

Costs and benefits of neurosurgical intervention for infant hydrocephalus in sub-Saharan Africa

Clinical article

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Object. Evidence from the CURE Children's Hospital of Uganda (CCHU) suggests that treatment for hydrocephalus in infants can be effective and sustainable in a developing country. This model has not been broadly supported or implemented due in part to the absence of data on the economic burden of disease or any assessment of the cost and benefit of treatment. The authors used economic modeling to estimate the annual cost and benefit of treating hydrocephalus in infants at CCHU. These results were then extrapolated to the potential economic impact of treating all cases of hydrocephalus in infants in sub-Saharan Africa (SSA).

Methods. The authors conducted a retrospective review of all children initially treated for hydrocephalus at CCHU via endoscopic third ventriculostomy or shunt placement in 2005. A combination of data and explicit assumptions was used to determine the number of times each procedure was performed, the cost of performing each procedure, the number of disability-adjusted life years (DALYs) averted with neurosurgical intervention, and the economic benefit of the treatment. For CCHU and SSA, the cost per DALY averted and the benefit-cost ratio of 1 year's treatment of hydrocephalus in infants were determined.

Results. In 2005, 297 patients (median age 4 months) were treated at CCHU. The total cost of neurosurgical intervention was \$350,410, and the cost per DALY averted ranged from \$59 to \$126. The CCHU's economic benefit to Uganda was estimated to be between \$3.1 million and \$5.2 million using a human capital approach and \$4.6 million–\$188 million using a value of a statistical life (VSL) approach. The total economic benefit of treating the conservatively estimated 82,000 annual cases of hydrocephalus in infants in SSA ranged from \$930 million to \$1.6 billion using a human capital approach and \$1.4 billion–\$56 billion using a VSL approach. The minimum benefit-cost ratio of treating hydrocephalus in infants was estimated to be 7:1.

Conclusions. Untreated hydrocephalus in infants exacts an enormous price from SSA. The results of this study suggest that neurosurgical intervention has a cost/DALY averted comparable to other surgical interventions that have been evaluated, as well as a favorable benefit-cost ratio. The prevention and treatment of hydrocephalus in SSA should be recognized as a major public health priority. (DOI: 10.3171/2011.8.PEDS11163)

KEY WORDS • hydrocephalus • economics • benefit-cost ratio • endoscopic third ventriculostomy • choroid plexus cauterization • ventriculoperitoneal shunt • Africa • disability-adjusted life year

CONDITIONS requiring surgical care, including neurosurgical interventions, account for a significant portion of the global burden of disease.^{4,11,24,40,46} Access to neurosurgical treatment can have a substantial

Abbreviations used in this paper: CCHU = CURE Children's Hospital of Uganda; CPC = choroid plexus cauterization; DALY = disability-adjusted life year; ETV = endoscopic third ventriculostomy; GNI = gross national income; IE-VSL = income elasticity of VSL; PIH = postinfectious hydrocephalus; PPP = purchasing power parity; SSA = sub-Saharan Africa; VSL = value of a statistical life.

impact on morbidity and mortality and is a key component in reducing the burden of disease and contributing to health system strengthening; however, its development in resource-limited countries has not been a global health priority. As with other surgical treatments, determining whether neurosurgical interventions can be cost-effective in the developing world should be evidence-based rather than relying on the conventional assumption that neurosurgery is impractical in resource-limited settings. Primary consideration should then be given to investing in innovative sustainable technologies, delineating ef-

ficient delivery systems, and training local providers to optimize interventions that are determined to be the most cost-effective.

In SSA, hydrocephalus in infants may alone represent more than 100,000 new cases per year.³⁵ Yet, excluding South Africa, SSA has fewer than 100 neurosurgeons.⁹ Treatment for hydrocephalus in infants at CCHU is effective and sustainable.^{36,38–41,43–45} Although it is a successful example of providing neurosurgical intervention in a resource-limited country, this model has not been broadly supported and implemented, in part because there are few data on the economic burden of disease or the cost and benefit of treatment.

There have been few attempts at measuring the costs and benefits of any surgical intervention in a developing country,^{13,14,29} and we are aware of no such analysis for a neurosurgical intervention. In the present study we used the CCHU as a case study, as well as a methodology that translated into dollars the DALYs averted by the treatment paradigm used in that institution, to provide an analysis of the costs and benefits of 1 year of hydrocephalus treatment at that facility.² We then considered the broader economic impact of hydrocephalus in infants and its treatment in SSA.

Methods

Estimating Averted DALYs and Economic Benefits of Treatment

Detailed explanations of the DALY and the methods used to estimate the costs and benefits of treatment are presented in the *Appendix*. Here, we provide an overview of essential features that are necessary for understanding the terminology and principles used in the results.

Health economists use the DALY to estimate the burden of disease and to perform cost-effectiveness analysis. One DALY is equal to 1 year of healthy life lost, which can result from either death or disability, with disability weights used to adjust for differences in severity across disabilities (0 = complete health, 1 = death). Averted DALYs provide a measure of the health benefits generated by medical interventions. We determined the number of averted DALYs by first calculating the number of DALYs assuming no treatment of hydrocephalus in infants, by then calculating the number assuming treatment, and by finally subtracting the latter from the former. We accounted for both the mortality and morbidity rates of treated and untreated infants. We calculated the DALYs from birth to death, and so our estimates of averted DALYs represent the long-term health benefits of treatment.

Disability-adjusted life years depend on assumptions about discounting and age weighting. Discounting converts future DALYs to present values and enables the DALYs that occur at different points in time to be compared and summed. Discounting future DALYs is standard practice, and we used the 3% discount rate suggested by Murray and Acharya.²⁶ Age weighting is a different concept that reflects the tendency of humans to value a year of healthy life more highly during the middle years of

life than at the beginning or the end. The notation DALYs (r, K, β) is used to signify whether DALYs have been adjusted for age and discounted, where r is the discount rate, K is the modulation of age weighting (0 = age weights off, 1 = age weights on), and β is the age-weighting parameter. We considered 3 scenarios: DALYs (0,0,0), that is, no discounting or age weighting; DALYs (3,1,0.04), discounting at 3% and an age-weighting parameter of 0.04; and DALYs (3,1, β), discounting at 3% and an age-weighting parameter linked to life expectancy.

Two approaches were applied in this study to translate DALYs to dollars. The first, known as the human capital approach, was originally suggested for use with DALYs in the WHO study *Macroeconomics and Health*.²⁸ This method assumes that a person, much like a machine, is annually worth what they produce and contribute to the national economy. To value a DALY using the human capital approach, we used PPP estimates of GNI/capita. The second approach utilizes a concept known as the VSL, which is related to individuals' willingness to pay for actions that reduce their risk of death. Sanctioned for use in cost-benefit analysis by the US government,^{10,32} the VSL methodology produces estimates that are 1 to 2 orders of magnitude greater than the human capital approach and, because it reflects attitudes toward changes in risk, it can exceed lifetime earnings. For example, the VSL used by the Environmental Protection Agency is \$7.4 million dollars.¹⁰ Assuming a 40-year working life, an annual income that equals the 2009 GNI/capita of \$45,640, and a discount rate of 3%, the lifetime earnings of an average American is approximately \$1,054,958 or just 14% of the VSL used by the Environmental Protection Agency. Economists have developed an approach for transferring estimates of VSL from countries where empirical studies have been performed to countries where they have not.³⁴ Central to this approach is a concept known as the "income elasticity of VSL" (IE-VSL), which indicates whether VSL increases more or less than proportionately with income. For example, an IE-VSL of 1.5 indicates that a 1% increase in income results in a 1.5% increase in VSL.

Study Cohort and Clinical Methods at CCHU

To assess the economic benefit of a previously reported treatment paradigm during 1 year at CCHU, a database review was undertaken to determine the method of treatment and the outcomes for all patients who underwent an initial operation for hydrocephalus at CCHU during the year 2005. This was a year during which one of the authors (B.C.W.) was living and working at CCHU full-time as the primary surgeon and was responsible for recording the operative data. Appropriate institutional approval was obtained.

Although ventriculoperitoneal shunts have been the standard treatment for hydrocephalus for 50 years, most shunts eventually fail. This failure presents a life-threatening emergency that requires urgent surgical intervention. Few children in SSA have access to this kind of care, rendering shunt dependence an especially life-threatening condition in this environment. Prospective clinical studies at CCHU have demonstrated the efficacy of ETV, along with improved outcomes in infants when combin-

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ing this procedure with CPC, as an alternative treatment for hydrocephalus of various etiologies.^{36,38,39,41,43–45} Endoscopic third ventriculostomy/CPC has a lower rate of infection and failure compared with shunt placement and, unlike shunt failure, which remains a life-long possibility, most ETV failures occur within 6 months during infancy when the clinical course is typically safer and less precipitous.⁴⁰ Furthermore, based on established clinical parameters, those children at higher risk for ETV failure can be identified early.^{43,44} When endoscopic treatment is unsuccessful, an inexpensive simple shunt has been shown to be as effective as a shunt commonly used in North America at 5% of the cost.³⁷ Thus, the initial treatment for hydrocephalus in all infants at CCHU was ETV (typically combined with CPC).³⁸ In those in whom treatment failed or those for whom ETV was not technically feasible, an inexpensive shunt was placed.³⁷

Cost of Treatment at CCHU

The financial cost per procedure for ETV as well as for shunt placement was determined for CCHU by using standard accounting methods, taking into account all salaries, overhead, capital costs (including depreciation of equipment and building), supplies, and all clinical services before and after surgery. The cost data were for 2010 and were reported in Ugandan shillings (2010 USh), while treatment in our patient cohort occurred in 2005. Changes in the treatment paradigm and the cost structure of CCHU between 2005 and 2010 were insubstantial. We converted 2010 USh to 2005 USh by using the gross domestic product deflator to adjust for inflation. We used the gross domestic product deflator instead of the consumer price index because the former includes prices of both consumption and investment goods and thus better reflects the mix of items included in treatment costs. We then converted from 2005 USh to US\$ using the 2005 official exchange rate (<http://www.oanda.com/currency/converter/>).

The average financial cost in 2005 was determined to be \$670 for each ETV/CPC procedure and \$470 for each shunt placement. The cost of shunting was kept low because we used an inexpensive shunt widely available in the developing world.³⁷ The use of shunts typically implanted in North America would more than double the total cost of each shunt operation. Patients who had a successful ETV beyond 6 months were considered “cured” with no need for further treatment since ETV failure beyond this time frame is rare.⁴⁰ Based on the work of previous investigators suggesting an average of 2–4 shunt revisions in the first 10 years after shunt placement, patients who underwent shunting were assumed to require an average of 2 additional operations for revisions over the course of their lifetime.²⁷ For the purposes of our analysis, we assumed that the first shunt revision took place during the 1st year of life and that the second revision took place in the 5th year of life. Because money has a time value, we discounted the cost of the second revision using the same 3% rate as described in the DALY section above. The total cost of these 2 additional operations was determined to be \$875 (\$470 + \$405).

Financial costs, which are the market-based costs ac-

tually incurred by an organization, are typically less than the full economic costs incurred by society. To facilitate comparison with other studies that have calculated a cost per DALY averted by using financial costs^{3,15,25} as opposed to economic costs, we used the above financial data when we calculated the cost per DALY averted (\$670 for ETV/CPC, \$470 for initial shunt, and \$875 for shunt revisions).

To calculate a benefit-cost ratio, however, additional adjustments had to be made to ensure that we did not underestimate economic costs. To convert financial costs to economic costs, we adjusted the salary component of the aforementioned costs upward by a factor of 2.93, which is the ratio of two estimates of 2005 Ugandan GNI per capita reported by the World Bank: the PPP estimate (\$880) and the Atlas estimate (\$300; <http://data.worldbank.org/>). The accounting estimates of CCHU salaries are conceptually more similar to the Atlas estimates, but development economists prefer PPP estimates, which better ensure comparability across countries. This adjustment ensures comparability of our cost estimates to our benefit estimates, which use PPP estimates in the calculation of VSL. It is also important for the extrapolation of costs to other countries in SSA.

Pertinent costs also include those incurred by the patient’s family. Mothers typically come with the child being treated. Although most mothers of children treated at CCHU are subsistence farmers rather than wage earners, the opportunity cost of their time must be accounted for. We made the simple assumption that this equals \$5.41/day (patients were in the hospital an average of 5 days), which is the 2005 GNI/capita (PPP) for SSA each divided by an assumed 300-day work year (<http://data.worldbank.org/>). We also assumed a \$10 round-trip cost for transportation between home and hospital.

With these adjustments, the average economic cost of the hospital procedures was determined to be \$1190 for each ETV/CPC procedure, \$980 for each shunt placement, and \$1830 for the 2 assumed shunt revisions. These costs were used to determine the benefit-cost ratio for neurosurgical intervention for hydrocephalus in infants.

Estimated Annual Cases of Hydrocephalus in Infants in SSA

To gauge the potential economic benefit of 1 year of neurosurgical intervention for all cases of hydrocephalus in infants in SSA, a modeling approach based on publicly available retrospective data was used to estimate the total number of new cases of hydrocephalus in 2005 in SSA. In developed countries the incidence of hydrocephalus in infancy (the 1st year of life) is 3–5/1000 live births.⁵ With an estimated 30,000,000 births in SSA in 2005, this rate implies that between 90,000 and 150,000 new infant cases of hydrocephalus occurred in that year. In marked contrast to developed countries, however, 60% of hydrocephalus cases in infants in Uganda is postinfectious.³⁹ It is therefore possible that the number of sub-Saharan African infants having hydrocephalus in 2005 was between 225,000 and 375,000 if one adds cases of PIH that would not have occurred in the developed world.³⁵ For the purposes of the present study, we assumed a conservative

estimate of 82,000 new cases of hydrocephalus in infants, which adjusts the minimum estimate of 90,000 cases of hydrocephalus in infancy for baseline SSA infant mortality (88 deaths/1000 live births in 2005), ignoring the fact that some of these infant deaths were themselves related to hydrocephalus (<http://data.worldbank.org/>).

Results

Clinical Data for 2005 at CCHU

Two hundred ninety-seven children received their initial treatment for hydrocephalus at CCHU in 2005 (Fig. 1). The mean and median ages at treatment were 10 and 4 months, respectively. Postinfectious hydrocephalus accounted for 187 of the cases (63%), consistent with our prior observations.³⁹ Of 215 patients who underwent ETV, 125 had combined ETV/CPC and 90 had ETV alone because of an age > 12 months, the presence of PIH with aqueduct obstruction (based on our previously reported results³⁸), or obliteration of the choroid plexus by scarring. Thirty of those who underwent ETV were lost to follow-up and 2 died within 30 days of surgery (1 from complications of a brain tumor). Of the remaining 183 patients who had a completed ETV and sufficient follow-up, treatment was successful in 113 (62%) in that they required no subsequent operations (mean and median follow-up 16 and 12 months, respectively). Given the rarity of late ETV failure, continued success in these patients was assumed. In 82 children, 90% of whom had PIH, the ETV attempt was abandoned (due to cisternal scarring, anatomical distortion, or poor visibility) for shunting (75 patients) or reservoir placement (7 patients); in this latter group, 3 patients underwent shunting and 4 were lost to further intervention. Initial treatment with ETV failed in 70 children and required an additional operation. Among these patients, 20 underwent repeat endoscopy (11 for re-opening of closed ETV and 9 for shunt placement). Of the 11 repeat ETVs, 5 were successful and 5 failed and required a third operation (4 shunts and 1 successful repeat ETV); 1 patient died of an unrelated accident. Of the other 50 patients in whom initial ETV failed, 49 underwent shunting at the second operation and 1 had a reservoir placed and was lost to further intervention.

Among the 265 patients with more than 1 month of follow-up, there were 3 operative deaths (1.1%). For all 297 children, there were 148 shunt operations (including reservoir placements) and 227 endoscopic procedures (total of 375 operations). Our previously reported operative mortality rate (death from any cause within 30 days) for patients who underwent ETV with or without CPC at CCHU for 2001–2007 was 1.3%,⁴⁴ and the operative mortality rate for patients who underwent shunt placement was 4%.³⁷ The higher mortality for shunt placement may reflect the higher risk for the PIH patient population in which ETV is most likely to be aborted or to fail. Given that a number of patients were lost to follow-up before 1 month, some of whom may have died, these previously established operative mortalities were assumed when calculating the DALYs averted. We also assumed that each patient who underwent shunting would undergo 2 revi-

sions, for a total of 3 operations per patient. This would result in 444 shunt operations, with an assumed 4% mortality per procedure. This would predict 18 shunt-related and 3 endoscopy-related deaths for the 2005 cohort over time. For the 2005 cohort of 297 patients, the total of 21 deaths would therefore estimate a cumulative 7% procedure-related mortality.

Economic Benefit to Uganda

Two hundred ninety-seven cases of infantile hydrocephalus were treated in 2005, averting 5921 DALYs (0,0,0), 3488 DALYs (3,1,0.04), or 2796 DALYs (3,1,β) (Table 1).

When the human capital approach is used to value averted DALYs, a lower bound estimate can be calculated by multiplying DALYs (3,1,0.04) by GNI/capita (PPP) and an upper bound can be calculated by multiplying DALYs (0,0,0) by GNI/capita (PPP). The resulting range of economic benefits of neurosurgical intervention at CCHU in 2005, not accounting for the cost of treatment (considered in the next section), was \$3.1 million–\$5.2 million (Table 2).

For the VSL approach, the range of economic benefits also depends on assumptions about the IE-VSL. We considered 3 scenarios: IE-VSL = 1.5 (Scenario 1), = 1 (Scenario 2), or = 0.55 (Scenario 3). The resulting total economic benefit of hydrocephalus treatment in infants at CCHU in 2005, again not accounting for treatment costs, was \$4.7 million for Scenario 1, \$32.5 million for Scenario 2, and \$188 million for Scenario 3 (Table 3).

Cost of Treatment

The total numbers of operations for the 2005 cohort were 148 shunt operations and 227 endoscopic procedures. This made for a total financial cost of (148 × \$470) + (227 × \$670), or \$221,650 for the calculated benefit of averting 5921 DALYs (0,0,0), 3488 DALYs (3,1,0.04), or 2796 DALYs (3,1,β), taking into account the expected sequelae and mortality of surgery. This resulted in an average overall cost of \$37–\$80/DALY averted during the initial treatment period. Assuming 2 more shunt operations over time for each shunt-treated patient meant an additional cost of 148 × \$875, or \$129,500. This would add \$22–\$46 to the total lifetime cost/DALY averted, or \$59–\$126/DALY averted over the lifetime of the 2005 cohort.

Potential Annual Economic Benefit if all Hydrocephalus in Infants Were Treated in SSA

If all of the conservatively estimated 82,000 annual cases of infant hydrocephalus in SSA in 2005 had been treated, assuming the same treatment methods, outcomes, and costs as those for CCHU, 1.79 million DALYs (0,0,0), 1.05 million DALYs (3,1,0.04), or 837,000 DALYs (3,1,β) would have been averted (Table 1). Using a human capital approach, the potential economic benefit, not accounting for costs, would be \$930 million–\$1.58 billion (Table 2), while a VSL approach suggested an economic benefit of \$1.4 billion using IE-VSL Scenario 1, \$9.8 billion using Scenario 2, and \$56.3 billion using Scenario 3 (Table 3).

To calculate the benefit-cost ratio for treating infant

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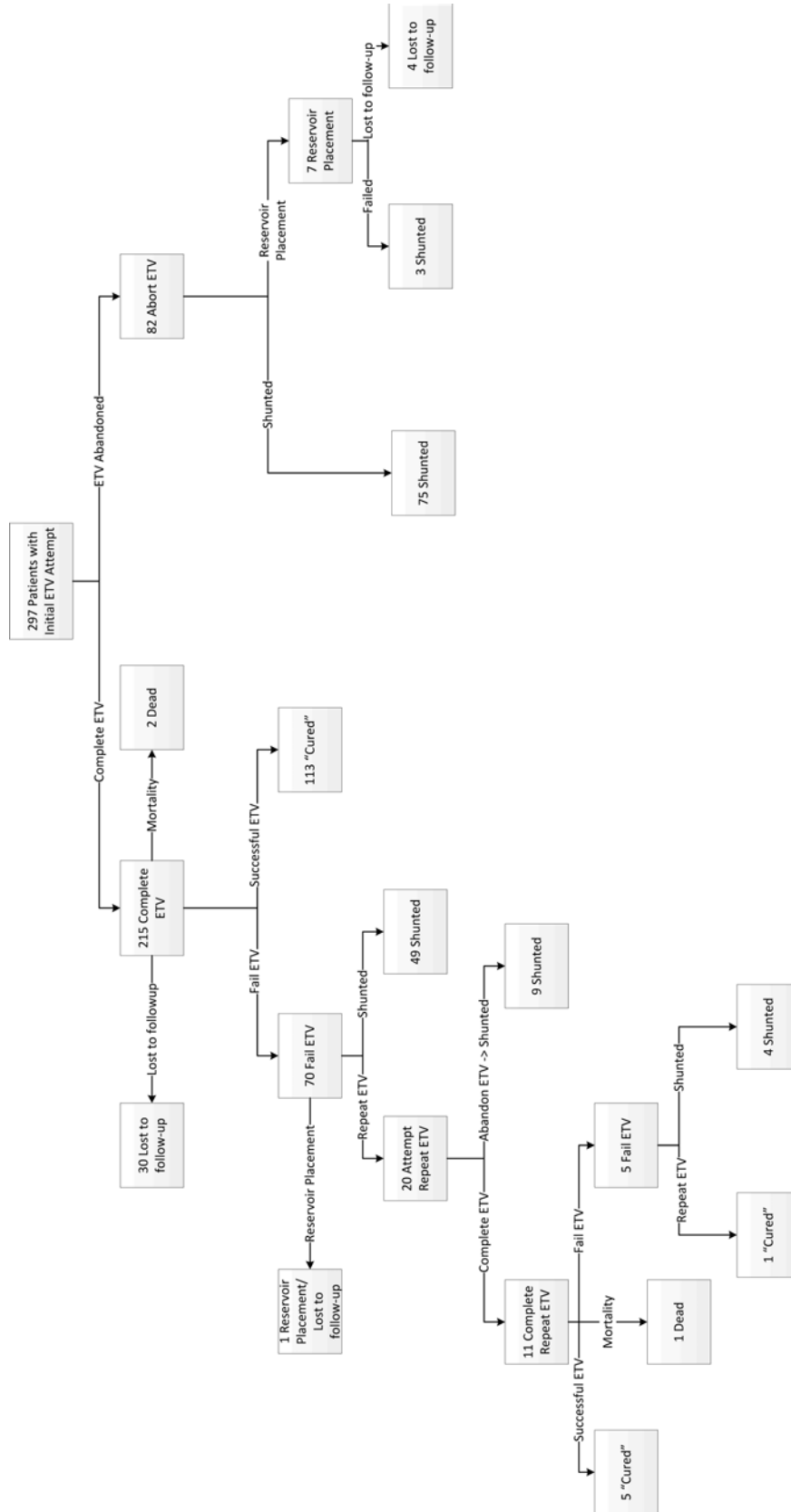


Fig. 1. Treatment and outcome flowchart for 2005 CCHU cohort.

TABLE 1: Total DALYs in Uganda (CCHU) and sub-Saharan Africa potentially averted with neurosurgical intervention

Area	Total DALYs (thousands)		
	3,1,β	3,1,0.04	0,0,0
Uganda	2.8	3.5	5.9
SSA	840	1,060	1,790

hydrocephalus in all of SSA in 2005, the total number of necessary ETV/CPC and shunt operations was extrapolated from the CCHU cohort of 297 patients to the estimated 82,000 cases of hydrocephalus in infants. The broader economic cost incurred by society, as opposed to the more restricted financial cost incurred by hospitals, was used to determine the total cost of each procedure. An estimated 62,700 ETV/CPC procedures at \$1190 per operation would cost \$74.6 million, and 40,900 shunt operations at an initial cost of \$980 per operation and an additional \$1830 for 2 shunt revision procedures would result in a cost of \$115 million. The total economic cost of treating all cases of infant hydrocephalus in 2005 would therefore have been \$189.6 million. Using the minimum potential economic benefit from the VSL approach, the treatment of all 82,000 cases would have resulted in \$1.4 billion of total lifetime economic benefits. These numbers imply a minimum benefit-cost ratio of 7:1. Using the benefit of \$9.8 billion from Scenario 2 implies a benefit-cost ratio of up to 50:1.

Discussion

This study is the first to assess the health burden, cost of treatment, and benefit of treatment for hydrocephalus in infants in a developing country or in SSA. Hydrocephalus is the most common neurosurgical disease in children and is a treatable condition. Nontreatment almost always leads to death or significant disability. An understanding of the disease burden in pediatric hydrocephalus in SSA has been evolving.^{35,40} Until recently, the important role of neonatal infection as an etiology for hydrocephalus in infants had not been appreciated.^{21,39} Postinfectious hydrocephalus arising from ventriculitis is the most common cause of pediatric hydrocephalus in Uganda, accounting for 60% of cases.³⁹ The majority of these cases arise from neonatal sepsis in the 1st month of life. These cases likely increases the overall expected incidence of hydrocephalus in infants beyond the 3–5/1000 live births reported for developed countries,⁵ where PIH is comparatively rare. We emphasize that PIH cases represent only a sub-

TABLE 2: Present value of economic impact of neurosurgical intervention for infant hydrocephalus using human capital approach*

Area	DALYs (3,1,0.04)	DALYs (0,0,0)
Uganda	3.1	5.2
SSA	930	1,600

* Values expressed in millions of US dollars.

TABLE 3: Present value of economic impact of neurosurgical intervention for infant hydrocephalus using VSLY approach*

Area	VSLY with DALYs (3,1,β)		
	Scenario 1†	Scenario 2‡	Scenario 3§
Uganda	4.6	32.5	188
SSA	1,400	9,800	56,300

* Values expressed in millions of US dollars.

† Scenario 1: Income Elasticity of VSL (IE-VSL) = 1.5.

‡ Scenario 2: IE-VSL = 1.0.

§ Scenario 3: IE-VSL = 0.55.

set of the infants who survive their initial neonatal sepsis and subsequently suffer hydrocephalus. It is estimated that sepsis develops in 1–2 million newborns each year in SSA.³³ Rates of neonatal sepsis as high as 170/1000 live births have been reported in developing countries, and community-based studies from several countries in SSA suggest around 10 deaths/1000 live births from neonatal infection.³¹ The incidence of PIH among surviving infants is not known.

In the present study, we attempted to derive the long-term economic impact of an actual treatment program for hydrocephalus in infants at 1 hospital in Uganda during a single year and, more broadly, the hypothetical long-term economic impact of similarly treating all cases that occur in a single year throughout SSA. Although an estimate of a quarter million sub-Saharan African infants who may have hydrocephalus in their 1st year of life is plausible, the present study assumes a conservative estimate of 82,000 cases per year. Therefore, the calculated results for the economic benefits of treating this disease are likely to be underestimates.

Results in the present study gauge the economic impact to Uganda of infant hydrocephalus treatment at CCHU during 2005, as well as the potential impact in SSA if all infant cases occurring in 1 year were treated using a similar paradigm. Of the 2 approaches used for valuing averted DALYs, we have more confidence in the VSL approach than in the human capital approach, as it is more widely accepted in the economic literature and is based more directly on actual human behavior.²

Burden of Disease and Benefit of Treatment

Little has been written about the burden of diseases requiring surgery in SSA. The annual total number of surgical DALYs, or the DALYs that could be averted with surgical intervention, was recently estimated for several conditions in Africa for 2002.⁸ The estimates were discounted but not age weighted [that is, DALYs (3,0,0)]. To make an appropriate comparison, we recalculated, according to the same assumptions, our estimate of the total number of DALYs for SSA in 2005 that could have been averted by treating hydrocephalus in infants. The resulting estimate, 895,000 DALYs (3,0,0) for SSA in 2005, is comparable to the published 2002 estimates of surgical DALYs for all malignancies (2 million), perinatal conditions (2 million), congenital anomalies (2 million), and cataracts and glaucoma (1 million) on the continent. Nev-

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ertheless, ours is the first report to highlight hydrocephalus in infants as a serious health burden in any region of the developing world.

Even less has been written about the economic benefits of addressing diseases requiring surgery. We assessed the annual economic benefit to Uganda of actual treatment at a single institution. Depending on whether one favors the human capital approach or (as we do) the VSL approach, the estimated long-term benefits of treating the 2005 cohort ranged from \$3.1 million to \$187 million. The result of applying the same analysis to SSA is arresting, even when using a conservative estimate of annual case numbers. According to the human capital approach, the potential economic benefit would be \$930 million–\$1.6 billion, whereas the VSL approach suggests an economic benefit of \$1.4 billion–\$56.3 billion. The closest comparison for these estimates is the potential economic benefit of treating all cases of cleft lip and palate in SSA in 1 year, which was recently assessed at \$252 million–\$441 million (human capital approach) or \$5.4 billion–\$9.7 billion (VSL approach).² In part, the much larger estimate for hydrocephalus in infants reflects the much higher mortality rate for untreated hydrocephalus than for untreated cleft lip and palate. In fact, the cleft lip and palate study focused exclusively on the consequences of morbidity.

Cost of Treatment

The cost of initial hydrocephalus treatment for the 2005 cohort was \$37–\$80/DALY, taking into consideration operative mortality and repeat surgery for early treatment failure. However, the expected cost over the lifetime of the cohort was estimated at \$59–\$126/DALY after accounting for an anticipated average of 2 additional operations for shunt failure among those who were shunt dependent. Thus, the greater the number of children who are shunt dependent, the more expensive the treatment, especially if more expensive shunt systems are used. It should also be noted that, unlike the case for shunt dependence, successful treatment via ETV carries a low risk of later failure in the older child after the fontanel has closed, when treatment failure becomes a life-threatening emergency. Therefore, the greater the fraction of patients successfully treated with ETV in a given cohort, the lower the cost and probably the greater the long-term survival in regions where urgent access to treatment for shunt failure is unavailable. Developing the capacity for endoscopy as the primary treatment strategy for hydrocephalus in infants receives additional support from the fact that shunt malfunctions are unlikely to be promptly treated in SSA, which raises the ultimate cost and mortality of shunt dependence to levels beyond those assumed in our analysis.

The initial (\$37–\$80/DALY) and estimated lifetime (\$59–\$126/DALY) cost of treatment for hydrocephalus at CCHU compare favorably with other public health interventions that have been studied. Nonsurgical examples include \$185–\$759/DALY averted for rotavirus vaccination in Thailand⁶ and \$670/DALY averted for a pneumococcal vaccination program in The Gambia.¹⁹ Comparable surgical examples include \$172 and \$223/DALY averted for trauma surgery in Nigeria and Haiti, respectively, and \$362/DALY averted for elective orthopedic operations in

Haiti.¹⁴ An analysis for groin hernia surgery at a hospital in Ghana suggested a low cost of around \$12.88/DALY averted.²⁹ Our findings strongly support development of the capacity to treat hydrocephalus in the developing world, especially in terms of a treatment paradigm that includes endoscopic treatment and avoids shunt dependence. This strategy has not been viewed as a funding priority by global health agencies, governments, and non-government organizations.

Untreated hydrocephalus in infants exacts an enormous price from SSA, and a large fraction of these cases could be prevented by public health strategies that prevent or efficiently treat neonatal sepsis. Preliminary work has identified *Acinetobacter* species as a potentially important pathogen in Uganda;²¹ however, the predominant organisms may vary over time and region. More work is necessary to identify the relevant pathogens and their patterns of infection in different regions of SSA to develop effective treatment and prevention strategies. Efficient evidence-based prevention and treatment of neonatal sepsis would not only prevent PIH, but should also protect even larger numbers of infants from death or irreversible neurocognitive disability. The prevention and treatment of hydrocephalus in SSA should be recognized as a major public health priority.

Limitations of the Study

The limitations of the DALY are well documented elsewhere.³ As pertains to this study, it is important to note that the DALY was not originally constructed to value the economic benefit of reducing the burden of disease. And yet, we believe it serves as a reasonable proxy for a lost year of life due to death, disability, or a combination of the two, and we adjusted parameter values in the DALY formulas (in particular, the age-weighting parameter) to make our DALY estimates conceptually consistent with the economic approaches we used to value them.

We adjusted the DALYs averted by neurosurgery by assuming that 60% of treated patients would have lifetime motor deficits, 25% would have hearing or visual deficits, 30% would have epilepsy, and 37% would have mild to severe cognitive impairment. These adjustments were based on studies from developed countries where, on the one hand, posthemorrhagic hydrocephalus of prematurity would be much more common than in SSA and, on the other hand, PIH would be much less common.^{18,22} As with posthemorrhagic hydrocephalus of prematurity, one would expect a substantial rate of disability among treated survivors of PIH. A recent assessment of PIH survivors 5–11 years following treatment at CCHU showed that approximately 40% had evidence of significant disability and around 60% were not attending school.⁴² This result appears reasonably consistent with the assumptions used for adjustments in the present study, where PIH cases accounted for 63% of the treatment group.

Conclusions

Our work suggests that total annual DALYs for hydrocephalus in infants in SSA are comparable to the total annual surgical DALYs for malignancies, perinatal con-

ditions, congenital anomalies, glaucoma, and cataracts, and 10 times those for cleft lip and palate. We concluded that a single year's treatment of hydrocephalus in infants can generate a long-term economic benefit of at least \$1.4 billion and perhaps as much as \$56 billion for SSA. A single hospital in eastern Uganda providing treatment for hydrocephalus in 297 children during 2005 generated \$4.6 million–\$187 million of long-run economic benefits in that country. The initial cost of treatment was \$37–\$80/DALY averted, with an estimated lifetime treatment cost (with shunt maintenance) of \$59–\$126/DALY averted. This cost compares favorably to the costs of a few other surgical interventions that have been studied in similar settings. The most conservative estimate of the benefit-cost ratio for treating hydrocephalus in infants in SSA is 7:1 and could be as high as 50:1.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Warf, Alkire, Vincent, Meara. Acquisition of data: Warf, Alkire. Analysis and interpretation of data: Warf, Alkire, Hughes, Schiff, Vincent, Meara. Drafting the article: Warf, Alkire, Bhai, Hughes, Meara. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Warf. Statistical analysis: Alkire, Vincent. Administrative/technical/material support: Alkire, Meara. Study supervision: Warf, Meara.

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Appendix

Economic Methodology and DALYs

We present a brief introduction to the techniques used in this study. For a complete discussion, see “Potential economic benefit of cleft lip and palate repair in sub-Saharan Africa” by Alkire et al.²

The basic formula for calculating the number of DALYs due to incident disease in a population is $DALYs = YLD + YLL$, $YLD = I$

$\times D \times DW$, and $YLL = N \times (LE - d)$, where YLD is years lost due to disability; YLL, years of life lost; I, incident cases; D, duration of illness; DW, disability weight; N, total number of deaths due to disease; LE, life expectancy; and d, age at death.

As noted in the text, 2 approaches were used to translate DALYs to dollars. We make 3 additional points about the VSL approach here. First, a VSL estimate from a country where empirical studies have been performed (Country A) can be transferred to one where they have not (Country B) by using information on the ratio of per capita income between the countries (Country B’s GNI per capita/Country A’s GNI per capita) and the income elasticity (IE-VSL).³⁴ When a VSL estimate is transferred from a higher-income country to a lower-income country, the predicted VSL for the lower-income country will be higher if the IE-VSL is lower. Viscusi and Aldy³⁴ suggest an IE-VSL of 0.5–0.6. A recent study by Hammitt and Robinson¹⁷ suggested that a substantially larger IE-VSL (≥ 1) should be used when transferring VSL estimates from high-income to low-income countries and that sensitivity analysis should be performed using a range of IE-VSL estimates. Consequently, in the present study we used 3 values for the IE-VSL: 0.55, 1, and 1.5. Following an authoritative review on valuing fatality risks,³⁴ in all cases we used GNI/capita estimates based on the PPP method.

Second, recent research suggests that the VSL of a child is around 1.8 times that of an adult. Therefore, the benefit of reducing fatality risks to children is valued at almost 2 times the benefit of reducing such risks to adults.¹⁶ Third, the value of a statistical life year (VSLY) is the annualized equivalent of VSL, and it is what was used in this study to value a DALY. Research indicates that the VSLY changes over one’s lifetime, peaking at about two-thirds of life expectancy.¹

Calculating DALYs Averted and the Economic Benefit of Treatment at CCHU During 2005

To calculate the DALYs averted due to neurosurgical intervention, we used previously published data that outline the natural history of untreated hydrocephalus in infants and the frequency of enduring sequelae (motor and sensory deficits, cognitive impairment) after neurosurgical intervention for hydrocephalus.^{7,18,22} For this model, we assumed that untreated hydrocephalus resulted in mortality outcomes similar to those described in the most robust analysis of the natural history of infant hydrocephalus known to us.²⁰ Neurosurgical intervention was assumed to avert these deaths, after adjusting for baseline SSA mortality. Since treated patients have substantial rates of disability, we adjusted the DALYs averted by neurosurgery by assuming that 60% of treated patients would have lifetime motor deficits, 25% would have hearing or visual deficits, 30% would have epilepsy, and 37% would have mild to severe cognitive impairment.^{18,22} Disability weights from the previously published studies^{23,30} were used to estimate the years lost to disability due to postsurgical sequelae. Furthermore, we assumed our previously reported 1.3% operative mortality rate for each ETV procedure³⁸ and 4% operative mortality rate for each shunt placement,³⁷ resulting in a cumulative operative mortality rate of 7% for patients. To calculate the DALYs averted as a result of treatment, we used the following equation: $DALYs \text{ averted} = (DALYs \text{ if untreated}) - (DALYs \text{ if treated})$.

Figures 2 and 3 provide a visual representation of the assumptions used in this paper for the 2005 CCHU cohort of 297 patients. The same assumptions were applied to the cohort of 82,000 cases in all of SSA. Figure 2 shows the assumed outcome of patients if there were no treatment, and Fig. 3 shows the assumed outcome of patients in the context of neurosurgical intervention.

Calculating DALYs

When valuing DALYs with the human capital approach, we used DALYs both without age weighting or discounting [DALYs (0,0,0)] and with the age-weighting factor from the Global Burden of Disease study and a 3% discount rate [DALYs (3,1,0.04)], as the

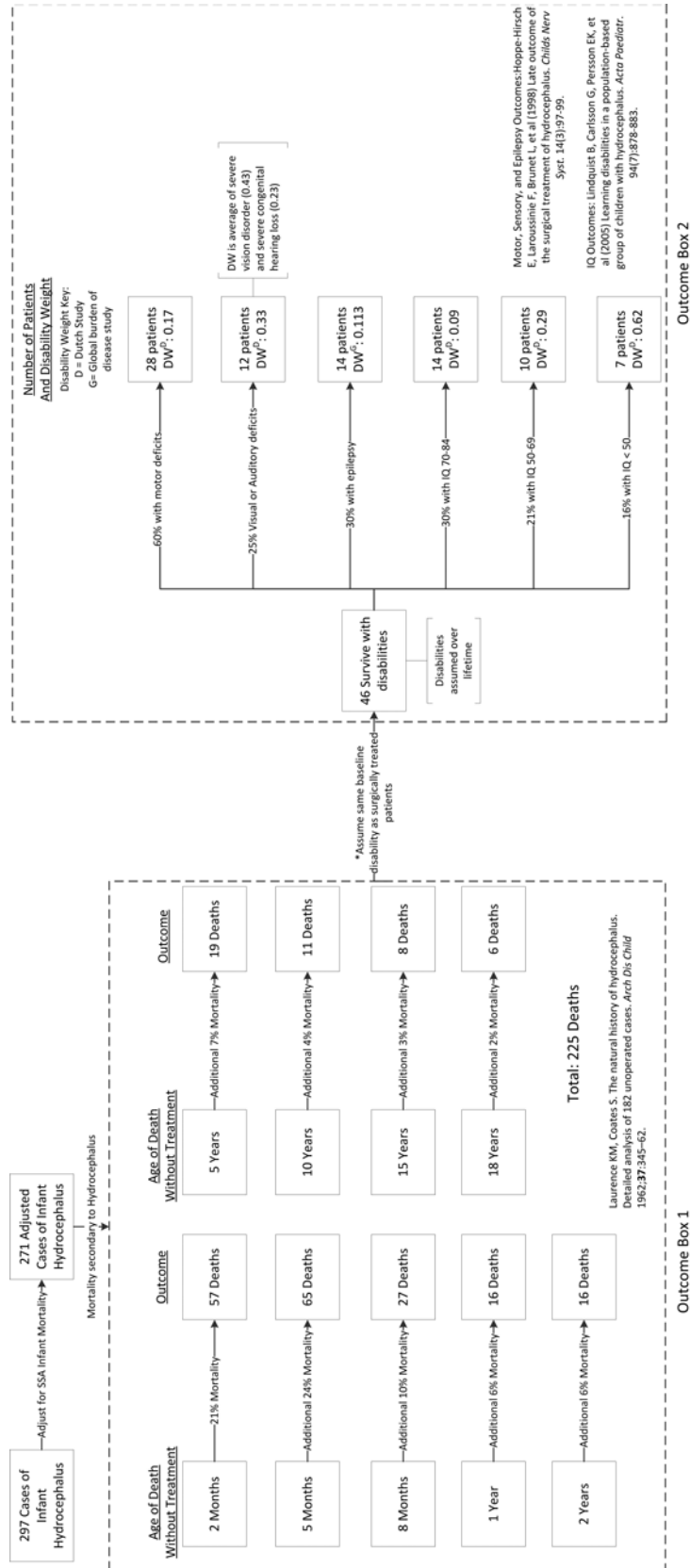


Fig. 2. Flowchart showing assumed outcomes for 2005 CCHU cohort if they had not undergone neurosurgical intervention (see Appendix). Dashed-line boxes indicate that the outcomes in that box contribute toward total DALYs; solid-line boxes indicate that the outcomes in that box do not contribute toward total DALYs.

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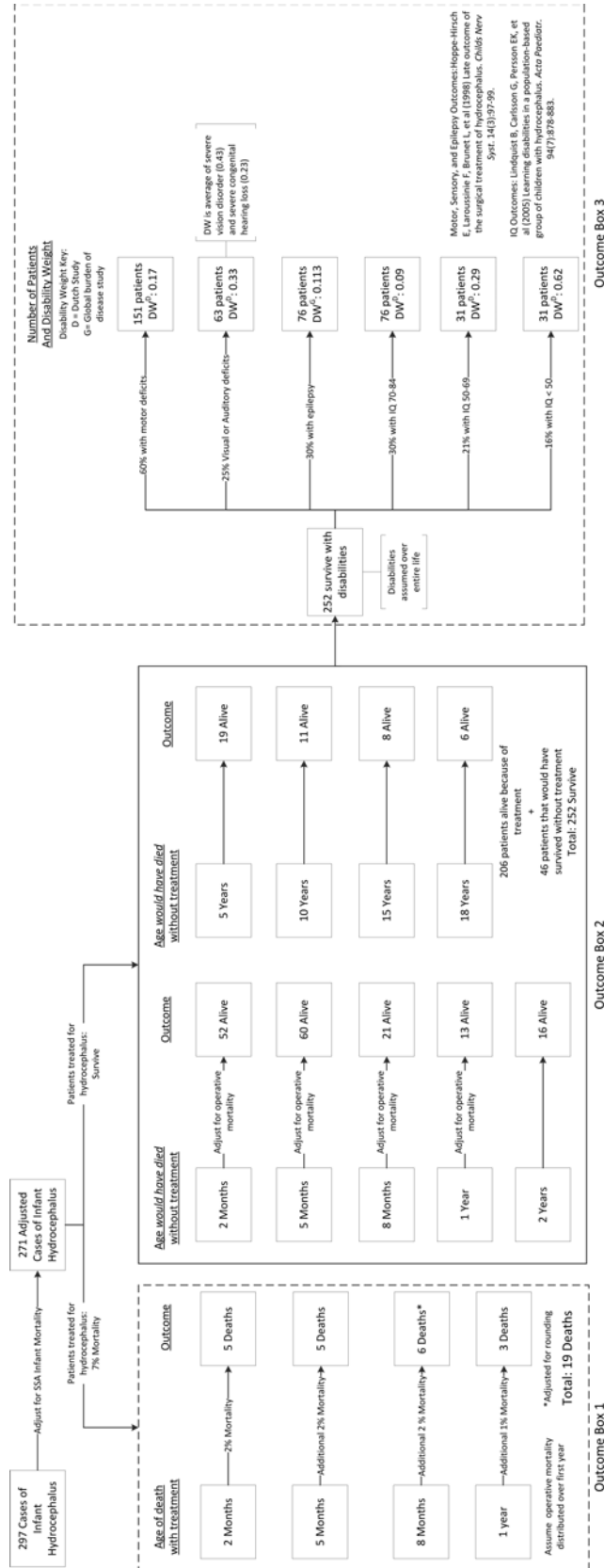


Fig. 3. Flowchart showing assumed outcomes for 2005 CCHU cohort having undergone neurosurgical intervention (see Appendix). Dashed-line boxes indicate that the outcomes in that box do not contribute toward total DALYs; solid-line boxes indicate that the outcomes in that box do contribute toward total DALYs.

cost-effectiveness literature suggests calculating both for the purpose of performing a sensitivity analysis.¹² We calculated them using the following equation:²⁶

$$DALYs = \int_a^L \{ [K \cdot DW \cdot C x e^{-\tilde{\alpha}x} e^{-r(x-a)}] + [DW \cdot (1-K) e^{-r(x-a)}] \} dx,$$

where a is age at the onset of disease; L is the country-specific life expectancy if calculating YLLs, or the age at the onset of disease plus the duration of disease if calculating YLDs; K is the age-weighting modulation constant (0 = no age weights, 1 = full age weights); DW is the disability weight (1 for death); C is the age-weighting correction constant from the Global Burden of Disease study; x is the age integrated over the duration of disease (YLDs), or age integrated over the duration of years of life lost (YLLs); r is the discount rate; and β is the age-weighting constant from the Global Burden of Disease study (0.04).²³ The function $(1/\beta)$ defines at which age the DALY age-weighting factor peaks. Hence, a β of 0.04 would result in the age-weighting factor peaking at age 25 years.

For DALYs valued using the VSLY approach, we calculated DALYs (3,1, $\tilde{\beta}$) using the following formula:

$$DALYs = \int_a^L \{ [DW \cdot \tilde{C} x e^{-\tilde{\beta}x} e^{-r(x-a)}] \} dx,$$

where the 2 key differences from the previous equation are as follows: 1) the absence of K – DALYs are always age-weighted ($K = 1$) when used with VSLY, as empirical research shows that VSLY varies with age;¹ and 2) the presence of $\tilde{\beta}$ and \tilde{C} . Since evidence indicates that VSLY peaks at about 2/3 of life expectancy,¹ we adjusted the age-weighting factor in the DALY formula so that it peaks at 2/3 of the life expectancy of each country in SSA. The tilde above β and C indicates that country-specific age-weighting parameters and correction constants were used. Since $(1/\beta)$ is the age at which the age-weighting factor peaks, we used the following expression to determine $\tilde{\beta}$ for each country in SSA so that its age-weighting factor peaked at 2/3 of the country's life expectancy (LE): $\tilde{\beta} = 1 / [(2/3) \cdot LE]$.

The value of C was also country specific, as it varies with β according to Table 5.2 in *The Global Burden of Disease and Risk Factors*.²³ We fit a cubic polynomial to the values in that table and used it to predict \tilde{C} for a given value of $\tilde{\beta}$.

Converting DALYs to Economic Benefits

We valued DALYs (3,1,0.04) and DALYs (0,0,0) using a human capital approach, so that each DALY averted was valued at a country's GNI/capita in 2005 (\$880 in Uganda) (<http://data.worldbank.org/>). To value DALYs using the VSLY approach, we first estimated country-specific VSL in Uganda using the following formula:³⁴

$$VSL(CSSA) = VSL(USA) \cdot \left[\frac{GNI\ p.c.\ (CSSA)}{GNI\ p.c.\ (USA)} \right]^{IE-VSL},$$

where $VSL(CSSA)$ is the value of a statistical life in a country in SSA, $VSL(USA)$ is the value of a statistical life in the US (\$7.4 million),¹⁰ $GNI\ p.c.(CSSA)$ is the GNI/capita in a country in SSA, $GNI\ p.c.(USA)$ is the GNI/capita in the US in 2005, and $IE-VSL$ is the income elasticity of VSL. We used 3 scenarios for $IE-VSL$ based on Viscusi and Aldy³⁴ and Hammitt and Robinson.¹⁷ Scenario 1 assumes an $IE-VSL$ of 1.5 and results in the lower limit of VSL estimates, Scenario 2 assumes an $IE-VSL$ of 1.0, and Scenario 3 assumes an $IE-VSL$ of 0.55 and results in the upper limit of VSL estimates. For childhood mortality, we adjusted the country-specific VSLs to account for the fact that society values the life of a child roughly 1.8 times an adult's VSL.¹⁶

To calculate the potential economic benefit of an intervention

that averts a given number of DALYs (3,1, $\tilde{\beta}$) using a VSL approach, we multiplied DALYs (3,1, $\tilde{\beta}$) by the value of a statistical life year. $VSLY_x$, the value of a statistical life-year at age x , is given by

$$VSLY_x = V \cdot \tilde{C} x e^{-\tilde{\beta}x},$$

where V is the age-neutral (constant) value of a statistical life year, and $\tilde{C} x e^{-\tilde{\beta}x}$ is the age-weighting factor found in the original DALY formula adjusted to peak at 2/3 of life expectancy. Note that using the DALY age-weighting factor creates internal consistency with the age weighting of DALYs and the VSLY.

The formula for estimating the economic benefit of an intervention using a VSLY approach with DALYs (3,1, $\tilde{\beta}$) can therefore be written as follows:

$$Economic\ Benefit = \int_a^L \{ [DW \cdot VSLY_x \cdot e^{-r(x-a)}] \} dx.$$

Substituting the equation for $VSLY_x$ in the economic benefit formula results in the following:

$$Economic\ Benefit = \int_a^L \{ [DW \cdot V \cdot \tilde{C} x e^{-\tilde{\beta}x} \cdot e^{-r(x-a)}] \} dx.$$

If the constant V is moved out of the integral, the economic benefit formula can be rewritten as follows:

$$Economic\ Benefit = V \int_a^L \{ [DW \cdot \tilde{C} x e^{-\tilde{\beta}x} \cdot e^{-r(x-a)}] \} dx,$$

which by substituting the equation for DALYs using the VSLY approach reduces to

$$Economic\ Benefit = V \cdot DALYs\ (3,1,\tilde{\beta}).$$

The DALY formula already contains the age-weighting factor ($\tilde{C} x e^{-\tilde{\beta}x}$), and so we need only multiply DALYs (3,1, $\tilde{\beta}$) by V , not $VSLY_x$, which would result in double age weighting.

Assuming one has already calculated DALYs (3,1, $\tilde{\beta}$), the only variable left to calculate is V , the age-neutral value of a statistical life year. It is defined by the following expression:

$$VSL = \int_0^{LE} V \cdot \tilde{C} x e^{-\tilde{\alpha}x} e^{-r(x-a)} dx,$$

where VSL is the country-specific value of a statistical life, LE is the country-specific life expectancy, and other variables are as defined above. Move the constants outside of the integral:

$$VSL = V \cdot \tilde{C} \int_0^{LE} x e^{-\tilde{\alpha}x} e^{-r(x-a)} dx.$$

Solve the formula for V and integrate:

$$V = \frac{VSL}{\tilde{C}} \cdot \frac{(\tilde{a} + r)^2}{1 - e^{-(\tilde{a} + r)LE} [1 + LE(\tilde{a} + r)]}.$$

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Calculating Annual Economic Benefit of Treating Hydrocephalus in all Infants in SSA

We used the natural history, sequelae, and surgical mortality assumptions found above, as well as country-specific life expectancies, to estimate DALYs (0,0,0), DALYs (3,1,0.04), and DALYs (3,1, β) averted if all of the estimated 82,000 cases of hydrocephalus in infants in SSA were treated. We then estimated the potential economic benefit of treating all of these cases by using the human capital approach to value DALYs (3,1,0.04) and DALYs (0,0,0) and the VSLY approach to value DALYs (3,1, β), and by summing the estimates across countries in SSA.