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ORIGINAL ARTICLE

Association of the quality of antenatal care with neonatal mortality: meta-analysis of individual participant data from 60 low- and middle-income countries

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Background: We investigated the quality of antenatal care (ANC) and its effect on neonatal mortality in 60 low- and middle-income countries (LMICs).

Methods: We used pooled comparable cross-sectional surveys from 60 LMICs (n=651 681). Cox proportional hazards multivariable regression models and meta-regression analysis were used to assess the effect of the quality of ANC on the risk of neonatal mortality. Kaplan–Meier survival curves were used to describe the time-to-event patterns of neonatal survival in each region.

Results: Pooled estimates from meta-analysis showed a 34% lower risk of neonatal mortality for children of women who were attended to at ANC by skilled personnel. Sufficient ANC advice lowered the risk of neonatal mortality by 20%. Similarly, children of women who had adequate ANC had a 39% lower risk of neonatal mortality. The pooled multivariable model showed an association of neonatal mortality with the ANC quality index (HR 0.85, 95% CI 0.77 to 0.93).

Conclusions: Improvement in the quality of ANC can reduce the risk of neonatal mortality substantially. Pursuing sustainable development goal 3, which aims to reduce neonatal mortality to 12 per 1000 live births by 2030, should improve the quality of ANC women receive in LMICs.

Keywords: Child health, Low- and middle-income countries, Meta-analysis, Neonatal mortality, Quality of ANC

Introduction

Although there has been considerable improvement in child health over the past few decades, neonatal, infant and child mortality remain high in most low- and middle-income countries (LMICs).[1,2] Many countries in these regions were unable to meet the millennium development goal (MDG) 4 of reducing under-5 mortality by two-thirds between 1990 and 2015.[3] Addressing neonatal mortality is therefore a global public health challenge of the twenty-first century, which requires global efforts with local actors. A renewed global effort at addressing the child health challenge is demonstrated in the sustainable development goals (SDGs).[4] In particular, SDG 3, target 3.2 aims to reduce neonatal mortality to 12 per 1000 live births by 2030. This renewed effort requires comprehensive data from LMICs in order to provide evidence-based information for interventions to improve neonatal survival and child health in general.

The SDGs also prioritised access to quality healthcare including antenatal care (ANC) during pregnancy.[5] Access to quality healthcare during pregnancy and after childbirth considerably improves health outcomes, including neonatal deaths.[6] In LMICs where obstetric and gynecological facilities may be unavailable, ANC can be one of the most cost-effective preventive services for maternal and child health. Adherence to commencing ANC in the first trimester of pregnancy and having at least four visits during the gestation period can reduce neonatal mortality.[6] However, research investigating the quality of ANC and its association with specific maternal and child health outcomes, including neonatal mortality, is lacking. The quality of ANC measures the continuum of healthcare services in various dimensions before the delivery care.[7] A lack of relevant quality data on the subject is therefore an important constraint to interventions aimed at improving child health in these countries. The goals of this study were twofold. We sought to, first, assess the quality of

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ANC at national and regional levels in LMICs, and second, investigate the association of the quality of ANC with neonatal mortality in these countries and regions.

Methods

Data

We used the most recent Demographic and Health Survey (DHS), which consists of nationally representative cross-sectional data collected using a standardised questionnaire, methodology and protocols in order to facilitate international comparison. The DHS has generated high quality important demographic, economic, social and health data for LMICs, which have been used in high quality research over recent decades. We pooled the most recent dataset which was publicly available from 60 LMICs conducted from 2001 to 2014/2015 to generate a large dataset with sufficient statistical power to investigate the association of ANC quality with neonatal death. The number of countries included in this study represents 43.2% of the LMICs in the world. We restricted our analyses to the most recent singleton live birth for each woman of reproductive age (15–49 y) (n=651 681).

The 60 countries were grouped into six regions in accordance with the WHO's regional classification. By this classification, 33 (53%) of the countries in this study were in Africa, four in East Asia and Pacific (6%), six in Europe and central Asia (2%), eight in Latin America and Caribbean (14%), four in the Middle East and North Africa (12%) and five in South Asia (13%). The full list of countries and survey years are shown in Table 1. Neonatal death, defined as death of a live born baby within the first 28 d of life, was calculated based on birth history, which consisted of information on the month and year of each birth and the child's survival status at the time of interview and current age or age at death, as applicable, which were recorded during the interviews. Age at death was recorded in days if the child died within 1 mo of birth.

We measured the quality of ANC as the main independent variable based on three main measures, namely, adequacy of ANC, sufficiency of advice and skilled ANC provider. These variables cover a wide range of quality interventions supported by the WHO guidelines for ANC.[8] Adequacy of ANC was constructed from the following: weight and height measurement and whether blood pressure and urine and blood samples were taken during ANC. Sufficiency of advice refers to whether a woman was told about the signs of pregnancy complications and where to go for care if complications occur. The ANC service provider was described as skilled if a doctor, a nurse/midwife or an obstetrician/gynecologist attended the ANC visits. For adequacy of ANC, 'yes' (coded as 1) refers to having had at least two of the three recommended ANC observations, measurements or tests while 'no' (coded as 0) refers to those who had less than two of the essential observations, measurements or tests. For sufficiency of advice 'yes' refers to having been either told of signs of pregnancy complications or where to go should complications arise and 'no' refers to those who were neither advised about signs of complications nor told where to go should they arise. Furthermore, an ANC quality index was constructed by summing three dummy variables, namely, adequacy of ANC (adequate vs not adequate), sufficiency of advice (sufficient advice vs not sufficient advice) and skilled ANC service provider (skilled provider vs other), and categorised as low (0–1), medium (2) or high (3).

The data on background characteristics of the mother (age, place of residence, wealth quintile, children ever born and education) as well as the place of delivery (categorised here as health facility vs other) were also collected during the interview and included in the analysis as covariates in order to investigate the independent association of ANC quality with the risk of neonatal death. The wealth quintile is a composite measure of the household's cumulative living standard based on ownership of specified assets split into quintiles: poorest, poorer, middle, richer and richest.[9]

Statistical analysis

We considered the sampling strategy of each survey by using sample weights to estimate the distribution of independent and dependent variables. We considered recommendations for strengthening the reporting of observational studies in epidemiology (STROBE) in reporting of the results.[10] We presented a weighted distribution of the main independent variables by country and pooled values for the regions and for the total sample (Table 1). Neonatal deaths per 1000 live births and the proportion of skilled ANC providers in each country are presented in a map of the world (Figures 1A and B). For those birth records for which the day of birth was missing, the 15th day of the month was imputed to estimate the survival time in days. For neonates who were still alive, survival time was estimated as the time elapsed between birth and the day of the survey, while for those who died it was estimated as the time between birth and death within the first 28 completed days of life. All children alive at 28 day were censored. We used Cox proportional hazard regression,[11] which is the most robust multivariate approach for estimating the HRs from survival data in medical research. The Cox proportional hazard is a survival analysis regression model that describes the relationship between the event incidence, as expressed by the hazard function, and a set of covariates to adjust their effect. The final Cox model was calculated as:

$$h(t) = h_0(t) \times \exp[b_1x_1 + b_2x_2 + \ldots + b_px_p]$$

where the hazard $h(t)$ at time t is dependent on a set of covariates (x_1, x_2, …, x_p) whose impact is measured by the size of the coefficients (b_1, b_2, …, b_p).[12]

The assumption is that each event (outcome) occurs independently, hence the probabilities of no event (survival) between time points are multiplied together to obtain the cumulative survival probability. We used the survey commands in Stata to adjust for the effect of the multistage cluster sampling on the estimates. The Schoenfeld residuals diagnostic test confirmed the adequacy of the multivariable proportional hazard model (p=0.139).[12,13]

We fitted separate Cox proportional models to estimate HRs for neonatal mortality with their 95% CIs for the pooled sample for each main independent variable (measured by adequacy of ANC, sufficiency of advice during ANC, whether ANC was administered by a skilled service provider and ANC quality index), adjusting for the sociodemographic variables, place of delivery, year of survey and country in separate models. The estimates for sociodemographic variables were obtained from the ANC

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Table 1. Distribution of the maternal content of antenatal care (ANC) (adequacy of test, sufficiency of advice and ANC provider) and the ANC quality index by country and region

	n=651 681	ANC content			
		Adequacy of test	Sufficiency of advice	ANC provider	ANC quality index
		Yes	Yes	Skilled	High
Africa					
Benin (2011–2012)	13 191	7767 (97.8)	5070 (63.7)	6847 (76.3)	4360 (54.9)
Burkina Faso (2010)	15 375	5968 (59.8)	5242 (52.7)	8034 (76.8)	2584 (25.9)
Burundi (2010)	7981	316 (6.3)	1822 (36.4)	4997 (98.7)	154 (3.1)
Cameroon (2011)	11 748	6203 (95.2)	3214 (49.4)	5598 (73.5)	2649 (40.7)
Chad (2014–2015)	18 635	5719 (79.6)	3336 (47.0)	5645 (50.9)	2225 (31.0)
Comoros (2012)	3235	1531 (79.7)	643 (33.6)	335 (16.3)	106 (5.5)
Congo (2011–2012)	8170	5390 (98.4)	3413 (62.3)	5244 (89.2)	3262 (59.5)
Democratic Republic of Congo (2013–2014)	18 390	7380 (74.2)	6249 (63.0)	5322 (48.2)	2761 (27.8)
Ivory Coast (2011–2012)	7492	3199 (66.1)	1769 (36.7)	4510 (86.4)	1329 (27.5)
Ethiopia (2011)	11 872	1130 (33.3)	679 (20.0)	2554 (32.4)	370 (10.9)
Gabon (2012)	5122	3480 (98.7)	1683 (48.1)	3375 (92.1)	1593 (45.2)
Ghana (2014)	5695	3879 (96.1)	3387 (84.0)	3651 (88.1)	3000 (74.3)
Guinea (2012)	7067	2222 (51.2)	1455 (33.5)	3188 (64.1)	809 (18.6)
Kenya (2014)	19 564	5646 (85.2)	3867 (58.4)	13 704 (95.1)	3482 (25.1)
Lesotho (2014)	3112	1964 (80.0)	1556 (63.4)	2427 (94.3)	1316 (53.6)
Liberia (2013)	6502	3881 (83.4)	3261 (70.2)	4298 (90.2)	2609 (56.1)
Madagascar (2008–2009)	12 686	6157 (78.2)	3829 (48.7)	7287 (84.3)	3280 (41.7)
Malawi (2010)	19 697	11 334 (84.3)	10 692 (79.6)	12 688 (92.9)	8866 (65.9)
Mali (2012–2013)	10 402	2192 (43.1)	2102 (41.4)	4793 (70.8)	1222 (24.1)
Mozambique (2011)	11 704	2765 (38.7)	2831 (39.6)	4333 (55.0)	769 (10.8)
Namibia (2013)	4804	3481 (93.7)	2729 (73.5)	3686 (96.2)	2578 (69.3)
Niger (2012)	13 347	1930 (28.2)	3828 (56.0)	6610 (82.8)	1403 (20.5)
Nigeria (2013)	31 828	10 330 (77.1)	9032 (67.8)	12 166 (60.0)	7148 (53.2)
Rwanda (2014–2015)	8004	3210 (53.4)	4746 (79.2)	5918 (97.8)	2700 (44.9)
Sao Tome (2008–2009)	1834	1356 (99.9)	899 (66.3)	1341 (98.1)	889 (65.4)
Senegal (2014)	11 479	6075 (71.7)	7590 (89.9)	5546 (75.3)	2084 (28.3)
Sierra Leone (2013)	12 198	5198 (70.6)	3333 (45.2)	5194 (60.4)	3687 (43.5)
Swaziland (2006–2007)	2829	2043 (98.4)	1115 (53.7)	1739 (81.6)	944 (45.5)
Tanzania (2010)	8176	2459 (45.5)	2860 (53.1)	4380 (79.6)	1451 (26.9)
Togo (2013–2014)	6706	3711 (82.4)	2974 (66.2)	1278 (26.3)	786 (17.4)
Uganda (2011)	8076	2726 (57.3)	2410 (50.7)	4406 (88.7)	1549 (32.6)
Zambia (2013–2014)	13 383	8096 (88.0)	8092 (88.0)	229 (2.5)	177 (1.9)
Zimbabwe (2010–2011)	5596	2099 (52.7)	2496 (62.7)	799 (18.1)	364 (9.1)
Africa pooled	345 898	140 836 (71.0)	1 181 193 (59.7)	162 122 (69.4)	72 504 (35.2)
East Asia and Pacific					
Cambodia (2014)	7253	5364 (94.0)	4684 (82.1)	5594 (93.7)	4420 (77.5)
Indonesia (2012)	16 948	13 373 (93.4)	7591 (53.0)	9796 (66.6)	5354 (37.4)
Philippines (2013)	6982	4825 (96.8)	4003 (80.3)	1508 (29.1)	1278 (25.6)
Timor-Leste (2009–2010)	9828	4903 (93.2)	2933 (55.7)	4694 (78.0)	2482 (47.1)
East Asia and Pacific pooled	41 011	28 465 (94.0)	19 211 (63.5)	21 593 (67.7)	13 533 (44.7)
Europe and central Asia					
Albania (2008–2009)	1576	1137 (86.8)	616 (47.0)	1275 (97.3)	595 (46.7)
Armenia (2010)	1448	1140 (99.1)	651 (56.6)	1103 (95.8)	625 (54.8)
Azerbaijan (2006)	2289	1034 (61.4)	558 (33.1)	1289 (76.5)	503 (38.3)
Kyrgyz Republic (2012)	4082	2911 (99.5)	1801 (61.9)	2569 (85.5)	1569 (53.6)
Moldova (2005)	1591	1351 (99.3)	1029 (75.9)	1295 (93.5)	975 (71.7)

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Table 1. *Continued*

	n=651 681	ANC content			
		Adequacy of test	Sufficiency of advice	ANC provider	ANC quality index
		Yes	Yes	Skilled	High
Ukraine (2007)	1177	1056 (100.0)	398 (37.7)	1053 (99.1)	396 (37.4)
Europe and central Asia pooled	12 164	8629 (95.2)	5051 (55.8)	8583 (89.4)	4662 (51.4)
Latin America and Caribbean					
Bolivia (2008)	8726	5622 (96.1)	3897 (66.7)	5814 (89.9)	3597 (61.5)
Colombia (2010)	15 856	12 801 (99.5)	10 465 (81.3)	12 785 (96.4)	10 370 (80.6)
Dominican Republic (2013)	3618	2905 (99.8)	2100 (72.0)	2844 (97.2)	2038 (69.9)
Guyana (2009)	1886	1352 (98.1)	925 (67.2)	1288 (90.7)	868 (62.3)
Haiti (2012)	6893	4526 (95.7)	3075 (65.0)	4463 (85.5)	2842 (60.1)
Honduras (2011–2012)	10 174	7901 (98.8)	6046 (75.7)	7419 (89.8)	5580 (69.8)
Peru (2012)	8804	7238 (99.3)	6753 (92.7)	1254 (16.9)	1120 (15.4)
Nicaragua (2001)	32 644	4100 (98.2)	3215 (77.0)	4106 (84.9)	3146 (75.3)
Latin America and Caribbean pooled	88 603	46 447 (98.4)	36 476 (77.3)	39 621 (79.6)	29 560 (62.6)
Middle East and North Africa					
Egypt (2014)	15 668	9184 (89.2)	4777 (46.5)	14 124 (90.2)	4500 (31.9)
Jordan (2012)	9833	6374 (97.8)	2209 (33.9)	6518 (99.1)	2180 (33.5)
Morocco (2003–2004)	31 696	2605 (81.6)	1248 (39.1)	3177 (67.8)	1082 (33.9)
Turkey (2003)	21 173	2564 (81.0)	NA	3138 (76.1)	0
Middle East and North Africa pooled	78 370	20 727 (89.5)	8234 (41.2)	26 975 (86.8)	7762 (28.8)
South Asia					
Bangladesh (2014)	8092	3006 (82.7)	1695 (46.7)	2563 (57.9)	1061 (29.4)
India (2005–2006)	56 438	18 635 (60.9)	14 269 (46.6)	28 152 (71.0)	11 139 (36.4)
Maldives (2009)	3736	3164 (84.3)	1647 (51.9)	3019 (94.9)	1557 (49.0)
Nepal (2011)	5391	1489 (42.3)	2777 (78.9)	2227 (53.7)	1023 (29.1)
Pakistan (2012–2013)	11 977	3377 (60.0)	2837 (50.5)	5338 (71.8)	2004 (35.6)
South Asia pooled	85 634	29 670 (63.7)	23 226 (49.9)	41 299 (70.2)	16 785 (36.1)
All countries					
Pooled	651 681	274 773 (66.1)	210 391 (50.6)	300 175 (72.4)	144 807 (39.6)

NA- not available.

quality index model. Next, estimates for ANC quality variables were analysed and plotted (forest plot) for each country and region using the fixed effect meta-analysis command in Stata. The fixed effects model considers that the variability between studies is due to random variations resulting from the size of the study. We also plotted smoothed hazard curves for the days of death to obtain the daily HRs for infants during the first 28 completed days of life stratified by the three main independent variables and the ANC quality index. Furthermore, we tested two-way and multiplicative interaction effects between the independent variables with respect to neonatal mortality. All statistical analyses were conducted using Stata/SE 14.0 (College Station, TX: StataCorp LP).

Results

The distribution of neonatal mortality and the quality of ANC across countries and regions are presented in Table 1 and Figures 1A and B; 40% of the total sample have a high ANC index and the quality of ANC varies across countries, with the lowest in Zambia (1.9%) and highest in Colombia (80.8%) (Table 1). After adjusting for potential confounding factors, the Cox proportional hazard model showed that babies of women who had adequate ANC had an 18% lower risk of dying at neonatal age compared with those who did not have adequate ANC (Table 2). Children of women who received sufficient advice had a lower risk of neonatal death (HR 0.90, 95% CI 0.84 to 0.97). Similarly, babies of women who were attended to by skilled personnel had a 29% reduced risk of death during the first 28 d of life. The ANC quality index shows that the higher the quality of ANC received by a woman, the lower the likelihood that her child would die within the first 28 d of life.

Country-level risk of neonatal death among children born to the women who had a skilled ANC provider is shown in Figure S1. The association of ANC with neonatal mortality varies across countries. The strongest associations of the quality of ANC with the risk of neonatal mortality were found in Moldova,

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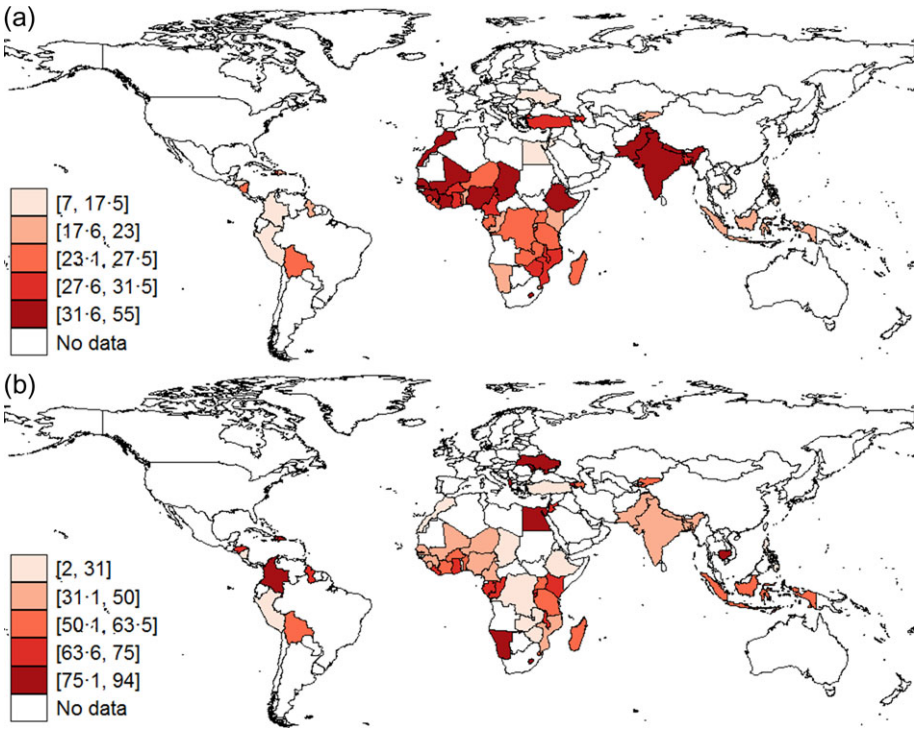

Figure 1. (a) Number of neonatal mortality per 1000 live births; (b) proportion of women who were attended to by a skilled antenatal care provider during pregnancy.

Burundi and Sao Tome. On the contrary, having ANC attended by skilled personnel seems to increase the risk of neonatal mortality in some countries, although these were not statistically significant.

The pooled HR showed 34% reduction in neonatal mortality among neonates of women who had ANC attended to by skilled personnel (Figure S1). Correspondingly, the pooled HR showed a 20% (Figure S2) and 39% (Figure S3) reduction in the risk of neonatal mortality for children of women who had received sufficient advice and an adequate test, respectively. This association, however, varied across countries, with significant heterogeneity for the effects (I^2 ranging from 41% to 76.6%) (Figures S1–3). Similarly, we found a lower risk of neonatal mortality among neonates of women who had ANC administered by skilled personnel, those who had sufficient ANC advice and those who had adequate ANC in all regions, with significant heterogeneity for the effect size across the regions (I^2 ranging from 87.2% to 98.2%) (Figures 2A–C). The only exception was in Africa, where no clear difference was found in the association of neonatal mortality and ANC attended to by skilled personnel (Figure 2A). Smoothed hazard functions for neonatal mortality during the first month of life are shown in Figures S4A–D stratified by adequacy of ANC, sufficiency of advice, skilled ANC service provider and the ANC quality index. The hazard was greatest among those who received no adequate test, insufficient advice and those at a lower level of the ANC quality index. Overall, the risk was highest at the beginning of life for all neonates and the differences in risk among the groups were also greater during the early neonatal period. We found statistically significant two-way interaction between the ANC quality index and place of delivery. Consequently, we plotted predictive margins to investigate graphically the association between the ANC quality index and place of delivery with respect to neonatal mortality (Figure S5). In further analyses of these associations we found multiplicative interactions between wealth index and maternal education, number of children ever born, maternal age and ANC quality index.

Discussion

This study found evidence in support of a positive association of the quality of ANC with neonatal survival in LMICs. Meta-analysis of individual level data suggests that children of women who were seen by skilled personnel during ANC visits had a 34% lower risk of dying during the neonatal period. Correspondingly, the pooled HR showed 20% and 39% reduced risk of neonatal mortality for children of women who received sufficient advice and an adequate test, respectively. However, these associations vary across countries. The differences in neonatal mortality by the quality of ANC were greater during the early neonatal period. With the exception of the African region, in all of the regions children whose mothers had ANC attended to by skilled personnel had a lower risk of dying during the first 28 d of life.

To the best of our knowledge, no other multi-country study has been conducted on LMICs examining the quality of ANC or how it is associated with child health in general and neonatal mortality in particular. This study is therefore the first to provide detailed analysis on the subject. In this regard there is a lack of

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Table 2. Association of neonatal death with content of antenatal care (ANC). HRs and their 95% CIs are adjusted for potential confounders (place of delivery, maternal age, area of residence, wealth quintile, children ever born, maternal education, country and year of survey variables) at the most recent birth

	n[a]	Weighted percentage	Neonatal death, %	Adjusted HR[b] (95% CI)	p-value[c]
Adequacy of test					<0.001
No	79 987	22.5	3.1	1.0	
Yes	274 773	77.5	2.2	0.82 (0.75 to 0.89)	
Sufficiency of advice					0.011
No	140 782	40.1	2.6	1.0	
Yes	210 391	59.9	2.2	0.90 (0.84 to 0.97)	
ANC provider					0.007
No care	49 183	11.9	3.5	1.0	
Non-skilled	65 262	15.7	2.4	0.62 (0.54 to 0.70)	
Skilled	300 175	72.4	2.4	0.71 (0.64 to 0.79)	
ANC quality index					<0.001
Low	80 961	22.1	2.9	1.0	
Medium	140 078	38.3	2.4	0.88 (0.80 to 0.96)	
High	144 807	39.6	2.1	0.85 (0.77 to 0.93)	
Place of delivery					0.838
Other	227 637	39.5	4.4	1.0	
Health facility	349 455	60.5	3.4	1.00 (0.92 to 1.10)	
Maternal age group, y					<0.001
15–19	35 156	5.4	5.0	1.0	
20–24	142 312	21.8	4.1	0.66 (0.57 to 0.76)	
25–29	172 849	26.5	3.4	0.55 (0.47 to 0.64)	
30–34	129 828	19.9	3.6	0.51 (0.43 to 0.61)	
35–39	91 677	14.1	4.7	0.58 (0.48 to 0.69)	
40–49	79 858	12.3	8.2	0.62 (0.50 to 0.76)	
Area of residence					0.335
Urban	234 027	35.9	4.0	1.0	
Rural	417 654	64.1	4.4	1.04 (0.95 to 1.14)	
Wealth quintile					<0.001
Poorest	141 770	22.9	4.5	1.0	
Poorer	133 479	21.6	4.4	1.06 (0.95 to 1.18)	
Middle	126 055	20.4	4.2	1.15 (1.03 to 1.28)	
Richer	117 417	19.0	4.0	1.20 (1.07 to 1.36)	
Richest	100 316	16.2	3.5	1.35 (1.17 to 1.55)	
Children ever born					<0.001
1	103 156	15.8	2.8	1.0	
2–3	258 510	39.7	3.7	0.86 (0.77 to 0.96)	
4–5	148 018	22.7	4.4	1.06 (0.91 to 1.22)	
≥6	141 973	21.8	6.7	1.48 (1.24 to 1.76)	
Maternal education					<0.001
No education	235 728	36.2	5.4	1.0	
Primary	205 021	31.5	4.4	0.87 (0.79 to 0.95)	
Secondary or more	210 932	32.4	3.1	0.69 (0.62 to 0.77)	

[a]The total for each of the variables may not be the same because of missing information in particular ANC variables.
[b]Each independent variable was adjusted separately for each sociodemographic factor in the table and for the place of delivery, country and year of survey variables.
[c]Global p-values for each variable were calculated from the multivariable Cox model.

previous studies with which to compare results. Our finding regarding the ability of the quality of ANC to reduce neonatal mortality is consistent with a recent cohort study, which reported that adherence to ANC guidelines decreased neonatal and delivery complications.[14] The differences between countries found in this study are consistent with smaller earlier studies.[15,16] Our

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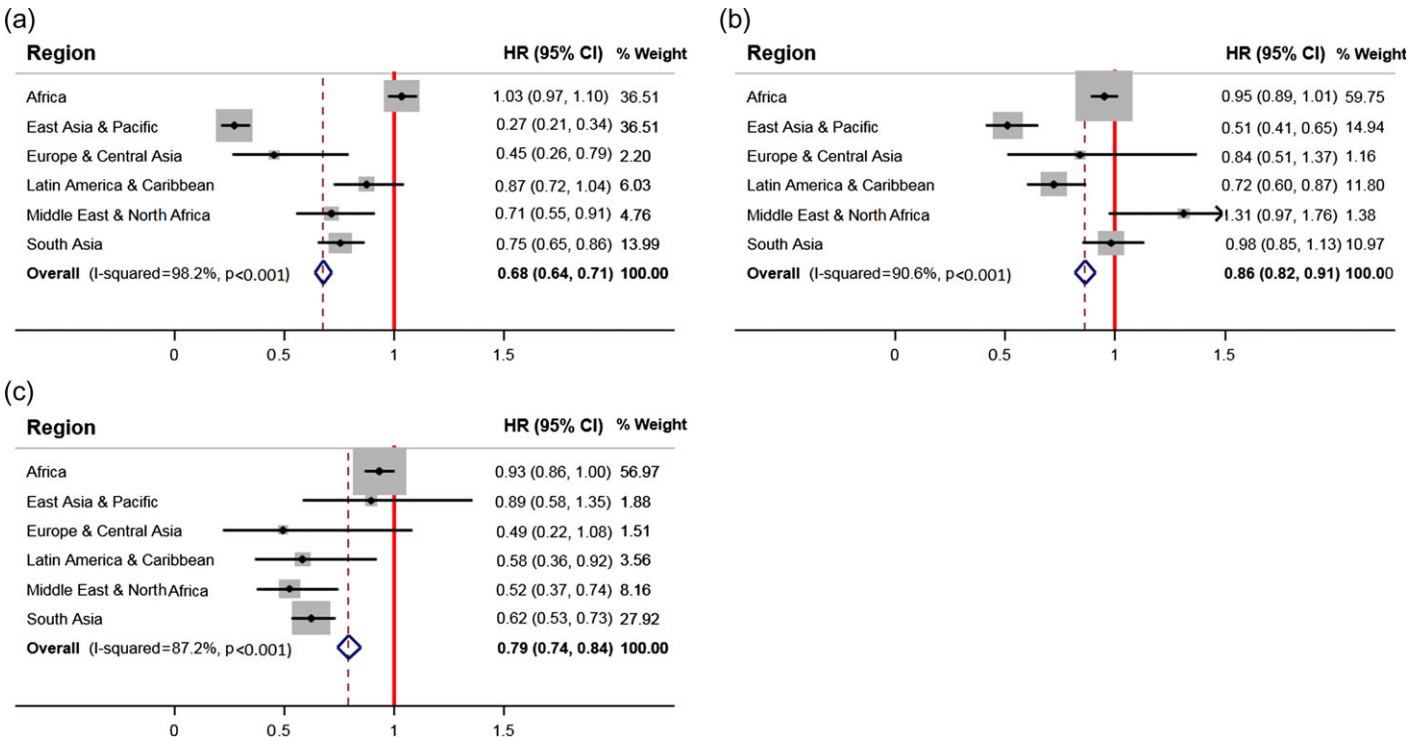

Figure 2. Meta-analysis of the association of antenatal care (ANC) quality indicators with neonatal mortality, adjusted HRs and their 95% CIs for the risk of neonatal mortality among children of mothers who had (a) ANC attended to by a skilled personnel during pregnancy across regions, (b) sufficiency of advice during pregnancy across regions and (c) adequacy of ANC during pregnancy across regions.

finding of a lack of evidence of the association of the quality of ANC with neonatal mortality in the African region varies from a previous study of 17 underdeveloped countries in the same region, which found reduced risk of neonatal mortality among children of women whose ANC was attended by skilled personnel.[17] Our data are more recent and include 33 countries from the African region that are a mixture of LMICs. These differences could explain the disparities in the findings. Future studies should investigate why the quality of ANC was not associated with reduced neonatal mortality in Africa.

Most of the ANC quality indicators used in our study, such as blood and urine tests and counselling, are essential, simple and low-cost clinical procedures which can be readily available and easily used in most LMICs. These measures are, nevertheless, very critical screening techniques that can contribute to identifying high-risk pregnancies in order to offer preventive remedies and consequently avoid complications and ensure the survival of both mother and child. The quality of ANC has also been reported to affect women's potential use of ANC services.[18] Our findings provide evidence for the need to promote adherence to simple ANC routine practices in order to improve the survival of neonates in LMICs. Aside from the availability of skilled personnel and resources, cultural beliefs, practices and the policies of health authorities and healthcare delivery systems in LMICs can affect the quality of ANC and healthcare delivery in general and influence women's access to healthcare.

In a prospective randomized trial in six LMICs, Baqui et al.[19] found that half of neonatal mortality occurred during the first couple of days of life, similar to that found in this study. Furthermore, our finding of greater differences in neonatal survival during the early days of life underscores the crucial role of quality ANC in preventing avoidable early neonatal deaths. Many of the countries in this region did not meet the MDG of reducing under-5 mortality by two-thirds between 1990 and 2015, although some have made significant progress. The SDG 3, which aims to reduce neonatal mortality to 12 per 1000 live births, has set a renewed agenda to address the global challenge of improving child health in pursuit of the unfinished agenda of the MDGs.[3] Moreover, improving access to quality healthcare, including utilisation of quality ANC, is an important priority in the SDG era. The provision of efficient low-cost ANC services such as essential tests and counselling/advice during ANC can contribute to the prevention of complications during delivery and save the lives of babies and their mothers while accelerating progress towards the attainment of SDG 3. A recent study has shown that neonates of women who deliver in a health facility have higher survival compared with those who do not deliver in a health facility.[20] Similarly, we found that the association between neonatal mortality and the ANC quality index was observed only when the delivery took place in a health facility. This highlights the importance of health facility delivery in achieving the goal of ANC. Overall, however, we found a strong association of the effect of quality ANC even after adjusting for the place of delivery and other potential confounders. Our findings therefore underscore the strong independent effect of the quality of ANC on neonatal mortality in LMICs.

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Besides the association between ANC quality indicators, we found associations of neonatal mortality with wealth index, maternal education, maternal age and the number of children ever born. These associations were similar to those reported in previous studies[6] except that we found multiplicative interactions between wealth index and maternal education, number of children ever born, maternal age and the ANC quality index. This suggests that the effect of wealth on neonatal mortality varies by these factors.

The pooled data used ensured a large sample size, which guaranteed sufficient power of the study. In addition, the meta-analysis conducted is strengthened by the use of data which were collected using similar protocols in all of the countries. Additionally, our data represent nearly half of all LMICs in the world and therefore provide a broad perspective on the subject in these regions. Despite these strengths, there are a number of constraints that should be considered during interpretation of the findings. All indicators used in this study were self-reported and may be biased by social desirability within the individual countries. Also, the cross-sectional nature of our data limits causal inference of the findings. Data on neonatal mortality were estimated from the births and deaths records, which were reported by the women retrospectively. The sociodemographic indicators such as age, wealth index and maternal education were measured at the time of the survey while the ANC variables and neonatal mortality were reported on the most recent births within 5 y of the survey. Therefore, it is possible that some of the sociodemographic factors have changed within the 5 y. The data may be subject to misclassification of stillbirth as neonatal death as well as by recall bias. However, previous studies, which validated such measures in retrospective and longitudinal surveys, found them to be accurate.[21] Initial assessment of the health data in the DHS-I suggests they are accurate estimates.[22] Moreover, a recent study of the validity of the DHS neonatal mortality measures concluded that, notwithstanding the limitations of the surveys, they provide the most reliable estimates of neonatal mortality in LMICs.[23] Although this study provides the most detailed analysis of the association of the quality of ANC on neonatal mortality, it is limited by the availability of data on the cause of death to investigate further to what extent the quality of ANC might have contributed to the cause of death. This notwithstanding, the independent association between the quality of ANC after adjusting for a large number of potential confounding factors strengthens our findings.

Overall, this study provides evidence regarding the potential of quality ANC in future interventions to reduce neonatal mortality in countries with low resources and towards the attainment of SDG 3, which targets reducing neonatal mortality to 12 per 1000 live births. Substantial improvement in the quality of ANC services is necessary to improve neonatal health in particular and maternal and child health in general. In LMICs where resources are very limited it is important to adapt and monitor ANC quality assessment criteria appropriate to the local setting in order to improve the quality of ANC. Middle-level health personnel such as nurses and midwives should be trained to perform basic maternal and foetal assessments and tests during ANC.

Supplementary data

Supplementary data are available at *International Health* online (http://inthealth.oxfordjournals.org/).

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