatically be classified as non-cases without being reviewed. But all the medical charts corresponding to EVR with potential ICD-10 codes for mTBI will be reviewed by the epidemiologist. The number of records that will actually be reviewed by the epidemiologist are specified below in the sample size section.

Criteria for the classification of medical charts:

No biological or radiological examination exists to help definitively diagnose an mTBI. Diagnosis of an mTBI is based solely on the search for symptoms and clinical signs reported by the patient or his/her family and on the physician's clinical examination. Accordingly, the diagnosis of mTBI is sometimes

uncertain. In order to take into account this uncertainty, we will distinguish 'certain cases' cases of mTBI, 'probable cases' and 'possible' cases based on the elements found in the medical charts.

Certain (i.e., conclusive) mTBI cases will be defined according to the most widely accepted criteria established by the WHO [3]:

(1) An explicit statement of head trauma:

- A direct or indirect blow to the head

Or

-A whiplash-like mechanism involving a violent head acceleration/deceleration movement.

AND

(2) A Glasgow coma scale (GCS) score between 13 and 15, 30 minutes post-injury or later upon presentation for healthcare

AND

(3) At least one of the following: post-traumatic amnesia of less than 24 hours, confusion or disorientation, loss of consciousness for 30 minutes or less, and/or other transient neurological abnormalities such as focal neurological deficits, seizures and intracranial lesions found by CT scans that do not require neurosurgical intervention.

The medical charts without GCS score and/or without duration of loss of consciousness and/or post-traumatic amnesia but which reflect other criteria of the WHO definition will be considered as certain cases. Indeed, we assume that if the GCS score is not indicated in the file, it is normal (GCS score= 15). Likewise, we hypothesize that if the duration of loss of consciousness or amnesia is not indicated in the medical charts, it is because it is not significant (loss of consciousness <30 minutes, amnesia <24 hours).

Then, in the category of "probable cases", all uncertain cases will be included.

Probable mTBI cases will be defined based on the following criteria **:**

(1) An explicit statement of head trauma:

- A direct or indirect blow to the head

Or

-A whiplash-like mechanism involving a violent head acceleration/deceleration movement.

AND

(2) At least one of the following criteria:

- Suspected loss of consciousness or amnesia

- At least one post-concussion symptom (symptoms frequently found in victims of mTBI but which are not specific to mTBI) of the Sport Concussion Assessment Tool 5th Edition (SCAT5) [19] (Table 2) .

- Criteria specific to <2 years old : scalp hematoma, abnormal behaviour according to parents

Table 2: List of symptoms of the SCAT5 checklist

The GCS score is not part of the criteria for probable cases; but if mentioned in the file it must be strictly superior to 12.

Possible mTBI cases will be defined based on the first WHO criteria only**:**

(1) An explicit statement of head trauma:

- A direct or indirect blow to the head

Or

-A whiplash-like mechanism involving a violent head acceleration/deceleration movement.

The GCS score is not part of the criteria for possible cases, but if mentioned in the file it must be strictly superior to 12.

Medical chart not classified in certain cases (no criteria of certain cases), probable cases (no criteria of probable cases) or possible cases (no criteria of possible cases) will be considered as “non-cases”.

Statistical analysis

Sample size

We estimate that a minimum sample size of 100 certain mTBI cases (our most restrictive definition) in patients' medical charts is needed to achieve a sensitivity and specificity of the algorithms of 50% (worst case scenario knowing that we do not know, *a priori*, the sensitivity and specificity of our algorithms applied to data in the OSCOUR® database) with a precision of 10% and a 5% α risk. Accordingly, assuming that mTBI certain cases account for 1% of ED visits [20], we would need a sample of at least 10,000 patients for our validation study. As is may not be possible to link or analyse some files (because of a lack of information to classify the patient) 12,000 files will be selected. An equal number of files will be randomly selected in each of the four ED sites (i.e., 3,000 cases per site).

Initially, the epidemiologist will review 2000 of the 12,000 medical charts. Of these 2000 files, based on the results of the pilot study, there should be about 140 medical charts of cases (certain, probable and possible cases) of mTBI. Then, in the 140 EVR corresponding to these 140 medical charts of cases of mTBI it should be possible to identify about 140 potential ICD-10 codes of mTBI. With these 140 potential case codes identified from the chart review and the other potential codes presented earlier, we should have a consistent and comprehensive list of potential ICD-10 codes of mTBI.

Thus, in a second step, among the 10,000 remaining medical charts, the epidemiologist will review "only" the medical charts of potential cases of mTBI (i.e medical charts corresponding to EVR with potential codes of mTBI). The EVR of potential cases as defined above represented approximately 35% of all EVR randomly selected for the pilote study (N=668). Thus, with the hypothese that this proportion is similar in the sample on which we worked in for the pilote study and in the sample on which we will work for the validation study, we can estimate that there we will probably be 3,500 records (35/100*10,000) of potential cases to review. As a result, the epidemiologist should read approximately 5 500 medical charts in total.

Accuracy of algorithms

Patients with medical charts that are not linkable or not analysable will be excluded from the analysis.

The sensitivity, specificity, PPV, and NPV of the different algorithms tested in the OSCOUR® database will be calculated, respectively, for 'certain' cases, for 'certain' and 'probable' cases and for 'total' cases (ie., certain, probable and possible cases combined). The calculation formulas used to calculate these different indicators are presented in Table 3. Ninety-five percent confidence intervals will be calculated for each of these four metrological qualities. All four qualities of the various algorithms will be measured globally (i.e., for all four ED) in the study . Statistical analyses will be performed using SAS Enterprise Guide 7.4.

Table 3: Formulas for Calculating Sensitivity, Specificity, PPV, and NPV of mTBI case selection algorithms in OSCOUR®

Patient and public involvement

No patients were involved in the design, or conduct, or reporting, or dissemination plans of the research.

Reporting

We will ensure that we present the methodology and results of our study in a transparent and accurate manner. We will follow guidelines proposed by Benchimol et al. in 2011 regarding the presentation of the methodology and results of validation studies [21].

Discussion

This protocol outlines the approach we will follow to study the accuracy of potential algorithms for identifying mTBI in the OSCOUR® database. The method we will use is based on the methodological framework and recommendations proposed by Widdifield et al. regarding the implementation of validation studies [22].

ED data (OSCOUR® database) are a particularly relevant source of data for national-level mTBI surveillance in France, and can be used to produce regularly updated information, for victims of all ages. More generally, the use of the OSCOUR® database for national surveillance of mTBI could help highlight this importance of this public health issue in France.

Before this database can be used for epidemiological monitoring of mTBI, it is essential to conduct a validation study to ensure that cases can be accurately defined using algorithms based on ICD-10 codes. We will seek to identify which of the algorithms tested has the highest sensitivity and specificity. If no algorithm is found to be effective in identifying mTBI cases, the results of the validation study will nevertheless be useful in making recommendations to improve the coding of mTBI in OSCOUR®.

Ethics and dissemination

The ethics committee of the French National Data Protection Authority (CNIL) approved this study (n° 921152, 1 August 2021). Results will be submitted to national and international peer-reviewed journals and presented at conferences dedicated to trauma and to methodologies for the construction and validation of algorithms.

Footnotes

Author Contributions:
LMP, AG, NB, FL, NA, MR and CF designed the study. LMP performed the review of literature. LMP drafted the first version of the manuscript. LMP, AG, NB, FL, NA, MR and CF critically revised the manuscript. All authors approved the final version.

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Data sharing statement: Not relevant

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Table 1: List of ICD-10 codes of mTBI cases identified during the pilot study

ICD-10 codes: Code title
S00.0: Superficial injury of scalp
S00.3: Superficial injury of nose
S00.7: Multiple superficial injuries of head
S00.9: Superficial injury of unspecified part of head
S01.0: Open scalp wound
S01.1: Open wound of eyelid and periocular area
S01.4: Open wound of cheek and temporomandibular area
S01.5: Open wound of lip and oral cavity
S01.8: Open wound from other parts of the head
S01.9: Open wound of unspecified part of head
S02.80: Fracture of other specified skull and facial bones
S06.0: Concussion

Table 2: List of symptoms of the SCAT5 checklist

Headache
“Pressure in head”
Neck Pain
Nausea or vomiting
Dizziness
Blurred vision
Balance problems
Sensitivity to light
Sensitivity to noise
Feeling slowed down
Feeling like “in a fog“
“Don’t feel right”
Difficulty concentrating
Difficulty remembering
Fatigue or low energy
Confusion[A]
Drowsiness
More emotional
Irritability
Sadness
Nervous or Anxious
Trouble falling asleep (if applicable)

A Patients with symptoms of confusion will be classified as certain cases because confusion is also part of the criteria of the WHO definition.

Table 3: Formulas for Calculating Sensitivity, Specificity, PPV, and NPV of mTBI case selection algorithms in OSCOUR®

		Medical chart: Reference standard		
		Case	**Non-case**	
OSCOUR® database	**Case**	True Positives (TP)	False Positives (FP)	PPV=TP/ (TP+FP)
	Non-case	False-negative (FN)	True-negative (TN)	NPV=TN/ (TN+FN)
		Sensitivity=TP/ (TP+FN)	Specificity=TN/ (TN+FP)	

Section & Topic	No	Item	Reported on page #
TITLE OR ABSTRACT			
	1	Identification as a study of diagnostic accuracy using at least one measure of accuracy (such as sensitivity, specificity, predictive values, or AUC)	1
ABSTRACT			
	2	Structured summary of study design, methods, results, and conclusions (for specific guidance, see STARD for Abstracts)	Not applicable : Protocol
INTRODUCTION			
	3	Scientific and clinical background, including the intended use and clinical role of the index test	3
	4	Study objectives and hypotheses	3
METHODS			
Study design	**5**	Whether data collection was planned before the index test and reference standard were performed (prospective study) or after (retrospective study)	4
Participants	**6**	Eligibility criteria	4
	7	On what basis potentially eligible participants were identified (such as symptoms, results from previous tests, inclusion in registry)	4
	8	Where and when potentially eligible participants were identified (setting, location and dates)	4
	9	Whether participants formed a consecutive, random or convenience series	4
Test methods	**10a**	Index test, in sufficient detail to allow replication	5
	10b	Reference standard, in sufficient detail to allow replication	6
	11	Rationale for choosing the reference standard (if alternatives exist)	Not applicable
	12a	Definition of and rationale for test positivity cut-offs or result categories of the index test, distinguishing pre-specified from exploratory	5
	12b	Definition of and rationale for test positivity cut-offs or result categories of the reference standard, distinguishing pre-specified from exploratory	6-7
	13a	Whether clinical information and reference standard results were available to the performers/readers of the index test	Not applicable
	13b	Whether clinical information and index test results were available to the assessors of the reference standard	6
Analysis	**14**	Methods for estimating or comparing measures of diagnostic accuracy	8
	15	How indeterminate index test or reference standard results were handled	6
	16	How missing data on the index test and reference standard were handled	8
	17	Any analyses of variability in diagnostic accuracy, distinguishing pre-specified from exploratory	Not applicable
	18	Intended sample size and how it was determined	8
RESULTS			
Participants	**19**	Flow of participants, using a diagram	Not applicable : Protocol
	20	Baseline demographic and clinical characteristics of participants	Not applicable : Protocol
	21a	Distribution of severity of disease in those with the target condition	Not applicable : Protocol
	21b	Distribution of alternative diagnoses in those without the target condition	Not applicable : Protocol
	22	Time interval and any clinical interventions between index test and reference standard	Not applicable : Protocol
Test results	**23**	Cross tabulation of the index test results (or their distribution) by the results of the reference standard	Not applicable : Protocol
	24	Estimates of diagnostic accuracy and their precision (such as 95% confidence intervals)	Not applicable : Protocol
	25	Any adverse events from performing the index test or the reference standard	Not applicable : Protocol
DISCUSSION			
	26	Study limitations, including sources of potential bias, statistical uncertainty, and generalisability	Not applicable : Protocol
	27	Implications for practice, including the intended use and clinical role of the index test	9

OTHER INFORMATION			
	28	Registration number and name of registry	1 et 10
	29	Where the full study protocol can be accessed	Not applicable : Protocol
	30	Sources of funding and other support; role of funders	Not applicable

STARD 2015

AIM

STARD stands for "Standards for Reporting Diagnostic accuracy studies". This list of items was developed to contribute to the completeness and transparency of reporting of diagnostic accuracy studies. Authors can use the list to write informative study reports. Editors and peer-reviewers can use it to evaluate whether the information has been included in manuscripts submitted for publication.

EXPLANATION

A **diagnostic accuracy study** evaluates the ability of one or more medical tests to correctly classify study participants as having a **target condition.** This can be a disease, a disease stage, response or benefit from therapy, or an event or condition in the future. A medical test can be an imaging procedure, a laboratory test, elements from history and physical examination, a combination of these, or any other method for collecting information about the current health status of a patient.

The test whose accuracy is evaluated is called **index test.** A study can evaluate the accuracy of one or more index tests. Evaluating the ability of a medical test to correctly classify patients is typically done by comparing the distribution of the index test results with those of the **reference standard**. The reference standard is the best available method for establishing the presence or absence of the target condition. An accuracy study can rely on one or more reference standards.

If test results are categorized as either positive or negative, the cross tabulation of the index test results against those of the reference standard can be used to estimate the **sensitivity** of the index test (the proportion of participants *with* the target condition who have a positive index test), and its **specificity** (the proportion *without* the target condition who have a negative index test). From this cross tabulation (sometimes referred to as the contingency or "2x2" table), several other accuracy statistics can be estimated, such as the positive and negative **predictive values** of the test. Confidence intervals around estimates of accuracy can then be calculated to quantify the statistical **precision** of the measurements.

If the index test results can take more than two values, categorization of test results as positive or negative requires a **test positivity cut-off**. When multiple such cut-offs can be defined, authors can report a receiver operating characteristic (ROC) curve which graphically represents the combination of sensitivity and specificity for each possible test positivity cut-off. The **area under the ROC curve** informs in a single numerical value about the overall diagnostic accuracy of the index test.

The **intended use** of a medical test can be diagnosis, screening, staging, monitoring, surveillance, prediction or prognosis. The **clinical role** of a test explains its position relative to existing tests in the clinical pathway. A replacement test, for example, replaces an existing test. A triage test is used before an existing test; an add-on test is used after an existing test.

Besides diagnostic accuracy, several other outcomes and statistics may be relevant in the evaluation of medical tests. Medical tests can also be used to classify patients for purposes other than diagnosis, such as staging or prognosis. The STARD list was not explicitly developed for these other outcomes, statistics, and study types, although most STARD items would still apply.

DEVELOPMENT

This STARD list was released in 2015. The 30 items were identified by an international expert group of methodologists, researchers, and editors. The guiding principle in the development of STARD was to select items that, when reported, would help readers to judge the potential for bias in the study, to appraise the applicability of the study findings and the validity of conclusions and recommendations. The list represents an update of the first version, which was published in 2003.

More information can be found on http://www.equator-network.org/reporting-guidelines/stard.

BMJ Open

Validity of algorithms for identifying mild traumatic brain injury in the French national Emergency department database OSCOUR®: a retrospective multicentre validation study protocol

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Validity of algorithms for identifying mild traumatic brain injury in the French national Emergency department database OSCOUR®: a retrospective multicentre validation study protocol

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Abstract

Introduction:

The French emergency department (ED) surveillance network OSCOUR® transmits data on ED visits to Santé publique France (the national public health agency). As these data are collected daily and are almost exhaustive at a national level, it would seem relevant to use them for national epidemiological surveillance of mild traumatic brain injury (mTBI). This article presents the protocol of a planned study to validate algorithms for identifying mTBI in the OSCOUR® database. Algorithms to be tested will be based on ICD-10 codes.

Methods and analysis

We will perform a multicentre validation study of algorithms for identifying mTBI in OSCOUR®. Different combinations of ICD-10 codes will be used to identify cases of mTBI in the OSCOUR® database. A random sample of mTBI cases and non-cases will be selected from four ED. Medical charts will serve as the reference standard to validate the algorithms. The sensitivity, specificity, positive and negative predictive values of the different algorithms, as well as their 95% confidence intervals, will be calculated and compared.

Ethics and dissemination

The ethics committee of the French National Data Protection Authority (CNIL) approved this study (n° 921152, 1 August 2021). Results will be submitted to national and international peer-reviewed journals and presented at conferences dedicated to trauma and to methodologies for the construction and validation of algorithms.

Article Summary

Strengths and limitations of this study

- **This is a multicentre study conducted in four ED in France; it will be the first in France to develop algorithms to identify cases of mTBI at a national level.**
- **The review of patients' medical charts will be used as the reference standard to validate the accuracy of the algorithms.**
- **A wide variety of algorithms will be evaluated, combining ICD-10 codes.**
- **In some cases, difficulties in diagnosing mTBI may complicate case identification in patient charts.**

Introduction

Between 50 and 60 million new cases of traumatic brain injury (TBI) of all levels of severity are recorded worldwide each year [1]. Of these, over 90% are mild traumatic brain injury (mTBI) [2], defined as "an acute brain injury resulting from mechanical energy to the head from external physical forces". Operational criteria for clinical identification include: (1) one or more of the following: confusion or disorientation, loss of consciousness for 30 minutes or less, post-traumatic amnesia for less than 24 hours, and/or other transient neurological abnormalities such as focal signs, seizure, and intracranial lesions not requiring surgery; (2) Glasgow Coma Scale score of 13–15 after 30 minutes post-injury or later upon presentation for healthcare [3].

An increase in mTBI incidence has been described in several recent international studies [4-7]. These very common traumas mainly affect men. All age groups are concerned but particularly young children under five years of age, people aged 15-24 years old, and those aged 75 years and over. The most common causes are falls and road accidents [8]. Although mTBI are classified as mild, they are not benign. While rarely life-threatening, the literature shows that a significant proportion of patients (20-36%) continue to have symptoms months and even years after the trauma occurs [9]. These symptoms, which are not specific to mTBI, are physical (headaches, fatigue, balance or hearing disorders, neck pain, etc.) and intellectual (attention, concentration, memory disorders, etc.) in nature; some patients have mood and behavioural disorders (impatience, anxiety, irritability, depression, guilt, etc.). All these symptoms cause personal and family suffering and can lead to situations of social withdrawal. They sometimes also affect employment or schooling opportunities in younger people. Moreover, several studies have shown that mTBI may be a risk factor for several neurodegenerative diseases [10].

In France, despite the severity of this issue, no recent epidemiological data exist to quantify and characterise the victims of mTBI at the national level. However, such data are essential to estimate the burden of mTBI, with a view to better adapting the offer of care - in particular for patients suffering from complications - and to implementing prevention measures. Using data from the French emergency department (ED) visits database (OSCOUR® network data) could be relevant for national epidemiological surveillance of mTBI, since these data are collected daily and are almost exhaustive at the national level. Moreover, a significant proportion of patients with mTBI who seek medical care are diagnosed and managed in ED [6]. However, the accuracy of potential algorithms which could be used in OSCOUR® is not as yet known.

A study conducted in the United States which evaluated the accuracy of a proposed algorithm based on the ICD-9 (ICD, International Classification of Diseases) codes proposed by the Centers for Disease Control and Prevention (CDC) to detect mTBI cases from medical and administrative databases [11], and which used the clinical examination of ED patients as the reference standard, showed that the algorithm had low sensitivity (45.9%) but high specificity (97.8%). While these results are informative, they do not predict the accuracy of algorithms based on ICD codes that could be used to detect cases of mTBI in the OSCOUR® database as each database has specific features and coding practices vary within and between countries. Accordingly, before OSCOUR® data can be used to monitor mTBI in France, a multicentre validation study of potential algorithms is essential.

The study protocol presented here aims to measure the accuracy of potential algorithms in the OSCOUR® database, which combine ICD-10 codes to identify visits for mTBI in France.

Methods and analysis

Study population selection

The validation study we will conduct is a retrospective multicentre study. Initially, three ED have been randomly selected from the OSCOUR® network and in addition, we also included the ED in which we conducted a pilot study. Of the 4 centers included for this study, 2 were teaching hospitals and 2 were non-teaching hospitals. These centers were located in different regions in France: Auvergne-Rhône-Alpes region, Centre-Val de Loire region, Grand-Est region, Ile-de France region (Paris region).
In each selected ED, a sample of visits (all ages) among all-cause visits occurring between 01/01/2019 and 31/12/2019 will be selected. This period reflects the most recent year before the COVID-19 pandemic for which we have consolidated data on ED visits which are representative of ED activity before the pandemic started.

Setting and data source

Administrative database

In France, data on ED visits are collected on a daily basis by ED participating in the OSCOUR® network.

In 2019, the network included 680 ED and covered 93% of all ED visits, including French overseas regions (except Martinique). An average of 56,700 ED visits per day were recorded in the OSCOUR® database.

For each ED visit, an Emergency Visit Report (EVR) is systematically produced. EVR contain medical information such the primary diagnosis (PD), up to 10 associated diagnoses (AD) coded according to the ICD-10 [12] (in 2019, the PD was recorded in 77% of EVR while AD were recorded in less than 10%), and chief complaints. EVR also contain demographic (sex, age, residence area code) and administrative (ED structural information, release date and time from ED, and orientation on discharge from ED (i.e., home, hospital ward, etc.)) data. Data for each visit are in the OSCOUR® database pseudonymized; accordingly individual patients cannot be directly identified.

Case and non-case identification in OSCOUR®

The EVR from the four selected ED will be classified as mTBI 'cases' and 'non-cases' by the different algorithms tested. In our article, the term algorithm is used simply to refer to a list of ICD-10 codes.

The first algorithm, we plan to test is based on the S06.0 "concussion" ICD-10 code alone. The S06.0 code is the only code which specifically describes mTBI in ICD-10 classification. In addition, a literature review we conducted earlier pointed out that the most frequently found mTBI identification algorithm included only the code of concussion.

Next, we plan to develop other algorithms in order to explore the feasibility of better accuracy in identifying mTBI cases compared to the algorithm based on the S06.0 code. These "broad algorithms" will be based on a list of ICD-10 codes which will include the S06.0 and all clinically relevant ICD-10 codes found in EVR which correspond to medical charts of cases that we will have identified during the review of the medical charts we will carry out in the 4 centers. From this list, different "broad algorithms" (i.e. combinations of ICD-10 codes) will be developed. Table 1 shows, for information purposes, the list of all clinically relevant ICD-10 codes identified during the pilot study. This list includes most of the codes identified in the literature previously [13-16] but also other codes never used such as open wound codes.

Table 1: List of ICD-10 codes of mTBI cases identified during the pilot study

All the algorithms ("S06.0 algorithm" and "broad algorithms") will be tested as such and then with the addition of exclusion criteria to try to exclude some severe forms of TBI:moderate and severe TBI that would have been wrongly selected by our algorithms.

The management of patients with moderate or severe TBI are quite different from that of patients with mild TBI patients. Patients with moderate or severe TBI are much more frequently referred to intensive care units or neurosurgery than patients with mild TBI [17]. Using the information coded in OSCOUR® that describes the patient's orientation after ED visits, it should be possible to exclude some cases of moderate to severe TBI.

Thus we will use the following two exclusion criteria:

-patient referred after ED visits to an intensive care unit,

-patient referred after ED visits to a surgical service (The type of surgical service is not specified in OSCOUR®. It will therefore not be possible to identify patients referred to neurosurgery).

These two exclusion criteria will be added to the "S06.0 algorithm" and to the "broad algorithms" first in isolation and then in combination.

EVR with at least one medical diagnosis (PD or AD) ICD-10 code included in the algorithm will be considered 'cases' in OSCOUR®. EVR containing no ICD-10 codes included in the algorithm in diagnostic will be considered 'non-cases'.

Medical Chart abstraction and case ascertainment

The computerized medical charts produced for each ED visit and stored on the hospital servers which the ED use, will be used as the reference standard to validate the mTBI case identification algorithms in the OSCOUR® database. We will identify the medical charts through the computerized medical charting systems (DMU, Cristal-Net, DxCare, and Crossway) of the ED selected for the study.

To identify medical charts which correspond to selected EVR, we will cross-link various variables (sex, residential postal code, date of birth, date and time of entry to ED, ED exit date and time, and orientation upon discharge from ED).

The medical charts will be read independently by two epidemiologists who will then categorise medical charts as an mTBI 'certain case','probable case', 'possible case' or 'non-case' using the validation criteria presented below. File classification will be blinded: the epidemiologists will not know the ICD-10 codes in the EVR corresponding to the medical chart analysed.

In order to ensure a good agreement between the two epidemiologists in the classification of medical charts, we will implement the following process:
Initially, the two epidemiologists will analyse, in one center, 100 identical medical charts, independently. The Kappa statistic will be used in order to quantify the agreement between the two epidemiologists in the classification of medical charts. Disagreements will be analysed and resolved by consensus between the two epidemiologists and by an expert physician if needed through telephone exchanges. This process will be repeated (review of 100 additional medical charts by the two epidemiologists) until the kappa statistic is greater than 0.8, meaning an almost perfect agreement [18]. At the end of this process, the review of the medical charts will continue to be carried out independently by the two epidemiologists but without measuring the agreement in the classification of medical charts. During the medical charts review, problems with classifying medical charts will be resolved through telephone exchanges with mTBI expert physicians who participate in the project.

For feasibility reasons, we will not review all medical charts. We will use an approach that allows to select all medical charts of mTBI cases while minimizing the number of medical charts of non-case. First we will identify all the ICD-10 corresponding to medical charts of mTBI cases. ICD-10 case codes will be searched in each of the 4 centers independently to take into account the coding specificities of each center. To identify , in each of the 4 centers, the list of ICD-10 codes corresponding to the medical charts of cases, a "saturation process" will be used. This saturation process will be implemented in the following way. At the end of each day of medical charts review, ICD-10 codes associated with medical charts of mTBI cases will be listed. Based on the results of a pilot study we conducted previously, about 10 medical charts of mTBI cases should be retrieved each day of medical charts review.

Then, the list of ICD-10 codes identified at the end of each day will be compared with that of the previous days (the list identified on the second day with that identified on the first day, the list identified on the third day with that of the two previous days and so on). When for one day no new codes will be identified compared to those identified the previous days, this could mean that saturation has been reached. To ensure that saturation has been reached, we will analyse the medical charts of a new day. At this stage, we will stop the process of saturation if no new codes are identified. At this stage, if new codes are identified the iterative process will continue as described above until reaching saturation (no new ICD-10 codes of mTBI cases are found for two consecutive days of medical charts review)

At the end of the saturation process we will have for each of the 4 centers a comprehensive list of ICD-10 codes of mTBI cases. Thus, in order to reduce the number of medical charts to be reviewed we will select and classified in each hospital only the medical charts corresponding to EVR with codes of mTBI cases identified with the saturation process. Medical charts corresponding to EVR without mTBI cases codes will be classified directly as non-cases without being reviewed. We cannot exclude that in some centers the saturation process does not succeed. If this scenario occurs, all the medical charts will have to be reviewed.

Criteria for the classification of medical charts:

No biological or radiological examination exists to help definitively diagnose an mTBI. Diagnosis of an mTBI is based solely on the search for symptoms and clinical signs reported by the patient or his/her family and on the physician's clinical examination. Accordingly, the diagnosis of mTBI is sometimes uncertain. In order to take into account this uncertainty, we will distinguish 'certain cases' cases of mTBI, 'probable cases' and 'possible' cases based on the elements found in the medical charts.

Certain (i.e., conclusive) mTBI cases will be defined according to the most widely accepted criteria established by the WHO [3]:

(1) An explicit statement of head trauma:

- A direct or indirect blow to the head

Or

-A whiplash-like mechanism involving a violent head acceleration/deceleration movement.

AND

(2) A Glasgow coma scale (GCS) score between 13 and 15, 30 minutes post-injury or later upon presentation for healthcare

AND

(3) At least one of the following: post-traumatic amnesia of less than 24 hours, confusion or disorientation, loss of consciousness for 30 minutes or less, and/or other transient neurological abnormalities such as focal neurological deficits, seizures and intracranial lesions found by CT scans that do not require neurosurgical intervention.

The medical charts, without GCS and with no evidence describing moderate or severe TBI but which reflect other criteria of the WHO definition will be considered as certain cases. Indeed, we assume that if the GCS is not indicated in the file, it is normal (GCS = 15).

The elements describing moderate to severe TBI to look for in the medical charts when the GCS is not mentioned are the following:

-1/ Items describing intracranial lesions associated with items describing a neurosurgical management

-2/ Items describing a coma or signs or symptoms specific to moderate and severe TBI

-3/ Items describing the three components assessed in the GCS (eye opening, verbal response and motor response) and indicative of moderate or severe TBI.

Examples of words to look for in the medical charts to identify cases of moderate and severe TBI when GCS is not mentioned are listed in table 2.

Table 2: Examples of words to look for in the medical charts to identify cases of moderate and severe TBI when the Glasgow Coma Scale score is not mentioned

Then, we hypothesized that if the duration of loss of consciousness or amnesia is not indicated in the medical charts, it is because it is not significant (loss of consciousness <30 minutes, amnesia <24 hours). Thus, in the same way as for the medical charts without GCS mentioned, we will considered as certain cases, the medical charts with loss of consciousness or amnesia mentioned but without duration of loss of consciousness and/or post-traumatic amnesia and without a GCS strictly inferior to 13 and/or without other evidence describing moderate or severe TBI (see above).

Then, in the category of "probable cases", all uncertain cases will be included.

Probable mTBI cases will be defined based on the following criteria **:**

(1) An explicit statement of head trauma:

- A direct or indirect blow to the head

Or

-A whiplash-like mechanism involving a violent head acceleration/deceleration movement.

AND

(2) At least one of the following criteria:

- Suspected loss of consciousness or amnesia

- At least one post-concussion symptom (symptoms frequently found in victims of mTBI but which are not specific to mTBI) of the Sport Concussion Assessment Tool 5th Edition (SCAT5) [19] (Table 3) .

- Criteria specific to <2 years old : scalp hematoma, abnormal behaviour according to parents

Table 3: List of symptoms of the SCAT5 checklist

(3): No evidence describing moderate or severe TBI: no mention of a GCS strictly lower than 13 and/or no mentions of other elements describing moderate or severe TBI (see above)

Possible mTBI cases will be defined based on the first WHO criteria only**:**

(1) An explicit statement of head trauma:

- A direct or indirect blow to the head

Or

-A whiplash-like mechanism involving a violent head acceleration/deceleration movement.

(2): No evidence describing moderate or severe TBI: no mention of a GCS strictly lower than 13 and/or no mentions of other elements describing moderate or severe TBI (see above)

Medical chart not classified in certain cases (no criteria of certain cases), probable cases (no criteria of probable cases) or possible cases (no criteria of possible cases) will be considered as "non-cases".

Analysis of medical charts corresponding to EVR without an ICD-10 code

As previously mentioned, not all visits recorded in the OSCOUR® database contain an ICD-10 code. To ensure that there is no systematic bias in the coding of mTBI cases (lower coding of mTBI cases, lower coding of non-hospitalized mTBI cases, etc.) we will review a sample of medical charts corresponding to visits without coded ICD-10 codes. In one of the 4 centers randomly selected (for feasibility reasons) participating in the study, 200 medical charts will be analyzed and classified using the criteria presented above. This additional analysis conducted in a single center will allow us to discuss the generalizability of the results obtained from our algorithms for identifying mTBI cases.

Statistical analysis

Sample size

We estimate that a minimum sample size of 100 certain mTBI cases (our most restrictive definition) in patients' medical charts is needed to achieve a sensitivity and specificity of the algorithms of 50% (worst case scenario knowing that we do not know, *a priori*, the sensitivity and specificity of our algorithms applied to data in the OSCOUR® database) with a precision of 10% and a 5% α risk. Accordingly, assuming that mTBI certain cases account for 1% of ED visits [20], we would need a sample of at least 10,000 patients for our validation study. As is may not be possible to link or analyse some files (because of a lack of information to classify the patient) 12,000 files will be selected. An equal number of files will be randomly selected in each of the four ED sites (i.e., 3,000 cases per site).

If saturation is not reached in any center, all the 12,000 medical charts (6,000 medical charts per epidemiologist) will need to be reviewed. If the saturation process is reached in one or more centers, the total number of medical charts that will be analysed is difficult to predict. Because we do not know in advance at what stage saturation will be reached. Finally, we do not know in advance the list of ICD-10 codes of mTBI cases that will be found in the centers where saturation will be reached.

Accuracy of algorithms

Patients with medical charts that are not linkable or not analysable will be excluded from the analysis.

The sensitivity, specificity, PPV, and NPV of the different algorithms tested in the OSCOUR® database will be calculated, respectively, for 'certain' cases, for 'certain' and 'probable' cases and for 'total' cases (ie., certain, probable and possible cases combined). The calculation formulas used to calculate these different indicators are presented in Table 4. Ninety-five percent confidence intervals will be calculated for each of these four metrological qualities. All four qualities of the various algorithms will be measured globally (i.e., for all four ED) in the study . Statistical analyses will be performed using SAS Enterprise Guide 7.4.

Table 4: Formulas for Calculating Sensitivity, Specificity, PPV, and NPV of mTBI case selection algorithms in OSCOUR®

Patient and public involvement

No patients were involved in the design, or conduct, or reporting, or dissemination plans of the research.

Reporting

We will ensure that we present the methodology and results of our study in a transparent and accurate manner. We will follow guidelines proposed by Benchimol et al. in 2011 regarding the presentation of the methodology and results of validation studies [21].

Discussion

This protocol outlines the approach we will follow to study the accuracy of potential algorithms for identifying mTBI in the OSCOUR® database. The method we will use is based on the methodological framework and recommendations proposed by Widdifield et al. regarding the implementation of validation studies [22].

ED data (OSCOUR® database) are a particularly relevant source of data for national-level mTBI surveillance in France, and can be used to produce regularly updated information, for victims of all ages. More generally, the use of the OSCOUR® database for national surveillance of mTBI could help highlight this importance of this public health issue in France.

Before this database can be used for epidemiological monitoring of mTBI, it is essential to conduct a validation study to ensure that cases can be accurately defined using algorithms based on ICD-10 codes. We will seek to identify which of the algorithms tested has the highest sensitivity and specificity. If no algorithm is found to be effective in identifying mTBI cases, the results of the validation study will nevertheless be useful in making recommendations to improve the coding of mTBI in OSCOUR®.

Our study has several limitations. First, we cannot exclude that some cases of mTBI in our study will not be identified. mTBI are complicated to identify and diagnose. The diagnosis of mTBI is based solely on the signs or symptoms reported by the patient or his or her family or highlighted by the physician during the clinical examination: there are no biological or radiological examinations that allow a diagnosis of certainty. To try to take into account this limitation inherent to all studies on mTBI, the epidemiologists who will classify the medical charts will be helped during the medical charts review by the mTBI expert physicians who participate in the project. Then, apart from the difficulties related to the identification of mTBI as such, another limitation of our study is related to the use of patient medical charts as a gold standard to validate our algorithms. The information written in the medical charts is not systematically complete and accurate and some records could be complicated to classify. In order to anticipate this difficulty, we determined precise criteria for the classification of cases with the mTBI expert physicians before the study. Moreover, the relevance of the criteria we had determined was checked thanks to a pilot study we conducted. Following this pilot study, some criteria were refined or adapted. Finally, the generalizability of our study could be questioned. For feasibility reasons, our study involved a limited number of centers (4 out of 700 ED in France). Nevertheless, among the 4 centers selected for this study, there were two university hospital emergency departments and 2 hospital emergency departments. Thus, the two main types of French emergency departments are represented in our study. Moreover, among the 4 selected centers, 3 were randomly selected in order to avoid potential biases inherent to volunteering (overrepresentation of "good coders" centers).

Ethics and dissemination

The ethics committee of the French National Data Protection Authority (CNIL) approved this study (n° 921152, 1 August 2021). Results will be submitted to national and international peer-reviewed journals and presented at conferences dedicated to trauma and to methodologies for the construction and validation of algorithms.

Footnotes

Author Contributions:
LMP, AG, NB, FL, NA, MR and CF designed the study. LMP performed the review of literature. LMP drafted the first version of the manuscript. LMP, AG, NB, FL, NA, MR and CF critically revised the manuscript. All authors approved the final version.

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Table 1: List of ICD-10 codes of mTBI cases identified during the pilot study

ICD-10 codes: Code title
S00.0: Superficial injury of scalp
S00.3: Superficial injury of nose
S00.7: Multiple superficial injuries of head
S00.9: Superficial injury of unspecified part of head
S01.0: Open scalp wound
S01.1: Open wound of eyelid and periocular area
S01.4: Open wound of cheek and temporomandibular area
S01.5: Open wound of lip and oral cavity
S01.8: Open wound from other parts of the head
S01.9: Open wound of unspecified part of head
S02.80: Fracture of other specified skull and facial bones
S06.0: Concussion

Items describing intracranial lesions associated with items describing a neurosurgical management *Items describing intracranial lesions:* -Epidural hemorrhage -Subdural hemorrhage -Intracerebral hemorrhage -Subarachnoid hemorrhage -Brain edema -Ischemic brain damage *Items describing a neurosurgical management:* - neurosurgical management - neurosurgical intervention
Items describing a coma or signs or symptoms specific to moderate and severe TBI -Coma -An inability to wake up from sleep - Increased confusion, nervousness or agitation - Prolonged loss of consciousness (>30 minutes) - Prolonged amnesia (>24 hours)
Items describing the three components assessed in the GCS (eye opening, verbal response and motor response) and indicative of moderate or severe TBI -The patient does not open eyes to a paintful stimuli or open eyes only to a paintful stimuli -The patient does not answer simple questions or is making incomprehensible sounds to answer simple questions -The patient has no motor answer, or abnormal extension to pain or abnormal flexion to pain

Table 2: Examples of words to look for in the medical charts to identify cases of moderate and severe TBI when the Glasgow Coma Scale score is not mentioned

TBI, Traumatic Brain Injury; GCS Glasgow Coma Scale;

Table 3: List of symptoms of the SCAT5 checklist

Headache
“Pressure in head”
Neck Pain
Nausea or vomiting
Dizziness
Blurred vision
Balance problems
Sensitivity to light
Sensitivity to noise
Feeling slowed down
Feeling like “in a fog“
“Don’t feel right”
Difficulty concentrating
Difficulty remembering
Fatigue or low energy
Confusion[A]
Drowsiness
More emotional
Irritability
Sadness
Nervous or Anxious
Trouble falling asleep (if applicable)

A Patients with symptoms of confusion will be classified as certain cases because confusion is also part of the criteria of the WHO definition.

Table 4: Formulas for Calculating Sensitivity, Specificity, PPV, and NPV of mTBI case selection algorithms in OSCOUR®

		Medical chart: Reference standard		
		Case	**Non-case**	
OSCOUR® database	**Case**	True Positives (TP)	False Positives (FP)	PPV=TP/ (TP+FP)
	Non-case	False-negative (FN)	True-negative (TN)	NPV=TN/ (TN+FN)
		Sensitivity=TP/ (TP+FN)	Specificity=TN/ (TN+FP)	

Section & Topic	No	Item	Reported on page #
TITLE OR ABSTRACT			
	1	Identification as a study of diagnostic accuracy using at least one measure of accuracy (such as sensitivity, specificity, predictive values, or AUC)	1
ABSTRACT			
	2	Structured summary of study design, methods, results, and conclusions (for specific guidance, see STARD for Abstracts)	Not applicable : Protocol
INTRODUCTION			
	3	Scientific and clinical background, including the intended use and clinical role of the index test	3
	4	Study objectives and hypotheses	3
METHODS			
Study design	**5**	Whether data collection was planned before the index test and reference standard were performed (prospective study) or after (retrospective study)	4
Participants	**6**	Eligibility criteria	4
	7	On what basis potentially eligible participants were identified (such as symptoms, results from previous tests, inclusion in registry)	4
	8	Where and when potentially eligible participants were identified (setting, location and dates)	4
	9	Whether participants formed a consecutive, random or convenience series	4
Test methods	**10a**	Index test, in sufficient detail to allow replication	5
	10b	Reference standard, in sufficient detail to allow replication	6
	11	Rationale for choosing the reference standard (if alternatives exist)	Not applicable
	12a	Definition of and rationale for test positivity cut-offs or result categories of the index test, distinguishing pre-specified from exploratory	5
	12b	Definition of and rationale for test positivity cut-offs or result categories of the reference standard, distinguishing pre-specified from exploratory	6-7
	13a	Whether clinical information and reference standard results were available to the performers/readers of the index test	Not applicable
	13b	Whether clinical information and index test results were available to the assessors of the reference standard	6
Analysis	**14**	Methods for estimating or comparing measures of diagnostic accuracy	8
	15	How indeterminate index test or reference standard results were handled	6
	16	How missing data on the index test and reference standard were handled	8
	17	Any analyses of variability in diagnostic accuracy, distinguishing pre-specified from exploratory	Not applicable
	18	Intended sample size and how it was determined	8
RESULTS			
Participants	**19**	Flow of participants, using a diagram	Not applicable : Protocol
	20	Baseline demographic and clinical characteristics of participants	Not applicable : Protocol
	21a	Distribution of severity of disease in those with the target condition	Not applicable : Protocol
	21b	Distribution of alternative diagnoses in those without the target condition	Not applicable : Protocol
	22	Time interval and any clinical interventions between index test and reference standard	Not applicable : Protocol
Test results	**23**	Cross tabulation of the index test results (or their distribution) by the results of the reference standard	Not applicable : Protocol
	24	Estimates of diagnostic accuracy and their precision (such as 95% confidence intervals)	Not applicable : Protocol
	25	Any adverse events from performing the index test or the reference standard	Not applicable : Protocol
DISCUSSION			
	26	Study limitations, including sources of potential bias, statistical uncertainty, and generalisability	Not applicable : Protocol
	27	Implications for practice, including the intended use and clinical role of the index test	9

OTHER INFORMATION			
	28	Registration number and name of registry	1 et 10
	29	Where the full study protocol can be accessed	Not applicable : Protocol
	30	Sources of funding and other support; role of funders	Not applicable

STARD 2015

AIM

STARD stands for "Standards for Reporting Diagnostic accuracy studies". This list of items was developed to contribute to the completeness and transparency of reporting of diagnostic accuracy studies. Authors can use the list to write informative study reports. Editors and peer-reviewers can use it to evaluate whether the information has been included in manuscripts submitted for publication.

EXPLANATION

A **diagnostic accuracy study** evaluates the ability of one or more medical tests to correctly classify study participants as having a **target condition.** This can be a disease, a disease stage, response or benefit from therapy, or an event or condition in the future. A medical test can be an imaging procedure, a laboratory test, elements from history and physical examination, a combination of these, or any other method for collecting information about the current health status of a patient.

The test whose accuracy is evaluated is called **index test.** A study can evaluate the accuracy of one or more index tests. Evaluating the ability of a medical test to correctly classify patients is typically done by comparing the distribution of the index test results with those of the **reference standard**. The reference standard is the best available method for establishing the presence or absence of the target condition. An accuracy study can rely on one or more reference standards.

If test results are categorized as either positive or negative, the cross tabulation of the index test results against those of the reference standard can be used to estimate the **sensitivity** of the index test (the proportion of participants *with* the target condition who have a positive index test), and its **specificity** (the proportion *without* the target condition who have a negative index test). From this cross tabulation (sometimes referred to as the contingency or "2x2" table), several other accuracy statistics can be estimated, such as the positive and negative **predictive values** of the test. Confidence intervals around estimates of accuracy can then be calculated to quantify the statistical **precision** of the measurements.

If the index test results can take more than two values, categorization of test results as positive or negative requires a **test positivity cut-off**. When multiple such cut-offs can be defined, authors can report a receiver operating characteristic (ROC) curve which graphically represents the combination of sensitivity and specificity for each possible test positivity cut-off. The **area under the ROC curve** informs in a single numerical value about the overall diagnostic accuracy of the index test.

The **intended use** of a medical test can be diagnosis, screening, staging, monitoring, surveillance, prediction or prognosis. The **clinical role** of a test explains its position relative to existing tests in the clinical pathway. A replacement test, for example, replaces an existing test. A triage test is used before an existing test; an add-on test is used after an existing test.

Besides diagnostic accuracy, several other outcomes and statistics may be relevant in the evaluation of medical tests. Medical tests can also be used to classify patients for purposes other than diagnosis, such as staging or prognosis. The STARD list was not explicitly developed for these other outcomes, statistics, and study types, although most STARD items would still apply.

DEVELOPMENT

This STARD list was released in 2015. The 30 items were identified by an international expert group of methodologists, researchers, and editors. The guiding principle in the development of STARD was to select items that, when reported, would help readers to judge the potential for bias in the study, to appraise the applicability of the study findings and the validity of conclusions and recommendations. The list represents an update of the first version, which was published in 2003.

More information can be found on http://www.equator-network.org/reporting-guidelines/stard.