Traumatic Brain Injury
Fact sheets and Policy brief

Can affect anyone, anywhere:
Causing death or changing lives forever

Created in collaboration with

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What is TBI?

TBI is defined as an alteration of brain function or other evidence of brain pathology, caused by an external force. TBI is not a single disease entity, but a collection of many different causes, disease types and severity.

**Key Facts:**

- 50 million new cases each year worldwide.
- 57,000 TBI-related deaths each year in the EU.
- 1.5 million hospital admissions for TBI in the EU each year.
- Over 80% of TBI occurs in low-middle income countries.
- Most common causes: Road traffic incidents, falls and violence.
- Adjusted for population, hospital admissions for TBI in the EU are three-fold higher than the USA.
- Official statistics report large variations in hospital admission rates for TBI across the EU, with eight-fold higher admission rates in Germany and Austria compared to Spain and Portugal.
- Reported mortality rates in the EU also vary enormously - with a six-fold difference between countries with the lowest and highest mortality.

The Human Burden

Worldwide, TBI is a leading cause of injury-related death and disability, with a devastating impact on patients and their families. Severe TBI can result in mortality rates as high as 30-40%. Survivors experience a substantial burden of physical, psychiatric, emotional and cognitive disabilities which disrupt the lives of individuals and their families. Such disabilities are not restricted to severe cases, but also occur frequently after moderate or mild TBI.

Life Long Disability Is Common and Includes:

- Impaired memory and problem solving.
- Difficulty in managing stress and emotional upsets.
- Problems in controlling one’s temper.
- Disturbed relationships.
- Increased risk of neurodegenerative disease and Parkinson.
- Reduced life expectancy (3 times more likely to die).

Costs to Society

- The global economic burden of TBI is estimated at about $400 billion. This means that 1 out of every 200 dollars generated in the global economy is spent on the costs and consequences of TBI.
- The direct medical costs for treatment of patients with TBI are high, but the greatest economic burden results from indirect costs - productivity loss, disability, reduced quality of life, and the need for family members to provide care, with resulting secondary loss of employment and productivity.
- TBI has a huge economic impact on individuals and families, and on society as a whole, but reported costs vary enormously. Some of these differences may be real, but most are likely explained by variation in how these costs are reported. The indirect costs of TBI and the impact of possible long term complications (such as dementia) are rarely accounted for. We need better data to understand the economic impact of TBI so that we can take rational and cost effective action to improve prevention and care – this demands uniformity in reporting of health economic data.

**Policy recommendations**

- An international consensus is needed on definitions and standardized epidemiological monitoring of TBI to allow accurate measurement of incidence, prevalence and mortality and comparison of rates of access to community, hospital and residential care.
- Studies are needed in children and adults to better understand links between TBI of all severities and later risks of neurological disease.
- Rigorous long-term health economic studies of direct and indirect costs are needed, which are necessary to inform rational decisions about allocation of resources for clinical care and research in TBI.
- International standardization of methods and health economic research is needed to enable consistent measurement and comparison of costs of TBI care.

Read more:


![Fig. 1 Rate of TBI-related emergency department visits is high and increasing in the very young. Data from the US derived from Centers for Disease Control and Prevention. Rates of TBI-related emergency department visits by age group—United States, 2001–2010. 2010.](https://www.cdc.gov/traumaticbraininjury/data/rates_ed_byage.html)

![Fig. 2 TBI-related hospitalizations are high and increasing in the elderly. Data from the US derived from Centers for Disease Control and Prevention. Rates of TBI-related emergency department visits by age group—United States, 2001–2010. 2010.](https://www.cdc.gov/traumaticbraininjury/data/rates_ed_byage.html)
Why we need to know about the epidemiology of TBI – and its changing patterns
Knowledge of epidemiology of TBI is essential to inform health care provision and prevention strategies.

Key facts:
- Patterns of TBI in high-income countries (HIC) are changing.
- The very young and the elderly are at high and increasing risk for TBI (fig. 1 and 2).
- The highest rate of emergency department visits because of TBI is in children under four years of age and increasing.
- The highest rate of hospital admissions is in the elderly and on the increase.
- The age of patients with more severe TBI has doubled since the ‘80s and the percentage of patients over 50 increased by a factor three (fig. 3).
- People over 65 years of age represent 10% of TBI cases, but account for 50% of TBI related mortality risk.
- Elderly patients with TBI are at high risk of age discrimination and suboptimal treatment.

TBI is very different in the elderly compared to young adult patients injured in road traffic incidents
Until recently, TBI was considered a disease of young, adult males who most commonly suffer injury from a road traffic incident. Improved road infrastructure, traffic safety legislation and personal safety measures (helmet use) have successfully reduced such injuries. However, patterns of TBI in high-income countries are changing and there is an increase of TBI in the very young and in the elderly. The increasing rate of TBI in the elderly is in excess of what may be expected in an ageing population. Individuals now remain mobile and semi-independent to much older ages than used to be the norm. This places them at increased risk of falls, and frailty increases this risk. Loneliness and depression can lead to alcohol abuse, which is increasingly recognized in older individuals. Chronic alcohol abuse can both increase the risk of a TBI and compromise recovery due to decreased cognitive reserve.

Elderly patients commonly suffer a TBI from a fall in which their head strikes a hard object, causing bruising of the brain (contusion). This pattern of injury is very different from that seen in road traffic incidents, where high velocity forces cause shearing of connecting fibres in the brain.

Older bodies react differently to an injury because of reduced reserve. Elderly TBI patients also often have pre-existing disease and are frequently on medication for this. For example, common drugs in this age group include anticoagulants and platelet aggregation inhibitors, both of which can increase the risk and severity of bleeding in the brain following a TBI. Fig. 4 illustrates how a small hemorrhagic contusion in an elderly patient on anticoagulant medication may expand rapidly within a few hours if the anticoagulant medication is not reversed.

The risk of age discrimination in TBI: beware of treatment nihilism
Age is one of the strongest predictors of TBI outcome: both mortality and disability increases continuously with age. Whilst this association is irrefutable, such poor outcomes may be partly avoidable. The false perception of a universally poor outcome in the elderly carries a substantial risk of therapeutic nihilism, often meaning such patients are treated less promptly, with less aggressive treatment, which is often withdrawn inappropriately early. The poor outcome resulting from such sub-optimal treatment fuels self-fulfilling prophecies of poor prognosis and reinforces current prejudices. Such therapeutic nihilism is unjustified: overall, favourable outcomes are seen in 39% of patients aged 60-69 years, when they are aggressively and promptly treated after admission. Elderly patients are underrepresented in most clinical studies and universally excluded from acute phase clinical trials.

Policy recommendations
- Rigorous epidemiologic studies are needed to capture the changing patterns of epidemiology and to identify high-risk groups and targets for improved prevention and management of TBI.
- Clinical research in the elderly is urgently needed to better understand the burden of TBI and response to treatment.

Read more:

Fig. 3 Since the ‘80s, the median age of patients with TBI enrolled in unselected observation studies has doubled and the % of patients over 50 years increased more than three times. Data derived from: Maas AIR, Stocchetti N, Bullock R. Moderate and severe traumatic brain injury in adults. Lancet Neurol 2008; 7: 728–41. Roozenbeek B, Maas AIR, Menon DK. Changing patterns in the epidemiology of traumatic brain injury. Nat Rev Neurol 2013; 9: 231–6.

Fig. 4 Hemorrhagic expansion of an initially small contusion in an elderly patient on anticoagulant medication
Prevention of TBI

Urgently implement known effective strategies for prevention of TBI

TBI is, to a great extent, preventable. Successful prevention has huge benefits for individuals and society: it saves lives, reduces disability, and decreases costs, both inside and outside the healthcare system.

The good news
Improved road safety management, enhanced road and vehicle safety, legislative actions and personal protection (helmets) have been highly effective in reducing TBI due to road traffic incidents.

The bad news
In low and middle-income countries, the incidence of TBI due to road traffic incidents is increasing due to increased use of motor vehicles in combination with an inadequate infrastructure and insufficient adoption of safety measures.

In high income countries, alcohol, other recreational drugs, and distracted driving (often linked to smart-phone use) are increasingly important contributors to road traffic incidents, in general, and to TBI in particular. The likelihood of a safety critically event occurring while driving has been reported to be six times higher for drivers dialing a cellphone and 23 times higher for those texting.

Focus of prevention
Prevention of TBI should be informed by knowledge of its epidemiology and causes, and by the identification of risk groups. Primary prevention aims to reduce the risk of injury in general; secondary prevention aims to reduce the occurrence of TBI or limit its severity if an injury happens. Both approaches can be effective in isolation, but combination of both strategies is needed to maximize benefits.

Some prevention initiatives are applied at a population level (e.g. legislation, improvement in infrastructure, vehicle safety design or workplace safety measures). Other prevention strategies can be specifically targeted at high risk subgroups. Examples include the targeting of drivers and cyclists to promote seat belt child restraint and helmet use. There are substantial potential opportunities to prevent injuries in elderly people at risk of falls – these are under-explored and need further attention.

Specific populations at increased risk for TBI
- **The very young:** children and adolescents are at particularly high risk of accidental TBI, and such injuries can have substantial and lifelong effects on individuals, families and communities. General prevention strategies, such as those related to helmet laws for bicycles and to concussion detection and prevention from sports injuries apply to both children and adults. Two specific aspects of injury prevention are unique to children: the use of car seats and safe guarding children at risk for abuse, with infants being the most vulnerable.
- **The elderly:** Increasing TBI in the elderly is of concern. Elderly people are more likely to fall, more likely to suffer a TBI when a fall occurs, and there is an increased risk for long-term adverse effects, even from an ostensibly mild TBI. A clear need exists to address causal risk factors and in particular to address the association between frailty and vulnerability to TBI through falls (fig. 5).

Sports related TBI: a sports related concussion is a frequent cause of TBI. Increasing evidence indicates that multiple concussive and sub concussive impacts can have a cumulative effect and may be associated with later cognitive decline and the development of a chronic neurodegenerative disease (chronic traumatic encephalopathy). In children and adolescents, there are additional concerns about effects of multiple concussion on brain development and learning. These concerns underscore the importance of immediately removing anyone from play when there is any suspicion of a possible TBI. We strongly recommend that professional sports organizations should be obliged to remove any player with suspected TBI from play immediately, thus setting an example for amateur athletes and young players.

Military personnel in conflict situations: combat related TBI is a substantial cause of mortality and morbidity and unlike civilian TBI, often includes blast related TBI. Blast as an injury mechanism was until recently largely confined to conflict settings, but has become more relevant also in civilian populations due to an increase in terrorist incidents. In the military setting, advances in body armor have increased survival chances, but conversely have led to an increase in survival with disability in patients who otherwise may have not survived the primary injury. In the civilian setting, primary prevention of terrorist attacks is of paramount importance. Lessons learned in military settings need to be transferred to civilian health care.

Offenders: a clear association exists between TBI and crime. This association is however complex as TBI may be a risk factor for criminal behavior, whilst criminal lifestyle will increase the risk of TBI. Screening for TBI in offenders should be considered more frequently and specialist services tailored to offenders with TBI. Studies are needed to understand how brain injury affects behavior, including risk of re-offending.

Policy recommendations
- Policies aimed at reducing the burden of TBI should focus on awareness campaigns and prevention of TBI in general and on strategies specifically to target high risk groups.
- The WHO recommendations on road safety need to be implemented in all countries.
- Any risk of an early second injury after even a mild TBI should be avoided: Professional sporting organizations should set an example for children and amateur athletes by immediately removing from play anyone with a suspected concussion.
- Prevention programs should target contexts specific to local settings and to high risk groups.
- A particular prevention focus is required in the elderly, with a focus on prevention of falls.

Read more:

www.center-tbi.eu
Translating knowledge to care

Key Facts:
- Substantial variation in outcome exists between centres.
- Access to health care is often inconsistent and continuity of care disrupted.
- Current approaches to classification of patients with TBI are insufficient to permit appropriate targeting of therapy to the needs of individual patients.
- No accepted quality indicators for TBI exist.
- Translation of evidence to clinical care is slow, imperfect and inconsistent.

What is the “best” treatment for patients with TBI?
Despite success in animal models of TBI, brain protective drugs have, thus far, mostly failed in patients with TBI. In more severe TBI, clinical care relies on optimizing physiology (e.g., blood pressure and oxygen levels), and trying to control elevated pressure inside the skull (intracranial pressure), which often develops as a consequence of swelling in the injured brain. Such approaches reduce mortality, but effects on functional outcome are less easy to demonstrate. This may be partly due to a “one size fits all” approach, which does not match therapies to disease severity and mechanisms in individual patients. Indeed, more aggressive approaches to reducing intracranial pressure (e.g., removing a portion of the skull to make more room for the swollen brain) may worsen outcome if used too early in the care of patients.

Does it matter how and where you are treated?
The best evidence that the quality of clinical care affects outcome comes from international research studies. Even when outliers are discarded, comparisons in these studies show four-fold differences between the best and worst performing hospitals – the implication being that the same patient might have a 10% chance of death or severe disability in the “best” hospital but a 40% chance of the same outcomes in the “worst” hospital (fig. 6). Many studies show that TBI patients cared for in specialist centres with high volume and protocol driven therapy achieve better outcomes in patients with severe TBI.

Why would such large differences exist in clinical outcome?
Strong evidence in support of many treatment options for TBI is lacking, and as a consequence there is great variability in management. Even where evidence exists, its translation to clinical care is slow, imperfect and inconsistent, and guidelines are inconsistently implemented. In addition, disconnects between acute care and post-acute treatment of TBI are common (fig. 7). These disconnects can result from resource limitation, but can also be the consequence of poorly designed and organized trauma systems, which compromises continuity care along and worsens patient outcome. Assessment of the quality of care in TBI is difficult because we have no accepted quality indicators.

Improving integration and implementation of research outputs into clinical care
Better knowledge implementation and care organization could improve outcome and potentially save costs. It is important to ensure that guidelines take account of such issues, and are tailored to local circumstances. Better integration of available evidence could be achieved by novel approaches such as the creation of “Living Systematic Reviews” which use innovative software to automatically facilitate updating of knowledge - which can then be rapidly integrated into “Living guidelines”.

Policy recommendations
- Health care policies should aim to improve access to and continuity of care for TBI.
- Incentives need to be implemented to stimulate transfer of adult and pediatric patients with TBI to specialist centres.
- Robust evidence is needed to inform guidelines on medical, surgical and rehabilitation interventions for TBI, and hence improve outcome.
- A set of Quality Indicators for TBI needs to be developed, that include structure, process and outcome metrics.
- Funders and publishers should support Living Systematic Reviews as a basis for up-to-date practical treatment recommendations.

Read more:
Developing proven new treatments that improve outcome

Support research to improve precision of therapy through better diagnosis and disease characterisation

Use comparative effectiveness research as an adjunct to randomised trials to identify best practice

Develop and validate multidimensional outcome constructs that quantify the overall burden of disability

Key Facts:
- Clinical trials in TBI have mostly been conducted in highly selected populations and rarely reflect real-world practice.
- Current classification systems for TBI are insufficient to permit targeting of treatments to the needs of individual patients.
- Trauma disturbs the brain in complex ways, affecting multiple outcome domains.

Conventional approaches to evidence generation have served TBI poorly

The Randomized Clinical Trial (RCT) is accepted as gold standard for demonstration of treatment benefit, but has been unable to identify effective therapeutics in TBI. Negative results might reflect the reality that none of our interventions have a substantial impact on outcome. However, it is more likely that they may benefit some, but not all patients. Moreover, our instruments for measuring outcome may be too insensitive, especially in patients with mild TBI. An additional criticism of past RCTs is that they rarely reflect the real-world practice of medicine — often excluding patients over the age of 65 (inappropriate given the discussions in page 2), and embedding the investigational treatment in a highly specified protocol. Finally, these studies have usually been based on a “one size fits all” approach. This is inappropriate for a disease which shows wide variation in mechanisms and severity. For example, a trial in “severe head injury” could result in inclusion of patients with all of the imaging abnormalities in the figure below (fig. 8), who have different injuries, prognosis and treatment needs, and are unlikely to respond equally to a single intervention.

Approaches to better evaluation of new and existing therapies in TBI

1. Precision medicine

We need to better characterize patients and match them to appropriate therapies — an approach now being characterized as Precision Medicine. Integration of data from multiple sources can improve disease characterization and monitoring of disease evolution. Application of Artificial Intelligence to such complex clinical data can deliver clinical decision support for TBI. In addition, three emerging clinical tools hold promise to improve our characterization of TBI patients.

Magnetic resonance imaging (MRI) detects lesions in areas where CT is insensitive (such as in the brainstem), and is far better at detecting some kinds of lesions; such as traumatic axonal injury, which involves shearing of nerve fibres (fig. 9). Blood-based biomarkers can provide measures of the presence and severity of injury. Indeed, the biomarker S100B has been included in the Scandinavian guidelines to decide whether patients with concussion might require a CT scan and the Federal Drug Administration in the USA recently approved the use of the protein biomarkers GFAP and UCHL-1 for this indication. Finally, genetics can characterize differences in the response to injury (the “Host response”). Differences in genetic make-up drive variations in the host response between patients, which can modulate the acute injury and recovery process, and the effects of TBI on long-term consequences of TBI.

2. Comparative Effectiveness Research (CER)

CER examines differences in treatment effects in real world settings. CER could be used to examine whether differences in outcome between centres are driven by treatment differences. Results of such studies could evidence of the benefit or harm of existing clinical interventions in real-world contexts.

3. Comprehensive approaches to outcome assessment

In TBI, functional outcome is perhaps more relevant than mortality because of the high rate of disability in survivors and is generally assessed with the 8-category extended Glasgow Outcome Scale. Its simplicity has clinical appeal, but the broad categories insufficiently account for the multidimensional nature of outcome following TBI, and are relatively insensitive at the higher end of the outcome spectrum. Moreover, it is increasingly becoming clear that a single outcome scale is insufficient to follow recovery in the clinical setting, or to serve as endpoint in clinical trials. Development and validation of multidimensional approaches to outcome assessment are essential.

Policy recommendations

- Comparative effectiveness research should be supported to identify best practices.
- Research is needed to improve the precision of diagnosis, classification and characterization of TBI using multidomain approaches.
- Research to develop multidimensional outcome constructs to quantify the burden of disability from TBI should be supported.
- Research is required to understand and mitigate the long term effects of TBI, both in mild and severe injuries.

Read more:

Fig. 8 Severe TBI: Very different types of disease
(A) Sheared brain: the typical picture of axonal injury on computed tomography. (B) Bruised brain: contusional brain injury (green arrows) on CT in an elderly patient with TBI. (C) Brain under pressure: a typical epidural haematoma (bleeding between the skull and outer coverings of the brain; green arrows) Modified from Maas et al. (2017) by permission of Elsevier

Fig. 9 Better detection of structural brain damage after traumatic brain injury with magnetic resonance imaging
Computed tomography (CT) scan from an adult patient with TBI on admission to hospital (left panel), and magnetic resonance imaging (MRI) scans (FLAIR: middle panel and GRE: right panel) within 2 days of admission. MRI shows a dorsolateral brainstem haemorrhage and surrounding oedema (green arrow) that was not detected with CT, and other haemorrhagic lesions (white arrows), which are most conspicuous on the GRE sequence (which is sensitized to blood products).
Global solutions: collaboration and data sharing

Key Facts:
• 80% of TBI occurs in LMIC, but over 80% of research comes from HICs.
• International collaboration and large studies are required to advance the care for TBI.
• Obtaining informed consent in unconscious patients is impossible.
• TBI is a global problem and mandates global efforts.

Large studies and collaboration: Past research in TBI has too often consisted of small, underpowered, inconclusive studies. The need for large research cohorts for high quality evidence led to establishment of the International TBI Research initiative (InTBIR; https://intbir.nih.gov/), a collaboration of funding agencies.

The InTBIR studies now include over 350 contributing centres and 50,000 patients with TBI of all severities, many of whom provide genomic, biomarker, and advanced imaging data (fig. 10) to support precision medicine and comparative effectiveness research. All projects comply with standards methods of data collection (Common Data Elements), which allow clinical investigators systematically to share data across the research community.

Two InTBIR studies are based in Europe: CENTER-TBI (Collaborative European Neurotrauma Effectiveness Research; www.center-tbi.eu), and CREACTIVE (Collaborative REsearch on ACute Traumatic brain Injury in intensive care medicine in Europe; http://creactive.marionegri.it/).

CENTER-TBI has a heavy emphasis on precision medicine and comparative effectiveness research, with an additional strong focus on knowledge translation. CREACTIVE builds on a European research network to better describe the epidemiology, prognosis and treatment of moderate-severe TBI in 7 countries. Biorepositories and databases from these studies will provide a legacy for future research.

3. Towards global collaborations
The greatest challenges from TBI come from LMICs, where 80% of cases occur, and where access to acute healthcare and late rehabilitation are variable and often poor. Conversely, the research which underpins guidelines originates from HICs. Making a real impact on the global burden of TBI requires that we look beyond the borders of HICs, and address research questions relevant to patients and clinicians in other settings. Emerging Global collaborations address this need: CENTER-TBI has partner studies in China and India, and several HICs have programs of global health research in TBI.

4. Building on the gains of InTBIR: Data sharing
The most substantial gains from InTBIR depend on meta-analyses across studies, maximising the use of publicly funded data collections. Although the principle of data sharing receives almost universal support, implementation is not easy. Any solution must comply with privacy and ethical regulations, account for deferred or waived consent (since many TBI patients lack capacity to consent at the time of research recruitment), ensure high-quality data standards, undertake rigorous data curation, promote sensible data use, whilst maintaining incentives for researchers who collect data, and appropriately accounting for the true costs of data sharing (fig. 11).

Balancing these competing demands is challenging, and requires adaptation to new legislation, novel technology, and changing social perceptions. Big data analysis and Artificial Intelligence offer huge opportunities, but their implementation in TBI research requires careful consideration. Relative advantages of a federated approach or implementation of an EU Health Cloud need to be assessed. Several current funding calls specifically address these issues and costs of data sharing and seek to facilitate interactions between research groups with large data repositories, allowing meta-analyses across studies, both within the EU and internationally.

The overall funding for InTBIR studies over 2012-2020 was approximately US$100 million - an enormous increase from past levels of funding for TBI research. However, this is still disproportionately low when compared with that for other neurological diseases - global funding for research into dementia, a disease with a comparable impact to TBI, was US$3-4 billion between 2008 and 2014. Given the large number of patients with TBI and the huge cost burden worldwide, substantial increases are warranted in the funding to support neurotrauma research.

Policy recommendations
• Co-ordinated research efforts on a global basis are needed to address the growing public health problem of TBI.
• Effective and productive data sharing is hampered by inappropriately restrictive privacy legislation and funding gaps – these require attention from funders and policymakers.
Traumatic brain injury: integrated approaches to improve prevention, clinical care, and research

50 million people suffer from a TBI worldwide every year—over 80% in developing countries
Annual global costs of care and consequences of TBI are up to US$400 billion
In developed countries, TBI increasingly affects the elderly and children under 4 years old
57 000 TBI-related deaths and 1-5 million hospitalisations occur in the EU-28 every year

**Recommendations to apply existing knowledge to improve prevention and clinical care**

1. **Urgently implement known effective strategies for prevention of TBI**
2. **Immediately remove from play any participants in sport with a suspected concussion**
3. **Develop and implement policies to improve timely access to acute and postacute care**
4. **Implement evidence-based guidelines on medical, surgical, and rehabilitation interventions**
5. **Tailor clinical care recommendations to local circumstances and resource availability**

**Recommendations to develop a common language for epidemiology and benchmarking care**

6. **Establish an international consensus for standardised epidemiological monitoring**
7. **Develop a set of quality indicators that includes structure, process, and outcome metrics**

**Recommendations to advance knowledge, clinical care, and outcomes through research**

8. **Support research to improve precision of therapy through better diagnosis and disease characterisation**
9. **Develop and validate multidimensional outcome constructs that quantify the overall burden of disability**
10. **Promote research on links between TBI and increased risk of later neurological disease**
11. **Use comparative effectiveness research as an adjunct to randomised trials to identify best practice**
12. **Increase global collaborations and establish national and international biorepositories and databases**