Linking World Bank Development Indicators and Outcomes of Congenital Heart Disease Survival in Low- and Middle-Income Countries: a Retrospective Analysis of Quality Improvement Data

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Linking World Bank Development Indicators and Outcomes of Congenital Heart Disease Survival in Low- and Middle-Income Countries: a Retrospective Analysis of Quality Improvement Data

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Abstract

Objective: Many Low- and Middle-Income Countries (LMICs) struggle to provide the health services investment required for life-saving Congenital Heart Disease (CHD) surgery. We explored associations between risk-adjusted CHD surgical mortality from 17 LMICs and global development indices to identify patterns that might inform investment strategies.

Design: A retrospective analysis. Country-specific Standardized Mortality Ratios were graphed against global development indices reflective of wealth and healthcare investment. Spearman correlation coefficients were calculated.

Setting and Participants: The International Quality Improvement Collaborative (IQIC) keeps a volunteer registry of outcomes of CHD surgery programs in low resource settings. Inclusion in the IQIC is voluntary enrollment by hospital sites. Patients in the registry underwent congenital heart surgery. Sites that actively participated in IQIC in 2013, 2014, or 2015 and passed a 10%

data audit were asked for permission to share data for this study. 31 sites in 17 countries are included.

Outcome Measures: In-hospital mortality. Standardized Mortality Ratios were calculated. Risk-adjustment for in-hospital mortality uses the RACHS method, a model including surgical risk category, age group, prematurity, presence of a major non-cardiac structural anomaly, and multiple congenital heart procedures during admission.

Results: The IQIC registry includes 24,917 congenital heart surgeries performed in children <18 years of age. The overall in-hospital mortality rate was 5.0 %. Country-level congenital heart surgery Standardized Mortality Ratios were negatively correlated with Gross Domestic Product (GDP) per capita (r= -0.34, p=0.18), and health expenditure per capita (r=-0.23, p=0.37) and positively correlated with under-5 mortality (r=.60, p=.01) and undernourishment (r=0.39, p=0.17). Countries with lower development had wider variation in mortality. GDP is a key driver of the association between other measures and mortality.

Conclusions: Results display a moderate relationship between wealth, healthcare investment and malnutrition, with significant variation, including superior results in many countries with low GDP. These findings provide context and optimism for investment in CHD procedures in low resource settings.

Strengths and Limitations of This Study

- This study uses data from the International Quality Improvement Collaborative for Congenital Heart Disease (IQIC), which offers a unique opportunity to study outcomes from low- and middle-income regions where little is known about outcomes for congenital heart surgery.
- This is the first study to directly compare development and investment to congenital heart surgery outcomes.
- This study adds context to the discussion of national investment in tertiary care in general and for congenital heart surgery in specific emerging economies.
- Study sample size is limited by the number of participants in IQIC.
- The study examines country-level outcomes, which may not reflect regional variability.

INTRODUCTION

In 2015, more than 150 world leaders at the United Nations agreed to adopt the 17 Sustainable Development Goals (SDGs) calling for a sustained investment globally to achieve a number of targets aiming at eradicating poverty and inequality, take action on climate change and the environment, improve access to health and education, and build strong institutions and partnerships.(1) Of particular importance is SDG3, ensure healthy lives and promote well-being for all at all ages and its demanding target to reduce neonatal mortality to at least as low as 12 per 1,000 live births and under-5 mortality to at least as low as 25 per 1,000 live births by 2030. Recent studies show that congenital anomalies, of which heart disease represents nearly half, are the fourth leading cause of neonatal deaths, especially for countries with lower overall childhood mortality,(2) which tend to be middle-, upper-middle- and high-income countries. Congenital Heart Disease (CHD) can also be a significant contributor to poverty as families can incur catastrophic health costs if care is not covered by health insurance.

Surgery for congenital heart disease requires substantial resources, and a highly specialized healthcare infrastructure. Low-and middle-income countries lack both access to care and capacity to perform congenital heart surgeries safely and effectively. Less developed countries have disproportionately higher amount of congenital heart disease per million Gross Domestic Product (GDP) compared to more economically developed countries.(3) In some cases, even countries that fall in the high-income group, or higher income regions within a country, struggle with allocating appropriate resources to CHD services. For example, Argentina is typically classified as high-income, but chose to be in the International Quality Improvement Collaborative because they felt they struggled with similar problems as LMICs for congenital heart surgery.

Literature has examined general surgical mortality in low- and middle-income countries, but to date, no studies have examined congenital heart surgery mortality in a comparative context to development. Lebrun et al. surveyed hospitals in multiple low income countries and found limited operative capacity for surgery with most countries having less than one surgeon or anesthesiologist per 100,000 population.(4) Bainbridge et al. found that in a mixed surgical population, perioperative mortality declined from the 1970s to 2011, especially in developing countries.(5) Hsuing and Abdallah highlight the need for more data on funding of paediatric surgery in LMICs.(6)

An analysis of congenital heart surgery outcomes within low- and middle-income countries adds context to the efforts of countries to reduce mortality for congenital heart disease. We retrospectively explored associations between risk-adjusted in-hospital survival after congenital heart surgery at the country level and indicators of national development and healthcare investment among low-and middle-income countries participating in an international quality improvement collaborative aimed at reducing congenital heart surgery mortality.

METHODS

Congenital Heart Surgery Outcomes

The International Quality Improvement Collaborative for Congenital Heart Disease (IQIC) collects surgical outcome data from participating centers in low-resource-settings around the world. The IQIC aims to reduce mortality for congenital heart surgery by collaborating with local sites to implement quality improvement strategies such as perioperative communication, infection reduction, and team-based practice.(7) The IQIC began collecting data in 2008 from five sites and has since grown to 64 sites across 25 countries in 2018. The database is housed at Boston Children's Hospital.

Outcome data (in-hospital mortality) in the IQIC registry was collected by individual programs on paediatric congenital heart surgeries performed at each site. Inclusion in the IQIC is voluntary enrollment by hospital sites. Patients included in the registry underwent congenital heart surgery. Sites that actively participated in IQIC in 2013, 2014, or 2015 and successfully passed a 10% data audit were asked for permission to share data for this study. A total of 31 sites in 17 countries (Afghanistan, Argentina, Brazil, China, Colombia, Costa Rica, Guatemala, India, Malaysia, Mexico, Pakistan, Peru, Russia, Serbia, Uganda, Ukraine, and Vietnam) chose to participate.

Development Indicators

The 2014 country-level development indicators are drawn from the publicly available World Bank World Development Indicators database.(8) Eight variables are included as indicators of country development and investment in health: Gross Domestic Product (GDP) per capita, health expenditure per capita, under-5 mortality rate, poverty headcount ratio at $5.50 per day, prevalence of undernourishment, life expectancy at birth, domestic general government health expenditure (% of GDP), and specialist surgical workforce (per 100,000 population).

GDP per capita (in constant 2010 US$) is the sum of gross value added by all resident producers (plus taxes, minus subsidies) divided by midyear population.(8) Health expenditure per capita (in current US$) is the sum of public and private health expenditures as a ratio of total population.(8) Prevalence of undernourishment is the percentage of the population whose food intake is insufficient to meet dietary energy requirements continuously.(8) Poverty headcount ratio is internationally comparable measure of the percentage of the population with income less than $5.50 a day (2011 international prices).(8) The under-5 mortality rate (per 1,000 live births) is the probability that a newborn baby will die before reaching age five, based on age-specific mortality rates of that year.(8) Life expectancy measures years of life for a newborn given current mortality patterns remain throughout their life.(8) Domestic general government health expenditure is the amount of public expenses on health as a share of the economy (GDP). (8) Specialist surgical workforce is the number of specialist surgical, anesthetic, and obstetric providers (per 100,000 of population). (8)

Data Analysis

We completed a retrospective analysis of IQIC registry data. For each country, we used the IQIC registry to determine the total number of cases of congenital heart surgery in children less than 18 years of age over the three-year period 2013-2015. The observed in-hospital mortality rate was calculated as the number of deaths occurring prior to hospital discharge divided by the total number of RACHS-classified surgical cases. The Risk Adjustment for Congenital Heart Surgery (RACHS) model is used to evaluate differences in mortality among groups of patients undergoing congenital heart surgery.(9) The outcome measure used is a Standardized Mortality Ratio (SMR) for each country, defined as the observed in-hospital mortality rate divided by the mortality rate that would be expected given the country's patient case mix. The expected in-hospital mortality rate was calculated using the previously validated RACHS risk adjustment method (7,10). The model included surgical risk category (categories 1 through 6, where 1 represents surgical procedures with the lowest risk for in-hospital mortality and 6 the highest), age group (≤30 days, 31 days to <1 year, 1 to 17 years), prematurity (<37 weeks), presence of a major non-cardiac structural anomaly, and multiple congenital heart procedures during the admission. The RACHS method was developed using U. S. outcomes data, but since the inception of the IQIC in 2008 has been successfully applied to LMICs.(7) An SMR greater than

1.0 suggests higher than expected mortality based on patient case mix, while an SMR less than 1.0 represents lower than expected mortality. Two-way scatter plots were used to examine the relationships between SMR and each development indicator; the strength of these relationships was quantified using Spearman correlation coefficients. We also used linear regression analysis to compare unadjusted regression coefficients relating each development indicator to SMR to coefficients adjusted for GDP per capita. The natural log of SMR was used as the outcome for these models since SMR itself was not normally distributed. Furthermore, we completed a stratified analysis between low complexity cases (RACHS categories 1 and 2) and high complexity cases (RACHS categories 3-6) and SMR. To do this, for each country we calculated a SMR for RACHS 1-2 and a SMR for RACHS 3-6 and compared correlations between the low RACHS SMR and each development indicator with the high RACHS SMR and each development indicator.

The institutional review board at Boston Children's Hospital gave permission for the IQIC data registry to be used for this research. Study data were collected and managed using REDCap electronic data capture tools hosted at Boston Children's Hospital.(11) REDCap (Research Electronic Data Capture) is a secure, web-based application designed to support data capture for research studies, providing 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources. The senior author had complete access to the registry data, and the authors are responsible for the study design, analysis and interpretation of data, and the decision to submit the paper for publication.

RESULTS

Among 31 programs in 17 countries, the IQIC database included 24,917 congenital heart surgeries performed in children <18 years of age. The number of programs per country ranged from one to six. The overall in-hospital mortality rate was 5.0 % and country-level mortality rate ranged from 1.7% to 25.0%. The age and RACHS category distribution of cases by country is shown in online supplementary Tables 1 and 2. The full RACHS model used to calculate country SMRs is shown in online supplementary Table 3.

Country SMRs range from 0.40 to 4.85. Unadjusted mortality rates and Standardized Mortality Rates by country are shown in online supplemental Figure 1. Correlation coefficients between each development index and SMR and regression coefficients, both unadjusted and adjusted by GDP per capita, by country are shown in Table 1.

Table 1. Correlation and Regression Coefficients for Development Indicators with SMR

Indicator	Number of Countries	Correlation Coefficient	Unadjusted Regression Coefficient	Regression Coefficient adjusted for GDP per capita
GDP per capita	17	r=-0.34	-0.047	--
Health Expenditure per capita	17	r= -0.23	-0.035	0.092
Undernourishment	14#	r=0.39	0.40	0.78
Under-5 Mortality Rate	17	r=.60*	0.13*	0.16
Poverty Headcount Ratio at $5.50 a day	11#	r=0.26	0.12	0.19
Life Expectancy	17	r= -0.35	-0.50	-0.49
Domestic General Government Health Expenditure	17	r=-0.22	-0.0937	-0.0297
Specialist Surgical Workforce	11#	r=-0.56	-0.0737	-0.0515

World Bank index not available for some countries

*significant at $p<0.05$

P-values: GDP correlation p=0.18, unadjusted regression coefficient p=.29, Health Expenditure correlation p=0.37, unadjusted regression p=0.55, adjusted regression p=0.47, Undernourishment correlation p=0.17, unadjusted regression p=0.14, adjusted regression p=0.20, Under-5 Mortality Rate correlation p=0.01, unadjusted regression p=0.04, adjusted regression p=0.08, Poverty Headcount ratio correlation p=0.43, unadjusted regression p=0.46, adjusted regression p=0.33, Life Expectancy correlation p=0.16, unadjusted regression p=0.11, adjusted regression p=0.24, Domestic General Government Health Expenditure correlation p=0.40, unadjusted regression p= 0.41 adjusted regression p=0.84 . Specialist Surgical Workforce p=0.07, unadjusted regression p=0.26, adjusted regression p=0.45.

Graphs showing the relationship between SMR by country and GDP per capita, health expenditure per capita, poverty headcount ratio, and specialist surgical workforce are shown in Figures 1-4 respectively. Graphs showing the relationship between SMR and other development indicators are shown in online supplemental figures 2-5.

Stratified analysis comparing congenital heart surgery mortality ratios from low complexity cases (low RACHS categories, 1-2) and high complexity cases (high RACHS categories, 3-6) are shown in online supplemental table 4. The low RACHS score SMR correlation largely mirror the overall SMR Spearman correlation, while the high RACHS score SMR has a lower correlation than the low RACHS score SMR with each development indicator except poverty headcount ratio and specialist surgical workforce.

DISCUSSION

We found negative associations of GDP per capita, Health Expenditure per capita, Domestic Government Health Expenditure, Specialist Surgical Workforce, and Life Expectancy with congenital heart surgery SMR: as these indicators increase, SMR decreases. We found positive associations of Poverty Headcount and Undernourishment with SMR: as poverty headcount or undernourishment increases, SMR increases. We also found the expected positive correlation between under-5 mortality and SMR, which was statistically significant. The association of GDP per capita and SMR suggests that overall development of a country may be an important component of surgical mortality, even more so than Health Expenditure per capita. The borderline statistically significant negative correlation between specialist surgical workforce and CHD mortality suggests that adequate workforce is integral to quality congenital heart surgical capacity. While most associations do not reach statistical significance, they display links between development and surgery outcomes.

Although these associations exist, a crucial finding of this study is that there is still substantial variation between countries in SMRs even at similar development levels. For example, Afghanistan and Pakistan have much higher SMRs than India, although they are at similar GDP per capita levels. Nations with high levels of conflict such as Afghanistan may have stressed health systems as a whole,(12,13) which would impact congenital heart surgery services. Similarly, Peru, Serbia and China are at similar GDP per capita levels yet vary widely in mortality, with China at the lowest SMR. China has a well-organized and efficient health system that likely contributes to better outcomes. (14) Although Peru appears to be an outlier, it is not influential – meaning it does not have a substantial impact on the correlation coefficients – with the exception of the association between SMR and undernourishment and SMR and specialist surgical workforce (both associations become stronger without Peru).

When adjusting for GDP per capita, regression coefficients decrease in magnitude for most indicators—health expenditure, poverty, life expectancy, and under-5 mortality. Therefore, the data indicates that GDP per capita is a main driver of the association between these indicators and congenital heart surgery mortality. However, the regression coefficient for undernourishment increases when controlling for GDP per capita, suggesting that population-wide undernourishment affects mortality after congenital heart surgery independently of GDP. This may be reflective of the higher likelihood of children undergoing CHD surgery while malnourished in countries where malnourishment is more prevalent, and potentially higher risk of death in such circumstances.(15–17)

Comparative analysis of low RACHS SMRs with development indicators and high RACHS SMRs with development indicators display that low RACHS SMRs correlations are similar to the overall SMR correlations and thus may contribute more to the overall correlation than high RACHS cases. Notably, high RACHS cases SMRs have a stronger correlation with poverty headcount ratio and with specialist surgery workforce than low RACHS cases SMRs, suggesting that low poverty and a present specialist surgery workforce are more important for positive outcomes in high complexity cases.

As poverty and infectious diseases decrease, non-communicable diseases such as congenital heart disease in LMICs account for a greater percentage of childhood deaths. Congenital defects represented 8.7% of global under-5 mortality in 2016.(18) Many stakeholders believe congenital heart surgery should be considered an "Essential Paediatric Surgical Procedure" due to the economic value of these surgeries in a community.(19) A substantial fraction (58%) of congenital heart defect burden (avertable disability years) could be alleviated with scaled up congenital heart surgery programs in low-and-middle-income countries.(20) Quality in high-specialty care is of paramount importance. A recent study estimated that cardiovascular diseases are the highest contributor to amenable mortality due to poor-quality care.(21) Quality tertiary care requires trained personnel and equipment and infection control.(22) Recommended strategies to improve surgical care include training and basic infrastructure and equipment,(23) which necessitates investment in healthcare systems.

Our method has several limitations. First, the sample size is only 17 countries and 31 sites (for some indicators, fewer), which limits statistical power, and may be why most associations, except under-5 mortality were not significant. Second, data are analyzed at the country-level but using facility-based clinical outcomes data from selected centers that participate in IQIC, which may not be representative of countrywide outcomes for CHD surgery. As a surgical quality improvement database, the IQIC collects data for in-hospital mortality and does not capture longer-term outcomes, therefore does not represent the broader socioeconomic factors that may affect survival from CHD surgery (24) and that could have been collected with a more population health focused database. IQIC sites are often large academic tertiary hospitals, and IQIC members are willing and able to collect data and participate in quality improvement activities. That may mean that sometimes hospital settings represented in this study do not always mirror the overall development level of their countries. However, most high-income countries tend to regionalize CHD surgical centers in several large urban areas, to avoid the creation of many small-volume centers. (25) Therefore, even though the overall quality of care of the health systems may be low, the centers themselves may have quite good CHD surgical outcomes. Country-level SMRs may also not accurately reflect regional variability in level of development or resources available for congenital heart surgery, especially in large countries such as China and India. For example, the sites in India are mostly from states in Southern India, which tend to have higher development levels than the Northern part of the country. There may also be variations in case mix of participating institutions due to gaps in the existing diagnosis and referral networks, healthcare financing, and social and cultural factors that may result in not treating the patients with the most severe disease, which may not be completely accounted for in risk-adjustment models. Regional differences in healthcare financing for CHD surgery and in-hospital care, including public and private insurance, is a particularly important factor not examined in this study, since care becomes unaffordable to most families if is not included in universal health insurance coverage package. On the other hand, institutions too could potentially suffer financial losses if reimbursement for CHD surgery is not at the appropriate level. Finally, our study only evaluates outcomes for children who underwent congenital heart surgery, and does not capture outcomes for children who did not have access to operations. Outcomes for these children are also likely associated with development and investment.

In conclusion, our results show correlations between various development indicators and congenital heart surgery mortality. Nonetheless, there is variation among countries of similar GDP levels, and lower risk-adjusted mortality in some countries with lower development offers hope and encourages investment in congenital heart surgery programs. Our findings can be helpful for national and sub-national planning by countries committed to achieving the SDGs, especially SDG3 target of ending preventable deaths of newborns and children under 5 years of age. As they consider development of different paediatric services, this study can give them guidance on areas they could invest in. Further study is required to truly understand why countries with similar development levels vary in congenital heart surgery mortality. Future studies ought to investigate why such variations exist, and examine the role of governments, NGOs or other stakeholders, training and retention of skilled professionals and other personnel, and infection control practices in particular countries. This inquiry can help establish effective strategies for successful congenital heart surgical programs in low- and middle-income countries.

Abbreviations

CHD Congenital Heart Disease

GDP Gross Domestic Product

IQIC International Quality Improvement Collaborative for Congenital Heart Disease

LMICs Low- and Middle-Income Countries

NGO Non-Governmental Organization

SDGs Sustainable Development Goals

SMR Standardized Mortality Ratio

RACHS Risk Adjustment for Congenital Heart Surgery

Contributors

SR and KJ had the primary responsibility to design the study and write the manuscript. BZ, KMC, JTC, KD, KG, PAH, RKK, JKK, WN, NS, and KJ coordinated the global study data concept and collection. BZ revised multiple manuscript drafts, and DF interpreted data. KG conducted statistical analyses.

Declaration of Interests

We declare no competing interests.

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Data Sharing Statement

Extra data is available by emailing the corresponding author.

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Figure Legends

Figure 1. This graph shows negative correlation of GDP per capita on the x-axis and SMR on the y-axis by country.

Figure 2. This graph shows negative correlation of Health Expenditure per capita on the x-axis and SMR on the y-axis by country.

Figure 3. This graph shows positive correlation of Poverty Ratio at $5.50 a day on the x-axis and SMR on the y-axis by country.

Figure 4. This graph shows a negative correlation of Surgical Specialist Workforce on the x-axis and SMR on the y-axis by country.

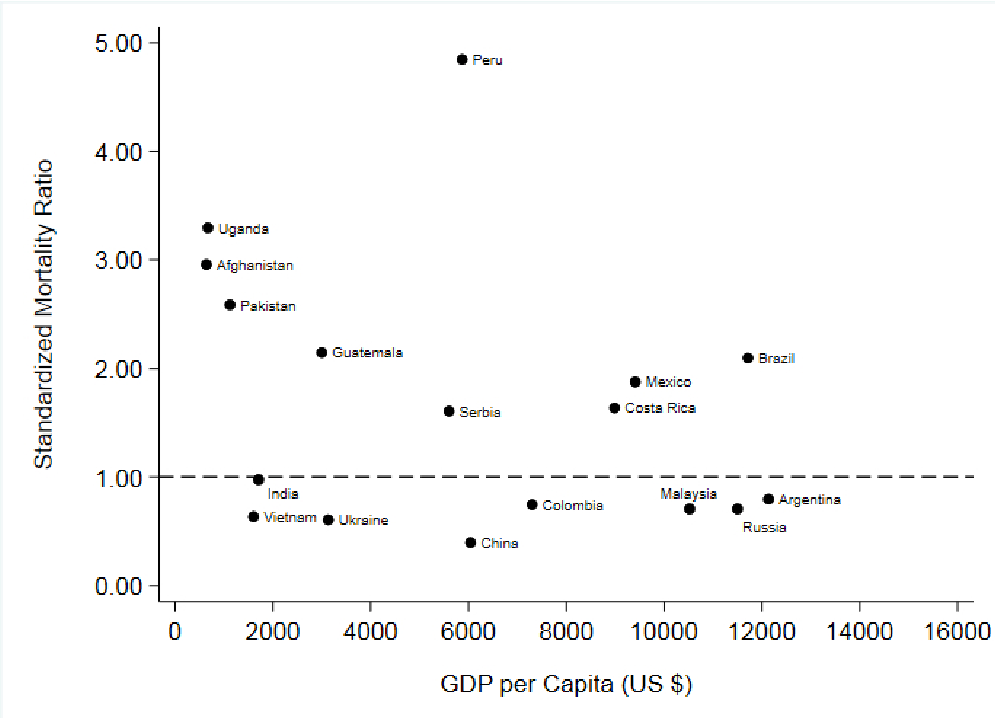
Online Supplemental Figure 1. This bar graph shows the unadjusted (observed) mortality rate for congenital heart surgery on the left y-axis and the Standardized Mortality Ratio (SMR) calculated using the RACHS model on the right y-axis. The x-axis show each country from lowest to highest number of cases.

Online Supplemental Figure 2. This graph shows positive correlation of Prevalence of Undernourishment on the x-axis and SMR on the y-axis by country.

Online Supplemental Figure 3. This graph shows positive correlation of Under-5 Mortality Rate on the x-axis and SMR on the y-axis by country.

Online Supplemental Figure 4. This graph shows negative correlation of Life Expectancy on the x-axis and SMR on the y-axis by country.

Online Supplemental Figure 5. This graph shows negative correlation of Domestic General Government Health Expenditure (% of GDP) on the x-axis and SMR on the y-axis by country.



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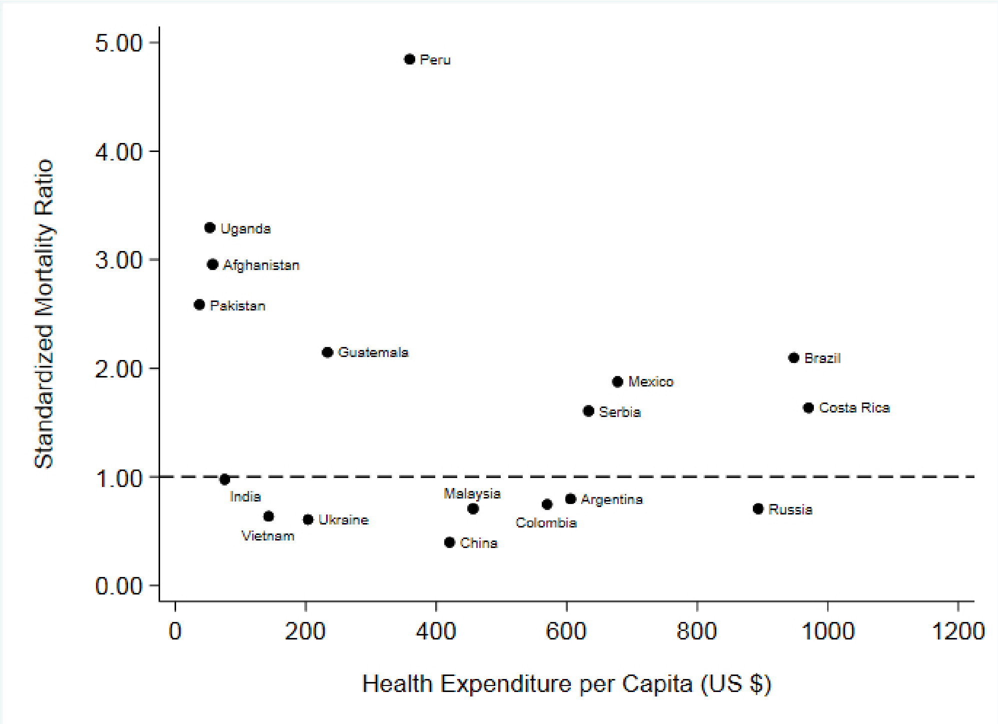

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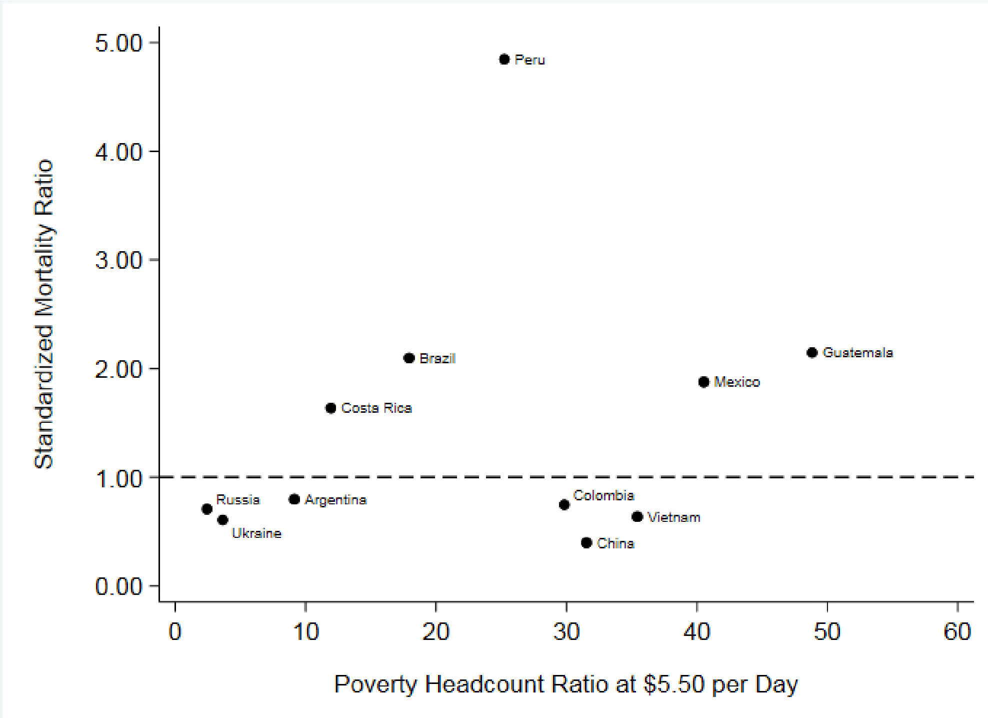
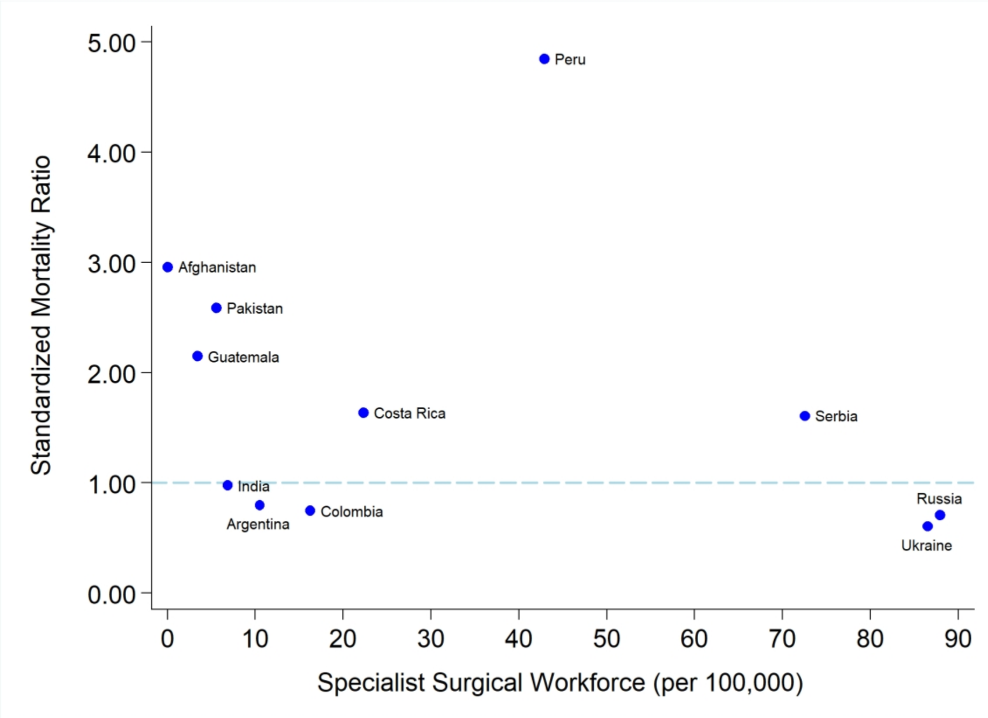


This graph shows positive correlation of Poverty Ratio at $5.50 a day on the x-axis and SMR on the y-axis by country.



This graph shows a negative correlation of Surgical Specialist Workforce on the x-axis and SMR on the y-axis by country.

Online Supplementary Figures and Tables

Online Supplemental Table 1. Age Distribution of Congenital Heart Surgery Cases by Country

Country	≤30 days	31 days to <1 year	1 to 17 years
Afghanistan	0 (0%)	39 (9%)	393 (91%)
Argentina	229 (13%)	615 (34%)	950 (53%)
Brazil	147 (10%)	587 (42%)	671 (48%)
China	164 (2%)	4335 (52%)	3832 (46%)
Colombia	169 (10%)	657 (40%)	835 (50%)
Costa Rica	27 (16%)	59 (35%)	81 (49%)
Guatemala	20 (3%)	282 (38%)	431 (59%)
India	345 (8%)	1942 (48%)	1780 (44%)
Malaysia	55 (4%)	404 (31%)	843 (65%)
Mexico	63 (12%)	139 (26%)	334 (62%)
Pakistan	38 (2%)	602 (26%)	1706 (73%)
Peru	5 (10%)	16 (33%)	27 (56%)
Russia	38 (11%)	187 (54%)	123 (35%)
Serbia	81 (27%)	125 (41%)	99 (32%)
Uganda	1 (<1%)	53 (24%)	165 (75%)
Ukraine	30 (11%)	104 (38%)	139 (51%)
Vietnam	50 (5%)	525 (55%)	375 (39%)
Total	**1462 (6%)**	**10671 (43%)**	**12784 (51%)**

Online Supplemental Table 2. RACHS Category by Country

Country	RACHS Risk Category				

	1	2	3	4	5+6
Afghanistan	229 (53%)	175 (41%)	27 (6%)	1 (<1%)	0 (0%)
Argentina	282 (16%)	682 (38%)	617 (34%)	162 (9%)	51 (3%)
Brazil	277 (20%)	440 (31%)	536 (38%)	127 (9%)	25 (2%)
China	859 (10%)	4935 (59%)	2192 (26%)	341 (4%)	4 (<1%)
Colombia	553 (33%)	573 (35%)	415 (25%)	97 (6%)	23 (1%)
Costa Rica	46 (28%)	74 (44%)	34 (20%)	12 (7%)	1 (1%)
Guatemala	411 (56%)	236 (32%)	66 (9%)	18 (2%)	2 (<1%)
India	548 (13%)	2009 (49%)	1066 (26%)	420 (10%)	24 (1%)
Malaysia	108 (8%)	684 (53%)	336 (26%)	165 (13%)	9 (1%)
Mexico	129 (24%)	202 (38%)	129 (24%)	66 (12%)	10 (2%)
Pakistan	357 (15%)	1482 (63%)	444 (19%)	63 (3%)	0 (0%)
Peru	10 (21%)	21 (44%)	14 (29%)	3 (6%)	0 (0%)
Russia	122 (35%)	105 (30%)	98 (28%)	22 (6%)	1 (<1%)
Serbia	52 (17%)	139 (46%)	79 (26%)	22 (7%)	13 (4%)
Uganda	119 (54%)	95 (43%)	5 (2%)	0 (0%)	0 (0%)
Ukraine	130 (48%)	69 (25%)	57 (21%)	17 (6%)	0 (0%)
Vietnam	123 (13%)	594 (63%)	151 (16%)	81 (9%)	1 (<1%)
Total	**4355 (17%)**	**12515 (50%)**	**6266 (25%)**	**1617 (6%)**	**164 (1%)**

Online Supplementary Table 3. Full RACHS Model

Cases Eligible for RACHS and Assigned to a Risk Category

	Odds Ratio	95% Confidence Interval	P Value
RACHS Risk Category			
1	1.0	-	-
2	2.3	(1.7, 3.2)	<0.001
3	6.7	(5.0, 9.1)	<0.001
4	9.5	(6.8, 13.1)	<0.001
5 + 6	43.6	(28.2, 67.6)	<0.001
Age at Surgery			
≤30 days	3.2	(2.6, 3.9)	<0.001
31 days to <1 year	1.6	(1.4, 1.8)	<0.001
1 to 17 years	1.0	-	-
Prematurity	1.4	(1.1, 1.7)	0.007
Major Non-Cardiac Structural Anomaly	2.0	(1.5, 2.6)	<0.001
Multiple Cardiac Procedures	1.0	(0.9, 1.2)	0.80

C statistic for this model is 0.75.

Online Supplemental Table 4. Development Indicators and Standardized Mortality Ratio Correlations Stratified by RACHS Category

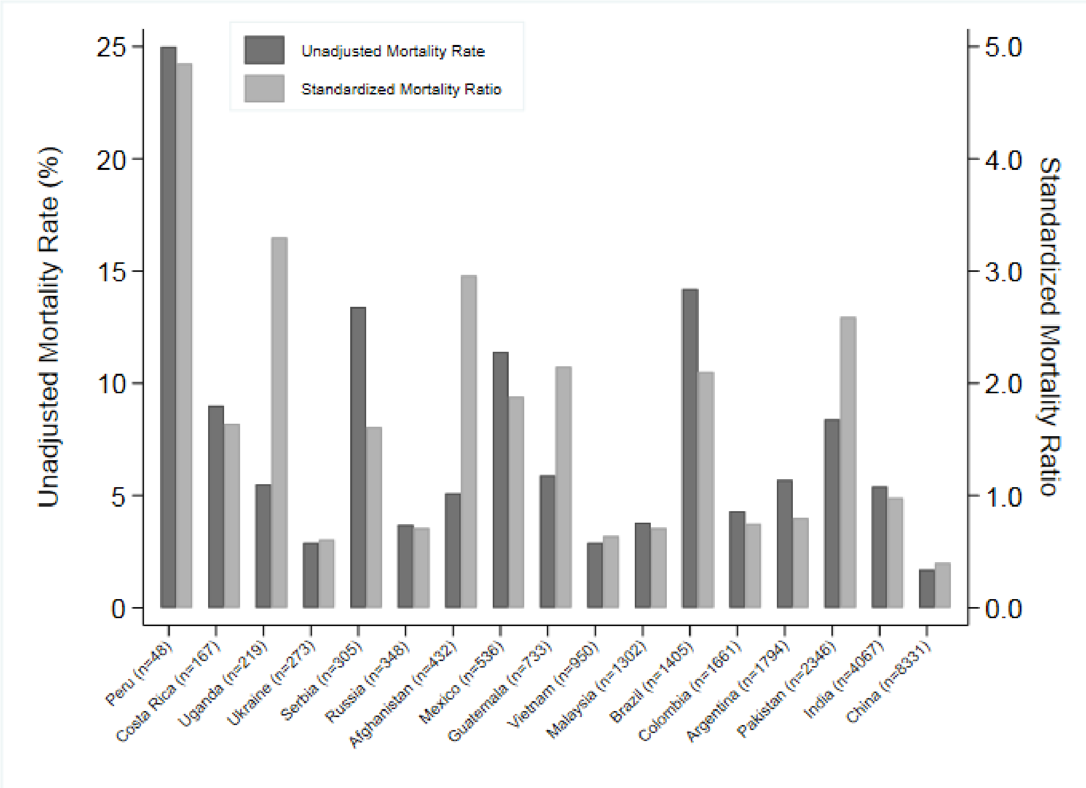
Correlations with SMR

	All Cases	RACHS 1-2	RACHS 3-6
	Spearman r (p value)	Spearman r (p value)	Spearman r (p value)
GDP per capita (US $)	-0.34 (0.18)	-0.38 (0.14)	-0.07 (0.81)

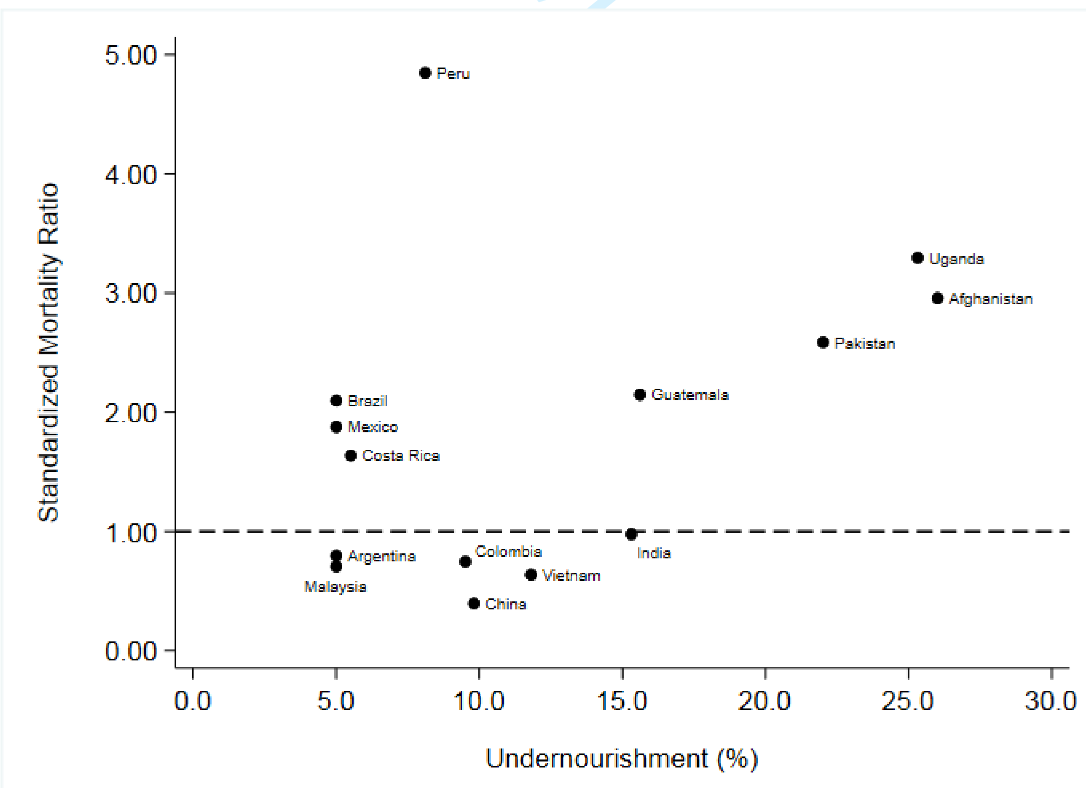
GNI per capita (US $)	-0.38 (0.13)	-0.40 (0.11)	-0.16 (0.58)
Health expenditure per capita (US $)	-0.23 (0.37)	-0.23 (0.38)	0.13 (0.66)
Undernourishment (%)	0.39 (0.17)	0.40 (0.15)	0.11 (0.74)
Life expectancy at birth (years)	-0.35 (0.16)	-0.38 (0.14)	-0.07 (0.82)
Under 5 mortality rate (per 1000)	0.60 (0.01)	0.54 (0.02)	0.43 (0.12)
Poverty headcount (%) V1	0.50 (0.12)	0.48 (0.13)	0.41 (0.24)
Poverty headcount ratio (%) V2	0.26 (0.43)	0.15 (0.65)	0.38 (0.28)
Domestic general government health expenditure (% of GDP)	-0.22 (0.40)	-0.19 (0.47)	-0.01 (0.97)
Specialist surgical workforce (per 100,000)	-0.56 (0.07)	-0.50 (0.12)	-0.70 (0.04)
Number of Countries	17	17	14#

3 countries (Afghanistan, Peru, and Uganda) were not used in the RACHS 3-6 correlations due to small number of cases.

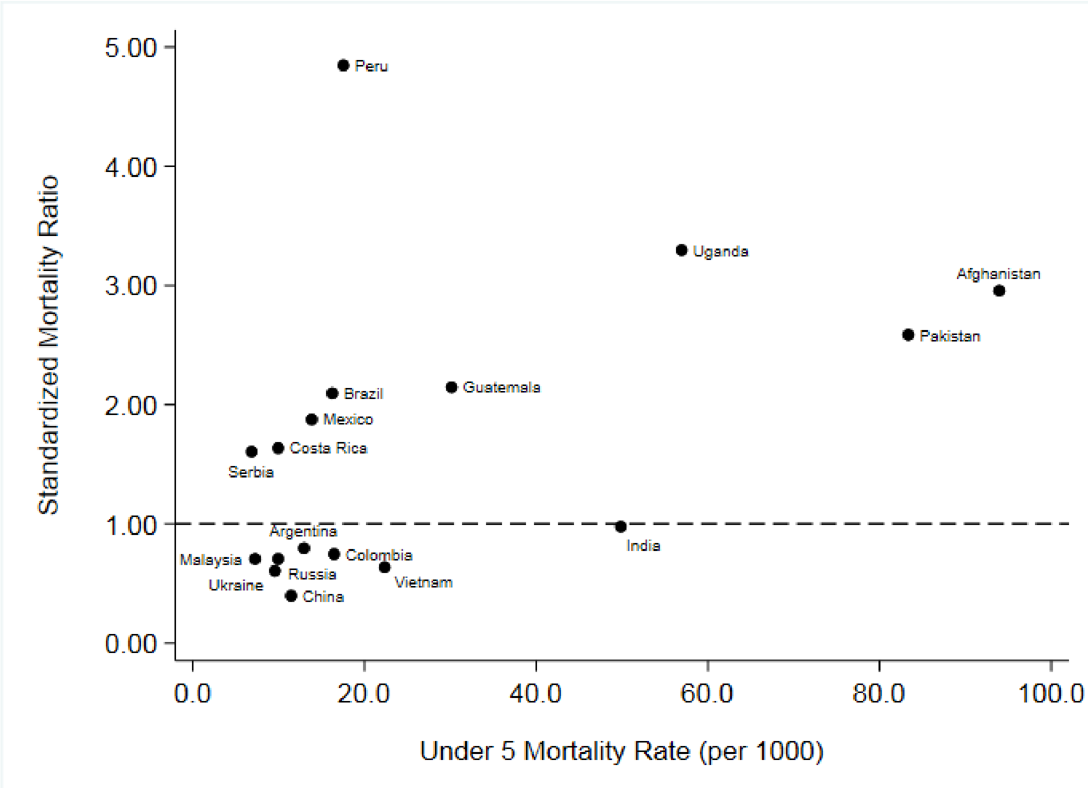
Online Supplemental Figure 1. Congenital Heart Surgery Unadjusted Mortality Rate and Standardized Mortality Ratio by Country



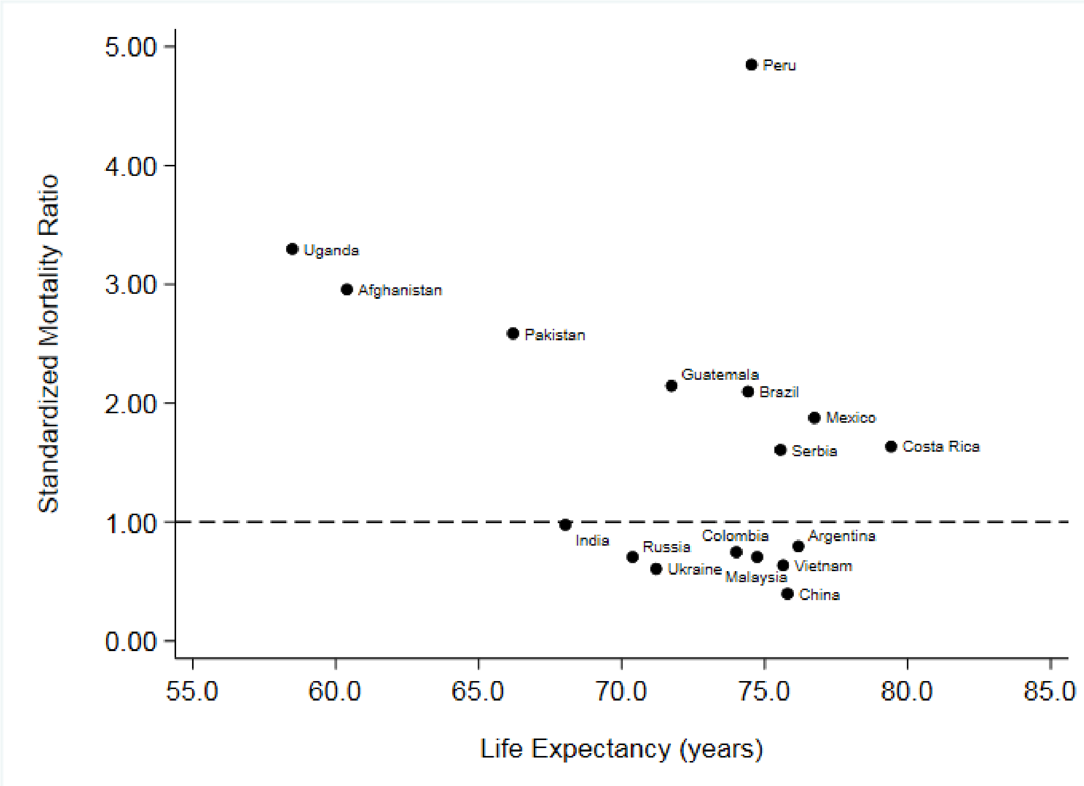
Online Supplemental Figure 2. Undernourishment and SMR



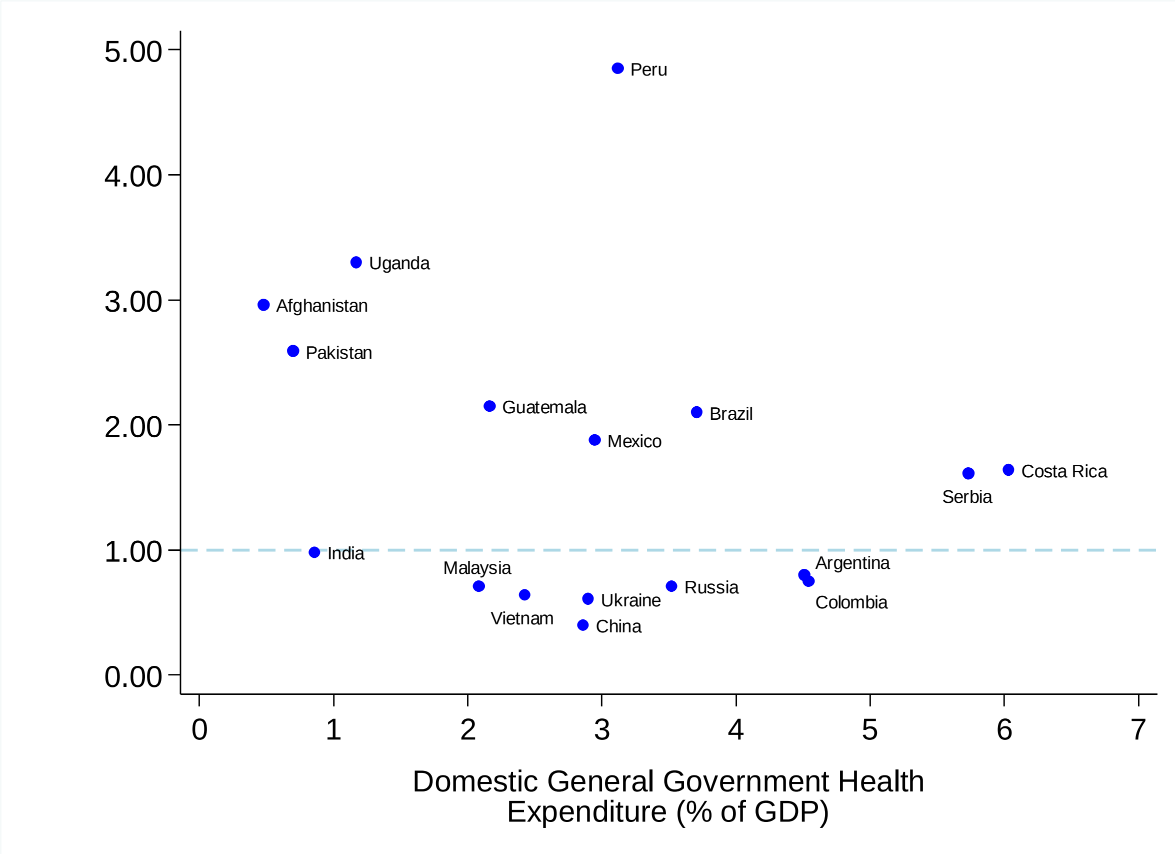
Online Supplemental Figure 3. Under-5 Mortality Rate and SMR



Online Supplemental Figure 4. Life Expectancy and SMR



Online Supplemental Figure 5. Domestic General Government Health Expenditure and SMR



Online Supplemental Figure Legends

Online Supplemental Figure 1. This bar graph shows the unadjusted (observed) mortality rate for congenital heart surgery on the left y-axis and the Standardized Mortality Ratio (SMR) calculated using the RACHS model on the right y-axis. The x-axis show each country from lowest to highest number of cases.

Online Supplemental Figure 2. This graph shows positive correlation of Prevalence of Undernourishment on the x-axis and SMR on the y-axis by country.

Online Supplemental Figure 3. This graph shows positive correlation of Under-5 Mortality Rate on the x-axis and SMR on the y-axis by country.

Online Supplemental Figure 4. This graph shows negative correlation of Life Expectancy on the x-axis and SMR on the y-axis by country.

Online Supplemental Figure 5. This graph shows negative correlation of Domestic General Government Health Expenditure (% of GDP) on the x-axis and SMR on the y-axis by country.

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3-4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6-7
		(*b*) Describe any methods used to examine subgroups and interactions	6-7
		(*c*) Explain how missing data were addressed	Table 1
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	n/a
		(*e*) Describe any sensitivity analyses	n/a
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	n/a
		(b) Give reasons for non-participation at each stage	5
		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	5
		(b) Indicate number of participants with missing data for each variable of interest	Table 1
Outcome data	15*	Report numbers of outcome events or summary measures	8
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8
		(*b*) Report category boundaries when continuous variables were categorized	8
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9
Discussion			
Key results	18	Summarise key results with reference to study objectives	9-10
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13
Generalisability	21	Discuss the generalisability (external validity) of the study results	12-13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Linking World Bank Development Indicators and Outcomes of Congenital Heart Surgery in Low- and Middle-Income Countries: a Retrospective Analysis of Quality Improvement Data

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Linking World Bank Development Indicators and Outcomes of Congenital Heart Surgery in Low- and Middle-Income Countries: a Retrospective Analysis of Quality Improvement Data

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Word Count: 3784

Abstract

Objective: Many Low- and Middle-Income Countries (LMICs) struggle to provide the health services investment required for life-saving Congenital Heart Disease (CHD) surgery. We explored associations between risk-adjusted CHD surgical mortality from 17 LMICs and global development indices to identify patterns that might inform investment strategies.

Design: Retrospective analysis. Country-specific Standardized Mortality Ratios were graphed against global development indices reflective of wealth and healthcare investment. Spearman correlation coefficients were calculated.

Setting and Participants: The International Quality Improvement Collaborative (IQIC) keeps a volunteer registry of outcomes of CHD surgery programs in low resource settings. Inclusion in the IQIC is voluntary enrollment by hospital sites. Patients in the registry underwent congenital heart surgery. Sites that actively participated in IQIC in 2013, 2014, or 2015 and passed a 10%

data audit were asked for permission to share data for this study. 31 sites in 17 countries are included.

Outcome Measures: In-hospital mortality. Standardized Mortality Ratios were calculated. Risk-adjustment for in-hospital mortality uses the RACHS method, a model including surgical risk category, age group, prematurity, presence of a major non-cardiac structural anomaly, and multiple congenital heart procedures during admission.

Results: The IQIC registry includes 24,917 congenital heart surgeries performed in children <18 years of age. The overall in-hospital mortality rate was 5.0 %. Country-level congenital heart surgery Standardized Mortality Ratios were negatively correlated with Gross Domestic Product (GDP) per capita (r= -0.34, p=0.18), and health expenditure per capita (r=-0.23, p=0.37) and positively correlated with under-5 mortality (r=.60, p=.01) and undernourishment (r=0.39, p=0.17). Countries with lower development had wider variation in mortality. GDP per capita is a driver of the association between some other measures and mortality.

Conclusions: Results display a moderate relationship between wealth, healthcare investment and malnutrition, with significant variation, including superior results in many countries with low GDP per capita. These findings provide context and optimism for investment in CHD procedures in low resource settings.

Strengths and Limitations of This Study

- This study uses data from the International Quality Improvement Collaborative for Congenital Heart Disease (IQIC), which offers a unique opportunity to study outcomes from LMICs where little is known about outcomes for congenital heart surgery.
- This is the first study to directly compare development and investment to congenital heart surgery outcomes.
- This study adds context to the discussion of national investment in tertiary care in general and for congenital heart surgery in specific emerging economies.
- Study sample size is limited by the number of participants in IQIC.
- The study does not examine regional variability within countries.

INTRODUCTION

In 2015, more than 150 world leaders at the United Nations agreed to adopt the 17 Sustainable Development Goals (SDGs) calling for a sustained investment globally to achieve a number of targets aiming at eradicating poverty and inequality, take action on climate change and the environment, improve access to health and education, and build strong institutions and partnerships.(1) Of particular importance is SDG3, ensure healthy lives and promote well-being for all at all ages and its demanding target to reduce neonatal mortality to at least as low as 12 per 1,000 live births and under-5 mortality to at least as low as 25 per 1,000 live births by 2030. Recent studies show that congenital anomalies, of which heart disease represents nearly half, are the fourth leading cause of neonatal deaths, especially for countries with lower overall childhood mortality,(2) which tend to be middle-, upper-middle- and high-income countries. Congenital Heart Disease (CHD) can also be a significant contributor to poverty as families can incur catastrophic health costs if care is not covered by health insurance.

Surgery for congenital heart disease requires substantial resources, and a highly specialized healthcare infrastructure. LMICs lack both access to care and capacity to perform congenital heart surgeries safely and effectively. Less developed countries have disproportionately higher amount of congenital heart disease per million Gross Domestic Product (GDP) compared to more economically developed countries.(3) In some cases, even countries that fall in the high-income group, or higher income regions within a country, struggle with allocating appropriate resources to CHD services. For example, Argentina is typically classified as high-income, but centers from Argentina chose to be in the International Quality Improvement Collaborative because they felt they struggled with similar problems as LMICs for congenital heart surgery.

Literature has examined general surgical mortality in LMICs, but to date, no studies have examined congenital heart surgery mortality in a comparative context to development. Lebrun et al. surveyed hospitals in multiple low income countries and found limited operative capacity for surgery with most countries having less than one surgeon or anesthesiologist per 100,000 population.(4) Bainbridge et al. found that in a mixed surgical population, perioperative mortality declined from the 1970s to 2011, especially in developing countries.(5) Hsuing and Abdallah highlight the need for more data on funding of paediatric surgery in LMICs.(6)

An analysis of congenital heart surgery outcomes within LMICs adds context to the efforts of countries to reduce mortality for congenital heart disease. We retrospectively explored associations between risk-adjusted in-hospital survival after congenital heart surgery and indicators of national development and healthcare investment among centers in LMICs participating in an international quality improvement collaborative aimed at reducing congenital heart surgery mortality.

METHODS

Congenital Heart Surgery Outcomes

The International Quality Improvement Collaborative for Congenital Heart Disease (IQIC) collects surgical outcome data from participating centers in low-resource-settings around the world. The IQIC aims to reduce mortality for congenital heart surgery by collaborating with local sites to implement quality improvement strategies such as perioperative communication, infection reduction, and team-based practice.(7) The IQIC began collecting data in 2008 from five sites and has since grown to 64 sites across 25 countries in 2018. The database is housed at Boston Children's Hospital.

Outcome data (in-hospital mortality) in the IQIC registry was collected by individual programs on paediatric congenital heart surgeries performed at each site. Inclusion in the IQIC is voluntary enrollment by hospital sites. Patients included in the registry underwent congenital heart surgery. Sites that actively participated in IQIC in 2013, 2014, or 2015 and successfully passed a 10% data audit were asked for permission to share data for this study. A total of 31 sites in 17 countries (Afghanistan, Argentina, Brazil, China, Colombia, Costa Rica, Guatemala, India, Malaysia, Mexico, Pakistan, Peru, Russia, Serbia, Uganda, Ukraine, and Vietnam) chose to participate.

Development Indicators

The 2014 country-level development indicators are drawn from the publicly available World Bank World Development Indicators database.(8) Eight variables are included as indicators of country development and investment in health: Gross Domestic Product (GDP) per capita, health expenditure per capita, under-5 mortality rate, poverty headcount ratio at $5.50 per day, prevalence of undernourishment, life expectancy at birth, domestic general government health expenditure (% of GDP), and specialist surgical workforce (per 100,000 population).

GDP per capita (in constant 2010 US$) is the sum of gross value added by all resident producers (plus taxes, minus subsidies) divided by midyear population.(8) Health expenditure per capita (in current US$) is the sum of public and private health expenditures as a ratio of total population.(8) Prevalence of undernourishment is the percentage of the population whose food intake is insufficient to meet dietary energy requirements continuously.(8) Poverty headcount ratio is internationally comparable measure of the percentage of the population with income less than $5.50 a day (2011 international prices).(8) The under-5 mortality rate (per 1,000 live births) is the probability that a newborn baby will die before reaching age five, based on age-specific mortality rates of that year.(8) Life expectancy measures years of life for a newborn given current mortality patterns remain throughout their life.(8) Domestic general government health expenditure is the amount of public expenses on health as a share of the economy (GDP). (8) Specialist surgical workforce is the number of specialist surgical, anesthetic, and obstetric providers (per 100,000 of population). (8)

Data Analysis

We completed a retrospective analysis of IQIC registry data. For each country, we used the IQIC registry to determine the total number of cases of congenital heart surgery in the registry in children less than 18 years of age over the three-year period 2013-2015. The observed in-hospital mortality rate was calculated as the number of deaths occurring prior to hospital discharge divided by the total number of RACHS-classified surgical cases. The Risk Adjustment for Congenital Heart Surgery (RACHS) model is used to evaluate differences in mortality among groups of patients undergoing congenital heart surgery.(9) The outcome measure used is a Standardized Mortality Ratio (SMR) for each country, defined as the observed in-hospital mortality rate divided by the mortality rate that would be expected given the country's patient case mix. The expected in-hospital mortality rate was calculated using the previously validated RACHS risk adjustment method (7,10). The model included surgical risk category (categories 1 through 6, where 1 represents surgical procedures with the lowest risk for in-hospital mortality and 6 the highest), age group (≤30 days, 31 days to <1 year, 1 to 17 years), prematurity (<37 weeks), presence of a major non-cardiac structural anomaly, and multiple congenital heart procedures during the admission. The RACHS method was developed using U. S. outcomes data, but since the inception of the IQIC in 2008 has been successfully applied to LMICs.(7) An SMR greater than 1.0 suggests higher than expected mortality based on patient case mix, while an SMR less than 1.0 represents lower than expected mortality. Two-way scatter plots were used to examine the relationships between SMR and each development indicator; the strength of these relationships was quantified using Spearman correlation coefficients. We also used linear regression analysis to compare unadjusted regression coefficients relating each development indicator to SMR to coefficients adjusted for GDP per capita. We adjusted for GDP per capita because it is a common broad representation of economic status that has been linked to health. (11) We did not adjust for any other indicators. The natural log of SMR was used as the outcome for these models since SMR itself was not normally distributed. An ancillary analysis without Peru was also completed after it appeared to be an outlier in figures generated.

Furthermore, we completed a stratified analysis between low complexity cases (RACHS categories 1 and 2) and high complexity cases (RACHS categories 3-6) and SMR. To do this, for each country we calculated a SMR for RACHS 1-2 and a SMR for RACHS 3-6 and compared correlations between the low RACHS SMR and each development indicator with the high RACHS SMR and each development indicator.

Ethical Considerations

The institutional review board at Boston Children's Hospital gave permission for the IQIC data registry to be used for this research. Study data were collected and managed using REDCap electronic data capture tools hosted at Boston Children's Hospital.(12) REDCap (Research Electronic Data Capture) is a secure, web-based application designed to support data capture for research studies, providing 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources. The senior author had complete access to the registry data, and the authors are responsible for the study design, analysis and interpretation of data, and the decision to submit the paper for publication.

Patient and Public Involvement Statement

Patients and public were not involved in the development of this study.

RESULTS

Among 31 programs in 17 countries, the IQIC database included 24,917 congenital heart surgeries performed in children <18 years of age. The number of programs per country ranged from one to six. The overall in-hospital mortality rate was 5.0 % and country-level mortality rate ranged from 1.7% to 25.0%. The number of congenital heart surgery cases by country and the proportion of cases in each country compared to the total cases is shown in online supplementary Figure 1. Centers in China represent the largest percentage of cases, with 33.4% of total cases. The age and RACHS category distribution of cases by country is shown in online supplementary Figures 2 and 3. In most countries, the majority of patients undergoing surgery in the centers are 1 to 17 years old. There is variation in the proportion of RACHS categories, but all countries have at least 50% of cases in low complexity RACHS category 1 or 2. The full RACHS model used to calculate country SMRs is shown in online supplementary Table 1.

Country SMRs range from 0.40 to 4.85. Unadjusted mortality rates and Standardized Mortality Rates by country are shown in online supplemental Figure 4. Correlation coefficients between each development index and SMR and regression coefficients, both unadjusted and adjusted by GDP per capita, by country are shown in Table 1.

Table 1. Correlation and Regression Coefficients for Development Indicators with SMR

Indicator	Number of Countries	Correlation Coefficient	Unadjusted Regression Coefficient	Regression Coefficient adjusted for GDP per capita
GDP per capita	17	r=-0.34	-0.047	--
Health Expenditure per capita	17	r= -0.23	-0.035	0.092
Undernourishment	14[#]	r=0.39	0.40	0.78

Under-5 Mortality Rate	17	r=.60*	0.13*	0.16
Poverty Headcount Ratio at $5.50 a day	11#	r=0.26	0.12	0.19
Life Expectancy	17	r= -0.35	-0.50	-0.49
Domestic General Government Health Expenditure	17	r=-0.22	-0.0937	-0.0297
Specialist Surgical Workforce	11#	r=-0.56	-0.0737	-0.0515

World Bank index not available for some countries

*significant at p<0.05

P-values: GDP correlation p=0.18, unadjusted regression coefficient p=.29, Health Expenditure correlation p=0.37, unadjusted regression p=0.55, adjusted regression p=0.47, Undernourishment correlation p=0.17, unadjusted regression p=0.14, adjusted regression p=0.20, Under-5 Mortality Rate correlation p=0.01, unadjusted regression p=0.04, adjusted regression p=0.08, Poverty Headcount ratio correlation p=0.43, unadjusted regression p=0.46, adjusted regression p=0.33, Life Expectancy correlation p=0.16, unadjusted regression p=0.11, adjusted regression p=0.24, Domestic General Government Health Expenditure correlation p=0.40, unadjusted regression p= 0.41 adjusted regression p=0.84 . Specialist Surgical Workforce p=0.07, unadjusted regression p=0.26, adjusted regression p=0.45.

The relationships between SMR by country and GDP per capita, health expenditure per capita, poverty headcount ratio, and specialist surgical workforce are shown in Figures 1-4 respectively. Notable in Figure 1 is a general trend towards lower SMR with increased GDP per capita, and Peru as a potential outlier in the data. Figure 2, health expenditure per capita, is similar to Figure 1; however, Serbia and Costa Rica seem to be at higher levels of health expenditure per capita than GDP per capita when compared with the other countries. The relationships between SMR and other development indicators (undernourishment, under-5 mortality rate, life expectancy, and domestic general government health expenditure) are shown in online supplemental figures 5-8.

Stratified analysis comparing congenital heart surgery mortality ratios from low complexity cases (low RACHS categories, 1-2) and high complexity cases (high RACHS categories, 3-6) are shown in Table 2. The low RACHS categories analysis includes a total of 16,870 cases, and the high RACHS categories analysis includes a total of 7,997 cases. The low RACHS score SMR correlation largely mirror the overall SMR Spearman correlation, while the high RACHS score SMR has a lower correlation than the low RACHS score SMR with each development indicator except poverty headcount ratio and specialist surgical workforce.

Table 2. Development Indicators and Standardized Mortality Ratio Correlations Stratified by RACHS Category

Correlations with SMR

	All Cases	RACHS 1-2	RACHS 3-6
	Spearman r (p value)	Spearman r (p value)	Spearman r (p value)
GDP per capita (US $)	-0.34 (0.18)	-0.38 (0.14)	-0.07 (0.81)
GNI per capita (US $)	-0.38 (0.13)	-0.40 (0.11)	-0.16 (0.58)
Health expenditure per capita (US $)	-0.23 (0.37)	-0.23 (0.38)	0.13 (0.66)
Undernourishment (%)	0.39 (0.17)	0.40 (0.15)	0.11 (0.74)
Life expectancy at birth (years)	-0.35 (0.16)	-0.38 (0.14)	-0.07 (0.82)
Under 5 mortality rate (per 1000)	0.60 (0.01)	0.54 (0.02)	0.43 (0.12)

Poverty headcount (%) V1	0.50 (0.12)	0.48 (0.13)	0.41 (0.24)
Poverty headcount ratio (%) V2	0.26 (0.43)	0.15 (0.65)	0.38 (0.28)
Domestic general government health expenditure (% of GDP)	-0.22 (0.40)	-0.19 (0.47)	-0.01 (0.97)
Specialist surgical workforce (per 100,000)	-0.56 (0.07)	-0.50 (0.12)	-0.70 (0.04)
Number of Countries	17	17	14[#]

3 countries (Afghanistan, Peru, and Uganda) were not used in the RACHS 3-6 correlations due to small number of cases.

DISCUSSION

We found the expected positive correlation between under-5 mortality and SMR, which was statistically significant. We also found a borderline statistically significant negative correlation between specialist surgical workforce and CHD mortality: as specialist surgical workforce increases, congenital heart surgery mortality decreases, suggesting that adequate workforce is integral to quality congenital heart surgical capacity. Other correlations found that are not statistically significant include negative associations of GDP per capita, Health Expenditure per capita, Domestic Government Health Expenditure, and Life Expectancy with congenital heart surgery SMR: as these indicators increase, SMR decreases. We found positive associations of Poverty Headcount and Undernourishment with SMR: as poverty headcount or undernourishment increases, SMR increases. The association of GDP per capita and SMR suggests that overall development of a country may be an important component of surgical mortality.. While most associations do not reach statistical significance, they display links between development and surgery outcomes.

Although it is difficult to be conclusive, an interesting finding of this study is that there is still substantial variation between countries in SMRs even at similar development levels. For example, Afghanistan and Pakistan have much higher SMRs than India, although they are at similar GDP per capita levels. Nations with high levels of conflict such as Afghanistan may have stressed health systems as a whole,(13,14) which would impact congenital heart surgery services. Also, while Afghanistan, Pakistan, and India have similar GDP per capita levels, they have very different overall GDP levels, which may affect access to surgery for patients and impact congenital heart surgery SMR variation. Similarly, Peru, Serbia and China are at similar GDP per capita levels yet vary widely in mortality, with China at the lowest SMR. China has a well-organized and efficient health system that likely contributes to better outcomes. (15) Although Peru appears to be an outlier, it is not influential – meaning it does not have a substantial impact on the correlation coefficients – with the exception of the association between SMR and undernourishment and SMR and specialist surgical workforce (both associations become stronger without Peru).

When adjusting for GDP per capita, regression coefficients decrease in magnitude for some indicators—poverty, life expectancy, and under-5 mortality. Therefore, the data indicates that GDP per capita is a driver of the association between these specific indicators and congenital heart surgery mortality. However, the regression coefficient for undernourishment increases when controlling for GDP per capita, suggesting that population-wide undernourishment affects mortality after congenital heart surgery outside the effect of GDP. This may be reflective of the higher likelihood of children undergoing CHD surgery while malnourished in countries where malnourishment is more prevalent, and potentially higher risk of death in such circumstances.(16–18) This also suggests that factors that correlate with general pediatric health, such as undernourishment, impact surgical mortality, offering a target for further improvement of health and surgical outcomes.

Comparative analysis of low RACHS SMRs with development indicators and high RACHS SMRs with development indicators display that low RACHS SMRs correlations are similar to the overall SMR correlations and thus may contribute more to the overall correlation than high RACHS cases. Notably, high RACHS cases SMRs have a stronger correlation with poverty headcount ratio and with specialist surgery workforce than low RACHS cases SMRs, suggesting that low poverty and a present specialist surgery workforce are more important for positive outcomes in high complexity cases. This potentially suggests that increasing training for a specialist surgery workforce is necessary in LMICs.

As poverty and infectious diseases decrease, non-communicable diseases such as congenital heart disease in LMICs account for a greater percentage of childhood deaths. Congenital defects represented 8.7% of global under-5 mortality in 2016.(19) Many stakeholders believe congenital heart surgery should be considered an "Essential Paediatric Surgical Procedure" due to the economic value of these surgeries in a community.(20) A substantial fraction (58%) of congenital heart defect burden (avertable disability years) could be alleviated with scaled up congenital heart surgery programs in LMICs.(21) Quality in high-specialty care is of paramount importance. A recent study estimated that cardiovascular diseases are the highest contributor to amenable mortality due to poor-quality care.(22) Quality tertiary care requires trained personnel and equipment and infection control.(23) Recommended strategies to improve surgical care include training and basic infrastructure and equipment,(24) which necessitates investment in healthcare systems.

Our method has several limitations. First, the sample size is only 17 countries and 31 sites (for some indicators, fewer), which limits statistical power, and may be why most associations, except under-5 mortality were not significant. Second, data are analyzed at the country-level but using only facility-based clinical outcomes data from selected centers that participate in IQIC, which are not representative of countrywide outcomes for CHD surgery and vary in the proportion of country cases that they represent, making firm conclusions difficult, but suggesting that country-specific analyses about patients at different poverty levels may be warranted. IQIC sites are often tertiary level hospitals with large referral bases and academic intent towards quality improvement; IQIC members are willing and able to collect data and participate in quality improvement activities. That may mean that sometimes hospital settings represented in this study do not always mirror the overall development level of their countries. However, most high-income countries tend to regionalize CHD surgical centers in several large urban areas, to avoid the creation of many small-volume centers. (25) Therefore, even though the overall quality of care of the health systems may be low, the centers themselves may have quite good CHD surgical outcomes. Country-level SMRs may also not accurately reflect regional variability in level of development or resources available for congenital heart surgery, especially in large countries such as China and India. For example, the sites in India are mostly from states in Southern India, which tend to have higher development levels than the Northern part of the country. There may also be variations in case mix of participating institutions due to gaps in the existing diagnosis and referral networks, healthcare financing, and social and cultural factors that may result in not treating the patients with the most severe disease, which may not be completely accounted for in risk-adjustment models. Regional differences in healthcare financing for CHD surgery and in-hospital care, including public and private insurance, is a particularly important factor not examined in this study, since care becomes unaffordable to most families if is not included in universal health insurance coverage package. On the other hand, institutions too could potentially suffer financial losses if reimbursement for CHD surgery is not at the appropriate level.

In conclusion, our results show correlations between various development indicators and congenital heart surgery mortality. Nonetheless, there is variation among countries of similar GDP per capita levels, and lower risk-adjusted mortality in some countries with lower development offers hope and encourages investment in congenital heart surgery programs. Our study can also be helpful for health policy decision-making. The recent global discourses on access to surgical services as well as on reduction of childhood mortality have been missing a macro analysis of the investments needed to develop surgical services in LMICs for high complexity diseases such as congenital heart disease. Our findings show that a link could be made between various development indicators and congenital heart surgery mortality, calling for more investigation at a regional level for quality and access improvement strategies and encouraging investment in congenital heart surgery programs and sub-specialty training, especially for all countries committed to achieving the SDG3 target of ending preventable deaths of newborns and children under 5 years of age. As governments consider development of different paediatric services, this study can give them guidance on areas they could invest in. The trend between economic factors and outcomes identified in this study can also be investigated by single centers using socioeconomic data of individual patients to see if a similar link arises, potentially helping to identify higher risk populations.

Further study is required to truly understand why countries with similar development levels vary in congenital heart surgery mortality. Future studies ought to investigate why such variations exist, and examine the role of governments, NGOs or other stakeholders, training and retention of skilled professionals and other personnel, and infection control practices in particular countries. Future studies should attempt to capture outcomes of children who did not have access to operations, as outcomes for these children are also likely associated with development and investment. Studies should also attempt to collect longer-term outcomes to represent the broader socioeconomic factors that may affect survival from CHD surgery (26) and that could be collected with a more population health focused database. This inquiry can help establish effective strategies for successful congenital heart surgical programs in LMICs.

Abbreviations

CHD Congenital Heart Disease

GDP Gross Domestic Product

IQIC International Quality Improvement Collaborative for Congenital Heart Disease

LMICs Low- and Middle-Income Countries

NGO Non-Governmental Organization

SDGs Sustainable Development Goals

SMR Standardized Mortality Ratio

RACHS Risk Adjustment for Congenital Heart Surgery

Contributors

SR and KJ had the primary responsibility to design the study and write the manuscript. BZ, KMC, JTC, KD, KG, PAH, RKK, JKK, WN, NS, and KJ coordinated the global study data concept and collection. BZ revised multiple manuscript drafts, and DF interpreted data. KG conducted statistical analyses.

Declaration of Interests
We declare no competing interests.

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Data Sharing Statement
Extra data is available by emailing the corresponding author.

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Figure Legends

Figure 1. This graph shows negative correlation of GDP per capita on the x-axis and SMR on the y-axis by country.

Figure 2. This graph shows negative correlation of Health Expenditure per capita on the x-axis and SMR on the y-axis by country.

Figure 3. This graph shows positive correlation of Poverty Ratio at $5.50 a day on the x-axis and SMR on the y-axis by country.

Figure 4. This graph shows a negative correlation of Surgical Specialist Workforce on the x-axis and SMR on the y-axis by country.

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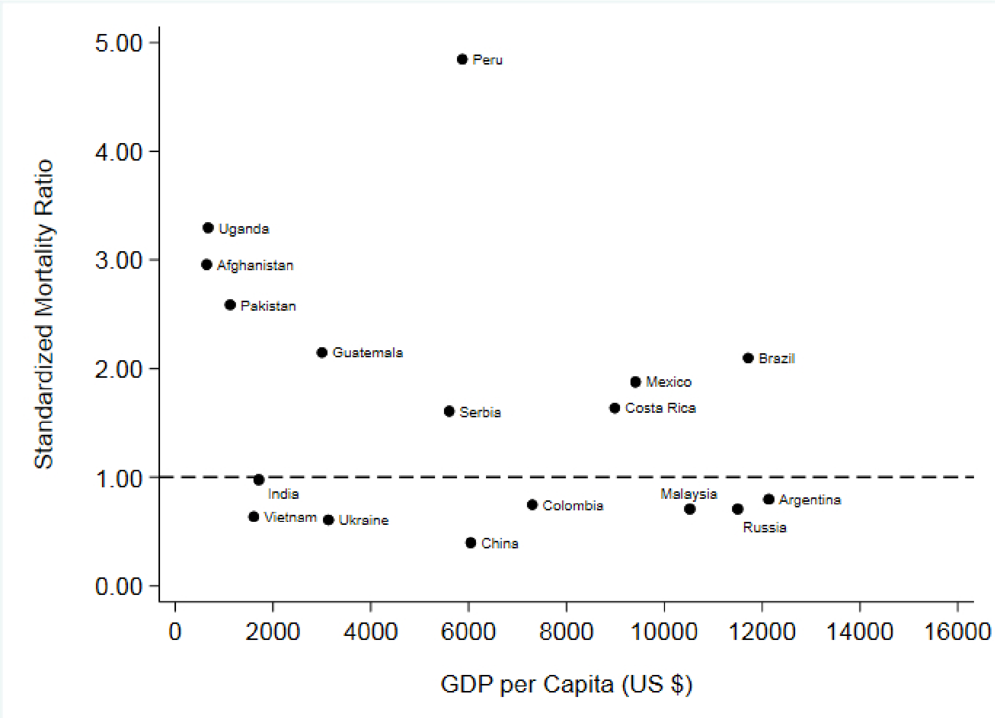
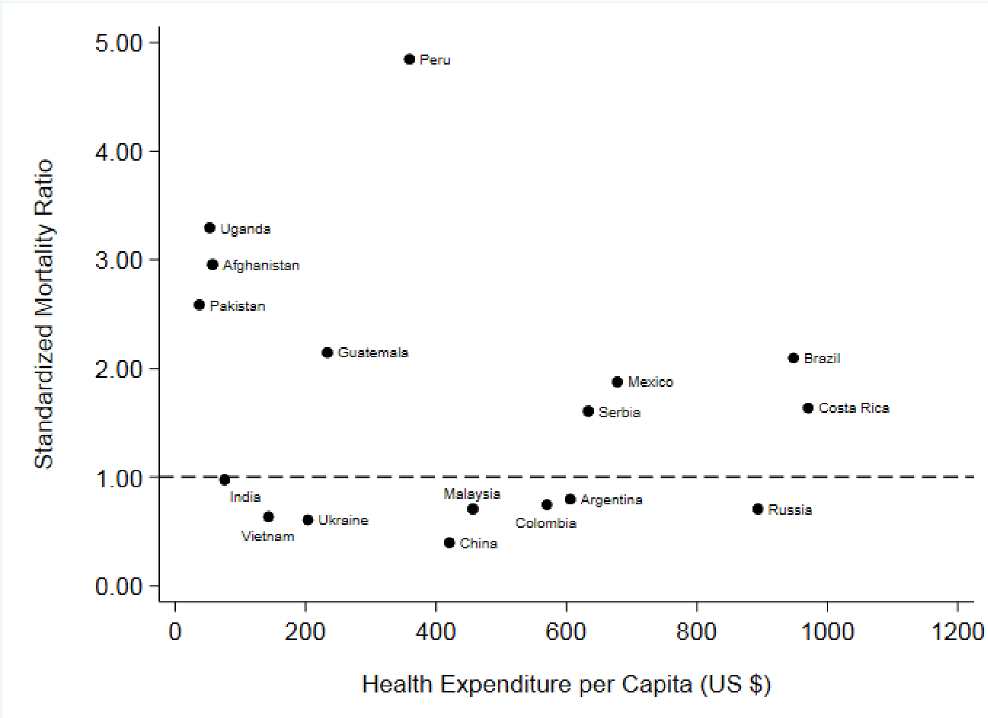
Online Supplemental Figure 7. This graph shows negative correlation of Life Expectancy on the x-axis and SMR on the y-axis by country.

Online Supplemental Figure 8. This graph shows negative correlation of Domestic General Government Health Expenditure (% of GDP) on the x-axis and SMR on the y-axis by country.



This graph shows negative correlation of GDP per capita on the x-axis and SMR on the y-axis by country.



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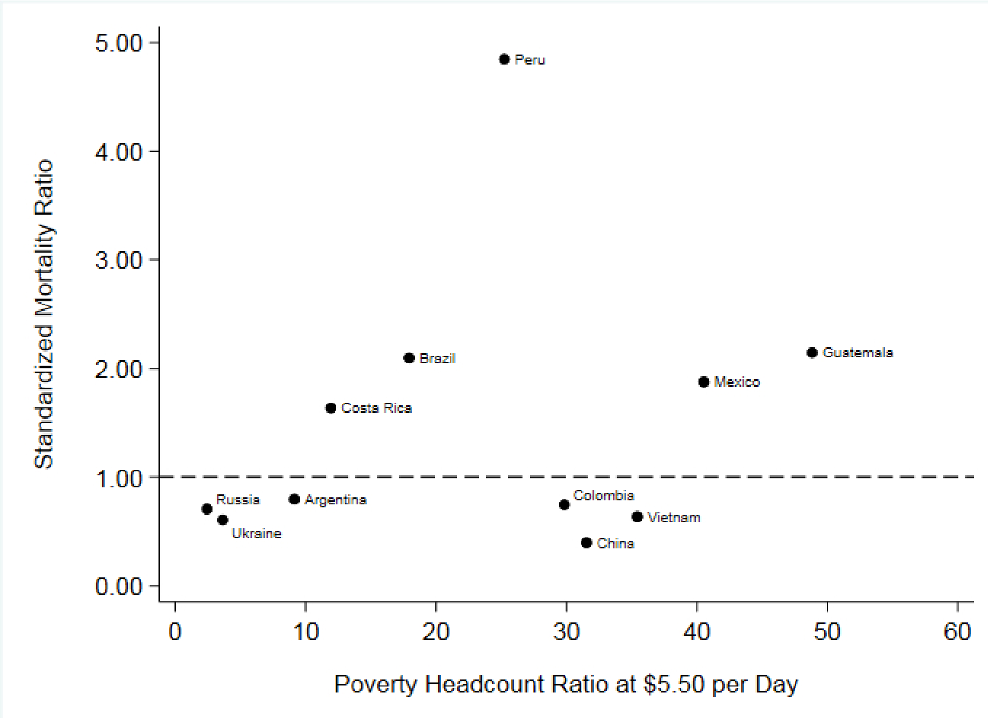

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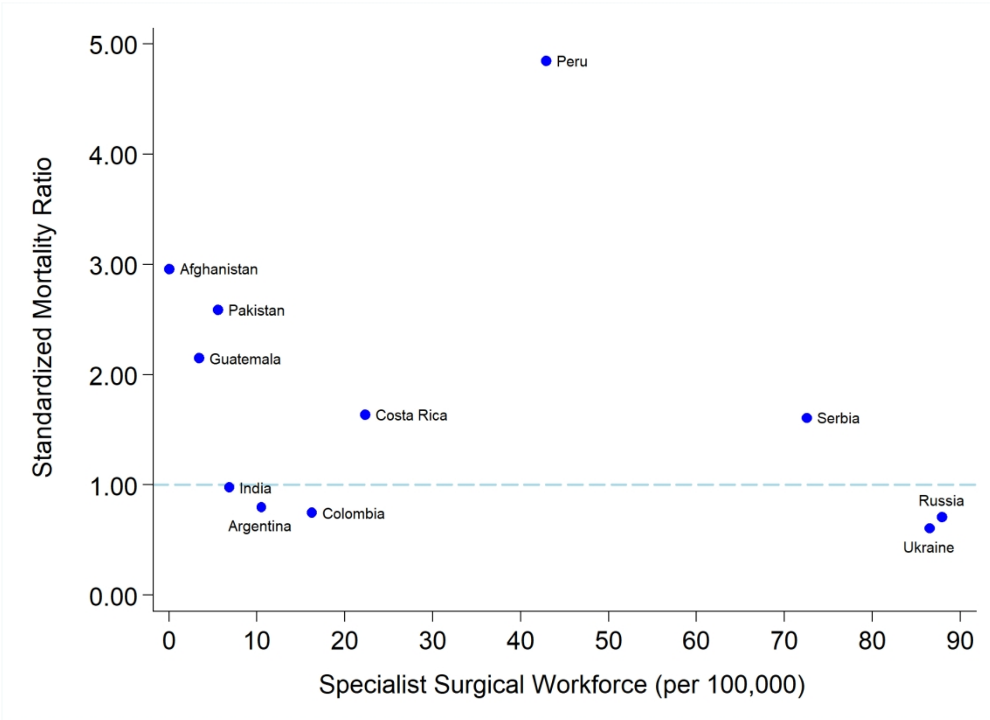

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Online Supplementary Figures and Tables

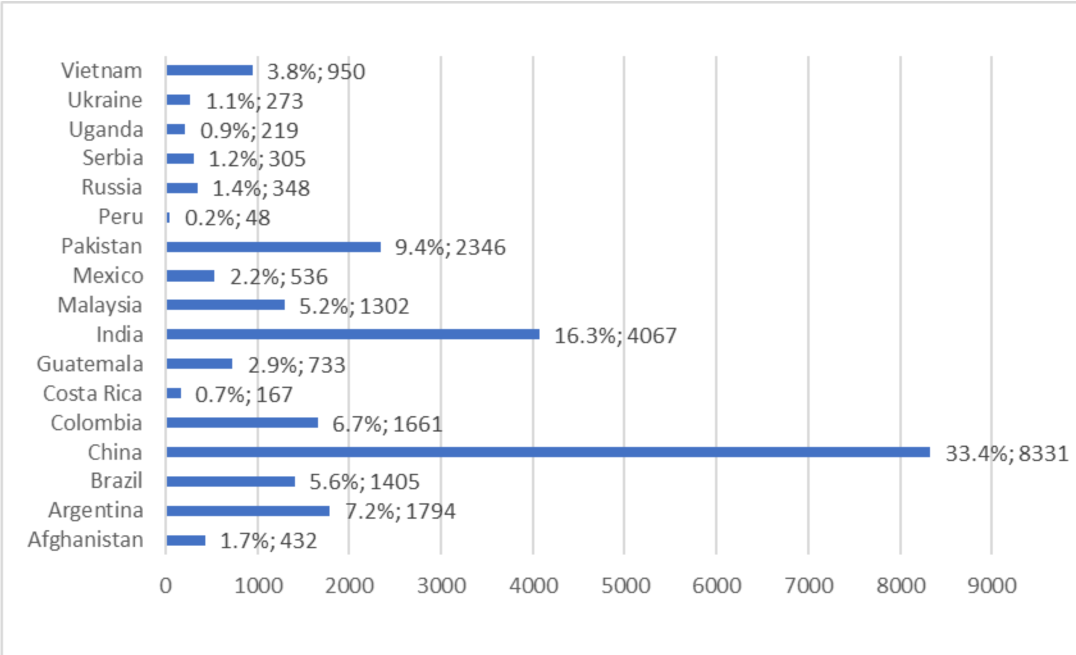
Online Supplementary Table 1. Full RACHS Model

Cases Eligible for RACHS and Assigned to a Risk Category

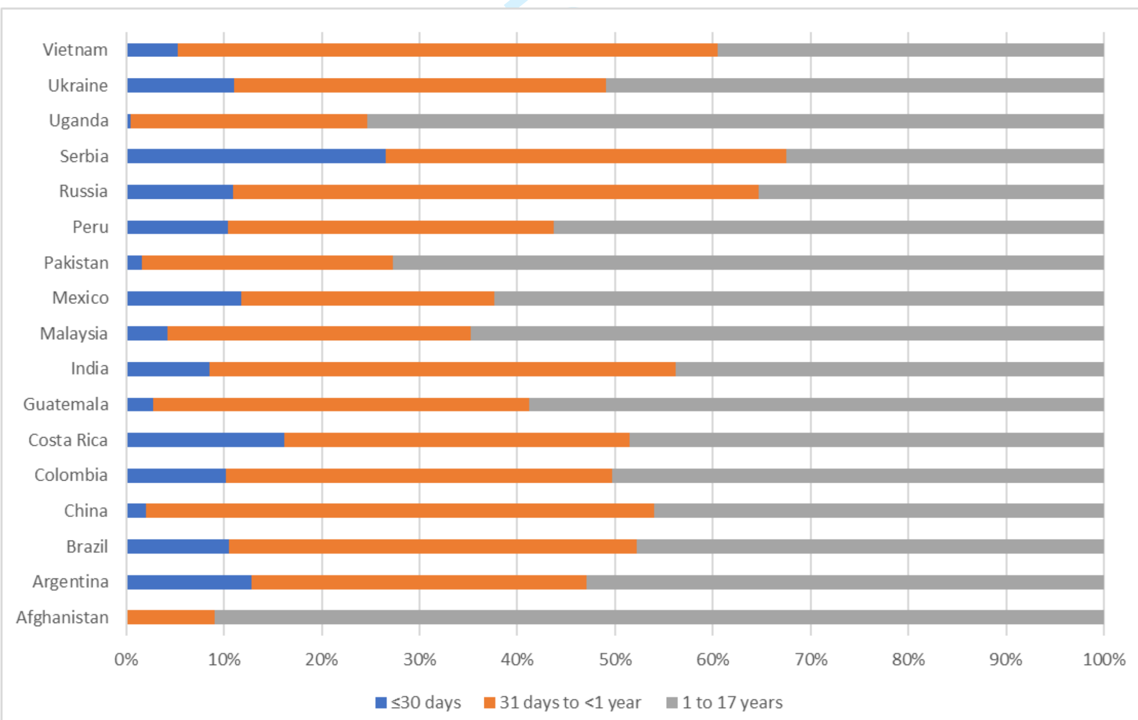
	Odds Ratio	95% Confidence Interval	P Value
RACHS Risk Category			
1	1.0	-	-
2	2.3	(1.7, 3.2)	<0.001
3	6.7	(5.0, 9.1)	<0.001
4	9.5	(6.8, 13.1)	<0.001
5 + 6	43.6	(28.2, 67.6)	<0.001
Age at Surgery			
≤30 days	3.2	(2.6, 3.9)	<0.001
31 days to <1 year	1.6	(1.4, 1.8)	<0.001
1 to 17 years	1.0	-	-
Prematurity	1.4	(1.1, 1.7)	0.007
Major Non-Cardiac Structural Anomaly	2.0	(1.5, 2.6)	<0.001
Multiple Cardiac Procedures	1.0	(0.9, 1.2)	0.80

C statistic for this model is 0.75.

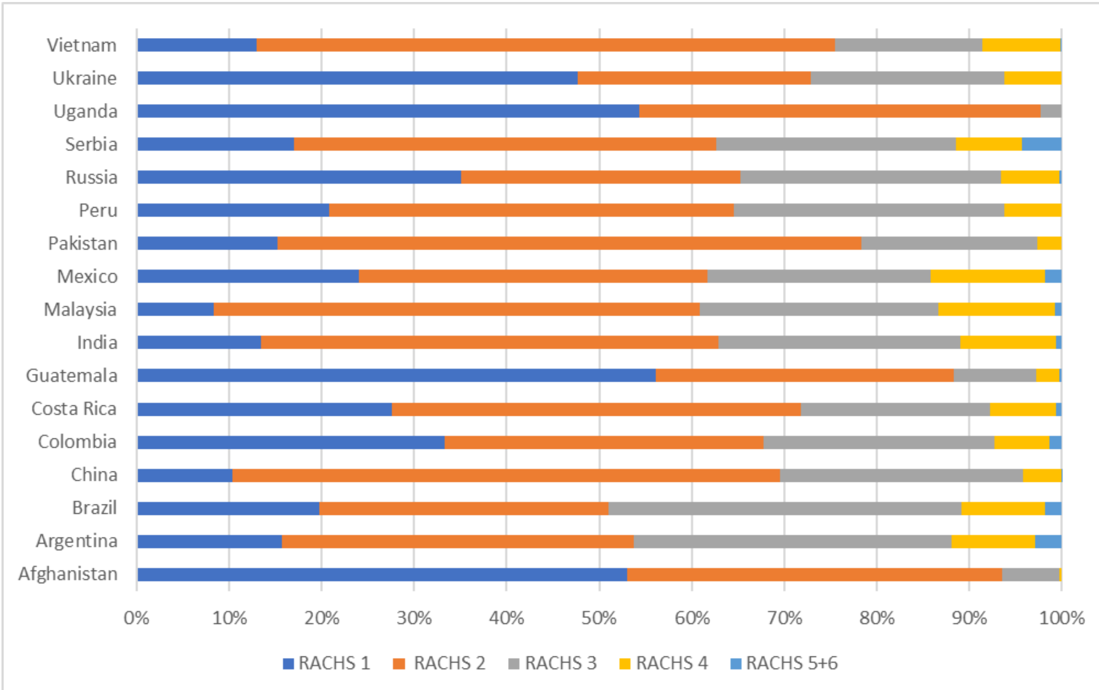
Online Supplementary Figure 1. Congenital Heart Surgery Cases by Country



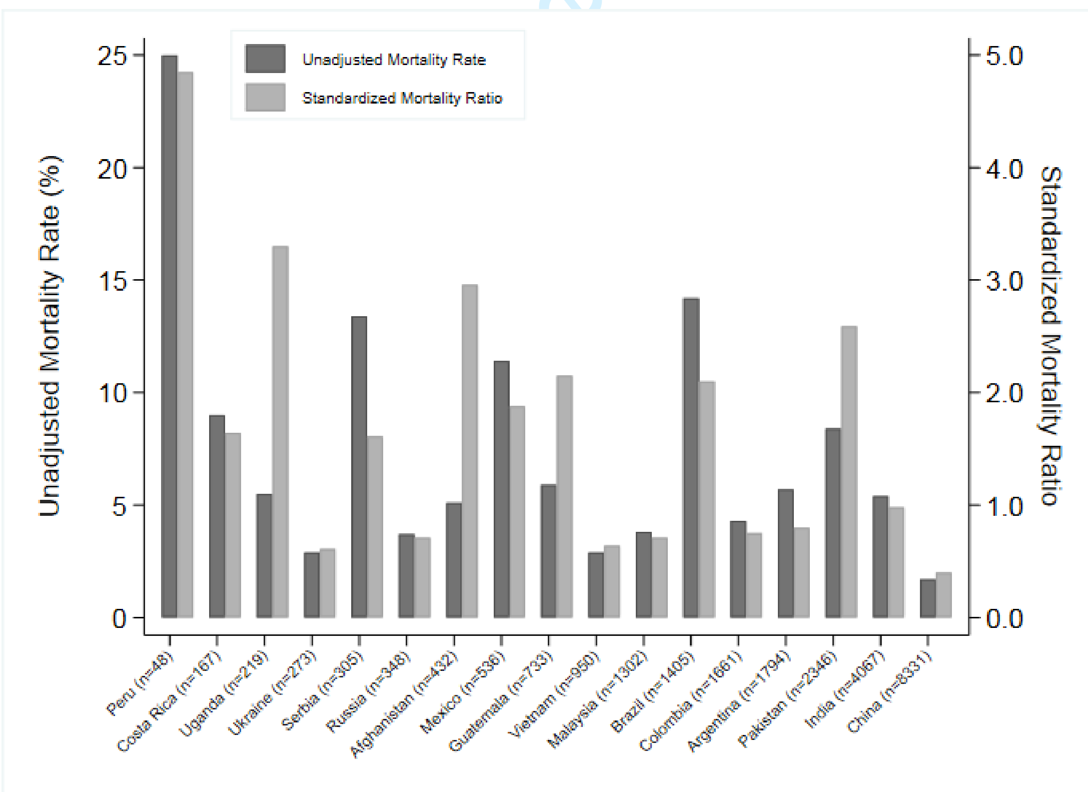
Online Supplemental Figure 2. Age Distribution of Cases by Country



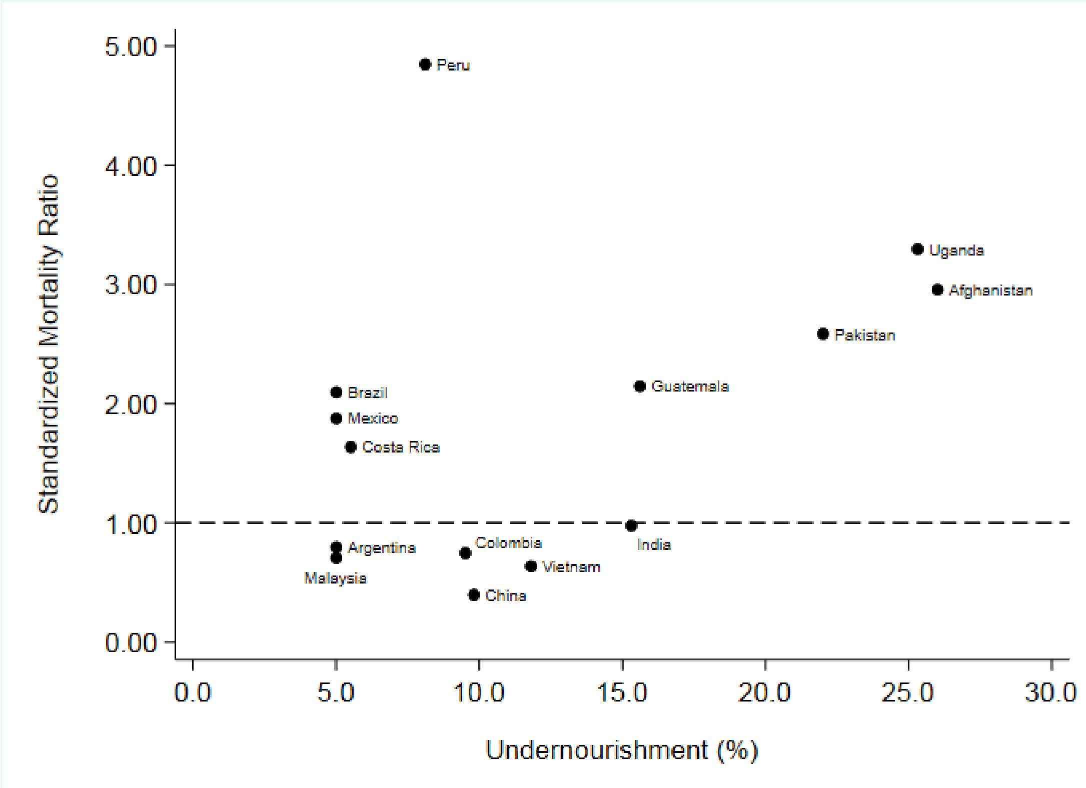
Online Supplemental Figure 3. RACHS Category Distribution by Country



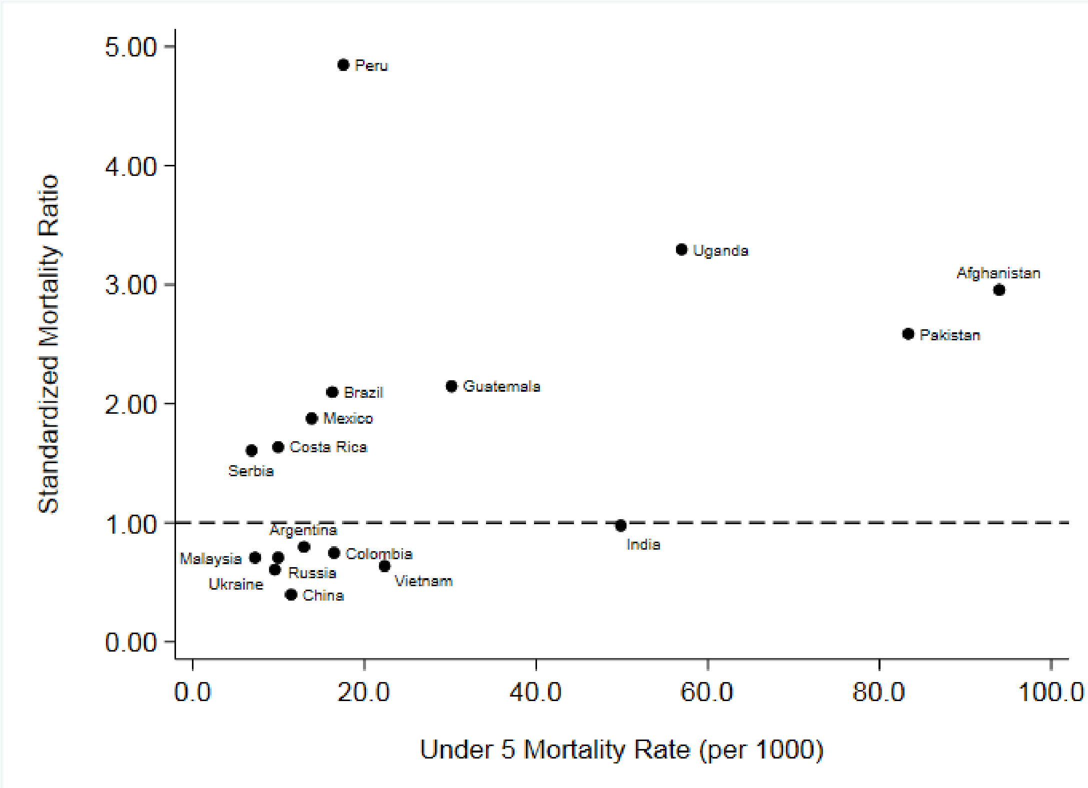
Online Supplemental Figure 4. Congenital Heart Surgery Unadjusted Mortality Rate and Standardized Mortality Ratio by Country



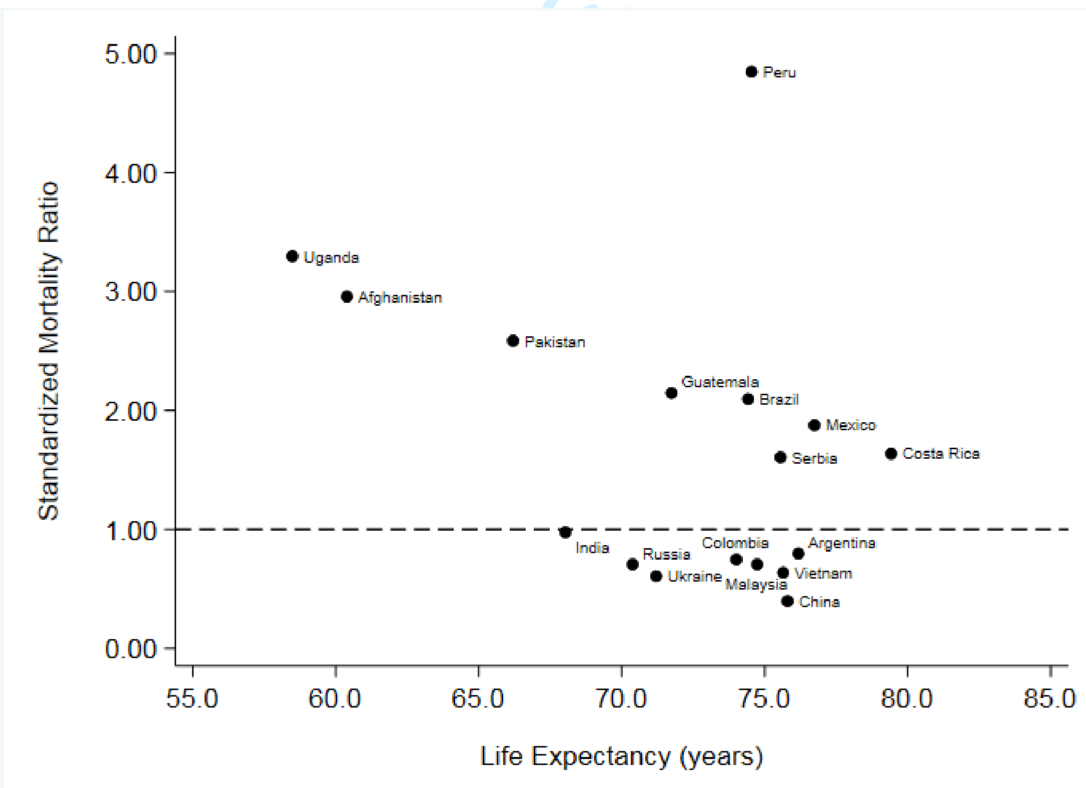
Online Supplemental Figure 5. Undernourishment and SMR



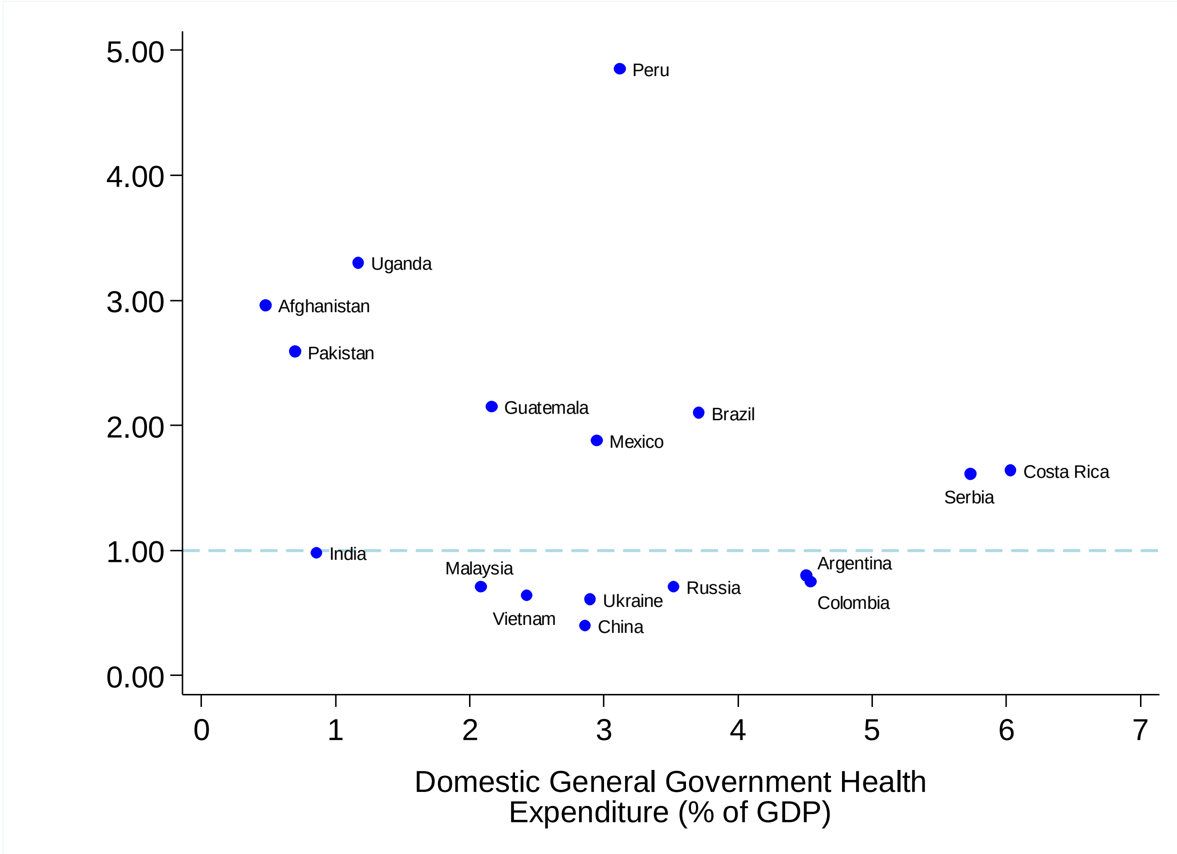
Online Supplemental Figure 6. Under-5 Mortality Rate and SMR



Online Supplemental Figure 7. Life Expectancy and SMR



Online Supplemental Figure 8. Domestic General Government Health Expenditure and SMR



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STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3-4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6-7
		(*b*) Describe any methods used to examine subgroups and interactions	6-7
		(*c*) Explain how missing data were addressed	Table 1
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	n/a
		(*e*) Describe any sensitivity analyses	n/a
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	n/a
		(b) Give reasons for non-participation at each stage	5
		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	5
		(b) Indicate number of participants with missing data for each variable of interest	Table 1
Outcome data	15*	Report numbers of outcome events or summary measures	8
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8
		(*b*) Report category boundaries when continuous variables were categorized	8
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9
Discussion			
Key results	18	Summarise key results with reference to study objectives	9-10
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13
Generalisability	21	Discuss the generalisability (external validity) of the study results	12-13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.