PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Incidence, course and risk factors of head injury in The Netherlands: a retrospective cohort study.
AUTHORS	Gerritsen, Herman; Samim, Mariam; Peters, Hans; Schers, Henk; Laar, Floris

VERSION 1 – REVIEW

REVIEWER	Jennifer Fishe University of Florida - Jacksonville United States of America
REVIEW RETURNED	18-Dec-2017

GENERAL COMMENTS	Strengths of study: comprehensive study of an entire country which collects data on each individual. The manual screening of patients in Cohort 1 is also a strength, given the limitations of diagnosis coding. Weaknesses: Why wasn't Cohort 2 also secondarily screened manually? Patients with complicated head injury often have multiple diagnoses, so it seems manual screening for this cohort would also have been warranted. The identified predictors of a complicated course are already known and extensively described in TBI literature. Specific comments: The authors continually refer to "guidelines" for head trauma. It is unclear what these guidelines are. Including them as a table would help orient readers that are not from The Netherlands. Results (1): Is it true that 34% of all patients in the country less than 15 years old had a head injury in the one year of Cohort 1 study? This seems remarkably high. Please clarify. Results (1): How many of the patients with positive CT findings, and how many of those who underwent neurosurgical intervention, were referred from the general practitioner? Results (2): Only 34 complicated head injuries over 10 years for a country with a population of around 17 million seems remarkably (or artificially) low. How does this number compare with previous studies in the same setting? Please justify that this is not due to a flawed study design. Results (3): Define High energy Trauma (HET) Results: Given the peak incidence in the age 0-1, this deserves a separate analysis, as often the mechanism of injury and risk factors

	in this age group varies greatly from older patients. For example, it is unlikely a 6 month old is on anticoagulants, intoxicated, and riding a bicycle. Regarding conclusion: "a more conservative referral policy for general practice may be desirable" - are the authors stating that they wish to reduce the rate of overtriage to urgent/emergent care for head injuries? In general for trauma, guidelines are written so as to avoid undertriage. Also regarding the use of "conservative," this would mean referring more patients to urgent/emergent care. I get the sense the authors meant more "liberal" instead of "conservative." Also regarding conclusion, the data presented in the Results (3) suggest that patients self triage (OR for those presenting first to primary care suggests extremely low odds of having a complicated head injury). It is a leap to say that this is as a result of guidelines rather than the patients self triaging based on their perceived severity. The identified predictors of complicated hospital course have already been extensively described in the literature, and are included in many prehospital and out-of-hospital trauma triage algorithms. Discussion: "Making it impossible to miss even the simplest case of head injury." A rather bold statement that should be avoided. Never say impossible in research. Discussion: "ongoing uncomplicated head injury may be associated with...significant disability, and neuropsychiatric symptoms." Is this really an uncomplicated head injury then? Most would say this is a complicated head injury. Discussion: "A more reserved management approach...in primary care". This cannot be concluded based on available evidence, as the authors do not report which of the complicated head injury cases attended to in secondary/tertiary care were originally referred from the primary care office.

REVIEWER	Norberto Andaluz University of Cincinnati/Mayfield Clinic
REVIEW RETURNED	21-Dec-2017

GENERAL COMMENTS	This is a very timely and welcome epidemiologic study on traumatic brain injury in the Primary Care setting. The authors take on the task of objectively evaluating data from a large population of head injury patients, and inherently evaluate the ability of general practitioners to identify patients who may suffer complications from their head injuries who would require referral to a specialist. Results from the study support the effectiveness of General Practitioners to identify such patients, challenging the conservative approach of current guidelines. The economic and healthcare policy implications of this study are substantial and set the ground for further discussion towards a more practical, reasonable approach to the management of head injury patients in the general practice. The authors should be congratulated on their researach and efforts in providing epidemiological data to help define a consistent approach to a growing problem in general practice due to increased awareness of head injury and its long term effects.

VERSION 1 – AUTHOR RESPONSE

Comments / questions editor

Please edit your title so that it does not include the subtitle.
We made an adjustment on the title of the paper.

See page 1, Line 1-2: Incidence, course and risk factors of head injury in The Netherlands.

Strengths and Limitations section should consist of one sentence bullet points.
The section on strengths and Limitations is adapted and partially re-written. We used the house style for BMJ-open wherever possible.

See page 3.

Please include a statement about ethical approval in your manuscript.
We added a statement about ethical approval into the paper.

Ethical approval, Page 4, Line 3-5: No formal ethical approval was needed for this study. Patients in the participating practices are informed about the continuous data collection. The data set is anonymized and encrypted before transfer to the researchers.

Comments / questions reviewer 1
Why wasn't Cohort 2 also secondarily screened manually?
We also screened cohort 2 manually for any indicator of head injury. The screened data was derived from a range of multiple episodes. We agree that the text suggests a different search and inclusion strategy between both cohorts. Therefore, we changed the text about cohort 2 to make clear that both study populations where screened and included in the same manner.

Methods, Page 7, Lines 14-16: All specialist letters from these preselected patients were then manually screened for a match to our inclusion criteria of head injury.

"guidelines" for head trauma. It is unclear what these guidelines are.
We intended to refer to the guideline of the Dutch Association of General Practitioners and the guideline of the Dutch Neurological Association. Both guidelines do have strong resemblance with the guidelines as used in the UK and US. We adjusted the text as follows:

Introduction, Page 5, Lines 28-29: Currently two different guidelines are used in the Netherlands, both have strong resemblance with the NICE guideline as used in the UK (12-14).

Is it true that 34% of all patients in the country less than 15 years old had a head injury in the one year of Cohort 1 study?
Obviously we were insufficiently clear because this is not what we meant to say. We intended to point out the fact that of the patients with a head injury, 34% was less than 15 years old. The text is adjusted to be clearer about the concerning population referred to:

Results, Page 10, Line 7: Out of all the patients with a head injury, 34% were under 15 years old.

How many of the patients with positive CT findings, and how many of those who underwent neurosurgical intervention, were referred from the general practitioner?

Out of the 36-complicated cases from cohort 2, 10 patients were referred by the general practitioner. Out of these 10 patients, 3 patients had positive CT findings and 2 of these 3 underwent neurosurgical intervention.

Only 34 complicated head injuries over 10 years for a country with a population of around 17 million seems remarkably (or artificially) low

We agree that 34 cases over ten years in the whole population would be remarkably low. However, the 34 cases refer to the complicated cases in the current cohort, and not to the whole population. On page 10, we wrote that 'over an observation period of ten years we identified 36 patients with complicated head injury (220.352 patient years)'. These 36 patients were identified in a representative cohort, a practice based research network (Family Medicine Network (FaMe-net)).

Define High energy Trauma (HET)

We applied the definition of the ACS-CT. HET is indeed defined as High Energy Transfer and not High Energy Trauma. We made adjustments in the text to be in accordance with literature. (American College of Surgeons Committee on Trauma (2000) (Amendments to) Resources for Optimal Care of the Injured Patient: 2000. Chicago: American College of Surgeons).

See Methods, Page 9, Line 6: high-energy transfer – during trauma (HET).
See Results, Page 11, Line 10: showed that a High Energy Transfer was related to

Given the peak incidence in the age 0-1, this deserves a separate analysis

We agree with the reviewer that trauma mechanisms and risk factors may vary between different age groups. We made an extra analysis on age and mechanism of trauma, as expected and shown in earlier literature the mechanism of trauma changes with the increasing of age:
(see uploaded document 'letter to editor'; the table cannot be uploaded in this 'plain text field')
We feel that this table does not add sufficient new information to be added in the paper. However, if wished we may supply the tables 'on request' or in an appendix.

I get the sense the authors meant more "liberal" instead of "conservative."

We understand that the phrasing "conservative" may lead to confusion. We meant that given the lower odds on a complicated course in the population out of hospital, the policy on referral could be more liberal in the sense of not referring if no evident neurological failure is seen. To avoid this confusion we now altered the term conservative into reserved.

See Abstract, Page 2, Line 28-29: A more reserved referral policy
See Discussion, Page 14, Line 5: A more reserved management of head

It is a leap to say that this is as a result of guidelines rather than the patients self triaging based on their perceived severity.

We agree with the reviewer that the conclusion of relation between self-selection and low odds is not justified by data from our study. Therefore, we deleted the related phrases.

Discussion, Page 15.

The identified predictors of complicated hospital course have already been extensively described in the literature

The identified predictors are indeed extensively described in literature. Previous studies on risk factors have mainly been based on hospital settings. Our study underlines the known risk factors and confirms them in out-of- hospital setting.

Never say impossible in research.

We agree with the reviewer and therefore we changed the text into 'hard' instead of 'impossible'.

Discussion, Page 12, Line 21: making it hard to miss

Is this really an uncomplicated head injury then? Most would say this is a complicated head injury.
In our study we defined ‘complicated’ and ‘uncomplicated’ in terms of the acute and short term danger leading to possible urgent medical interventions. We agree that this may be misleading in a way because ‘uncomplicated’ (acute) head injury may still lead to disability and negative health effects in the long term. Therefore, we changed this line as follows:
Discussion, Page 13, Line 22-25: We are furthermore convinced that identifying patients with mild trauma (including those not seen in a hospital setting) is relevant because (un-)complicated head injury may still be associated with significant cost in terms of disability, lost work or neuropsychiatric complications (28, 29).
"A more reserved management approach...in primary care". This cannot be concluded based on available evidence, as the authors do not report which of the complicated head injury cases attended to in secondary/tertiary care were originally referred from the primary care office.
Unfortunately, the data supporting this conclusion was unclear. This data can be found scattered throughout the text; in table 1 we reported the following: (see uploaded document 'letter to editor'; the table cannot be uploaded in this 'plain text field')

Next, we report on page 10 “A total of eight patients (1.7%) died during study period; two were not sent to a hospital and died without an autopsy, these were the same patients as found in cohort 1.”. Dead is a complicated head injury. 2 persons were not referred by the GP, and 2 persons were seen exclusively by the GP. So, these 2 persons can be no one else than the 2 who died. To clarify this, we have made an adjustment in the text.

Results, Page 10, Line 28-29: were referred directly to the hospital without involvement of a GP. If the initial contact was in primary care (22.2% [n=8)

Comments / questions reviewer 2

We thank the reviewer for his positive comments, and agree that our study may have healthcare policy implications. The comments underpin the relevance of our study.

VERSION 2 – REVIEW

REVIEWER	Jennifer Fishe, MD University of Florida - Jacksonville, United States
REVIEW RETURNED	14-Mar-2018

GENERAL COMMENTS	Manuscript reads much more clear than previous version. A few comments: Page 6 Line 38 - please clarify what 'clinical setting' you are referring to. Page 7 Line 6 - revise 'incidence of head injury in primary care' - because you really looked at incidence of head injury in the network you searched, which included primary care and ED care Page 9 line 23 - why wasn't trauma surgery included in the specialist list Page 9 line 50 - please specify how you dealt with patients who had more than one isolated case of head injury Page 14 line 52 - please specify of the complicated patients who first presented to primary care, how many were referred to an ED Page 16 - would be nice to perform risk factor analysis for JUST the subgroup who presented first to primary care, as this is stated in your introduction is your intent to develop head injury triage guidelines for primary care pediatricians. if you do not perform this

	risk factor analysis then please justify why and adjust conclusions and discussion accordingly. as your data supports, those who first present to primary care vs ED self select in part based on the severity of symptoms, and thus are different populations. developing a triage rule for primary care based on a population which includes those who first present to an ED has a selection bias problem.

VERSION 2 – AUTHOR RESPONSE

Comments / questions reviewer (1)
Please clarify what 'clinical setting' you are referring to.
Currently almost all available data of patients with head injury is based on studies from secondary or tertiary care. The comments made about incidence does refer to almost exclusive hospital populations. We adjusted the text as follows:

Introduction, Page 6: About 90% of head injuries in hospital setting are considered to be mild (6, 7).

Revise 'incidence of head injury in primary care' - because you really looked at incidence of head injury in the network you searched, which included primary care and ED care
We agree with the reviewer that the description ‘head injury in primary care' is not explicit enough in describing g the scope of the study/studied population. In accordance with the description as used in the abstract we adjusted the text as follows:

Introduction, Page 7: In this study, we aim to assess the incidence of head injury across the care continuum, and to identify risk factors for intracranial injury.

Why wasn't trauma surgery included in the specialist list.
Patients with (complicated) head trauma who had received trauma surgery are included in our study. In the Dutch health care system all secondary care involvement is reported back to patients primary care physician. Patients with (multi) trauma who (also) have significant head injury will (also) have (diagnostic and / or therapeutic) involvement of neurology, neurosurgery or rehabilitation medicine, which in turn will lead to correspondence to primary care. If the patient died before a neurologist (etc) had the chance to get involved, l these patients would have been found by our search because of our review of autopsy reports.

Please specify how you dealt with patients who had more than one isolated case of head injury.
Indeed, our description of methods were not clear enough about this topic. We adjusted the text as follows:

Methods, Page 9: Some patients had more than one isolated case of head injury, each case was scored as a new finding.

Please specify of the complicated patients who first presented to primary care, how many were referred to an ED
Out of the complicated patients who first presented to primary care, 8 out of 10 were referred to the ED. In both cases of non-referral, a palliative approach was chosen.

Results, Page 15: A total of eight patients (1.7%) died during study period; two were not sent to a hospital and died without an autopsy, these were the same patients as found in cohort 1.

It would be nice to perform risk factor analysis for JUST the subgroup who presented first to primary care, as this is stated in your introduction is your intent to develop head injury triage guidelines for

primary care pediatricians. if you do not perform this risk factor analysis then please justify why and adjust conclusions and discussion accordingly. as your data supports, those who first present to primary care vs ED self select in part based on the severity of symptoms, and thus are different populations. developing a triage rule for primary care based on a population which includes those who first present to an ED has a selection bias problem.

We agree with the reviewer that a risk factor analysis for the subgroup analysis for the subset of patients who presented primarily to primary care would be desirable. However, the number of patients who presented first to primary care and who turned out to have complicated head injury is extremely low: in total we found 10 cases of complicated head injury who first presented to primary care. Moreover, the “risk factors” that led to referral to secondary care by the general practitioners were obvious, as all complicated patients had neurological deficits such as mental dysfunction (loss of overview, severe amnesia and slowness), evident coordination disorders. As discussed in the manuscript a triage tool for out of hospital use would be a logical instrument to desire. But based on our data, it turns out that normal clinical judgment is sufficient guidance in decision making.
We hope that with these answers we have addressed the concerns of the reviewer. Otherwise, we would be pleased to answer any further questions or requests.