Potential Economic Benefit of Treatment for Severe Traumatic Brain Injury in Uganda

By

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A Master's Paper submitted to the faculty of the University of North Carolina at Chapel Hill in partial fulfillment of the requirements for the degree of Master of Public Health in the Public Health Leadership Program

Chapel Hill
2012

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Abstract

**Background**  Traumatic brain injury (TBI) is a leading cause of death and disability worldwide. Although the majority of the global burden of disease likely occurs in low- and middle-income countries, particularly in sub-Saharan Africa, there is a paucity of data surveillance and analysis reporting on incidence rate, morbidity, mortality, and economic costs attributable to traumatic brain injury.

**Methods**  A systematic review of all of the epidemiological studies published on TBI in East Africa over the past decade and assessed the available data from those studies was performed. We used a prognostic model to estimate outcomes of conservative and neurosurgical treatment for severe TBI data from a cohort of patients at the national referral hospital of Uganda in the capital city of Kampala during a 13-month study period. To evaluate the long-term impact of treatment for severe TBI, averted DALYs were calculated and converted to dollars using the human capital approach and the value of a statistical life (VSL) approach. This cohort was then used as a representative sample for assessing severe TBI-related benefit for all of Uganda using a combination of this data and explicit assumptions.

**Results**  From May 2008 to June 2009, 127 cases of severe TBI were treated at New Mulago Hospital averting 1,448 DALYs [0,0,0], 1,075 DALYs [3,1,0.04], or 974 DALYs [3,1,0.03]. Using the human capital approach, the economic benefit of intervention ranged from approximately $1.3 million to $1.7 million. The VSL approach estimated an economic benefit of $282,902 to over $11 million. The health benefit of severe TBI for all Ugandans was estimated at between about 11,000 and 17,000 averted DALYs per year with an annual potential economic benefit of $15 million to $20 million using the human capital approach and $3.3 million to $130 million using the VSL approach.

**Conclusions**  Our study suggests that treatment of severe TBI in Uganda has the potential to reduce a significant proportion of morbidity, mortality, and economic burden. The amount of
economic gain produced from treating a small cohort of patients indicates the importance of treatment for severe TBI in developing countries in sub-Saharan Africa.
Severe Traumatic Brain Injury in East Africa: Systematic Review

Introduction

The World Health Organization reports that traumatic brain injury (TBI) is a leading cause of global morbidity and mortality, resulting in death or hospitalization for at least 10 million people and contributing to an estimated 425 years of healthy life lost due to disability (YLDs) per 100,000 people every year.¹-³ Yet, this reported global burden of TBI is only an approximation. Accurate measures of the burden of disease attributable to TBI worldwide are not available due to the lack of systematic data collection, particularly in developing countries, many of which are in Sub-Saharan Africa. Moreover, countries that systematically collect injury data often undercount the two extremes of TBI, mild and severe.⁴ Mild TBI does not manifest clear symptoms and patients often do not present to health care facilities in resource poor settings where access is an issue. Similarly, severe traumatic brain injuries often result in death prior to patient arrival to a health care facility, particularly if pre-hospital care is not present. Furthermore, there are not internationally accepted standards defining what constitutes disability resulting from head trauma.²

For the purposes of this assessment, TBI is defined as trauma to the head that results in brain concussion, skull fracture, brain damage with clear neurological deficits and clinically observable cognitive deficits, post-traumatic amnesia, neurological sequelae and/or any evidence of intracerebral hemorrhage.⁵ In resource intensive settings where adequate imaging is present, a distinction is made between head injury and traumatic brain injury, as the former includes external injury to the face or scalp, while the latter specifically denotes neurologic impairment and damage to brain tissue. However, literature from resource poor settings without three-dimensional neuroimaging [¹][²] often refer to TBI as head injury, therefore due to the setting of this review, the terms are considered interchangeable.
Road traffic injuries are the leading cause of TBI worldwide. Developing countries, such as those in East Africa, currently have the highest disease burden of TBI due to massive growth in motor vehicle numbers, higher numbers of people injured per crash, poor enforcement of traffic safety regulations, inadequate public health infrastructure, and poor access to health services. These countries are also known to experience worse outcomes and higher mortality rates associated with severe TBI when compared to high- and middle-income countries. Given its predilection for young adults and projected increase in incidence within the next decade, TBI death and disability will continue to affect the most productive sector of the sub-Saharan African workforce.

Due to lack of standardized TBI surveillance systems in most countries throughout the world, data on the global burden of disease attributable to TBI are based on expert-derived estimates. Therefore in 2006, the World Health Organization called for increased efforts to strengthen evidence-based data collection on regional epidemiology in order to improve measures for prevention and intervention. Hence, in order to assess what information exists in the literature, this systematic review aims to answer the following question: What data have been published regarding the epidemiology of TBI in East Africa within the past decade?
Methods

Setting

A literature review was undertaken to determine the epidemiology of traumatic brain injury (TBI) within the East African Community (EAC). In 2000, the EAC, which consists of Tanzania, Kenya, Uganda, Rwanda, and Burundi, established to intensify political, economic, and social collaboration. Generally, these low-income developing countries in sub-Saharan Africa have similar geographic and demographic features as well as comparable burdens of disease.

Searches and Selection Process

Sources were obtained via MEDLINE searches using the MeSH major topic term “Craniocerebral Trauma/epidemiology”, which includes brain injuries, closed head injuries, penetrating head injuries, traumatic intracranial hemorrhages, skull fractures, and others. Results were reviewed by titles and abstracts. Full-length articles were obtained and analyzed when they seemed pertinent to the study question and when meta-analyses and systematic reviews included international cohorts. Additional sources were obtained from searches for “traumatic brain injury,” “head trauma,” and “head injury” on African journal websites (i.e. East African Medical Journal, East African Journal of Surgery, African journals online). References from the retrieved sources were checked to identify additional potential sources. Articles selected for review were limited to those with publish dates after January 2002 that focused on traumatic brain injury in East African populations without restriction to age, gender, severity of TBI, setting, or study design. When more than one article used the same study population without offering additional information pertinent to the review, the article with the most breadth of data was used. Data were extracted (when available) on country, setting, study design, number of patients, case criteria, inclusion criteria, incidence, TBI characteristics, TBI etiology, patient demographics, and other relevant factors.
Quality Assessment

One investigator independently screened all abstracts for inclusion. All ten of the studies included were epidemiological cohort studies; four of them were retrospective and the remaining six were prospective. Quality was determined by assessing the risk of bias and external validity of each study. Three of the studies lacked internal validity due to large potential for selection and measurement bias; these three studies were identified as poor quality.\textsuperscript{10-12} The other seven studies were determined to be of fair quality as their potential for bias was moderately low.\textsuperscript{13-19} All ten studies had poor external validity.
Results

An initial MEDLINE search yielded 1,798 English articles published after January 2002, which were reviewed by title and abstract to yield 179 articles involving an African population. Two articles obtained from this search studied an East African population and addressed TBI.\textsuperscript{13,16} Six articles were obtained from African journal website searches.\textsuperscript{10,11,14,15,17,19} An additional two articles were obtained after being identified in reference sections.\textsuperscript{12,18} Of the ten studies used, three took place in Tanzania, three took place in Kenya, two took place in Uganda, two took place in Rwanda, and none took place in Burundi. A brief description of each study, including country, setting, study design, number of patients, case criteria, inclusion criteria, and result section data was used for is summarized in Table 1. Variation in study design and inclusion criteria necessitates cautious comparison.

Incidence

None of the studies reported overall hospital incidence, however many studies reported the incidence of TBI among other subpopulations. Chalya et al. found that head injury patients presenting to a Tanzanian urban referral hospital represented 21\% of 12,140 trauma patients over a 2-year period.\textsuperscript{15} In Tanzania, Maier et al. found that among patients receiving cranial CT scans, 10.3\% had traumatic pathologies in the urban private hospital setting and 21.6\% had traumatic pathologies in the rural referral hospital setting.\textsuperscript{13} At the same rural hospital, prior to becoming a referral hospital and obtaining a CT scan, head trauma represented 6\% of all neurological pathology.\textsuperscript{18} Akama et al. found that in Kenya, among patients received to an urban referral hospital following road traffic injuries, 7\% suffered from head injury.\textsuperscript{16} In the same urban referral hospital, patients with severe TBI (Glasgow Coma Score, GCS ≤ 8) represented 14.3\% of adult intensive care unit (ICU) admissions, with 92\% of these patients having additional extracranial pathology on admission.\textsuperscript{17} In 2001, as boda-bodas (i.e. bicycle and motorcycle taxis) were gaining in popularity, 10\% of boda-boda patients presenting to the national referral
hospital in Uganda had head injuries,\textsuperscript{12} which by 2009 increased to over 35% of boda-boda injury patients presenting with head injury.\textsuperscript{10} Rwanda’s national referral hospital found that 18% of road traffic injury patients presented with head injury as mono-trauma while an additional 2% experienced poly-trauma involving the head.\textsuperscript{11} Another Rwanda study found that traumatic brain injury represented 49.3% of all neurosurgical admissions.\textsuperscript{14}

\textit{TBI Characteristics}

Several studies reported on the severity of TBI in admitted patients. For the purposes of this review, mild TBI is GCS of 13 through 15, moderate TBI is GCS of 9 through 12, and severe TBI is a GCS of 8 or below. Of patients with head injury from a road traffic accident, 52% were reported as mild TBI, whereas 31% were reported as moderate TBI, and 17% were reported as severe TBI at a Kenyan urban referral hospital.\textsuperscript{16} In the same hospital, 39% of traumatic intracranial hematomas caused mild TBI, 33% of traumatic intracranial hematomas caused moderate TBI, and 24% of traumatic intracranial hematomas caused severe TBI. The mortality rates for mild, moderate, and severe TBI in these patients were 3%, 11%, and 59% respectively.\textsuperscript{19} In a Tanzanian urban referral hospital, 66% of patients sustained a mild TBI, 20% of patients sustained a moderate TBI, and 14% of patients sustained a severe TBI. The mortality rates for these patients were 14%, 24%, and 62% respectively.\textsuperscript{15} Hitimana et al. found that 47% of neurosurgical head injury patients had mild TBI, 9% had moderate TBI, and 28% had severe TBI at a Rwandan rural referral hospital. The mortality rates for these patients were 0%, 14%, and 52% respectively.\textsuperscript{14} In a Kenyan study that only investigated severe traumatic brain injury, a mortality rate of 54% was reported.\textsuperscript{17}

Two studies commented on the types of lesions and presenting features associated with the TBI. Chalya et al found that CT scan brain findings at a Tanzanian urban referral hospital, 92% had scalp hematoma, 79% had generalized cerebral edema, 38% had skull fractures, 37% had epidural hematomas, 24% had pneumocephalus, 14% had subdural hematomas, 10% had
intracerebral hematomas, and 7% had subarachnoid hemorrhage. In addition, 42% of TBI patients presented with a history of loss of consciousness, 19% of TBI patients presented with a systolic blood pressure (SBP) of 90 mmHg or below, and 14% sustained additional injuries that were severe (Injury Severity Score, ISS ≥ 16). Mortality, which occurred in 11% of patients, was found to be significantly associated with extremes of age, comorbid conditions, severe ISS, severe TBI by GCS, SBP < 90 mmHg, loss of consciousness duration, need for ICU admission, and space occupying lesion on CT scan. Of patients admitted to a Kenyan urban referral hospital with a diagnosis of traumatic intracranial hematoma, 48% had extradural hematoma, 42% had subdural hematomas, 28% had skull fractures, 21% had intracranial hemorrhage, and 8% had brain contusions. A history of a loss of consciousness, which occurred in 67% of these patients, along with poor GCS and extremes of age were significantly associated with mortality in these patients.

TBI Etiologies

Many studies reported that road traffic injuries caused the majority of TBI in urban settings but this was not necessarily the case in rural settings. Medical records of cranial CT patients from the Maier et al study in Tanzania showed that head injuries were caused by road traffic injuries, non-specified trauma, and crimes/violence in 46%, 31%, and 8% of patients, respectively, in the urban private hospital; whereas those causes represented 25%, 43%, and 32% of head injuries in the rural referral hospital. Road traffic injuries, assault, and falls caused 49.2%, 30.8% and 16.2% of head injuries, respectively, in a Tanzanian urban referral hospital. Fifty-two percent of the road traffic injuries involved motorcycles with motorcyclists most commonly injured (48%), followed by passengers (27%), and pedestrians (10%); helmets were used in 19% of these patients. Also, the majority of the TBIs were blunt (79%) as opposed to penetrating, none of these patients received any pre-hospital care, and 78% of these patients were brought in by friends, relatives, or bystanders. In the ICU of a Kenyan urban referral
hospital, 59% of patients experienced severe TBI due to a motor vehicle injury, while 32% and 2% experienced severe TBI due to assaults and falls, respectively. In the same hospital, traumatic intracranial hematomas were caused by assault, motor vehicle collisions, and falls in 28%, 15%, and 14% of patients, respectively.

Many studies investigated TBI etiology as it relates to TBI incidence and mortality. According to Akama et al., head injury was the predominant cause of death among those fatally injured following a road traffic accident; it was identified as the sole cause of death in 14% of fatally injured patients and a contributor to the cause of death in an additional 22% of fatally injured patients. Of these patients, 48% had SDH, 29%, had skull fractures, 23% had brain contusions/lacerations, and 6% had brain evisceration on autopsy. Also, pedestrians represented more head injury cases (55%) than either passengers (24%) or drivers (21%). In rural Rwanda, Hitimana et al. found that 71% of road traffic injuries resulted in TBI and among all neurosurgical pathology etiologies, road traffic injuries accounted for the most deaths (44%). In this study population, 15% of falls, 9% of assaults, and 3% of other incidents (e.g. landslide, sports) resulted in head injury. Of note, 79% of TBI patients were admitted within 24 hours of injury/symptom onset, while 16% were admitted within one week and 5% were admitted after 2 weeks.

**Patient Demographics**

Males were found to suffer a greater frequency of TBI than females. In Tanzania, Maier et al reported a male to female incidence ratio of 2.1:1 on cranial CT in the urban private hospital setting and 5.7:1 on cranial CT in the rural referral hospital setting. Another Tanzanian study at an urban referral hospital found a male to female incidence ratio of 1.5:1. Additionally, this study found that the mean age for TBI was 26.8 years with a range of 1 to 82 years. The incidence ratio of males to females with severe TBI at a Kenyan urban referral center was 5.2:1 and the majority of patients were between the ages of 25 and 39 years (51%), as opposed to 40
to 60 year olds who represented 21% of patients, and patients over 60 years old who
represented 5% of the patients. The male to female traumatic intracranial hematoma incidence
ratio at the same hospital was 8.4:1. In this study population, the majority of the patients were
between the ages of 26 to 45 years (49%), while 26% of patients were between the ages of 14
and 25 year and 10% patients were between the ages of 46 and 60 years.
Discussion

This systematic review sought to analyze the data regarding the epidemiology of TBI in East Africa within the past decade. Variation between countries, hospital settings, and inclusion criteria complicate extrapolation, however, some themes were observed. Patients with TBI represented a substantial proportion of traumatic and neurological pathology in these hospitals. Most patients presented to the hospital with mild TBI as opposed to moderate or severe TBI. Road traffic injuries resulted in a significant amount of TBI morbidity and mortality, especially in urban settings. Also, males and young to middle-aged individuals were disproportionately affected by TBI. The distribution of TBI severity and associated mortality rates among patients presenting for admission to the hospital was likely affected by accessibility, affordability, awareness, and availability of pre- and in-hospital care. Much of the data presented here is consistent with the epidemiology of TBI in other developing low- and middle-income countries in Sub-Saharan Africa.4,20-22

Although this compilation of data is interesting and informative, this systematic review is limited by contextual variety, methodological shortcomings of studies, and lack of generalizability. This review highlights the need for demographic surveillance tools, including community surveys and trauma registries, for determination of both the met and unmet need due to TBI in the East African population. Systematic injury data collection has tremendous potential for further identification of strategies to combat TBI. Innovative effort will be required to obtain epidemiological data that can direct allocation of resources in an evidence-based cost-effective manner. New incidence of TBI, frequently referred to as a silent epidemic, is a major public health problem that needs and deserves urgent international attention. Standardized surveillance is essential for devising strategies to prevent and treat it.
References

Table 1. Description of sources included in the mini-systematic review

<table>
<thead>
<tr>
<th>Source</th>
<th>Country</th>
<th>Setting</th>
<th>Study design</th>
<th>Study size</th>
<th>Cases; case criteria</th>
<th>Inclusion criteria</th>
<th>Acquired Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Akama et al, 2007</td>
<td>Kenya</td>
<td>Urban referral hospital</td>
<td>Prospective cohort</td>
<td>482</td>
<td>29; Injuries to the head ranged from abrasions to brain evisceration, scored by GCS</td>
<td>All patients and fatally injured victims involved in road traffic injuries brought to the casualty and dental departments of the hospital from 9/2004-12/2004</td>
<td>Incidence, TBI characteristics, TBI etiology</td>
</tr>
<tr>
<td>Galukan de et al, 2009</td>
<td>Uganda</td>
<td>Urban referral hospital</td>
<td>Prospective cohort</td>
<td>124</td>
<td>44; head injuries were defined as concussions or brain contusions</td>
<td>Consecutive patients presenting every 3rd day who sustained boda-boda injuries and were managed in the accident and emergency wards over 9 month period</td>
<td>Incidence</td>
</tr>
<tr>
<td>Twagirye et al, 2008</td>
<td>Rwanda</td>
<td>Urban referral hospital</td>
<td>Retrospective cohort</td>
<td>1101</td>
<td>224; 196 were mono-trauma and 28 were poly-trauma involving the head</td>
<td>All of the road traffic injury victims who consulted the emergency department from 1/2005-12/2005</td>
<td>Incidence</td>
</tr>
<tr>
<td>Hitiman a et al, 2009</td>
<td>Rwanda</td>
<td>Rural referral hospital</td>
<td>Prospective cohort</td>
<td>152</td>
<td>75; traumatic brain injury determined by clinical exam, xray, and CT when available, differentiated from spinal trauma</td>
<td>All patients with neurosurgical conditions treated over 8 month period from 10/2007 to 5/2008</td>
<td>Incidence, TBI characteristics, TBI etiology</td>
</tr>
<tr>
<td>Chalya et al, 2011</td>
<td>Tanzania</td>
<td>Urban referral hospital</td>
<td>Prospective cohort</td>
<td>260</td>
<td>260; diagnosis of head injury was made by clinical history, physical examination, and abnormal skull radiographs and CT scan</td>
<td>All consecutive head injury patients who presented to the Accident and Emergency department were recruited into the study during a 2-year period between 4/2008 and 3/2010</td>
<td>Incidence, TBI characteristics, TBI etiology, patient demographics</td>
</tr>
<tr>
<td>Opondo et al, 2007</td>
<td>Kenya</td>
<td>Urban referral hospital</td>
<td>Prospective cohort</td>
<td>87</td>
<td>87; severe traumatic brain injury by GCS of 8 or below</td>
<td>All consecutive adult patients with severe traumatic brain injury admitted to the ICU between April and September 2005</td>
<td>Incidence, TBI characteristics, TBI etiology, patient demographics</td>
</tr>
<tr>
<td>Nadduma et al, 2004</td>
<td>Uganda</td>
<td>Urban referral hospital</td>
<td>Retrospective cohort</td>
<td>182</td>
<td>9; head injuries</td>
<td>All patient admitted with traffic injuries from July to September 2001</td>
<td>Incidence</td>
</tr>
<tr>
<td>Winkler et al, 2008</td>
<td>Tanzania</td>
<td>Rural missionary hospital</td>
<td>Prospective cohort</td>
<td>740</td>
<td>55, head trauma with neurological impairment ranging from temporary loss of consciousness to deep coma</td>
<td>All patients with neurological signs and/or symptoms were seen in consecutive order by a specialist neurologist over a period of 8 months in 2003</td>
<td>Incidence</td>
</tr>
<tr>
<td>Kithikii et al, 2011</td>
<td>Kenya</td>
<td>Urban referral hospital</td>
<td>Retrospective cohort</td>
<td>608</td>
<td>608; traumatic intracranial hematoma</td>
<td>All pts who were admitted and diagnosed with traumatic intracranial hematoma between 1/2000 and 12/2009</td>
<td>TBI characteristics, TBI etiology, patient demographics</td>
</tr>
</tbody>
</table>
Potential Economic Benefit of Treatment for Severe Traumatic Brain Injury in Uganda:

Research Master's Paper

Introduction

Traumatic brain injury (TBI) is a leading cause of morbidity and mortality, resulting in death or hospitalization for at least 10 million people every year. Globally, TBI contributes to an estimated 425 years of healthy life lost due to disability (YLDs) per 100,000 annually, making it the foremost cause of death and disability in people under the age of 40 years old. As of 1996, worldwide approximately 57 million people were living with TBI serious enough to require at least one hospitalization. The largest burden of disease attributable to TBI is in low- and middle-income countries (LMICs), particularly those within sub-Saharan Africa. Increasing trends in incidence of TBI in these countries are due to greater population density and higher rates of injury. Limited health care access and resources further exacerbate TBI death and disability. For example, an estimated 15% of incident skull fracture injury patients receive treatment in sub-Saharan Africa compared to 90% in high-income countries. LMICs are also known to experience worse outcomes and higher mortality rates associated with severe TBI, defined by a Glasgow Coma Scale (GCS) score from 3 to 8, when compared to high- and middle-income countries. Given its predilection for young adults and projected increase in incidence within the next decade, TBI death and disability will continue to affect the most productive sector of the sub-Saharan African workforce.

Appropriate hospital intervention, including prompt critical care and neurosurgical treatment to minimize secondary brain injury, plays a crucial role in decreasing the morbidity and mortality attributable to severe TBI. Expanding access to critical care and neurosurgical treatment through investment in training and technology not only improves community health status, increases the number and quality of health care professionals, and contributes to overall health care capacity development and systems strengthening, but it also has potential to
reduce the significant economic burden posed by TBI in low and middle income countries (LMICs). Unfortunately, standardization of treatment across a wide variety of settings is complicated by severe resource limitations within many of the countries that are disproportionately affected.\textsuperscript{6} This reality necessitates evidence-based decision making in resource allocation prioritization and health care sector planning. Cost-effectiveness analysis is a mechanism used by policymakers in many countries and the World Health Organization for determining whether the initiation or continuation of a medical or surgical intervention is providing benefit that is reasonably proportional to cost.\textsuperscript{10,11} Although interventions focusing on infectious disease (e.g. immunizations) have been traditionally emphasized throughout the global health community for their low benefit to cost ratios, recent evidence suggests that surgical treatment and emergency care for potentially disabling traumatic injuries are comparably cost-effective.\textsuperscript{12-14}

While the economic burden on TBI in the United States has been extensively studied,\textsuperscript{15} we are not aware of any studies assessing the potential economic impact of treatment for TBI in a sub-Saharan African (SSA) or other LMIC. For this study, we used a cohort of patients with severe TBI at the primary national hospital in Uganda as a case study to evaluate the benefit in terms of disability-adjusted life years (DALYs) averted and the broader economic impact of severe TBI treatment, including neurosurgical and critical care.
Methods

Setting and Subjects

New Mulago Hospital is a 1,500-bed national referral hospital located in Kampala, which is the largest city and capital of Uganda. It serves approximately 1.6 million people living in Kampala residents and 1.5 million people living in neighboring districts and beyond. Since 2007, the hospital has benefited from a twinning program with Duke University Medical Center and Duke Global Health Institute called the Duke Global Health PLUS (Placement of Life-changing and Usable Surplus) Program. The Duke Global Health PLUS Program provided contextually appropriate anesthesia machines, hemodynamic monitoring equipment, and surgical equipment for the five elective operating rooms, a recovery room, and an intensive care unit (ICU) at New Mulago Hospital. Additionally, the program began training camps run by Duke neurosurgeons, anesthesiology personnel, surgical operating room nurses and technicians, ICU specialists, recovery and floor nurses and clinical engineers. Annual training camps and continuing medical educations (CME) courses are held for four of Uganda’s five neurosurgeons, in addition to Ugandan anesthesiology personnel, nurses, and clinical engineers.

A 13-month period from May 2008 to June 2009 was selected as a representative sample of patients with severe TBI (n=127) who were treated through the efforts of the New Mulago Hospital faculty and staff with support from the Duke Global Health PLUS Program. We performed secondary analysis of data collected through retrospective clinical surveillance on all patients who received conservative and surgical treatment for severe TBI, defined by a presenting GCS of 3 to 8, at New Mulago Hospital during this study period. The following variables were included in the data set: age, gender, mechanism of injury, computed tomography (CT) result, lowest and highest GCS with dates, presenting blood pressure, signs/symptoms (i.e. vomiting, pupil fixation, pupil symmetry), surgical procedure, ancillary treatment, incident date, admission date, operation date, discharge date, and discharge status. The Ugandan health care providers were trained to treat severe TBI according to the Brain
Trauma Foundation guidelines. Therefore we assumed that all patients were treated in adherence to these guidelines to the extent possible given limitations associated with the resource setting.\textsuperscript{17} We scored each patient using the core International Mission for Prognosis and Analysis of Clinical Trials in TBI (IMPACT) model, which is an international, externally validated prognostic model that provides the probability of outcomes at 6 months following treatment by GOS category (i.e. mortality represented by GOS 1, unfavorable outcome represented by GOS 2-3, and favorable outcome represented by GOS 4-5).\textsuperscript{18}

\textit{Quantification of Averted DALYs}

The DALY is a health parameter that measures premature mortality and morbidity associated with an illness or disease, where one DALY represents one year of healthy life lost. DALYs are calculated by adding years lost due to disability (YLD) to years of life lost (YLL) using the following basic formulas: $\text{DALYs} = \text{YLD} + \text{YLL}$, where $\text{YLD} = I \times D \times DW$, $\text{YLL} = N \times LD$, $I$ = incident cases, $D$ = duration of illness, $DW$ = disability weight (i.e. expert-derived determinations of social preferences and valuations of health ranging from 0 to 1, where 0 represents complete health and 1 represents death), $N$ = number of deaths and $LD$ is life expectancy at age of death. For the purpose of sensitivity analysis, DALY calculations are frequently modified to take into account discounting (i.e. factoring in preference for health in the present relative to health in the future) and age-weighting (i.e. factoring in relative value for a year of health life depending on age). By calculating the difference between DALYs in a cohort of treated individuals and DALYs in a cohort of counterfactual untreated individuals, averted DALYs are provided as a measure of the premature death and disability averted by treatment.\textsuperscript{19}

We calculated the number of averted DALYs attributable to treatment for incident severe TBI at New Mulago Hospital during the study period. We assumed that untreated patients would die without treatment and have no years of life lost due to disability (i.e. $\text{YLD}=0$ and $\text{DALYs} = \text{YLL}$); and we assumed that treated patients would have an average-weighted outcome based
on GOS category probabilities predicted using the IMPACT core model.\textsuperscript{18} Disability weights were determined for each GOS category using World Health Organization (WHO) definitions of disability weighting.\textsuperscript{20} The disability weight for GOS-1, that is death, is 1; GOS-2 and GOS-3, characterized by vegetative state and severe disability respectively, have a combined disability weight of 0.8275; and the most favorable outcome, GOS-4 and GOS-5, representing moderate disability and good recovery respectively, have a combined disability weight of 0.203. For simplification, outcome-associated disability weights were applied immediately at the age of the severe TBI diagnosis as opposed to 6 months following the severe TBI diagnosis as predicted by the IMPACT core model.\textsuperscript{18} Duration of illness was assumed to be the mean Ugandan life expectancy at the age of death.\textsuperscript{21} As recommended in the DALY literature, we calculated unweighted averted DALYs with no age-weighing or discounting (i.e. DALYs[0,0,0]); weighted averted DALYs with an age weighting factor that peaks at 25 years ($\beta=0.04$) and a 3\% discount rate (i.e. DALYs[3,1,0.04]); and weighted averted DALYs with an age weighting factor peaking at two-thirds of mean Ugandan life expectancy during the study period ($\beta=0.03$) and a 3\% discount rate (i.e. DALYs[3,1,0.03]).\textsuperscript{22}

\textit{Quantification of Economic Benefit}

The potential benefits attributable to treatment for severe TBI were translated into economic terms using two methodologically sound approaches. Economists advocate converting DALYs averted into dollars using the concepts of human capital by way of the Gross National Income (GNI) per capita and the value of a statistical life (VSL).\textsuperscript{23} The human capital approach, calculated by multiplying the GNI per capita by DALYs averted, is considered a more conservative estimate of economic benefit because it is based on the idea that an individual’s societal value is determined by their potential contribution to the national economy and it does not factor in associated social benefits (e.g. decreased expense for family). We calculated an upper and lower limit of economic benefit with the human capital approach using the
unweighted [0,0,0] and weighted [3,1,0.04] averted DALYs, respectively. The mean Uganda GNI per capita was calculated from the World Bank data.\textsuperscript{24}

The VSL approach represents a more generous estimate of economic benefit that reflects the amount of money a group of people is willing to pay to reduce premature mortality. As such, the VSL approach takes the value of welfare into consideration more so than the value of productivity produced by the human capital approach.\textsuperscript{23,25,26} Uganda, like many LMICs, does not report a VSL, thus country-specific VSL was estimated using of the VSL in the USA using the following formula: VSL(Uganda) = VSL(USA)\times[GNI(Uganda)/GNI(USA)]^{IE-VSL}, where VSL(USA) is $8.3 million (in 2012 USD),\textsuperscript{27,28} GNI(USA) is $46,380 (in 2012 USD) and GNI(Uganda) is $1,180 (in 2012 USD),\textsuperscript{24} and IE-VSL is income elasticity of VSL (IE-VSL of 0.55 estimates the upper limit and IE-VSL of 1.5 estimates the lower limit of VSL).\textsuperscript{23,29} We then calculated the economic benefit with the VSL approach using the following formula: Economic benefit = V\times avertedDALYs(3,1,0.03), where V is the constant value of a statistical life year.\textsuperscript{25,29}

To estimate broader health and economic benefit, we calculated the average averted DALYs and economic gain per patient for each method by dividing the total averted DALYs and economic benefit by the number of patients in each group. Assuming the New Mulago Hospital catchment area population of around 3 million people is a representative sample of the Ugandan population of around 34 million people, roughly 1,500 Ugandans could potentially benefit from treatment for severe TBI every year.\textsuperscript{16,30} Using this ratio and the average averted DALYs and economic gain per patient, potential health and economic benefit for all of Uganda was approximated.
Results

Clinical Data

One hundred twenty-seven patients received treatment for severe TBI at New Mulago Hospital from May 2008 to June 2009. The mean age at treatment was 26 years and 69% of the patients were under the age of 40 years (n=88). Road traffic accidents (68%) and assault (17%) accounted for the majority of cases. Of the 28 patients who underwent neurosurgery, half received craniotomies, 8 received craniectomies, and 6 received burr holes. The in-hospital surgical mortality rate was 53%. Sixteen surgical patients (57%) were discharged or died with improved GCS scores (i.e. greater than 8). The majority of patients were treated conservatively (n=99); 18% of conservatively treated patients died before discharge and 84% were discharged or died with improved GCS scores.

Averted DALYs and Economic Benefit

One hundred twenty-seven cases of severe TBI were treated at New Mulago Hospital averting 1,448 DALYs [0,0,0], 1,075 DALYs [3,1,0.04], or 974 DALYs [3,1,0.03] (Table 1). Using the human capital approach, the economic benefit of intervention ranged from approximately $1.3 million to $1.7 million. The VSL approach estimated an economic benefit of $282,902 to over $11 million (Table 2). Conservatively treated patients were estimated to receive more economic gain than patients treated with neurosurgical intervention (Table 3). For Uganda, this correlates to between about 11,000 and 17,000 averted DALYs per year and an annual potential economic benefit of $15 million to $20 million using the human capital approach and $3.3 million to $130 million using the VSL approach, without taking into account the cost of treatment.
Discussion

To our knowledge, this study is the first to attempt quantification of the health and economic benefits of conservative and neurosurgical treatment for severe TBI in an LMIC or in SSA. Traumatic brain injury is a leading cause of loss of life and function in the developing world. Consistent with the findings in our study, the majority of TBI in countries worldwide is caused by road traffic injuries. LMICs have the highest disease burden of TBI due to massive growth in motor vehicle numbers, higher numbers of people injured per crash, poor enforcement of traffic safety regulations, inadequate public health infrastructure, and poor access to health services. Moreover, our study demonstrated TBI’s predilection for males and young adults, who are the most productive sector of the developing world workforce. Given the growing incidence of TBI, and understanding of the health and economic burden associated with TBI is paramount.

Data on the burden of disease attributable to TBI in SSA are based on expert-derived estimates due to lack of standardized TBI surveillance systems in most countries throughout the world. Increased data collection efforts are required in order to strengthen our understanding of the most pressing problems affecting LMICs. In the present study, we used the data from a cohort of patients at the national referral hospital of Uganda to evaluate the long-term impact of treatment for severe TBI during a 13-month study period. This cohort was used as a representative sample for assessing severe TBI-related health benefit using averted DALYs and economic benefit using the human capital and VSL approaches for all of Uganda. The VSL approach for converting averted DALYs into dollars is the more widely accepted methodology for approximating economic benefit due to its basis in human behavior. However, even the most conservative estimates reveal a health benefit of 974 averted DALYs [3,1,0.03] with a respective economic benefit of over $280,000 (VSL approach) for patients treated at New Mulago Hospital and a health benefit of 11,00 averted DALYs [3,1,0.03] with a respective
economic benefit of $3.3 million (VSL approach) for patients treated all throughout Uganda over the course of 13-months.

The present study is limited by its reliance on a set of assumptions. Long-term data was not available for any of the patients, which necessitated the use of a predictive model. While the IMPACT models have been externally validated and are widely used, other prognostic models have been shown to be more accurate for cohorts with TBI in LMICs.\textsuperscript{18,33,34} However, our data set contained an inadequate amount of detail to fill in all of the variables necessary to compute outcome probabilities using these other models. Another limitation is the lack of published literature investigating the effects of severe TBI on the life expectancy of Ugandans. While severe TBI has been shown to confer an increased risk of mortality in high-income countries, the practical effect that this may have on premature mortality given poorer general health and shorter life expectancies remains unclear.\textsuperscript{30,35} Also, many studies that assess the economic benefit associated with treatment include the treatment cost per averted DALY, however, inadequate cost data prevented us from doing so.\textsuperscript{25,29} Finally, the limitations associated with using averted DALYs as an appropriate measure of avoidable morbidity and mortality, have been well-documented elsewhere.\textsuperscript{36,37}

Conclusions

Our study suggests that the health and economic burden associated with severe TBI is extensive in Kampala and we conclude that nationwide treatment for severe TBI may provide economic benefit between $3.3 million and $130 million for Uganda. The amount of economic gain produced from treating a small cohort of patients indicates the importance of treatment for severe TBI in developing countries in sub-Saharan Africa. We hypothesize that other LMICs would similarly benefit significantly from decreasing the death and disability associated severe TBI. Programs focusing on increased training and technology transfers in order to contribute to
health care capacity development and systems strengthening, as well as growth of initiatives focusing on prevention, are essential to reducing the global burden of TBI.
References


Table 1. Total DALYs averted from severe TBI treatment at New Mulago Hospital

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<thead>
<tr>
<th>Treatment</th>
<th>Cases</th>
<th>Total DALYs Averted</th>
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<tr>
<td></td>
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<td>DALYs [3,1,0.04]</td>
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<tr>
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<td>952</td>
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<tr>
<td>Neurosurgical</td>
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<td>123</td>
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<td>Total</td>
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<td>1075</td>
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Table 2. Economic benefit of severe TBI at New Mulago Hospital (in USD)

<table>
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<tr>
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<th>Upper Limit</th>
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<tbody>
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<tr>
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<td>$1,708,640</td>
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<tr>
<td>VSL</td>
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### Table 3. Economic gain per patient (in USD)

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<th>Methodology</th>
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</thead>
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