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Factors associated with declining under-five mortality rates from 2000 to 2011: An ecological analysis of 46 African countries

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ABSTRACT

Background: Inadequate overall progress is being made towards the 4th Millennium Development Goal of reducing mortality rates in children under five years of age by two-thirds between 1990 and 2015. However, child survival progress has been variable across African countries. Understanding country-level factors that have influenced rapid reductions in child mortality could facilitate improvement of child survival in the post-2015 era.

Methods and Findings: We examined 70 potential health, economic, and social predictors of under-five mortality for the 46 nations within the World Health Organization African Region from 2000 to 2011. We assessed completeness of indicator data over time, the annual rate of change of such indicators, and the impact of indicators on the annual rate of reduction (ARR) of under-five mortality rates by country. The median (interquartile range) ARR was 2.4% (1.6-4.6). Seven indicators demonstrated a strong and significant association with national ARRs, adjusted for potential confounders in robust regression models. Larger ARRs were associated with more rapidly increasing coverage of seeking treatment for acute respiratory infection (β=0.27 [i.e., a 1% increase in the indicator rate of change was associated with a 0.27% increase in ARR]; p=0.02), increasing gross domestic product (GDP) per capita (β=0.23; p=0.09), increasing health expenditure relative to GDP (β= 0.22; p=0.07), decreasing out-of-pocket health expenses (β= -0.26; p=0.04), decreasing public spending on education relative to GDP (β= -0.20; p=0.06), decreasing prevalence of underweight in children (β= -0.30; p=0.07), and decreasing maternal mortality ratio (β= -0.86; p<0.01).

Conclusions: Key predictive indicators generally correlate with improved health care access and/or health financing. The strongest predictor of favorable ARR was more rapid reduction in maternal mortality ratio, underscoring the essential role of maternal health on child health. Surveillance of indicators could help monitor which nations will need additional support in reducing under-five mortality.

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STRENGTHS AND LIMITATIONS OF THIS STUDY

- This study represents the most comprehensive analysis to date of health indicators and other determinants of health as predictors of declining under-five mortality in Africa.
- Study findings highlight the role of financing, economy, and the broader health system in more rapidly reducing an already declining, albeit slowly, under-five mortality rate above and beyond the contribution of individual interventions.
- This study highlights the ongoing challenge of obtaining indicator reporting from 100% of countries, including interventions monitored by Countdown to 2015.
- The ecological, cross-sectional study design the time periods for change in indicator coverage did not always fully overlap with time periods for change in under-five mortality, and temporality and causality inferences may be limited.
- The small sample size (at most n=46 countries, but often smaller due to missing indicator coverage data) limits the validity of some associations and prevents adjustment for too many covariates.

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INTRODUCTION

Under-five mortality (U5M) rates have declined worldwide from an estimated 90 deaths per 1,000 live births in 1990 to 48 deaths per 1,000 in 2012, representing an average annual rate of reduction (ARR) of 2.9% [1]. Higher income regions had an estimated U5M rate of 6 deaths per 1,000 live births in 2012 (3.8% ARR); they account for only 1.4% of all under-five deaths. In contrast, the World Health Organization (WHO) African Region (including 46 countries in 2012; Figure 1, Table 1) experienced 95 under-five deaths per 1,000 live births in 2012 and a 1990-2012 ARR of 2.7%[1]. Thus, African children are nearly 16 times more likely to die under age five than children from high income nations, though progress in Africa is being made.

Table 1. Under-five mortality rates and annual rate of reduction (ARR) for the 46 countries in the WHO African Region.

	Under-five mortality rate (per 1,000) in the given year[a]				ARR (%) 1990 to 2011	ARR (%) 1990 to 2000	ARR (%) 2000 to 2011	ARR (%) in 2000-2015 needed to meet MDG
Country	1990	2000	2011	MDG for 2015				
Algeria[b]	65.6	45.7	29.8	21.9	3.7	3.6	3.8	4.8
Angola	243.2	199.3	157.6	81.1	2.0	2.0	2.1	5.8
Benin	177.3	139.7	106.0	59.1	2.4	2.4	2.5	5.6
Botswana[b]	52.8	81.1	25.9	17.6	3.3	-4.4	9.9	9.7
Burkina Faso	208.4	181.5	146.4	69.5	1.7	1.4	1.9	6.2
Burundi	182.6	164.6	139.1	60.9	1.3	1.0	1.5	6.4
Cameroon	145.2	139.5	127.2	48.4	0.6	0.4	0.8	6.8
Cape Verde	58.0	38.9	21.3	19.3	4.7	3.9	5.3	4.6
Central African Republic	169.1	172.0	163.5	56.4	0.2	-0.2	0.5	7.2
Chad	208.3	188.5	169.0	69.4	1.0	1.0	1.0	6.4
Comoros	121.7	99.6	79.3	40.6	2.0	2.0	2.1	5.8
Congo	118.8	108.8	98.8	39.6	0.9	0.9	0.9	6.5
Côte d'Ivoire	151.4	138.6	114.9	50.5	1.3	0.9	1.7	6.5
Dem. Rep. of the Congo	181.4	181.4	167.7	60.5	0.4	0.0	0.7	7.1
Equatorial Guinea	189.6	152.2	118.1	63.2	2.2	2.2	2.3	5.7
Eritrea	137.7	98.2	67.8	45.9	3.3	3.3	3.3	4.9
Ethiopia	198.3	138.6	77.0	66.1	4.4	3.5	5.2	4.8
Gabon	94.4	82.4	65.6	31.5	1.7	1.4	2.1	6.2
Gambia	164.6	130.3	100.6	54.9	2.3	2.3	2.3	5.6
Ghana	120.9	98.7	77.6	40.3	2.1	2.0	2.2	5.8
Guinea	228.2	174.5	125.8	76.1	2.8	2.6	2.9	5.4
Guinea-Bissau	210.4	185.8	160.6	70.1	1.3	1.2	1.3	6.3
Kenya	97.8	113.1	72.8	32.6	1.4	-1.5	3.9	8.0
Lesotho	87.5	117.3	86.0	29.2	0.1	-3.0	2.8	8.9
Liberia	241.2	163.8	78.3	80.4	5.2	3.8	6.5	4.6
Madagascar	161.2	104.1	61.6	53.7	4.5	4.3	4.7	4.3
Malawi	227.0	164.1	82.6	75.7	4.7	3.2	6.0	5.0
Mali	257.3	214.4	175.6	85.8	1.8	1.8	1.8	5.9
Mauritania	124.7	117.9	112.1	41.6	0.5	0.6	0.5	6.7
Mauritius[b]	23.9	18.6	15.1	8.0	2.2	2.5	1.9	5.5

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Country	Under-five mortality rate (per 1,000) in the given year[a]				ARR (%) 1990 to 2011	ARR (%) 1990 to 2000	ARR (%) 2000 to 2011	ARR (%) in 2000-2015 needed to meet MDG
	1990	2000	2011	MDG for 2015				
Mozambique	225.7	172.1	103.1	75.2	3.7	2.7	4.6	5.4
Namibia	72.8	73.5	41.5	24.3	2.6	-0.1	5.1	7.1
Niger	313.7	215.6	124.5	104.6	4.3	3.7	4.9	4.7
Nigeria	213.6	187.9	124.1	71.2	2.6	1.3	3.7	6.3
Rwanda	156.3	183.0	54.1	52.1	4.9	-1.6	10.5	8.0
São Tome and Principe	96.0	92.5	88.8	32.0	0.4	0.4	0.4	6.8
Senegal	135.9	130.4	64.8	45.3	3.5	0.4	6.2	6.8
Seychelles[b]	16.6	13.8	13.8	5.5	0.9	1.8	0.0	5.9
Sierra Leone	266.7	240.6	185.3	88.9	1.7	1.0	2.3	6.4
South Africa	62.3	74.1	46.7	20.8	1.4	-1.7	4.1	8.1
Swaziland	83.3	114.2	103.6	27.8	-1.0	-3.2	0.9	9.0
Togo	147.0	127.8	110.1	49.0	1.4	1.4	1.3	6.2
Uganda	178.0	140.5	89.9	59.3	3.2	2.3	4.0	5.6
United Rep. of Tanzania	157.9	126.4	67.6	52.6	4.0	2.2	5.5	5.7
Zambia	192.8	153.8	82.9	64.3	3.9	2.2	5.5	5.6
Zimbabwe	79.2	105.8	67.1	26.4	0.8	-2.9	4.1	8.8

[a] U5M rate data obtained from www.childmortality.org, accessed January 2013
[b] Countries with U5M rates <40 per 1,000 in 2011 are considered to be on track despite having 1990-2011 ARRs of less than 4%.
Abbreviations: ARR, annual rate of reduction; MDG, Millennium Development Goal

In 2000, the 4th Millennium Development Goal (MDG4)[2] proposed the reduction of the U5M rate by two-thirds between 1990 and 2015, requiring a global average ARR of 4.4% to reach this goal. Africa has nearly tripled its U5M ARR from 1.4% in 1990-2000 to 3.8% in 2000-2012, but the ARR achievements are inadequate to achieve the MDG4 targets[1]. Proven cost-effective child survival interventions and proposed delivery channels for those interventions need to be scaled-up[3-7]. The *Countdown to 2015 for Maternal, Newborn, and Child Survival* initiative was created in 2005 to monitor use of evidence-based interventions for maternal, neonatal, and child health[8]. In 2012, the Countdown's 75 priority countries accounted for >95% of all maternal and child deaths[9,10]. Of note, 41 (55%) of the 75 Countdown priority countries come from the 46 WHO African Region countries (the exceptions were Algeria, Cape Verde, Mauritius, Namibia, and Seychelles).

In 2006, WHO, the United Nations Children's Fund, and the World Bank developed Child Survival Strategy for the African Region aimed to support countries' efforts to reduce child deaths from preventable and treatable conditions by scaling up coverage of effective interventions[6]. These include antenatal care, post-natal care, infant and young child feeding, the expanded program on immunizations, integrated management of common childhood illness, prevention of mother-to-child transmission of human immunodeficiency virus (HIV) and use of insecticide treated nets, among others. As of 2013, 38 of the 46 African countries had developed or updated national child survival policies, strategies, and plans. Population coverage in the African Region has increased with time, including coverage of measles vaccination, neonatal tetanus protection, antiretroviral drugs for prevention of mother-to-child transmission of HIV, and at least one antenatal care visit for every pregnant woman[11]. Coverage of other interventions,

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however, remains low, particularly for exclusive breastfeeding, pneumococcus and *Haemophilus influenzae* vaccination, treatment of childhood diarrhea, pneumonia and malaria, and use of insecticide treated nets. Despite progress, Africa is not on track to reach MDG4 due to inconsistent and suboptimal implementation and scale-up of evidence-based maternal, neonatal, and child health interventions[10]. With variable progress across countries in improving child survival in Africa, understanding factors associated with the most rapid changes in U5M reductions could assist regional and country efforts to improve child survival in the post-2015 era.

We sought to identify direct and indirect factors influencing how rapidly countries reduce U5M, as evidenced by their ARR. An ecological analysis of country-level data was used to determine which factors previously reported to reduce U5M are also the strongest predictors of larger ARRs in Africa.

METHODS

The study was approved by the Institutional Review Boards of both WHO and Vanderbilt University.

Under-five mortality data

We obtained country-specific U5M rates from annual estimates provided by www.childmortality.org, the data used in the United Nations Children's Fund Reports on *Levels and Trends in Child Mortality*. For each of the 46 WHO African Region countries, the estimated U5M rates for 2000 and 2011 (the latest estimates available at the time of the analysis [accessed January 2013]) were obtained and the ARR from 2000 to 2011 was calculated. Use of the ARR as an outcome facilitates interpretation of results in the context of MDG4 progress metrics. Under-five mortality estimates for 1990, and the corresponding ARR for the period 1990 to 2000 and 1990 to 2011 are presented for comparison but were not utilized in the analyses.

The U5M ARR is an exponential function, defined as one minus the n^{th} root of the later mortality (i.e., 2011) divide by the initial mortality (i.e., 2000)[12]. We multiplied by 100 to express ARR as a percentage (*Equation 1*):

$$\text{ARR} = \left(1 - \left[\frac{y_{t+n}}{y_t}\right]^{\frac{1}{n}}\right) \times 100$$

where y_t is the mortality rate for a given year (e.g., 2000) and n is the number of years between the two rates (e.g., 11 years when calculating ARR from 2000 and 2011 rates). The ARR will have a positive value when a country is reducing its mortality rate, consistent with how ARR is typically reported. This represents the year-to-year relative reduction in the U5M and slightly underestimates the ARR calculations used by others[13], particularly at ARRs >5%.

Factors (indicators) potentially associated with child mortality

Identification. Potential factors to be included in the analyses included those monitored by Countdown to 2015 as well as those identified through a comprehensive literature search of the PubMed database. We searched for studies on under-five, infant, or

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neonatal mortality within any of the 46 countries in WHO African Region that were published between 2002 and 2012. Abstracts were reviewed to identify those factors reported to be associated with under-five, infant, or neonatal mortality. Thirty-five factors were identified to be the most commonly reported. Because we wanted to explore these factors in an ecological analysis, we included in the current analysis those that were not already on the Countdown 2015 indicator list and had aggregate country-level data available for analysis. By adding these additional indicators, we constructed a final list of 70 indicators to assess for associations with U5M ARR, including the following categories: socio-demographics (18 indicators), access to health care (16), governance and financing (11), maternal health (6), child survival interventions (7), clinical and health conditions (7), and other country infrastructure (5) (see Supplemental Table S1). Thirty-six indicators are regularly monitored by Countdown to 2015 while the remaining 34 were identified through the literature and are not monitored by Countdown to 2015.

Data sources and inclusion criteria. Data for 58 (83%) of the 70 indicators were obtained from the World Bank Data Catalogue[14]. The World Bank Data Catalogue is a repository of national, regional, and global indicator data that have been compiled from officially-recognized international sources. In many instances, a single indicator may be derived from multiple data sources using modeling or aggregation techniques. Data for another 12 indicators not available through the World Bank Data Catalogue were obtained directly from each country's Demographic and Health Surveys[15] (10 indicators) or Countdown 2015 country profiles (2 indicators)[8,10]. In total, 24 (34%) of 70 indicators were obtained entirely or in part from country Demographic and Health Surveys or other household survey data, including the majority of the maternal health, access to health care, and child survival intervention indicators. Other sources included data collected and maintained by WHO, various UN divisions, UNAIDS, the Organisation for Economic Co-operation and Development, and the World Bank.

For each of the 46 WHO African Region countries, data on the 70 indicators were obtained that corresponded as close as possible to the years 2000 and 2011. To be considered sufficient for inclusion in the analyses, indicator data had to meet the following three criteria: a) reported for one of the years between 1998 and 2003, termed *2000 indicator data*, b) reported for one of the years between 2006 and 2011, termed *2011 indicator data,* and c) the pair of indicator data had to be at least five years apart in order to minimize incorrect extrapolation when calculating changes in the indicator. If any of these criteria were not met from a given country, the change in the coverage for that particular indicator was not calculated and was deemed missing. As with the U5M estimates, limited 1990 data are also presented for comparison purposes. Consistent with the requirements for 2000 and 2011 indicator data, 1990 indicator data had to be reported for one of the years between 1990 and 1995 and be at least five years apart from the data reported for the 2000 indicator data.

Indicator annual rate of change (ARC) calculation. The ARC for each indicator is conceptually similar to the ARR for U5M and was calculated using the same ARR equation shown above in *Equation 1* but with one difference: a value of one is now subtracted from the exponential function so that the ARC has a negative value when the indicator decreases over time (i.e., $Coverage_{2011} < Coverage_{2000}$) and a positive value when the indicator increases over time (*Equation 2*):

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$$\text{ARC} = \left(\left[\frac{y_{t+n}}{y_t}\right]^{\frac{1}{n}} - 1\right) \times 100$$

This is in contrast to the U5M ARR which has a positive value when mortality is decreasing over time (i.e., $U5M_{2011} < U5M_{2000}$).

Statistical analysis

The dependent variable of interest was the U5M ARR for 2000-2011. Each indicator ARC was an independent variable of interest. Both indicator ARCs and U5M ARR were analyzed as continuous variables and no transformations were performed. Bivariate associations were explored using the Wilcoxon rank-sum test and linear regression. Given the sample size (n=46 countries), results from traditional linear regression methods may be overly influenced by outliers. These outliers, however, likely represent true data rather than data errors, and exclusion would unnecessarily decrease the sample size. Hence, robust linear regression was used to minimize the influence of outlying observations, without excluding them[16-18] using iteratively reweighted least squares (M-estimation with Huber weighting).

Multivariable robust linear regression models were fit for each indicator of interest while adjusting for a small number of covariates (i.e., other indicators that may confound the specific indicator association being analyzed). A standard set of indicators were identified *a priori* to be included as covariates in all analyses. Given the sample size of 46 countries, at most, a decision was also made *a priori* to include no more than five covariates in the multivariable analyses to avoid overfitting. We selected the following indicator ARCs for inclusion as covariates in each model based on previous ecological studies, consideration of what macro- or system-level factors would influence the majority of the indicators, and having nearly complete data: 1) access to improved water source, 2) health expenditure (relative to gross domestic product [GDP]), 3) adult HIV prevalence, 4) urban population prevalence, and 5) receipt of antenatal care (when applicable). All regression models included these core indicator ARCs as covariates unless expected to be highly correlated with the predictor indicator of interest. Changes in the receipt of antenatal care was only included when the indicator being analyzed would occur following the pregnancy period (e.g., maternal mortality ratio, births delivered at a health facility, measles immunization, wasting prevalence), and was not included for socio-demographic indicators, macro-level indicators such as health expenditure, and system-level indicators such as physician density.

The estimated robust linear regression beta coefficient for each indicator ARC and U5M ARR association can be interpreted as the absolute change in ARR for every one percent increase in the indicator ARC. For example, a beta coefficient of 0.20 indicates that for every 1.0% increase in the indicator ARC there is a corresponding 0.2% increase in the ARR. Stated differently, a 5.0% increase in the indicator ARC (e.g., 6% ARC compared to 1% ARC) corresponds to a 1% increase in the ARR (e.g., 4% ARR versus 3% ARR). To avoid false negatives, we reported all associations when the p-values were <0.10, acknowledging that some of these associations may be due to chance alone, especially with higher p values. We report an indicator to be a strong

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predictor when the adjusted beta coefficient for the association with ARR is ≥0.20 or ≤ -0.20. Results are presented below only for those indicators for which at least 50% of countries (i.e., 23 or more countries) have non-missing indicator ARC data. Results for all indicators are available in Supplemental Tables S1 through S5.

RESULTS

Country-specific progress in under-five mortality

As of 2011, U5M rates and corresponding ARRs for each of the 46 WHO African countries vary widely (Figure 1; Table 1). Seven countries (Cape Verde, Ethiopia, Liberia, Madagascar, Malawi, Niger, and Rwanda) have 1990-2011 ARRs of at least 4.3%, sufficient to meet their MDG4 target. Tanzania is also considered to be on track with an ARR of 4.0%, as is Zambia (ARR of 3.9%). An additional four countries (Algeria, Botswana, Mauritius, and Seychelles) are considered on track due to U5M rates <40 per 1,000. Nine countries were making little to no progress with ARRs <1.0%: Cameroon, Central African Republic, Congo, Democratic Republic of Congo, Lesotho, Mauritania, São Tome and Principe, Swaziland, and Zimbabwe. The remaining 23 countries were making insufficient progress. Considerable progress towards MDG4 has occurred since 2000 (the referent point for this analysis), with eight countries (Botswana, Kenya, Mozambique, Namibia, Senegal, South Africa, Uganda, and Zimbabwe) accelerating their ARRs to at least 3.9%, despite slower progress from 1990 to 2000 (Table 1).

Descriptive results of selected indicators

Of the 70 indicators identified, 61 (87%) had sufficient data from at least one country for the period 2000 to 2011 to be included. Of these, 41 (67%) indicators had data for at least 50% of the countries (See Supplemental Table S2). When considered by country, reporting of the 61 indicators improved over time (Figure 2). For the 2011 indicator data alone, 63 (90%) had data for at least 50% of the countries, with 27 countries (59%) reporting 50 of the 61 indicators. Only Ghana reported all 61 indicators. Notably, 13 countries reported *fewer* indicators for 2011 compared with 2000.

For indicators reported by at least 50% of countries, there were few differences in median U5M ARRs when comparing countries with missing and non-missing data (see Supplemental Table S3). Notable differences, however, were observed for 1) households with a television, 2) availability of physicians, 3) diarrhea treatment, and 4) population coverage of cell phones. When considering completeness of indicator data by country, there was a small correlation between U5M ARRs and the number of indicators reported by a country (Figure 3).

Large to moderately large median ARCs (Table 2) were noted with the use of insecticide treated nets (34.0%), non-health infrastructure indicators of internet users (34.0%), population coverage of cell phones (8.5%), and households with a television (6.7%), and various indicators of donor funding (6.4% to 9.1%). Lower median ARCs (Table 2) occurred for socio-demographic indictors of GDP per capita (4.3%) and women with at least some secondary education (3.2%); maternal mortality ratio (-3.6%); health care access and treatment indicators of children with fever receiving antimalarial drugs (-4.8%), diarrhea treatment (2.3%) and births attended by skilled health staff

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(2.0%); intervention indicators of exclusive breastfeeding (4.1%) and children ages 1-2 years receiving all basic vaccinations (2.8%); and governance and financing indicators of health expenditure as a proportion of total government expenditure (2.5%) and public spending on education as a proportion of GDP (2.1%). Details of all indicator ARCs are in Supplemental Table S4.

Table 2. Median 2000 indicator values and corresponding indicator annual rate of change (ARC) for the 2000-2011 period.

Indicator	N	Median 2000 value (IQR)	Median 2000-2011 ARC (IQR)
Socio-demographics			
Adult female literacy rate (%)	35	54 (37 - 72)	1.2 (0.8 - 2.8)
Female labor participation rate (%)	45	46 (43 - 49)	0.1 (-0.1 - 0.3)
Fertility rate (rate per 1,000 persons)	46	6 (5 - 6)	-1.4 (-2.0 - -0.9)
Gross domestic product (GDP) per capita (PPP int'l $)	45	990 (680 – 1,900)	4.3 (2.8 - 6.1)
Human development index (0 to 1)	39	0.38 (0.31 - 0.48)	1.1 (0.7 - 1.9)
Improved sanitation facilities (%)	45	25 (13 - 45)	1.6 (0.4 - 2.7)
Improved water source (%)	45	62 (51 - 79)	1.1 (0.2 - 1.8)
Labor force participation rate among women (%)	45	66 (50 - 76)	0.3 (-0.1 - 0.6)
Urban population prevalence (%)	46	35 (22 - 44)	1.3 (0.7 - 1.7)
Women with at least some secondary education (%)	23	16 (10 - 30)	3.2 (2.5 - 5.3)
Maternal health			
Pregnant women receiving prenatal care (%)	38	77 (64 - 88)	1.3 (0.6 - 2.7)
Adult female mortality rate (rate per 1,000 persons)	46	360 (280 - 420)	-1.2 (-1.8 - -0.6)
Maternal mortality ratio (rate per 100,000 births)	45	550 (400 - 840)	-3.6 (-4.5 - -20)
Access to health care			
Seeking ARI treatment (%)	33	40 (27 - 55)	1.7 (-0.3 - 5.0)
Births attended by skilled health staff (%)	37	47 (39 - 60)	2.0 (0.3 - 3.4)
Children with fever receiving antimalarial drugs (%)	30	53 (32 - 61)	-4.8 (-7.5 - -0.2)
Diarrhea treatment (%)	25	39 (28 - 45)	2.3 (-1.3 - 5.7)
Physicians (rate per 100,000 persons)	23	5.7 (2.9 – 12.0)	1.2 (-0.6 - 5.2)
Child survival interventions			
Children 1 year old receiving all basic vaccinations (%)	26	41 (29 - 65)	2.8 (1.1 - 5.3)
Exclusive breastfeeding (%)	36	25 (14 - 37)	4.1 (-0.2 - 8.6)
Measles immunization (%)	46	69 (49 - 76)	1.3 (0.3 - 2.5)
Use of insecticide-treated bed nets (%)	30	2 (1 - 4)	34.0 (28.0 - 42.0)
Vitamin A supplementation coverage (%)	37	91 (78 - 96)	-0.3 (-2.0 - 0.7)
Clinical and health conditions			
Adult prevalence of HIV (%)	43	4 (1 - 8)	-0.8 (-3.5 - 1.7)
Low-birthweight babies (%)	30	13 (11 - 17)	-0.3 (-3.6 - 1.0)
Malnutrition prevalence (height for age) (%)	34	40 (34 - 48)	-1.1 (-2.3 - 0.2)
Malnutrition prevalence (weight for age) (%)	34	22 (18 - 27)	-1.7 (-3.2 - -0.9)
Prevalence of wasting (%)	34	9 (7 - 12)	-1.9 (-5.2 - 0.5)
Governance and financing			
External resources for health (%)	45	13 (4.6 - 20)	6.4 (-1.0 - 10.0)
Health expenditure (% of GDP) (%)	45	5 (4 - 6)	1.4 (0.5 - 3.3)
Health expenditure (% of government expenditures) (%)	45	9 (7 - 10)	2.5 (-0.4 - 3.7)
Net bilateral aid flows from DAC donors (US$ in millions)	46	120 (40 - 260)	9.1 (5.0 - 16.0)
Net ODA received (% of GNI) (%)	46	9 (4 - 13)	-0.9 (-5.4 - 5.4)
Net ODA received per capita (US$)	46	23 (15 - 41)	7.4 (2.4 - 13.0)
Out-of-pocket health expenditure (%)	45	43 (26 - 58)	-1.7 (-3.9 - -0.6)
Public spending on education (% of GDP) (%)	34	4 (3 - 5)	2.1 (0.2 - 3.9)

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Public spending on education (% of government expenditure)(%)	25	16 (14 - 19)	1.6 (-0.2 - 3.0)
Safety and Rule of Law (0 to 100)	46	54 (43 - 66)	-0.0 (-0.9 - 0.4)
Other factors			
Households with television (%)	24	18 (6 - 29)	6.7 (4.1 – 10.0)
Internet users (rate per 100 persons)	46	0.2 (0.1 - 0.5)	34.0 (25.0 - 46.0)
Population coverage of cell phones (%)	26	37 (17 - 82)	8.5 (1.3 - 16.0)

Abbreviations: ARC, annual rate of change; IQR, inter-quartile range; PPP int'l $, purchasing power parity of GDP converted to international dollars; ARI, acute respiratory infection; DAC, Development Assistance Committee; ODA, Official Development Assistance; GNI, gross national income; HIV, human immunodeficiency virus

Associations between indicator ARCs & under-five mortality ARRs

Seven indicator ARCs were strongly associated with positive or negative ARR trends. For three of the indicators, larger increases in ARCs were associated with larger U5M ARRs: seeking treatment for acute respiratory infection (ARI) (β=0.27; p=0.02), GDP per capita (β=0.23; p=0.09), and health expenditure relative to GDP (β= 0.22; p=0.07) (Table 3). For four indicators, larger increases in ARCs were inversely associated with unfavorable and larger *decreases* in U5M ARR: malnutrition (underweight) prevalence (β= -0.30; p=0.07), the maternal mortality ratio (β= -0.86; p<0.01), increases in out-of-pocket expenses (β= -0.26; p=0.04), and public spending on education as a proportion of GDP (β= -0.20; p=0.06). These indicate that larger decreases in ARC were associated with improved U5M ARR.

Of the remaining 63 indicators, 34 also had sufficient sample sizes (at least 23 of 46 countries providing sufficient data) to warrant consideration (14 of these are also included in Table 3): five had large ($\beta \geq 0.20$ or $\beta \leq -0.20$) but statistically non-significant ($p \geq 0.10$) associations with U5M ARR after adjusting for potential confounders, three had small associations (β<0.20 with p<0.10), and 26 had no association (β<0.20 with p≥0.10). The final 29 factors had insufficient data for analyses or their small sample sizes (fewer than 23 of 46 countries providing sufficient data): 10 indicators with no data, 4 indicators with insufficient data for adjusted analyses, and 15 indicators with <50% of countries reporting sufficient data. Details of all indicator and ARR associations are in Supplemental Table S5.

Table 3. Crude and adjusted associations between select indicators and under-five mortality annual rate of reduction, 2000-2011.

		Crude		Adjusted[b]	
Indicator[g]	**N**	***B***	**p-value**	***β***	**p-value**
Socio-demographics					
Access to improved water source (%)	45	-0.05	0.39	0.01	0.40
Female labor participation rate (%)	45	-0.39	0.33	-0.58	0.33
Fertility rate (births per woman)	46	0.09	0.38	0.18	0.35
GDP per capita (PPP int'l $)[f]	45	0.20	0.13	**0.23**	**0.09**
Human development index (0 to 1)	39	0.50	0.21	0.48	0.29
Labor force participation rate among women (%)	45	-0.01	0.40	0.23	0.37
Urban population prevalence (%)	46	0.42	0.21	0.28	0.31
Maternal health					
Adult female mortality rate (rate per 1,000 persons)	46	-0.39	0.10	-0.35	0.18

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Maternal mortality ratio (rate per 100,000 births)[c]	45	-0.40	<0.01	**-0.86**	**<0.01**
Pregnant women receiving prenatal care (%)	38	-0.24	0.22	-0.08	0.38
Access to health care					
Births attended by skilled health staff (%)[c]	37	-0.08	0.34	0.04	0.39
Children with fever receiving antimalarial drugs (%)[c]	30	0.08	0.04	0.14	0.02
Seeking ARI treatment (%)[c]	33	0.25	0.02	**0.27**	**0.02**
Clinical and health conditions					
Adult prevalence of HIV (%)	43	-0.08	0.22	-0.06	0.32
Malnutrition prevalence (weight for age) (%)[c]	34	-0.13	0.24	**-0.30**	**0.07**
Prevalence of wasting (%)[d]	34	-0.05	0.33	-0.10	0.22
Governance and financing					
Health expenditure (% of GDP) (%)	45	0.21	0.05	**0.22**	**0.07**
Health expenditure (% of government expenditure) (%)[f]	45	0.04	0.32	0.11	0.16
Net ODA received per capita (US$)	46	-0.04	0.24	-0.09	0.09
Out-of-pocket health expenditure (%)[f]	45	-0.13	0.17	**-0.26**	**0.04**
Public spending on education (% of GDP) (%)	34	-0.10	0.23	**-0.20**	**0.06**

[a] Insufficient data, Indicators for which fewer than 23 countries had sufficient data for the analysis period; other results not shown if β <0.20 and p≥0.10 (all results for all indicators available in Supplemental Table S5).

[b] All results adjusted for improved water source, health expenditure (relative to GDP), adult HIV prevalence, and urban population prevalence unless otherwise noted:

[c] further adjusted for receipt of prenatal care; [e] not adjusted for improved water source; [f] not adjusted for health expenditure (relative to GDP)

[g] Indicators shown in **bold** have an adjusted β ≥0.20 and p<0.10

Abbreviations: GDP, gross domestic product; PPP int'l $, purchasing power parity of GDP converted to international dollars; ARI, acute respiratory infection; HIV, human immunodeficiency virus; ODA, Official Development Assistance.

DISCUSSION

Our study represents the most comprehensive analysis to date of health indicators and other determinants of health as predictors of declining U5M in Africa. From 70 factors considered, we could use 41 indicators meaningfully. More rapid scale-up of seven factors were associated with a favorable ARR rise (i.e., higher rate of U5M decline) between 2000 and 2011. Six of the indicators might be expected: higher rates of seeking treatment for ARI, higher GDP per capita, higher health expenditure relative to GDP, lower out-of-pocket expenses, lower prevalence of underweight, and lower maternal mortality ratio. The strongest association was for maternal mortality ratio (β= -0.86), indicating that a 1.0% increase in the annual reduction of the maternal mortality ratio was associated with a 0.86% increase in the U5M ARR. The other six factors had similar magnitudes of association ranging from an absolute value of β=0.20 to β=0.30.

The inverse association between increasing ARC for public spending on education relative to GDP and declines in U5M ARR was counterintuitive. A possible explanation is that it represents the challenge of competing priorities for extremely resource-limited countries, where increases in education relative to GDP may adversely affect spending in other areas, such as health.

Fotso et al. studied U5M ARRs from 22 African countries using data from 1988-2004. Larger increases in access to clean water and receipt of basic vaccinations (*Bacillus*

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Calmette-Guérin [BCG]; diphtheria, pertussis, tetanus; measles; and polio) were associated with larger ARRs, while higher increases in urban populations were associated with lower ARRs[19]. We did not find these associations in this 2000-2011 analysis.

Binkin et al. studied U5M ARRs from 19 African countries using data primarily from the late 1990s to mid-2000s and grouping specific interventions into composite indices representing antenatal care, access to delivery services, seeking treatment, immunizations, breastfeeding, and nutritional status[13]. Of these, antenatal care, access to delivery services (including a skilled attendant at delivery, delivery in a health facility, and/or caesarean section), and improved nutritional status (including reductions in underweight, stunting, and/or wasting) were associated with higher ARRs. Our findings also suggested that reductions in the prevalence of being underweight were associated with a high ARR from 2000-2011. Unlike our finding of increased coverage of seeking ARI treatment to be associated with higher ARRs, Binkin et al. did not find seeking health treatment (including ARI treatment and diarrhea treatment) to be associated with ARR.

Lawn et al.[20] assessed how annual rates of change in 11 indicators representing context (gross national income, general and adolescent fertility rate, female literacy, total health expenditure, government effectiveness, political stability, and female HIV prevalence) and coverage (skilled birth attendance, tetanus prevention at birth, and diphtheria, pertussis, tetanus vaccine coverage) were associated with neonatal mortality (i.e., not U5M) ARR between 2000 and 2010. Of these, only improved coverage of tetanus protection at birth was found to be associated with lower neonatal mortality ARR, a counterintuitive finding. The authors argued that the paradox arose from the fact that the nations investing the most in scaling up tetanus coverage were those with the weakest health systems, high neonatal mortality, and lower coverage of interventions.

Other ecological studies of country-level indicators and under-five or infant mortality rates (not ARRs) have found the following to be associated with lower mortality in Africa: having a skilled attendant at delivery[21], exclusive breast feeding[22], prevention of mother-to-child transmission of HIV and ART for children[23], diphtheria, pertussis, tetanus or measles vaccination[23], use of insecticide treated nets[23], HIV [24,25], health expenditure[24], income[21,25], urban population prevalence[26], access to clean water[23], female education[21,25,26], and fertility rate[26]. Stunting[23] and underweight[22] were associated with increased mortality. While our study found associations between U5M ARRs and changes in only a few of these factors, we note that a lack of association between an indicator ARC and mortality ARR does not imply that the intervention is not associated with reduced mortality. Rather, it means that more rapid scale-up or change in a particular factor does not appear to be associated with a more rapid decline in mortality based on the ARR. During the study period, nearly every African country had declining U5M. A non-significant ARC-ARR association could present if such a decline was relatively constant, regardless of whether there was a slow or rapid change in the factor over the corresponding period. It also highlights the need for further research on delivery and subsequent measurement, including assessing quality, of these proven interventions[27,28].

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Our findings highlight the role of financing, economy, and the broader health system to more rapidly reduce an already declining, albeit slowly, U5M rate above and beyond the contribution of individual interventions. As the Millennium Development Goals give way to Sustainable Development Goals for 2030, these factors must be addressed to enable further increases in maternal, neonatal, and child health interventions[29]. Model projections suggest that 3.8 million children will still die in 2030 if current U5M rate ARRs remain steady, and that 2.4 million will die even if ARRs increase substantially[25]. As U5M rates continue to decline, increasing attention must be paid to neonatal mortality which now accounts for 44% of all deaths in children under five years of age (34% in Sub-Saharan African)[30,31]. Facility-based interventions and improving quality care for pregnant women and newborns are needed[31]. The same financial, economic, and broader health system factors that would increase U5M ARRs would also increase reductions in neonatal mortality.

Our study's strongest and most statistically significant association by far with U5M ARR was for more rapid declines in the maternal mortality ratio. This may well represent the direct negative effect of maternal death on subsequent child survival. It may also be indicative of health systems that do poorly in preventing both maternal and child deaths. More rapid increases in treatment seeking behavior for ARI was the only health-related access or intervention factor found to associate with a larger U5M ARR. Validation studies suggest that indicators of access to care or behavior (e.g., seeking ARI treatment) may be more reliably measured than actual treatment (e.g., children with ARI receiving treatment; we had insufficient data to analyze this), since quality of care and ability to recall symptoms may bias the coverage estimates[28,32]. Similar concerns exist about reliability of vaccination coverage estimates due to information bias on the vaccination card or recall bias from maternal reports[33].

Our study highlights the ongoing challenge of obtaining indicator reporting from all countries. Results for 29 of the 70 indicators could not be calculated, or the results could not be considered representative, given that more than half the countries were missing the necessary data. Of particular importance, seven of the 27 interventions monitored by Countdown to 2015 were unreported by at least 50% of countries during the 2000-2011 period. While this improved to only three in 2011 (i.e., any year between 2006 and 2011), 15 of the intervention indicators were still reported by <40 of the 46 countries. This reflects a similar finding by the *Every Woman, Every Child* independent Expert Review Group that only 11 of the 75 countries contributing to more than 95% of global child mortality had recent data on all eight coverage indicators that are recommended for global monitoring[34].

In our current study, only exclusive breast feeding, having a skilled attendant at delivery, and immunization coverage (measles or all immunizations instead of diphtheria, pertussis, and tetanus) had sufficient data for analysis. The other five Expert Review Group indicators lacked sufficient data for analysis or interpretation (unmet need for contraception, antenatal care at least four times, antiretroviral prophylaxis for prevention of mother-to-child transmission of HIV, postnatal care within two days, and children with ARI provided antibiotics). While reporting of key indicators has improved over the last 20 years, missing indicator data from a number of countries, even in 2011, means that future analyses of indicators and child mortality outcomes, not to mention global

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monitoring of progress, will continue to suffer from small samples sizes and potential bias.

Limitations should be considered when interpreting the findings from this report. First, mortality and indicator data were obtained from secondary sources and some may have suboptimal methods of data collection and model-based estimation, though the World Bank, United Nations Children's Fund, the Inter-agency Group for Child Mortality Estimation, Demographic and Health Surveys, Multiple Indicator Cluster Surveys, and Countdown to 2015 seek to be as authoritative sources as they can. A recent *PLoS Medicine* Collection highlighted the challenges in obtaining valid coverage data from community-based household surveys[28]. Second, the study design was an ecological, cross-sectional study. As such, changes in the indicators of interest were occurring simultaneously with changes in mortality, and temporality and causality inferences are limited. Ecological studies are prone to bias and associations at the aggregate level (e.g., country) may not reflect the cause-effect relationship at the individual or local level. Nevertheless, we felt this design was appropriate given the interest in achieving MDG4, which is monitored at a country level. Third, the time period for calculating the indicator ARCs did not always fully overlap with the time period for calculating mortality ARRs (e.g., indicator ARC for 2000-2011 may have been calculated from data for 2003 and 2010). We attempted to minimize any potential bias by only considering indicator data for which at least a five year period of the 11 year time period were available for calculating ARCs. Finally, the small sample size (at most n=46 countries) limits the validity of many associations and prevents adjustment for many covariates. We cannot exclude residual confounding and low power to detect certain associations. In spite of these limitations, the unique strengths of our study include our broad identification of factors potentially relevant to child survival, beyond those typically used from Demographic and Health Surveys and Countdown to 2015. We also made statistical efforts to minimize bias or distortion from outliers, without excluding them.

There are numerous interventions, health indicators, and other determinants of health that influence child mortality rates. However, there are very few studies assessing which of these factors are associated with higher ARR reflecting more rapid declines in U5M. Policy makers now have evidence that can back decisions to propose increasing access to care for children under age five (extrapolating from our ARI access finding), increasing health investments per GDP, notably towards maternal mortality reduction and reducing childhood undernutrition and out-of-pocket expenses for health care.

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CONTRIBUTORSHIP STATEMENT

AMK helped with the stuy design, acquisition of data, assisted with data analysis, interpretation of results, and drafting the manuscript. He had full access to all of the data

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in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. He affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained. MB assisted with acquisition of data, conducted the analysis, and critically revised manuscript. CAH contributed to the study design, interpretation of results, and drafting the manuscript. KM helped with conception and design of the study and critically revising the manuscript. PH helped with conception and design of the study and critically revising the manuscript. BES assisted with data analysis and critically revising the manuscript. MHA assisted with the study design and interpretation and critically revising the manuscript. TK helped with conception and design of the study and critically revising the manuscript. SHV helped with conception and design of the study and drafting the manuscript. All authors have participated sufficiently in the work to take public responsibility for its content.

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COMPETING INTERESTS

KM, PH, and TM are paid employees of the WHO. All other authors have no competing interests to report.

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DATA SHARING

Additional data is available at http://biostat.mc.vanderbilt.edu/wiki/Main/WHOUnder5Mortality, or by emailing Dr. Aaron Kipp at aaron.kipp@vanderbilt.edu

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FIGURE LEGENDS

Figure 1. Annual rate of reduction (ARR) in under-five mortality for the 46 countries in the WHO African Region, 2000 to 2011 (Higher ARRs indicate more progress, represented by a greener color on the map).

Figure 1 footnote: The WHO African Region excludes Djibouti, Egypt, Libya, Morocco, Somalia, Sudan, and Tunisia; all are included in the WHO Eastern Mediterranean Region. From May 2012, South Sudan is now officially part of the African Region but was not an independent WHO member nation during the study period through 2011.

Figure 2. Completeness of 61 indicators reported by country, 1990, 2000, and 2011.

Figure 2 footnote: hashed bars indicate how many fewer indicators were reported in 2011 compared with 2000; 1990 defined as any indicator reported between 1990 and 1995, 2000 defined as 1998-2003, and 2011 defined as 2006-2011.

Figure 3. Correlation between under-five mortality ARR and completeness of indicator data for 46 countries in the WHO African Region for the period 2000-2011.

Figure 3 footnote: The coefficient of 0.08 suggests that for every additional 12 indicators reported by a country, there is a corresponding 1% increase in the ARR.

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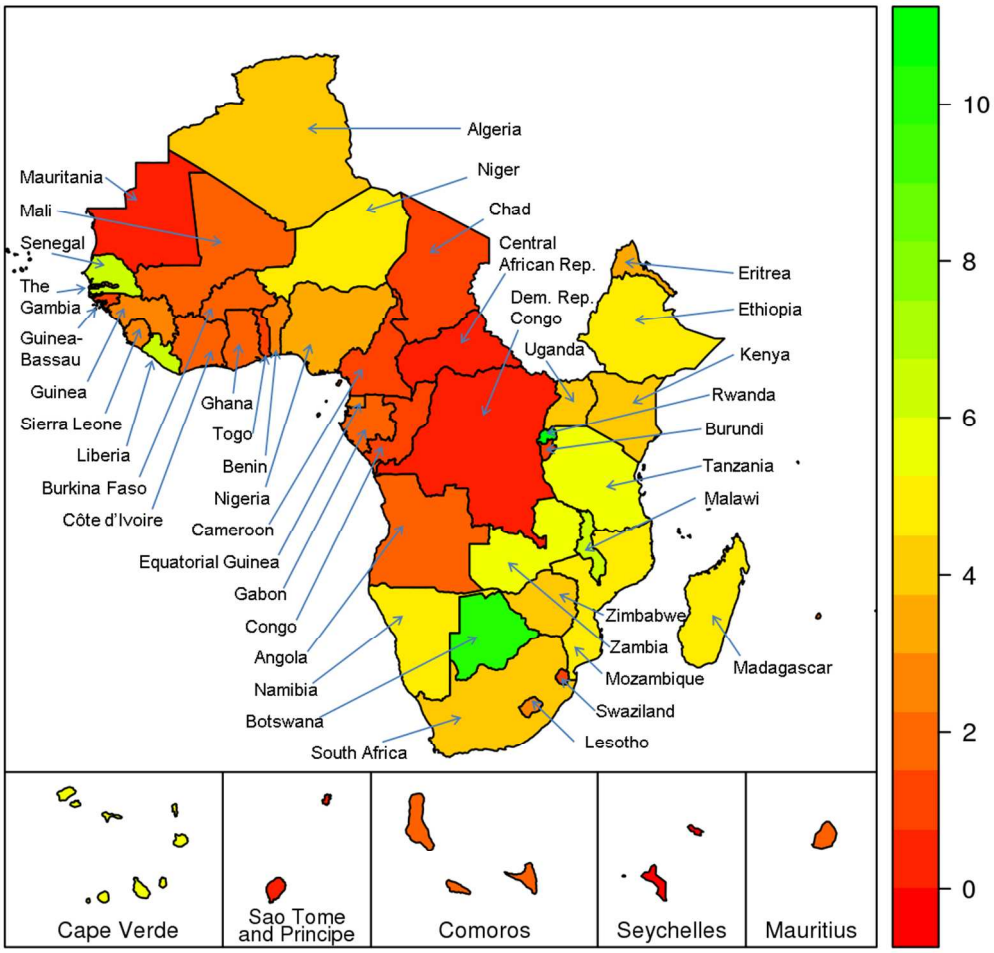

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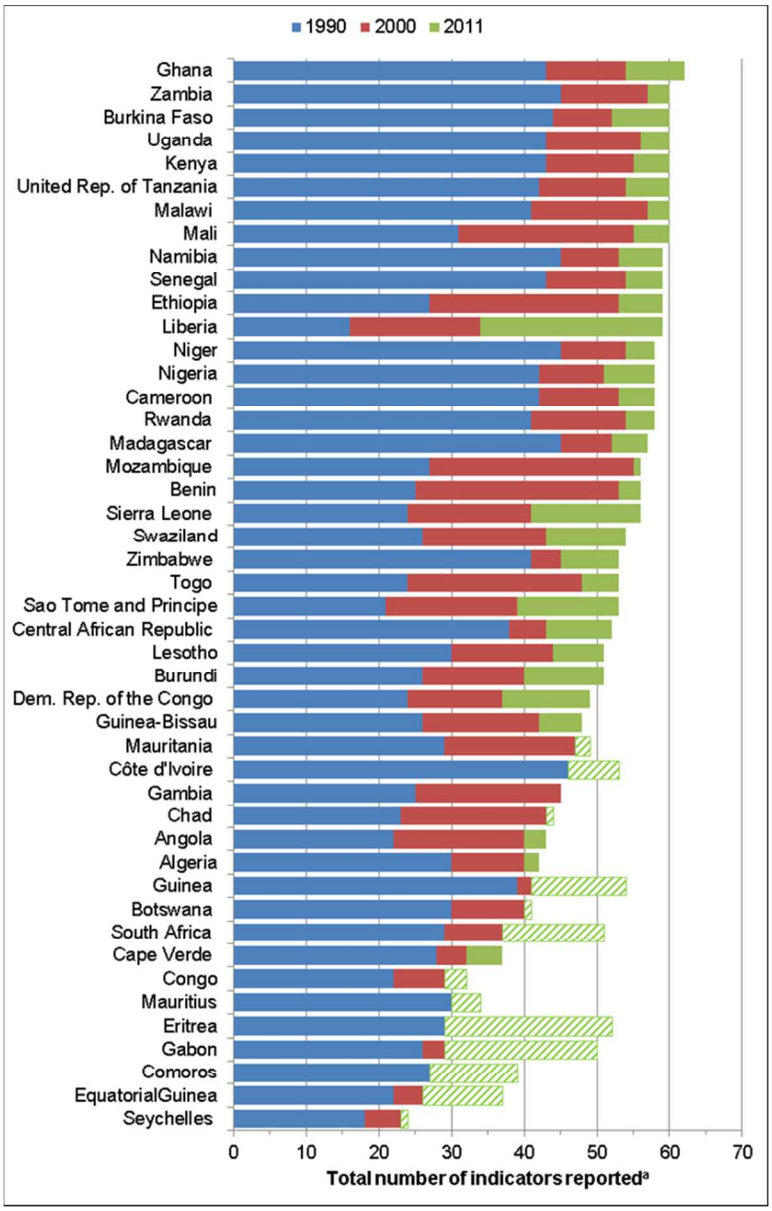

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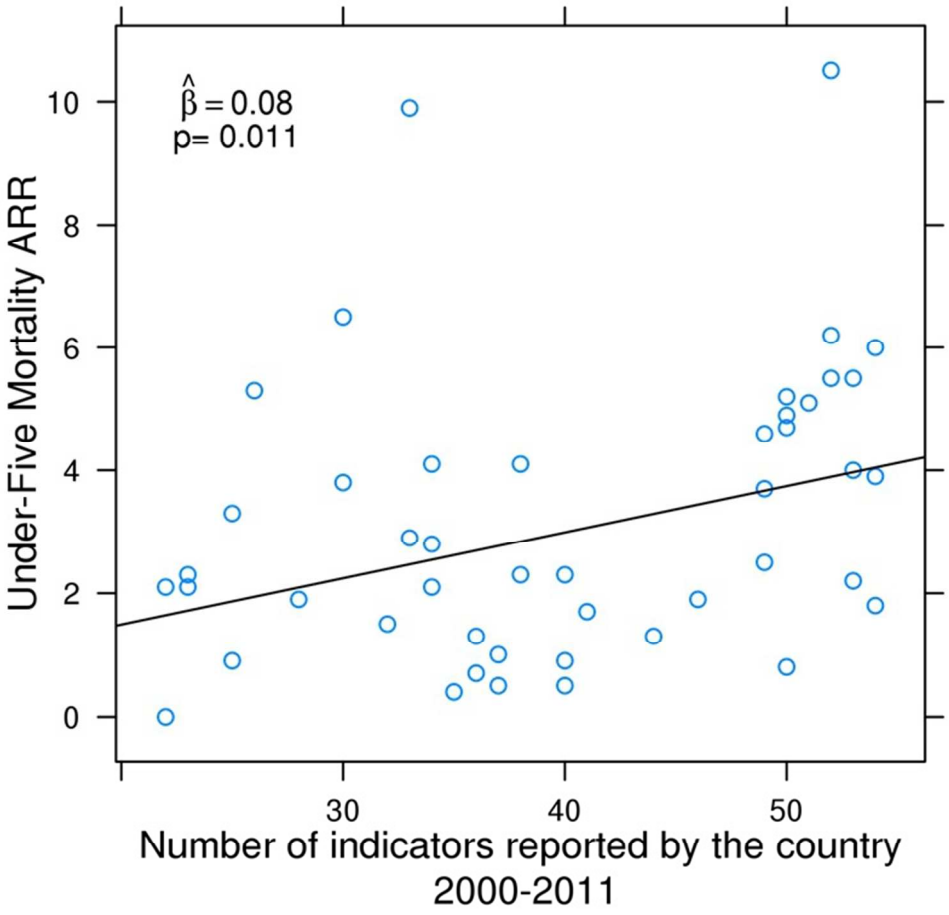

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SUPPLEMENTAL MATERIAL

Table S1. Factors (indicators) used in the ecological analysis.

Category	Indicator name[a]
Socio-demographic (18 indicators listed)	
Age	• Age at first marriage, female • Teenage mothers (% of women ages 15-19 who have had children or are currently pregnant) • Age at first birth of women 20-49 yrs
Education	• Years of education completed among women 15-49 yrs • Percent of women 15-49 yrs old with at least some secondary education
Literacy	• Literacy rate, females (% of females ages 15 and above)
Children	• Number of living children per household • Fertility rate, total (births per woman)[c]
Employment	• Labor force participation rate, female (% of female population ages 15-64) • Labor force, female (% of total labor force)
Water and Sanitation	• Access to improved water source (% of population with access)[b] • Access to improved sanitation facilities (% of population with access)[b]
Socio-economic status	• Gini index[d] • Poverty headcount ratio at national poverty line (% of population) • Households with television (%) • Human development index (HDI)[e] • Gross Domestic Product (GDP) per capita (PPP Int'l $)
Rural/urban residence	• Urban population (% of total)
Maternal health (6 indicators listed)	
Family planning	• Unmet need for contraception (% of married women ages 15-49)[b]
Antenatal care	• Pregnant women receiving prenatal care (%)[b] • Pregnant women receiving prenatal care of at least four visits (%)[b] • Percent of women with live births who received antenatal care during first 5 months of pregnancy
Maternal mortality	• Maternal mortality ratio (per 100,000 live births)[c] • Mortality rate, adult, female (per 1,000 female adults)
Access to health care (16 indicators listed)	
Availability	• Physicians (per 1,000 persons)[c] • Nurses and midwives (per 1,000 persons)[c] • **Nurses (per 1,000 persons)** • Community health workers (per 1,000 persons)

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	• Hospital beds (per 1,000 persons) • Births attended by skilled health staff (% of total)[b] • % of births delivered by caesarean section[b]
Utilization	• % of births delivered at a health facility • % of births with a postnatal visit within the first 2 days after delivery[b] • Seeking ARI treatment (% of children under 5 taken to a health provider)[b]
Treatment	• % of children 0-59 months of age with ARI who received antibiotics[b] • Diarrhea treatment (% of children under 5 receiving oral rehydration and continued feeding)[b] • Children with fever receiving antimalarial drugs (% of children under age 5 with fever)[b] • Use of preventive treatment for malaria (% of pregnant women)[b] • **Adoption of low osmolarity Oral Rehydration Salts and zinc for management of diarrhea**[c] • **Community treatment of pneumonia with antibiotics**[c]
Child survival interventions (7 indicators listed)	
PMTCT	• **HIV positive pregnant women receiving antiretrovirals, using WHO/UNAIDS methodology (%)**[b] • **Antiretroviral therapy coverage (% of persons with advanced HIV infection)**[b]
Breastfeeding	• Exclusive breastfeeding (% of children under 6 months)[b]
Vitamin A supplementation	• Vitamin A supplementation coverage rate (% of children ages 6-59 months)[b]
Immunizations	• Immunization, measles (% of children ages 12-23 months)[b] • % of 12-23 month old children receiving all basic vaccinations[b,f]
Bed nets	• Use of insecticide-treated bed nets (% of under-5 population)[b]
Clinical and health conditions (7 indicators listed)	
HIV	• Prevalence of HIV, total (% of population ages 15-49) • **Female adults with HIV (% of population ages 15+ with HIV)** • **Prevalence of HIV, female (% ages 15-24)**
Preterm/birth weight	• Low-birth weight babies (% of births)[c]
Malnutrition	• Malnutrition prevalence, height for age (% of children under 5)[c] • Malnutrition prevalence, weight for age (% of children under 5)[c] • Prevalence of wasting (% of children under 5)[c]
Governance and financing (11 indicators listed)	
Health financing	• Health expenditure, total (% of GDP)[c] • Health expenditure, public (% of government expenditure)[c] • Out-of-pocket health expenditure (% of total expenditure on health)[c]
Education financing	• Public spending on education, total (% of GDP) • Public spending on education, total (% of government expenditure)
Donor funding	• External resources for health (% of total expenditure on health) • Net bilateral aid flows from DAC donors, Total (current US$)[g] • Net official development aid (ODA) received (% of Gross National Income)[c,h]

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	• Net ODA received per capita (current US$)[c,h] • **Net ODA received (constant 2010 US$)**[c,h]
Quality of governance	• Safety and Rule of Law (Ibrahim index with 4 indicators)[i]
Other (5 indicators listed)	
Country infrastructure	• Road density (km of road per 100 sq. km of land area) • Roads, paved (% of total roads) • **Access to electricity (% of population)** • Population coverage of mobile cellular telephony (%) • Internet users (per 100 persons)

[a] 9 indicators in bold were not included in the database due to 100% insufficient data (see methods); analysis dataset has 61 indicators.
[b] one of the 27 Countdown to 2015 intervention indicators (or closely related)
[c] one of the Countdown to 2015 country profile indicators (or closely related)
[d] The GINI index is a measure of income inequality, where 0 represents perfect equality and 100 represents perfect inequality
[e] The Human Development Index is a composite measure of development incorporating life expectancy at birth, mean years of schooling and expected years of schooling, and gross national income per capita, where 0 represents very low development and 1 represents very high development
[f] Includes BCG, measles and three doses each of DPT and polio vaccine (excluding polio vaccine given at birth)
[g] DAC, Development Assistance Committee. DAC members are Australia, Austria, Belgium, Canada, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Japan, Republic of Korea, Luxembourg, Netherlands, New Zealand, Norway, Portugal, Spain, Sweden, Switzerland, United Kingdom, United States, and European Union Institutions
[h] ODA, Official Development Assistance. ODA includes loans and grants made by DAC members, non-DAC countries, and multilateral institutions
[i] Ibrahim index is a composite measure of a countries provision of political, social and economic public goods and services. It is comprised of four indicates: Personal safety, Rule of law, Accountability and corruption and, National security. The index ranges from 0 to 100, with higher values representing better governance.

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Table S2. Completeness of data for 61[a] indicators for the periods 1990-2011, 1990-2000, 2000-2011, and 2011 alone.

	1990-2011	1990-2000	2000-2011	2011[b]
Indicator	**# countries (% complete)**	**# countries (% complete)**	**# countries (% complete)**	**# countries (% complete)**
Fertility rate	46 (100%)	46 (100%)	46 (100%)	46 (100%)
Net bilateral aid flows from DAC donors	46 (100%)	46 (100%)	46 (100%)	46 (100%)
Net ODA received per capita	46 (100%)	46 (100%)	46 (100%)	46 (100%)
Urban population prevalence	46 (100%)	46 (100%)	46 (100%)	46 (100%)
Female labor participation rate	45 (98%)	45 (98%)	45 (98%)	45 (98%)
Labor force participation rate among women	45 (98%)	45 (98%)	45 (98%)	45 (98%)
Maternal mortality ratio	45 (98%)	45 (98%)	45 (98%)	45 (98%)
External resources for health	44 (96%)	45 (98%)	45 (98%)	45 (98%)
GDP per capita (PPP int'l $)	44 (96%)	44 (96%)	45 (98%)	45 (98%)
Health expenditure (% of GDP)	44 (96%)	45 (98%)	45 (98%)	45 (98%)
Health expenditure (% of government expenditures)	44 (96%)	45 (98%)	45 (98%)	45 (98%)
Access to improved sanitation facilities	44 (96%)	44 (96%)	45 (98%)	45 (98%)
Access to improved water source	44 (96%)	44 (96%)	45 (98%)	45 (98%)
Measles immunization	44 (96%)	44 (96%)	46 (100%)	46 (100%)
Net ODA received (% of GNI)	44 (96%)	44 (96%)	46 (100%)	46 (100%)
Out-of-pocket health expenditure	44 (96%)	45 (98%)	45 (98%)	45 (98%)
Adult prevalence of HIV	43 (93%)	43 (93%)	43 (93%)	43 (93%)
Physicians	33 (72%)	24 (52%)	23 (50%)	36 (78%)
Human development index	31 (67%)	31 (67%)	39 (85%)	46 (100%)
Hospital beds	29 (63%)	8 (17%)	8 (17%)	39 (85%)
Births attended by skilled health staff	24 (52%)	27 (59%)	37 (80%)	37 (80%)
Malnutrition prevalence (height for age)	24 (52%)	25 (54%)	34 (74%)	35 (76%)
Malnutrition prevalence (weight for age)	23 (50%)	25 (54%)	34 (74%)	34 (74%)
Prevalence of wasting	23 (50%)	25 (54%)	34 (74%)	34 (74%)
Public spending on education (% of GDP)	23 (50%)	19 (41%)	34 (74%)	41 (89%)
Pregnant women receiving prenatal care	22 (48%)	23 (50%)	38 (83%)	38 (83%)
Children 1-2yrs old receiving all basic vaccinations	18 (39%)	20 (43%)	26 (57%)	31 (67%)
Gini index	18 (39%)	17 (37%)	22 (48%)	28 (61%)
Paved roads	18 (39%)	33 (72%)	19 (41%)	20 (43%)
Adult female literacy rate	17 (37%)	12 (26%)	35 (76%)	44 (96%)
Antenatal care during first 5 months of pregnancy	16 (35%)	19 (41%)	19 (41%)	23 (50%)
Seeking ARI treatment	16 (35%)	16 (35%)	33 (72%)	34 (74%)
Births delivered at a health facility	16 (35%)	19 (41%)	19 (41%)	32 (70%)
Births delivered by caesarean section	16 (35%)	18 (39%)	18 (39%)	30 (65%)

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Median age at pregnancy (or first birth)	16 (35%)	18 (39%)	18 (39%)	24 (52%)
Median number of living children per household	16 (35%)	18 (39%)	18 (39%)	24 (52%)
Pregnant women receiving ≥4 prenatal care visits	16 (35%)	18 (39%)	21 (46%)	32 (70%)
Unmet need for contraception	15 (33%)	14 (30%)	18 (39%)	30 (65%)
Women with at least some secondary education	15 (33%)	19 (41%)	23 (50%)	29 (63%)
Teenage mothers	14 (30%)	15 (33%)	15 (33%)	25 (54%)
Low-birthweight babies	13 (28%)	14 (30%)	30 (65%)	33 (72%)
Female age at first marriage	12 (26%)	15 (33%)	17 (37%)	27 (59%)
Poverty headcount ratio at national poverty line	8 (17%)	9 (20%)	15 (33%)	31 (67%)
Maternal mortality ratio	6 (13%)	0 (0%)	17 (37%)	31 (67%)
Households with television	5 (11%)	5 1(1%)	24 (52%)	30 (65%)
Adult female mortality rate	4 (9%)	4 (9%)	46 (100%)	46 (100%)
Births with a postnatal visit ≤2 days after delivery	0 (0%)	0 (0%)	10 (22%)	22 (48%)
Children with fever receiving antimalarial drugs	0 (0%)	0 (0%)	30 (65%)	35 (76%)
Community health workers	0 (0%)	0 (0%)	2 (4%)	11 (24%)
Diarrhea treatment	0 (0%)	0 90%)	25 (54%)	30 (65%)
Exclusive breastfeeding	0 (0%)	1 (2%)	36 (78%)	36 (78%)
Internet users	0 (0%)	0 (0%)	46 (100%)	46 (100%)
Median years of maternal education	0 (0%)	0 (0%)	6 (13%)	18 (39%)
Nurses and midwives	0 (0%)	0 (0%)	6 (13%)	34 (74%)
Population coverage of cell phones	0 (0%)	0 (0%)	26 (57%)	44 (96%)
Pregnant women using malaria preventive treatment	0 (0%)	0 (0%)	3 (7%)	16 (35%)
Public spending on education (% of government expenditure)	0 (0%)	0 (0%)	25 (54%)	37 (80%)
Road density	0 (0%)	0 (0%)	8 (17%)	22 (48%)
Safety and Rule of Law	0 (0%)	0 (0%)	46 (100%)	46 (100%)
Use of insecticide-treated bed nets	0 (0%)	0 (0%)	30 (65%)	35 (76%)
Vitamin A supplementation coverage	0 (0%)	0 (0%)	37 (80%)	42 (91%)

[a] Of the 70 indicators identified, only these 61 had sufficient data from at least one country for the period 2000 to 2011 to be included, see Methods.

[b] defined as in the Methods: indicator data between 2006 and 2011

Abbreviations: DAC= Development Assistance Committee; ODA= Official Development Assistance; GDP= gross domestic product; ARI= acute respiratory infection; HIV= Human Immunodeficiency Virus

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Table S3. Difference in median under-five mortality ARRs between countries reporting and countries not reporting indicator data for the 2000-2011 period.

		Under-five mortality	
Indicator	**No. (%) of countries reporting indicator**	**Difference in median ARR[a]**	**p-value[b]**
Adult female mortality rate	46 (100%)	n/a	n/a
Fertility rate	46 (100%)	n/a	n/a
Internet users	46 (100%)	n/a	n/a
Measles immunization	46 (100%)	n/a	n/a
Net bilateral aid flows from DAC donors	46 (100%)	n/a	n/a
Net ODA received (% of GNI)	46 (100%)	n/a	n/a
Net ODA received per capita	46 (100%)	n/a	n/a
Safety and Rule of Law	46 (100%)	n/a	n/a
Urban population prevalence	46 (100%)	n/a	n/a
External resources for health	45 (98%)	1.8	0.52
Female labor participation rate	45 (98%)	-2.5	0.10
GDP per capita	45 (98%)	1.8	0.52
Health expenditure (% of GDP)	45 (98%)	1.8	0.52
Health expenditure (% of government expenditure)	45 (98%)	1.8	0.52
Access to improved sanitation facilities	45 (98%)	-2.5	0.10
Access to improved water source	45 (98%)	-2.5	0.10
Labor force participation rate among women	45 (98%)	-2.5	0.10
Maternal mortality ratio	45 (98%)	-2.5	0.10
Out-of-pocket health expenditure	45 (98%)	1.8	0.52
Adult prevalence of HIV	43 (93%)	-1.8	0.12
Human development index	39 (85%)	-0.4	0.26
Pregnant women receiving prenatal care	38 (83%)	-0.7	0.25
Births attended by skilled health staff	37 (80%)	-0.7	0.40
Exclusive breastfeeding	36 (78%)	-0.7	0.34
Adult female literacy rate	35 (76%)	1.8	0.16
Vitamin A supplementation coverage	35 (76%)	-0.8	0.18
Malnutrition prevalence (height for age)	34 (74%)	-0.7	0.22
Malnutrition prevalence (weight for age)	34 (74%)	-0.7	0.22
Prevalence of wasting	34 (74%)	-0.7	0.22
Public spending on education (% of GDP)	34 (74%)	0.6	0.81
Seeking ARI treatment	33 (72%)	-0.2	0.87
Children with fever receiving antimalarial drugs	30 (65%)	0.5	0.76
Low-birthweight babies	30 (65%)	-1.0	0.47
Use of insecticide-treated bed nets	30 (65%)	1.0	0.52
Children 1 year old receiving all basic vaccinations	26 (57%)	-1.6	0.13
Population coverage of cell phones	26 (57%)	-1.6	0.22
Diarrhea treatment	25 (54%)	**1.0**	**0.09**
Public spending on education (% of gov. expenditure)	25 (54%)	-0.5	0.60
Households with television	24 (52%)	**-1.7**	**0.04**
Physicians	23 (50%)	**-1.9**	**<0.01**
Women with at least some secondary education	23 (50%)	-1.8	0.17
Gini index	22 (48%)	0.4	0.98
Pregnant women receiving ≥4 prenatal care visits	21 (46%)	**-2.0**	**<0.01**
Antenatal care during first 5 months of pregnancy	19 (41%)	**-2.5**	**<0.01**
Births delivered at a health facility	19 (41%)	**-2.5**	**<0.01**
Paved roads	19 (41%)	0.3	0.75

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Births delivered by caesarean section	18 (39%)	**-2.2**	**<0.01**
Median age at pregnancy (or first birth)	18 (39%)	**-2.7**	**<0.01**
Median number of living children per household	18 (39%)	**-2.7**	**<0.01**
Unmet need for contraception	18 (39%)	-1.5	0.24
Female age at first marriage	17 (37%)	**-1.9**	**0.05**
Poverty headcount ratio at national poverty line	15 (33%)	0.3	0.98
Teenage mothers	15 (33%)	**-2.0**	**<0.01**
Births with a postnatal visit ≤2 days after delivery	10 (22%)	**-2.2**	**0.02**
Hospital beds	8 (17%)	-2.0	0.20
Road density	8 (17%)	-1.1	0.86
Median years of maternal education	6 (13%)	**-2.7**	**0.01**
Nurses and midwives	6 (13%)	-1.6	0.13
Pregnant women using malaria preventive treatment	3 (7%)	-1.6	0.22
Community health workers	2 (4%)	-1.4	0.50

[a] Calculated as (median ARR of countries not reporting the indicator) – (median ARR of countries reporting the indicator)
[b] Indicators with statistically significant (p<0.10) differences are **bold**

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Table S4. Median baseline indicator values and corresponding ARC for the 2000-2011 period.

Indicator	N	Median 2000 value (IQR)	Median 2000-2011 ARC (IQR)
Socio-demographics			
Access to improved sanitation facilities (%)	45	25 (13 - 45)	1.6 (0.4 - 2.7)
Access to improved water source (%)	45	62 (51 - 79)	1.1 (0.2 - 1.8)
Adult female literacy rate (%)	35	54 (37 - 72)	1.2 (0.8 - 2.8)
Female age at first marriage (years)	17	21 (20 - 22)	0.2 (-0.1 - 0.6)
Female labor participation rate (%)	45	46 (43 - 49)	0.1 (-0.1 - 0.3)
Fertility rate (births per woman)	46	6 (5 - 6)	-1.4 (-2.0 - -0.9)
GDP per capita (PPP int'l $)	45	990 (680 – 1,900)	4.3 (2.8 - 6.1)
Gini index (0 to 100)	22	43 (41 - 50)	0.0 (-1.0 - 0.6)
Human development index (0 to 1)	39	0.38 (0.31 - 0.48)	1.1 (0.7 - 1.9)
Labor force participation rate among women (%)	45	66 (50 - 76)	0.3 (-0.1 - 0.6)
Median age at pregnancy (or first birth) (years)	18	19 (19 - 20)	0.2 (0.1 - 0.2)
Median number of living children per household (N)	18	2 (2 - 3)	0.1 (-0.6 - 0.4)
Median years of maternal education (years)	6	4 (3 - 6)	2.4 (0.9 - 4.2)
Poverty headcount ratio at national poverty line (%)	15	46 (39 - 55)	-1.2 (-3.0 - -0.5)
Teenage mothers (%)	15	22 (19 - 32)	-1.1 (-2.5 - -0.6)
Urban population prevalence (%)	46	35 (22 - 44)	1.3 (0.7 - 1.7)
Women with at least some secondary education (%)	23	16 (10 - 30)	3.2 (2.5 - 5.3)
Maternal health			
Adult female mortality rate (rate per 1,000 persons)	46	360 (280 - 420)	-1.2 (-1.8 - -0.6)
Antenatal care during first 5 months of pregnancy (%)	19	57 (45 - 67)	1.4 (0.5 - 3.4)
Maternal mortality ratio (rate per 100,000 births)	45	550 (400 - 840)	-3.6 (-4.5 - -20)
Pregnant women receiving ≥4 prenatal care visits (%)	21	46 (23 - 62)	1.7 (-0.3 - 4.0)
Pregnant women receiving prenatal care (%)	38	77 (64 - 88)	1.3 (0.6 - 2.7)
Unmet need for contraception (%)	18	27 (22 - 32)	0.6 (-1.2 - 1.9)
Access to health care			
Births attended by skilled health staff (%)	37	47 (39 - 60)	2.0 (0.3 - 3.4)
Births delivered at a health facility (%)	19	43 (34 - 55)	1.8 (0.1 - 3.7)
Births delivered by caesarean section (%)	18	3 (1 - 4)	5.3 (1.6 - 7.6)
Births with a postnatal visit ≤2 days after delivery (%)	10	8 (5 - 12)	16.0 (8.0 - 21.0)
Children with fever receiving antimalarial drugs (%)	30	53 (32 - 61)	-4.8 (-7.5 - -0.2)
Community health workers (rate per 1,000 persons)	2	0.2 (0.2 - 0.3)	15.0 (13.0 - 17.0)
Diarrhea treatment (%)	25	39 (28 - 45)	2.3 (-1.3 - 5.7)
Hospital beds (rate per 1,000 persons)	8	1.2 (0.4 – 2.0)	-2.3 (-4.6 - -1.0)
Nurses and midwives (rate per 1,000 persons)	6	1.2 (0.6 - 1.6)	-3.0 (-5.0 - -1.0)

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Physicians (rate per 100,000 persons)	23	5.7 (2.9 – 12.0)	1.2 (-0.6 - 5.2)
Pregnant women using malaria preventive treatment (%)	3	36 (29 - 37)	10.0 (-1.8 - 15.0)
Seeking ARI treatment (%)	33	40 (27 - 55)	1.7 (-0.3 - 5.0)
Child survival interventions			
Children 1 year old receiving all basic vaccinations (%)	26	41 (29 - 65)	2.8 (1.1 - 5.3)
Exclusive breastfeeding (%)	36	25 (14 - 37)	4.1 (-0.2 - 8.6)
Measles immunization (%)	46	69 (49 - 76)	1.3 (0.3 - 2.5)
Use of insecticide-treated bed nets (%)	30	2 (1 - 4)	34.0 (28.0 - 42.0)
Vitamin A supplementation coverage (%)	37	91 (78 - 96)	-0.3 (-2.0 - 0.7)
Clinical and health conditions			
Adult prevalence of HIV (%)	43	4 (1 - 8)	-0.8 (-3.5 - 1.7)
Low-birthweight babies (%)	30	13 (11 - 17)	-0.3 (-3.6 - 1.0)
Malnutrition prevalence (height for age) (%)	34	40 (34 - 48)	-1.1 (-2.3 - 0.2)
Malnutrition prevalence (weight for age) (%)	34	22 (18 - 27)	-1.7 (-3.2 - -0.9)
Prevalence of wasting (%)	34	9 (7 - 12)	-1.9 (-5.2 - 0.5)
Governance and financing			
External resources for health (%)	45	13 (4.6 - 20)	6.4 (-1.0 - 10.0)
Health expenditure (relative to GDP) (%)	45	5 (4 - 6)	1.4 (0.5 - 3.3)
Health expenditure (relative to government) (%)	45	9 (7 - 10)	2.5 (-0.4 - 3.7)
Net bilateral aid flows from DAC donors (US $ in millions)	46	120 (40 - 260)	9.1 (5.0 - 16.0)
Net ODA received (% of GNI) (%)	46	9 (4 - 13)	-0.9 (-5.4 - 5.4)
Net ODA received per capita (US$)	46	23 (15 - 41)	7.4 (2.4 - 13.0)
Out-of-pocket health expenditure (%)	45	43 (26 - 58)	-1.7 (-3.9 - -0.6)
Public spending on education (% of GDP) (%)	34	4 (3 - 5)	2.1 (0.2 - 3.9)
Public spending on education (% of gov. expenditure) (%)	25	16 (14 - 19)	1.6 (-0.2 - 3.0)
Safety and Rule of Law (0 to 100)	46	54 (43 - 66)	-0.0 (-0.9 - 0.4)
Other			
Households with television (%)	24	18 (6 - 29)	6.7 (4.1 – 10.0)
Internet users (rate per 100 persons)	46	0.2 (0.1 - 0.5)	34.0 (25.0 - 46.0)
Paved roads (%)	19	12 (10 - 29)	1.2 (-1.4 - 3.1)
Population coverage of cell phones (%)	26	37 (17 - 82)	8.5 (1.3 - 16.0)
Road density (km of road per 100 sq km)	8	8 (4 - 20)	1.4 (0.3 - 6.2)

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Table S5. Crude and adjusted associations between indicators and under-five mortality ARR[a].

		Crude		Adjusted[b,c]	
Indicator	N	β	p-value	β	p-value
Socio-demographics					
Access to improved sanitation facilities (%)[e]	45	0.07	0.36	0.17	0.27
Access to improved water source (%)	45	-0.05	0.39	0.01	0.40
Adult female literacy rate (%)	35	-0.07	0.37	-0.06	0.38
Female age at first marriage (years)	17	-0.07	0.39	-0.33	0.32
Female labor participation rate (%)	45	-0.39	0.33	-0.58	0.33
Fertility rate (births per woman)	46	0.09	0.38	0.18	0.35
GDP per capita (PPP int'l $)[f]	45	0.20	0.13	0.23	0.09
Gini index (0 to 100)	22	-0.15	0.32	0.35	0.22
Human development index (0 to 1)	39	0.50	0.21	0.48	0.29
Labor force participation rate among women (%)	45	-0.01	0.40	0.23	0.37
Median age at pregnancy (or first birth) (years)	18	1.39	0.34	-0.23	0.39
Median number of living children per household (N)	18	-0.08	0.39	-1.06	<0.01
Median years of maternal education (years)	6	-0.02	0.37		
Poverty headcount ratio at national poverty line (%)	15	-0.26	0.20	-0.44	0.05
Teenage mothers (%)	15	-0.25	0.30	-0.81	0.12
Urban population prevalence (%)	46	0.42	0.21	0.28	0.31
Women with at least some secondary education (%)	23	-0.09	0.24	-0.04	0.36
Maternal health					
Adult female mortality rate (rate per 1,000 persons)	46	-0.39	0.10	-0.35	0.18
Antenatal care during first 5 months of pregnancy (%)	19	0.21	0.17	0.59	0.01
Maternal mortality ratio (rate per 100,000 births)[d]	45	-0.40	<0.01	-0.86	<0.01
Pregnant women receiving ≥4 prenatal care visits (%)	21	0.09	0.28	0.11	0.24
Pregnant women receiving prenatal care (%)	38	-0.24	0.22	-0.08	0.38
Unmet need for contraception (%)	18	0.08	0.24	0.07	0.30
Access to health care					
Seeking ARI treatment (%)[d]	33	0.25	0.02	0.27	0.02
Births attended by skilled health staff (%)[d]	37	-0.08	0.34	0.04	0.39
Births delivered at a health facility (%)[d]	19	0.01	0.39	0.12	0.30
Births delivered by caesarean section (%)[d]	18	0.12	0.20	0.18	0.10
Births with a postnatal visit ≤2 days after delivery (%)[d]	10	-0.05	0.25	-0.32	<0.01
Children with fever receiving antimalarial drugs (%)[d]	30	0.08	0.04	0.14	0.02
Community health workers (rate per 1,000 persons)	2				
Diarrhea treatment (%)[d]	25	-0.06	0.19	-0.06	0.29
Hospital beds (rate per 1,000 persons)	8	-0.07	0.37	-0.81	0.01
Nurses and midwives (rate per 1,000 persons)	6	0.17	0.08		
Physicians (rate per 100,000 persons)	23	0.04	0.35	0.12	0.12
Pregnant women using malaria preventive treatment (%)	3	0.04	0.12		
Child survival interventions					
Children 1 year old receiving all basic vaccinations (%)[d]	26	-0.12	0.24	-0.11	0.34
Exclusive breastfeeding (%)[d]	36	-0.01	0.38	-0.01	0.39
Measles immunization (%)[d]	46	-0.03	0.38	0.10	0.31
Use of insecticide-treated bed nets (%)[d]	30	0.02	0.27	0.03	0.25
Vitamin A supplementation coverage (%)[d]	35	0.05	0.33	0.04	0.37
Clinical and health conditions					
Adult prevalence of HIV (%)	43	-0.08	0.22	-0.06	0.32
Low-birthweight babies (%)[d]	30	0.15	0.11	0.18	0.10
Malnutrition prevalence (height for age) (%)[d]	34	0.05	0.38	-0.01	0.40

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Malnutrition prevalence (weight for age) (%)[d]	34	-0.13	0.24	-0.30	0.07
Prevalence of wasting (%)[d]	34	-0.05	0.33	-0.10	0.22
Governance and financing					
External resources for health (%)	45	0.03	0.29	0.04	0.23
Health expenditure (% of GDP) (%)	45	0.21	0.05	0.22	0.07
Health expenditure (% of government expenditure) (%)[f]	45	0.04	0.32	0.11	0.16
Net bilateral aid flows from DAC donors (US$ in millions)	46	-0.02	0.34	-0.05	0.24
Net ODA received (relative to GNI) (%)	46	-0.01	0.37	-0.04	0.24
Net ODA received per capita (US$)	46	-0.04	0.24	-0.09	0.09
Out-of-pocket health expenditure (%)[f]	45	-0.13	0.17	-0.26	0.04
Public spending on education (% of GDP) (%)	34	-0.10	0.23	-0.20	0.06
Public spending on education (% of gov. expenditure) (%)	25	0.00	0.40	-0.10	0.31
Safety and Rule of Law (0 to 100)	46	0.05	0.38	-0.03	0.39
Other					
Households with television (%)	24	0.04	0.36	-0.11	0.29
Internet users (rate per 100 persons)	46	0.03	0.17	0.02	0.27
Paved roads (%)	19	0.04	0.36	0.07	0.23
Population coverage of cell phones (%)	26	-0.04	0.31	-0.07	0.13
Road density (km of road per 100 sq. km)	8	0.01	0.38	-0.05	0.28

[a] 10 of 70 indicators not shown in table because sufficient data were missing for all 46 countries

[b] N>2 required to run crude robust linear regression models; N>6 required to run adjusted robust linear regression models which include a minimum of four covariates.

[c] All results adjusted for improved water source, health expenditure (relative to GDP), adult HIV prevalence, and urban population prevalence unless otherwise noted below:

[d] further adjusted for receipt of prenatal care

[e] not adjusted for improved water source

[f] not adjusted for health expenditure (relative to GDP)

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STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	
Title and abstract	1	Title: Factors associated with declining under-five mortality rates from 2000 to 2011: An ecological analysis of 46 African countries An abstract is provided in the manuscript summarizing what was done and what was found
Introduction		
Background/rationale	2	Under-five mortality (U5M) rates have declined worldwide yet African children are nearly 16 times more likely to die under age five than children from high income nations and the decline in mortality has not been as rapid as hoped. Despite progress, Africa is not on track to reach Millennium Development Goal #4 of reducing U5M by two-thirds between 1990 and 2015. With variable progress across countries in improving child survival in Africa, understanding factors associated with the most rapid changes in U5M reductions could assist regional and country efforts to improve child survival.
Objectives	3	We sought to identify direct and indirect factors influencing how rapidly countries reduce U5M, as evidenced by their annual rate of reduction (ARR).
Methods		
Study design	4	An ecological analysis of country-level data was used to determine which factors previously reported to reduce U5M are also the strongest predictors of larger ARRs in Africa.
Setting	5	Available data from the 46 countries in the WHO African Region during the period 2000 to 2011.
Participants	6	As an ecological study, the "participants" include the 46 countries and not individuals.
Variables	7	Outcome: country-specific U5M rates from annual estimates provided by www.childmortality.org, the data used in the UNICEF Reports on *Levels and Trends in Child Mortality,* were used to calculate country-specific ARRs for the period 2000-2011.
Data sources/ measurement	8*	See #7 above.
Bias	9	Because survey data used in this study is not collected on an annual basis, actual data for 2000 and 2011 were often not available, data from years close to 2000 and 2011 had to be used to calculated the change in indicator coverage (predictor variable of interest). To minimize bias due to improperly extrapolating data over the time period, the following criteria were used. Indicator data had to be reported for one of the years between 1998 and 2003, termed *2000 indicator data*, and also reported for one of the years between 2006 and 2011, termed *2011 indicator data*. Furthermore, indicator values that most closely corresponded to the years 2000 and 2011 had to also be at least five years apart. If any of these criteria were not met from a given country, change in the coverage for that particular indicator was not calculated and was considered missing. Additionally, with the small sample size of 46 countries, regression modelling may have been susceptible to bias from data outliers. To minimize this possibility while retaining as much data in the analysis as possible, robust regression was used in the analysis using iteratively reweighted least squares to minimize the influence of outlying observations.
Study size	10	46 is the number of countries in the WHO African Region, our collaborator and funding agency for the project.
Quantitative variables	11	All predictor variables were modelled as continuous variables (e.g., range of vaccination coverage levels, median age of first pregnancy, etc.)

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Statistical methods	12	As described in the Methods section, robust linear regression was used to model the association between the change in coverage of an indicator and U5M ARR, while controlling for potential confounders. A separate model was used for each predictor of interest. Given the small sample size (n=46 at most), a decision was also made *a priori* to include no more than five covariates in the multivariable analyses to avoid overfitting. We selected the following indicator ARCs for inclusion as covariates in each model based on previous ecological studies, consideration of what macro- or system-level factors would influence the majority of the indicators, and having nearly complete data: access to improved water source, health expenditure (relative to gross domestic product [GDP]), adult HIV prevalence, urban population prevalence, and receipt of ANC (when applicable). All regression models included these core indicator ARCs as covariates unless expected to be highly correlated with the predictor indicator of interest. No subgroup, interaction, or sensitivity analyses were conducted. Figure 2 and Supplemental Table S2 show the completeness of reporting of indicators by country. For many indicators, a number of countries were missing sufficient data to calculate the ARC. Regression modelling was conducted for all predictor indicators regardless of the number of countries missing data, and these are presented in Supplemental Table S5. However, out of concern that missing data was associated with ARR (Figure 3 and Supplemental Table S3), main results are only provided for indicators with at least 50% complete reporting (e.g., >=23 of the 46 countries).
Results		
Participants	13*	Not applicable.
Descriptive data	14*	Not applicable.
Outcome data	15*	Table 1 shows the U5M ARR for each country in the analysis.
Main results	16	Of the 70 indicators considered in the analysis, seven indicators shows a strong and statistically significant association with U5M ARR. These included seeking treatment for ARI, GDP per capita, health expenditure relative to GDP, out-of-pocket expenses, prevalence of underweight, maternal mortality ratio, and public spending on education relative to GDP. Crude and adjusted associations are provided in Table 3 and for all associations in Supplemental Table S5).
Other analyses	17	Not applicable.
Discussion		
Key results	18	Our study represents the most comprehensive analysis to date of health indicators and other determinants of health as predictors of declining U5M in Africa. From 70 factors considered, we could use 41 indicators meaningfully. A more rapid scale-up of six factors were associated with a favorable ARR rise (i.e., higher rate of U5M decline) between 2000 and 2011: higher rates of seeking treatment for ARI, higher GDP per capita, higher health expenditure relative to GDP, lower out-of-pocket expenses, lower prevalence of underweight, and lower maternal mortality ratio. The strongest association was for maternal mortality ratio (β= -0.86), indicating that a one-percent increase in the annual reduction of the maternal mortality ratio was associated with a 0.86 percent increase in the U5M ARR. An inverse association between increasing ARC for public spending on education relative to GDP and declines in U5M ARR was counterintuitive. A possible explanation is that it represents the challenge of competing priorities for extremely resource-limited countries, where increases in education relative to GDP may adversely affect spending in other areas, such as health.
Limitations	19	Four important limitations are discussed in the Discussion section: a. Mortality and indicator data were obtained from secondary data sources. b. The ecological, cross-sectional study design. c. The time period for calculating the indicator ARCs did not always fully overlap with the time period for calculating mortality ARRs.

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		d. The small sample size (at most n=46 countries) limits the validity of many associations and prevents adjustment for many covariates. In spite of these limitations, the unique strengths of our study include our broad identification of factors potentially relevant to child survival, beyond those typically used from Demographic and Health Surveys and Countdown to 2015. We also made statistical efforts to minimize bias or distortion from outliers, without excluding them.
Interpretation	20	Our findings highlight the role of financing, economy, and the broader health system to more rapidly reduce an already declining, albeit slowly, U5M rate above and beyond the contribution of individual interventions. Our study also highlights the ongoing challenge of obtaining indicator reporting from 100% of countries. Results for 29 of the 70 indicators could not be calculated, or the results could not be considered representative, given that more than half the countries were missing the necessary data.
Generalisability	21	By design, our results are generalizable to the WHO African Region. Our findings may not be valid outside of the African context.
Other information		
Funding	22	Funding for this project was provided by the World Health Organization. Support for data management came from the Vanderbilt Institute for Clinical and Translational Research (grant UL1 TR000445 from the National Center for Advancing Translational Sciences at the National Institutes of Health).

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Factors associated with declining under-five mortality rates from 2000 to 2013: An ecological analysis of 46 African countries

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Factors associated with declining under-five mortality rates from 2000 to 2013: An ecological analysis of 46 African countries

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ABSTRACT

Objective: Inadequate overall progress has been made towards the 4th Millennium Development Goal of reducing under-five mortality rates by two-thirds between 1990 and 2015. Progress has been variable across African countries. We examined health, economic, and social factors potentially associated with reductions in under-five mortality (U5M) from 2000-2013

Setting: Ecological analysis using publicly available data from the 46 nations within the World Health Organization African Region.

Outcome measures: We assessed the annual rate of change (ARC) of 70 different factors and their association with the annual rate of reduction (ARR) of U5M rates using robust linear regression models.

Results: Most factors improved over the study period for most countries, with the largest increases seen for economic or technological development and external financing factors. The median (interquartile range) U5M ARR was 3.6% (2.8-5.1%). Only four of 70 factors demonstrated a strong and significant association with U5M ARRs, adjusting for potential confounders. Higher ARRs were associated with more rapidly increasing coverage of seeking treatment for acute respiratory infection (β=0.22 [i.e., a 1% increase in the ARC was associated with a 0.22% increase in ARR]; 90% confidence interval: 0.09 - 0.35; p=0.01), increasing health expenditure relative to gross domestic product (β= 0.26; 95% CI: 0.11 - 0.41; p=0.02), increasing fertility rate (β=0.54; 95% CI: 0.07 - 1.02; p=0.07), and decreasing maternal mortality ratio (β= -0.47; 95% CI: -0.69 - -0.24; p<0.01). The majority of factors showed no association or raised validity concerns due to missing data from a large number of countries.

Conclusions: Improvements in socio-demographic, maternal health, and governance and financing factors were more likely associated with U5M ARR. These underscore the essential role of contextual factors facilitating child health interventions and services. Surveillance of these factors could help monitor which countries need additional support in reducing under-five mortality.

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STRENGTHS AND LIMITATIONS OF THIS STUDY

- This study represents a comprehensive analysis of health factors and other determinants of health associated with declining under-five mortality in Africa.
- Study findings highlight the role of financing, economy, and the broader health system in more rapidly reducing an already declining, albeit slowly, under-five mortality rate above and beyond the contribution of individual interventions.
- Inferences of causality may be limited due to the ecological study design and that the time periods for change in coverage of the factors did not always fully overlap with time periods for change in under-five mortality.
- The small sample size (at most n=46 countries, but often smaller due to missing data) limits the validity of some associations and prevents adjustment for too covariates.

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INTRODUCTION

Under-five mortality (U5M) rates have declined worldwide from an estimated 90 deaths per 1,000 live births in 1990 to 46 deaths per 1,000 in 2013, representing an average annual rate of reduction (ARR) of 3.0% [1]. Higher income regions had an estimated U5M rate of 6 deaths per 1,000 live births in 2012 (3.8% ARR); they account for only 1.4% of all under-five deaths. In contrast, the World Health Organization (WHO) African Region (including 46 countries in 2012; Figure 1, Table 1) experienced 90 under-five deaths per 1,000 live births in 2013 and a 1990-2013 ARR of 2.9%[1]. Thus, African children are nearly 16 times more likely to die under age five than children from high income nations, though progress in Africa is being made.

Table 1. Under-five mortality rates and annual rate of reduction (ARR) for the 46 countries in the WHO African Region, 2000-2013.

	Under-five mortality rate (per 1,000) in the given year[a]			ARR (%) 2000 to 2013	ARR (%) in 2000-2015 needed to meet MDG
Country	2000	2013	MDG for 2015		
Algeria[b]	39.6	25.2	15.7	3.5	6.2
Angola	216.7	167.4	75.3	2.0	7.0
Benin	146	85.3	59.8	4.1	6.0
Botswana	85.1	46.6	16.5	4.6	10.9
Burkina Faso	185.8	97.6	67.4	5.0	6.8
Burundi	148.9	82.9	56.9	4.5	6.4
Cameroon	151.2	94.5	45.5	3.6	8.0
Cape Verde[b]	35.3	26	21.0	2.4	3.5
Central African Republic	174.1	139.2	59.0	1.7	7.2
Chad	190.7	147.5	71.6	2.0	6.5
Comoros	101.3	77.9	41.8	2.0	5.9
Congo	121.4	49.1	30.7	7.0	9.2
Côte d'Ivoire	146.1	100	50.5	2.9	7.1
Dem. Rep. of the Congo	175.9	118.5	58.7	3.0	7.3
Equatorial Guinea	142.4	95.8	61.3	3.0	5.6
Eritrea	89.3	49.9	50.2	4.5	3.8
Ethiopia	145.5	64.4	68.3	6.3	5.0
Gabon	84.6	56.1	30.9	3.2	6.7
Gambia	119	73.8	56.6	3.7	5.0
Ghana	101.3	78.4	42.7	2.0	5.8
Guinea	170.2	100.7	79.2	4.0	5.1
Guinea-Bissau	180.8	123.9	74.9	2.9	5.9
Kenya	110.9	70.7	32.9	3.5	8.1
Lesotho	114.6	98	28.8	1.2	9.2
Liberia	175.2	71.1	82.7	6.9	5.0
Madagascar	110.6	56	53.6	5.2	4.8
Malawi	174.2	67.9	81.8	7.2	5.0
Mali	219.9	122.7	84.7	4.5	6.4
Mauritania	113.1	90.1	39.3	1.7	7.0
Mauritius[b]	18.6	14.3	7.7	2.0	5.9
Mozambique	168.5	87.2	79.0	5.1	5.0
Namibia	75.5	49.8	24.5	3.2	7.5

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Country	Under-five mortality rate (per 1,000) in the given year[a]			ARR (%) 2000 to 2013	ARR (%) in 2000-2015 needed to meet MDG
	2000	2013	MDG for 2015		
Niger	226.9	104.2	109.1	6.0	4.9
Nigeria	187.7	117.4	71.1	3.6	6.5
Rwanda	181.9	52	50.6	9.6	8.5
Sao Tome and Principe	89.3	51	36.8	4.3	5.9
Senegal	137	55.3	47.0	7.0	7.1
Seychelles[b]	14.2	14.2	5.5	0.0	6.3
Sierra Leone	231.5	160.6	89.2	2.8	6.4
South Africa	74.3	43.9	20.3	4.0	8.6
Swaziland	122.5	80	24.6	3.3	10.7
Togo	121.8	84.7	48.8	2.8	6.1
Uganda	147	66.1	59.6	6.1	6.0
United Rep. of Tanzania	131.5	51.8	55.7	7.2	5.7
Zambia	168.8	87.4	64.2	5.1	6.4
Zimbabwe	102.6	88.5	24.9	1.1	9.4

[a] U5M rate data obtained from www.childmortality.org, accessed June 2015
[b] Countries with U5M rates <40 per 1,000 in 2013 are considered to be on track despite having 1990-2013 ARRs of less than 4%.
Abbreviations: ARR, annual rate of reduction; MDG, Millennium Development Goal

In 2000, the 4th Millennium Development Goal (MDG4)[2] proposed the reduction of the U5M rate by two-thirds between 1990 and 2015, requiring a global average ARR of 4.4% to reach this goal. Africa has more than tripled its U5M ARR from 1.3% in 1990-2000 to 4.2% in 2000-2013, but the ARR achievements are inadequate to meet the MDG4 targets[1]. Proven cost-effective child survival interventions and proposed delivery channels for those interventions need to be scaled-up[3-7]. The *Countdown to 2015 for Maternal, Newborn, and Child Survival* initiative was created in 2005 to monitor the use of these evidence-based interventions for maternal, neonatal, and child health[8]. In 2012, the Countdown's 75 priority countries accounted for >95% of all maternal and child deaths[9,10]. Of note, 41 (55%) of the 75 Countdown priority countries come from the 46 WHO African Region countries (the exceptions were Algeria, Cape Verde, Mauritius, Namibia, and Seychelles).

In 2006, WHO, the United Nations Children's Fund, and the World Bank developed Child Survival Strategy for the African Region aimed to support countries' efforts to reduce child deaths from preventable and treatable conditions by scaling up coverage of effective interventions[6]. These include antenatal care, post-natal care, infant and young child feeding, the expanded program on immunizations, integrated management of common childhood illness, prevention of mother-to-child transmission of human immunodeficiency virus (HIV) and use of insecticide treated nets, among others. As of 2013, 38 of the 46 African countries had developed or updated national child survival policies, strategies, and plans. Population coverage in the African Region has increased with time, leading to high coverage of measles vaccination, neonatal tetanus protection, antiretroviral drugs for prevention of mother-to-child transmission of HIV, and at least one antenatal care visit for every pregnant woman[11]. Coverage of other interventions remain low, however, in spite of recent increases in coverage, including exclusive breastfeeding, pneumococcus and *Haemophilus influenzae* vaccination, treatment of

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childhood diarrhea, pneumonia and malaria, and use of insecticide treated nets. Despite progress, Africa is not on track to reach MDG4 due to inconsistent and suboptimal implementation and scale-up of evidence-based maternal, neonatal, and child health interventions[10]. With variable progress across countries in improving child survival in Africa, understanding factors associated with the most rapid changes in U5M reductions could assist regional and country efforts to improve child survival in the post-2015 era.

We sought to identify proximal (e.g., interventions and services) and distal (e.g., socio-economic) factors influencing how rapidly countries reduce U5M, as evidenced by their ARR. An ecological analysis of country-level data was used to determine which factors previously reported to reduce U5M are also the factors most strongly associated with higher ARRs in Africa.

METHODS

The study was approved by the Institutional Review Boards at Vanderbilt University.

Mortality data were obtained for the period 2000-2013, while data on all factors of interest were obtained for the period 1998-2011. These are described in detail below.

Under-five mortality data

We obtained country-specific U5M rates from annual estimates provided by www.childmortality.org, the data used in the United Nations Children's Fund (UNICEF) Report on *Levels and Trends in Child Mortality*. For each of the 46 WHO African Region countries, the estimated U5M rates for 2000 and 2013 (the latest estimates available at the time of the analysis [accessed June 2014]) were obtained and the ARR from 2000 to 2011 was calculated. Use of the ARR as an outcome facilitates interpretation of results in the context of MDG4 progress metrics.

The U5M ARR reflects a constant rate of change in the U5M rate between two time periods and is calculated using the following equation (Equation 1):

$$\text{ARR} = \left(\frac{ln\left[\frac{y_{t+n}}{y_t}\right]}{n} \right) \times (-100)$$

where y_t is the mortality rate for a given year (e.g., 2000) and n is the number of years between the two rates (e.g., 13 years when calculating ARR from 2000 and 2013 rates). Consistent with how it is calculated and reported by UNICEF[1] and others[12], the ARR is expressed as a percent and will have a positive value when a country is reducing its mortality rate. As an example, an ARR of 4.4% or greater is needed for a country to meet MDG4 of reducing U5M by two-thirds between 1990 and 2015. In the years leading up to 2015, expressing the reduction in U5M as an ARR made it possible to monitor progress across countries and over different time periods..

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Factors potentially associated with child mortality

Identification. Because we wanted to assess a broad range of factors potentially associated with U5M ARR, factors to be used in the analysis included those monitored by Countdown to 2015 as well as others identified through a comprehensive literature search of the PubMed database. We searched for studies on under-five, infant, or neonatal mortality within any of the 46 countries in the WHO African Region that were published between 2002 and 2012. Abstracts were reviewed to identify factors that were 1) associated with under-five, infant, or neonatal mortality, 2) not already reported by Countdown to 2015, and 3) had aggregate country-level data available for the analysis. Thirty-four factors met these criteria. These were combined with 20 Countdown 2015 intervention indicators (or closely related) and 16 non-intervention indicators reported in the Countdown 2015 country profiles (or were closely related). The final list used in the analysis included 70 factors from the following categories: socio-demographics (18 factors), access to health care (16), governance and financing (11), maternal health (6), child survival interventions (7), clinical and health conditions (7), and other country infrastructure (5) (see Supplemental Table S1).

Data sources and inclusion criteria. Data for 58 (83%) of the 70 indicators were obtained from the World Bank Data Catalogue[13]. The World Bank Data Catalogue is a repository of national, regional, and global indicator data that have been compiled from officially-recognized international sources. In many instances, a single indicator may be derived from multiple data sources using modeling or aggregation techniques. Data for the remaining 12 factors not available through the World Bank Data Catalogue were obtained directly from each country's Demographic and Health Surveys[14] (10 factors) or Countdown 2015 country profiles (2 factors)[8,10]. In total, 26 (37%) of 70 factors were obtained entirely or in part from country Demographic and Health Surveys or other household survey data, including the majority of the maternal health, access to health care, and child survival intervention factors. Other sources included data collected and maintained by WHO, various UN divisions, UNAIDS, the Organisation for Economic Co-operation and Development, and the World Bank (See Supplemental Tables S2 and S3 for further details).

For each of the 46 WHO African Region countries, data on the 70 factors were obtained that corresponded as close as possible to the years 2000 and 2011. To be considered sufficient for inclusion in the analyses, data for each factor had to meet the following three criteria: a) reported for one of the years between 1998 and 2003, termed *2000 data*, b) reported for one of the years between 2006 and 2011, termed *2011 data,* and c) the pair of data points for each factor had to be at least five years apart in order to minimize incorrect extrapolation when calculating changes in the indicator. If any of these criteria were not met, the change over time for that particular factor was not calculated and was deemed missing.

Indicator annual rate of change (ARC) calculation. The ARC for each indicator is conceptually similar to the ARR for U5M and was calculated using the same ARR equation shown above in *Equation 1* but with one difference: a value of one is now subtracted from the exponential function so that the ARC has a negative value when the indicator decreases over time (i.e., $Coverage_{2011} < Coverage_{2000}$) and a positive value when the indicator increases over time (*Equation 2*):

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$$\text{ARC} = \left(\frac{ln\left[\frac{y_{t+n}}{y_t}\right]}{n} \right) \times (100)$$

This is in contrast to the U5M ARR which has a positive value when mortality is decreasing over time (i.e., $U5M_{2013} < U5M_{2000}$).

Statistical analysis

The dependent variable of interest was the U5M ARR for 2000-2013. Each indicator ARC was an independent variable of interest. Both indicator ARCs and U5M ARR were analyzed as continuous variables and no transformations were performed. The distribution of ARRs was inspected visually and was confirmed to be approximately normal by the Shapiro-Wilk test for normality (p=0.33). Associations were explored using linear regression. Given the sample size (n=46 countries), results from traditional linear regression methods may be overly influenced by outliers. These outliers, however, likely represent true data rather than data errors, and exclusion would unnecessarily decrease the sample size. Hence, robust linear regression was used to minimize the influence of outlying observations, without excluding them[15-17] using iteratively reweighted least squares (M-estimation with Huber weighting).

Multivariable robust linear regression models were fit for each factor of interest, resulting in 70 different regression models (one for each factor). A standard set of factors was identified *a priori* to be included in each model as covariates to adjust for potential confounding of the specific factor association being analyzed. Given the sample size of 46 countries, at most, a decision was also made *a priori* to include no more than five covariates in the multivariable analyses to avoid overfitting. We selected the following factor ARCs for inclusion as covariates in each model based on previous ecological studies, consideration of what macro- or system-level factors would influence the majority of the factors, and having nearly complete data: 1) access to improved water source, 2) health expenditure (relative to gross domestic product [GDP]), 3) adult HIV prevalence, 4) urban population prevalence, and 5) receipt of antenatal care (when applicable). All regression models included these core factor ARCs as covariates unless expected to be highly correlated with the primary indicator of interest (e.g. improved water sources was excluded from the model for the association between improved sanitation facilities; health expenditure relative to GDP was excluded from the model for the association between health expenditure relative to government expenditure). Changes in the receipt of antenatal care was only included when the indicator being analyzed would occur following the pregnancy period (e.g., maternal mortality ratio, births delivered at a health facility, measles immunization, wasting prevalence), and was not included for socio-demographic factors, macro-level factors such as health expenditure, and system-level factors such as physician density.

The estimated robust linear regression beta coefficient for each indicator ARC and U5M ARR association can be interpreted as the change in ARR associated with every one percent increase in the indicator ARC. For example, a beta coefficient of 0.20 indicates

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that for every 1.0% increase in the indicator ARC there is a corresponding 0.2% increase in the ARR. Stated differently, a 5.0% increase in the indicator ARC (e.g., 6% ARC compared to 1% ARC) corresponds to a 1% increase in the ARR (e.g., 4% ARR versus 3% ARR). To help avoid Type II errors, which can occur with small samples, we reported all associations when the p-values were <0.10, acknowledging that some of these associations may be due to chance alone, especially with higher p values. We report an indicator to be strongly associated with ARR when the adjusted beta coefficient is ≥0.20 or ≤ -0.20.

A preliminary analysis showed significantly different ARRs between countries reporting a specific indicator and countries not reporting a specific indicator when the indicator was reported by <50% of the countries. Because these differences suggest selection bias, we only present results for those factors for which at least 23 countries (≥50%) have sufficient data (i.e., non-missing indicator data for both time periods). Results for all factors are available in Supplemental Tables S4 and S5.

All analyses were conducted using R-software 2.15.2 (www.r-project.org).

RESULTS

Country-specific progress in under-five mortality

As of 2013, U5M rates and corresponding ARRs for each of the 46 WHO African countries vary widely, with a median (interquartile range) of 3.6% (2.8% - 5.1%) (Figure 1; Table 1). Eleven countries (Eritrea, Ethiopia, Liberia, Madagascar, Malawi, Mozambique, Niger, Rwanda, Senegal, Tanzania, and Uganda) have met or are on track to meet their MDG4 target. An additional four countries (Algeria, Cape Verde, Mauritius, and Seychelles) are considered on track due to U5M rates <40 per 1,000. Eight countries were making very little progress with ARRs ≤2.0%: Angola, Central African Republic, Chad, Comoros, Ghana, Lesotho, Mauritania, and Zimbabwe. Of the remaining 23 countries, some were making good progress but will fall just short of their MDG4 target (e.g., Congo, Mali, and Zambia), while others were making some progress but still have a considerable ways to go before reaching MDG4 (e.g., Cameroon, Kenya, and South Africa) (Table 1).

Descriptive results of selected factors

Of the 70 factors identified, 60 (86%) had sufficient data from at least one country for the period 2000 to 2011. Of these, 41 (68%) factors had data for at least 50% of the countries and are shown in Table 2. The largest ARCs were generally observed for factors related to economic or technological development and external financing, ranging from an ARC of 4.2% (GDP per capita) to 29.0% (internet users) and including, for example, external resources for health (ARC of 6.2%). An extremely large ARC also occurred for use of insecticide-treated bednets (ARC of 29.0%), an intervention which can be rapidly scaled up and which also had the lowest coverage at the start of the study period (2% in 2000). In contrast, vitamin A supplementation had very high coverage at the start of the study period (91%) and did not change dramatically over time (ARC of -0.3%). Coverage of other child survival interventions or access to health care generally improved over the study period with ARCs from 1.2% to 4.0%. Some

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countries, however, had worsening coverage over time as indicated by negative ARCs in the inter-quartile range. Adverse health conditions improved slowly over the study period with ARCs from -0.3% to -1.9%, and the largest improvement was seen for maternal mortality ratio (ARC of -3.7%). Similar to the adverse health conditions, socio-demographic factors improved over the study period for nearly all countries, with ARCs ranging from 0.1% to 3.2%.Details of all indicator ARCs are in Supplemental Table S4.

Table 2. Median 2000 indicator values and corresponding indicator annual rate of change (ARC) for the 2000-2011 period.

Indicator	N	Median 2000 value (IQR)	Median 2000-2011 ARC (IQR)
Socio-demographics			
Adult female literacy rate (%)	35	54 (37 - 72)	1.2 (0.8 - 2.7)
Female labor participation rate (%)	45	46 (43 - 49)	0.1 (-0.1 - 0.3)
Fertility rate (births per woman)	46	6 (5 - 6)	-1.4 (-2.1 - -0.9)
Gross domestic product (GDP) per capita (PPP int'l $)	45	990 (680 – 1,900)	4.2 (2.8 – 5.9)
Human development index (0 to 1)	39	0.38 (0.31 - 0.48)	1.1 (0.7 - 1.9)
Improved sanitation facilities (%)	45	25 (13 - 45)	1.6 (0.4 - 2.6)
Improved water source (%)	45	62 (51 - 79)	1.1 (0.2 - 1.8)
Labor force participation rate among women (%)	45	66 (50 - 76)	0.3 (-0.1 - 0.6)
Urban population prevalence (%)	46	35 (22 - 44)	1.3 (0.7 - 1.6)
Women with at least some secondary education (%)	23	16 (10 - 30)	3.2 (2.5 - 5.2)
Maternal health			
Pregnant women receiving prenatal care (%)	38	77 (64 - 88)	1.3 (0.6 - 2.7)
Adult female mortality rate (rate per 1,000 persons)	46	360 (280 - 420)	-1.2 (-1.8 - -0.6)
Maternal mortality ratio (rate per 100,000 births)	45	550 (400 - 840)	-3.7 (-4.6 - -2.0)
Access to health care			
Seeking ARI treatment (%)	33	40 (27 - 55)	1.7 (-0.3 - 4.9)
Births attended by skilled health staff (%)	37	47 (39 - 60)	2.0 (0.3 - 3.3)
Children with fever receiving antimalarial drugs (%)	30	53 (32 - 61)	-4.9 (-7.8 - -0.2)
Diarrhea treatment (%)	25	39 (28 - 45)	2.2 (-1.4 - 5.5)
Physicians (rate per 100,000 persons)	23	5.7 (2.9 – 12.0)	1.2 (-0.6 - 5.1)
Child survival interventions			
Children 1 year old receiving all basic vaccinations (%)	26	41 (29 - 65)	2.7 (1.1 - 5.1)
Exclusive breastfeeding (%)	36	25 (14 - 37)	4.0 (-0.2 - 8.2)
Measles immunization (%)	46	69 (49 - 76)	1.3 (0.3 - 2.5)
Use of insecticide-treated bed nets (%)	30	2 (1 - 4)	29.0 (24.0 - 35.0)
Vitamin A supplementation coverage (%)	37	91 (78 - 96)	-0.3 (-2.0 - 0.7)
Clinical and health conditions			
Adult prevalence of HIV (%)	43	4 (1 - 8)	-0.8 (-3.6 - 1.7)
Low-birthweight babies (%)	30	13 (11 - 17)	-0.3 (-3.7 - 1.0)
Malnutrition prevalence (height for age) (%)	34	40 (34 - 48)	-1.1 (-2.4 - 0.2)
Malnutrition prevalence (weight for age) (%)	34	22 (18 - 27)	-1.8 (-3.3 - -1.0)
Prevalence of wasting (%)	34	9 (7 - 12)	-1.9 (-5.3 - 0.5)
Governance and financing			
External resources for health (%)	45	13 (4.6 - 20)	6.2 (-1.1 – 9.8)
Health expenditure (% of GDP) (%)	45	5 (4 - 6)	1.4 (0.5 - 3.2)
Health expenditure (% of government expenditures) (%)	45	9 (7 - 10)	2.5 (-0.4 - 3.6)
Net bilateral aid flows from DAC donors (US$ in millions)	46	120 (40 - 260)	8.7 (4.9 - 15.0)
Net ODA received (% of GNI) (%)	46	9 (4 - 13)	-0.9 (-5.6 - 5.3)
Net ODA received per capita (US$)	46	23 (15 - 41)	7.1 (2.4 - 13.0)

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Out-of-pocket health expenditure (%)	45	43 (26 - 58)	-1.7 (-4.0 - -0.6)
Public spending on education (% of GDP) (%)	34	4 (3 - 5)	2.0 (0.2 - 3.8)
Public spending on education (% of government expenditure)(%)	25	16 (14 - 19)	1.6 (-0.2 - 3.0)
Safety and Rule of Law (0 to 100)	46	54 (43 - 66)	-0.0 (-0.9 - 0.4)
Other factors			
Households with television (%)	24	18 (6 - 29)	6.5 (4.0 – 10.0)
Internet users (rate per 100 persons)	46	0.2 (0.1 - 0.5)	29.0 (22.0 - 38.0)
Population coverage of cell phones (%)	26	37 (17 - 82)	8.2 (1.3 - 15.0)

Abbreviations: ARC, annual rate of change; IQR, inter-quartile range; PPP int'l $, purchasing power parity of GDP converted to international dollars; ARI, acute respiratory infection; DAC, Development Assistance Committee; ODA, Official Development Assistance; GNI, gross national income; HIV, human immunodeficiency virus

Associations between indicator ARCs & under-five mortality ARRs

There was evidence that ARRs were higher for countries that had more complete data reported for use in the analyses (Figure 2). However, of the results presented below, all but one factor was reported by >30 countries.

Four indicator ARCs were strongly and statistically associated with U5M ARR after adjusting for potential confounders (Table 3, in bold). With three of these, larger ARCs were associated with larger U5M ARRs: fertility rate (β=0.54; p=0.07), health expenditure relative to GDP (β= 0.26; p=0.01), and seeking treatment for acute respiratory infection (ARI) (β=0.22; p=0.01). With the fourth, larger ARCs for maternal mortality ratio were inversely associated with unfavorable and larger *decreases* in U5M ARR (β= -0.47; p<0.01).

An additional four factors had large ($\beta \geq 0.20$ or $\beta \leq -0.20$) but statistically non-significant ($p \geq 0.10$) associations with U5M ARR, while another four showed small but statistically significant associations (β<0.20 with p<0.10) (Table 3). Of the remaining 58 factors considered in this analysis, 27 had sufficient data from at least 23 of the 46 countries, but there was no association with U5M ARR (β<0.20 and $p \geq 0.10$) (seven are shown in Table 3). The final 31 factors had no data available for analysis (n=10) or were reported by <23 countries and not presented here due to concerns about selection bias. Results for all 70 factors are available in Supplemental Table S5.

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Table 3. Crude and adjusted associations for select factors[a] and under-five mortality annual rate of reduction, 2000-2013.

		Crude			Adjusted[b]		
	N[e]	***β***	**90% CI**	**p-value**	***β***	**90% CI**	**p-value**
Socio-demographics							
Adult female literacy rate (%)	33	0.02	(-0.26, 0.31)	0.39	0.11	(-0.19, 0.41)	0.32
Female labor participation rate (%)	42	-1.07	(-2.42, 0.29)	0.17	-0.32	(-1.56, 0.92)	0.36
Fertility rate (births per woman)	42	0.78	(0.26, 1.31)	0.02	**0.54**	**(0.07, 1.02)**	**0.07**
Human development index (0 to 1)[e]	35	0.12	(0.04, 0.20)	0.02	0.09	(0.01, 0.17)	0.07
Improved water source (%)	42	0.40	(-0.05, 0.85)	0.14	0.36	(-0.07, 0.78)	0.16
Labor force participation rate among women (%)	42	-0.33	(-1.19, 0.53)	0.33	0.19	(-0.57, 0.96)	0.36
Urban population prevalence (%)	42	0.53	(-0.03, 1.09)	0.12	0.39	(-0.15, 0.93)	0.20
Maternal Health							
Adult female mortality rate (rate per 1,000 persons)	42	-0.49	(-0.83, -0.16)	0.03	-0.25	(-0.61, 0.10)	0.20
Maternal mortality ratio (rate per 100,000 births)[c]	35	-0.57	(-0.80, -0.35)	<0.01	**-0.47**	**(-0.69, -0.24)**	**<0.01**
Pregnant women receiving prenatal care (%)	35	0.09	(-0.30, 0.48)	0.37	0.09	(-0.24, 0.41)	0.36
Access to Health Care							
Seeking ARI treatment (%)[c]	31	0.26	(0.10, 0.42)	0.02	**0.22**	**(0.09, 0.35)**	**0.01**
Births attended by skilled health staff (%)[c]	34	0.21	(-0.03, 0.45)	0.14	0.18	(-0.07, 0.43)	0.19
Clinical and Health Conditions							
Adult prevalence of HIV (%)	42	-0.13	(-0.25, -0.01)	0.07	-0.09	(-0.20, 0.02)	0.17
Malnutrition prevalence (height for age) (%)[c]	32	0.11	(-0.15, 0.38)	0.31	0.15	(-0.10, 0.40)	0.24
Governance and Financing							
Health expenditure (% of GDP) (%)	42	0.24	(0.07, 0.40)	0.03	**0.26**	**(0.11, 0.41)**	**0.01**
Health expenditure (% of government expenditures) (%)[d]	42	0.11	(-0.01, 0.23)	0.12	0.08	(-0.04, 0.19)	0.22
Net ODA received per capita (US$)	42	-0.01	(-0.09, 0.07)	0.39	-0.08	(-0.15, -0.01)	0.07
Out-of-pocket health expenditure (%)[d]	42	-0.19	(-0.37, -0.02)	0.08	-0.19	(-0.34, -0.03)	0.06
Other							
Households with television (%)	23	0.29	(0.13, 0.46)	0.01	0.19	(0.05, 0.33)	0.04

[a] Includes all factors for which 1) β >0.20 or β < -0.20, or 2) p<0.10. **Factors having both are shown in bold**. Additional factors of interest are shown if N≥23. (Results for all factors available in Supplemental Table S5).

[b] All results adjusted for improved water source, health expenditure (% of GDP), adult HIV prevalence, and urban population prevalence unless otherwise noted: [c] further adjusted for receipt of prenatal care; [d] not adjusted for health expenditure (% of GDP)

[e] N=sample size of the adjusted analyses and is <46 due to missing country data on some of the factors, including those included as covariates

[f] Because the range of the HDI is only from 0 to 1, the β represents the change in ARR for each 0.10 increase in HDI ARC.

Abbreviations: ARI, acute respiratory infection; CI, confidence interval; GDP, gross domestic product; HIV, human immunodeficiency virus; ODA, Official Development Assistance.

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DISCUSSION

Our study represents a comprehensive analysis of health-related factors and other determinants of health associated with declining U5M in Africa. From 70 factors considered, only four were found to have a strong and statistically significant association with higher rates of reduction in U5M between 2000 and 2013: more rapid increases in fertility rate, health expenditure relative to GDP, and seeking treatment for ARI, and a more rapid decrease in maternal mortality ratio. Maternal mortality ratio showed a particularly strong association (β= -0.47), indicating that a 1.0% increase in the annual reduction of the maternal mortality ratio was associated with a 0.47% increase in the U5M ARR. The associations for health expenditure relative to GDP and seeking treatment for ARI were half this magnitude (β=0.26 to β=0.22, respectively.

The strong and statistically significant association between more rapid declines in the maternal mortality ratio and U5M ARR may well represent the direct negative effect of maternal death on subsequent child survival. It may also be indicative of health systems that do poorly in preventing both maternal and child deaths. More rapid increases in treatment seeking behavior for ARI was the only health-related access or intervention factor found to associate with a larger U5M ARR. Validation studies suggest that factors of access to care or behavior (e.g., seeking ARI treatment) may be more reliably measured than actual treatment (e.g., children with ARI receiving treatment; we had insufficient data to analyze this), since quality of care and ability to recall symptoms may bias the coverage estimates[18,19]. Similar concerns exist about reliability of vaccination coverage estimates due to information bias on the vaccination card or recall bias from maternal reports[20]. This may explain, in part, why some of these factors were not associated with ARR in our study.

The association between fertility rate and higher U5M ARRs is at first counterintuitive. However, as shown in Table 2, fertility rates are declining (negative ARC) in nearly all 46 of the countries. Thus, slower declines in fertility rates are associated with more rapid reductions in U5M – something that becomes more intuitive in the context of demographic transition, Birth rates begin to decline typically only after mortality rates have begun to decline. The observed association may therefore reflect that much of Africa is in the early and middle stages of the demographic transition. Countries with the most rapid reductions in U5M have just begun to reduce their fertility rates, while countries that previously had substantial reductions in mortality (and therefore smaller ARRs in the recent past) have the most rapid reductions in fertility rate as the transition enters the final stages such the fertility rates once again come to parallel mortality rates.

Few other studies have explored the association between changes in health, economic, and financing factors and ARRs in child mortality. Fotso et al. studied U5M ARRs from 22 African countries using data from 1988-2004. Larger increases in access to clean water and receipt of basic vaccinations (*Bacillus Calmette-Guérin* [BCG]; diphtheria, pertussis, tetanus; measles; and polio) were associated with larger ARRs, while higher increases in urban populations were associated with lower ARRs[21]. Our analyses found increases in access to clean water and urban population to be related to ARR, but these were not statistically significant. Findings from Fotso et al.[21] are not directly

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comparable to ours, however, given their earlier time period under study, inclusion of fewer countries and focus on urban areas, and no multivariable analyses.

Binkin et al. studied U5M ARRs from 19 African countries using data primarily from the late 1990s to mid-2000s and grouping specific interventions into composite indices representing antenatal care, access to delivery services, seeking treatment, immunizations, breastfeeding, and nutritional status[12]. Of these, antenatal care, access to delivery services (including a skilled attendant at delivery, delivery in a health facility, and/or caesarean section), and improved nutritional status (including reductions in underweight, stunting, and/or wasting) were associated with higher ARRs. We did not find these associations in our analysis. And unlike our finding of increased coverage of seeking ARI treatment to be associated with higher ARRs, Binkin et al.[12] did not find seeking health treatment (including ARI treatment and diarrhea treatment) to be associated with ARR. Again, however, their analyses differed from ours in terms of time period of study and number of countries included.

Lawn et al.[22] assessed how annual rates of change in 11 factors representing context (gross national income, general and adolescent fertility rate, female literacy, total health expenditure, government effectiveness, political stability, and female HIV prevalence) and coverage (skilled birth attendance, tetanus prevention at birth, and diphtheria, pertussis, tetanus vaccine coverage) were associated with neonatal mortality (not U5M) ARR between 2000 and 2010. Of these, only improved coverage of tetanus protection at birth was found to be associated with lower neonatal mortality ARR, a counterintuitive finding. The authors argued that the paradox arose from the fact that the nations investing the most in scaling up tetanus coverage were those with the weakest health systems, high neonatal mortality, and lower coverage of interventions. Many of the contextual factors analyzed by Lawn et al were found to have small and statistically non- significant associations in our analysis of U5M ARR.

Other ecological studies of country-level factors and under-five or infant mortality rates (not ARRs) have found the following to be associated with lower mortality in Africa: having a skilled attendant at delivery[23], exclusive breast feeding[24], prevention of mother-to-child transmission of HIV and ART for children[25], diphtheria, pertussis, tetanus or measles vaccination[25], use of insecticide treated nets[25], HIV [26,27], health expenditures[26], income[23,27], urban population prevalence[28], access to clean water[25,29], female education[23,27,28], fertility rate[28], and maternal mortality[29]. Stunting[25] and underweight[24] were associated with increased mortality. While our study found associations between U5M ARRs and changes in only someof these factors, we note that a lack of association between a factor'sARC and mortality ARR does not imply that the intervention or other factor is not associated with reduced mortality. Rather, it means that more rapid scale-up or change in a particular factor does not appear to be associated with a more rapid decline in mortality based on the ARR. During the study period, nearly every African country had declining U5M. A non-significant ARC-ARR association could present if such a decline was relatively constant, regardless of whether there was a slow or rapid change in the factor over the corresponding period. It also highlights the need for further research on delivery and subsequent measurement, including assessing quality, of these proven interventions[19,30].

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Our findings highlight the role of financing, economy, and the broader health system to more rapidly reduce an already declining, albeit slowly, U5M rate above and beyond the contribution of individual interventions. As the Millennium Development Goals give way to Sustainable Development Goals for 2030, these factors must be addressed to enable further increases in maternal, neonatal, and child health interventions[31]. Model projections suggest that 3.8 million children will still die in 2030 if current U5M rate ARRs remain steady, and that 2.4 million will die even if ARRs increase substantially[27]. As U5M rates continue to decline, increasing attention must be paid to neonatal mortality which now accounts for 44% of all deaths in children under five years of age (34% in Sub-Saharan African)[32,33]. Facility-based interventions and improving quality care for pregnant women and newborns are needed[33]. The same financial, economic, and broader health system factors that would increase U5M ARRs would also increase reductions in neonatal mortality.

Limitations should be considered when interpreting the findings from this report. First, mortality and indicator data were obtained from secondary sources and some may have suboptimal methods of data collection and model-based estimation, though the World Bank, United Nations Children's Fund, the Inter-agency Group for Child Mortality Estimation, Demographic and Health Surveys, Multiple Indicator Cluster Surveys, and Countdown to 2015 seek to be as authoritative sources as they can. A recent *PLoS Medicine* Collection highlighted the challenges in obtaining valid coverage data from community-based household surveys[19]. Second, the study design was an ecological, study. As such, changes in the factors of interest were occurring simultaneously with changes in mortality, and temporality and causality inferences are limited. Ecological studies are prone to bias and associations at the aggregate level (e.g., country) may not reflect the cause-effect relationship at the individual or local level. Nevertheless, we felt this design was appropriate given the interest in achieving MDG4, which is monitored at a country level. Third, the time period for calculating the ARCs did not always fully overlap with the time period for calculating mortality ARRs (e.g., ARCs for 2000-2011 may have been calculated from data for 2003 and 2010). We attempted to minimize any potential bias by only considering data from factors for which at least a five year period of the 11 year time period were available for calculating ARCs. Finally, the small sample size (at most n=46 countries) limits the validity of many associations and prevents adjustment for many covariates. We cannot exclude residual confounding and low power to detect certain associations. In spite of these limitations, the unique strengths of our study include our broad identification of factors potentially relevant to child survival, beyond those typically used from Demographic and Health Surveys and Countdown to 2015. We also made statistical efforts to minimize bias or distortion from outliers, without excluding them.

There are numerous interventions, health factors, and other determinants of health that influence child mortality rates. However, there are very few studies assessing which of these are associated with higher ARR reflecting more rapid declines in U5M. Policy makers now have evidence that can back decisions to propose increasing access to care for children under age five (extrapolating from our ARI access finding), and increasing health investments, notably towards both child and maternal health.

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CONTRIBUTORSHIP STATEMENT

AMK helped with the stuy design, acquisition of data, assisted with data analysis, interpretation of results, and drafting the manuscript. He had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. He affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained. MB assisted with acquisition of data, conducted the analysis, and critically revised manuscript. CAH contributed to the study design, interpretation of results, and drafting the manuscript. KM helped with conception and design of the study and critically revising the manuscript. PH helped with conception and design of the study and critically revising the manuscript. BES assisted with data analysis and critically revising the manuscript. MHA assisted with the study design and interpretation and critically revising the manuscript. TK helped with conception and design of the study and critically revising the manuscript. SHV helped with conception and design of the study and drafting the manuscript. All authors have participated sufficiently in the work to take public responsibility for its content.

I, Aaron M. Kipp, The Corresponding Author of this article contained within the original manuscript which includes any diagrams & photographs within and any related or stand alone film submitted (the Contribution") has the right to grant on behalf of all authors and does grant on behalf of all authors, a licence to the BMJ Publishing Group Ltd and its licencees, to permit this Contribution (if accepted) to be published in the BMJ and any other BMJ Group products and to exploit all subsidiary rights, as set out in our licence set out at: http://www.bmj.com/about-bmj/resources-authors/forms-policies-and-checklists/copyright-open-access-and-permission-reuse. I am one author signing on behalf of all co-owners of the Contribution.

COMPETING INTERESTS

KM, PH, and TM are paid employees of the WHO. All other authors have no competing interests to report.

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DATA SHARING

Additional data is available at http://biostat.mc.vanderbilt.edu/wiki/Main/WHOUnder5Mortality, or by emailing Dr. Aaron Kipp at aaron.kipp@vanderbilt.edu

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FIGURE LEGENDS

Figure 1. Annual rate of reduction (ARR) in under-five mortality for the 46 countries in the WHO African Region, 2000 to 2013 (Higher ARRs indicate more progress, represented by a greener color on the map).

Figure 1 footnote: The WHO African Region excludes Djibouti, Egypt, Libya, Morocco, Somalia, Sudan, and Tunisia; all are included in the WHO Eastern Mediterranean Region. From May 2012, South Sudan is now officially part of the African Region but was not an independent WHO member nation during the study period.

Figure 2. Correlation between under-five mortality ARR and completeness of indicator data for 46 countries in the WHO African Region for the period 2000-2013

Figure 3 footnote: The coefficient of 0.09 suggests that for every additional 11 factors reported by a country, there is a corresponding 1% increase in the ARR.

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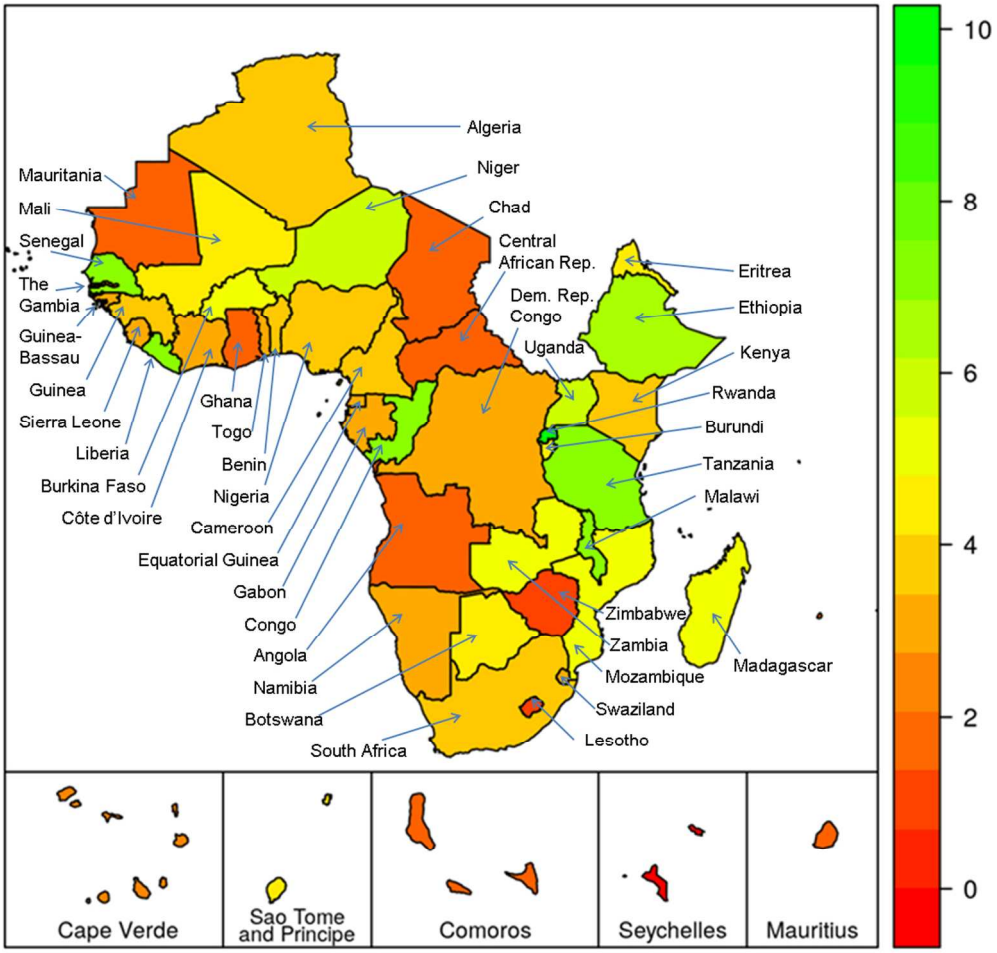

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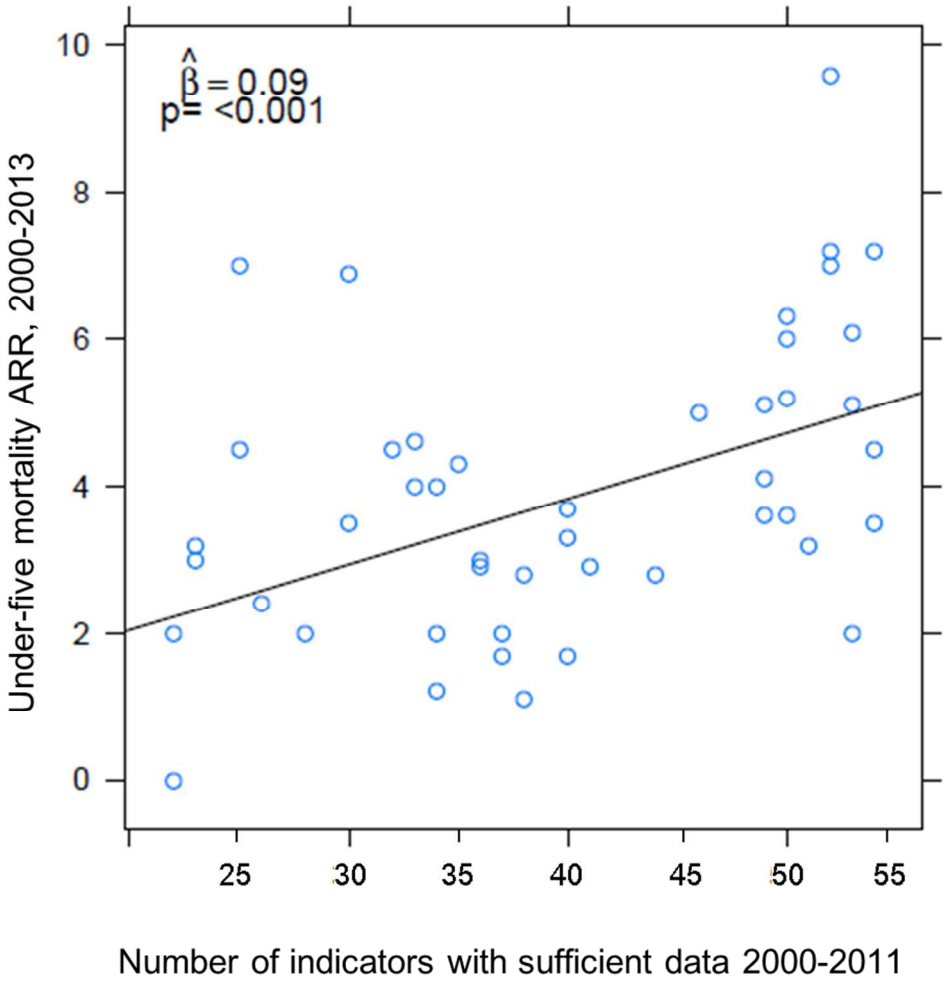

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SUPPLEMENTAL MATERIAL

Table S1. Factors assessed in the ecological analysis.

Category	Indicator name[a]
Socio-demographic (18 indicators listed)	
Age	• Age at first marriage, female • Teenage mothers (% of women ages 15-19 who have had children or are currently pregnant) • Age at first birth of women 20-49 yrs
Education	• Years of education completed among women 15-49 yrs • Percent of women 15-49 yrs old with at least some secondary education
Literacy	• Literacy rate, females (% of females ages 15 and above)
Children	• Number of living children per household • Fertility rate, total (births per woman)[c]
Employment	• Labor force participation rate, female (% of female population ages 15-64) • Labor force, female (% of total labor force)
Water and Sanitation	• Access to improved water source (% of population with access)[b] • Access to improved sanitation facilities (% of population with access)[b]
Socio-economic status	• Gini index[d] • Poverty headcount ratio at national poverty line (% of population) • Households with television (%) • Human development index (HDI)[e] • Gross Domestic Product (GDP) per capita (PPP Int'l $)
Rural/urban residence	• Urban population (% of total)
Maternal health (6 indicators listed)	
Family planning	• Unmet need for contraception (% of married women ages 15-49)[b]
Antenatal care	• Pregnant women receiving prenatal care (%)[b] • Pregnant women receiving prenatal care of at least four visits (%)[b] • Percent of women with live births who received antenatal care during first 5 months of pregnancy
Maternal mortality	• Maternal mortality ratio (per 100,000 live births)[c] • Mortality rate, adult, female (per 1,000 female adults)
Access to health care (16 indicators listed)	
Availability	• Physicians (per 1,000 persons)[c] • Nurses and midwives (per 1,000 persons)[c] • **Nurses (per 1,000 persons)** • Community health workers (per 1,000 persons)

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	• Hospital beds (per 1,000 persons) • Births attended by skilled health staff (% of total)[b] • % of births delivered by caesarean section[b]
Utilization	• % of births delivered at a health facility • % of births with a postnatal visit within the first 2 days after delivery[b] • Seeking ARI treatment (% of children under 5 taken to a health provider)[b]
Treatment	• **% of children 0-59 months of age with ARI who received antibiotics[b]** • Diarrhea treatment (% of children under 5 receiving oral rehydration and continued feeding)[b] • Children with fever receiving antimalarial drugs (% of children under age 5 with fever)[b] • Use of preventive treatment for malaria (% of pregnant women)[b] • **Adoption of low osmolarity Oral Rehydration Salts and zinc for management of diarrhea[c]** • **Community treatment of pneumonia with antibiotics[c]**
Child survival interventions (7 indicators listed)	
PMTCT	• **HIV positive pregnant women receiving antiretrovirals, using WHO/UNAIDS methodology (%)[b]** • **Antiretroviral therapy coverage (% of persons with advanced HIV infection)**
Breastfeeding	• Exclusive breastfeeding (% of children under 6 months)[b]
Vitamin A supplementation	• Vitamin A supplementation coverage rate (% of children ages 6-59 months)[b]
Immunizations	• Immunization, measles (% of children ages 12-23 months)[b] • % of 12-23 month old children receiving all basic vaccinations[b,f]
Bed nets	• Use of insecticide-treated bed nets (% of under-5 population)[b]
Clinical and health conditions (7 indicators listed)	
HIV	• Prevalence of HIV, total (% of population ages 15-49) • **Female adults with HIV (% of population ages 15+ with HIV)** • **Prevalence of HIV, female (% ages 15-24)**
Preterm/birth weight	• Low-birth weight babies (% of births)[c]
Malnutrition	• Malnutrition prevalence, height for age (% of children under 5)[c] • Malnutrition prevalence, weight for age (% of children under 5)[c] • Prevalence of wasting (% of children under 5)[c]
Governance and financing (11 indicators listed)	
Health financing	• Health expenditure, total (% of GDP)[c] • Health expenditure, public (% of government expenditure)[c] • Out-of-pocket health expenditure (% of total expenditure on health)[c]
Education financing	• Public spending on education, total (% of GDP) • Public spending on education, total (% of government expenditure)
Donor funding	• External resources for health (% of total expenditure on health) • Net bilateral aid flows from DAC donors, Total (current US$)[g] • Net official development aid (ODA) received (% of Gross National Income)[c,h]

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	• Net ODA received per capita (current US$)[c,h] • **Net ODA received (constant 2010 US$)**[c,h]
Quality of governance	• Safety and Rule of Law (Ibrahim index with 4 indicators)[i]
Other (5 indicators listed)	
Country infrastructure	• Road density (km of road per 100 sq. km of land area) • Roads, paved (% of total roads) • **Access to electricity (% of population)** • Population coverage of mobile cellular telephony (%) • Internet users (per 100 persons)

[a] 10 indicators in bold were not included in the database due to 100% insufficient data (see methods); analysis dataset has 61 indicators.
[b] one of the 27 Countdown to 2015 intervention indicators (or closely related)
[c] one of the Countdown to 2015 country profile indicators (or closely related)
[d] The GINI index is a measure of income inequality, where 0 represents perfect equality and 100 represents perfect inequality
[e] The Human Development Index is a composite measure of development incorporating life expectancy at birth, mean years of schooling and expected years of schooling, and gross national income per capita, where 0 represents very low development and 1 represents very high development
[f] Includes BCG, measles and three doses each of DPT and polio vaccine (excluding polio vaccine given at birth)
[g] DAC, Development Assistance Committee. DAC members are Australia, Austria, Belgium, Canada, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Japan, Republic of Korea, Luxembourg, Netherlands, New Zealand, Norway, Portugal, Spain, Sweden, Switzerland, United Kingdom, United States, and European Union Institutions
[h] ODA, Official Development Assistance. ODA includes loans and grants made by DAC members, non-DAC countries, and multilateral institutions
[i] Ibrahim index is a composite measure of a countries provision of political, social and economic public goods and services. It is comprised of four indicates: Personal safety, Rule of law, Accountability and corruption and, National security. The index ranges from 0 to 100, with higher values representing better governance.

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Table S2. Detailed description of data sources for each of the 70 factors assessed in the ecological study.

Indicator[a]	Source for data analysis[j]	Primary source reported by World Bank Data Catalogue (if applicable)[k]	Additional notes [k]
Socio-demographic (18 indicators listed)			
Age at first marriage, female	WB-HNPS	UN, Department of Economic and Social Affairs, Population Division. World Marriage Data.	
Teenage mothers (% of women ages 15-19 who have had children or are currently pregnant)	WB-WDI	DHS (Macro Int.)	
Age at first birth of women 20-49 yrs	Country DHS		
Years of education completed among women 15-49 yrs	Country DHS		
Percent of women 15-49 yrs old with at least some secondary education	Country DHS		
Literacy rate, females (% of females ages 15 and above)	WB-WDI	UN Educational, Scientific, and Cultural Organization (UNESCO) Institute for Statistics.	
Number of living children per household	Country DHS		
Fertility rate, total (births per woman)[c]	WB-WDI	(1) UN Population Division. World Population Prospects, (2) United Nations Statistical Division. Population and Vital Statistics Report (various years), (3) Census reports and other statistical publications from national statistical offices	Annual data series are interpolated from 5-year period data; for countries without vital registration systems fertility rates are extrapolated from earlier censuses or other surveys. If no empirical information available, a model is used to estimate the share of births to adolescents.
Labor force participation rate, female (% of female population ages 15-64)	WB-WDI	International Labour Organization, Key Indicators of the Labour Market database.	ILO modeled estimates using both nationally reported and imputed data.
Labor force, female (% of total labor force)	WB-WDI	International Labour Organization, using World Bank population estimates.	
Improved water source (% of population with access)[b]	WB-WDI	WHO and UN Children's Fund, Joint Measurement Programme http://www.wssinfo.org	Linear trend line through data points to provide estimates for all years between 1990 and 2015
Improved sanitation facilities (% of population with access)[b]	WB-WDI		
GINI index[d]	WB-WDI	World Bank, Development Research Group.	Data based on household survey data obtained from government statistical agencies and World Bank country

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			departments (http://iresearch.worldbank.org/PovcalNet/index.htm)
Poverty headcount ratio at national poverty line (% of population)	WB-WDI	World Bank, Global Poverty Working Group.	Data are based on World Bank's country poverty assessments and country Poverty Reduction Strategies.
Households with television (%)	WB-ADI	International Telecommunication Union	
Human development index (HDI)[e]	WB-ADI	UN Development Program, Human Development Reports http://hdr.undp.org/en/statistics/data/	
Gross Domestic Product (GDP) per capita (PPP Int'l $)	WB-WDI	World Bank, International Comparison Program database.	
Urban population (% of total)	WB-WDI	UN, World Urbanization Prospects.	The indicator is calculated using World Bank population estimates and urban ratios from the UN World Urbanization Prospects. Annual data series are interpolated from census and other national population data using demographic modeling
Maternal health (6 indicators listed)			
Unmet need for contraception (% of married women ages 15-49)[b]	WB-WDI	Household surveys, including DHS (Macro Int.) and MICS (UNICEF)	
Pregnant women receiving prenatal care (%)[b]	WB-WDI	UNICEF, State of the World's Children, Childinfo, and DHS (Macro Int.)	
Pregnant women receiving prenatal care of at least four visits (%)[b]	WB-HNPS		
Percent of women with live births who received antenatal care during first 5 months of pregnancy	Country DHS		
Maternal mortality ratio (per 100,000 live births)[c]	WB-WDI	WHO, UNICEF, UNFPA, The World Bank, and the United Nations Population Division. Trends in Maternal Mortality: 1990 to 2013. Geneva, World Health Organization, 2014	Modeled estimates are based on the Maternal Mortality Estimation Inter-Agency Group (WHO, UNICEF, UNFPA, and World Bank) and use a multilevel regression model utilizing national maternal mortality data and socioeconomic information, including fertility, birth attendants, and GDP.
Mortality rate, adult, female (per 1,000 female adults)	WB-WDI	(1) UN Population Division. World Population Prospects. New York, UN, Department of Economic and Social Affairs	Annual data series are linear interpolations from 5-year period data; for countries without vital registration

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		http://esa.un.org/wpp/unpp/panel_population.htm, (2) University of California, Berkeley, and Max Planck Institute for Demographic Research. Human Mortality Database. www.mortality.org or www.humanmortality.de	systems fertility rates are extrapolated from earlier censuses or other surveys.
Access to health care (16 indicators listed)			
Physicians (per 1,000 people)[c]	WB-WDI	WHO, Global Atlas of the Health Workforce http://apps.who.int/globalatlas/.	
Nurses and midwives (per 1,000 people)[c]	WB-HNPS		
Nurses (per 1,000 people)	WB-WDI		100% insufficient for analysis
Community health workers (per 1,000 people)	WB-WDI	WHO, OECD, supplemented by country data.	
Hospital beds (per 1,000 people)	WB-WDI	Data after 2005 are extracted from the World Health Statistics Table 6 published by WHO. WHS data is based on PAHO basic indicators (2011) www.paho.org/English/SHA/coredata/tabulator/newTabulator.htm	
Births attended by skilled health staff (% of total)[b]	WB-WDI	UNICEF, State of the World's Children, Childinfo, and DHS (Macro Int.)	For many countries, includes MICS data reanalyzed by UNICEF
% of births delivered by caesarean section[b]	Country DHS		
Adoption of low osmolarity Oral Rehydration Salts and zinc for management of diarrhea[c]	Countdown 2015 reports		100% insufficient for analysis
Community treatment of pneumonia with antibiotics[c]	Countdown 2015 reports		100% insufficient for analysis
% of births delivered at a health facility	Country DHS		
% of births with a postnatal visit within the first 2 days after delivery[b]	Country DHS		
Seeking ARI treatment (% of children under 5 taken to a health provider)[b]	WB-WDI	UNICEF, State of the World's Children, Childinfo, and DHS (Macro Int.)	For many countries, includes DHS or MICS data reanalyzed by UNICEF
% of children 0-59 months of age with ARI who received antibiotics[b]	Country DHS		100% insufficient for analysis
Diarrhea treatment (% of children under 5 receiving oral rehydration and continued feeding)[b]	WB-WDI	UNICEF, State of the World's Children, Childinfo, and DHS (Macro Int.)	For many countries, includes DHS or MICS data reanalyzed by UNICEF
Children with fever receiving	WB-WDI		

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antimalarial drugs (% of children under age 5 with fever)[b]			
Use of preventive treatment for malaria (% of pregnant women)[b]	WB-HNPS	DHS (Macro Int.)	
Child survival interventions (7 indicators listed)			
HIV positive pregnant women receiving antiretrovirals, using WHO/UNAIDS methodology (%)[b]	WB-ADI	UNAIDS and the WHO's Report on the Global AIDS Epidemic. http://data.unaids.org/pub/GlobalReport/2008/	100% insufficient for analysis
Antiretroviral therapy coverage (% of people with advanced HIV infection)[b]	WB-WDI	UNAIDS and the WHO's Report on the Global AIDS Epidemic.	100% insufficient for analysis
Exclusive breastfeeding (% of children under 6 months)[b]	WB-WDI	UNICEF, State of the World's Children, Childinfo, and DHS (Macro Int.)	For some countries, includes MICS data reanalyzed by UNICEF
Vitamin A supplementation coverage rate (% of children ages 6-59 months)[b]	WB-WDI	UN Children's Fund, State of the World's Children.	
Immunization, measles (% of children ages 12-23 months)[b]	WB-WDI	WHO and UNICEF http://www.who.int/immunization_monitoring/routine/en/	
% of 12-23 month old children receiving all basic vaccinations[b,f]	Country DHS		
Use of insecticide-treated bed nets (% of under-5 population)[b]	WB-WDI	UNICEF, State of the World's Children, Childinfo, and DHS (Macro Int.)	
Clinical and health conditions (7 indicators listed)			
Prevalence of HIV, total (% of population ages 15-49)	WB-WDI	UNAIDS and the WHO's Report on the Global AIDS Epidemic.	All years are model based estimates from 2012 report
Female adults with HIV (% of population ages 15+ with HIV)	WB-HNPS		100% insufficient for analysis
Prevalence of HIV, female (% ages 15-24)	WB-HNPS		100% insufficient for analysis
Low-birth weight babies (% of births)[c]	WB-WDI	UNICEF, State of the World's Children, Childinfo, and DHS (Macro Int.)	For many countries, includes DHS or MICS data reanalyzed by UNICEF
Malnutrition prevalence, height for age (% of children under 5)[c]	WB-WDI	WHO, Global Database on Child Growth and Malnutrition. Aggregation is based on UNICEF/WHO Joint Global Malnutrition Analysis Date Set 2011 and additional analysis by UNICEF.	MICS and other UNICEF surveys, DHS, national nutrition surveys
Malnutrition prevalence, weight for age (% of children under 5)[c]	WB-WDI		
Prevalence of wasting (% of children under 5)[c]	WB-WDI		
Governance and financing (11 indicators listed)			

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Health expenditure, total (% of GDP)[c]	WB-WDI	WHO National Health Account database http://apps.who.int/nha/database	Many low-income countries use DHS or MICS funded by donors to obtain health system data.
Health expenditure, public (% of government expenditure)[c]	WB-WDI	WHO Global Health Expenditure database http://apps.who.int/nha/database	
Out-of-pocket health expenditure (% of total expenditure on health)[c]	WB-HNPS	WHO National Health Account database http://apps.who.int/nha/database/DataExplorerRegime.aspx	Many low-income countries use DHS or MICS funded by donors to obtain health system data.
Public spending on education, total (% of GDP)	WB-WDI	UN Educational, Scientific, and Cultural Organization (UNESCO) Institute for Statistics.	
Public spending on education, total (% of government expenditure)	WB-WDI		
External resources for health (% of total expenditure on health)	WB-WDI	WHO National Health Account database http://apps.who.int/nha/database for the most recent updates	Many low-income countries use DHS or MICS funded by donors to obtain health system data.
Net bilateral aid flows from DAC donors, Total (current US$)[g]	WB-WDI	DAC of the Organisation for Economic Co-operation and Development, Geographical Distribution of Financial Flows to Developing Countries, Development Co-operation Report, and International Development Statistics database. www.oecd.org/dac/stats/idsonline	
Net ODA received (constant 2010 US$)[c,h]	WB-WDI		100% insufficient for analysis
Net official development aid (ODA) received (% of Gross National Income)[c,h]	WB-WDI	DAC of the Organisation for Economic Co-operation and Development, Geographical Distribution of Financial Flows to Developing Countries, Development Co-operation Report, and International Development Statistics database. www.oecd.org/dac/stats/idsonline. World Bank estimates are used for the denominator.	
Net ODA received per capita (current US$)[c,h]	WB-WDI		
Safety and Rule of Law (Ibrahim index with 4 indicators)[i]	WB-ADI	Mo Ibrahim Foundation, electronic files and web site.	
Road density (km of road per 100 sq. km of land area)	WB-WDI	International Road Federation, World Road Statistics and electronic files	
Roads, paved (% of total roads)	WB-WDI		
Access to electricity (% of population)	WB-WDI	International Energy Agency, World Energy Outlook 2010.	100% insufficient for analysis
Population coverage of mobile cellular telephony (%)	WB-ADI	International Telecommunication Union	
Internet users (per 100 people)	WB-WDI		

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[a] 10 indicators in bold were not included in the database due to 100% insufficient data (see methods); analysis dataset has 60 indicators.
[b] one of the 27 Countdown to 2015 intervention indicators (or closely related)
[c] one of the Countdown to 2015 country profile indicators (or closely related)
[d] The GINI index is a measure of income inequality, where 0 represents perfect equality and 100 represents perfect inequality
[e] The Human Development Index is a composite measure of development incorporating life expectancy at birth, mean years of schooling and expected years of schooling, and gross national income per capita, where 0 represents very low development and 1 represents very high development
[f] Includes BCG, measles and three doses each of DPT and polio vaccine (excluding polio vaccine given at birth)
[g] DAC, Development Assistance Committee. DAC members are Australia, Austria, Belgium, Canada, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Japan, Republic of Korea, Luxembourg, Netherlands, New Zealand, Norway, Portugal, Spain, Sweden, Switzerland, United Kingdom, United States, and European Union Institutions
[h] ODA, Official Development Assistance. ODA includes loans and grants made by DAC members, non-DAC countries, and multilateral institutions
[i] Ibrahim index is a composite measure of a countries provision of political, social and economic public goods and services. It is comprised of four indicates: Personal safety, Rule of law, Accountability and corruption and, National security. The index ranges from 0 to 100, with higher values representing better governance.
[j] Data source for the current analysis: WB, World Bank Data Catalogue; WDI, World Development Index; ADI, Africa Development Index; HNPS, Health Nutrition & Population Statistics; Country DHS indicates data were obtained directly from each country's Demographic and Health Survey; Countdown to 2015 indicates data were obtained directly from each country's Country Profile in the Countdown to 2015 reports.
[k] Summarized from the indicator/country metadata provided in the World Bank Data Catalogue. See metadata in World Bank Data Catalogue for more details (Data Catalogue code listed in Supplemental Table S3). http://databank.worldbank.org.

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Table S3. World Bank Data Catalogue source and code for each of the 70 factors assessed in the ecological study.

Indicator[a]	Source for Data analysis	World Bank Data Catalogue Code[k]
Socio-demographic (18 indicators listed)		
Age at first marriage, female	WB-HNPS	SP.DYN.SMAM.FE
Teenage mothers (% of women ages 15-19 who have had children or are currently pregnant)	WB-WDI	SP.MTR.1519.ZS
Age at first birth of women 20-49 yrs	Country DHS	
Years of education completed among women 15-49 yrs	Country DHS	
Percent of women 15-49 yrs old with at least some secondary education	Country DHS	
Literacy rate, females (% of females ages 15 and above)	WB-WDI	SE.ADT.LITR.FE.ZS
Number of living children per household	Country DHS	
Fertility rate, total (births per woman)[c]	WB-WDI	SP.DYN.TFRT.IN
Labor force participation rate, female (% of female population ages 15-64)	WB-WDI	SL.TLF.CACT.FE.ZS
Labor force, female (% of total labor force)	WB-WDI	SL.TLF.TOTL.FE.ZS
Improved water source (% of population with access)[b]	WB-WDI	SH.H2O.SAFE.ZS
Improved sanitation facilities (% of population with access)[b]	WB-WDI	SH.STA.ACSN
GINI index[d]	WB-WDI	SI.POV.GINI
Poverty headcount ratio at national poverty line (% of population)	WB-WDI	SI.POV.NAHC
Households with television (%)	WB-ADI	IT.TVS.HOUS.ZS
Human development index (HDI)[e]	WB-ADI	UNDP.HDI.XD
Gross Domestic Product (GDP) per capita (PPP Int'l $)	WB-WDI	NY.GDP.PCAP.PP.CD
Urban population (% of total)	WB-WDI	SP.URB.TOTL.IN.ZS
Maternal health (6 indicators listed)		
Unmet need for contraception (% of married women ages 15-49)[b]	WB-WDI	SP.UWT.TFRT
Pregnant women receiving prenatal care (%)[b]	WB-WDI	SH.STA.ANVC.ZS
Pregnant women receiving prenatal care of at least four visits (%)[b]	WB-HNPS	SH.STA.ANV4.ZS
Percent of women with live births who received antenatal care during first 5 months of pregnancy	Country DHS	
Maternal mortality ratio (per 100,000 live births)[c]	WB-WDI	SH.STA.MMRT
Mortality rate, adult, female (per 1,000 female adults)	WB-WDI	SP.DYN.AMRT.FE
Access to health care (16 indicators listed)		
Physicians (per 1,000 people)[c]	WB-WDI	SH.MED.PHYS.ZS
Nurses and midwives (per 1,000 people)[c]	WB-HNPS	SH.MED.NURS.P3
Nurses (per 1,000 people)	WB-WDI	SH.MED.NUMW.P3
Community health workers (per 1,000 people)	WB-WDI	SH.MED.CMHW.P3
Hospital beds (per 1,000 people)	WB-WDI	SH.MED.BEDS.ZS
Births attended by skilled health staff (% of total)[b]	WB-WDI	SH.STA.BRTC.ZS
% of births delivered by caesarean section[b]	Country DHS	
Adoption of low osmolarity Oral Rehydration Salts and zinc for management of diarrhea[c]	Countdown 2015	

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Community treatment of pneumonia with antibiotics[c]	Countdown 2015	
% of births delivered at a health facility	Country DHS	
% of births with a postnatal visit within the first 2 days after delivery[b]	Country DHS	
Seeking ARI treatment (% of children under 5 taken to a health provider)[b]	WB-WDI	SH.STA.ARIC.ZS
% of children 0-59 months of age with ARI who received antibiotics[b]	Country DHS	
Diarrhea treatment (% of children under 5 receiving oral rehydration and continued feeding)[b]	WB-WDI	SH.STA.ORCF.ZS
Children with fever receiving antimalarial drugs (% of children under age 5 with fever)[b]	WB-WDI	SH.MLR.TRET.ZS
Use of preventive treatment for malaria (% of pregnant women)[b]	WB-HNPS	SH.MLR.PREG.ZS
Child survival interventions (7 indicators listed)		
HIV positive pregnant women receiving antiretrovirals, using WHO/UNAIDS methodology (%)[b]	WB-ADI	SH.HIV.PREG.VIRALS.ZS
Antiretroviral therapy coverage (% of people with advanced HIV infection)[b]	WB-WDI	SH.HIV.ARTC.ZS
Exclusive breastfeeding (% of children under 6 months)[b]	WB-WDI	SH.STA.BFED.ZS
Vitamin A supplementation coverage rate (% of children ages 6-59 months)[b]	WB-WDI	SN.ITK.VITA.ZS
Immunization, measles (% of children ages 12-23 months)[b]	WB-WDI	SH.IMM.MEAS
% of 12-23 month old children receiving all basic vaccinations[b,f]	Country DHS	
Use of insecticide-treated bed nets (% of under-5 population)[b]	WB-WDI	SH.MLR.NETS.ZS
Clinical and health conditions (7 indicators listed)		
Prevalence of HIV, total (% of population ages 15-49)	WB-WDI	SH.DYN.AIDS.ZS
Female adults with HIV (% of population ages 15+ with HIV)	WB-HNPS	SH.DYN.AIDS.FE.ZS
Prevalence of HIV, female (% ages 15-24)	WB-HNPS	SH.HIV.1524.FE.ZS
Low-birth weight babies (% of births)[c]	WB-WDI	SH.STA.BRTW.ZS
Malnutrition prevalence, height for age (% of children under 5)[c]	WB-WDI	SH.STA.STNT.ZS
Malnutrition prevalence, weight for age (% of children under 5)[c]	WB-WDI	SH.STA.MALN.ZS
Prevalence of wasting (% of children under 5)[c]	WB-WDI	SH.STA.WAST.ZS
Governance and financing (11 indicators listed)		
Health expenditure, total (% of GDP)[c]	WB-WDI	SH.XPD.TOTL.ZS
Health expenditure, public (% of government expenditure)[c]	WB-WDI	SH.XPD.PUBL.GX.ZS
Out-of-pocket health expenditure (% of total expenditure on health)[c]	WB-HNPS	SH.XPD.OOPC.TO.ZS
Public spending on education, total (% of GDP)	WB-WDI	SE.XPD.TOTL.GD.ZS
Public spending on education, total (% of government expenditure)	WB-WDI	SE.XPD.TOTL.GB.ZS
External resources for health (% of total expenditure on health)	WB-WDI	SH.XPD.EXTR.ZS
Net bilateral aid flows from DAC donors, Total (current US$)[g]	WB-WDI	DC.DAC.TOTL.CD
Net official development aid (ODA) received (% of Gross National Income)[c,h]	WB-WDI	DT.ODA.ODAT.GN.ZS
Net ODA received per capita (current US$)[c,h]	WB-WDI	DT.ODA.ODAT.PC.ZS
Net ODA received (constant 2010 US$)[c,h]	WB-WDI	DT.ODA.OATL.CD
Safety and Rule of Law (Ibrahim index with 4 indicators)[i]	WB-ADI	MO.INDEX.SRLW.XQ
Other (5 indicators listed)		
Road density (km of road per 100 sq. km of land area)	WB-WDI	IS.ROD.DNST.K2

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Roads, paved (% of total roads)	WB-WDI	IS.ROD.PAVE.ZS
Access to electricity (% of population)	WB-WDI	EG.ELC.ACCS.ZS
Population coverage of mobile cellular telephony (%)	WB-ADI	IT.MOB.COV.ZS
Internet users (per 100 people)	WB-WDI	IT.NET.USER.P2

[a] 10 indicators in bold were not included in the database due to 100% insufficient data (see methods); analysis dataset has 60 indicators.

[b] one of the 27 Countdown to 2015 intervention indicators (or closely related)

[c] one of the Countdown to 2015 country profile indicators (or closely related)

[d] The GINI index is a measure of income inequality, where 0 represents perfect equality and 100 represents perfect inequality

[e] The Human Development Index is a composite measure of development incorporating life expectancy at birth, mean years of schooling and expected years of schooling, and gross national income per capita, where 0 represents very low development and 1 represents very high development

[f] Includes BCG, measles and three doses each of DPT and polio vaccine (excluding polio vaccine given at birth)

[g] DAC, Development Assistance Committee. DAC members are Australia, Austria, Belgium, Canada, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Japan, Republic of Korea, Luxembourg, Netherlands, New Zealand, Norway, Portugal, Spain, Sweden, Switzerland, United Kingdom, United States, and European Union Institutions

[h] ODA, Official Development Assistance. ODA includes loans and grants made by DAC members, non-DAC countries, and multilateral institutions

[i] Ibrahim index is a composite measure of a countries provision of political, social and economic public goods and services. It is comprised of four indicates: Personal safety, Rule of law, Accountability and corruption and, National security. The index ranges from 0 to 100, with higher values representing better governance.

[j] Data source for the current analysis: WB, World Bank Data Catalogue; WDI, World Development Index; ADI, Africa Development Index; HNPS, Health Nutrition & Population Statistics; Country DHS indicates data were obtained directly from each country's Demographic and Health Survey; Countdown to 2015 indicates data were obtained directly from each country's Country Profile in the Countdown to 2015 reports.

[k] Indicator code as documented by the World Bank Data Catalogue; http://databank.worldbank.org.

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Table S4. Median baseline indicator values and corresponding ARC for the 2000-2011 period.

Indicator	N	Median 2000 value (IQR)	Median 2000-2011 ARC (IQR)
Socio-demographics			
Access to improved sanitation facilities (%)	45	25 (13 - 45)	1.6 (0.4 - 2.7)
Access to improved water source (%)	45	62 (51 - 79)	1.1 (0.2 - 1.8)
Adult female literacy rate (%)	35	54 (37 - 72)	1.2 (0.8 - 2.8)
Female age at first marriage (years)	17	21 (20 - 22)	0.2 (-0.1 - 0.6)
Female labor participation rate (%)	45	46 (43 - 49)	0.1 (-0.1 - 0.3)
Fertility rate (births per woman)	46	6 (5 - 6)	-1.4 (-2.0 - -0.9)
GDP per capita (PPP int'l $)	45	990 (680 – 1,900)	4.3 (2.8 - 6.1)
Gini index (0 to 100)	22	43 (41 - 50)	0.0 (-1.0 - 0.6)
Human development index (0 to 1)	39	0.38 (0.31 - 0.48)	1.1 (0.7 - 1.9)
Labor force participation rate among women (%)	45	66 (50 - 76)	0.3 (-0.1 - 0.6)
Median age at pregnancy (or first birth) (years)	18	19 (19 - 20)	0.2 (0.1 - 0.2)
Median number of living children per household (N)	18	2 (2 - 3)	0.1 (-0.6 - 0.4)
Median years of maternal education (years)	6	4 (3 - 6)	2.4 (0.9 - 4.2)
Poverty headcount ratio at national poverty line (%)	15	46 (39 - 55)	-1.2 (-3.0 - -0.5)
Teenage mothers (%)	15	22 (19 - 32)	-1.1 (-2.5 - -0.6)
Urban population prevalence (%)	46	35 (22 - 44)	1.3 (0.7 - 1.7)
Women with at least some secondary education (%)	23	16 (10 - 30)	3.2 (2.5 - 5.3)
Maternal health			
Adult female mortality rate (rate per 1,000 persons)	46	360 (280 - 420)	-1.2 (-1.8 - -0.6)
Antenatal care during first 5 months of pregnancy (%)	19	57 (45 - 67)	1.4 (0.5 - 3.4)
Maternal mortality ratio (rate per 100,000 births)	45	550 (400 - 840)	-3.6 (-4.5 - -20)
Pregnant women receiving ≥4 prenatal care visits (%)	21	46 (23 - 62)	1.7 (-0.3 - 4.0)
Pregnant women receiving prenatal care (%)	38	77 (64 - 88)	1.3 (0.6 - 2.7)
Unmet need for contraception (%)	18	27 (22 - 32)	0.6 (-1.2 - 1.9)
Access to health care			
Births attended by skilled health staff (%)	37	47 (39 - 60)	2.0 (0.3 - 3.4)
Births delivered at a health facility (%)	19	43 (34 - 55)	1.8 (0.1 - 3.7)
Births delivered by caesarean section (%)	18	3 (1 - 4)	5.3 (1.6 - 7.6)
Births with a postnatal visit ≤2 days after delivery (%)	10	8 (5 - 12)	16.0 (8.0 - 21.0)
Children with fever receiving antimalarial drugs (%)	30	53 (32 - 61)	-4.8 (-7.5 - -0.2)
Community health workers (rate per 1,000 persons)	2	0.2 (0.2 - 0.3)	15.0 (13.0 - 17.0)
Diarrhea treatment (%)	25	39 (28 - 45)	2.3 (-1.3 - 5.7)
Hospital beds (rate per 1,000 persons)	8	1.2 (0.4 – 2.0)	-2.3 (-4.6 - -1.0)
Nurses and midwives (rate per 1,000 persons)	6	1.2 (0.6 - 1.6)	-3.0 (-5.0 - -1.0)

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Physicians (rate per 100,000 persons)	23	5.7 (2.9 – 12.0)	1.2 (-0.6 - 5.2)
Pregnant women using malaria preventive treatment (%)	3	36 (29 - 37)	10.0 (-1.8 - 15.0)
Seeking ARI treatment (%)	33	40 (27 - 55)	1.7 (-0.3 - 5.0)
Child survival interventions			
Children 1 year old receiving all basic vaccinations (%)	26	41 (29 - 65)	2.8 (1.1 - 5.3)
Exclusive breastfeeding (%)	36	25 (14 - 37)	4.1 (-0.2 - 8.6)
Measles immunization (%)	46	69 (49 - 76)	1.3 (0.3 - 2.5)
Use of insecticide-treated bed nets (%)	30	2 (1 - 4)	34.0 (28.0 - 42.0)
Vitamin A supplementation coverage (%)	37	91 (78 - 96)	-0.3 (-2.0 - 0.7)
Clinical and health conditions			
Adult prevalence of HIV (%)	43	4 (1 - 8)	-0.8 (-3.5 - 1.7)
Low-birthweight babies (%)	30	13 (11 - 17)	-0.3 (-3.6 - 1.0)
Malnutrition prevalence (height for age) (%)	34	40 (34 - 48)	-1.1 (-2.3 - 0.2)
Malnutrition prevalence (weight for age) (%)	34	22 (18 - 27)	-1.7 (-3.2 - -0.9)
Prevalence of wasting (%)	34	9 (7 - 12)	-1.9 (-5.2 - 0.5)
Governance and financing			
External resources for health (%)	45	13 (4.6 - 20)	6.4 (-1.0 - 10.0)
Health expenditure (relative to GDP) (%)	45	5 (4 - 6)	1.4 (0.5 - 3.3)
Health expenditure (relative to government) (%)	45	9 (7 - 10)	2.5 (-0.4 - 3.7)
Net bilateral aid flows from DAC donors (US $ in millions)	46	120 (40 - 260)	9.1 (5.0 - 16.0)
Net ODA received (% of GNI) (%)	46	9 (4 - 13)	-0.9 (-5.4 - 5.4)
Net ODA received per capita (US$)	46	23 (15 - 41)	7.4 (2.4 - 13.0)
Out-of-pocket health expenditure (%)	45	43 (26 - 58)	-1.7 (-3.9 - -0.6)
Public spending on education (% of GDP) (%)	34	4 (3 - 5)	2.1 (0.2 - 3.9)
Public spending on education (% of gov. expenditure) (%)	25	16 (14 - 19)	1.6 (-0.2 - 3.0)
Safety and Rule of Law (0 to 100)	46	54 (43 - 66)	-0.0 (-0.9 - 0.4)
Other			
Households with television (%)	24	18 (6 - 29)	6.7 (4.1 – 10.0)
Internet users (rate per 100 persons)	46	0.2 (0.1 - 0.5)	34.0 (25.0 - 46.0)
Paved roads (%)	19	12 (10 - 29)	1.2 (-1.4 - 3.1)
Population coverage of cell phones (%)	26	37 (17 - 82)	8.5 (1.3 - 16.0)
Road density (km of road per 100 sq km)	8	8 (4 - 20)	1.4 (0.3 - 6.2)

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Table S5. Crude and adjusted associations between indicators and under-five mortality ARR, 2000-2013.

Indicator[a]	Crude				Adjusted[b,c]		
	N	β	90% CI	p-value	β	90% CI	p-value
Socio-demographics							
Access to improved sanitation facilities (%)[e]	42	0.08	(-0.20, 0.37)	0.350	0.04	(-0.23, 0.31)	0.385
Access to improved water source (%)	42	0.40	(-0.05, 0.85)	0.139	0.36	(-0.07, 0.78)	0.155
Adult female literacy rate (%)	33	0.02	(-0.26, 0.31)	0.392	0.11	(-0.19, 0.41)	0.324
Female age at first marriage (years)	16	0.07	(-0.83, 0.98)	0.388	-0.16	(-0.66, 0.34)	0.334
Female labor participation rate (%)	42	-1.07	(-2.42, 0.29)	0.171	-0.32	(-1.56, 0.92)	0.362
Fertility rate (births per woman)	42	0.78	(0.26, 1.31)	0.023	0.54	(0.07, 1.02)	0.069
GDP per capita (PPP int'l $)[f]	42	0.00	(-0.21, 0.21)	0.396	0.06	(-0.14, 0.26)	0.352
GINI index (0 to 100)	21	-0.04	(-0.46, 0.39)	0.389	0.22	(-0.16, 0.60)	0.248
Human development index (0 to 1)[g]	35	0.12	(0.04, 0.20)	0.023	0.09	(0.01, 0.17)	0.066
Labor force participation rate among women (%)	42	-0.33	(-1.19, 0.53)	0.325	0.19	(-0.57, 0.96)	0.363
Median age at pregnancy (or first birth) (years)	17	-0.43	(-5.16, 4.30)	0.388	-0.45	(-3.71, 2.82)	0.379
Median number of living children per household (N)	17	0.78	(-0.06, 1.62)	0.123	-0.21	(-0.84, 0.42)	0.334
Median years of maternal education (years)	6	0.01	(-0.23, 0.26)	0.373	-0.08	(NA, NA)	
Poverty headcount ratio at national poverty line (%)	15	-0.08	(-0.46, 0.30)	0.367	-0.25	(-0.63, 0.13)	0.215
Teenage mothers (%)	14	-0.41	(-1.09, 0.26)	0.230	-0.44	(-0.72, -0.17)	0.022
Urban population prevalence (%)	42	0.53	(-0.03, 1.09)	0.117	0.39	(-0.15, 0.93)	0.196
Women with at least some secondary education (%)	21	-0.11	(-0.26, 0.04)	0.187	-0.05	(-0.17, 0.07)	0.303
Maternal health							
Adult female mortality rate (rate per 1,000 persons)	42	-0.49	(-0.83, -0.16)	0.025	-0.25	(-0.61, 0.10)	0.199
Antenatal care during first 5 months of pregnancy (%)	18	0.35	(0.12, 0.58)	0.022	0.29	(0.10, 0.47)	0.024
Maternal mortality ratio (rate per 100,000 births)[d]	35	-0.57	(-0.80, -0.35)	<0.001	-0.47	(-0.69, -0.24)	0.003
Pregnant women receiving ≥4 prenatal care visits (%)	20	0.22	(0.06, 0.37)	0.034	0.07	(-0.01, 0.16)	0.134
Pregnant women receiving prenatal care (%)	35	0.09	(-0.30, 0.48)	0.369	0.09	(-0.24, 0.41)	0.359
Unmet need for contraception (%)	18	0.02	(-0.10, 0.14)	0.373	0.03	(-0.06, 0.11)	0.331
Access to health care							
Seeking ARI treatment (%)[d]	31	0.26	(0.10, 0.42)	0.016	0.22	(0.09, 0.35)	0.012
Births attended by skilled health staff (%)[d]	34	0.21	(-0.03, 0.45)	0.142	0.18	(-0.07, 0.43)	0.192
Births delivered at a health facility (%)[d]	18	0.17	(-0.01, 0.36)	0.112	0.05	(-0.10, 0.20)	0.335
Births delivered by caesarean section (%)[d]	17	0.18	(0.04, 0.32)	0.052	0.13	(0.05, 0.20)	0.017
Births with a postnatal visit ≤2 days after delivery (%)[d]	9	-0.10	(-0.22, 0.01)	0.134	-0.14	(-0.14, -0.14)	<0.001
Children with fever receiving antimalarial drugs (%)[d]	28	0.05	(-0.02, 0.12)	0.176	0.06	(-0.01, 0.12)	0.143

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Community health workers (rate per 1,000 persons)	2						
Diarrhea treatment (%)[d]	24	-0.10	(-0.18, -0.01)	0.072	-0.09	(-0.18, 0.00)	0.111
Hospital beds (rate per 1,000 persons)	8	-0.09	(-0.29, 0.11)	0.283	-0.32	(-0.45, -0.19)	0.013
Nurses and midwives (rate per 1,000 persons)	5						
Physicians (rate per 100,000 persons)	21	0.03	(-0.09, 0.15)	0.360	0.06	(0.00, 0.13)	0.089
Pregnant women using malaria preventive treatment (%)	3						
Child survival interventions							
Children 1 year old receiving all basic vaccinations (%)[d]	23	0.09	(-0.09, 0.28)	0.278	-0.14	(-0.39, 0.10)	0.236
Exclusive breastfeeding (%)[d]	33	-0.01	(-0.08, 0.06)	0.388	-0.03	(-0.09, 0.04)	0.308
Measles immunization (%)[d]	35	0.03	(-0.19, 0.26)	0.382	0.11	(-0.08, 0.30)	0.254
Use of insecticide-treated bed nets (%)[d]	28	0.02	(-0.02, 0.07)	0.277	0.01	(-0.04, 0.05)	0.381
Vitamin A supplementation coverage (%)[d]	31	0.11	(0.01, 0.21)	0.085	0.06	(-0.04, 0.16)	0.241
Clinical and health conditions							
Adult prevalence of HIV (%)	42	-0.13	(-0.25, -0.01)	0.073	-0.09	(-0.20, 0.02)	0.171
Low-birthweight babies (%)[d]	27	0.04	(-0.10, 0.17)	0.359	0.05	(-0.07, 0.17)	0.303
Malnutrition prevalence (height for age) (%)[d]	32	0.11	(-0.15, 0.38)	0.306	0.15	(-0.10, 0.40)	0.244
Malnutrition prevalence (weight for age) (%)[d]	32	-0.07	(-0.28, 0.15)	0.344	-0.02	(-0.23, 0.19)	0.390
Prevalence of wasting (%)[d]	32	0.01	(-0.12, 0.14)	0.390	0.03	(-0.09, 0.15)	0.357
Governance and financing							
External resources for health (%)	42	0.01	(-0.05, 0.07)	0.373	-0.01	(-0.06, 0.05)	0.390
Health expenditure (% of GDP) (%)	42	0.24	(0.07, 0.40)	0.028	0.26	(0.11, 0.41)	0.010
Health expenditure (% of government expenditure) (%)[f]	42	0.11	(-0.01, 0.23)	0.120	0.08	(-0.04, 0.19)	0.217
Net bilateral aid flows from DAC donors (US$ in millions)	42	0.01	(-0.06, 0.07)	0.394	-0.05	(-0.12, 0.03)	0.224
Net ODA received (relative to GNI) (%)	42	-0.01	(-0.09, 0.07)	0.392	-0.08	(-0.15, -0.01)	0.074
Net ODA received per capita (US$)	42	0.02	(-0.03, 0.08)	0.301	-0.01	(-0.06, 0.05)	0.388
Out-of-pocket health expenditure (%)[f]	42	-0.19	(-0.37, -0.02)	0.079	-0.19	(-0.34, -0.03)	0.061
Public spending on education (% of GDP) (%)	33	0.03	(-0.13, 0.19)	0.379	-0.06	(-0.21, 0.10)	0.329
Public spending on education (% of gov. expenditure) (%)	24	0.19	(0.00, 0.38)	0.106	0.06	(-0.14, 0.27)	0.345
Safety and Rule of Law (0 to 100)	42	0.10	(-0.14, 0.34)	0.316	-0.07	(-0.30, 0.15)	0.342
Other							
Households with television (%)	23	0.29	(0.13, 0.46)	0.009	0.19	(0.05, 0.33)	0.044
Internet users (rate per 100 persons)	42	0.05	(0.01, 0.09)	0.048	0.03	(-0.02, 0.07)	0.221
Paved roads (%)	17	0.07	(-0.10, 0.24)	0.309	0.06	(-0.07, 0.19)	0.294
Population coverage of cell phones (%)	24	0.01	(-0.07, 0.09)	0.387	0.01	(-0.05, 0.07)	0.383
Road density (km of road per 100 sq. km)	7	-0.05	(-0.37, 0.26)	0.364	-0.12	(-0.46, 0.22)	0.240

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[a] 10 of 70 indicators not shown in table because sufficient data were missing for all 46 countries
[b] N>2 required to run crude robust linear regression models; N>6 required to run adjusted robust linear regression models which include a minimum of four covariates.
[c] All results adjusted for improved water source, health expenditure (relative to GDP), adult HIV prevalence, and urban population prevalence unless otherwise noted below:
[d] further adjusted for receipt of prenatal care
[e] not adjusted for improved water source
[f] not adjusted for health expenditure (relative to GDP)
[g] Because the range of the HDI is only from 0 to 1, the β represents the change in ARR for each 0.10 increase in HDI ARC.

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STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	
Title and abstract	1	Title: Factors associated with declining under-five mortality rates from 2000 to 2011: An ecological analysis of 46 African countries An abstract is provided in the manuscript summarizing what was done and what was found
Introduction		
Background/rationale	2	Under-five mortality (U5M) rates have declined worldwide yet African children are nearly 16 times more likely to die under age five than children from high income nations and the decline in mortality has not been as rapid as hoped. Despite progress, Africa is not on track to reach Millennium Development Goal #4 of reducing U5M by two-thirds between 1990 and 2015. With variable progress across countries in improving child survival in Africa, understanding factors associated with the most rapid changes in U5M reductions could assist regional and country efforts to improve child survival.
Objectives	3	We sought to identify direct and indirect factors influencing how rapidly countries reduce U5M, as evidenced by their annual rate of reduction (ARR).
Methods		
Study design	4	An ecological analysis of country-level data was used to determine which factors previously reported to reduce U5M are also the strongest predictors of larger ARRs in Africa.
Setting	5	Available data from the 46 countries in the WHO African Region during the period 2000 to 2011.
Participants	6	As an ecological study, the "participants" include the 46 countries and not individuals.
Variables	7	Outcome: country-specific U5M rates from annual estimates provided by www.childmortality.org, the data used in the UNICEF Reports on *Levels and Trends in Child Mortality,* were used to calculate country-specific ARRs for the period 2000-2011.
Data sources/ measurement	8*	See #7 above.
Bias	9	Because survey data used in this study is not collected on an annual basis, actual data for 2000 and 2011 were often not available, data from years close to 2000 and 2011 had to be used to calculated the change in indicator coverage (predictor variable of interest). To minimize bias due to improperly extrapolating data over the time period, the following criteria were used. Indicator data had to be reported for one of the years between 1998 and 2003, termed *2000 indicator data*, and also reported for one of the years between 2006 and 2011, termed *2011 indicator data*. Furthermore, indicator values that most closely corresponded to the years 2000 and 2011 had to also be at least five years apart. If any of these criteria were not met from a given country, change in the coverage for that particular indicator was not calculated and was considered missing. Additionally, with the small sample size of 46 countries, regression modelling may have been susceptible to bias from data outliers. To minimize this possibility while retaining as much data in the analysis as possible, robust regression was used in the analysis using iteratively reweighted least squares to minimize the influence of outlying observations.
Study size	10	46 is the number of countries in the WHO African Region, our collaborator and funding agency for the project.
Quantitative variables	11	All predictor variables were modelled as continuous variables (e.g., range of vaccination coverage levels, median age of first pregnancy, etc.)

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Statistical methods	12	As described in the Methods section, robust linear regression was used to model the association between the change in coverage of an indicator and U5M ARR, while controlling for potential confounders. A separate model was used for each predictor of interest. Given the small sample size (n=46 at most), a decision was also made *a priori* to include no more than five covariates in the multivariable analyses to avoid overfitting. We selected the following indicator ARCs for inclusion as covariates in each model based on previous ecological studies, consideration of what macro- or system-level factors would influence the majority of the indicators, and having nearly complete data: access to improved water source, health expenditure (relative to gross domestic product [GDP]), adult HIV prevalence, urban population prevalence, and receipt of ANC (when applicable). All regression models included these core indicator ARCs as covariates unless expected to be highly correlated with the predictor indicator of interest. No subgroup, interaction, or sensitivity analyses were conducted. Figure 2 and Supplemental Table S2 show the completeness of reporting of indicators by country. For many indicators, a number of countries were missing sufficient data to calculate the ARC. Regression modelling was conducted for all predictor indicators regardless of the number of countries missing data, and these are presented in Supplemental Table S5. However, out of concern that missing data was associated with ARR (Figure 3 and Supplemental Table S3), main results are only provided for indicators with at least 50% complete reporting (e.g., >=23 of the 46 countries).
Results		
Participants	13*	Not applicable.
Descriptive data	14*	Not applicable.
Outcome data	15*	Table 1 shows the U5M ARR for each country in the analysis.
Main results	16	Of the 70 indicators considered in the analysis, seven indicators shows a strong and statistically significant association with U5M ARR. These included seeking treatment for ARI, GDP per capita, health expenditure relative to GDP, out-of-pocket expenses, prevalence of underweight, maternal mortality ratio, and public spending on education relative to GDP. Crude and adjusted associations are provided in Table 3 and for all associations in Supplemental Table S5).
Other analyses	17	Not applicable.
Discussion		
Key results	18	Our study represents the most comprehensive analysis to date of health indicators and other determinants of health as predictors of declining U5M in Africa. From 70 factors considered, we could use 41 indicators meaningfully. A more rapid scale-up of six factors were associated with a favorable ARR rise (i.e., higher rate of U5M decline) between 2000 and 2011: higher rates of seeking treatment for ARI, higher GDP per capita, higher health expenditure relative to GDP, lower out-of-pocket expenses, lower prevalence of underweight, and lower maternal mortality ratio. The strongest association was for maternal mortality ratio (β= -0.86), indicating that a one-percent increase in the annual reduction of the maternal mortality ratio was associated with a 0.86 percent increase in the U5M ARR. An inverse association between increasing ARC for public spending on education relative to GDP and declines in U5M ARR was counterintuitive. A possible explanation is that it represents the challenge of competing priorities for extremely resource-limited countries, where increases in education relative to GDP may adversely affect spending in other areas, such as health.
Limitations	19	Four important limitations are discussed in the Discussion section: a. Mortality and indicator data were obtained from secondary data sources. b. The ecological, cross-sectional study design. c. The time period for calculating the indicator ARCs did not always fully overlap with the time period for calculating mortality ARRs.

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		d. The small sample size (at most n=46 countries) limits the validity of many associations and prevents adjustment for many covariates. In spite of these limitations, the unique strengths of our study include our broad identification of factors potentially relevant to child survival, beyond those typically used from Demographic and Health Surveys and Countdown to 2015. We also made statistical efforts to minimize bias or distortion from outliers, without excluding them.
Interpretation	20	Our findings highlight the role of financing, economy, and the broader health system to more rapidly reduce an already declining, albeit slowly, U5M rate above and beyond the contribution of individual interventions. Our study also highlights the ongoing challenge of obtaining indicator reporting from 100% of countries. Results for 29 of the 70 indicators could not be calculated, or the results could not be considered representative, given that more than half the countries were missing the necessary data.
Generalisability	21	By design, our results are generalizable to the WHO African Region. Our findings may not be valid outside of the African context.
Other information		
Funding	22	Funding for this project was provided by the World Health Organization. Support for data management came from the Vanderbilt Institute for Clinical and Translational Research (grant UL1 TR000445 from the National Center for Advancing Translational Sciences at the National Institutes of Health).

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