GLOBAL BURDEN AND UNMET NEED FOR HYPERBILIRUBINEMIA TREATMENT

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INTRODUCTION
Severe neonatal hyperbilirubinemia (SNH) that is untreated poses a significant global public health challenge. However, national-level data from resource-limited countries are scarce, and global and regional estimates for the unmet need for phototherapy treatment are unavailable.

OBJECTIVE
To provide an initial estimate of the total and unmet need for neonatal phototherapy globally, with an emphasis on resource-limited settings.

METHODS
Based on our literature review of the incidence of SNH requiring phototherapy, we modeled regional incidences of SNH using International Classification of Diseases, Ninth Revision (ICD-9) coded data on phototherapy treatment in the United States,1 with adjustments for term/preterm birth ratios,2 differences in hereditary risk factors for hyperbilirubinemia (glucose-6-phosphate dehydrogenase deficiency).3 We also adjusted for under-reporting in ICD-9 codes for neonatal noninvasive procedures.4 We estimated availability of phototherapy, for which data is also adjusted for under-reporting in ICD-9 codes for neonatal noninvasive procedures.4 We adjusted for genetic differences in risk by scaling the portion of SNH due to G6PD deficiency according to prevalence of the enzyme disorder. G6PD deficiency may have a varying relationship to severe neonatal hyperbilirubinemia according to prevalence of the enzyme disorder. Our estimate is conservative, as we do not account for the higher prevalence of environmental risks, including sulfa drug exposure and hemolytic triggers, as well as the effect of sub-optimal health infrastructure, which increases the incidence of sepsis and thereby hyperbilirubinemia.

RESULTS
Our preliminary effort to estimate the global burden of SNH suggests that the unmet need for effective phototherapy treatment exceeds 6 million newborns annually. Increasing the global availability of effective phototherapy could reduce the adverse consequences of SNH and kernicteric mortality, as well as reduce the need for exchange transfusions.

LIMITATIONS
We adjusted for genetic differences in risk by scaling the portion of SNH due to G6PD deficiency according to prevalence of the enzyme disorder. G6PD deficiency may have a varying relationship to severe neonatal hyperbilirubinemia in countries with a different prevalence of this disorder. Our estimate is conservative, as we do not account for the higher prevalence of environmental risks, including sulfa drug exposure and hemolytic triggers, as well as the effect of sub-optimal health infrastructure, which increases the incidence of sepsis and thereby hyperbilirubinemia.

SUMMARY
We estimate that annually at least 14.1 million babies worldwide (10.5% of live births) require phototherapy (see Table 1). Of these, more than 6 million infants of those requiring treatment (~45%) do not receive effective treatment, and approximately 100,000 reach extreme hyperbilirubinemia of TSB ≥30 mg/dL, a threshold associated with brain damage. The largest unmet need in absolute and percentage terms is in South Asia and Africa, particularly because of a high number of births and pre-term births, weak health systems, and hereditary risk factors.

CONCLUSIONS
Our preliminary effort to estimate the global burden of SNH suggests that the unmet need for effective phototherapy treatment exceeds 6 million newborns annually. Increasing the global availability of effective phototherapy could reduce the adverse consequences of SNH and kernicteric mortality, as well as reduce the need for exchange transfusions.

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REFERENCES

Table 1. Regional estimates for total and unmet need for phototherapy treatment and incidence of elevated bilirubin concentrations. Inadequate data was available for estimation of unmet need and bilirubin concentrations in Europe, North America, and Oceania, thus leading to an underestimation of the world total (indicated by *)

US total PT incidence = (US reported PT incidence/ICD-9 underreporting coefficient)

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Figure 1. Flow chart of illustrating burden calculation methodology

Figure 2. Estimated total annual need for phototherapy treatment by region.

Figure 3. Estimated total unmet need for phototherapy treatment by region.