# CHAPTER 8

## General discussion

# General discussion

This thesis describes the epidemiology, risk factors, preventive measures and decision rules for diagnostics in patients with head trauma and traumatic brain injury (TBI) in emergency departments (EDs) in the Netherlands.

**Interpretation and clinical implications of main findings**

*Current situation and trends in traumatic brain injury*

Chapter 2 of this thesis demonstrated a 75% increase in ED visits and a 95% increase in hospitalizations for TBI in the Netherlands between 1998 and 2012. In contrast, TBI-related mortality remained stable. Similar trends in TBI-related ED visits and mortality are observed in other high-income countries.[1,2]

In most high-income countries the epidemiology of patients with TBI is changing.[3] Nowadays the average patient with TBI is older and more often female than one or two decades ago. This trend was confirmed in our own studies (chapter 6). Moreover, the relative and absolute increase in ED visits by elderly TBI patients is higher than expected based on ageing of the population alone. Several explanations for these changes are: increased awareness of TBI especially in the elderly, changed guidelines and increased use of antiplatelet and anticoagulant drugs. Finally, the elderly participate in society until a higher age and live longer independently than in the past. These developments could lead to more fall accidents. [4-6]

The major changes in epidemiology and causative trauma mechanism we observed in our studies have significant clinical implications. Almost all decision rules for minor head injury that are being used globally have been based on studies from the beginning of this century [7-9]. The results of these studies have been adopted in (inter)national guidelines and are still being used in daily practice today. It is highly questionable whether the results and decision aids from those studies are still as valid today in a totally different population, in comparison with the population two decades ago. For example head injury caused by ground level falls leads less often to death or severe TBI compared to other (high energetic) trauma mechanisms.[10] Nonetheless, given a certain Glasgow Coma Scale (GCS) score the mortality is higher in older patients than in young patients with TBI.[11] This implies that identification of head injury patients with (intra)cranial lesions is potentially unreliable in guidelines that are based on old decision rules. Therefore, guidelines should be validated in the current population, as we did for the Dutch population (Chapter 6).

In chapter 3 of this thesis we demonstrated that the current Dutch guideline did not have the desired effect of less CT-scans and/or less hospitalizations. In contrast both CT ratio and hospitalizations increased. These effects are not solely the consequence of the new guideline. Nonetheless a critical appraisal of the guideline is needed as the effects of the introduction of the guideline are the opposite to what was expected. Examples of possible adjustments to the guideline that could be considered to limit the number of CT-scans are adjustment of the guideline to the current population, a higher threshold for performing a CT-scan and more emphasis on clinical judgement or the implementation of other diagnostic modalities such as biomarkers. Furthermore, a multimodal intervention focusing on physicians could be of importance to reduce the number of CT scans and or the number of hospitalizations.[12]

*Prevention of traumatic brain injury*

Not only the demographics of patients changed, also causative trauma mechanisms changed in our studies. In the ageing population more injuries resulted from ground level falls compared to the past when violence and motorized vehicle accidents were predominant causative mechanisms (chapters 2,6,7). These changes are in line with changes observed in other high-income countries.[1,13] In light of the rapidly increasing number of ED visits for TBI in combination with limited treatment options, much effort should be made to prevent head injury and TBI.

As mentioned above, ground level falls, especially in the elderly, are the most important and increasing cause of TBI in the Netherlands. Not only are falls the most important cause, falls in elderly individuals also lead relatively more often to head/brain injury than in the past.[14] Besides a major cause of (head)injury, falls are also a major cause of death in the Netherlands.[6] The number of deaths caused by falls is increasing rapidly. In 2018 the mortality caused by ground level falls was almost three times higher than at the beginning of this century.[15] An important cause for the increase in fall-related injury is ageing of the population. However, fall rates in the elderly exceed the expected number of falls which would be expected by ageing of the population alone.[4,16,17] In the Netherlands increased fall rates in the elderly, amongst other explanations such as increased awareness, might be caused by the fact that elderly live independently until a higher age than in the past.[18]

Falls in elderly individuals can be reduced by exercise and fall prevention programs.[19-25] The increase in the number of fall-related TBIs in older adults suggests an urgent need to enhance fall-prevention efforts in that population.[14,26]

Besides ground level falls another increasingly important, typically Dutch cause of TBI are bicycle accidents. Compared to other countries the use of bicycle helmets is low by commuter and recreational cyclists in the Netherlands. While the mortality risk (number of traffic deaths per kilometer) of other modes of transportation decreased in the past 20 years in the Netherlands, bicycle-related mortality did not decrease. [27] International studies have shown that bicycle helmet use may decrease TBI.[28] In chapter 5 of this thesis we demonstrated that more frequent use of bicycle helmets would probably lead to a decrease in TBI in the Netherlands. After a recent appeal from a group of physicians, helmets will become obligatory for light mopeds (up to 25km/h) in the Netherlands.[29], Introduction of helmet laws for bicyclists could lead to a reduction of bicycle use and therefore turn out to be counter-productive for public health.[30] Hence, provision of good information and stimulation of voluntary bicycle helmet use seems to be the best option.

*Risk factors for traumatic brain injury, antiplatelet therapy*

Controversy exists whether antiplatelet therapy should be considered as a risk factor for intracranial complications in patients with head injury. Several mostly low to moderate quality studies have been conducted that studied the effect of antiplatelet therapy on the risk of intracranial complications in head injury. In this thesis we conducted a systematic review and meta-analysis of these studies (chapter 4). This review suggests that pre-injury antiplatelet therapy, other than acetylsalicylic acid (ASA) monotherapy, is associated with an increased incidence of traumatic intracranial hemorrhage. However, this should be interpreted with caution given the high heterogeneity and methodological flaws of several studies included in the systematic review. For patients on ASA monotherapy the available evidence was insufficient to establish whether this should be considered as a risk factor as well. Besides the fact that patients with antiplatelet therapy seem to have a higher risk of intracranial complications, there are indications that these patients also have higher risk of an unfavorable outcome. [31-33] Hence, a low scanning threshold is warranted for patients on antiplatelet therapy.

*Decision rules for patients with minor head injury and mild traumatic brain injury*

Several decision rules have been developed to efficiently identify patients with head injury that have intracranial complications. As mentioned before, most of these decision rules have been developed at the beginning of this century, when the demographics of patients with head injury were quite different from nowadays. Four frequently used decision rules were validated and compared in chapter 6 of this thesis. The New Orleans Criteria (NOC), the Canadian CT Head Rule (CCHR), the National Institute for Health and Care Excellence (NICE) and the CT in Head Injury

Patients (CHIP) rule.[7-9,34] We concluded that all four decision rules (NICE, CCHR, NOC, CHIP) that were validated could be used. However, all of them have important limitations, either scanning almost all patients or missing significant lesions. On the one hand the NOC had the highest sensitivity, but at the cost of a low specificity; on the other hand the NICE had the highest specificity but at the cost of a low sensitivity. Which decision rule is preferred depends on how many unnecessary CT scans you are willing to make to prevent one missed traumatic lesion. The clinical implication from chapter 6 is clear, the decision rules should be updated.

Consequently we performed an update of the CHIP rule which is described in chapter 7. The updated CHIP rule consists of 12 variables, compared to 15 in the original CHIP rule. Compared to the original CHIP the updated rule could better identify patients with (potential) neurosurgical lesions without increasing, or potentially decreasing, the CT rate. In accordance with our findings from chapter 4 of this thesis, the use of antiplatelet therapy was associated with traumatic findings on CT and was included in the decision rule. Surprisingly anticoagulant (e.g. coumarins) use was not identified as independent risk factor for traumatic findings. Nonetheless a low threshold for scanning these patients is advised both because of potentially worse outcome of traumatic intracranial hemorrhage in the presence of anticoagulant use, and because these results have not yet been confirmed in a validation study.[31-33]

Instead of a fixed scan threshold we gave insight to an increase or decrease in scanning threshold, with subsequently a shift in balance between specificity and sensitivity. In this way clinicians or guidelines can tailor their advice depending on how many unnecessary CT scans they are willing to make to prevent one missed traumatic lesion.

## Limitations

The limitations of each individual study included in this thesis have been discussed in the relevant chapters. Some general limitations will be mentioned here.

Different data sources have been used for different studies included in this thesis. Chapters 3, 6 and 7 contain data collected by our own study group, for chapters 2 and 5 we used data from external sources and chapter 4 is a systematic review. This may lead to a difference in interpretation or definition of TBI. As a consequence the presented incidence figures have to be interpreted with caution.

An important limitation of the CREST (CT Refinement Study), presented in chapters 6 and 7, is that not all consecutive MHI patients received a CT-scan. Participating centers followed the applicable guidelines for CT scanning, patients without risk factors or with one minor criteria did not have a CT-scan. Therefore, patients who did not receive a CT but had intracranial traumatic findings (false negative patients) could have been missed. Possible solutions for this problem could have been either scanning all participating patients or a follow-up study. Scanning all patients did not seem completely ethical and would have led to longer throughput times in the participating busy EDs and would therefore probably have jeopardized the completeness of our study. Both more CT-scans and a follow-up study would have increased costs of the study substantially, this was not feasible considering the available budget. In the studies presented in chapters 6 and 7 we solved this problem by using imputation of the outcome based on present risk factors.

All studies included in this thesis have been conducted in a limited number of EDs in the Netherlands (except for the systematic review). Circumstances in other countries, or other EDs may differ. Therefore, extrapolating results from this thesis should be done with caution in other countries or other hospitals. Even more important, all studies have been conducted in EDs and results may not be valid for other settings such as general practitioners' practices or emergency medical services.

## Future perspectives

Future studies will have to externally validate the updated CHIP rule, not only in the Netherlands, but preferably also in other countries. Besides that an increasing body of evidence exists that blood-based biomarkers for TBI can improve the diagnostic accuracy and clinical decision making.[35] In the past decades several potential **biomarkers** have been identified for this purpose. Some promising examples of these are: S100B, Glial fibrillary acidic protein (GFAP), Ubiquitin carboxy terminal hydrolase L1 (UCH-L1) and NSE (neuron-specific enolase). However, apart from S100B which is included in the Scandinavian Neurotrauma Guidelines, the use of biomarkers in clinical practice is still very limited at the moment.[36] Future studies should aim to study the effectiveness of incorporation of these biomarkers into clinical decision rules. For biomarkers to be of added value to current practice they should naturally be valid and reliable. Besides, they should be readily available and affordable. Finally, biomarkers should offer added value by either increasing precision or reducing costs and throughput times.

We demonstrated that CT rates increased after implementation of new minor head injury guidelines. We aimed to increase diagnostic accuracy to improve the existing CHIP rule on which the Dutch guideline was based. Nonetheless, it has not been proven that clinical decision rules for minor head injury do outperform **clinical judgement** (clinical gestalt). Therefore, future research should also compare clinical judgement with existing decision rules for minor head injury. Off course the experience of the physician has to be considered in this kind of research as clinical judgement is likely to improve with more experience. It is important to mention that guidelines are tools to facilitate clinical decision making and are not carved in stone. Whenever possible, the patient should be involved in decision making to come to a shared decision.

In the Netherlands, as well as in other countries, there are different guidelines for head injury for general practitioners, emergency medical services (EMS) and emergency departments (EDs).[37-39] As long as these guidelines are well aligned there does not have to be a problem. However, for each of these guidelines a different interpretation of available literature is being made. As we discussed in an opinion article, this leads to different, not well aligned guidelines and different treatment under similar circumstances.[40] Future guidelines for general practitioners, EDs and EMS should ideally be made jointly, or at least be **harmonized** and offer similar treatment under similar circumstances.

In this thesis we used fairly large patient series, nonetheless there are many more patients with TBI in the Netherlands than we could possibly include in our study. A **population-based registry** for patients with (mild) TBI could potentially include tens of thousands of patients annually in the Netherlands alone. Clinical information from such a database could be used to enhance decision making regarding diagnostics and the (acute) treatment of TBI. This could be done either by machine learning algorithms or by traditional regression models.

As discussed before we should focus on ways to prevent TBI, especially in the elderly. Fall prevention programs should be evaluated and effective **fall prevention programs** should be implemented. Implementation of such programs can be challenging and ways to better implement these programs should be studied.

Finally, the studies presented in this thesis as well as other TBI decision rules focus on CT results and short-term outcomes. Naturally, these are not the real outcomes of primary interest. It would be very valuable to relate clinical and CT findings in the acute setting to **long-term outcomes**.

# References


1. Centers for Disease Control and Prevention. Surveillance Report of Traumatic Brain Injury-related Emergency Department Visits, Hospitalizations, and Deaths. Centers for Disease Control and Prevention, U.S. Department of Health and Human Services; 2019.
2. Centers for Disease Control and Prevention. Surveillance of TBI related Emergency Department visits, Hospitalizations, and Deaths United States, 2001-2010. Centers for Disease Control and Prevention; 2010.
3. Roozenbeek B, Maas AI, Menon DK. Changing patterns in the epidemiology of traumatic brain injury. Nat Rev Neurol 2013; 9 (4):231-236.
4. Cigolle CT, Ha J, Min LC, Lee PG, Gure TR, Alexander NB, et al. The epidemiologic data on falls, 1998-2010: more older Americans report falling. JAMA Intern Med 2015; 175 (3):443-445.
5. VeiligheidNL. Privé- valongevallen bij ouderen. Cijfers valongevallen in de privésfeer 2018. Amsterdam2019.
6. Statistics Netherlands. Dagelijks 13 doden door een val. 2019.
7. Haydel MJ, Preston CA, Mills TJ, Luber S, Blaudeau E, DeBlieux PM. Indications for computed tomography in patients with minor head injury. N Engl J Med 2000; 343 (2):100-105.
8. Stiell IG, Wells GA, Vandemheen K, Clement C, Lesiuk H, Laupacis A, et al. The Canadian CT Head Rule for patients with minor head injury. Lancet 2001; 357 (9266):1391-1396.
9. Smits M, Dippel DW, Steyerberg EW, de Haan GG, Dekker HM, Vos PE, et al. Predicting intracranial traumatic findings on computed tomography in patients with minor head injury: the CHIP prediction rule. Ann Intern Med 2007; 146 (6):397-405.
10. Centers for Disease Control and Prevention. Report to Congress on Traumatic Brain Injury in the United States: Epidemiology and Rehabilitation. Atlanta, GA: National Center for Injury Prevention and Control; Division of Unintentional Injury Prevention; 2014.
11. Kehoe A, Smith JE, Bouamra O, Edwards A, Yates D, Lecky F. Older patients with traumatic brain injury present with a higher GCS score than younger patients for a given severity of injury. Emerg Med J 2016; 33 (6):381-385.
12. Sharp AL, Huang BZ, Tang T, Shen E, Melnick ER, Venkatesh AK, et al. Implementation of the Canadian CT Head Rule and Its Association With Use of Computed Tomography Among Patients With Head Injury. Ann Emerg Med 2018; 71 (1):54-63.e52.
13. Kehoe A, Smith JE, Edwards A, Yates D, Lecky F. The changing face of major trauma in the UK. Emerg Med J 2015; 32 (12):911-915.
14. Olij BF, Panneman MJM, van Beeck EF, Haagsma JA, Hartholt KA, Polinder S. Fall-related healthcare use and mortality among older adults in the Netherlands, 1997-2016. Exp Gerontol 2019; 120:95-100.
15. Statistic Netherlands. Overledenen; belangrijke doodsoorzaken (korte lijst), leeftijd, geslacht. 2019.
16. Statistics Netherlands. Steeds meer doden door een val. 2017.
17. Statistics Netherlands. Meer ouderen in ziekenhuis met hoofdletsel. 2018.
18. van Duin CS, L; van Roon, D; Harmsen, C;. Huishoudensprognose 2015–2060: jongeren en ouderen langer thuis. Statistics Netherlands; 2016.
19. Olij BF, Erasmus V, Kuiper JI, van Zoest F, van Beeck EF, Polinder S. Falls prevention activities among community-dwelling elderly in the Netherlands: A Delphi study. Injury 2017; 48 (9):2017-2021.

20. Olij BF, Erasmus V, Barmentloo LM, Burdorf A, Smilde D, Schoon Y, et al. Evaluation of Implementing a Home-Based Fall Prevention Program among Community-Dwelling Older Adults. Int J Environ Res Public Health 2019; 16 (6).
21. Hopewell S, Adedire O, Copsey BJ, Boniface GJ, Sherrington C, Clemson L, et al. Multifactorial and multiple component interventions for preventing falls in older people living in the community. Cochrane Database Syst Rev 2018; 7:Cd012221.
22. Karlsson MK, Magnusson H, von Schewelov T, Rosengren BE. Prevention of falls in the elderly--a review. Osteoporos Int 2013; 24 (3):747-762.
23. Sherrington C, Michaleff ZA, Fairhall N, Paul SS, Tiedemann A, Whitney J, et al. Exercise to prevent falls in older adults: an updated systematic review and meta-analysis. Br J Sports Med 2017; 51 (24):1750-1758.
24. Stubbs B, Brefka S, Denkinger MD. What Works to Prevent Falls in Community-Dwelling Older Adults? Umbrella Review of Meta-analyses of Randomized Controlled Trials. Phys Ther 2015; 95 (8):1095-1110.
25. Tricco AC, Thomas SM, Veroniki AA, Hamid JS, Cogo E, Strifler L, et al. Comparisons of Interventions for Preventing Falls in Older Adults: A Systematic Review and Meta-analysis. Jama 2017; 318 (17):1687-1699.
26. Taylor CA, Bell JM, Breiding MJ, Xu L. Traumatic Brain Injury-Related Emergency Department Visits, Hospitalizations, and Deaths - United States, 2007 and 2013. MMWR Surveill Summ 2017; 66 (9):1-16.
27. research Sifrs. Road deaths in the Netherlands. SWOV Fact sheet. The Hague: SWOV; 2019.
28. Hoye A. Bicycle helmets - To wear or not to wear? A meta-analyses of the effects of bicycle helmets on injuries. Accid Anal Prev 2018; 117:85-97.
29. van Nieuwenhuizen C. Kamerbrief over planning ontwerpbesluit helmplicht snorfiets. The Hague: Ministry of Infrastructure and Water Management; 2019.
30. Lemon J. Changes in participation, demographics and hazard associated with mandatory bicycle helmets in New South Wales, Australia. Journal of Transport & Health 2018; 9:195-202.
31. Nishijima DK, Shahlaie K, Sarkar K, Rudisill N, Holmes JF. Risk of unfavorable long-term outcome in older adults with traumatic intracranial hemorrhage and anticoagulant or antiplatelet use. Am J Emerg Med 2013; 31 (8):1244-1247.
32. Peck KA, Calvo RY, Schechter MS, Sise CB, Kahl JE, Shackford MC, et al. The impact of preinjury anticoagulants and prescription antiplatelet agents on outcomes in older patients with traumatic brain injury. J Trauma Acute Care Surg 2014; 76 (2):431-436.
33. Seddighi AS, Motiei-Langroudi R, Sadeghian H, Moudi M, Zali A, Asheghi E, et al. Factors predicting early deterioration in mild brain trauma: a prospective study. Brain Inj 2013; 27 (13-14):1666-1670.
34. National Institute for Health and Care Excellence (NICE). Head injury: assessment and early management. NICE; 2017.
35. Mondello S, Sorinola A, Czeiter E, Vamos Z, Amrein K, Synnot A, et al. Blood-Based Protein Biomarkers for the Management of Traumatic Brain Injuries in Adults Presenting to Emergency Departments with Mild Brain Injury: A Living Systematic Review and Meta-Analysis. J Neurotrauma 2018.
36. Unden J, Ingebrigtsen T, Romner B. Scandinavian guidelines for initial management of minimal, mild and moderate head injuries in adults: an evidence and consensus-based update. BMC Med 2013; 11:50.
37. Nederlands Huisartsen Genootschap (NHG). NHG-Standaard Hoofdtrauma. 2015.

38. Ambulancezorg Nederland. Landelijk Protocol Ambulancezorg 8.1 (LPA). 106 Hoofd-/hersenletsel. Zwolle: Ambulancezorg Nederland; 2016.
39. Hageman G, Pols MA, Schipper DM, Boerman RH, Cremers JPM, van Dijk KGJ. Richtlijn licht traumatich hoofd/hersenletsel (LTH). Federatie Medisch Specialisten; 2010.
40. van den Brand CL, Jellema K. Behandeling hoofdletsel verre van uniform. Medisch Contact 2016; 12 (24 maart 2016):38-39.