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Global Burden of Head and Neck Cancer: Economic Consequences, Health, and the Role of Surgery

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Abstract

Objective. We aimed to describe the mortality burden and macroeconomic effects of head and neck cancer as well as delineate the role of surgical workforce in improving head and neck cancer outcomes.

Study Design. Statistical and economic analysis.

Setting. Research group.

Subjects and Methods. We conducted a statistical analysis on data from the World Development Indicators and the 2016 Global Burden of Disease study to describe the relationship between surgical workforce and global head and neck cancer mortality-to-incidence ratios. A value of lost output model was used to project the global macroeconomic effects of head and neck cancer.

Results. Significant differences in mortality-to-incidence ratios existed between Global Burden of Disease study superregions. An increase of surgical, anesthetic, and obstetric provider density by 10% significantly correlated with a reduction of 0.76% in mortality-to-incidence ratio ($P < .0001$; adjusted $R^2 = 0.84$). There will be a projected global cumulative loss of $535 billion US dollars (USD) in economic output due to head and neck cancer between 2018 and 2030. Southeast Asia, East Asia, and Oceania will suffer the greatest gross domestic product (GDP) losses at $180 billion USD, and South Asia will lose $133 billion USD.

Conclusion. The mortality burden of head and neck cancer is increasing and disproportionately affects those in low- and middle-income countries and regions with limited surgical workforces. This imbalance results in large and growing economic losses in countries that already face significant resource constraints. Urgent investment in the surgical workforce is necessary to ensure access to timely surgical services and reverse these negative trends.

Keywords

head and neck cancer, cancer, surgery, global surgery, global health, otolaryngology, macroeconomics, workforce

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Cancer represents an immense and growing burden of disease worldwide, causing 8.9 million deaths in 2016.[1] An estimated 70% of these deaths occur in low- and middle-income countries.[1] Due to modest improvements in health care delivery and decreasing premature death, the populations in these countries are aging.[1,2] Along with the tobacco epidemic, this contributes to an epidemiologic transition in which low- and middle-income countries bear an increasing burden of noncommunicable diseases, including head and neck cancer (HNC).[1,3] In 2016, 1.1 million new cases and 4.1 million prevalent cases of HNC were

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reported, contributing to 512,770 deaths. HNC constituted 5.7% of global cancer-related mortality, which is comparable to that of breast cancer (6.1%) and pancreatic cancer (4.5%). An estimated 67% of HNC cases and 82% of HNC deaths occurred in low- and middle-income countries.[1]

In addition to causing avertable morbidity and mortality, HNC can impose a substantial economic burden. While the microeconomic impact of providing surgical care for HNC has not been thoroughly investigated, it is known that many patients in low- and middle-income countries pay out of pocket for health care and bear a great risk of financial catastrophe.[4] One prospective, 8-country cohort study of adults in Southeast Asia found that 30% of participants incurred financial catastrophe from cancers of the oral cavity and pharynx.[4] Meanwhile, an analysis of the effects of HNC on macroeconomic welfare in Bangladesh, India, and Pakistan in 2010 conservatively estimated that US$16.9 billion was lost due to HNC in just 1 year.[3]

As HNC is often preventable and can be cured when identified at early stages, this represents a missed opportunity to improve population health outcomes.[3,5,6] Given the inadequate global chemotherapy and radiotherapy capacity,[7,8] surgical care is a particularly important intervention as it is often the primary mode of diagnosis and treatment for early stage HNC.[3,5,9] However, many low- and middle-income country health systems have limited surgical capacity in part due to surgical workforce shortages and geographic maldistribution of providers, reducing the likelihood that patients receive timely surgical care.[10] In 2015, the Lancet Commission on Global Surgery (LCoGS) convened a group of experts to provide estimates on the global burden of surgical disease and to identify avenues to advance surgical system strengthening.[10] By correlating increases in surgical, anesthetic, and obstetric (SAO) provider density with decreases in the maternal mortality ratio (MMR), they showed that surgical workforce is a vital component to providing an adequate volume of surgical procedures and improving health outcomes.[10]

The LCoGS set forth goals and recommendations intended to reduce preventable suffering and death due to surgical disease by 2030, including minimum surgical workforce requirements (20 SAO providers per 100,000 people) and volume of surgical procedures (5000 operations per 100,000 people per year).[10] More broadly, the United Nations has designated the Sustainable Development Goals (SDGs) as a global commitment to end poverty. Surgical care is essential to achieving 8 of these 17 goals, including SDG 3, which promotes "good health and wellbeing," and SDG 8, which highlights the need for "decent work and economic growth."[11,12] To prioritize appropriate surgical care in pursuit of these goals, it is important to describe the trends of HNC health outcomes and the resulting macroeconomic impact through 2030. Furthermore, while SAO provider density has been correlated with MMR, the relationship between the surgical workforce and HNC outcomes has not been well defined. Given the significant burden of HNC, we hypothesize that increasing the surgical workforce is essential to improving HNC survival, reducing the associated macroeconomic burden, and achieving the LCoGS goals and the SDGs.

Table 1. Global Burden of Disease Study (GBD) Superregions.[1]

GBD Superregions
High-income
Central Europe, Eastern Europe, and Central Asia
Latin America and Caribbean
North Africa and Middle East
South Asia
Southeast Asia, East Asia, and Oceania
Sub-Saharan Africa

Methods

Data Sources

This study used data on HNC mortality and incidence estimates for 195 countries from the Global Burden of Disease Study (GBD) 2016 by the Institute of Health Metrics and Evaluation (IHME).[1] Five GBD causes were selected to define HNC: "lip and oral cavity cancer," "other pharynx cancer," "larynx cancer," "nasopharynx cancer," and "thyroid cancer."[1] "Other pharynx cancer" includes neoplasms of the oropharynx and hypopharynx.[13] In addition, estimates of the impact of risk factors, measured in disability-adjusted life years, for the 5 groupings of cancers were identified through IHME.[1,14] These risk factors are reported in Appendix 1 (in the online version of the article). Countries were classified using GBD superregions as listed in **Table 1**.

This study did not involve participation of human subjects or require use of patient-level data. For this analysis, we relied on economic and population health estimates at the national level from publicly available data repositories. As such, institutional review board review was not applicable for this study.

Measures and Outcomes: Mortality-to-Incidence Ratios and Surgical Workforce Density

The mortality-to-incidence ratio (MIR) was calculated by dividing the mortality count by the incidence count in a given year. Although a crude measure of survival, MIR has greater utility in identifying inequities in cancer outcomes and allows for international comparisons of survival due to the availability of incidence and mortality data for most countries.[15] Lower MIRs have been shown to reflect the implementation of effective cancer control programs, including cancer screening and treatment.[16] Higher-than-predicted MIRs have conversely been shown to be associated with inadequate health policies, recommendations, and treatment for cancer control.[17,18]

SAO provider density was used as an indicator of surgical workforce level. SAO provider density can also serve as a proxy for other facets of surgical system functioning, as it has been shown to correlate with both surgical volume and MMR.[10,19] Data on SAO provider density were obtained

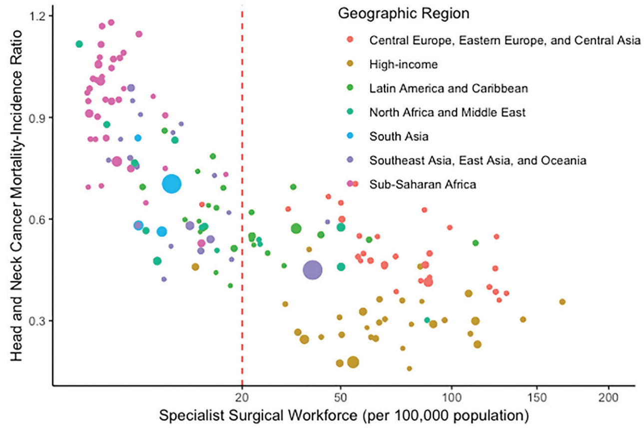

Figure 1. Head and neck cancer mortality-to-incidence ratios plotted against surgical, anesthetic, and obstetric (SAO) provider density across Global Burden of Disease Study (GBD) superregions in 2016. Population density is represented by data point size.

from the World Development Indicators.[20] Country-specific SAO provider densities are available in Appendix 2 (in the online version of the article).

Statistical Analysis

MIR by GBD superregion was compared using a 1-way analysis of variance (ANOVA), with subsequent group differences compared using pairwise *t* tests with the Bonferroni adjustment for multiple comparisons. *P* values less than .0238 (.05/21) were considered significant. Both SAO provider density and MIR were log-transformed, and a multivariate regression model using GBD superregion and IHME risk factors was fit. Statistical analyses were performed in SAS 9.4 (SAS Institute, Cary, North Carolina), and **Figure 1** was created using R version 3.5.2 (Vienna, Austria) and RStudio 1.1.463 (Boston, Massachusetts).

Macroeconomic Consequences of Head and Neck Cancer

The macroeconomic consequences of HNC were modeled using the value of lost output (VLO) approach, which has previously been described by the authors (M.G.S., B.C.A.)[21-23] and others.[24-26] The VLO approach is based on a model that was originally supplied by the World Health Organization (WHO) known as EPIC (Projecting the Economic Cost of Ill Health), which is a calibrated simulation model that can be used to project market economy losses, measured as foregone gross domestic product (GDP) due to disease and injury. The VLO approach assesses how changes in disease-specific mortality affect economic output (GDP) of a country over time by modeling the effect of said mortality on a country's labor supply and fixed capital assets, both of which drive economic productivity.[27] The model is first calibrated using exogenously sourced projections of disease mortality,[28] GDP,[29] and the labor supply[30] from 2014 to 2030. We then presume a counterfactual of no head and neck cancer mortality to derive the counterfactual GDP by perturbing the labor supply and capital stock variables. Foregone GDP is estimated by subtracting the status quo GDP from the counterfactual GDP. It is important to note that mortality estimates are included from 2014 to 2017 to calibrate the model, and therefore those deaths contribute to economic losses, even though we begin estimating economic losses in 2018. Although more recent iterations of EPIC do include a morbidity module, we have elected not to include morbidity until additional verification of the proposed morbidity approach is assessed in the literature.

The VLO model was applied to estimate annual and cumulative GDP losses during 2018 to 2030 for countries in which the necessary econometric data were available. Results are presented in 2017 international dollars (IND) or US dollar (USD) adjusted for purchasing power parity.[31] The purchasing power parity method establishes a conversion rate by comparing the price levels of a fixed basket of goods between countries, such that the price is the same between countries when stated in the reference currency, in this case the United States. For each approach, countries were evaluated by income classification (as classified by the 2017 World Bank scheme) and by region (as defined by the GBD IHME).[31,32] JMP version 14.2 (SAS Institute) was used for the VLO analysis. Appendix 3 (in the online version of the article) provides additional mathematical details, assumptions, and data sources.

Table 2. Mortality-to-Incidence Ratio (MIR) by Global Burden of Disease Study (GBD) Superregion.

GBD Superregion	MIR
High-income	0.31
Central Europe, Eastern Europe, and Central Asia	0.51
Latin America and Caribbean	0.57
North Africa and Middle East	0.60
Global	**0.62**
Southeast Asia, East Asia, and Oceania	0.66
South Asia	0.69
Sub-Saharan Africa	0.93

Results

Head and Neck Cancer Care Outcomes

To assess relative HNC care outcomes, MIRs by GBD superregion are reported in **Table 2**. The sub-Saharan Africa GBD superregion had a significantly greater MIR than any other region, with differences in MIR mean ranging from 0.24 (compared to South Asia) to 0.62 (compared to high-income). In addition, all other GBD superregions had significantly greater MIRs than that of the high-income region. Finally, Southeast Asia had a significantly higher MIR than Central Europe, Eastern Europe, and Central Asia (difference = 0.15). A full list of MIRs by country is available in Appendix 2 (in the online version of the article).

Table 3. Combined Cumulative Losses in International Dollars (IND) from 2018-2030 by Global Burden of Disease Study (GBD) Superregion.

GBD Superregion	Combined Cumulative GDP Losses from 2018-2030 (Millions, 2017 IND)	Proportion of Gross Domestic Product Lost in 2030, %
Central Europe, Eastern Europe, and Central Asia	$40,265	0.042
High-income	$125,460	0.022
Latin America and Caribbean	$21,036	0.023
North Africa and Middle East	$22,081	0.020
South Asia	$133,146	0.087
Southeast Asia, East Asia, and Oceania	$180,085	0.040
Sub-Saharan Africa	$12,833	0.026

Surgical Workforce and Head and Neck Cancer

Figure 1 is a plot of HNC MIR against SAO provider density. In a univariate regression model for MIR, an increase in SAO provider density by 10% significantly correlated with a reduction of 1.7% in MIR ($P < .0001$; adjusted R^2 = 0.61). After controlling for cancer risk factors, an increase of SAO provider density by 10% significantly correlated with a reduction of 1.3% in MIR ($P < .0001$; adjusted R^2 = 0.70). Finally, after controlling for cancer risk factors *and* geographic location, an increase of SAO provider density by 10% significantly correlated with a reduction of 0.76% in MIR ($P < .0001$; adjusted R^2 = 0.84).

Macroeconomic Consequences of Head and Neck Cancer

We estimate that deaths from HNC will result in a global cumulative loss of $535 billion USD in economic output between 2018 and 2030. The GBD superregion Southeast Asia, East Asia, and Oceania will suffer the greatest GDP losses at $180 billion USD, while South Asia will lose $133 billion USD. The proportion of potential GDP lost is most substantial in South Asia. **Table 3** contains projected macroeconomic loss by GBD superregion, and Appendix 4 (in the online version of the article) contains projected macroeconomic loss by country.

Discussion

These results show that lower surgical workforce correlates with worse outcomes in patients with HNC and that negative health outcomes due to HNC translate into substantial macroeconomic impact. The global cumulative macroeconomic loss between 2018 and 2030 was estimated at $535 billion USD, which will largely be shouldered by countries in South Asia and Southeast Asia, East Asia, and Oceania. This suggests that countries and regions with inadequate health systems and constrained financial capacity will bear greater health and macroeconomic consequences of HNC.

The underlying epidemiological trends of HNC currently exhibit a substantial and inequitably distributed burden of disease. In 2016, the GBD superregions of South Asia and Southeast Asia, East Asia, and Oceania were disproportionately affected by HNC. South Asia had 1.3 million cases and 290,225 deaths, while Southeast Asia, East Asia, and Oceania had 1.5 million cases and 126,221 deaths.[1] See Appendix 2 (in the online version of the article) for a region and country breakdown of HNC mortality and incidence rates as reported by the GBD.

The global mortality burden due to HNC is expected to increase. An estimated 705,902 people worldwide will die from HNC in 2030—a 38% increase over 2016.[1,28] Furthermore, the distribution of this burden will grow more unequal across all regions. Compared to 2016, the 2030 mortality predictions reveal decreases in mortality for only some countries in the high-income and Central Europe, Eastern Europe, and Central Asia regions.[1,28] Previous studies support and nuance these HNC epidemiological trends. Saunders et al[33] highlighted the increasing global HNC prevalence and the resulting morbidity and mortality from 2005 to 2015, while Gupta et al[34] and others[35-41] have presented HNC epidemiology by type of neoplasm or by geographic location. Current and predicted absolute mortality due to HNC are listed in **Table 4** by GBD superregion and represented visually in **Figure 2** by country. Appendix 2 (in the online version of the article) lists these GBD predictions by both region and country.

Although this background can help inform effective HNC interventions, existing literature largely focuses on disease prevention to alleviate this burden. To address this gap, we present MIRs in the context of absolute mortality of HNC. As incidence is the denominator of MIR, this accounts for differences in HNC mortality that are due to prevention efforts.[17] Thus, this analysis provides a novel understanding of disparities in mortality due to inadequate surgical capacity for HNC control.

SAO provider density is a widely reported indicator used to assess surgical workforce, and it has also been suggested as a marker of surgical system functioning.[10] A previous study estimated that 1,272,586 new surgical workforce providers are needed to achieve the LCoGS recommendation of 20 surgeons, anesthetists, and obstetricians per 100,000 people by 2030, costing an estimated $71 to $146 billion

Table 4. Head and Neck Cancer (HNC) Mortality Estimates for 2016 and 2030 by Global Burden of Disease Study (GBD) Superregion.[1,28]

GBD Superregion	2016 Mortality	Predicted 2030 Mortality	Percentage Change from 2016 to 2030
Global	**512,492**	**705,901**	**+38**
Central Europe, Eastern Europe, and Central Asia	43,883	45,474	+4
High-income	78,273	83,546	+6
Latin America	27,047	35,882	+33
North Africa and Middle East	15,018	22,894	+52
South Asia	199,280	307,213	+54
Southeast Asia, East Asia, and Oceania	126,006	176,534	+40
Sub-Saharan Africa	22,985	34,359	+49

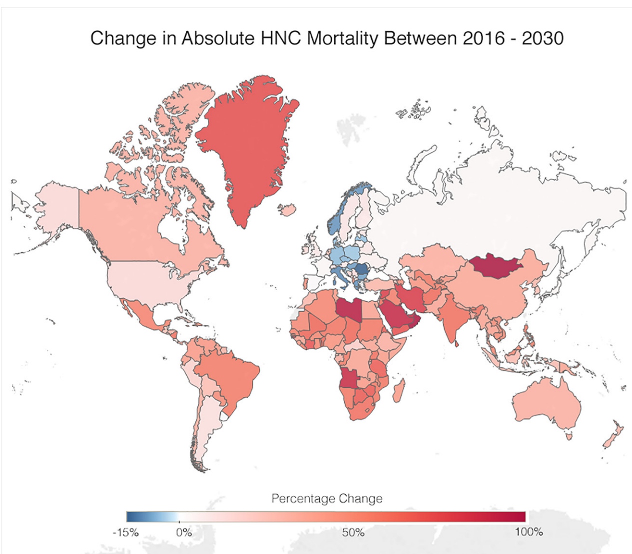

Figure 2. Heat map of predicted changes in absolute head and neck cancer mortality by country between 2016 and 2030.[1,28]

USD.[10,42] Below 20 SAO providers per 100,000 population, the LCoGS found that MMR decreased sharply with increasing SAO provider density. Our results support this recommendation. **Figure 1** illustrates that below the threshold of 20 SAO providers per 100,000 population, the trend of HNC MIRs decreases sharply with an increasing SAO provider density.

The relationship between surgical workforce and HNC outcomes supports the utility of SAO provider density as an indicator, and it suggests that countries that develop a surgical workforce will also see improvements in HNC care outcomes. However, SAO provider density is a broad indicator and does not account for the entire surgical workforce, including nurses, midlevel providers, and specialists, who are responsible for HNC care. Further work is needed to delineate the density and distribution of surgical HNC care providers to most effectively address gaps in HNC care.

Previous estimates of the macroeconomic impact of surgical disease provide context for the findings reported here. Alkire et al[23] estimated that the global macroeconomic burden of surgical disease could contribute up to 2.5% of lost GDP output in low- and middle-income countries (LMICs) by the year 2030. Meanwhile, Verguet et al[43] predicted that the scaleup of surgical services to achieve the recommended surgical volume of 5000 operations/100,000 population per year would cost $300 to $420 billion USD. This investment is substantially smaller than the estimated $12.3 trillion gross loss in economic growth in LMICs if the status quo persists and surgical services are not scaled up by 2030.[10]

While human suffering is reason alone for action, evidence about the economic impact of disease can be useful to inspire and inform the creation of comprehensive health policy.[44] As an intrinsic link exists between health and economic growth,[45] these data can support interventions that foment bidirectional impact on both health and the economy while also advancing progress toward the LCoGS goals and the SDGs. This is timely because an increasing number of governments are developing national surgical policy in the form of national surgical, obstetric, and anesthesia plans (NSOAPs).[46,47]

LCoGS recommended NSOAPs as national strategic plans designed to incorporate surgical service delivery and financing into overarching national health plans, and they present an opportunity to address HNC surgical care at a national level.[10] NSOAPs are developed through a national surgical planning process with local stakeholders to address 6 pillars of health systems: financing, governance, information management, infrastructure, service delivery, and workforce. This permits the systematic integration of surgery, anesthesia, and obstetrics within the existing health care system. Since 2016, 5 NSOAPs have been signed (Ethiopia, Nigeria, Rwanda, Tanzania, and Zambia) and over 20 more are being developed across Latin America, Asia, and Africa.[46,47] Policy directed at growing the health care workforce, increasing infrastructure, and expanding financial access to surgery will directly benefit patients with HNC, and our findings can spur the explicit and thoughtful inclusion of otolaryngology–head and neck surgery within NSOAPs.

The growing momentum for surgery presents additional opportunities to address HNC care policy. International professional societies like the World Federation of Societies of Anesthesiologists and programs like the Global Initiative for

Children's Surgery have successfully elevated the urgency to address conditions relevant to their respective fields, and they have created relevant data to inform policy.[48,49] The global community of otolaryngologists can look to these successes as examples in efforts to address the burden of HNC through research, policy, and advocacy.

National governments and the global otolaryngology community should support surgical system strengthening. Yet, developing effective policy requires an understanding of both the mortality burden and economic impact of specific categories of surgical disease. Previous HNC modeling studies have calculated the macroeconomic burden only for specific cancer types or a limited number of locations.[50-52] To address this gap, we have used VLO modeling to show that HNC is a significant detriment to the growth of countries and regions across the world. Our VLO findings are not directly comparable to other macroeconomic estimates due to disparate methodologies. However, these macroeconomic results, combined with the relationship between surgical workforce and HNC outcomes, emphatically support the inclusion of surgical HNC care in national surgical policy.

This study has a number of strengths. There has been no previous analysis of global HNC epidemiology with regard to surgical treatment. We present a robust regression model that shows a statistical relationship between HNC outcomes and surgical workforce while controlling for both risk factors and geographic regions. Thus, efforts to avert HNC mortality must also consider surgical workforce. Furthermore, while each GBD HNC cause was also incorporated into the estimates by Alkire et al,[23] the global macroeconomic burden of HNC has not been independently studied. This analysis provides a country- and regional-level breakdown of the macroeconomic burden of HNC, which can be used to support and frame HNC care within national surgical policy.

We must also recognize the limitations of this study. Data availability and quality are primary among these. While SAO provider density is the best-reported surgical indicator, variation in definitions of surgical providers limits its comparability between countries.[53] In addition, the GBD reports that its cause-specific data on cancer and mortality can have wide uncertainty depending on the data collection practices and reliability of data sources for each country. The resulting relative data quality can vary substantially between GBD superregions and countries.[54,55]

For the macroeconomic modeling, the VLO approach is limited by the underlying GBD data quality, availability, and modeling; these limitations are inherently carried over into the VLO model predictions. Missing national-level econometric data limits the accuracy of macroeconomic estimates for GBD superregions. However, we have reported the most conservative estimates so as not to inflate the findings. Furthermore, neither the MIRs nor the VLO model address the impact of morbidity on HNC care outcomes or macroeconomic trends. As with any models that use forecasting, these results represent our best understanding of future health scenarios, but they contain a measure of uncertainty as unforeseen geopolitical events can substantially alter these trajectories.

Conclusion

The mortality burden of HNC is increasing, and it disproportionately affects those in low- and middle-income countries and regions with limited surgical workforce. This imbalance results in large and growing economic losses in countries that already face significant resource constraints. Given the integral role of surgical care for HNC control, urgent investment is necessary to ensure access to safe, timely, and affordable surgical services to reverse the negative health and economic trends due to HNC. By expanding access to surgical HNC care, we can avert needless death and advance progress toward the LCoGS 2030 goals and the SDGs. Local actors, national governments, and international agencies must support surgical system strengthening for HNC care through national surgical policy.

Author Contributions

Rolvix H. Patterson, contributed to the design, data acquisition, data analysis, data interpretation, drafting, and revising of the work; gave final approval of the version to be published and agreed to be accountable for all aspects of the work; **Victoria G. Fischman**, contributed to the data analysis, drafting, and revising of the work; gave final approval of the version to be published and agreed to be accountable for all aspects of the work; **Isaac Wasserman**, contributed to the data acquisition, data analysis, and revising of the work; gave final approval of the version to be published and agreed to be accountable for all aspects of the work; **Jennifer Siu**, contributed to the design, drafting, and revising of the work; gave final approval of the version to be published and agreed to be accountable for all aspects of the work; **Mark G. Shrime**, contributed to the interpretation of the data, drafting, and revising of the work; gave final approval of the version to be published and agreed to be accountable for all aspects of the work; **Johannes J. Fagan**, contributed to the interpretation of the data and revising of the work; gave final approval of the version to be published and agreed to be accountable for all aspects of the work; **Wayne Koch**, contributed to the interpretation of the data and revising of the work; gave final approval of the version to be published and agreed to be accountable for all aspects of the work; **Blake C. Alkire**, contributed to the design, data acquisition, data analysis, data interpretation, drafting, and revising of the work; gave final approval of the version to be published and agreed to be accountable for all aspects of the work.

Disclosures

Competing interests: Mark G. Shrime, grant funding from Mercy Ships to perform outcomes research; Blake C. Alkire, grant funding from Mercy Ships to perform outcomes research.

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Supplemental Material

Additional supporting information is available in the online version of the article.

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