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Long-term healthcare utilisation, costs and quality of life after invasive group B *Streptococcus* disease: a cohort study in five low-income and middle-income countries

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ABSTRACT

Introduction There are no published data on the long-term impact of invasive group B *Streptococcus* disease (iGBS) on economic costs or health-related quality of life (HRQoL) in low-income and middle-income countries. We assessed the impact of iGBS on healthcare utilisation, costs and HRQoL in Argentina, India, Kenya, Mozambique and South Africa.

Methods Inpatient and outpatient visits, out-of-pocket (OOP) healthcare payments in the 12 months before study enrolment, and health-state utility of children and caregivers (using the EuroQol 5-Dimensions-3-Level) were collected from iGBS survivors and an unexposed cohort matched on site, age at recruitment and sex. We used logistic or Poisson regression for analysing healthcare utilisation and zero-inflated gamma regression models for family and health system costs. For HRQoL, we used a zero-inflated beta model of disutility pooled data.

Results 161 iGBS-exposed and 439 unexposed children and young adults (age 1–20) were included in the analysis. Compared with unexposed participants, iGBS was associated with increased odds of any healthcare utilisation in India (adjusted OR 11.2, 95% CI 2.9 to 43.1) and Mozambique (6.8, 95% CI 2.2 to 21.1) and more frequent healthcare visits (adjusted incidence rate ratio (IRR) for India 1.7 (95% CI 1.4 to 2.2) and for Mozambique 6.0 (95% CI 3.2 to 11.2)). iGBS was also associated with more frequent days in inpatient care in India (adjusted IRR 4.0 (95% CI 2.3 to 6.8) and Kenya 6.4 (95% CI 2.9 to 14.3)). OOP payments were higher in the iGBS cohort in India (adjusted mean: Int$682.22 (95% CI Int$364.28 to Int$1000.16) vs Int$133.95 (95% CI Int$72.83 to Int$195.06)) and Argentina (Int$244.86 (95% CI Int$47.38 to Int$442.33) vs Int$52.38 (95% CI Int$−1.39 to Int$106.1)). For all remaining sites, differences were in the same direction but not statistically significant for almost all outcomes. Health-state disutility was higher in iGBS survivors (0.08, 0.04–0.13 vs 0.06, 0.02–0.10).

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Internationally, there is a scarcity of data on the long-term health utilisation, costs and health-related quality of life after invasive group B *Streptococcus* disease (iGBS). This is the first study to assess these outcomes in low-income and middle-income countries (LMICs).

WHAT THIS STUDY ADDS

⇒ Indicators suggest that iGBS is associated with significantly higher healthcare utilisation and costs compared with unexposed children in Mozambique, Kenya and India. Similar non-statistically significant trends were found in Argentina and South Africa. These are the first estimates showing that iGBS might be associated with increased long-term costs to families and to the healthcare system in at least some LMIC countries, and the first LMIC estimates of health-related quality of life among iGBS survivors and their caregivers.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Maternal vaccines against iGBS are in development but their cost-effectiveness needs to be assessed before there is a case to bring them to market. To enable a comprehensive understanding of the economic burden of iGBS, there is a need for larger studies in LMICs with population-based surveillance, more reliable measures of exposure (including severity) and longer cohort follow-up with more frequent and comparable assessment of healthcare usage and costs. Our findings underline the importance of large cohort studies and the need for earlier identification and care of affected families, including financial protection.

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Conclusion The iGBS health and economic burden may persist for years after acute disease. Larger studies are needed for more robust estimates to inform the cost-effectiveness of iGBS prevention.

INTRODUCTION

Group B *Streptococcus* (GBS) is a leading cause of invasive bacterial disease in neonates and young infants (<90 days old), causing substantial mortality and morbidity from sepsis and meningitis.[1 2] Globally, it is estimated that there are 231 800 (114 100–455 000) early-onset and 162 200 (70 200–394 400) late-onset invasive GBS disease (iGBS) cases a year in infants, causing 58 000–91 000 deaths. The burden of iGBS morbidity and mortality is higher in low-income and middle-income countries (LMICs), with nearly half of the global burden in sub-Saharan Africa, even though the continent only has 13% of the world's population.[3]

Several studies have recently addressed knowledge gaps about the long-term outcomes of iGBS. One study across five LMICs found that infants who survived acute iGBS meningitis or sepsis have an increased long-term risk of neurodevelopmental impairment (NDI), including intellectual, motor, vision and hearing impairments.[4] The adjusted risk ratio (aRR) for any NDI in children with a history of iGBS was 1.74 (95% CI 1.34 to 2.26) when compared with non-exposed children, however, the aRR for moderate/severe NDI among iGBS survivors in the study was 1.27 (95% CI 0.65 to 2.45).[4] In Denmark and the Netherlands, infants with a history of iGBS were approximately two times more likely to suffer from long-term NDI compared with those who did not experience iGBS.[5] Globally, it was estimated that 37 100 (14 600–96 200) infants who recover from iGBS develop moderate or severe NDI every year.[3]

Despite the growing evidence on the risk of long-term sequelae, there remains a scarcity of data on the long-term economic outcomes of iGBS, especially in LMICs.[6] Until recently, the only estimates available on long-term costs of iGBS were for children aged two or younger in the UK.[7] Authors observed that health and social care costs for children who had iGBS were two times higher compared with non-iGBS children. The mean societal cost was £6145 higher among iGBS cases than among non-iGBS controls (95% CI £4370.8 to £7918.6).[7] Recently, in Denmark, history of iGBS was associated with more frequent outpatient clinic visits (incidence rate ratio (IRR) 1.83, 95% CI 1.67 to 2.00) and hospital admissions (1.43, 95% CI 1.37 to 1.50) in children aged 10 years or younger.[5]

Data on health-related quality of life (HRQoL) are also scarce, particularly in LMICs. A Dutch cost-effectiveness study assessed HRQoL using the HUI-3 instrument among survivors of early-onset iGBS aged 2–8 years old whose parents were members of the Dutch Foundation of Parents of GBS patients. However, this study did not report the health-state utility values.[8] A more recent cost-effectiveness study in the UK, using the PedsQL to assess HRQoL in iGBS survivors aged 3–5 years old, reported health-state utility decrements of 0.002 in children with mild sequelae, 0.056 with moderate sequelae and 0.299 with severe sequelae.[9]

Understanding the long-term impact of iGBS on economic outcomes and HRQoL is vital to inform assessments of the value of interventions such as screening and future maternal vaccines.[10–13] As highlighted by Hutubessy *et al*'s framework, in addition to direct health benefits, data on the broader benefits of vaccination, such as societal, economic and educational outcomes, are necessary to fully capture the full value of vaccination.[14] However, there are no published data on the long-term costs or HRQoL for children with a history of iGBS in LMICs. This is especially important given that Africa and Asia suffer the largest burden of iGBS.

The aim of this study was to compare long-term healthcare utilisation, healthcare-related costs and HRQoL between children with a history of iGBS and those with no history of iGBS in five LMIC sites.

METHODS

Study design and data collection

This study is part of a larger multicountry matched cohort study that assessed the long-term outcomes after iGBS including NDI and the acute costs of neonatal sepsis and meningitis (protocol and results previously reported).[4 15] Here, we present and analyse previously unpublished data on long-term healthcare utilisation, costs and HRQoL after iGBS. The outcomes are described in more detail below and in online supplemental table 1. Costs were calculated from both the perspective of the patient and patient's family for out-of-pocket (OOP) payments (which included hospital and clinicians' fees, tests, medications and assistive devices) and from the perspective of the healthcare provider for health system costs. For health system costs, we asked patients and their families about their utilisation of healthcare and converted this into financial costs in local currency using 2010 WHO-CHOICE costs.[16] WHO-CHOICE costs take the health system perspective, regardless of payer. The WHO-CHOICE inpatient unit costs present the estimated cost per hospital bed-day, excluding the cost of drugs and diagnostic tests but including costs such as personnel, capital and food costs. The WHO-CHOICE outpatient unit costs define the estimated cost per outpatient visit and include all cost components except drugs and diagnostics.

Participants and exposure

We identified five sites in three regions with a high burden of iGBS: Asia (India), Latin America (Argentina) and sub-Saharan Africa (Kenya, Mozambique and South Africa). Information on each site and detailed methods have been published separately[15] and are summarised in online supplemental methods. Briefly, children with a

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previous bacteriologically confirmed diagnosis of either GBS meningitis or sepsis (see online supplemental methods for case definitions) in the first 90 days of life and who were at least 18 months old were identified via hospital records, Health and Demographic Surveillance Systems, or from previous epidemiological studies. Children with no history of iGBS in the hospital records, the Health and Demographic Surveillance Systems or from previous epidemiological studies were matched to iGBS survivors based on site, sex and age. The matching ratio was targeted at 1:3.

Trained fieldworkers contacted the parents/primary caregivers of potential participants about the study. Reasons for non-participation were recorded. Children enrolled in the study and their main caregiver attended an in-person assessment visit. Written informed consent was obtained in-person before the assessment. At the assessment, data relevant to this study were collected on paper or a tablet-based custom-designed application (see online supplemental methods for questionnaire).

Outcomes and potential confounding variables

We compared the following outcomes reported by families of iGBS survivors and of matched non-iGBS children for the 12 months preceding study recruitment separately in each of the five sites: usage of any health service (outcome 1), total number of healthcare visits (outcome 2a) and number of each type of healthcare visit, for example, inpatient care, emergency care, outpatient clinic, etc (outcome 2b), number of days spent in inpatient care (outcome 3), OOP healthcare payments (outcome 4), total cost of healthcare to the health system (outcome 5a), costs of each type of healthcare visit to the health system (outcome 5b), costs of coping with healthcare payments (outcome 6) and HRQoL measured using the EuroQoL 5-Dimensions-3-Level (EQ-5D-3L) instrument (outcome 7)[17] (see online supplemental table 1 for details). All costs (outcomes 4 and 5) were inflated and presented in undiscounted 2022 Int$ using methods from Turner *et al*.[18]

We captured information on the following potential confounding variables: participants' age at recruitment, sex (male, female), preterm birth (<37 weeks, ≥37 weeks) and main caregiver education at time of recruitment (no/early childhood education, primary, secondary, college/university) as a proxy for socioeconomic position. We selected these variables a priori and decided we would retain them in the analyses irrespective of the statistical significance of their association because of their potential importance as confounding factors.

Statistical analysis

We conducted a complete case analysis. To compare any healthcare utilisation (outcome 1) between study cohorts separately in each country, we first calculated frequencies and percentages of healthcare utilisation and corresponding 95% CIs. We estimated unadjusted ORs and associated 95% CIs using logistic regression models and applied multivariable logistic regressions with the inclusion of potential confounding variables to estimate adjusted ORs. For outcomes 2–5, we first used medians and IQRs given the skewed zero-inflated distribution of the data (see online supplemental table 2). For the total number of healthcare visits (outcome 2a), number of each type of healthcare visit (outcome 2b) and number of days in inpatient care (outcome 3), we used Poisson regression to calculate unadjusted and adjusted IRRs, predicted number of events, and corresponding 95% CIs for iGBS and unexposed children.

To estimate the unadjusted and adjusted mean OOP healthcare costs (outcome 4) and the mean health system costs (outcome 5a), along with corresponding 95% CIs, we used a mixed model, previously used to analyse cost data.[19 20] Because of the zero-inflated distribution, the mixed model allowed us to first model the proportion of patients with zero costs using a logit function, and then model a second component for the above-zero cost using a generalised linear model with the log link function and gamma distribution. We described the costs of each type of healthcare visit to the health system (outcome 5b) using unadjusted means and SD. For each cost of coping (outcome 6), we described the frequencies and percentages, separately for iGBS survivors and unexposed children and calculated the exact binomial 95% CIs.

For both child and caregiver HRQoL (outcome 7), we summarised the frequency and percentage of responses for each category of the five EQ-5D-3L dimensions stratified by iGBS exposure and country. For health-state utility values based on the Visual Analogue Scale (VAS) and time-trade-off valuations of the five dimensions, we reported means and exact binomial 95% CIs. To convert EQ-5D-3L dimension responses to health-state valuations we used the R 'eq5d' package[21] and specified the Argentina value-set for the Argentina data, and the Zimbabwe value-set for data from other countries, for which no country-specific value sets were available.

To compare HRQoL between iGBS and non-iGBS children, we first converted health-state utility to disutility (1—utility). We used a Bayesian zero-inflated beta model and pooled data to estimate the mean and 95% CIs of disutility for iGBS survivors and unexposed children in each country while adjusting for confounders. This type of model was chosen to account for the high proportion of EQ-5D respondents reporting perfect health (zero disutility) and that (dis)utility is restricted to the interval (0, 1). As an additional analysis, we used a similar model incorporating an interaction term between country and iGBS, to see if the effect of iGBS was the same across study sites.

We described the categorical confounding variables using frequencies and percentages and the continuous confounding and outcome variables using means and SD, separately for iGBS survivors and unexposed children. We used Pearson's χ^2 test to compare participants who completed the questionnaire versus those who did

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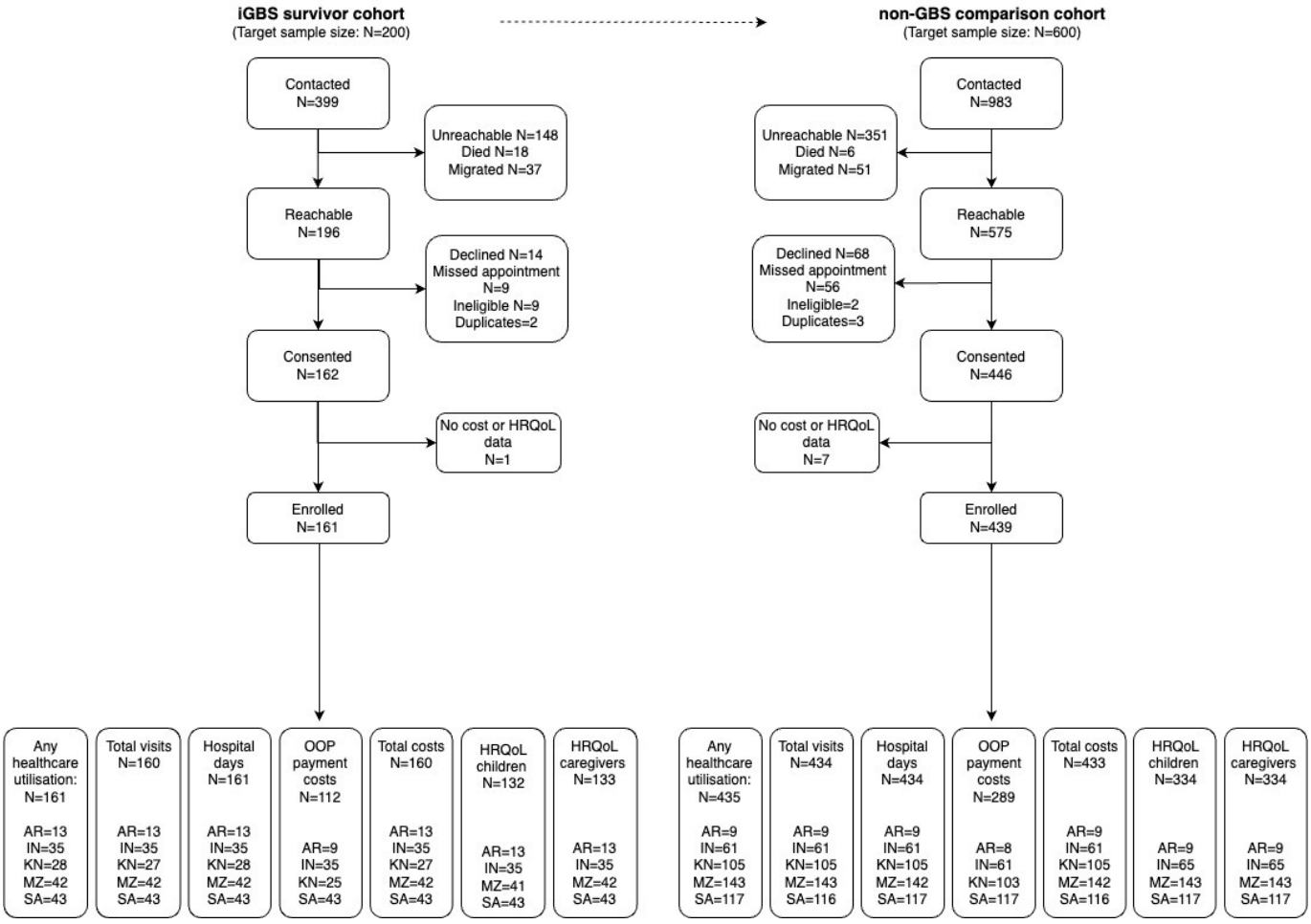

Figure 1 Flow chart of iGBS (invasive group B *Streptococcus*) and non-iGBS children and young adults recruited in multicountry study. In Mozambique, only 21 exposed and 8 unexposed participants completed data on out-of-pocket (OOP) payments and only 2 (exposed) participants had costs above 0. Therefore, Mozambique was removed from the analysis for OOP payments, leaving 401 participants (112 iGBS survivors; 289 unexposed individuals). HRQoL, health-related quality of life; AR, Argentina; IN, India; KN, Kenya; MZ, Mozambique; SA, South Africa.

not, and to compare confounding variables between iGBS survivors and unexposed children.

Analysis of healthcare utilisation and cost data were conducted using STATA V.17.0 and analysis of the EQ-5D-3L data was conducted using R V.4.2.1.

Patient and public involvement

No patients were involved in the design of this study.

RESULTS

Participants

We identified 399 iGBS survivors and 983 eligible unexposed individuals across the five sites. Of these, 161 iGBS survivors and 439 unexposed individuals were recruited and completed data for this study (see figure 1 with exclusion criteria). Argentina enrolled only 50% of their targeted iGBS cohort due to strict COVID-19 restrictions and in South Africa, 57% (103/180) of the cohort of iGBS survivors could not be contacted by phone; in the remaining sites, over 85% of identified individuals were contacted. In Mozambique, only 21 exposed and 8 unexposed individuals completed data on OOP payments and only 2 (exposed) participants had costs above 0. Therefore, Mozambique was removed from the analysis for OOP payments.

There were 22 participants in the Argentinian site (13 iGBS; 9 non-iGBS), 100 in India (35, 65), 133 in Kenya (28, 105), 185 in Mozambique (42, 143) and 160 in South Africa (43, 117). 10 participants who completed other parts of the questionnaire did not have any cost or utilisation data (4 in India and 6 in Kenya). The only notable difference between them and participants who did have information for any cost or utilisation outcome was a higher percentage of participants under 5 years of age (50% vs 23%, respectively). Across four sites, excluding Kenya, 466 participants and 467 caregivers completed the ED-5D-3L.

The demographic characteristics of iGBS and non-iGBS participants in each site are reported in online supplemental table 3. The mean age across the whole cohort was 7.9 years (SD 4.7, 1–20 years, see online supplemental figure 1 for distribution of ages in each exposure group).

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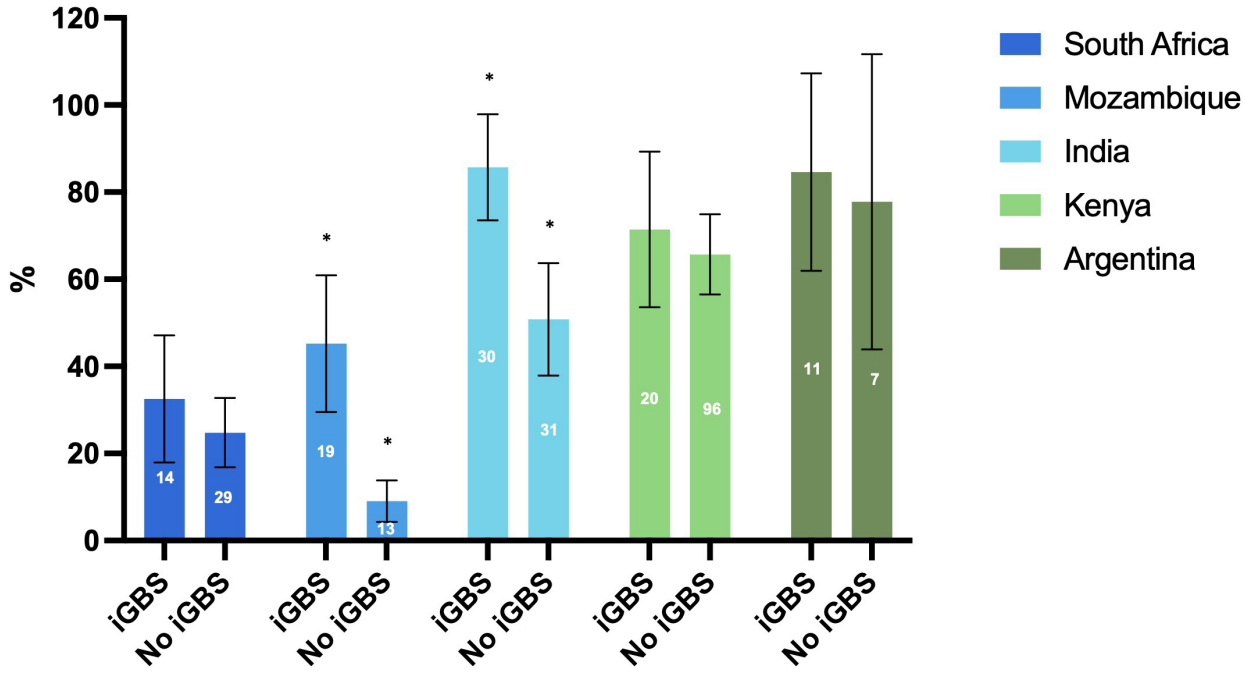

Country	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Argentina	1.57 (0.18- 13.86)	3.24 (0.18-57.12)
India	5.81 (1.99-16.95)	11.19 (2.91-43.09)
Kenya	1.30 (0.52-3.25)	1.10 (0.42-2.84)
Mozambique	8.26 (3.59-19.01)	6.77 (2.17-21.09)
South Africa	1.46 (0.68-3.14)	1.42 (0.65-3.10)

Figure 2 Frequency of any usage of healthcare in the 12 months preceding study recruitment in iGBS survivors versus the unexposed cohort, stratified by country. Bars show the proportion of individuals with any visit to inpatient care, emergency department, outpatient care, community clinic or traditional healers in South Africa, Mozambique, India, Kenya and Argentina for iGBS exposed and unexposed participants. The number in the middle of each bar is the numerator for each percentage. The table shows the unadjusted and adjusted ORs with 95% CI for usage of healthcare in iGBS survivors compared with the unexposed cohort. Adjustments were made for age, sex, preterm birth and main caregiver's education where possible. *The differences that were significant. GBS, invasive group B *Streptococcus;* iGBS, invasive GBS.

A higher proportion of iGBS survivors was born preterm compared with unexposed individuals (12.8% vs 6.5%, respectively). In Mozambique, caregivers of unexposed participants were more likely to have no or early childhood education compared with exposed participants.

Healthcare utilisation in the 12 months preceding study recruitment (outcomes 1, 2, 3)

Figure 2 shows that within each country site the use of any healthcare service (outcome 1) in the 12 months preceding the study was consistently higher in iGBS survivors than the matched comparison cohort. In Argentina, Kenya and South Africa, the absolute difference between iGBS survivors and unexposed individuals was 6%–8%, whereas in India and Mozambique, there was a larger difference of around 35%–36%. This is reflected in the ORs also shown in figure 2. Although differences were only significant in India (adjusted ORs 11.19, 95% CI 2.91 to 43.09) and Mozambique (6.77, 95% CI 2.17 to 21.09), all countries showed the same overall direction of increased odds of any healthcare utilisation in iGBS-exposed versus unexposed participants.

Similarly, the unadjusted and adjusted IRRs for healthcare visits (outcome 2a) in the 12 months preceding the study were also higher in iGBS survivors than unexposed individuals across each of the sites (see table 1A). In Mozambique, for example, the adjusted IRRs for iGBS

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Table 1 (A) Estimates of unadjusted and adjusted incidence rate ratios for the number of healthcare visits in the 12 months preceding study recruitment in iGBS survivors versus unexposed participants, stratified by country

(A)	*N*	Zero visits (%)	Unadjusted IRR (95% CIs)	Adjusted IRR (95% CIs)
South Africa				
Unexposed	*116*	75.9	1.0 (ref)	1.0 (ref)
iGBS exposed	*43*	67.4	1.1 (0.7 to 1.7)	1.1 (0.7 to 1.7)
Mozambique				
Unexposed	*143*	90.9	1.0 (ref)	1.0 (ref)
iGBS exposed	*42*	54.8	6.7 (4.0 to 11.1)	6.0 (3.2 to 11.2)*
India				
Unexposed	*61*	49.2	1.0 (ref)	1.0 (ref)
iGBS exposed	*35*	14.3	1.5 (1.2 to 1.9)	1.7 (1.4 to 2.2)
Kenya				
Unexposed	*105*	34.3	1.0 (ref)	1.0 (ref)
iGBS exposed	*27*	29.6	1.4 (1.1 to 1.8)	1.2 (0.9 to 1.5)
Argentina				
Unexposed	*9*	22.2	1.0 (ref)	1.0 (ref)
iGBS exposed	*13*	15.4	1.3 (0.9 to 2.1)	1.4 (0.9 to 2.3)
(B)	***N***	**Zero visits (%)**	**Unadjusted IRR (95% CIs)**	**Adjusted IRR (95% CIs)**
India				
Unexposed	*61*	90.2	1.0 (ref)	1.0 (ref)
iGBS exposed	*35*	80.0	4.4 (2.7 to 7.5)	4.0 (2.3 to 6.8)
Kenya				
Unexposed	*105*	95.2	1.0 (ref)	1.0 (ref)
iGBS exposed	*28*	89.3	6.0 (2.7 to 13.2)	6.4 (2.9 to 14.3)
Mozambique				
Unexposed	*142*	98.6	1.0 (ref)	1.0 (ref)
iGBS exposed	*42*	95.2	5.1 (0.9 to 30.4)	4.4 (0.3 to 72.1)*

Adjusted for age, sex, preterm birth and main caregiver's education, where possible using Poisson regression.
(B) Estimates of the unadjusted and adjusted incidence rate ratio for the number of days spent in inpatient care in the 12 months preceding study recruitment in iGBS-exposed versus unexposed participants, stratified by country
N in italics is the number of participants in each cohort.
*N for iGBS cohort in the adjusted analysis is 29.
iGBS, invasive Group B *Streptococcus*; IRR, incidence rate ratio.

survivors was 6.0 (95% CI 3.2 to 11.2) while in India it was 1.7 (95% CI 1.4 to 2.2) compared with non-exposed individuals. Likewise, the percentage of individuals with at least one visit in each cohort was higher in iGBS survivors compared with unexposed individuals.

Figure 3 and online supplemental table 4 show the adjusted number of visits for each type of healthcare service (outcome 2b) in the 12 months preceding the study for iGBS survivors and unexposed individuals, by country. The distributions highlight that the adjusted number of visits of most, but not all, healthcare services was higher in exposed versus unexposed participants, especially for outpatient and community clinic visits, which was generally more consistent across sites. There were slight variations across the sites in the trends of the different services used and the magnitude of the differences between exposure cohorts (see figure 3). Nevertheless, the healthcare service with the largest difference in the adjusted number of visits between the cohorts was outpatient visits in South Africa (iGBS 0.3, 0.1–0.4 vs non-iGBS 0.2, 0.1–0.3, respectively), India (3.5, 2.8–4.1 vs 2.0, 1.7–2.4), Kenya (1.4, 1.0–1.9 vs 0.4, 0.3–0.5) and Argentina (2.3, 1.3–3.3 vs 1.0, 0.4–1.6), whereas in Mozambique, it was inpatient visits (0.4, 0.03–0.8 vs 0.03, 0.00–0.06).

Finally, the number of days spent in inpatient care (outcome 3) in the 12 months preceding this study was calculated for India, Kenya and Mozambique. The number of days spent in inpatient care was generally low; over 80% of participants in each exposure cohort in each country had no inpatient care days (see table 1B). Nevertheless, the percentage of participants with at least one visit was higher for iGBS-exposed versus unexposed participants. In line with this, the adjusted IRRs for

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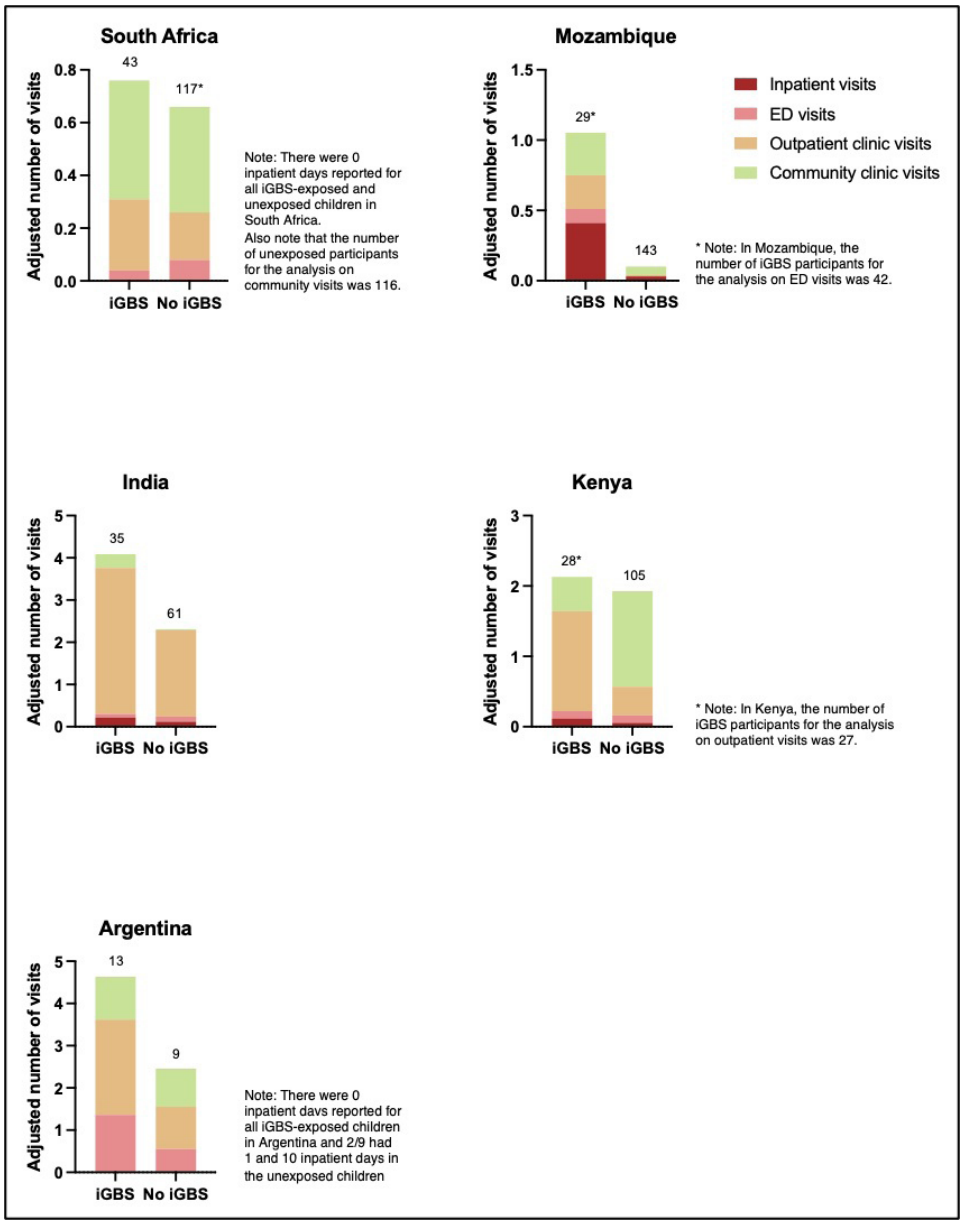

Figure 3 Health system visits for each type of healthcare service used in the 12 months preceding study recruitment in iGBS survivors and the unexposed cohort, stratified by country. Adjusted mean number of visits for each healthcare service in South Africa, Mozambique, India and Argentina for iGBS exposed and unexposed cohort, using Poisson regression. Adjustments made for age, sex, preterm birth and main caregiver's education where possible. Number above each bar represents the number of participants in each cohort for each analysis of the different healthcare services. ED, emergency department; iGBS, invasive group B *Streptococcus.*

inpatient days were higher in iGBS survivors than unexposed individuals, with the difference reaching statistical significance in India (IRR 4.0, 95% CI 2.3 to 6.8) and Kenya (6.4, 95% CI 2.9 to 14.3). In Argentina, none of the unexposed individuals had any inpatient days whereas 2 of 9 iGBS survivors had 1 and 10 inpatient days, while in South Africa there were no inpatient days for iGBS survivors and unexposed participants.

Healthcare costs in the 12 months preceding study recruitment (outcomes 4 and 5)

Overall, 40.2% (N=45/112) of iGBS survivors and 44.6% (N=129/289) of unexposed individuals in Argentina, India, Kenya and South Africa did not incur any OOP payment costs for healthcare (outcome 4) in the 12 months preceding the study. The proportion of participants with zero OOP payments was highest in South Africa (exposed 69.8%; unexposed 82.1%). In all country sites except Kenya, adjusted mean OOP payments were higher in exposed compared with unexposed participants, although the difference was only significant in Argentina and India. Indeed, the highest difference in the adjusted mean OOP healthcare payments between cohorts was in India (Int$682.22, 95% CI Int$364.28 to Int$1000.16 vs Int$133.95, 72.83 to Int$195.06) for

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Table 2 Estimates of the unadjusted and adjusted mean out-of-pocket healthcare payments in international dollars (Int$) spent in the 12 months preceding study recruitment in iGBS-exposed versus unexposed participants, stratified by country

	N	Zero visits (%)	Unadjusted mean int $ (95% CI)	Adjusted mean int $ (95% CI)
South Africa*				
Unexposed	*117*	82.1	15.67 (7.59 to 23.75)	16.10 (7.30 to 24.91)
GBS exposed	*43*	69.8	34.25 (12.77 to 55.73)	34.22 (10.71 to 57.74)
India†				
Unexposed	*61*	36.1	129.43 (66.51 to 192.34)	133.95 (72.83 to 195.06)
GBS exposed	*35*	8.6	800.10 (396.09 to 1204.11)	682.22 (364.28 to 1000.16)
Kenya				
Unexposed	*103*	8.7	92.21 (52.53 to 131.88)	87.23 (52.08 to 122.38)
GBS exposed	*25*	44.0	118.30 (–18.63 to 255.23)	75.62 (–40.34 to 191.58)
Argentina§				
Unexposed	*8*	25.0	189.05 (–46.74 to 424.84)	52.38 (–1.39 to 106.15)
GBS exposed	*9*	11.1	335.66 (–16.39 to 687.71)	244.86 (47.38 to 442.33)

Adjusted for age, sex, preterm birth and main caregiver's education where possible, using mixed modelling (logit and a Generalised Linear Model with the log link and gamma distribution).
N in italics is the number of participants in each cohort.
N for adjusted models: India: 94, Kenya: 118, Argentina: 11.
Negative CIs appear because of delta method used for calculations of CIs.
*Adjusted for age, sex and preterm birth.
†p<0.001.
‡p<0.05.
iGBS, invasive Group B *Streptococcus*.

iGBS survivors and unexposed individuals, respectively) and Argentina (Int$244.86, Int$47.38 to Int$442.33 vs Int$52.38 (Int$–1.39 to Int$106.15) although with wide 95% CIs (see table 2). There was no apparent consistency in differences in the costs of coping with such healthcare payments across different countries (outcome 6, online supplemental table 5).

Mean adjusted health system costs (outcome 5a) in the 12 months preceding the study in all countries, except Argentina, were higher in iGBS survivors compared with unexposed participants (see online supplemental table 6). However, differences were generally small and only statistically significant in Kenya (Int$26.63, 95% CIs Int$11.78 to Int$41.48 in iGBS survivors vs Int$11.66, Int$8.37 to Int$14.95 in unexposed individuals). India also had a relatively higher difference between the two exposure cohorts (Int$90.33, 95% CI Int$38.34 to Int$142.32 vs Int$32.99, 95% CI Int$15.42 to Int$50.57, p>0.05). Comparing the distribution of the unadjusted costs for each type of health service (outcome 5b, online supplemental figure 2) to the number of visits to each type of healthcare service (outcome 2b, figure 3), reveals that, even though the number of inpatient care visits across countries is low because the cost of inpatient care is high, inpatient care represents a relatively higher proportion of total costs.

Health-related quality of life (outcome 7)

Overall, the mean health-state utility based on the EQ-5D-3L index score pooled across countries was 0.96 (SD 0.1) among participants exposed to iGBS, compared with 0.98 (SD 0.07) in unexposed individuals. When assessed using the VAS the corresponding mean health-state utilities were 0.91 (SD 0.13) and 0.96 (SD 0.08), respectively. On average caregivers of children exposed to GBS reported slightly lower health state utility of 0.95 (SD 0.1) compared with 0.96 (SD 0.09) for caregivers of unexposed children, and 0.88 (SD 0.17) compared with 0.94 (SD 0.11) using VAS. Across all children and caregivers, problems were most commonly reported in the anxiety and depression domain (children: 30/466, caregivers: 43/467) and in the pain and discomfort domain (children: 19/466, caregivers: 71/467).

In our adjusted model, the overall disutility was higher among participants exposed to iGBS (0.082, 95% CI 0.043 to 0.130) compared with unexposed participants (0.057, 95% CI 0.023 to 0.099). However, the average disutility in both the exposed and unexposed participants varied substantially between countries and was lowest in Mozambique and highest in Argentina (table 3). In the adjusted model with an interaction term, the estimated marginal effect of iGBS on disutility varied by country, although the 95% CI all overlap (online supplemental table 18). When using the VAS with no interaction term, overall exposure to iGBS was associated with a larger difference in disutility (iGBS exposed: 0.112, 0.084–0.145 vs unexposed: 0.071, 0.0494–0.094), and a similar pattern of variation was seen between countries (online supplemental table 29).

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Table 3 Estimated child and caregiver health state disutility valued using time-trade-off among iGBS-exposed versus unexposed participants, by country

		Unadjusted model		Adjusted model	
	N	Zero disutility (%)	Marginal estimate (95% CI)	Zero disutility (%)	Marginal estimate (95% CI)
Child EQ-5D-3L					
Argentina					
iGBS exposed	*13*	47	0.103 (0.048 to 0.167)	47	0.156 (0.080 to 0.239)
Unexposed	*9*	65	0.061 (0.021 to 0.112)	65	0.120 (0.046 to 0.207)
India					
iGBS exposed	*35*	88	0.023 (0.007 to 0.046)	88	0.059 (0.014 to 0.120)
Unexposed	*65*	94	0.010 (0.003 to 0.021)	94	0.036 (0.006 to 0.083)
Mozambique					
iGBS exposed	*41*	85.4	0.037 (0.017 to 0.063)	82	0.032 (0.011 to 0.061)
Unexposed	*143*	92.7	0.017 (0.078 to 0.029)	93	0.018 (0.049 to 0.039)
South Africa					
iGBS exposed	*43*	85	0.035 (0.015 to 0.062)	86	0.077 (0.021 to 0.153)
Unexposed	*117*	93	0.016 (0.007 to 0.027)	92	0.048 (0.011 to 0.106)
Overall					
iGBS exposed	*132*		0.051 (0.031 to 0.074)		0.082 (0.043 to 0.130)
Unexposed	*334*		0.027 (0.014 to 0.042)		0.057 (0.023 to 0.099)
Caregiver EQ-5D-3L					
Argentina					
iGBS exposed	*13*	25	0.153 (0.104 to 0.206)	28	0.179 (0.107 to 0.247)
Unexposed	*9*	30	0.145 (0.092 to 0.200)	26	0.184 (0.110 to 0.264)
India					
iGBS exposed	*35*	55	0.105 (0.070 to 0.143)	58	0.172 (0.107 to 0.243)
Unexposed	*65*	61	0.093 (0.065 to 0.122)	59	0.175 (0.108 to 0.249)
Mozambique					
iGBS exposed	*42*	86	0.029 (0.015 to 0.047)	83	0.020 (0.008 to 0.038)
Unexposed	*143*	89	0.024 (0.013 to 0.035)	89	0.020 (0.008 to 0.037)
South Africa					
iGBS exposed	*43*	93	0.012 (0.004 to 0.024)	93	0.037 (0.009 to 0.078)
Unexposed	*117*	95	0.010 (0.004 to 0.018)	94	0.036 (0.009 to 0.076)
Overall					
iGBS exposed	*133*		0.075 (0.056 to 0.095)		0.103 (0.068 to 0.141)
Unexposed	*334*		0.068 (0.051 to 0.086)		0.105 (0.067 to 0.145)

Full specification of the zero-inflated beta models and model coefficients are provided in online supplemental tables 7–54. Unadjusted model using pooled data across countries includes covariates for GBS exposure and country. Adjust model using pooled data also includes covariates for age, sex, preterm birth and caregiver highest education.
N in italics is the number of participants in each cohort.
EQ-5D-3L, EuroQol 5-Dimensions-3-Level; iGBS, invasive Group B *Streptococcus*.

For caregivers when using the health-state utility index based on the EQ-5D-3L index score, there was no difference in the overall adjusted mean disutility between those whose children were exposed to GBS (0.103, 0.068–0.141) and those who were not (0.105, 0.067–0.145), although the overall level of disutility again varied between countries (table 3 and online supplemental table 37). In contrast when health-state utility was based on the VAS, adjusted disutility was higher among caregivers of exposed children (0.174, 0.136–0.214) vs unexposed (0.122, 0.092–0.154).

DISCUSSION

In this study, we presented data on the long-term healthcare utilisation, healthcare-related costs and HRQoL for

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children with a history of iGBS and those with no history of iGBS in five LMIC sites. Compared with unexposed children, iGBS was associated with greater healthcare utilisation in the 12 months preceding the study, as measured by the use of any healthcare service and frequency of visits in India and Mozambique, even when adjusting for age, sex, preterm birth and caregiver's education. The adjusted odds of any healthcare service were up to 11 times higher in iGBS-exposed children. Although not reaching statistical significance, utilisation in Argentina, Kenya and South Africa followed similar trends. iGBS was associated with an increased frequency of days spent in inpatient care in the 12 months preceding the study compared with unexposed children in India and Kenya even after adjusting for potential confounders. Adjusted OOP healthcare payments in the 12 months preceding the study were higher in families of participants exposed to iGBS in India and Argentina while adjusted health system costs were higher in the iGBS-exposed cohort in Kenya. Overall, adjusted disutility based on both the VAS and the five dimensions of the EQ-5D-3L was higher (ie, HRQoL was lower) among children with a history of iGBS, than those with no such history, although this difference was not statistically significant for the health-state utility index based on the five dimensions. There was no apparent difference in adjusted disutility between caregivers of iGBS-exposed and unexposed children.

There has been a paucity of data on long-term economic costs from iGBS or neonatal sepsis and meningitis.[6] Our findings in Africa, Asia and South America that there may be long-term differences in utilisation and costs in some LMIC settings, are in line with the higher long-term healthcare utilisation and costs of iGBS found in high-income countries as well as the substantial economic burden estimated for neonatal sepsis in LMIC countries. Although our finding of lower HRQoL in children exposed to iGBS was not statistically significant, we note that our study was not specifically powered for this outcome. The fact that we did observe a statistically significant difference when measuring health-state utility with the VAS, further suggests that there is a true difference in HRQoL. Furthermore, this finding is consistent with two previous studies in high-income countries that reported fewer quality-adjusted life-years accrued among survivors of iGBS in the Netherlands[8] and lower health-state utility among iGBS survivors with sequelae.[22] However, we are not able to make a quantitative comparison due to differences in the way that results were reported in these studies. Our estimates also showed variation in both baseline HRQoL and the marginal effect of iGBS between study sites, which may be due to heterogeneity in the prevalence of NDI and behavioural problems between the study population, as already report by Paul *et al*.[4]

In addition to contributing to the limited literature on the topic, our results highlight an important area for investigation to inform clinical and health policy. LMICs in Asia and Africa have a higher burden of iGBS and consequently may have a higher burden of economic costs from iGBS. Early intervention such as screening and vaccination could prevent the adverse impact on patients and families in long-term mortality, morbidity and associated economic costs. However, iGBS screening has very low uptake in most LMICs, while vaccine candidates will need further investment to reach the market.[23] Preventing acute episodes of iGBS may not be sufficient economic justification for investing in these preventive interventions given the competing demands for healthcare resources in LMICs. Hence, these interventions are unlikely to see widespread uptake in LMICs without data from studies such as ours to inform cost-effectiveness analyses of such interventions. This is especially important as LMICs are susceptible to the 'poverty trap', a cycle where the combination of economic hardship and the high incidence of infectious diseases inhibits the sustained improvement of both health standards and economic growth in a society.[24]

This is the first published study on the long-term costs and HRQoL of iGBS in LMIC contexts. We enrolled participants across a wide age range and included representation from five LMICs across three continents thus increasing geographical representativeness. As a result of self-reported primary data collection, we were able to capture comprehensive data on healthcare use and associated costs in the 12 months preceding the study.

Some limitations should be noted. The key limitation is the relatively small sample size within each country site, partly because of COVID-19-related disruptions, leading to wide CIs for the estimates. This may also be a reason for the contradictory results between countries. For example, in Kenya, the adjusted OOP payments were non-significantly higher in the iGBS-unexposed cohort whereas the opposite trend was found in the remaining countries. Likewise, adjusted costs to the health system in Argentina were non-significantly higher in the iGBS-unexposed cohort compared with the opposite trend in the remaining countries. The difference in results may be because of differences in the characteristics of the populations across the sites, For example, the non-iGBS cohort in Argentina had a very high rate of moderate/severe NDI.[4] This again could be due to issues with a small sample size. Another limitation is that, as data collection was self-reported, all cost and utilisation outcomes were reliant on the caregivers' ability to recall accurately. Additionally, outcomes were only for a snapshot of the 12 months preceding study recruitment, therefore healthcare usage and costs may not reflect costs in other calendar years or ages, although we recruited participants across a wide age range. Also, while we were able to adjust for two potentially important confounders in our analysis (preterm birth and caregiver education), differences may be driven by residual confounding due to other variables on which we were not able to collect information. For example, we did not adjust for other health conditions in either group, which could influence the costs, utilisation or quality of life.

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Given these limitations, studies with larger sample sizes are needed to generate robust estimates of the average annual utilisation and costs for iGBS survivors compared with controls. However, we acknowledge that it is a challenge to obtain larger sample sizes given the relatively low incidence of iGBS. Therefore, it might be useful to invest in long-term follow-up surveillance studies with frequent data collection points in a few sites, especially as studies on the impact of vaccination draw closer. Clinical trials of GBS vaccines may present a unique opportunity to set up long-term follow-up studies with minimal bias. It may also be valuable for future researchers to do a more granular assessment on the influence of iGBS severity (ie, iGBS onset, syndrome and NDI status) and age (ie, whether the impact of iGBS attenuates as the children get older or whether it is largely constant) on long-term healthcare utilisation and costs, and HrQoL. Similarly, researchers may wish to explore the different types of direct non-medical costs (such as travel and childcare) and indirect costs (such as hours spent caring and lost productivity) of iGBS in LMICs. Finally, it may be valuable to collect data from the health system or health practitioners directly to support the self-reported findings here.

CONCLUSIONS

These are the first published estimates from five LMICs showing that iGBS may be associated with long-term healthcare utilisation and costs, and lower HRQoL in affected children and their families. Given the high burden of iGBS in LMICs, it is crucial to understand these costs to establish the value of interventions such as screening and future maternal GBS vaccination. Our study underlines the need for cohort studies and long-term surveillance to provide more robust data on social and economic inputs to better understand the value of iGBS prevention approaches including maternal vaccination.

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Long-term healthcare utilisation, costs, and quality of life after invasive group B *Streptococcus* disease: a cohort study in five low- and middle-income countries

Supplementary table 1. Description of the outcomes developed for this study

Objective	Outcome	Description
1	Any healthcare utilisation	Binary variable (Yes/No) according to any of the following questions answered yes or no: visits to inpatient, emergency department, outpatient, community, or traditional healer clinics in the last 12 months
2	a. Total number of healthcare visits b. Number of each type of healthcare visit	a. Summed number of visits reported in questionnaire for: inpatient, emergency department, outpatient, community, or traditional healer clinics in the last 12 months b. Individual number of visits reported in questionnaire for: inpatient, emergency department, outpatient, community, or traditional healer clinics in the last 12 months
3	Number of days spent in inpatient care	Number of days reported for hospital stay in the last 12 months from questionnaire
4	Out of pocket (OOP) healthcare payments	Question on amount in local currency spent on healthcare in the last 12 months (incl. hospital and clinicians' fees, tests, medications, assistive devices, minus any fees reimbursed) inflated to 2022 local currency using GDP deflators and converted into international dollars (Int$) using 2022 PPP conversion factors from the World Development Indicators of the World Bank,(1) as described by Turner et al. (2019).(2)
5	a. Total cost of healthcare to the health system b. Cost of each type of healthcare visit	Multiplied number of days admitted to hospital and the number of outpatient visits with unit costs, as estimated by the latest 2010 WHO-CHOICE costs(3) for each country in local currency inflated to 2022 and converted to international dollars (Int $) as described above using GDP deflators and PPP conversion factors the World Development Indicators of the World Bank and methods from Turner et al. (2019).(2, 4) a. Total costs: Summed all costs in Int$ together b. Costs: Costs for each type of healthcare visit presented separately For inpatient unit costs, we used WHO-CHOICE costs for secondary level hospital inpatient care, for emergency unit costs we used secondary-level outpatient care, for outpatient visits we used primary-level outpatient care, and for community visits we used outpatient health centre care with no beds. We did not include costs for traditional healer visits.
6	Costs of coping with healthcare payments	Binary variables (Yes/No) for each of the following questions: whether (a) money was borrowed, (b) assets were sold, (c) additional work was undertaken, (d) or whether a child in the family dropped out of education, to cover healthcare costs.
7	Health related quality of life (HrQoL)	HRQoL of both the participant and the main caregiver an EQ-5D-3L questionnaire was administered in three countries where country-approved translations are available: Argentina (Spanish), India (English, Telugu, Tamil) and South Africa (English, Zulu). The EQ-5D-3L was self-reported for caregivers and individuals aged 11 and over whereas it was proxy-reported for children aged 3 to 10.

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Supplementary table 2a. Distribution of healthcare visits and cost outcomes of survivors of invasive Group B *Streptococcus* disease (iGBS) in infancy and matched comparison cohort, stratified by country

	South Africa				Mozambique				India				Kenya				Argentina			
	No iGBS		iGBS		No iGBS		iGBS		No iGBS		iGBS		No iGBS		iGBS		No iGBS		iGBS	
Outcomes	**Med**	**IQR**	**Med**	**IQR**	**Med**	**IQR**	**Med**	**IQR**	**Med**	**IQR**	**Med**	**IQR**	**Med**	**IQR**	**Med**	**IQR**	**Med**	**IQR**	**Med**	**IQR**
Total number of healthcare visits	0.00	0.00	0.00	1.00	0.00	0.00	0.00	1.00	1.00	3.00	3.00	3.00	1.00	3.00	2.00	4.00	2.00	4.00	2.00	3.00
Inpatient care	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.22	0.00	0.00	0.00
Emergency department	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.00	1.00
Outpatient	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	3.00	3.00	4.00	0.00	0.00	0.00	3.00	1.00	1.00	1.00	2.00
Community	0.00	0.00	0.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	2.00	0.00	1.00	0.00	1.00	0.00	1.00
Traditional healer	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Days spent in inpatient care	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Out of pocket healthcare payments (int$)	0.00	0.00	0.00	56.03	0.00	0.00	0.00	0.00	51.32	205.27	256.58	487.51	38.64	72.13	10.30	103.05	32.96	122.16	217.17	360.65
Total cost of healthcare to the health system	0.00	0.00	0.00	17.71	0.00	0.00	0.00	2.90	9.01	36.04	36.04	59.28	6.68	13.68	10.97	32.05	76.82	172.39	89.84	134.76

	South Africa				Mozambique				India				Kenya				Argentina			
	No iGBS		iGBS		No iGBS		iGBS		No iGBS		iGBS		No iGBS		iGBS		No iGBS		iGBS	
Outcomes	**Med**	**IQR**	**Med**	**IQR**	**Med**	**IQR**	**Med**	**IQR**	**Med**	**IQR**	**Med**	**IQR**	**Med**	**IQR**	**Med**	**IQR**	**Med**	**IQR**	**Med**	**IQR**
Inpatient care	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Emergency department	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	46.83	0.00	46.83
Outpatient	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	27.03	27.03	36.04	0.00	0.00	0.00	19.23	44.92	44.92	44.92	89.84
Community	0.00	0.00	0.00	17.71	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	4.56	9.12	0.00	4.56	0.00	31.90	0.00	31.90

Int$=international dollars, IQR=Interquartile range, Med=Median

Supplementary table 2b. Distribution of health-related quality of life outcomes of survivors of invasive Group B *Streptococcus* disease (iGBS) in infancy and matched comparison cohort, stratified by country

	South Africa		Mozambique		India		Argentina	
	iGBS	No iGBS	iGBS	No iGBS	iGBS	No iGBS	GBS	No iGBS
Participant EQ-5D-3L								
Total	43	117	46	145	35	65	13	9
Mobility								
No problems in walking	43 (100.0%)	116 (99.1%)	44 (95.7%)	143 (98.6%)	34 (97.1%)	65 (100.0%)	12 (92.3%)	9 (100.0%)
Some problems in walking	0 (0.0%)	1 (0.9%)	2 (4.3%)	1 (0.7%)	1 (2.9%)	0 (0.0%)	1 (7.7%)	0 (0.0%)
Confined to bed	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Self Care								
No problems with self-care	43 (100.0%)	115 (98.3%)	45 (97.8%)	144 (99.3%)	35 (100.0%)	65 (100.0%)	11 (84.6%)	9 (100.0%)
Some problems bathing or dressing himself/herself	0 (0.0%)	2 (1.7%)	1 (2.2%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	2 (15.4%)	0 (0.0%)
Unable to bathe or dress himself/herself	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Usual Activities								

	South Africa		Mozambique		India		Argentina	
	iGBS	**No iGBS**	**iGBS**	**No iGBS**	**iGBS**	**No iGBS**	**GBS**	**No iGBS**
No problems with performing his/her usual activities	42 (97.7%)	115 (98.3%)	45 (97.8%)	144 (99.3%)	34 (97.1%)	65 (100.0%)	10 (76.9%)	9 (100.0%)
Some problems with performing his/her usual activities	0 (0.0%)	1 (0.9%)	1 (2.2%)	0 (0.0%)	1 (2.9%)	0 (0.0%)	2 (15.4%)	0 (0.0%)
Unable to perform his/her usual activities	1 (2.3%)	1 (0.9%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (7.7%)	0 (0.0%)
Pain Discomfort								
No pain or discomfort	43 (100.0%)	114 (97.4%)	40 (87.0%)	142 (97.9%)	32 (91.4%)	64 (98.5%)	12 (92.3%)	7 (77.8%)
Moderate pain or discomfort	0 (0.0%)	2 (1.7%)	5 (10.9%)	2 (1.4%)	3 (8.6%)	1 (1.5%)	1 (7.7%)	2 (22.2%)
Extreme pain or discomfort	0 (0.0%)	1 (0.9%)	1 (2.2%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Anxiety Depression								
Not anxious or depressed	39 (90.7%)	110 (94.0%)	40 (87.0%)	142 (97.9%)	35 (100.0%)	62 (95.4%)	9 (69.2%)	6 (66.7%)
Moderate anxious or depressed	3 (7.0%)	7 (6.0%)	6 (13.0%)	3 (2.1%)	0 (0.0%)	3 (4.6%)	3 (23.1%)	3 (33.3%)
Extremely anxious or depressed	1 (2.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (7.7%)	0 (0.0%)
HSValue (VAS)								
Mean (SD)	0.99 (0.05)	0.99 (0.04)	0.89 (0.14)	0.98 (0.07)	0.84 (0.15)	0.91 (0.09)	0.86 (0.14)	0.86 (0.15)
HSValue (TTO)								
Mean (SD)	0.98 (0.07)	0.98 (0.06)	0.95 (0.10)	0.99 (0.08)	0.98 (0.06)	0.99 (0.04)	0.88 (0.19)	0.95 (0.06)
Caregiver EQ-5D-3L								
Total	43	117	47	145	35	65	13	9
Mobility								
No problems in walking	43 (100.0%)	114 (97.4%)	46 (97.9%)	144 (99.3%)	33 (94.3%)	57 (87.7%)	10 (76.9%)	9 (100.0%)
Some problems in walking	0 (0.0%)	3 (2.6%)	1 (2.1%)	1 (0.7%)	2 (5.7%)	8 (12.3%)	3 (23.1%)	0 (0.0%)
Confined to bed	0 (0.0%)	0 (0.0%)	0 (0.0%)	0(0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Self Care								
No problems with self-care	43 (100.0%)	117 (100.0%)	45 (95.7%)	144 (99.3%)	35 (100.0%)	64 (98.5%)	13 (100.0%)	9 (100.0%)
Some problems bathing or dressing himself/herself	0 (0.0%)	0 (0.0%)	2 (4.3%)	1 (0.7%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)
Unable to bathe or dress himself/herself	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

	South Africa		Mozambique		India		Argentina	
	iGBS	**No iGBS**	**iGBS**	**No iGBS**	**iGBS**	**No iGBS**	**GBS**	**No iGBS**
Usual_Activities								
No problems with performing his/her usual activities	43 (100.0%)	116 (99.1%)	46 (97.9%)	143 (98.6%)	31 (88.6%)	60 (92.3%)	11 (84.6%)	9 (100.0%)
Some problems with performing his/her usual activities	0 (0.0%)	1 (0.9%)	1 (2.1%)	2 (1.4%)	4 (11.4%)	5 (7.7%)	2 (15.4%)	0 (0.0%)
Unable to perform his/her usual activities	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Pain_Discomfort								
No pain or discomfort	40 (93.0%)	114 (97.4%)	41 (87.2%)	135 (93.1%)	26 (74.3%)	37 (56.9%)	5 (38.5%)	4 (44.4%)
Moderate pain or discomfort	3 (7.0%)	3 (2.6%)	5 (10.6%)	10 (6.9%)	8 (22.9%)	26 (40.0%)	8 (61.5%)	4 (44.4%)
Extreme pain or discomfort	0 (0.0%)	0 (0.0%)	1 (2.1%)	0 (0.0%)	1 (2.9%)	2 (3.1%)	0 (0.0%)	1 (11.1%)
Anxiety_Depression								
Not anxious or depressed	42 (97.7%)	116 (99.1%)	38 (80.9%)	144 (99.3%)	30 (85.7%)	50 (76.9%)	7 (53.8%)	4 (44.4%)
Moderate anxious or depressed	1 (2.3%)	1 (0.9%)	9 (19.1%)	1 (0.7%)	5 (14.3%)	13 (20.0%)	6 (46.2%)	4 (44.4%)
Extremely anxious or depressed	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (3.1%)	0 (0.0%)	1 (11.1%)
HSValue (VAS)								
Mean (SD)	0.99 (0.04)	0.99 (0.03)	0.88 (0.14)	0.98 (0.05)	0.75 (0.20)	0.79 (0.14)	0.83 (0.18)	0.79 (0.19)
HSValue (TTO)								
Mean (SD)	0.99 (0.05)	0.99 (0.04)	0.95 (0.11)	0.99 (0.05)	0.93 (0.12)	0.89 (0.13)	0.86 (0.12)	0.81 (0.22)

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Supplementary table 3. Descriptive characteristics of survivors of invasive Group B *Streptococcus* disease (iGBS) in infancy and matched comparison cohort, stratified by country

	South Africa				Mozambique				India				Kenya				Argentina			
	No iGBS		iGBS		No iGBS		iGBS		No iGBS		iGBS		No iGBS		iGBS		No iGBS		iGBS	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Total	117	100.0	43	100	143	100.0	42	100.0	65	100.0	35	100.0	105	100.0	28	100.0	9	100.0	13	100.0
Age at recruitment																				
Less than 5 years	0	0.0	0	0.0	19	13.3	8	19.1	40	61.5	21	60.0	38	36.2	13	46.4	1	11.1	1	7.7
5-9 years	117	100.0	43	100	27	18.9	8	19.1	17	26.2	9	25.7	27	25.7	4	14.3	7	77.8	7	53.9
10 years and over	0	0.0	0	0.0	97	67.8	26	61.9	8	12.3	5	14.3	40	38.1	11	39.3	1	11.1	5	38.5
Sex																				
Male	60	51.3	22	51.2	73	51.1	22	52.4	26	40.0	16	45.7	55	52.4	17	60.7	4	44.4	7	53.9
Female	57	48.7	21	48.8	70	49.0	20	47.6	39	60.0	19	54.3	50	47.6	11	39.3	5	55.6	6	46.2
Preterm birth																				
37+wks	100	85.5	34	79.1	127	88.8	25	86.2	62	95.4	32	91.4	99	94.3	23	82.1	7	77.8	12	92.3
<37wks	17	14.5	9	20.9	1	0.7	1	3.5	3	4.6	3	8.6	6	5.7	5	17.9	2	22.2	1	7.7
Don't know	0	0.0	0	0.0	15	10.5	3	10.3	0	0.0	0	0	0	0.0	0	0.0	0	0.0	0	0.0
Carer Education																				

	South Africa				Mozambique				India				Kenya				Argentina			
	No iGBS		iGBS		No iGBS		iGBS		No iGBS		iGBS		No iGBS		iGBS		No iGBS		iGBS	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
No or Early Childhood	0	0.0	0	0.0	107	74.8	7	16.7	0	0.0	2	5.7	96	91.4	24	85.7	0	0.0	1	7.7
Primary	1	0.9	1	2.3	34	23.8	20	47.6	11	16.9	4	11.4	7	6.7	4	14.3	4	44.4	4	30.8
Secondary	84	71.8	32	74.4	1	0.7	10	23.8	14	21.5	7	20.0	2	1.9	0	0.0	4	44.4	6	46.2
College or University	32	27.4	10	23.3	1	0.7	5	11.9	40	61.5	22	62.9	0	0.0	0	0.0	1	11.1	2	15.4

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Supplementary table 4. Estimates of the adjusted number of visits (and 95% confidence intervals) for each type of healthcare service for invasive group B Streptococcus (iGBS) exposed and unexposed participants, stratified by country

	GBS exposed		**Not exposed**	
	N	**Adjusted number of visits (95% CIs)**	***N***	**Adjusted number of visits (95% CIs)**
South Africa				
ED visits	*43*	0.04 (-0.03-0.10)	*117*	0.08 (0.03-0.13)
Outpatient visits	*43*	0.27 (0.11-0.44)	*117*	0.18 (0.11-0.26)
Community visits	*43*	0.45 (0.25-0.65)	*116*	0.40 (0.29-0.52)
Mozambique				
Inpatient visits	*29*	0.41 (0.03-0.79)	*143*	0.03 (0.00-0.06)
ED visits	*42*	0.10 (-0.04-0.24)	*143*	0.00 (0.00-0.00)
Outpatient visits	*29*	0.24 (-0.06-0.53)	*143*	0.01 (-0.01-0.02)
Community visits	*29*	0.31 (0.12-0.51)	*143*	0.06 (0.02-0.10)
Healer visits	*29*	0.05 (-0.01-0.11)	*143*	0.07 (0.02-0.13)
India				
Inpatient visits	*35*	0.22 (0.06-0.38)	*61*	0.12 (0.03-0.20)
ED visits	*35*	0.08 (-0.01-0.17)	*61*	0.12 (0.03-0.21)
Outpatient visits	*35*	3.46 (2.80-4.11)	*61*	2.04 (1.69-2.39)
Community visits	*35*	0.33 (0.13-0.52)	*61*	0.05 (-0.01-0.10)
Healer visits	*35*	0.00 (0.00-0.00)	*61*	0.09 (-91.18-91.36)
Kenya				
Inpatient visits	*28*	0.11 (-0.02-0.24)	*105*	0.05 (0.01-0.09)
ED visits	*28*	0.11 (-0.00-0.22)	*105*	0.11 (0.05-0.18)
Outpatient visits	*27*	1.42 (0.97-1.87)	*105*	0.41 (0.29-0.53)
Community visits	*28*	0.49 (0.24-0.73)	*105*	1.36 (1.13-1.59)
Healer visits	*28*	0.10 (0.00-0.19)	*105*	0.02 (-0.01-0.06)
Argentina				

ED visits	*13*	1.36 (0.55-2.17)	*9*	0.55 (0.08-1.02)
Outpatient visits	*13*	2.26 (1.27-3.26)	*9*	1.00 (0.38-1.63)
Community visits	*13*	1.06 (0.37-1.75)	*9*	0.93 (0.19-1.66)

CIs=confidence intervals, ED=emergency department
Notes:
1. Counts adjusted for age, sex, gestational age, and main caregiver education where possible using Poisson regression.
2. Negative CIs appear because of delta method used for calculations of confidence intervals.

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Supplementary table 5. Frequency and exact binomial 95% confidence intervals for the costs of copying with healthcare out of pocket payments in the last 12 months for invasive group B *Streptococcus* (iGBS) exposed and unexposed participants, stratified by country

	iGBS-exposed			Unexposed		
	N	**Freq.**	**% (Exact binomial 95% CIs)**	**N**	**Freq.**	**% (Exact binomial 95% CIs)**
South Africa						
Borrowed	*43*	1	2.3 (0.1-12.3)	*117*	1	0.9 (0.0-4.7)
Sold asset	*43*	0	0.0	*117*	0	
Other child dropped education	*43*	1	2.3 (0.1-12.3)	*117*	2	1.7 (0.2-6.0)
Took extra work	*43*	0	0.0	*117*	0	
Mozambique						
Borrowed	*42*	1	2.4 (0.1-12.6)	*143*	1	0.7 (0.0-3.8)
Sold asset	*42*	1	2.4 (0.1-12.6)	*143*	0	0.0
Other child dropped education	*42*	3	7.1 (1.5-19.5)	*143*	5	3.5 (1.1-8.0)
Took extra work	*42*	1	2.4 (0.1-12.6)	*143*	6	4.2 (1.6-8.9)
India						
Borrowed	*35*	8	22.9 (10.4-40.1)	*61*	6	9.8 (3.7-20.2)
Sold asset	*35*	3	8.6 (1.8-23.1)	*61*	3	4.9 (1.0-13.7)
Other child dropped education	*35*	0	0.0	*61*	0	0.0
Took extra work	*35*	1	2.9 (0.1-14.9)	*61*	0	0.0
Kenya						
Borrowed	*28*	5	17.9 (6.1-36.9)	*104*	10	9.6 (4.7-17.0)
Sold asset	*28*	1	3.6 (0.1-18.3)	*104*	12	11.5 (6.1-19.3)
Other child dropped education	*28*	4	14.3 (4.0-32.7)	*104*	7	6.7 (2.7-13.4)
Took extra work	*28*	2	7.1 (0.9-23.5)	*104*	2	1.9 (0.2-6.8)

Argentina						
Borrowed	*13*	5	38.5 (13.9-68.4)	*9*	5	55.6 (21.2-86.3)
Sold asset	*13*	2	15.4 (1.9-45.4)	*9*	0	0.0
Other child dropped education	*13*	1	7.7 (0.2-0.36.0)	*9*	2	22.2 (2.8-60.0)
Took extra work	*13*	2	15.4 (1.9-45.4)	*9*	1	11.1 (0.0-48.2)

CI=confidence interval

Long-term healthcare utilisation, costs, and quality of life after invasive group B *Streptococcus* disease: a cohort study in five low- and middle-income countries

Supplementary table 6. Estimates of the unadjusted and adjusted mean health system costs in international dollars (Int$) spent on healthcare in the last 12 months in invasive group B *Streptococcus* (iGBS) exposed versus unexposed participants, stratified by country

	N	Zero visits (%)	Unadjusted mean Int $ (95% CIs)	Adjusted mean Int $ (95% CIs)
South Africa				
Unexposed	*116*	75.86	14.21 (4.75-23.66)	14.28 (5.34-23.23)
iGBS exposed	*43*	67.44	15.21 (1.08-29.34)	16.62 (1.66-31.59)
Mozambique				
Unexposed	*142*	95.77	0.25 (0.01-0.48)	0.28 (0.00-0.57)
iGBS exposed	*42*	64.29	2.16 (1.03-3.29)	1.94 (0.39-3.49)
India				
Unexposed	*35*	14.29	34.24 (15.36-53.12)	32.99 (15.42-50.57)
iGBS exposed	*61*	49.18	91.11 (43.81-138.41)	90.33 (38.34-142.32)
Kenya*				
Unexposed	*105*	34.29	11.35 (8.23-14.47)	11.66 (8.37-14.95)
iGBS exposed	*27*	33.33	27.25 (12.64-41.85)	26.63 (11.78-41.48)
Argentina				
Unexposed	*9*	22.22	531.10 (29.18-1091.38)	324.49 (-78.89-727.88)
iGBS exposed	*13*	15.38	172.32 (29.77-314.87)	183.31 (120.81-487.43)

CI=Confidence intervals

Notes:

1. Means adjusted for age, sex, gestational age, and main caregiver's education where possible using GLM mixed modelling (logit and a GLM with the log link and gamma distribution)
2. Negative CIs appear because of delta method used for calculations of confidence intervals.

N for adjusted models: South Africa: 159, Mozambique: 169, India: 94, Kenya: 130, Argentina: 15

*p<0.01

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Supplementary tables for Health-related quality of life

Child health-state disutility based on EQ-5D-3L Index

Model coefficients

Supplementary table 7. Unadjusted model of child health-state disutility based on EQ-5D-3L valued using time trade off.

Fixed effects (conditional)

Parameter	Median	95% CI
(Intercept)	-1.1611	(-1.6446, -0.6768)
phi_Intercept	2.2783	(1.6523, 2.8207)
gbsNoGBS	-0.0949	(-0.5428, 0.3507)
CountryCodeMozambique	0.0397	(-0.4743, 0.5650)
CountryCodeIndia	-0.2250	(-0.8872, 0.4110)
CountryCodeArgentina	-0.2487	(-0.8644, 0.3586)
phi_gbsNoGBS	-0.0605	(-0.8886, 0.7620)

Fixed effects (zero-inflated)

Parameter	Median	95% CI
(Intercept)	1.7416	(1.0969, 2.4224)
gbsNoGBS	0.8071	(0.1622, 1.4259)
CountryCodeMozambique	-0.0286	(-0.7758, 0.7012)
CountryCodeIndia	0.2688	(-0.6409, 1.2108)
CountryCodeArgentina	-1.8876	(-2.9350, -0.8535)

Model: disutility_TTO ~ gbs + CountryCode (466 Observations)

Supplementary table 8. Adjusted model of child health-state disutility based on EQ-5D-3L valued using time trade off.

Fixed effects (conditional)

Parameter	Median	95% CI
(Intercept)	-2.1429	(-3.6592, -0.6999)
phi_Intercept	2.5698	(1.6248, 3.4025)
gbsNoGBS	-0.0160	(-0.5005, 0.4766)
ageband	-0.0071	(-0.0597, 0.0454)
sexmale	0.2851	(-0.1803, 0.7306)
pretermTerm	0.3459	(-0.5870, 1.4639)
pretermUnknown	1.2894	(-0.0114, 2.6333)
carerhighesteducationNoOrEarlyChildhoodEducation	0.4836	(-0.2366, 1.2158)

Parameter	Median	95% CI
carerhighesteducationPrimaryEducation	0.7874	(0.0767, 1.4976)
carerhighesteducationSecondaryEducation	0.4408	(-0.2540, 1.1334)
CountryCodeMozambique	-0.4119	(-1.2326, 0.3868)
CountryCodeIndia	-0.1793	(-1.0622, 0.6548)
CountryCodeArgentina	-0.1092	(-0.8561, 0.5897)
phi_gbsNoGBS	-0.2501	(-1.6338, 1.3438)

Fixed effects (zero-inflated)

Parameter	Median	95% CI
(Intercept)	3.0889	(1.4340, 4.8647)
gbsNoGBS	0.6923	(0.0050, 1.3729)
ageband	-0.0421	(-0.1304, 0.0426)
sexmale	-0.3295	(-0.9656, 0.3078)
pretermTerm	-0.7104	(-2.1570, 0.6140)
pretermUnknown	-1.9397	(-3.7984, -0.1852)
carerhighesteducationNoOrEarlyChildhoodEducation	-0.3067	(-1.6600, 1.0859)
carerhighesteducationPrimaryEducation	-0.5793	(-1.7242, 0.5897)
carerhighesteducationSecondaryEducation	-0.1980	(-1.1129, 0.7143)
CountryCodeMozambique	0.9031	(-0.4799, 2.2925)
CountryCodeIndia	0.2448	(-0.7831, 1.2713)
CountryCodeArgentina	-1.7165	(-2.8588, -0.5424)

Model: disutility_TTO ~ gbs + ageband + sex + preterm + carerhighesteducation + CountryCode (466 Observations)

Supplementary table 9. Adjusted model of child health-state disutility based on EQ-5D-3L valued using time trade off including GBS-Country interaction term.

Fixed effects (conditional)

Parameter	Median	95% CI
(Intercept)	-1.6267	(-2.9642, -0.4112)
phi_Intercept	2.4977	(1.7273, 3.2853)
gbsNoGBS	-0.0785	(-0.8329, 0.7232)
ageband	-0.0290	(-0.0767, 0.0193)
sexmale	0.1157	(-0.2838, 0.5219)
pretermTerm	0.0849	(-0.6693, 0.9171)
pretermUnknown	2.2206	(0.8874, 3.4774)
carerhighesteducationNoOrEarlyChildhoodEducation	0.1194	(-0.5997, 0.8279)
carerhighesteducationPrimaryEducation	0.8205	(0.0937, 1.5590)
carerhighesteducationSecondaryEducation	0.4094	(-0.2348, 1.0917)
CountryCodeMozambique	-1.3816	(-2.8779, -0.0522)
CountryCodeIndia	0.0794	(-1.0075, 1.1007)
CountryCodeArgentina	0.2262	(-0.7567, 1.1954)

Parameter	Median	95% CI
gbsNoGBS:CountryCodeMozambique	1.5697	(0.3707, 2.7790)
gbsNoGBS:CountryCodeIndia	-0.7274	(-2.0326, 0.5937)
gbsNoGBS:CountryCodeArgentina	-0.8526	(-2.0193, 0.2753)
phi_gbsNoGBS	0.6205	(-0.8338, 1.9602)

Fixed effects (zero-inflated)

Parameter	Median	95% CI
(Intercept)	3.6664	(1.8953, 5.7179)
gbsNoGBS	-0.0244	(-1.3721, 1.1523)
ageband	-0.0469	(-0.1357, 0.0400)
sexmale	-0.3605	(-1.0107, 0.2989)
pretermTerm	-0.7227	(-2.2397, 0.5814)
pretermUnknown	-1.6719	(-3.5766, 0.1162)
carerhighesteducationNoOrEarlyChildhoodEducation	-1.0409	(-2.5572, 0.4913)
carerhighesteducationPrimaryEducation	-0.6537	(-1.8215, 0.4790)
carerhighesteducationSecondaryEducation	-0.1864	(-1.1315, 0.6979)
CountryCodeMozambique	-0.0090	(-1.7302, 1.6907)
CountryCodeIndia	-0.1692	(-1.7705, 1.4782)
CountryCodeArgentina	-1.8396	(-3.5526, -0.2173)
gbsNoGBS:CountryCodeMozambique	2.0890	(0.2616, 4.0156)
gbsNoGBS:CountryCodeIndia	0.6884	(-1.2854, 2.7137)
gbsNoGBS:CountryCodeArgentina	-0.0369	(-2.2930, 2.2746)

Model: vdisutility_TTO ~ gbs + ageband + sex + preterm + carerhighesteducation + CountryCode + CountryCode * gbs (466 Observations)

Estimated proportion with zero-disutility by GBS status

Supplementary table 10. Unadjusted proportion of children by iGBS exposure status and country reporting zero disutility based on EQ-5D-3L valued using time trade off.

gbs	CountryCode	Proportion reporting zero disutility
GBS	SouthAfrica	0.85
GBS	Mozambique	0.84
GBS	India	0.88
GBS	Argentina	0.47
NoGBS	SouthAfrica	0.93
NoGBS	Mozambique	0.92
NoGBS	India	0.94
NoGBS	Argentina	0.65

Supplementary table 11. Adjusted proportion of children by iGBS exposure status and country reporting zero disutility based on EQ-5D-3L valued using time trade off.

gbs	CountryCode	Proportion reporting zero disutility
GBS	SouthAfrica	0.86
GBS	Mozambique	0.82
GBS	India	0.88
GBS	Argentina	0.47
NoGBS	SouthAfrica	0.92
NoGBS	Mozambique	0.93
NoGBS	India	0.94
NoGBS	Argentina	0.65

Supplementary table 12. Adjusted proportion of children by iGBS exposure status and country reporting zero disutility based on EQ-5D-3L valued using time trade off including GBS-Country interaction term.

gbs	CountryCode	Proportion reporting zero disutility
GBS	SouthAfrica	0.90
GBS	Mozambique	0.75
GBS	India	0.88
GBS	Argentina	0.54
NoGBS	SouthAfrica	0.90
NoGBS	Mozambique	0.95
NoGBS	India	0.94
NoGBS	Argentina	0.55

Estimated marginal means by GBS status

Supplementary table 13. Unadjusted marginal estimate of child disutility by iGBS exposure status and country based on EQ-5D-3L valued using time trade off.

Parameter	Median	Median.1	95% CI
GBS, SouthAfrica	0.0353	0.0353	(0.0152, 0.0621)
NoGBS, SouthAfrica	0.0160	0.0160	(0.0072, 0.0274)
GBS, Mozambique	0.0374	0.0374	(0.0169, 0.0630)
NoGBS, Mozambique	0.0170	0.0170	(0.0078, 0.0286)
GBS, India	0.0233	0.0233	(0.0072, 0.0462)
NoGBS, India	0.0103	0.0103	(0.0030, 0.0214)
GBS, Argentina	0.1030	0.1030	(0.0483, 0.1672)
NoGBS, Argentina	0.0608	0.0608	(0.0211, 0.1121)

Supplementary table 14. Adjusted marginal estimate of child disutility by iGBS exposure status and country based on EQ-5D-3L valued using time trade off.

Parameter	Median	Median.1	95% CI
GBS, SouthAfrica	0.0770	0.0770	(0.0211, 0.1531)
NoGBS, SouthAfrica	0.0478	0.0478	(0.0108, 0.1062)
GBS, Mozambique	0.0322	0.0322	(0.0113, 0.0609)
NoGBS, Mozambique	0.0180	0.0180	(0.0049, 0.0390)
GBS, India	0.0589	0.0589	(0.0143, 0.1201)
NoGBS, India	0.0355	0.0355	(0.0056, 0.0832)
GBS, Argentina	0.1560	0.1560	(0.0803, 0.2392)
NoGBS, Argentina	0.1201	0.1201	(0.0461, 0.2065)

Supplementary table 15. Adjusted marginal estimate of child disutility by iGBS exposure status and country based on EQ-5D-3L valued using time trade off including GBS-Country interaction term.

Parameter	Median	Median.1	95% CI
GBS, SouthAfrica	0.0785	0.0785	(0.0116, 0.1797)
NoGBS, SouthAfrica	0.0786	0.0786	(0.0191, 0.1644)
GBS, Mozambique	0.0384	0.0384	(0.0145, 0.0688)
NoGBS, Mozambique	0.0154	0.0154	(0.0022, 0.0406)
GBS, India	0.0918	0.0918	(0.0158, 0.1938)
NoGBS, India	0.0397	0.0397	(0.0034, 0.1028)
GBS, Argentina	0.2250	0.2250	(0.1022, 0.3530)
NoGBS, Argentina	0.1469	0.1469	(0.0461, 0.2552)

Average marginal effect by GBS status

Supplementary table 16. Unadjusted average marginal effect of iGBS exposure on child disutility by country based on EQ-5D-3L valued using time trade off.

Parameter	Median	Median.1	95% CI
NoGBS - GBS, SouthAfrica	-0.0188	-0.0188	(-0.0426, -0.0007)
NoGBS - GBS, Mozambique	-0.0200	-0.0200	(-0.0437, -0.0013)
NoGBS - GBS, India	-0.0124	-0.0124	(-0.0308, -0.0002)
NoGBS - GBS, Argentina	-0.0405	-0.0405	(-0.0879, 0.0009)

Supplementary table 17. Adjusted average marginal effect of iGBS exposure on child disutility by country based on EQ-5D-3L valued using time trade off.

Parameter	Median	Median.1	95% CI
NoGBS - GBS, SouthAfrica	-0.0268	-0.0268	(-0.0723, 0.0081)
NoGBS - GBS, Mozambique	-0.0133	-0.0133	(-0.0343, 0.0032)
NoGBS - GBS, India	-0.0213	-0.0213	(-0.0580, 0.0056)
NoGBS - GBS, Argentina	-0.0346	-0.0346	(-0.0920, 0.0233)

Supplementary table 18. Adjusted average marginal effect of iGBS exposure on child disutility by country based on EQ-5D-3L valued using time trade off including GBS-Country interaction term.

Parameter	Median	Median.1	95% CI
NoGBS - GBS, SouthAfrica	-0.0002	-0.0002	(-0.0777, 0.0709)
NoGBS - GBS, Mozambique	-0.0214	-0.0214	(-0.0554, 0.0078)
NoGBS - GBS, India	-0.0477	-0.0477	(-0.1414, 0.0261)
NoGBS - GBS, Argentina	-0.0768	-0.0768	(-0.2147, 0.0618)

Child health-state disutility based on EQ-5D-3L VAS

Model coefficients

Supplementary table 19. Unadjusted model of child health-state disutility based on EQ-5D-3L VAS.

Fixed effects (conditional)

Parameter	Median	95% CI
(Intercept)	-1.8615	(-2.2679, -1.4523)
phi_Intercept	2.2909	(1.9408, 2.6305)
gbsNoGBS	-0.4411	(-0.6975, -0.1945)
CountryCodeMozambique	0.2780	(-0.1300, 0.7141)
CountryCodeIndia	0.4948	(0.1175, 0.9166)
CountryCodeArgentina	0.7194	(0.2118, 1.2254)
phi_gbsNoGBS	0.2598	(-0.1899, 0.7081)

Fixed effects (zero-inflated)

Parameter	Median	95% CI
(Intercept)	1.4545	(0.8957, 2.0385)
gbsNoGBS	0.8495	(0.3528, 1.3443)
CountryCodeMozambique	-1.1550	(-1.7526, -0.5683)
CountryCodeIndia	-3.1668	(-3.8673, -2.5110)
CountryCodeArgentina	-2.6374	(-3.6998, -1.5687)

Model: disutility_VAS ~ gbs + CountryCode (466 Observations)

Supplementary table 20. Adjusted model of child health-state disutility based on EQ-5D-3L VAS.

Fixed effects (conditional)

Parameter	Median	95% CI
(Intercept)	-2.1351	(-2.9078, -1.3856)
phi_Intercept	2.2830	(1.9173, 2.6204)
gbsNoGBS	-0.3840	(-0.6614, -0.1167)
ageband	-0.0086	(-0.0375, 0.0197)
sexmale	0.1280	(-0.1046, 0.3619)
pretermTerm	0.1594	(-0.4188, 0.7989)
pretermUnknown	0.4358	(-0.2920, 1.1997)
carerhighesteducationNoOrEarlyChildhoodEducation	-0.0494	(-0.5840, 0.4856)
carerhighesteducationPrimaryEducation	0.2726	(-0.0998, 0.6402)
carerhighesteducationSecondaryEducation	0.0319	(-0.2877, 0.3494)
CountryCodeMozambique	0.1724	(-0.4086, 0.7423)
CountryCodeIndia	0.5074	(0.0888, 0.9488)
CountryCodeArgentina	0.6768	(0.1287, 1.2080)
phi_gbsNoGBS	0.2962	(-0.1644, 0.7646)

Fixed effects (zero-inflated)

Parameter	Median	95% CI
(Intercept)	1.9753	(0.6845, 3.3110)
gbsNoGBS	0.5517	(0.0145, 1.1051)
ageband	0.0679	(0.0094, 0.1256)
sexmale	-0.0544	(-0.5355, 0.4262)
pretermTerm	-1.0182	(-2.1383, 0.0388)
pretermUnknown	-2.5916	(-4.0118, -1.1833)
carerhighesteducationNoOrEarlyChildhoodEducation	0.9022	(-0.1125, 1.8816)
carerhighesteducationPrimaryEducation	-0.0793	(-0.9822, 0.7937)
carerhighesteducationSecondaryEducation	0.2920	(-0.4247, 0.9831)
CountryCodeMozambique	-1.3630	(-2.3585, -0.3811)
CountryCodeIndia	-2.8963	(-3.6546, -2.1700)
CountryCodeArgentina	-2.8440	(-4.0319, -1.7596)

Model: disutility_VAS ~ gbs + ageband + sex + preterm + carerhighesteducation + CountryCode (466 Observations)

Supplementary table 21. Adjusted model of child health-state disutility based on EQ-5D-3L VAS including GBS-Country interaction term.

Fixed effects (conditional)

Parameter	Median	95% CI
(Intercept)	-2.4738	(-3.5027, -1.5093)
phi_Intercept	2.2932	(1.9249, 2.6363)
gbsNoGBS	0.1215	(-0.7760, 1.1000)
ageband	-0.0084	(-0.0375, 0.0198)
sexmale	0.1513	(-0.0844, 0.3907)
pretermTerm	0.0785	(-0.5259, 0.7261)
pretermUnknown	0.3006	(-0.4617, 1.1010)
carerhighesteducationNoOrEarlyChildhoodEducation	0.0385	(-0.5542, 0.6410)
carerhighesteducationPrimaryEducation	0.2817	(-0.0826, 0.6462)
carerhighesteducationSecondaryEducation	0.0391	(-0.2803, 0.3543)
CountryCodeMozambique	0.6306	(-0.2931, 1.6407)
CountryCodeIndia	0.9027	(0.0606, 1.8353)
CountryCodeArgentina	1.0587	(0.1215, 2.0652)
gbsNoGBS:CountryCodeMozambique	-0.6643	(-1.7633, 0.3931)
gbsNoGBS:CountryCodeIndia	-0.5009	(-1.5082, 0.4499)
gbsNoGBS:CountryCodeArgentina	-0.5485	(-1.7324, 0.6215)
phi_gbsNoGBS	0.2783	(-0.1860, 0.7535)

Fixed effects (zero-inflated)

Parameter	Median	95% CI
(Intercept)	2.5092	(1.0095, 4.1153)
gbsNoGBS	-0.0342	(-1.1919, 1.0805)
ageband	0.0699	(0.0109, 0.1307)
sexmale	-0.0669	(-0.5409, 0.4386)
pretermTerm	-1.1481	(-2.3295, -0.0304)
pretermUnknown	-2.6113	(-4.1319, -1.1512)
carerhighesteducationNoOrEarlyChildhoodEducation	0.6373	(-0.4636, 1.7571)
carerhighesteducationPrimaryEducation	-0.1588	(-1.0795, 0.7425)
carerhighesteducationSecondaryEducation	0.3165	(-0.4042, 1.0102)
CountryCodeMozambique	-2.0095	(-3.4189, -0.6706)
CountryCodeIndia	-3.5681	(-4.9917, -2.2313)
CountryCodeArgentina	-2.6633	(-4.3226, -1.1705)
gbsNoGBS:CountryCodeMozambique	1.1195	(-0.3588, 2.6244)
gbsNoGBS:CountryCodeIndia	0.9521	(-0.5830, 2.5556)
gbsNoGBS:CountryCodeArgentina	-1.0062	(-3.5899, 1.3823)

Model: disutility_VAS ~ gbs + ageband + sex + preterm + carerhighesteducation + CountryCode + CountryCode * gbs (466 Observations)

Estimated proportion with zero-disutility by GBS status

Supplementary table 22. Unadjusted proportion of children by iGBS exposure status and country reporting zero disutility based on EQ-5D-3L VAS.

gbs	CountryCode	Proportion reporting zero disutility
GBS	SouthAfrica	0.81
GBS	Mozambique	0.57
GBS	India	0.16
GBS	Argentina	0.24
NoGBS	SouthAfrica	0.91
NoGBS	Mozambique	0.76
NoGBS	India	0.30
NoGBS	Argentina	0.42

Supplementary table 23. Adjusted proportion of children by iGBS exposure status and country reporting zero disutility based on EQ-5D-3L VAS.

gbs	CountryCode	Proportion reporting zero disutility
GBS	SouthAfrica	0.84
GBS	Mozambique	0.49
GBS	India	0.20
GBS	Argentina	0.27
NoGBS	SouthAfrica	0.90
NoGBS	Mozambique	0.78
NoGBS	India	0.27
NoGBS	Argentina	0.39

Supplementary table 24. Adjusted proportion of children by iGBS exposure status and country reporting zero disutility based on EQ-5D-3L VAS including GBS-Country interaction term.

gbs	CountryCode	Proportion reporting zero disutility
GBS	SouthAfrica	0.88
GBS	Mozambique	0.44
GBS	India	0.17
GBS	Argentina	0.38
NoGBS	SouthAfrica	0.88
NoGBS	Mozambique	0.80
NoGBS	India	0.29
NoGBS	Argentina	0.22

Estimated marginal means by GBS status

Supplementary table 25. Unadjusted marginal estimate of child disutility by iGBS exposure status and country based on EQ-5D-3L VAS.

Parameter	Median	Median.1	95% CI
GBS, SouthAfrica	0.0253	0.0253	(0.0122, 0.0413)
NoGBS, SouthAfrica	0.0082	0.0082	(0.0040, 0.0136)
GBS, Mozambique	0.0724	0.0724	(0.0486, 0.0987)
NoGBS, Mozambique	0.0281	0.0281	(0.0192, 0.0383)
GBS, India	0.1715	0.1715	(0.1383, 0.2076)
NoGBS, India	0.0987	0.0987	(0.0777, 0.1212)
GBS, Argentina	0.1825	0.1825	(0.1182, 0.2492)
NoGBS, Argentina	0.0978	0.0978	(0.0524, 0.1499)

Supplementary table 26. Adjusted marginal estimate of child disutility by iGBS exposure status and country based on EQ-5D-3L VAS.

Parameter	Median	Median.1	95% CI
GBS, SouthAfrica	0.0348	0.0348	(0.0137, 0.0630)
NoGBS, SouthAfrica	0.0175	0.0175	(0.0060, 0.0339)
GBS, Mozambique	0.0783	0.0783	(0.0527, 0.1074)
NoGBS, Mozambique	0.0449	0.0449	(0.0270, 0.0649)
GBS, India	0.1569	0.1569	(0.1090, 0.2137)
NoGBS, India	0.1022	0.1022	(0.0667, 0.1422)
GBS, Argentina	0.1758	0.1758	(0.1135, 0.2466)
NoGBS, Argentina	0.1150	0.1150	(0.0659, 0.1702)

Supplementary table 27. Adjusted marginal estimate of child disutility by iGBS exposure status and country based on EQ-5D-3L VAS including GBS-Country interaction term.

Parameter	Median	Median.1	95% CI
GBS, SouthAfrica	0.0184	0.0184	(0.0027, 0.0448)
NoGBS, SouthAfrica	0.0214	0.0214	(0.0072, 0.0414)
GBS, Mozambique	0.0900	0.0900	(0.0571, 0.1276)
NoGBS, Mozambique	0.0356	0.0356	(0.0176, 0.0595)
GBS, India	0.1659	0.1659	(0.1092, 0.2299)
NoGBS, India	0.1009	0.1009	(0.0640, 0.1430)
GBS, Argentina	0.1524	0.1524	(0.0767, 0.2375)
NoGBS, Argentina	0.1357	0.1357	(0.0700, 0.2136)

Average marginal effect by GBS status

Supplementary table 28. Unadjusted average marginal effect of iGBS exposure on child disutility by country based on EQ-5D-3L VAS.

Parameter	Median	Median.1	95% CI
NoGBS - GBS, SouthAfrica	-0.0169	-0.0169	(-0.0302, -0.0064)
NoGBS - GBS, Mozambique	-0.0441	-0.0441	(-0.0684, -0.0222)
NoGBS - GBS, India	-0.0725	-0.0725	(-0.1070, -0.0399)
NoGBS - GBS, Argentina	-0.0835	-0.0835	(-0.1252, -0.0453)

Supplementary table 29. Adjusted average marginal effect of iGBS exposure on child disutility by country based on EQ-5D-3L VAS.

Parameter	Median	Median.1	95% CI
NoGBS - GBS, SouthAfrica	-0.0168	-0.0168	(-0.0341, -0.0036)
NoGBS - GBS, Mozambique	-0.0329	-0.0329	(-0.0562, -0.0128)
NoGBS - GBS, India	-0.0541	-0.0541	(-0.0918, -0.0204)
NoGBS - GBS, Argentina	-0.0597	-0.0597	(-0.1003, -0.0230)

Supplementary table 30. Adjusted average marginal effect of iGBS exposure on child disutility by country based on EQ-5D-3L VAS including GBS-Country interaction term.

Parameter	Median	Median.1	95% CI
NoGBS - GBS, SouthAfrica	0.0028	0.0028	(-0.0233, 0.0251)
NoGBS - GBS, Mozambique	-0.0537	-0.0537	(-0.0955, -0.0151)
NoGBS - GBS, India	-0.0644	-0.0644	(-0.1171, -0.0145)
NoGBS - GBS, Argentina	-0.0164	-0.0164	(-0.1193, 0.0870)

Caregiver health-state disutility based on EQ-5D-3L Index

Model coefficients

Supplementary table 31. Unadjusted model of caregiver health-state disutility based on EQ-5D-3L valued using time trade off.

Fixed effects (conditional)

Parameter	Median	95% CI
(Intercept)	-1.4409	(-1.8558, -1.0494)
phi_Intercept	3.0115	(2.5112, 3.4736)
gbsNoGBS	0.0083	(-0.2370, 0.2519)
CountryCodeMozambique	0.1034	(-0.3211, 0.5524)
CountryCodeIndia	0.2634	(-0.1279, 0.6779)
CountryCodeArgentina	0.0845	(-0.3737, 0.5475)
phi_gbsNoGBS	-0.1430	(-0.7513, 0.4778)

Fixed effects (zero-inflated)

Parameter	Median	95% CI
(Intercept)	2.6725	(1.9034, 3.4742)
gbsNoGBS	0.2310	(-0.3358, 0.7974)
CountryCodeMozambique	-0.8375	(-1.6754, -0.0494)
CountryCodeIndia	-2.4598	(-3.2810, -1.7029)
CountryCodeArgentina	-3.8107	(-5.0232, -2.6350)

Model: disutility_TTO ~ gbs + CountryCode (467 Observations)

Supplementary table 32. Adjusted model of caregiver health-state disutility based on EQ-5D-3L valued using time trade off.

Fixed effects (conditional)

Parameter	Median	95% CI
(Intercept)	-1.4938	(-2.0731, -0.9145)
phi_Intercept	3.2136	(2.6776, 3.7031)
gbsNoGBS	0.0794	(-0.1682, 0.3246)
ageband	0.0052	(-0.0244, 0.0373)
sexmale	-0.0529	(-0.3042, 0.1935)
pretermTerm	-0.1830	(-0.5752, 0.2148)
pretermUnknown	0.5266	(-0.1610, 1.1609)
carerhighesteducationNoOrEarlyChildhoodEducation	0.2194	(-0.2807, 0.7274)
carerhighesteducationPrimaryEducation	0.4160	(0.0871, 0.7396)
carerhighesteducationSecondaryEducation	0.2002	(-0.1269, 0.5315)
CountryCodeMozambique	-0.2753	(-0.8334, 0.2751)
CountryCodeIndia	0.2646	(-0.1485, 0.7122)
CountryCodeArgentina	-0.0277	(-0.4943, 0.4462)
phi_gbsNoGBS	-0.3398	(-0.9710, 0.3244)

Fixed effects (zero-inflated)

Parameter	Median	95% CI
(Intercept)	3.2540	(1.8566, 4.6877)
gbsNoGBS	0.1082	(-0.4973, 0.7131)
ageband	-0.0986	(-0.1776, -0.0208)
sexmale	-0.0287	(-0.5925, 0.5416)
pretermTerm	0.2883	(-0.8576, 1.4064)
pretermUnknown	0.1025	(-1.6304, 1.7962)
carerhighesteducationNoOrEarlyChildhoodEducation	0.0112	(-1.2810, 1.2497)
carerhighesteducationPrimaryEducation	-1.8023	(-2.8305, -0.8177)
carerhighesteducationSecondaryEducation	-0.0079	(-0.8211, 0.7878)
CountryCodeMozambique	0.5241	(-0.8523, 1.9433)

Parameter	Median	95% CI
CountryCodeIndia	-2.4905	(-3.4272, -1.5966)
CountryCodeArgentina	-3.3755	(-4.7076, -2.1189)

Model: disutility_TTO ~ gbs + ageband + sex + preterm + carerhighesteducation + CountryCode (467 Observations)

Supplementary table 33. Adjusted model of caregiver health-state disutility based on EQ-5D-3L valued using time trade off including GBS-Country interaction term.

Fixed effects (conditional)

Parameter	Median	95% CI
(Intercept)	-1.4144	(-2.1808, -0.6871)
phi_Intercept	3.1930	(2.6487, 3.7064)
gbsNoGBS	-0.0418	(-0.8257, 0.7338)
ageband	0.0053	(-0.0259, 0.0363)
sexmale	-0.0722	(-0.3323, 0.1839)
pretermTerm	-0.1899	(-0.5845, 0.2257)
pretermUnknown	0.6385	(-0.1145, 1.3605)
carerhighesteducationNoOrEarlyChildhoodEducation	0.1619	(-0.3838, 0.6735)
carerhighesteducationPrimaryEducation	0.4290	(0.0955, 0.7659)
carerhighesteducationSecondaryEducation	0.1928	(-0.1379, 0.5240)
CountryCodeMozambique	-0.4451	(-1.2093, 0.3804)
CountryCodeIndia	0.2238	(-0.4332, 0.9248)
CountryCodeArgentina	-0.0730	(-0.7565, 0.6523)
gbsNoGBS:CountryCodeMozambique	0.3224	(-0.6379, 1.2879)
gbsNoGBS:CountryCodeIndia	0.0862	(-0.7834, 0.9249)
gbsNoGBS:CountryCodeArgentina	0.0537	(-0.9178, 0.9774)
phi_gbsNoGBS	-0.3456	(-1.0102, 0.3243)

Fixed effects (zero-inflated)

Parameter	Median	95% CI
(Intercept)	3.3076	(1.6621, 5.1220)
gbsNoGBS	0.2150	(-1.4129, 1.6813)
ageband	-0.1082	(-0.1885, -0.0282)
sexmale	-0.0825	(-0.6632, 0.4969)
pretermTerm	0.2836	(-0.8885, 1.4225)
pretermUnknown	0.5719	(-1.1615, 2.4081)
carerhighesteducationNoOrEarlyChildhoodEducation	-0.5637	(-1.9188, 0.7819)
carerhighesteducationPrimaryEducation	-1.9142	(-2.9880, -0.9207)
carerhighesteducationSecondaryEducation	0.0195	(-0.7939, 0.8254)
CountryCodeMozambique	-0.0348	(-1.9205, 1.8004)
CountryCodeIndia	-1.8650	(-3.5158, -0.4076)
CountryCodeArgentina	-3.1357	(-5.1239, -1.3411)

Parameter	Median	95% CI
gbsNoGBS:CountryCodeMozambique	1.2597	(-0.6803, 3.1989)
gbsNoGBS:CountryCodeIndia	-0.9694	(-2.7171, 0.9208)
gbsNoGBS:CountryCodeArgentina	-0.6174	(-3.4481, 2.1753)

Model: disutility_TTO ~ gbs + ageband + sex + preterm + carerhighesteducation + CountryCode + CountryCode * gbs (467 Observations)

Estimated proportion with zero-disutility by GBS status

Supplementary table 34. Unadjusted proportion of caregivers by iGBS exposure status and country reporting zero disutility based on EQ-5D-3L valued using time trade off.

gbs	CountryCode	Proportion reporting zero disutility
GBS	SouthAfrica	0.93
GBS	Mozambique	0.86
GBS	India	0.55
GBS	Argentina	0.25
NoGBS	SouthAfrica	0.95
NoGBS	Mozambique	0.89
NoGBS	India	0.61
NoGBS	Argentina	0.30

Supplementary table 35. Adjusted proportion of caregivers by iGBS exposure status and country reporting zero disutility based on EQ-5D-3L valued using time trade off.

gbs	CountryCode	Proportion reporting zero disutility
GBS	SouthAfrica	0.93
GBS	Mozambique	0.83
GBS	India	0.58
GBS	Argentina	0.28
NoGBS	SouthAfrica	0.94
NoGBS	Mozambique	0.89
NoGBS	India	0.59
NoGBS	Argentina	0.26

Supplementary table 36. Adjusted proportion of caregivers by iGBS exposure status and country reporting zero disutility based on EQ-5D-3L valued using time trade off including GBS-Country interaction term.

gbs	CountryCode	Proportion reporting zero disutility
GBS	SouthAfrica	0.93
GBS	Mozambique	0.74
GBS	India	0.68
GBS	Argentina	0.31
NoGBS	SouthAfrica	0.95
NoGBS	Mozambique	0.92

gbs	CountryCode	Proportion reporting zero disutility
NoGBS	India	0.54
NoGBS	Argentina	0.22

Estimated marginal means by GBS status

Supplementary table 37. Unadjusted marginal estimate of caregiver disutility by iGBS exposure status and country based on EQ-5D-3L valued using time trade off.

Parameter	Median	Median.1	95% CI
GBS, SouthAfrica	0.0122	0.0122	(0.0040, 0.0235)
NoGBS, SouthAfrica	0.0100	0.0100	(0.0038, 0.0180)
GBS, Mozambique	0.0286	0.0286	(0.0145, 0.0467)
NoGBS, Mozambique	0.0235	0.0235	(0.0134, 0.0353)
GBS, India	0.1049	0.1049	(0.0698, 0.1425)
NoGBS, India	0.0926	0.0926	(0.0654, 0.1217)
GBS, Argentina	0.1529	0.1529	(0.1042, 0.2060)
NoGBS, Argentina	0.1449	0.1449	(0.0918, 0.2001)

Supplementary table 38. Adjusted marginal estimate of caregiver disutility by iGBS exposure status and country based on EQ-5D-3L valued using time trade off.

Parameter	Median	Median.1	95% CI
GBS, SouthAfrica	0.0369	0.0369	(0.0090, 0.0776)
NoGBS, SouthAfrica	0.0359	0.0359	(0.0086, 0.0757)
GBS, Mozambique	0.0204	0.0204	(0.0077, 0.0376)
NoGBS, Mozambique	0.0198	0.0198	(0.0075, 0.0368)
GBS, India	0.1722	0.1722	(0.1070, 0.2433)
NoGBS, India	0.1747	0.1747	(0.1083, 0.2492)
GBS, Argentina	0.1787	0.1787	(0.1106, 0.2471)
NoGBS, Argentina	0.1842	0.1842	(0.1099, 0.2636)

Supplementary table 39. Adjusted marginal estimate of caregiver disutility by iGBS exposure status and country based on EQ-5D-3L valued using time trade off including GBS-Country interaction term.

Parameter	Median	Median.1	95% CI
GBS, SouthAfrica	0.0404	0.0404	(0.0040, 0.0983)
NoGBS, SouthAfrica	0.0339	0.0339	(0.0062, 0.0767)
GBS, Mozambique	0.0305	0.0305	(0.0110, 0.0554)
NoGBS, Mozambique	0.0112	0.0112	(0.0025, 0.0254)
GBS, India	0.1421	0.1421	(0.0714, 0.2237)
NoGBS, India	0.1945	0.1945	(0.1211, 0.2727)
GBS, Argentina	0.1754	0.1754	(0.0929, 0.2611)
NoGBS, Argentina	0.1924	0.1924	(0.0956, 0.2925)

Average marginal effect by GBS status

Supplementary table 40. Unadjusted average marginal effect of iGBS exposure on caregiver disutility by country based on EQ-5D-3L valued using time trade off.

Parameter	Median	Median.1	95% CI
NoGBS - GBS, SouthAfrica	-0.0022	-0.0022	(-0.0107, 0.0042)
NoGBS - GBS, Mozambique	-0.0049	-0.0049	(-0.0209, 0.0087)
NoGBS - GBS, India	-0.0122	-0.0122	(-0.0499, 0.0255)
NoGBS - GBS, Argentina	-0.0080	-0.0080	(-0.0439, 0.0309)

Supplementary table 41. Adjusted average marginal effect of iGBS exposure on caregiver disutility by country based on EQ-5D-3L valued using time trade off.

Parameter	Median	Median.1	95% CI
NoGBS - GBS, SouthAfrica	-0.0007	-0.0007	(-0.0206, 0.0191)
NoGBS - GBS, Mozambique	-0.0005	-0.0005	(-0.0123, 0.0111)
NoGBS - GBS, India	0.0026	0.0026	(-0.0440, 0.0502)
NoGBS - GBS, Argentina	0.0057	0.0057	(-0.0365, 0.0477)

Supplementary table 42. Adjusted average marginal effect of iGBS exposure on caregiver disutility by country based on EQ-5D-3L valued using time trade off including GBS-Country interaction term.

Parameter	Median	Median.1	95% CI
NoGBS - GBS, SouthAfrica	-0.0060	-0.0060	(-0.0620, 0.0421)
NoGBS - GBS, Mozambique	-0.0184	-0.0184	(-0.0446, 0.0012)
NoGBS - GBS, India	0.0509	0.0509	(-0.0190, 0.1226)
NoGBS - GBS, Argentina	0.0167	0.0167	(-0.0957, 0.1312)

Caregiver health-state disutility based on EQ-5D-3L VAS

Model coefficients

Supplementary table 43. Unadjusted model of caregiver health-state disutility based on EQ-5D-3L VAS.

Fixed effects (conditional)

Parameter	Median	95% CI
(Intercept)	-1.7059	(-2.2576, -1.1838)
phi_Intercept	1.8212	(1.4872, 2.1262)
gbsNoGBS	-0.3633	(-0.6305, -0.1131)
CountryCodeMozambique	0.2901	(-0.2531, 0.8576)
CountryCodeIndia	0.7854	(0.2837, 1.3352)
CountryCodeArgentina	0.7941	(0.1720, 1.4268)
phi_gbsNoGBS	0.5305	(0.1054, 0.9622)

Fixed effects (zero-inflated)

Parameter	Median	95% CI
(Intercept)	1.8231	(1.1716, 2.5408)
gbsNoGBS	1.3345	(0.7458, 1.9176)
CountryCodeMozambique	-1.7377	(-2.4724, -1.0317)
CountryCodeIndia	-5.5084	(-6.5784, -4.4935)
CountryCodeArgentina	-3.5019	(-4.7205, -2.3387)

Model: disutility_VAS ~ gbs + CountryCode (467 Observations)

Supplementary table 44. Adjusted model of caregiver health-state disutility based on EQ-5D-3L VAS.

Fixed effects (conditional)

Parameter	Median	95% CI
(Intercept)	-1.5822	(-2.2615, -0.9476)
phi_Intercept	1.8832	(1.5537, 2.1962)
gbsNoGBS	-0.3162	(-0.5771, -0.0581)
ageband	0.0202	(-0.0098, 0.0498)
sexmale	0.0740	(-0.1541, 0.3130)
pretermTerm	-0.6446	(-1.0601, -0.2200)
pretermUnknown	-0.4477	(-1.0950, 0.2056)
carerhighesteducationNoOrEarlyChildhoodEducation	-0.2854	(-0.8279, 0.2388)
carerhighesteducationPrimaryEducation	0.1573	(-0.1790, 0.4767)
carerhighesteducationSecondaryEducation	0.1377	(-0.1729, 0.4433)
CountryCodeMozambique	0.3780	(-0.3014, 1.0661)
CountryCodeIndia	1.0506	(0.4966, 1.6446)
CountryCodeArgentina	0.7941	(0.1461, 1.4543)
phi_gbsNoGBS	0.5489	(0.1183, 0.9913)

Fixed effects (zero-inflated)

Parameter	Median	95% CI
(Intercept)	1.7581	(0.3183, 3.3232)
gbsNoGBS	0.7215	(0.0559, 1.3793)
ageband	0.0307	(-0.0362, 0.0981)
sexmale	-0.2045	(-0.7929, 0.3917)
pretermTerm	0.4780	(-0.7526, 1.6195)
pretermUnknown	-0.9394	(-2.5064, 0.5883)
carerhighesteducationNoOrEarlyChildhoodEducation	1.5092	(0.2776, 2.7238)
carerhighesteducationPrimaryEducation	-0.3904	(-1.5427, 0.7323)
carerhighesteducationSecondaryEducation	-0.0012	(-0.9918, 0.9436)
CountryCodeMozambique	-2.2455	(-3.4816, -1.0996)
CountryCodeIndia	-5.4958	(-6.7154, -4.3936)

Parameter	Median	95% CI
CountryCodeArgentina	-3.6588	(-4.9843, -2.4364)

Model: disutility_VAS ~ gbs + ageband + sex + preterm + carerhighesteducation + CountryCode (467 Observations)

Supplementary table 45. Adjusted model of caregiver health-state disutility based on EQ-5D-3L VAS including GBS-Country interaction term.

Fixed effects (conditional)

Parameter	Median	95% CI
(Intercept)	-1.7341	(-2.8428, -0.7611)
phi_Intercept	1.8762	(1.5441, 2.1970)
gbsNoGBS	-0.1287	(-1.2513, 1.1088)
ageband	0.0213	(-0.0088, 0.0508)
sexmale	0.0920	(-0.1423, 0.3340)
pretermTerm	-0.6558	(-1.0820, -0.2268)
pretermUnknown	-0.5809	(-1.2738, 0.1298)
carerhighesteducationNoOrEarlyChildhoodEducation	-0.1841	(-0.7485, 0.3794)
carerhighesteducationPrimaryEducation	0.1662	(-0.1633, 0.4950)
carerhighesteducationSecondaryEducation	0.1292	(-0.1847, 0.4351)
CountryCodeMozambique	0.6625	(-0.4382, 1.8288)
CountryCodeIndia	1.1720	(0.1558, 2.2845)
CountryCodeArgentina	0.8026	(-0.2877, 2.0321)
gbsNoGBS:CountryCodeMozambique	-0.4533	(-1.7589, 0.8185)
gbsNoGBS:CountryCodeIndia	-0.1544	(-1.3840, 1.0487)
gbsNoGBS:CountryCodeArgentina	0.0453	(-1.4059, 1.3965)
phi_gbsNoGBS	0.5589	(0.1242, 0.9953)

Fixed effects (zero-inflated)

Parameter	Median	95% CI
(Intercept)	2.0417	(0.4021, 3.8030)
gbsNoGBS	0.3947	(-0.9513, 1.7432)
ageband	0.0301	(-0.0368, 0.1004)
sexmale	-0.2543	(-0.8425, 0.3547)
pretermTerm	0.4515	(-0.7971, 1.6451)
pretermUnknown	-0.8084	(-2.4266, 0.7878)
carerhighesteducationNoOrEarlyChildhoodEducation	1.0890	(-0.2313, 2.3792)
carerhighesteducationPrimaryEducation	-0.5737	(-1.7798, 0.5848)
carerhighesteducationSecondaryEducation	0.0106	(-0.9499, 0.9818)
CountryCodeMozambique	-2.7097	(-4.3083, -1.2319)
CountryCodeIndia	-5.1154	(-7.0089, -3.4229)
CountryCodeArgentina	-3.4266	(-5.2226, -1.7468)
gbsNoGBS:CountryCodeMozambique	1.0378	(-0.6018, 2.7277)

Parameter	Median	95% CI
gbsNoGBS:CountryCodeIndia	-0.6080	(-2.7320, 1.6513)
gbsNoGBS:CountryCodeArgentina	-0.7141	(-3.3949, 1.8411)

Model: disutility_VAS ~ gbs + ageband + sex + preterm + carerhighesteducation + CountryCode + CountryCode * gbs (467 Observations)

Estimated proportion with zero-disutility by GBS status

Supplementary table 46. Unadjusted proportion of caregivers by iGBS exposure status and country reporting zero disutility based on EQ-5D-3L VAS.

gbs	CountryCode	Proportion reporting zero disutility
GBS	SouthAfrica	0.86
GBS	Mozambique	0.52
GBS	India	0.03
GBS	Argentina	0.17
NoGBS	SouthAfrica	0.96
NoGBS	Mozambique	0.80
NoGBS	India	0.09
NoGBS	Argentina	0.42

Supplementary table 47. Adjusted proportion of caregivers by iGBS exposure status and country reporting zero disutility based on EQ-5D-3L VAS.

gbs	CountryCode	Proportion reporting zero disutility
GBS	SouthAfrica	0.89
GBS	Mozambique	0.45
GBS	India	0.05
GBS	Argentina	0.24
NoGBS	SouthAfrica	0.95
NoGBS	Mozambique	0.83
NoGBS	India	0.08
NoGBS	Argentina	0.32

Supplementary table 48. Adjusted proportion of caregivers by iGBS exposure status and country reporting zero disutility based on EQ-5D-3L VAS including GBS-Country interaction term.

gbs	CountryCode	Proportion reporting zero disutility
GBS	SouthAfrica	0.91
GBS	Mozambique	0.38
GBS	India	0.09
GBS	Argentina	0.31
NoGBS	SouthAfrica	0.94
NoGBS	Mozambique	0.85
NoGBS	India	0.06

gbs	CountryCode	Proportion reporting zero disutility
NoGBS	Argentina	0.22

Estimated marginal means by GBS status

Supplementary table 49. Unadjusted marginal estimate of caregiver disutility by iGBS exposure status and country based on EQ-5D-3L VAS.

Parameter	Median	Median.1	95% CI
GBS, SouthAfrica	0.0211	0.0211	(0.0080, 0.0390)
NoGBS, SouthAfrica	0.0045	0.0045	(0.0016, 0.0089)
GBS, Mozambique	0.0930	0.0930	(0.0617, 0.1268)
NoGBS, Mozambique	0.0281	0.0281	(0.0181, 0.0397)
GBS, India	0.2771	0.2771	(0.2322, 0.3268)
NoGBS, India	0.1971	0.1971	(0.1678, 0.2269)
GBS, Argentina	0.2374	0.2374	(0.1622, 0.3192)
NoGBS, Argentina	0.1253	0.1253	(0.0646, 0.1935)

Supplementary table 50. Adjusted marginal estimate of caregiver disutility by iGBS exposure status and country based on EQ-5D-3L VAS.

Parameter	Median	Median.1	95% CI
GBS, SouthAfrica	0.0252	0.0252	(0.0068, 0.0524)
NoGBS, SouthAfrica	0.0108	0.0108	(0.0027, 0.0244)
GBS, Mozambique	0.1186	0.1186	(0.0753, 0.1678)
NoGBS, Mozambique	0.0683	0.0683	(0.0371, 0.1040)
GBS, India	0.3226	0.3226	(0.2484, 0.3989)
NoGBS, India	0.2500	0.2500	(0.1892, 0.3157)
GBS, Argentina	0.2280	0.2280	(0.1499, 0.3107)
NoGBS, Argentina	0.1564	0.1564	(0.0914, 0.2283)

Supplementary table 51. Adjusted marginal estimate of caregiver disutility by iGBS exposure status and country based on EQ-5D-3L VAS including GBS-Country interaction term.

Parameter	Median	Median.1	95% CI
GBS, SouthAfrica	0.0181	0.0181	(0.0015, 0.0494)
NoGBS, SouthAfrica	0.0121	0.0121	(0.0022, 0.0286)
GBS, Mozambique	0.1430	0.1430	(0.0865, 0.2048)
NoGBS, Mozambique	0.0479	0.0479	(0.0202, 0.0831)
GBS, India	0.3065	0.3065	(0.2255, 0.3912)
NoGBS, India	0.2571	0.2571	(0.1953, 0.3258)
GBS, Argentina	0.1892	0.1892	(0.0966, 0.2939)
NoGBS, Argentina	0.1894	0.1894	(0.0988, 0.2863)

Average marginal effect by GBS status

Supplementary table 52. Unadjusted average marginal effect of iGBS exposure on caregiver disutility by country based on EQ-5D-3L VAS.

Parameter	Median	Median.1	95% CI
NoGBS - GBS, SouthAfrica	-0.0163	-0.0163	(-0.0316, -0.0053)
NoGBS - GBS, Mozambique	-0.0646	-0.0646	(-0.0969, -0.0352)
NoGBS - GBS, India	-0.0801	-0.0801	(-0.1296, -0.0308)
NoGBS - GBS, Argentina	-0.1103	-0.1103	(-0.1649, -0.0582)

Supplementary table 53. Adjusted average marginal effect of iGBS exposure on caregiver disutility by country based on EQ-5D-3L VAS.

Parameter	Median	Median.1	95% CI
NoGBS - GBS, SouthAfrica	-0.0138	-0.0138	(-0.0324, -0.0016)
NoGBS - GBS, Mozambique	-0.0493	-0.0493	(-0.0849, -0.0164)
NoGBS - GBS, India	-0.0719	-0.0719	(-0.1251, -0.0196)
NoGBS - GBS, Argentina	-0.0705	-0.0705	(-0.1203, -0.0249)

Supplementary table 54. Adjusted average marginal effect of iGBS exposure on caregiver disutility by country based on EQ-5D-3L VAS including GBS-Country interaction term.

Parameter	Median	Median.1	95% CI
NoGBS - GBS, SouthAfrica	-0.0055	-0.0055	(-0.0377, 0.0178)
NoGBS - GBS, Mozambique	-0.0936	-0.0936	(-0.1564, -0.0374)
NoGBS - GBS, India	-0.0489	-0.0489	(-0.1207, 0.0204)
NoGBS - GBS, Argentina	-0.0001	-0.0001	(-0.1270, 0.1297)

Long-term healthcare utilisation, costs, and quality of life after invasive group B *Streptococcus* disease: a cohort study in five low- and middle-income countries

Supplementary Methods

Summary of study settings

In 2018, a call for data was shared through multiple channels to reach the widest number of potential study sites in low- and middle-income countries. This included contacting experts, known GBS researchers and previous collaborators, looking through scientific conferences and meetings, placing posts on social media platforms, and sending direct requests from the WHO head office to country offices. Of those who responded, we identified potential study sites based on the following criteria: (a) they had at least 10 surviving iGBS cases post-discharge that could be enrolled; (b) they had neurodevelopmental follow-up data or the ability to collect this type of data in children aged at least 3 years; (c) their expected loss to follow-up was <20%. Research teams from Argentina, India, Kenya, Mozambique, and South Africa met the criteria and agreed to participate in this work and lead investigations locally.

The sites identified children with a history of iGBS in the first 90 days after birth, and who were at least 18 months old at time of recruitment via a Health and Demographic Surveillance System (HDSS) (Kenya, Mozambique) or hospital records (Argentina, India). The sites identified a comparison cohort (children with no history of iGBS) matched on age and sex via HDSS or hospital-birth registries. In South Africa, a cohort of iGBS survivors and controls from three epidemiological studies that were conducted between 2012 and 2015 were contacted for re-enrolment.

Case definition for iGBS

Clinical presentation	iGBS case definition
Possible serious bacterial infection (pSBI)	One of the following: temperature ≥37.5°C or ≤35.5°C, history of difficulty feeding, movement only when stimulated, respiratory rate of ≥60 breaths per min, severe chest in-drawing, history of convulsions
Sepsis	Clinical signs of pSBI and/or GBS-positive blood culture or latex agglutination or PCR
Meningitis	Clinical signs of pSBI and [(GBS-positive CSF culture or latex agglutination or PCR) or (GBS-positive blood culture or latex agglutination or PCR and CSF leucocyte count of >20x106/l)]

CSF, cerebrospinal fluid; PCR, polymerase chain reaction; pSBI, possible serious bacterial infection

Demographic, health, and economic impact of long-term outcomes in survivors of neonatal GBS disease questionnaire

Introduction

Thank you for coming into the clinic today for your child's GBS study appointment.

We will be looking at your child's health and development by asking you questions about your child's and will also ask you some questions about your household .

We will also be asking your child's to perform a few tasks. We will be taking notes of what your child's is able to do.

It is expected that your time at the clinic will take about 2.5 hours. We will have a break and snack after about an hour, and please let us know if you and/or your child's need a break at anytime.

Thank you again for your participation in the study, which aims to understand the health and financial needs of children who had Group B Streptococcus disease when they were babies. Your participation in our study is voluntary, and non-participation will not influence your health care or your relationship with your midwife, doctor or other health care professional. You can stop the interview at any point if you no longer want to be part of the study.

We have an information form about our study that I will read to you now and ask your consent for ongoing participation in this study.

INTERVIEWER READS INFORMATION AND CONSENT FORM, GIVES INFORMATION FORM TO CAREGIVER/MOTHER AND KEEPS CONSENT FORM. GO TO CONSENT SECTION TO SELECT CONSENT 'YES' OR 'NO' AS APPROPRIATE.

IF CONSENT YES, CONTINUE TO GBS QUESTIONNAIRE

SECTION 1 – PARTICIPANT AND HOUSEHOLD DETAILS

This section captures background information on the participant, main caregiver and household. Where possible data items should be automatically pre-populated in the tablet-based survey platform using existing data and responses from other survey modules.

Study information

ID	Question / Data Item	Response Options	Comments/Filter
1.1	Study Site	☐ CHBAH	*(tick one appropriate answer)*
1.2	Country code	(01) ☐ Argentina (02) ☐ India (03) ☐ Kenya (04) ☐ Mozambique	*(tick one appropriate answer)*

		(05) ☐ South Africa	
1.3	Clinic/Hospital code	☐☐☐☐☐☐☐	***(indicate clinic code, interviewer ID and interview date correctly)***
1.4	Interviewer ID	☐☐☐☐☐☐☐	
1.5	Interview Date	d d m m y y y y	
	Respondent Identification		
1.6	What is **YOUR** relationship to **THE CHILD**?	☐ Mother ☐ Father ☐ Grandparent ☐ Aunt / Uncle ☐ Sibling ☐ Other (biological relation) ☐ Other (not biological relation)	
1.7	Are you the main caregiver for this child?	☐ YES ☐ NO	If yes, skip to 2.1
1.8	What is **the main caregiver** relationship to **THE CHILD**?	☐ Mother ☐ Father ☐ Grandparent ☐ Aunt / Uncle ☐ Sibling ☐ Other (biological relation) ☐ Other (not biological relation)	main caregiver, which is the person from your household who usually spends the most time caring for THIS CHILD.

Participant information

ID	Question / Data Item	Response Options	Comments
	Child Identification		
2.1	Study Participant ID	☐☐☐☐☐☐☐	***Unique for the study and auto generated when participant list***

ID	Question / Data Item	Response Options	Comments
			imported into database
2.1a	HDSS Participant ID	☐☐☐☐☐☐☐	*Only in sites with health and Demographic Surveillance System (HDSS)*
2.1b	HDSS Household ID	☐☐☐☐☐☐☐	*Only in sites with health and Demographic Surveillance System (HDSS)*
2.2	Participant Name	Surname …… First name……	***(indicate name correctly)***
2.3	Participant Sex	Boy (Male) Girls (Female) Ambiguous Others	*(tick one appropriate answer)*
2.4	Participant Age	☐☐ ☐ Don't Know	***(indicate Age)*** ***(tick the box if don't know)***
2.5	Participant Date of Birth	d d m m y y y y	***(indicate date of birth)***
2.6	Participant Ethnic Group	Combined for site-specific list	*(tick appropriate answer and specify where needed)*
2.7	Participant Religion	Combined for site-specific list	*(tick one appropriate answer)*
2.8	Language	Combined for site-specific list	*(tick appropriate answer and specify where needed)*
	Birth history		
3.1	Birth weight (g)	.☐ ☐ Don't Know	***(indicate grams)*** ***(tick the box if don't know)***

ID	Question / Data Item	Response Options	Comments
3.2	Gestational age	☐ Term (≥ 37 weeks) ☐ Preterm (< 37 weeks) ☐☐ ☐ Don't Know	*(If preterm, please record gestational age -- Numerical value (weeks)*
3.3	What is the birth order of **your child**?	☐ First born ☐ Second born ☐ Third born ☐ Specify if higher _____ ☐ Don't Know	*(tick one appropriate answer)*
3.4	Did **your child** have any perinatal/neonatal complications?	☐ YES ☐ NO ☐ Don't Know	*(tick one appropriate answer)*
3.5	Did **your child** require admission as a baby?	☐ YES ☐ NO ☐ Don't Know If yes, please explain ……	*(tick one appropriate answer)*
	Current and past health status		
3.5	Do you think **your child** is generally well today?	☐ Yes ☐ No ☐ Don't know	*(tick one appropriate answer)*
3.6	Does **your child** have any of the following symptoms?	☐ High fever ☐ Severe headache ☐ Severe pain ☐ Croupy cough ☐ Severe diarrhoea ☐ Unable to drink or eat	
3.7	Self-reported medical history of major illness with neurodevelopment complication Has **your child** ever had:		
	a. Major illness with admission to hospital or ongoing health problems	☐ Yes ☐ No ☐ Don't know If yes, please specify: HIV	*(tick one appropriate answer)*

ID	Question / Data Item	Response Options	Comments
		Meningitis Other, don't know Other, specify _____	
	b. Convulsions or other neurologic problems	☐ Yes ☐ No ☐ Don't know	*(tick one appropriate answer)*
	c. Malnutrition or growth problems	☐ Yes ☐ No ☐ Don't know	*(tick one appropriate answer)*
	d. Developmental delays	☐ Yes ☐ No ☐ Don't know	*(tick one appropriate answer)*
	e. Attention deficit hyperactivity disorder (ADHD)/anxiety/mood problems/depression	☒ Yes ☐ No ☐ Don't know	*(tick one appropriate answer)*
	f. Any other injury (e.g., loss of fingers, toes, limb)	☐ Yes ☐ No ☐ Don't know	*(tick one appropriate answer)*
	g. Any other significant problem that has ongoing implications	☐ Yes ☐ No ☐ Don't know If yes, please specify ……	
3.8	Does your child have difficulty hearing sounds like people's voices or music?	☐ (0) No difficulty ☐ (1) Some difficulty ☐ (2) A lot of difficulty ☐ (3) Cannot hear at all	
3.9	Does your child have difficulty seeing?	☐ (0) No difficulty ☐ (1) Some difficulty ☐ (2) A lot of difficulty ☐ (3) Cannot see at all	
	Participant Education		
4.1	Can **your child** read and write a simple sentence?	☐ YES ☐ NO	*(tick one appropriate answer)*

ID	Question / Data Item	Response Options	Comments
4.2	Has **your child** ever attended school or any early childhood education programme?	☐ YES ☐ NO	**If no skip to 5.1**
4.3	How many years has **your child** completed in formal education?	☐☐ ☐ Don't Know	***(indicate years)*** ***(tick the box if don't know)***
4.4	Is **your child** currently in formal education?	☐ YES ☐ NO	*(tick one appropriate answer)*
4.5	Has **your child** ever repeated a school year (grade)?	☐ YES ☐ NO	**If no skip to 4.7**
4.6	If yes, how many times did **your child** repeat a school year (grade)?	☐☐ ☐ Don't Know	***(indicate number of times)*** ***(tick the box if don't know)*** ***IF MAIN GIVER***
4.7	What is the highest level and grade or year of school **your child** has ever attended?	☐ EARLY CHILDHOOD EDUCATION ☐ PRIMARY ☐ LOWER SECONDARY ☐ UPPER SECONDARY ☐ HIGHER	

Main caregiver information

The following questions relate to the main caregiver, which is the person from your household who usually spends the most time caring for THIS CHILD. If the respondent is not the main caregiver, then please ask them to answer the remaining questions from the perspective of the main caregiver.

ID	Question / Data Item	Response Options	Comments
5.1	**RECORD** the sex of the **MAIN CAREGIVER**	☐ Male ☐ Female	*(tick one appropriate answer)*
5.2	How old are **YOU/MAIN CAREGIVER**?	☐☐ ☐ Don't Know	***(indicate Age)*** ***(tick the box if don't know)***
5.3	Can **YOU/MAIN CAREGIVER** read or write a simple sentence?	☐ YES ☐ NO	*(tick one appropriate answer)*

ID	Question / Data Item	Response Options	Comments
5.4	How many years did **YOU/MAIN CAREGIVER** spend in formal education?	☐☐ ☐ Don't Know	***(indicate years)*** ***(tick the box if don't know)***
5.5	What is **YOU/MAIN CAREGIVER** highest level of education?	☐ No formal ☐ Early childhood education ☐ Primary ☐ Secondary ☐ College/technical training ☐ University	*(tick one appropriate answer)*
5.6	Are **YOU/MAIN CAREGIVER** the main income earner of the household?	☐ YES ☐ NO	
5.7	What is **YOUR/MAIN CAREGIVER** occupation?	☐ Working (formal/informal employment) ☐ Seeking work ☐ Homemakers ☐ Students ☐ Others (Specify)_____	*(tick one appropriate answer)*
5.8	What is **YOUR/MAIN CAREGIVER** current work status?	☐ Income from paid employment ☐ Income from self-employment ☐ Unpaid work ☐ Housework (including caring responsibilities) ☐ Retired ☐ Other	**If unpaid / housework / retired / other skip to 7.1**
5.9	On average how much do **YOU/MAIN CAREGIVER** earn per hour from paid work or self-employment?	In local currency ☐☐☐☐☐☐ ☐ Don't know	***(indicate amount)*** ***(tick the box if don't know)***

ID	Question / Data Item	Response Options	Comments
5.10	On average how many hours paid work or self-employment do **YOU/MAIN CAREGIVER** work per week?	H H M M ☐ Don't know	***(indicate hours, if they don't work put zero)*** ***(tick the box if don't know)***

Household information

ID	Question / Data Item	Response Options	Comments
	Household location		
6.1	Location of household (name of village, town, district)	Location name ……	
6.2	Location type?	☐ Urban ☐ Traditional ☐ Farm	"."
	Household Occupants		
7.1	How many people in total live in the household?	☐ Don't Know	***(indicate whole number)*** ***(tick the box if don't know)***
7.2	How many of these people are children aged under 18?	☐ Don't Know	***(indicate whole number)*** ***(tick the box if don't know)***
7.3	How many of these people are adults over the age of 60?	☐ Don't Know	***(indicate whole number)*** ***(tick the box if don't know)***
7.4	Have any children from the household ever been given up for adoption?	☐ YES ☐ NO	*Including informal adoption.*
	Socio-Economic Status		
8.1	Is location linked wealth index available?	☐ YES ☐ NO	**If no skip to 8.3**
8.2	DHS Wealth Index	Numerical value ☐ Don't know	From DHS database, part of Participant Details and should be

ID	Question / Data Item	Response Options	Comments
			shown automatically if already extracted
8.3	Does any member of your household have the following:		
	a. radio	☐ Yes ☐ No ☐ Don't know If yes, how many _____	
	b. television	☐ Yes ☐ No ☐ Don't know If yes, how many _____	
	c. landline telephone	☐ Yes ☐ No ☐ Don't know If yes, how many _____	
	d. computer	☐ Yes ☐ No ☐ Don't know If yes, how many _____	
	e. refrigerator	☐ Yes ☐ No ☐ Don't know If yes, how many _____	
	f. vacuum cleaner	☐ Yes ☐ No ☐ Don't know If yes, how many _____	
	g. microwave oven	☐ Yes ☐ No ☐ Don't know If yes, how many _____	

ID	Question / Data Item	Response Options	Comments
	h. stove	☐ Yes ☐ No ☐ Don't know If yes, how many _____	
	i. washing machine	☐ Yes ☐ No ☐ Don't know If yes, how many _____	
	j. watch	☐ Yes ☐ No ☐ Don't know If yes, how many _____	
	k. cell phone	☐ Yes ☐ No ☐ Don't know If yes, how many _____	
	l. Motor bike	☐ Yes ☐ No ☐ Don't know If yes, how many _____	
	m. bicycle	☐ Yes ☐ No ☐ Don't know If yes, how many _____	
	n. animal drawn cart	☐ Yes ☐ No ☐ Don't know If yes, how many _____	
	o. car/bakkie/van/truck	☐ Yes ☐ No ☐ Don't know	

ID	Question / Data Item	Response Options	Comments
		If yes, how many _____	
	p. boat with motor	☐ Yes ☐ No ☐ Don't know If yes, how many _____	
8.4	What is the main source of drinking water for your household?	☐ PIPED INTO DWELLING/HOUSE . . . . ☐ PIPED TO YARD/PLOT . . . . . . ☐ PIPED TO NEIGHBOUR . . . . . . ☐ PUBLIC/COMMUNAL TAP . . . . . . ☐ BOREHOLE . . . . . . ☐ PROTECTED WELL . . . . . . ☐ UNPROTECTED WELL . . . . . . ☐ PROTECTED SPRING . . . . . . ☐ UNPROTECTED SPRING . . . . . . ☐ RAINWATER . . . . . . ☐ WATER-CARRIER/TANKER TRUCK . . . ☐ CART WITH SMALL TANK/WATER VENDOR ☐ SURFACE WATER (RIVER/DAM/LAKE/POND/STREAM / CANAL/IRRIGATION CHANNEL) . . . . . ☐ BOTTLED WATER . . . . . . ☐ OTHER	
8.5	What kind of toilet flush do members of your household usually use?	☐ FLUSH TO PIPED SEWER SYSTEM . . . . ☐ FLUSH TO SEPTIC TANK . . . . . . ☐ FLUSH TO PIT LATRINE . . . . . . ☐ FLUSH TO SOMEWHERE ELSE . . . . . . ☐ FLUSH, DON'T KNOW WHERE . . . . . ☐ VENTILATED IMPROVED PIT LATRINE	

ID	Question / Data Item	Response Options	Comments
		□ PIT LATRINE WTH VENTILATION PIPE BUT NO GAUZE MESH/NETTING . . . . . □ PIT LATRINE WTHOUT VENTILATION PIPE □ COMPOSTING TOILET/ ECOLOGICAL SANITATION SYSTEM . . . . . . □ CHEMICAL TOILET . . . . . . □ BUCKET TOILET . . . . . . □ NO FACILITY/BUSH/FIELD . . . . □ OTHER	
8.6	What is the household's main source of cooking fuel?	□ ELECTRICITY FROM MAINS . . . . . . □ ELECTRICITY FROM GENERATOR . . . . □ ELECTRICITY FROM OTHER SOURCE . □ SOLAR ENERGY . . . . . . □ GAS . . . . . . □ PARAFFIN . . . . . . □ COAL . . . . . . □ WOOD . . . . . . □ STRAW/SHRUBS/GRASS . . . . . . □ AGRICULTURAL CROP . . . . . . □ ANIMAL DUNG . . . . . . □ NO FOOD COOKED IN HOUSEHOLD . . □ OTHER	
8.7	Does your household own the land on which the structure (house) sits	□ (01) Owns □ (02) Pays rent □ (03) No rent with consent from owner (04) No rent, squatting	
8.8	How many rooms in this household are used for sleeping?	☐☐ rooms	

ID	Question / Data Item	Response Options	Comments
8.9	What is the main source for heating/warming your household?	☐ ELECTRICITY FROM MAINS . . . . ☐ ELECTRICITY FROM GENERATOR . . . . ☐ ELECTRICITY FROM OTHER SOURCE . ☐ SOLAR ENERGY . . . . ☐ GAS . . . . ☐ PARAFFIN . . . . ☐ COAL . . . . ☐ WOOD . . . . ☐ STRAW/SHRUBS/GRASS . . . . ☐ AGRICULTURAL CROP . . . . ☐ ANIMAL DUNG . . . . ☐ NO FOOD COOKED IN HOUSEHOLD . . ☐ OTHER	
8.10	Does your household have electricity that is connect to the mains?	☐ No ☐ Yes ☐	
8.11	ow is the refuse or rubbish in this household mainly collected or removed? PROBE: How often is it removed?	☐ REMOVED BY LOCAL AUTHORITY/PRIVATE COMPANY AT LEAST ONCE A WEEK . . . . . ☐ REMOVED BY LOCAL AUTHORITY/PRIVATE COMPANY LESS OFTEN THAN ONCE A WEEK ☐ REMOVED BY COMMUNITY MEMBERS, CONTRACTED BY THE MUNICIPALITY AT LEAST ONCE A WEEK . . . . ☐ REMOVED BY COMMUNITY MEMBERS, CONTRACTED BY THE MUNICIPALITY LESS OFTEN THAN ONCE A WEEK . . . . ☐ REMOVED BY COMMUNITY MEMBERS AT LEAST ONCE A WEEK . . . . ☐ REMOVED BY COMMUNITY MEMBERS LESS OFTEN THAN ONCE A WEEK . . . . . ☐ COMMUNAL REFUSE DUMP	

ID	Question / Data Item	Response Options	Comments
		☐ COMMUNAL CONTAINER/CENTRAL COLLECTION POINT . . . . . . ☐ OWN REFUSE DUMP . . . . . . ☐ OWN REFUSE BURNED . . . . . . ☐ NO RUBBISH DISPOSAL/DUMP OR LEAVE ANYWHERE . . . . . . ☐ OTHER ☐	
8.12	What are the ***walls*** of the main dwelling (house) predominantly made of?	☐ NO WALLS . . . . . . ☐ DIRT/MUD . . . . . . ☐ PLASTIC . . . . . . ☐ WATTLE AND DAUB . . . . . . ☐ STONE WITH MUD . . . . . . ☐ MUD WITH CEMENT MIX . . . . . . ☐ CARDBOARD . . . . . . ☐ REUSED WOOD . . . . . . ☐ CEMENT . . . . . . ☐ STONE WITH LIME/CEMENT . . . . . . ☐ BRICKS . . . . . . ☐ CEMENT BLOCK/CONCRETE . . . . . . ☐ WOOD PLANKS . . . . . . ☐ CORRUGATED IRON/ZINC . . . . . . ☐ OTHER	
8.13	What is the ***roof*** of the main dwelling predominantly made of?	☐ NO ROOF . . . . . . ☐ THATCHING/GRASS . . . . . . ☐ MUD/SOD . . . . . . ☐ PLASTIC . . . . . . ☐ WATTLE AND DAUB . . . . . . ☐ MUD WITH CEMENT MIX	

ID	Question / Data Item	Response Options	Comments
		□ BRICKS . . . . . . □ WOOD PLANKS . . . . . . □ CARDBOARD . . . . . . □ CORRUGATED IRON/ZINC . . . . . . □ WOOD . . . . . . □ ASBESTOS . . . . . . □ TILES . . . . . . □ CEMENT . . . . . . □ OTHER	
8.14	What is the ***floor*** of the main dwelling predominantly made of?	□ EARTH/SAND . . . . . . □ DUNG . . . . . . □ WOOD PLANKS . . . . . . □ LAMINATED OR POLISHED WOOD . . □ VINYL/ASPHALT STRIPS . . . . . . □ CERAMIC TILES . . . . . . □ CEMENT . . . . . . □ CARPET . . . . . . □ OTHER	
8.15	What type of dwelling/building?	□ DWELLING/HOUSE OR BRICK/CONCRETE BLOCK STRUCTURE ON A SEPARATE STAND/YARD/FARM . . . . . . □ TRADITIONAL DWELLING/HUT STRUCTURE MADE OF TRADITIONAL MATERIALS . . . . . □ FLAT OR APARTMENT IN BLOCK OF FLATS . . □ CLUSTER HOUSE IN COMPLEX . . . . . □ TOWN HOUSE/SEMI-DETACHED HOUSE IN COMPLEX . . . . . . □ SEMI-DETACHED HOUSE . . . . . . □ DWELLING/HOUSE/FLAT/ROOM IN BACKYARD 07	

ID	Question / Data Item	Response Options	Comments
		☐ INFORMAL DWELLING/SHACK IN BACKYARD . . ☐ INFORMAL DWELLING/SHACK NOT IN BACKYARD (E.G., IN AN INFORMAL/SQUATTER SETTLEMENT OR ON FARM) . . . . . . ☐ ROOM/FLATLET ON A PROPERTY OR LARGER DWELLING/SERVANTS' QUARTERS/GRANNY FLAT . . . . . . ☐ CARAVAN OR TENT . . . . . . ☐ OTHER	
	Household Income		
	What is the average **MONTHLY** income of your household from each of the following sources?		
9.1	What is the average total monthly income that you receive from all sources (i.e., total after any deductions)?	In local currency ☐☐☐☐☐☐ ☐ Don't know	***(indicate income)*** ***(tick the box if don't know)*** **If DON'T KNOW, SKIP to 12.1**
9.2	Income after tax from employment by adults living in your household?	In local currency ☐☐☐☐☐☐ ☐ Don't know	***(indicate income)*** ***(tick the box if don't know)***
9.3	Income after tax from paid employment by children of school age living in your household?	In local currency ☐☐☐☐☐☐ ☐ Don't know	***(indicate income)*** ***(tick the box if don't know)***
9.4	Income received from pensions by members of your household?	In local currency ☐☐☐☐☐☐ ☐ Don't know	***(indicate income)*** ***(tick the box if don't know)***
9.5	Income received from social welfare, cash-transfers or other government payments?	In local currency ☐☐☐☐☐☐	***(indicate income)*** ***(tick the box if don't know)***

ID	Question / Data Item	Response Options	Comments
		☐ Don't know	
9.6	What is the estimated market value of food consumed by your household each **MONTH** that you produce yourselves?	In local currency ☐☐☐☐☐☐ ☐ Don't know	Aim is to estimate value of production.
9.7	What is the estimated market value clothes produced by your household each **MONTH** that you use yourselves?	In local currency ☐☐☐☐☐☐ ☐ Don't know	Aim is to estimate value of production.
9.8	Did your total household income decrease as a result of caring for **your child**? (Consider changes to all income including paid work and benefit payments.)	☐ YES ☐ NO	***(Note for data collector: it should be made clear that this should be in reference to the before and after care for this particular child)***

Household expenditure

ID	Question / Data Item	Response Options	Comments
	Total Expenditure		
10.1	Over the past **MONTH** what was your estimated total household expenditure?	In local currency ☐☐☐☐☐☐ ☐ Don't know	***(indicate expenditure)*** ***(tick the box if don't know)***
	Expenditure by Category		
11.1	Over the past **MONTH** how much has your household spent in total on healthcare? (e.g. hospital or clinic fees, doctor's fees, traditional healers, medical tests, medications, assistive devices such as spectacles, hearing aids, walking canes)	In local currency ☐☐☐☐☐☐ ☐ Don't know	***(indicate amount)*** ***(tick the box if don't know)***
11.2	Over the past **MONTH** how much has your household spent on transportation?	In local currency ☐☐☐☐☐☐	***(indicate amount)*** ***(tick the box if don't know)***

ID	Question / Data Item	Response Options	Comments
	(e.g. Taxi / bus / train fares, petrol / oil, vehicle maintenance, parking fees, air travel)	☐ Don't know	
11.3	Over the past **MONTH** how much has your household spent on education? (e.g. school / tuition / university fees, tutoring or extra classes, school material such as books and uniforms)	In local currency ☐☐☐☐☐☐ ☐ Don't know	***(indicate amount)*** ***(tick the box if don't know)***
11.4	Over the past **MONTH** how much has your household spent on food?	In local currency ☐☐☐☐☐☐ ☐ Don't know	***(indicate amount)*** ***(tick the box if don't know)***
11.5	Over the past **MONTH** what is the estimated value of food your household has consumed that you received as gifts or produced yourselves?	In local currency ☐☐☐☐☐☐ ☐ Don't know	***(indicate amount)*** ***(tick the box if don't know)***
	Health Insurance		
12.1	Are the members of your household covered by any form of private or government health insurance/medical aid scheme?	☐ No insurance ☐ Government insurance/NHI ☐ Private Insurance ☐ Others (specify)	**If "no insurance" skip to section 2.**
12.2	If you have healthcare insurance how much of your household healthcare expenditure from the past **MONTH** was or will be reimbursed/covered directly by the insurer?	In local currency ☐☐☐☐☐☐ ☐ Don't know	***(indicate amount)*** ***(tick the box if don't know)*** ***GO TO SECTION 2***

SECTION 2 – CHILD'S HEALTH RELATED QUALITY OF LIFE

Proxy version of the EQ-5D:

By placing a tick in one box in each group below, please indicate which statements (*insert name of person whose health is being assessed, e.g. Mr. Kumar or Mohan*) would choose to describe his/her health state today if he/she was able to tell us.

Do not tick more than one box in each group.

Mobility

No problems in walking ❑

Some problems in walking ❑

Confined to bed ❑

Self-Care

No problems with self-care ❑

Some problems bathing or dressing himself/herself ❑

Unable to bathe or dress himself/herself ❑

Usual Activities (*e.g. work, study, household work, family or leisure activities)*

No problems with performing his/her usual activities ❑

Some problems with performing his/her usual activities ❑

Unable to perform his/her usual activities ❑

Pain / **Discomfort**

No pain or discomfort ❑

Moderate pain or discomfort ❑

Extreme pain or discomfort ❑

Anxiety / **Depression**

Not anxious or depressed ❑

Moderately anxious or depressed ❑

Extremely anxious or depressed ❑

(Please check that you have ticked the boxes that the subject would choose to describe his/her health state today if he/she was able to tell us)

Health state today: ____

Self version

By placing a tick in one box in each group below, please indicate the statements that best describe your own health state today.

Mobility

I have no problems in walking	❑
I have some problems in walking	❑
I am confined to bed	❑

Self-Care

I have no problems with self-care	❑
I have some problems bathing or dressing myself	❑
I am unable to bathe or dress myself	❑

Usual Activities *(e.g. work, study, household work, family or leisure activities)*

I have no problems in performing my usual activities	❑
I have some problems in performing my usual activities	❑
I am unable to perform my usual activities	❑

Pain / Discomfort

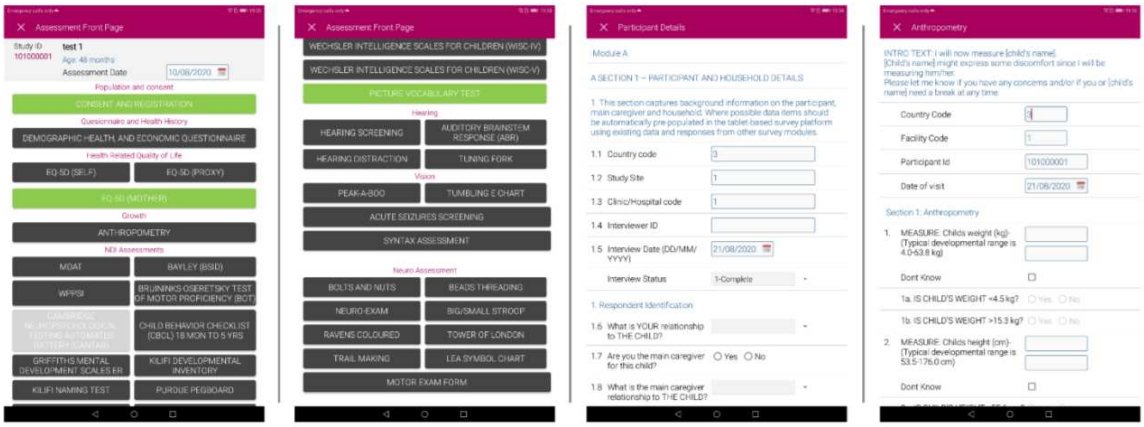
I have no pain or discomfort	❑
I have moderate pain or discomfort	❑
I have extreme pain or discomfort	❑

Anxiety / Depression

I am not anxious or depressed	❑
I am moderately anxious or depressed	❑
I am extremely anxious or depressed	❑

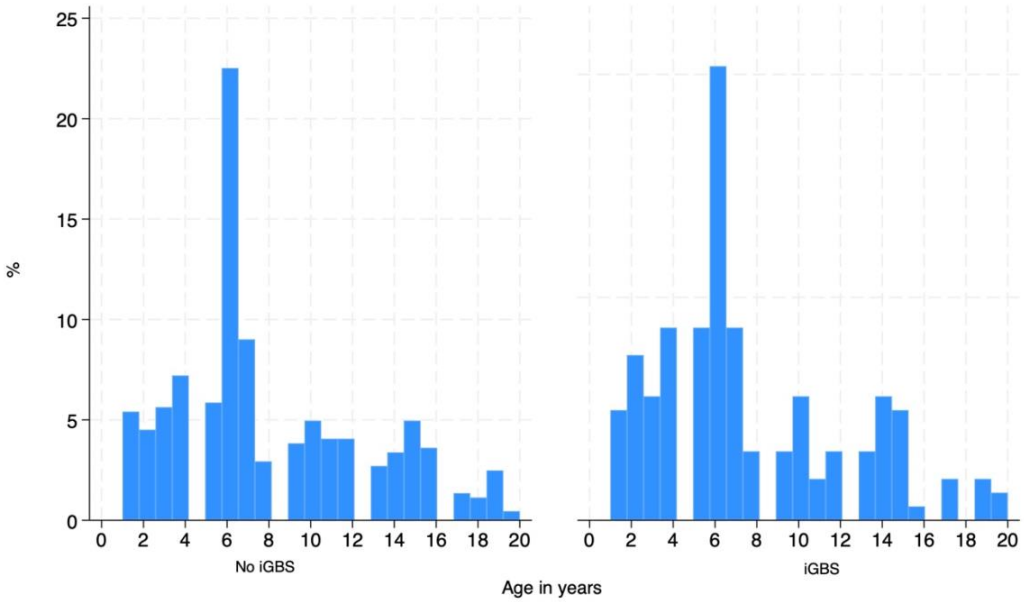
Health state today: ____

Data app



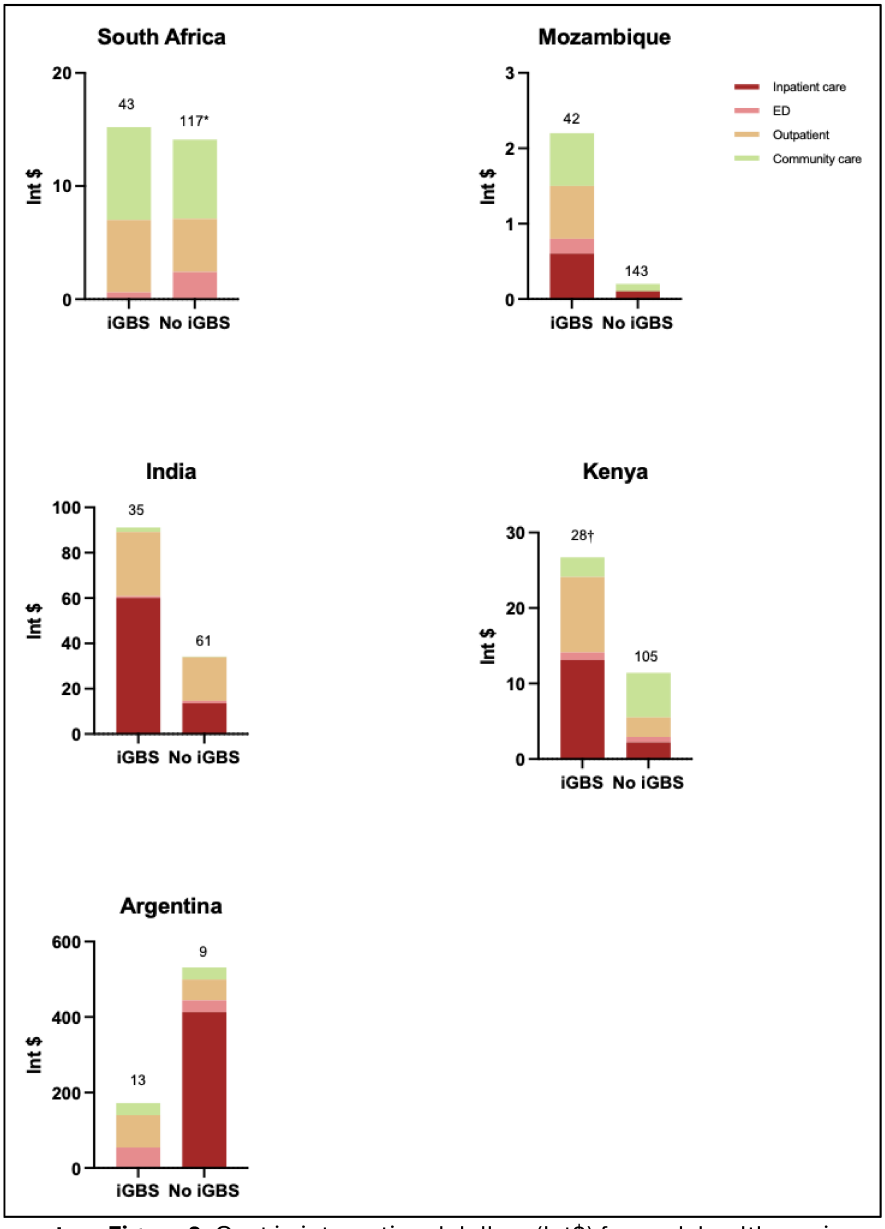
App is available on request

Long-term healthcare utilisation, costs, and quality of life after invasive group B *Streptococcus* disease: a cohort study in five low- and middle-income countries



Supplementary Figure 1. Distribution of age by exposure type. iGBS=invasive group B *Streptococcus*

Long-term healthcare utilisation, costs, and quality of life after invasive group B *Streptococcus* disease: a cohort study in five low- and middle-income countries



Supplementary Figure 2. Cost in international dollars (Int$) for each health service used in the last 12 months in iGBS survivors and the unexposed cohort, stratified by country. Stacked unadjusted mean costs for each healthcare service in South Africa, Mozambique, India, Kenya, and Argentina for GBS exposed and unexposed cohort. Number above each bar represents the number of participants in each cohort for the cost of each healthcare service. *Except for community care costs where the N for the unexposed cohort is 116. †Except for outpatient costs where the N for the iGBS exposed cohort is 27. ED=emergency department iGBS=invasive group B *Streptococcus*

Long-term healthcare utilisation, costs, and quality of life after invasive group B *Streptococcus* disease: a cohort study in five low- and middle-income countries

Reflexivity Statement

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* Joint first authors

1. How does this study address local research and policy priorities?

This study was part of a wider multi-country study to address evidence gaps on the long-term health and economic impacts of Group B Streptococcus (GBS) in low- and middle-income countries (LMICs), which bear the highest burden of GBS disease. This study provides new evidence from LMICs on the health-related quality of life and healthcare costs beyond infancy in children who survived invasive GBS disease. The result can help to inform studies on cost-effectiveness of interventions to prevent invasive GBS disease, including new maternal vaccines that are under development. The need for such studies arose from discussions with country partners that such vaccines were unlikely to be introduced in many LMICs without strong donor support, and that donors would require evidence of high burden to unlock funding.

2. How were local researchers involved in study design?

Researchers from the different study sites were part of the initial concept of the study. They then attended a planning workshop in London prior to the start of the project. This workshop was used to develop ideas for data collection and associated analysis. Participants from this workshop then contributed to development of an overarching and local study protocols, which was subsequently published in an open access journal including all researchers as co-authors.

3. How has funding been used to support the local research team?

Funding was provided to local research teams to support/recruit staff conducting data collection.

4. How are research staff who conducted data collection acknowledged?

Research staff involved in data collection who did not meet the criteria for being named authors on this study are acknowledged as named members of a collaborative authorship group.

5. Do all members of the research partnership have access to study data?

All members of the partnership have access to data in accordance with a data-sharing agreement.

6. How was data used to develop analytical skills within the partnership?

As part of the overarching multi-country study an online analysis workshop was held to allow all researchers to opportunity to contribute to developing analysis plans for different papers, including this one. The multi-country study has resulted in more than 10 manuscripts enabling different partners to take the lead for different analyses, with other co-authors providing specific expertise when needed.

7. How have research partners collaborated in interpreting study data?

As noted above as part of the overarching study different research partners have taken the lead on analysis and data interpretation for different manuscripts. For this particular study the lead authors included research partners in data interpretation through sharing of early analysis via online meetings and soliciting comments and suggestions from all co-authors on multiple drafts of the manuscript.

8. How were research partners supported to develop writing skills?

The research team writing this study was predominantly composed of experienced academics, who did not require development of their writing skills.

9. How will research products be shared to address local needs?

All the research outputs from the overarching multi-country study, including this study, have been published in open access journals so that they are openly available to everyone. They have also been disseminated in conferences around the world e.g., South Africa, Brazil.

10. How is the leadership, contribution and ownership of this work by LMIC researchers recognised within the authorship?

As mentioned above the overarching multi-country study results in more than 10 publications, with different research partners taking the lead on different manuscripts including first and senior authorship positions. This manuscript includes named authors from each of the study sites and all participants in the wider project are recognised through the collaborative authorship group.

11. How have early career researchers across the partnership been included within the authorship team?

We included mix of senior and early career researchers from all research teams within named authorship, and all other researchers were included in the collaborative authorship group.

12. How has gender balance been addressed within the authorship?

Twelve authors are female and six authors are male. First authorship is shared between one male and one female author.

13. How has the project contributed to training of LMIC researchers?

This project did not provide direct training to LMIC researchers.

14. How has the project contributed to improvements in local infrastructure?

This project has not directly contributed to improvements in local infrastructure.

15. What safeguarding procedures were used to protect local study participants and researchers?

Local data collection was conducted in accordance with a standardised protocol developed in collaboration with all partners and reviewed by local institutional review boards in each study site.