Individual- and population-based interventions to improve survival in early life in a low resource setting

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Verbetering van overleving in de vroege levensjaren door interventies op individueel en populatie niveau in een omgeving met beperkte middelen

(met een samenvatting in het Nederlands)

Proefschrift

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Chapter 2

Kayode GA, Amoakoh-Coleman M, Brown-Davies C, Grobbee DE, Agyepong IA, Ansah E, et al. Quantifying the validity of routine neonatal healthcare data in the Greater Accra Region, Ghana. *PloS one* 2014;9(8):e104053.

Chapter 3

Kayode GA, Grobbee DE, Amoakoh-Coleman M, Agyepong IA, Ansah E, van Dijk H, et al. Temporal Trends in Neonatal Mortality in Ghana: Impacts and Challenges of Health Policies and Programs. *(Submitted)*

Chapter 4

Kayode GA, Ansah E, Agyepong IA, Amoakoh-Coleman M, Grobbee DE, Klipstein-Grobusch K. Individual and community determinants of neonatal mortality in Ghana: a multilevel analysis. *BMC pregnancy and childbirth* 2014;14:165.

Chapter 5

Kayode GA, Amoakoh-Coleman M, Agyepong IA, Ansah E, Grobbee DE, Klipstein-Grobusch K. Contextual risk factors for low birth weight: a multilevel analysis. *PloS one* 2014;9(10):e109333.

Chapter 6

Kayode GA, Grobbee DE, Amoakoh-Coleman M, Ansah E, Uthman OA, Klipstein-Grobusch K. Exploring variation in neonatal mortality and its relation to country characteristic in 49 sub-Saharan African countries. *(Submitted)*

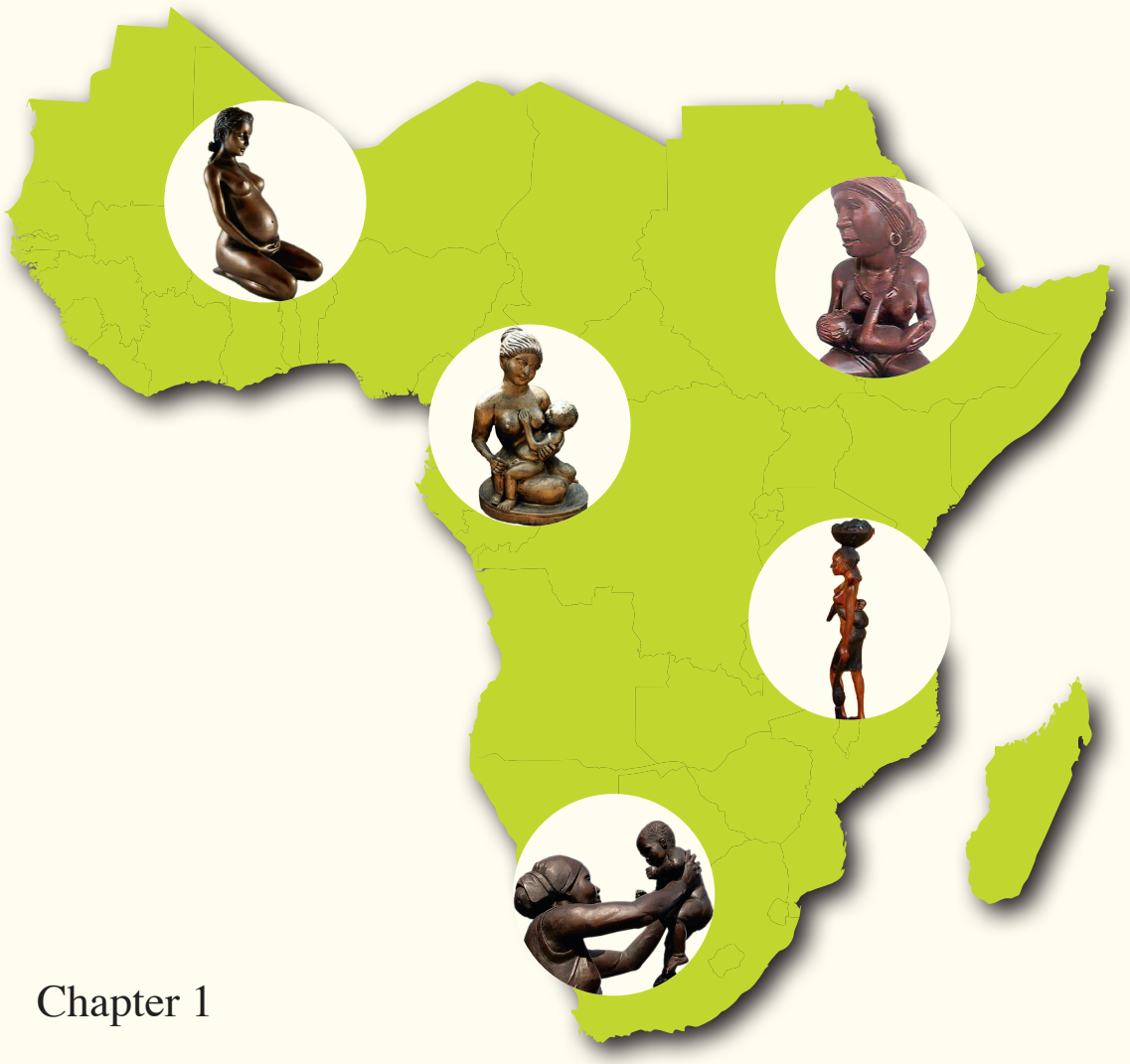
Chapter 7

Browne JL, Kayode GA, Arhinful D, Fidder SAJ, Grobbee DE, Klipstein-Grobusch K. Impact of maternal health insurance on continuum of care services utilization. *(Submitted)*

Chapter 8

Kayode GA, de Groot JAH, Amoakoh-Coleman M, Adeleke IT, Ansah E, Grobbee DE, Klipstein-Grobusch K. Predicting stillbirth in a low resource setting. *(Submitted)*

Contents



Chapter 1

General introduction

The major causes of neonatal deaths (low birth weight / prematurity, infection, birth asphyxia, and birth trauma) are well known,(1) yet its high occurrence continues unabated.(2) After twenty-five year of pursuing attainment of Millennium Development Goals 4 (MDG 4) that aimed to lower under-five mortality by two-thirds by 2015, it is now obvious that without substantial decline in neonatal mortality rate, it will be difficult to improve survival in early life. Given the limited success recorded by the MDG 4,(3) it has been included in the newly formulated Sustainable Development Goal (SDG). The Sustainable Development Goal 3 (SDG 3) aims to ensure healthy lives and promotes well-being for all at all ages. Under this goal, the Sustainable Development Goal 3.2 specifically aims at ending avoidable / preventable neonatal deaths by 2030. This new initiative will likely improve global attention being paid to neonatal mortality and will thus be of major importance for SSA to utilize this initiative to address persistently high neonatal death of about 1.2 million per annum.(2, 4)

To achieve a substantial reduction in neonatal mortality in SSA as targeted by SDG 3.2, it is important to learn from prior efforts aimed at reduction of neonatal mortality. During the era of the MDGs, government and non-governmental organizations have made considerable efforts to actualize MDG 4 in SSA. Most interventions, however, directly targeted under-five and infant mortality assumed that non-neonatal specific interventions will also improve neonatal survival.(5) This has proven to be an erroneous assumption and several calls(5-9) were issued to increase attention to neonatal mortality. As a result, neonatal specific interventions have been implemented such as Kangaroo Mother Care (KMC),(10) integration of neonatal healthcare into Safe Motherhood Program(11) and Integrated Management of Childhood Illness (IMCI)(12), Save Newborn Lives/Save the Children,(13) Maternal and Neonatal Tetanus Elimination Initiative,(14) and prevention of mother-to-child transmission of HIV(15) to name the most important. However, considering the persistently high neonatal mortality rate,(2) and increases in the proportion of infant and under-five mortality attributed to neonatal deaths,(16) these efforts so far have only yielded paucity declines in neonatal mortality. This might be the reason why some stakeholders in maternal and child health believe that a substantial decline in neonatal mortality can only be achieved with the utilization of high-tech medical equipment, a conclusion that fails to realize that most high-incomes countries achieved a significant reduction in neonatal mortality before the advent of high-tech medical equipment.(8, 17) For SDG 3.2 to achieve its aim, it is important to unravel why the implemented programs could not achieve a significant decline in neonatal mortality especially in SSA.

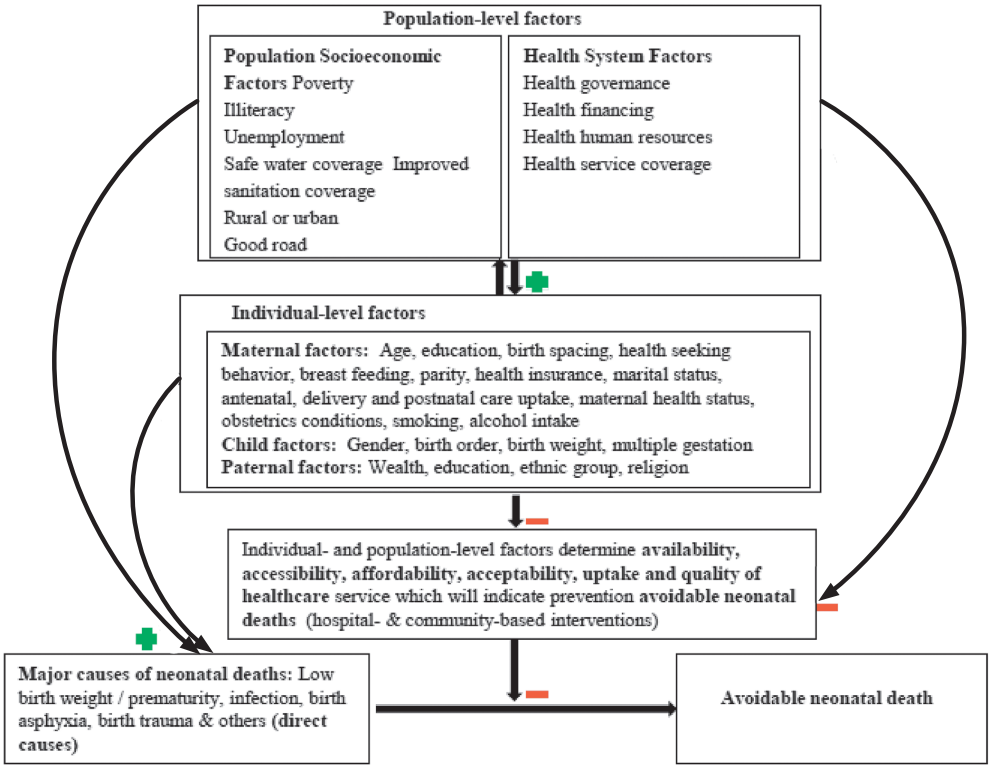


Figure 1. Conceptual framework for neonatal mortality(18)

Further, a clear understanding of the underlying mechanisms for neonatal survival may both reveal reasons for persistently high neonatal mortality in SSA and indicate effective interventions to realize SDG 3.2. Based on medical knowledge and literature the conceptual framework for child survival was modified to explain neonatal death (figure 1).(18) The framework consists of two major components: direct factors (leading causes of neonatal deaths) and indirect factors (population- and individual-level factors). Both individual- and population-level factors interact and influence neonatal survival via two mechanisms: (i) increase the occurrence of the main causes of neonatal death (low birth weight / prematurity, infections, birth asphyxia, birth trauma and others)(19-21) and (ii) hinder the prevention of neonatal death by influencing availability, accessibility, affordability, acceptability, uptake and quality of healthcare services.(22) For example, living in high-poverty neighborhoods was shown to increase the likelihood of neonatal mortality;(23) this might be due to high risk of infections and poor access to quality healthcare in such a neighbourhood. In contrary, wealthy, educated, city-dwelling mothers were more likely to utilize antenatal, skilled delivery and postnatal health care(22) which likely improves neonatal survival. Based on this framework it is important to identify population-based interventions that will

improve neonatal survival. Similarly, it is important to utilize individual-level factors to develop decision-making tools that will improve risk-based management in maternal and neonatal healthcare.

Since the reduction of neonatal mortality remains as the main priority to improve survival in early life, this thesis aims to contribute towards actualizing a substantial reduction in neonatal mortality by achieving the following objectives: (i) to understand why the rate of survival in early life has not improved, (ii) to identify population-based interventions for survival in early life, and (iii) to improve prevention of death in early life. Achieving these objectives will generate evidence that could be used to improve existing interventions implemented and formulate new interventions to address neonatal survival.

Outline of the thesis

Chapter 1 of this thesis presents the public health importance of neonatal mortality in SSA and efforts to address it. Chapter 2 examines the validity of routine data being used to monitor progress towards actualizing MDG 4. Chapter 3 describes trends in neonatal mortality in the last two decades and compares these trends to that of infant and under-5 mortality; it further assesses the impact and challenges of polices and implemented intervention programs to achieve a reduction in neonatal mortality. Chapter 4 identifies individual- and population-level determinants for neonatal mortality while chapter 5 determines population-level factors for low birth weight. Chapter 6 examines variation in neonatal mortality in sub-Saharan Africa and underlying factors for the observed variation. Chapter 7 reports on the effect of maternal health insurance status on the uptake of antenatal, delivery and postnatal care, while chapter 8 describes the development of prediction models to identify pregnancies with a high risk of stillbirth. Chapter 9 provides recommendations on how to address avoidable neonatal deaths in SSA.

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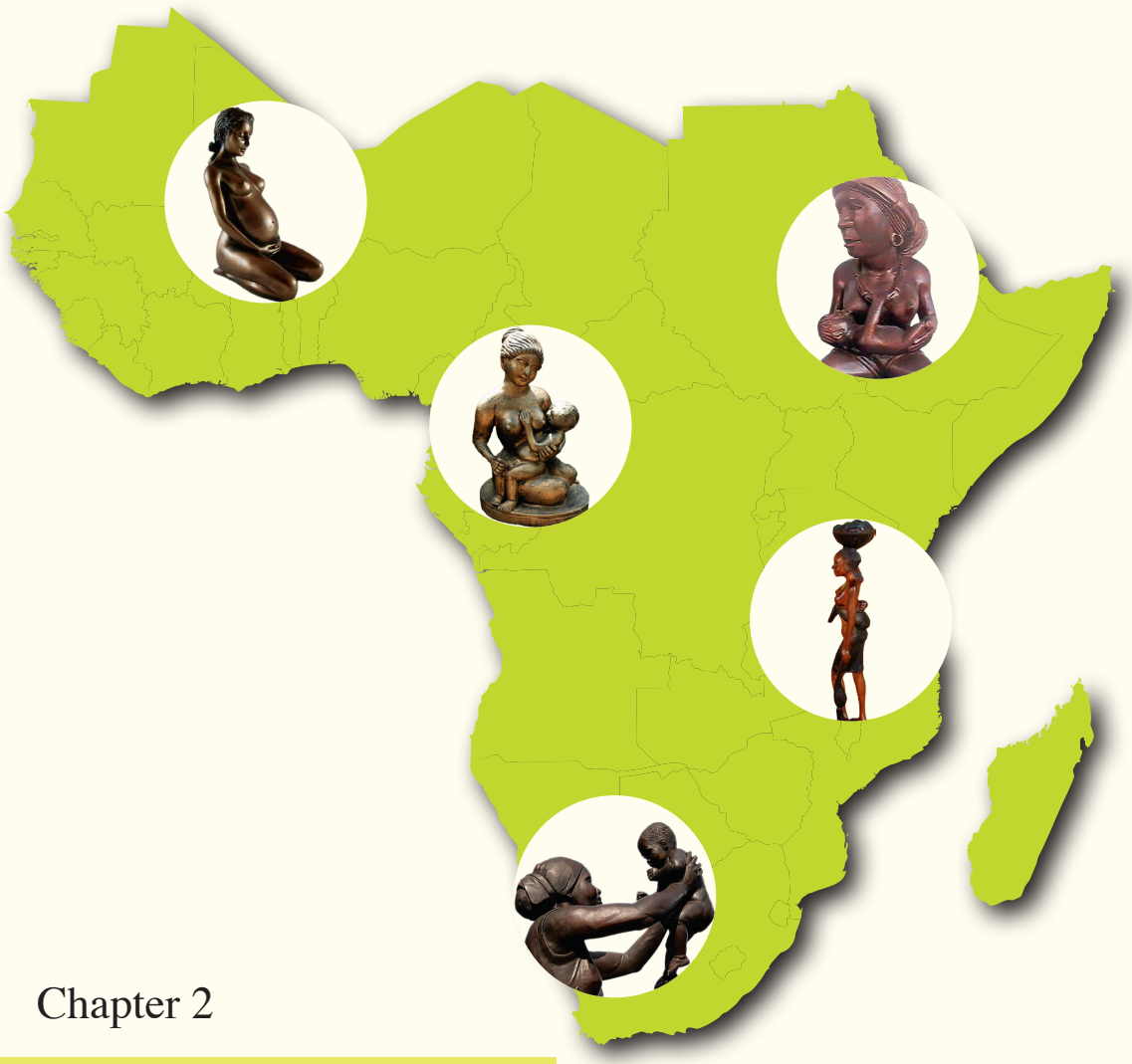
Part 1

Unravelling why the rate of survival in early life remains stagnant



Chapter 2

Quantifying the Validity of Routine Neonatal Healthcare Data in the Greater Accra Region, Ghana

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Diederick E Grobbee
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Evelyn Ansah
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Abstract

Objectives

The District Health Information Management System–2 (DHIMS–2) is the database for storing health service data in Ghana, and similar to other low and middle income countries, paper-based data collection is being used by the Ghana Health Service. As the DHIMS-2 database has not been validated before this study aimed to evaluate its validity.

Methods

Seven out of ten districts in the Greater Accra Region were randomly sampled; the district hospital and a polyclinic in each district were recruited for validation. Seven pre-specified neonatal health indicators were considered for validation: antenatal registrants, deliveries, total births, live birth, stillbirth, low birthweight, and neonatal death. Data were extracted on these health indicators from the primary data (hospital paper-registers) recorded from January to March 2012. We examined all the data captured during this period as these data have been uploaded to the DHIMS-2 database. The differences between the values of the health indicators obtained from the primary data and that of the facility and DHIMS–2 database were used to assess the accuracy of the database while its completeness was estimated by the percentage of missing data in the primary data.

Results

About 41,000 data were assessed and in almost all the districts, the error rates of the DHIMS-2 data were less than 2.1% while the percentages of missing data were below 2%. At the regional level, almost all the health indicators had an error rate below 1% while the overall error rate of the DHIMS-2 database was 0.68% (95% C I = 0.61–0.75) and the percentage of missing data was 3.1% (95% C I = 2.96–3.24).

Conclusion

This study demonstrated that the percentage of missing data in the DHIMS-2 database was negligible while its accuracy was close to the acceptable range for high quality data.

Background

Data quality assurance is of high priority in any clinical research because the quality of the data is a major determinant of the validity of the conclusions drawn. High quality data can be ensured by adherence to Good Clinical Data Management Practice (GCDMP) [1] although there is no consensus on what should be regarded as guidelines for GCDMP for all the fields of healthcare research [2]. Generally, it is believed that the information on regulations and guidelines for GCDMP can be obtained from the International Conference on Harmonisation (ICH), Food Drug Agency (FDA) and Society for Good Clinical Data Management [3]–[5] to inform formulation of Standard Operating Procedures (SOPs) for data collection.

Data can be captured by Electronic Data Capturing (EDC) and Paper-based Data Collection (PDC) method. Both methods are prone to errors thus, careful assessment of data quality prior to analysis is essential. Errors can be detected in clinical data by double data entry, logic check (range check, detection of outliers, relational conflicts and more) and visual verification [6]. All these methods have their own limitations. The quality of a dataset can be quantified by estimating its accuracy (error rate) and completeness (% of the missing data) [6]. Validation of PDC is usually done by comparing the Case Report Form (CRF) to the database even though this is not in accordance with Good Clinical Practice recommendations [7]. Ideally, in data validation, the database should be compared to the data source i.e. patient's folder or register (primary data source) [7] to avoid the underestimation of the error rate as previously reported by Nahm and colleagues [8]. In the CRF - database validation, some data collection processes that precede CRF will not be examined. Routine clinical data collection in low and middle income countries (LMICs) are mostly paper-based before uploading them to the database.

Similar to other LMICs, routine clinical data in Ghana rely on PDC and prior to May 2012, the District Health Information Management System (DHIMS) was used to manage routine data collected by the health facilities. Health facilities collated and forwarded their data to the districts. The district offices further collated and forwarded the data to regional and subsequently national level before data were uploaded to the national database (data acquisition process). Recently, a web-based database called DHIMS-2 was launched with the aim of improving the quality of the DHIMS data by shortening data acquisition processes. This new method still relies on PDC but the number of data acquisition processes have considerably reduced suggesting possible improvement in the quality of the DHIMS-2 database compared to the previous DHIMS database [9], [10].

Further, the new data management system allows health facilities to collate and upload their data directly to the DHIMS-2 database with instant access at the district, regional and national level. Small health facilities that lack internet facilities and manpower to upload their data to the database

continue to forward data to the district office for uploading. This is a great achievement when compared to the former system of handling data (DHIMS). Despite the introduction of this new improved data management system, the quality of the DHIMS-2 data has not been assessed in detail. Thus, this study aimed to quantify the quality of routine neonatal data in the DHIMS-2 database by evaluating its accuracy (error rate) and completeness (% of missing data) for subsequent use in clinical research, evidence-based health policy formulation, and monitoring progress towards attaining Millennium Development Goal 4 (MDG 4 aims to reduce under-five mortality by two-thirds between 1990 and 2015).

Methods

Setting

This study was conducted in the Greater Accra Region (GAR), one of the ten administrative regions of Ghana. The region is located in the southern part of Ghana with a population of about 4 million [11] and a neonatal mortality rate of 21 per 1,000 live births [12]. The GAR has ten administrative districts: Accra Metropolis, Ga South Municipality, Dangme East District, Dangme West District, Tema Metropolis, Ledjokuku-Krowor Municipality, Ashaiman Municipality, Adenta Municipality, Ga East Municipality and Ga West Municipality. Communities in this region are mostly urban and the region is served by both public and private health facilities. The DHIMS-2 database covers all the public and few private health facilities.

Design of data collection

Collection of data to validate the DHIMS-2 database was carried out in the GAR. Given the financial limitations, data collection could not be extended beyond the GAR. Seven out of the ten districts in the GAR were randomly sampled for inclusion in the study; we anonymized the sampled districts as district A, B, C, D, E, F and G. The district hospital (secondary level of care in low resource setting) and a polyclinic (primary level of care in low resource setting) in each of the sampled districts were recruited for the study and where one of these health facilities was not available, a health centre (primary level of care in low resource setting but smaller than a polyclinic) in that district was considered. Seven neonatal health indicators were pre-specified for validation: antenatal registrants, deliveries, live birth, stillbirth, low birth weight and neonatal death. Data captured on these health indicators during the first quarter of 2012, were retrieved from thirteen health facilities in the sampled districts with the support of trained research assistants who collected information in a standardized manner. We examined all the data captured on the pre-specified health indicators during the first quarter of 2012 because all the districts have uploaded the data captured during this period to the DHIMS-2 database. Data were retrieved from the primary data sources (antenatal, delivery and neonatal register), facility data and DHIMS-2 data. Antenatal,

delivery and neonatal registers are paper register where clinical and non-clinical profiles of the patients are recorded when they present at antenatal, delivery or neonatal intensive care unit. Data were extracted from the primary data sources on the pre-specified health indicators and the differences between the estimated values of the health indicators obtained from the primary data and that of the facility and DHIMS–2 data were used to estimate the accuracy of the DHIMS-2 database. Completeness of the DHIMS-2 database was estimated by calculating the percentage of missing data in the primary data. Primary data (individual patient data) were obtained from the antenatal, delivery and neonatal register while the facility and DHIMS-2 data (aggregate data) were provided by the health facilities and the Biostatistics Department of the Greater Accra Regional Health Directorate respectively. In addition, semi-structured questionnaires were used to gather information on the data acquisition processes as shown in Figure 1.

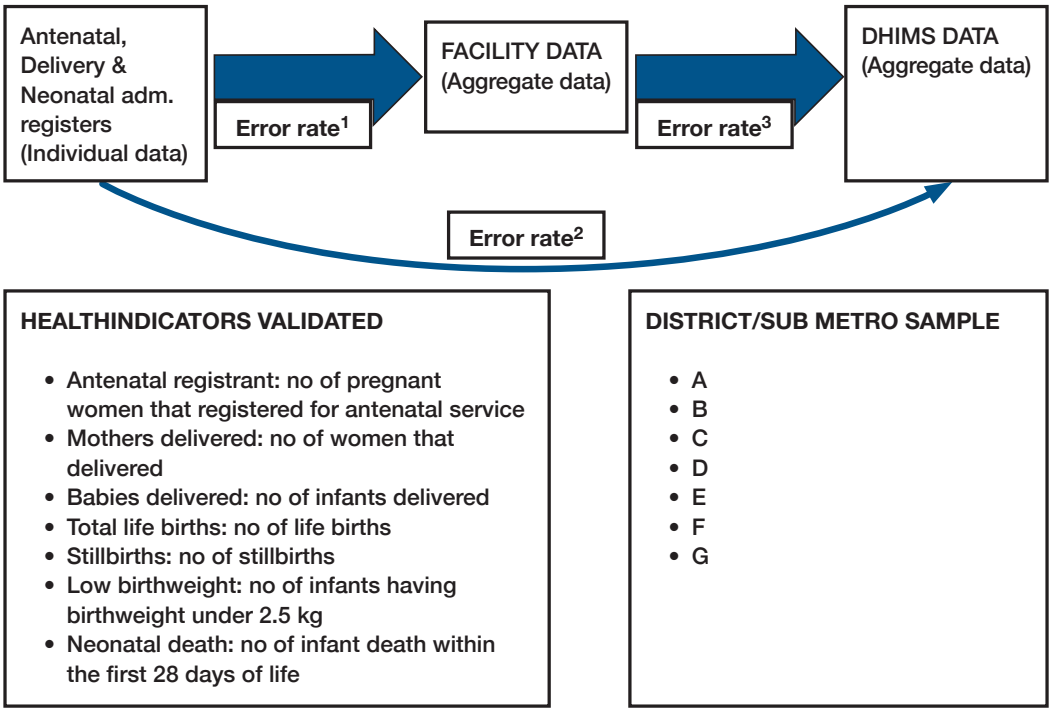

Figure 1. Data flow from the primary data sources to DHIMS-2 database

Data recording

Table 1 shows the different codes used to denote stillbirth. The delivery service data were recorded in the delivery register with different codes across the facilities. The nurses in-charge of the data recording and collation gave the precise interpretation of the codes used to denote different health

indicators in order to avoid misinterpretation errors during data assessment. For instance stillbirth was denoted differently (0, 0/10, 0/0, IUFD, SB, FSB, MSB) across the health facilities but clarified for the purpose of this study by the staff in-charge.

Table 1. Different codes used at the facilities

FACILITY NAME	STILLBIRTH CODES
Facility I	SB; 0; 0/10; Macerated
Facility II	0/10; 0/0
Facility III	SB
Facility IV	SB
Facility V	SB; FSB; IUFD; Macerated SB; MSB
Facility VI	Fresh SB; Stillbirth; MSB; IUFD;
Facility VII	SB
Facility VIII	SB
Facility IX	0; 0/10; Macerated
Facility X	Macerated baby

Statistical analysis

The quality of the DHIMS-2 database was quantified by assessing the accuracy (error rate) and completeness (percentage of missing data) of the pre-specified neonatal health indicators. A double-visual verification procedure and logic check were applied to estimate the accurate values of the pre-specified health indicators from the primary data. The differences between the estimated values of the health indicators obtained from the primary data and that of the facility and DHIMS-2 data indicated the total number of error in the facility and DHIMS-2 database respectively. Error rates were calculated by dividing the total number of error by the total number of data inspected. Double visual verification is an analogue of double data entry; we applied it because of the inaccuracy of visual verification [6]. The same procedure was also applied to estimate the total number of missing data in the primary data. The percentage of missing data was subsequently calculated by dividing the total number of missing data by the total number of data inspected. The differences between the estimated values of the health indicators in the primary data and that of the DHIMS-2 database were calculated; we subsequently divided the estimated difference (total number of errors) by the total number of data inspected to obtain the error rate and we denoted the estimated error rate as error rate^{1}. We repeated this procedure between the primary and facility data; the estimated error rate between both data was denoted as error rate^{2}. The same process was applied to estimate the error

rate between the facility to DHIMS-2 data and we named the estimated error rate as error rate[3]. All the different error rates estimated are shown in Figure 1.

Completeness was defined as:

$$Completeness = (md - di) \times 100$$

Where ***md*** = total number of missing data; ***di*** = total number of data inspected

The error rate was defined as:

$$Er = (ne \div di) \times 100$$

Where ***Er*** = error rate; ***di*** = total number of data inspected

Finally, the 95% confidence interval of the overall missing data (completeness) and error rates were estimated

$$y = p \pm z\sqrt{p(1-p) \div di}$$

Where ***y*** = 95% confidence interval of the estimate; ***p*** = % of missing data or error rate; ***z*** = 1.645 (1-sided alpha level of 0.5); and ***di*** = total number of data inspected. SPSS (version 20) was used for the analysis [13].

Ethical approval

This study was conducted in the GAR in conjunction with the Biostatistics Department of the Ghana Health Service which is saddled with the responsibility of collecting, monitoring, managing, and verifying routine GHS clinical data. Written permission to conduct this study in collaboration with the Biostatistics Department of the Ghana Health Service was obtained from the Regional Director of Health Services, Greater Accra Regional Health Directorate, Ghana Health Service. Ethical approval was not required because we only received and analysed anonymous data.

Table 2: Completeness and Accuracy of DHIMS-2 data

District / Sub-Metro	Completeness (% of missing data)	Accuracy (Error rates in %)
A	1.97	0.22
B	0.09	0.15
C	1.76	3.25
D	25.6	1.27
E	1.27	2.03
F	0	2.66
G	0.88	2.01
Total Estimate of the DHIMS-2 Data Validity in the GAR	**3.10 % (95% C. I = 2.96 - 3.24)**	**0.68% (95% C. I = 0.61 - 0.75)**

Results

Data processing

Thirteen health facilities from seven districts were recruited into the study and a total of 41,000 data recorded on the selected health indicators from January to March 2012. On average 5,800 data entries were inspected per district using logic check and double visual verification procedure. Figure 1 shows the neonatal health indicators considered and the pathway of data flow from the primary data to the DHIMS-2 database. All the health facilities were using a PDC method before uploading their data to the DHIMS-2 database.

After the monthly collation of the primary data from the antenatal, delivery and neonatal admission register by the nurses in their respective departments; data uploading into the DHIMS-2 database was done within the health facilities in all the district hospitals and some of the polyclinics. The facility public health nurses, health information officers and biostatistician were responsible for data uploading depending on the health facility whereas the district public health nurses were uploading data sent from the maternity and health centres.

Overall completeness of data in the districts and GAR

Table 2 shows the completeness of the DHIMS-2 data in each district and the GAR. We estimated the percentage of the missing data in the primary data source and in almost all the districts, the percentages of the missing data that were less than 2% with an exception of district D where the value exceeded 25%. Overall percentage of missing data in the GAR was 3.10% (95% C. I = 2.96–3.24).

Overall data accuracy in the districts and GAR

Table 2 shows the overall accuracy of the DHIMS-2 data in each district and the GAR. District B had the lowest error rate of 0.15% while most of the districts had an error rate less than 2.1% with the exception of district F and C. The overall error rate of the DHIMS-2 database in the GAR was 0.68% (95% C. I = 0.61–0.75).

Accuracy of health indicators at the regional level

Estimated error rates of the DHIMS-2 data in the Greater Accra Region (data flow from the primary data source to the DHIMS-2 database) are shown in **Table 3**. The results showed that approximately all the examined health indicators had error rates below 1% except for two parameters: total antenatal registrants and number of babies delivered for which error rates of 1.05% were estimated.

Table 3. Error rates of each health indicator in the DHIMS-2 data at the regional level

GREATER ACCRA REGION (INVOLVING ONLY THE SAMPLED DISTRICTS/SUB-METRO)							
HEALTH INDICATORS	**1° DATA**	**FACILITY DATA**	**DHIMS – 2 DATA**	**TOTAL DATA INSPECTED**	**ERROR RATE[1] (%)**	**ERROR RATE[2] (%)**	**ERROR RATE[3] (%)**
Total registrants	8984	9079	9079	9012	1.05	1.05	0
Mothers delivered	5903	5875	5912	5925	0.47	0.15	0.62
Babies delivered	5988	5955	5998	6010	0.55	0.17	0.72
Total live birth	5847	5868	5910	6010	0.35	1.05	0.70
Stillbirths	141	87	88	6010	0.90	0.88	0.02
LBW	436	399	399	6010	0.62	0.62	0
Neonatal death	53	52	52	433	0.23	0.23	0
The overall accuracy of the DHMIS-2 database = 0.68 % (95% C. I = 0.61 - 0.75)							

Error rate[1] represents the percentage of error in the facility data compared to the 1° data

Error rate[2] represents the percentage of error in the DHIMS-2 data compared to the 1° data

Error rate[3] represents the percentage of error in the DHIMS-2 data compared to the facility data

Accuracy of health indicators at the district level

Table 4 shows the estimated error rates of all the health indicators in each of the district as the data flow from the primary data to the DHIMS-2 database. Generally in all the districts, the facility and DHIMS-2 data were almost identical when compared with the exception of district A where facility data differed substantially from the primary and DHIMS-2 data and some of the error rates (error rate[1] & error rate[3]) exceeded 4%. However, in district A, the primary data were observed to be very similar to the DHIMS-2 data and none of the error rates (error rate[2]) of the health indicators exceeded 0.5%.

Table 4. Error rates of each health indicator in the DHIMS-2 data at the district level

HEALTH INDICATORS	1° DATA	FACILITY DATA	DHIMS – 2 DATA	TOTAL DATA INSPECTED	ERROR RATE[1] (%)	ERROR RATE[2] (%)	ERROR RATE[3] (%)
DISTRICT A							
Total registrants	264	265	265	266	0.38	0.38	0
Total delivery	935	897	934	937	4.06	0.11	3.95
Total births	938	894	937	940	4.68	0.11	4.57
Total live birth	933	885	929	940	5.11	0.43	4.68
Stillbirths	7	8	8	940	0.11	0.11	0
LBW	33	36	36	940	0.32	0.32	0
Neonatal death	***	***	***	***	***	***	***
DISTRICT B							
Total registrants	1382	1381	1381	1384	0	0	0
Total delivery	543	543	543	545	0	0	0
Total births	545	545	545	547	0	0	0
Total live birth	541	541	541	547	0	0	0
Stillbirths	4	4	4	547	0	0	0
LBW	20	15	15	547	0.91	0.91	0
Neonatal death	7	7	***	1232	0	***	***
DISTRICT C							
Total registrants	1474	1455	1455	1478	1.29	1.29	0
Total delivery	975	917	917	979	5.92	5.92	0
Total births	982	926	926	986	5.68	5.68	0
Total live birth	968	915	915	986	5.38	5.38	0
Stillbirths	14	11	11	986	0.30	0.30	0
LBW	48	29	29	986	1.93	1.93	0
Neonatal death	***	***	***	***	***	***	***
DISTRICT D							
Total registrants	1448	1453	1453	1452	0.34	0.34	0
Total delivery	536	548	548	540	2.22	2.22	0
Total births	540	552	552	544	2.21	2.21	0
Total live birth	536	551	551	544	2.76	2.76	0
Stillbirths	4	1	1	544	0.55	0.55	0
LBW	65	59	59	544	1.10	1.10	0
Neonatal death	***	***	***	***	***	***	***
DISTRICT E							

Total registrants	1362	1421	1421	1364	4.33	4.33	0
Mothers delivered	971	976	976	973	0.51	0.51	0
Babies delivered	986	992	992	988	0.61	0.61	0
Total live birth	957	979	979	988	2.23	2.23	0
Stillbirths	29	13	14	988	1.62	1.52	0.1
LBW	75	49	49	988	2.36	2.36	0
Neonatal death	10	12	***	65	3.08	***	***
DISTIRCT F							
Total registrants	766	762	762	770	0.52	0.52	0
Mothers delivered	231	247	247	235	6.81	6.81	0
Babies delivered	233	249	249	237	6.75	6.75	0
Total live birth	232	248	248	237	6.75	6.75	0
Stillbirths	1	1	1	237	0	0	0
LBW	12	12	12	237	0	0	0
Neonatal death	***	***	***	***	***	***	***
DISTIRCT G							
Total registrants	2294	2342	2342	2298	2.36	2.36	0
Mothers delivered	1712	1747	1747	1716	2.04	2.04	0
Babies delivered	1764	1797	1797	1768	1.87	1.87	0
Total live birth	1682	1748	1748	1768	3.73	3.73	0
Stillbirths	82	49	49	1768	1.87	1.87	0
LBW	183	199	199	1768	0.90	0.90	0
Neonatal death	53	52	52	433	0.23	0.23	0

Error rate[1] represents the percentage of error in the facility data compared to the 1° data

Error rate[2] represents the percentage of error in the DHIMS-2 data compared to the 1° data

Error rate[3] represents the percentage of error in the DHIMS-2 data compared to the facility data

*** denotes data that were not available when the study was conducted

Further, in other districts the facility and DHIMS-2 data were error-free (error rate^{3}) or almost error-free when compared. However, both the facility and DHIMS-2 data were observed to have some degree of discrepancies when compared to the primary data; in district C and F, half of their health indicators had error rates up to 5% and 6% (error rate^{1} and error rate^{2}) respectively. In district D, E, and G almost all the error rates (error rate^{1} and error rate^{2}) were below 3% whereas in district B almost all the health indicators were error-free.

Discussion

Main findings

This study quantified the quality of the DHIMS-2 data by estimating its completeness and accuracy as the data flow from the primary data to the national database. The overall error rate in the DHIMS-2 database was 0.68% (95% C. I = 0.61–0.75) and the percentage of missing data was 3.10% (95% C. I = 2.96–3.24) indicating that the overall accuracy of the DHIMS-2 database was close to an acceptable value of the error rate (0.5%) for high quality data [14], [15]. The accuracy of the DHIMS-2 database was well above the reported average error rates (9.76%) of forty-two source-database validation studies [8] and was observed to be more accurate and complete than a similar database (HMIS database) assessed in Tanzania [9].

It is important to note that there is no consensus on what should be regarded as an acceptable error rate for high quality data; so this value varies across clinical and pharmaceutical fields [6]. The variation in the cut-off point for the acceptable error rate depends on the outcome and the consequences of committing errors. Generally, the majority of the experts agreed that 0.5%, 0–0.1% and 0.2–1%, should be considered as the acceptable error rate for the overall, critical and non-critical variables respectively [14], [15]. Judging from this perspective the overall error rate of the DHIMS-2 data was very close to the acceptable value. However, it is important to emphasise that the final error rate of this data greatly depends on the size of the data inspected. In other words, as the inspected dataset increases the magnitude of the error rate declines.

Overall percentage of missing data in the DHIMS-2 database in each of the districts was negligible with the exception of district D where the percentage of missing data exceeded 25%. This was because one of the facilities in this district was not recording the status of the newborn adequately post-delivery. In all the districts, the facility and DHIMS-2 data were identical or almost identical when compared except for district A where both data differed substantially. The most likely reason for the discrepancy was that the authentic copy of the facility data that was uploaded to the DHIMS-2 database might have been misplaced. In district B all the three data (primary, facility and DHIMS-2) were almost identical, indicating the ability of the public facilities to provide high quality data. The commonest source of error was inaccurate collation of the primary data; others were inaccurate

numbering of the registers, collation of the facility data before the end of the month and inadequate supply of delivery and antenatal register. Other challenges were inadequate training of data collectors (midwives, public health nurses, health information officer and biostatistician), incomplete data capturing, lack of periodic data verification, and more. Variation in coding of health indicators is another important issue that needs attention.

This study evaluated the validity of the DHIMS-2 database and identified plausible sources of errors that should be addressed to improve the quality of the data. At the time of the study, Standard Operating Procedures (SOPs) for the DHIMS-2 database were under development; its application during data acquisition will contribute significantly to the collection of high-quality data. Although introduction of electronic data collection could improve the quality of the database even further the cost associated with electronic data collection may make EDC not a suitable option for low resource settings. Therefore, the focus should be on optimizing PDC procedures, e.g. to implement appropriate quality improvement measures to ensure high quality data. This will require adherence to the SOPs by the data collectors and avoidance of the common sources of errors mentioned earlier.

This study clearly showed that most of the errors in the data were committed during collation of the primary data; indicating that the introduction of double check procedures will reduce the occurrence of errors in the database to a negligible level. This procedure is an analogue of double data entry thus, it is expected to reduce the error rate to 0.001% [16]. Provision of well-designed registers tailored to capture only the required data will enhance uniformity in data capturing processes and accelerate the attainment of high-quality data. Provision of periodic training on data collection will increase staff knowledge and resolve the lack of uniformity in data coding. A concerted effort should be made to integrate more private hospitals and traditional birth attendants into the DHIMS-2 database.

Study limitations and strengths

The districts involved in this study were randomly sampled and the health facilities that were recruited within the sampled districts were selected based on pre-specified criteria to avoid selection bias. This study recruited about 50% of the districts in the Greater Accra Region in order to have a clearer insight about the quality of the DHIMS-2 data. It has been reported that the visual verification of data has an inherent weakness of committing 15% error [17]. Thus, we adopted double visual verification; an analogue of double data entry which has been shown to be very sensitive with an error rate of 0.001% [16]. Two people verified the data separately and compared their results in order to resolve any disparity which implies that the probability of committing any error during the verification of the data is directly proportional to the chance that these two

assessors will commit the same error. Further, we performed a source – database validation which is in accordance with GCP standard. However, this study only covered the neonatal component of the database; thus it might be argued that the results cannot be generalised to the other components of the database. However, this will only hold grounds if the underlying mechanisms of committing errors in other components of the database are different.

Conclusion

This study demonstrated that the DHIMS-2 data have a negligible level of missing data while its accuracy was very close to an acceptable standard. It is very clear that the DHIMS-2 data in the GAR can be transformed to high-quality data as demonstrated in district B if other districts can replicate this excellent achievement.

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Author Contributions

Analyzed the data: GAK. Wrote the paper: GAK. Jointly conceived the study idea: GAK MAC KKG EA DEG. Developed material for data collection: GAK. Conducted the literature review and wrote the first draft of the manuscript: GAK. Supervised the first draft of the manuscript: KKG EA DEG. Collected the data for this study: GAK MAC. Assisted with sampling and data collection: CBD. Scientifically reviewed the manuscript and approved the final manuscript: GAK MAC KKG EA DEG CBD IA.

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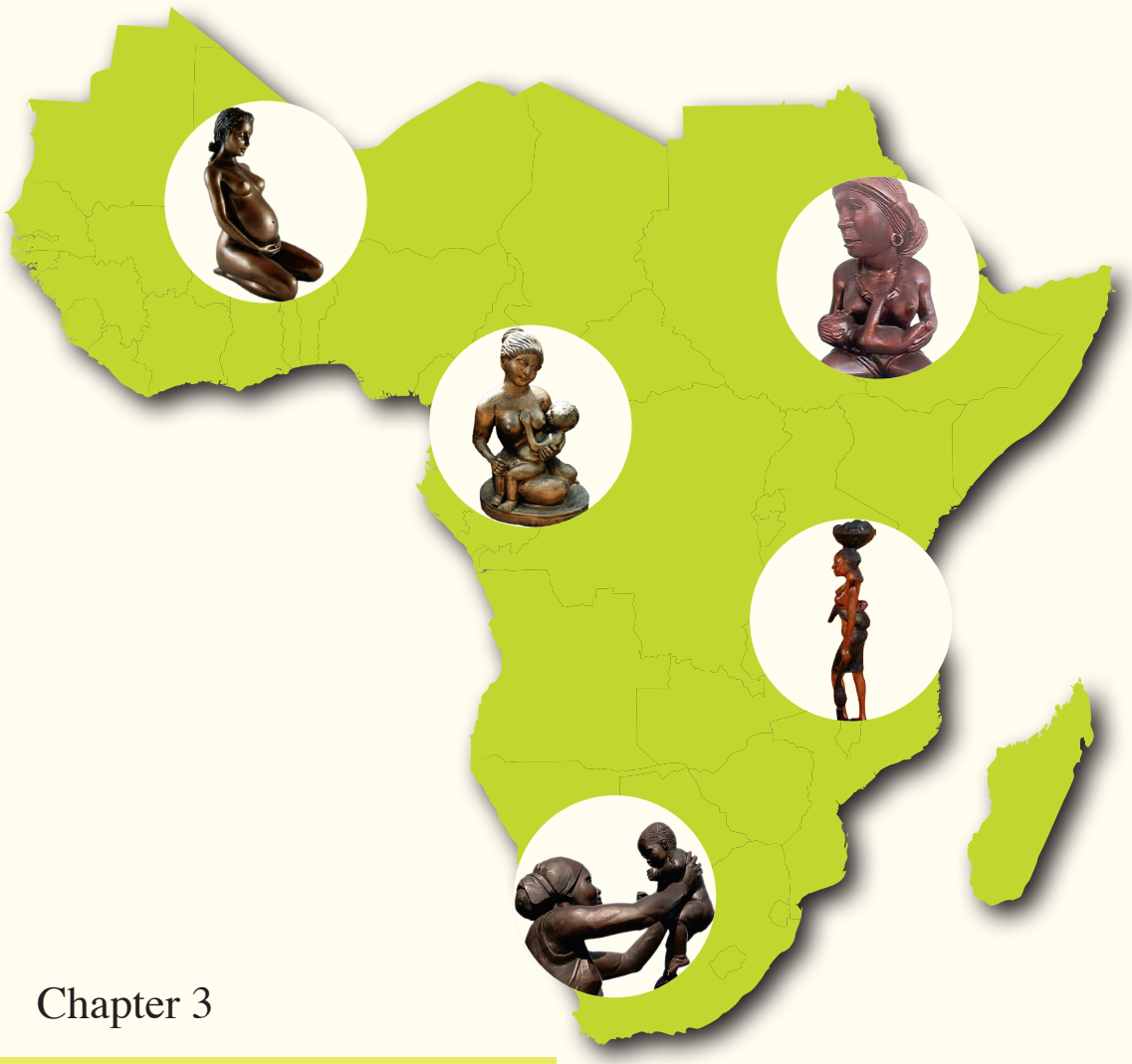

Chapter 3

Temporal Trends in Neonatal Mortality in Ghana: Impacts and Challenges of Health Policies and Program

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Abstract

Background

Various efforts have been made in Ghana since the adoption of Millennium Development Goal 4 to reduce under-five mortality by two-thirds between 1990 and 2015. Thus, this study aimed to describe trends in neonatal, infant and under-5 mortality and highlight the impacts and challenges of health policies and intervention programs implemented.

Methods

Ghana Demographic and Health Survey data (1988 to 2008) were used for a trend analysis, applying poisson regression analysis to estimate the incidence rate ratio of the trends and to compare the incidence rate of neonatal death to that of infant and under-5 death. Implemented health policies and intervention programs were reviewed to identify their impact on childhood mortality in Ghana.

Results

Since 1988 neonatal, infant, and under-five mortality in Ghana have been declining by 0.6, 1.0 and 1.2 % annually. From 1988-1989 neonatal, infant, and under-5 mortality were observed to decline by 31%, 31% and 24% respectively, whereas from 1989-2008, neonatal mortality increased by 7% while infant and under-five mortality further declined by 10% and 20% respectively. Thus, the proportion of infant and under-5 mortality attributed to neonatal death has increased. Most programs implemented were directed at infant and under-five mortality, but seem not to have been implemented comprehensively.

Conclusion

Progress towards attaining MDG 4 in Ghana was below the targeted rate, particularly in neonatal mortality. Most health policies and programs were targeting infant and under-five mortality and appeared not to have been well implemented. Thus, neonatal specific interventions should be implemented and improve existing programs.

Background

Neonatal mortality continues to remain a prominent global health issue even though Millennium Development Goal 4 (MDG 4) was universally adopted to reduce under-five mortality by two-thirds between 1990 – 2015.[1] As the deadline for the attainment of this goal has almost elapsed, ninety-nine percent of childhood mortality still occur in low and middle income countries (LMICs),[2] indicating the persistence of a great inequality between LMICs and high income countries (HICs). Several "calls for action" have been made to raise awareness,[2-5] and in response, both governmental and non-governmental bodies have committed considerable resources to this public health challenge, although their level of financial commitment has been seriously criticized to be inadequate.[6]

Despite the financial commitment, the decline observed in neonatal mortality has not been as expected. Thus, neonatal mortality accounts for a large part of the failure to attain MDG 4. To date, 40% of under-5 mortality and 50% of infant mortality occur in neonatal life;[7] even though three-quarters of neonatal deaths are preventable.[3] Globally, attainment of MDG 4 will thus remain elusive without a substantial reduction in neonatal mortality.

In the last two to three decades in Ghana covering a period both before and after the declaration and acceptance of the MDGs, the government of Ghana has formulated several maternal and child health policies and in some cases implemented accompanying intervention programs. During the first decade from 1988 to 1998 the Safe Motherhood Program (SMP)[8] was initiated with the aim of securing safe delivery for women and improving child health services. Likewise, the Life Saving Skills (LSS) program[9] was commenced to sharpen the clinical skills of midwives. Similarly, the Integrated Management of Childhood Illness (IMCI)[10] that was first launched in the 1990s seeks to improve child survival through the provision of clinical guidelines for management of childhood illnesses, health system strengthening and improving community health practices. Further intervention programs and policies were implemented from 1998 to 2008 such as: The Community-Based Health Planning and Services (CHPS),[11] aiming to improve primary health care service; the User Fees Exemption for Delivery[12] to ease the financial burden of delivery service and serving as an addition to the User Fees Exemption for Antenatal, Postnatal and Child Welfare Clinic that was introduced in the 1980s. In 2002, antenatal care service was reformed leading to the introduction of focused antenatal care. Focused antenatal care (FANC)[13] aims to achieve safe delivery through individualization of antenatal care and consideration of socio-cultural, beliefs, lifestyle and medical characteristics of pregnant women in the management of their pregnancies. FANC was implemented to improve maternal and child survival through targeted assessment of pregnant women in order to provide essential antenatal care services which include early detection and

treatment of illness and pregnancy complications, administer tetanus toxoid, health education on birth preparedness, nutrition and more. In an effort to remove financial barriers to health services access and improve equity in financing and access to care the National Health Insurance Scheme (NHIS)[14] was established by the Ghanaian government under the Act 650 of 2003 and by 2008, 55% of the population had registered.[15]

Apart from all these national programs and policies, various regions also implemented different intervention programs; for instance the Kybele program in the Greater Accra region,[16;17] Accelerated Child Survival and Development (ACSD)[18] sponsored by United Nation Children and Education Fund (UNICEF) in the Upper East, Northern and Upper West region and Kangaroo Mother Care[19] which commenced in six regions in 2007; just to mention a few.

To the best of our knowledge, no study has examined trends in neonatal mortality either at national or regional level. Thus, this study aimed to evaluate temporal trends in neonatal mortality in relation to that of infant and under-5 mortality over two decades (1998-2008); and reviewed health policies and intervention programs implemented during this time period for their impact. Questions investigated were (1) what have been the temporal trends in neonatal mortality from 1988 to 2008 in Ghana, (2) do these trends differ from trends in infant and under-five mortality in Ghana over the same period, (3) do the observed temporal trends in national neonatal mortality rates differ across regions in Ghana over the same time period, and (4) has there been an impact of the implemented health policies and intervention programs on neonatal, infant and under-5 mortality in Ghana.

Methods

Setting

Ghana is located in sub-Saharan Africa, along the Gulf of Guinea with a total area of about 239,000 Km²,[20] and a population of about 24.4 million.[21] It has an annual growth rate of about 2.4 % per year,[22] and the geographic coordinate is 8 00 N, 2 00 W. Ghana shares boundaries with Togo at the Eastern part, Cote d'Ivore at the Western part, Burkina Faso at the Northern part, and the Atlantic Ocean at the base of the country. It has about 100 ethnic groups with different languages and culture making it rich in ethnic diversity.[23] The major ethnic groups are Akan, Ewe, Mole-Dagbani, Guan, and Ga-Adangbe.[23] It has a Gross Domestic Product (GDP) of about 31.3 billion US dollars, a Gross National Income (GNI) of 1,230 US dollars with an unemployment rate of about 10.4%.[21] According to World Health Organization, the county spends about 8.1% of her GDP on health and is considered a lower middle-income country.[21]

Design of data collection

This is a longitudinal study describing the trends in neonatal mortality, and the proportion of infant and under-5 mortality attributed to neonatal deaths in Ghana, from 1988 to 2008, using five consecutive Ghana Demographic and Health Survey datasets.[24] complemented by a longitudinal assessment of formulated and implemented maternal and child health policy agendas in Ghana over the same time period. GDHS datasets utilized in this study were obtained in 1988, 1993, 1998, 2003, and 2008. All the GDHSs followed the same sampling technique. During the data collection, households were randomly sampled for interview by applying a stratified two-stage cluster randomized sampling technique. All women and men in all the selected households, within the age range 15 – 49 years and 15 – 59 years respectively were interviewed using questionnaires. The datasets are nationally representative with an individual response rate of 95 - 97% and a household response rate of 97 – 99%. Detailed information on the sampling techniques and procedures for the data collection have been published elsewhere.[24] For the longitudinal assessment of maternal and child health policies and interventions, MEDLINE, EMBASE, Google Scholar, African Index Medicus and Ghana Medical Journal were searched for relevant articles. After reviewing the articles information was extracted from the studies that have assessed these health policies and programs.

Statistical analysis

Neonatal, infant and under-five mortality rates at national and regional level were estimated from each GDHS. Trend analysis was performed primarily at the national level. In addition, regional trends in neonatal mortality were examined to investigate for regional variation in neonatal mortality. Temporal trend patterns were depicted by plotting the number of neonatal death per 1000 live births against time (year); infant and under-5 mortality underwent similar analysis. In addition, the proportion of infant and under-five mortality accounted for by neonatal mortality was examined by plotting the percentage of infant and under-five mortality attributed to neonatal death against time (year). Further, a Poisson regression analysis was applied to estimate the incidence rate ratios in the trends. Statistical significance was determined by two-tailed Wald test at significant level of alpha equal to 5%.

$$\ln(Y) = a + \beta*(t) + e$$

Where "**a**"= intercept of the model, "**β**"= is the trend, **Y**= total number of neonatal deaths per 1000 live births (will be repeated for infant and under-5 deaths), "**ln**" = natural logarithm, "**t**" = measured in years (year the survey was done), and "**e**" = residual of the model. Also, the incidence rate ratio of death at each stage of life (neonatal, postnatal and aged 1 < 5 years) was estimated in a Poisson

regression model and all the analyses were performed in Stata statistical software package version 11.[25]

Ethical approval

Ethical approval to conduct the GDHS was approved by the Ethics Committee of ICF Macro in Calverton, United States and the Ethics Committee, Ghana Health Service, Accra, Ghana. Approval to utilize this data was obtained from the Ethics Committee of ICF Macro in Calverton, United States.

Table 1. Cases of Neonatal, Infant and Under-five Deaths Per Each Ghana DHS

GDHS	Total Live Births Number (n)	Neonatal Deaths Number (n)	Infant Deaths Number (n)	Under-Five Deaths Number (n)
GDHS 1988	4136	198	299	446
GDHS 1993	2204	94	130	148
GDHS 1998	3298	109	192	272
GDHS 2003	3844	166	235	314
GDHS 2008	2992	106	157	198

GDHS Ghana Demographic and Health Survey

Results

Table 1 shows the total number of live births captured per each GDHS and the total number of deaths that occurred among neonates, infants and under-five children. Over the two decades from 1988 to 2008 five demographic health surveys were conducted in Ghana for which a total of 16,474 live births and 673 neonatal deaths were captured. Total live births and neonatal deaths captured per survey ranged from 2204 to 4136 and 94 to 198 respectively while infant and under-five deaths recorded ranged from 130 to 299 and 148 to 499 respectively.

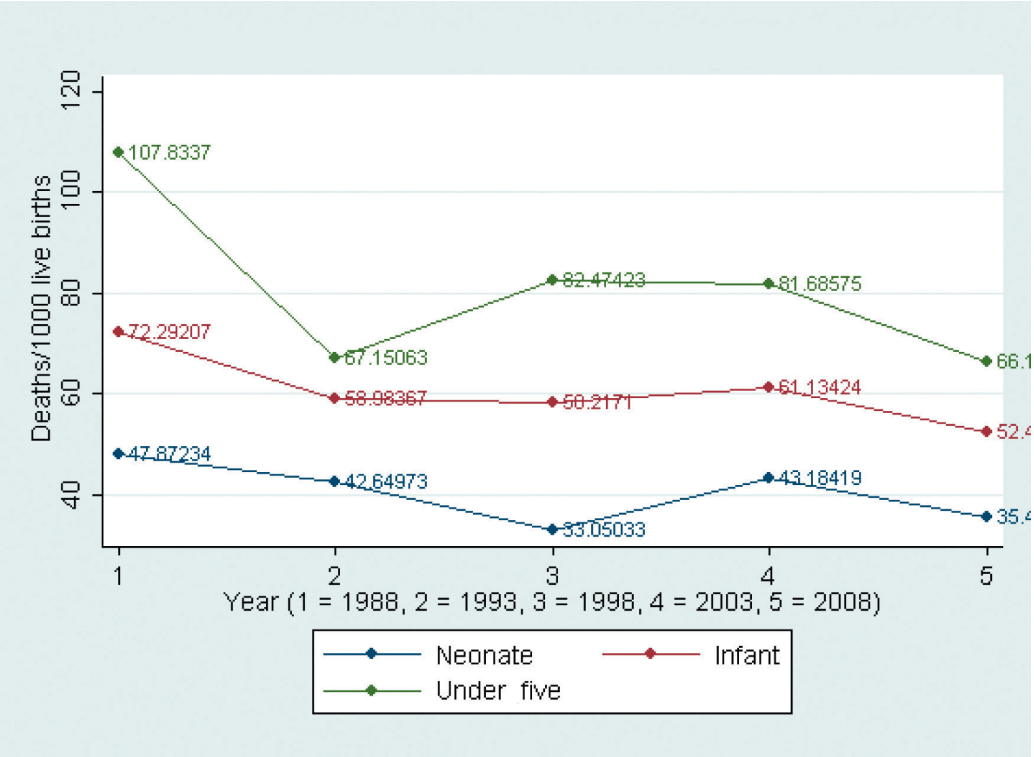


Figure 1. Trends in neonatal, infant and under five mortality from the 1988 to the 2008

Trend in neonatal mortality compared to that of infant and under five mortality

Figure 1 shows the trends in neonatal, infant and under five mortality from the 1988 to the 2008 GDHS. During the first half of this era, 1988 to 1998, neonatal mortality was observed to decline by 31% while infant and under five mortality reduced by 31% and 24% respectively. However, in the following decade, 1999 to 2008, neonatal mortality was observed to increase by 7% whereas infant and under five mortality declined further by 10% and 20% respectively. Annually, over the period of two decades (1988 to 2008), neonatal infant and under five mortality declined by 0.6%, 1.0% and 2.1% respectively.

Table 2. Poisson regression analyses of the trend in neonatal, infant and under five mortality, 1988 to 2008 Ghana Demographic & Health Survey

Year	Neonatal Death	Infant Death	Under-five Death
	IRR (95% CI)	IRR (95% CI)	IRR (95% CI)
1988 GDHS	1 (reference)	1 (reference)	1 (reference)
1993 GDHS	0.90 (0.60 – 1.35)	0.82 (0.58 – 1.15)	0.62 (0.46 – 0.84)**
1998 GDHS	0.69 (0.44 – 1.07)	0.81 (0.57 – 1.14)	0.76 (0.57 – 1.01)
2003 GDHS	0.90 (0.59 – 1.35)	0.85 (0.60 – 1.19)	0.76 (0.57 – 1.01)
2008 GDHS	0.73 (0.47 – 1.12)	0.72 (0.50 – 1.03)	0.61 (0.45 – 0.83)**

IRR: Incidence Risk Ratio; CI: confidence interval; ***P-value > 0.001; **P-value > 0.01; *P-value > 0.05

Table 2 shows the results of Poisson regression analyses, where neonatal, infant and under five mortality rates obtained in the first GDHS (1988 GDHS) were compared to the estimates in the subsequent GDHS (1993, 1998, 2003 & 2008). No statistically significant decline was observed in neonatal and infant mortality. In contrast, the risk of under five death was observed to be reduced significantly by 38% and 39% from 1988 to 1998 and 1988 to 2008 GDHS, respectively. Considering the risk of dying in childhood in the last two decade, from 1988 to 2008, no significant reduction was observed in neonatal and infant life whereas for under five mortality relatively witnessed more reduction. This was not unexpected considering the observed annual rate of decline in neonatal, infant and under five mortality, indicating lack of adequate attention to neonatal healthcare as reported in the literature.[26]

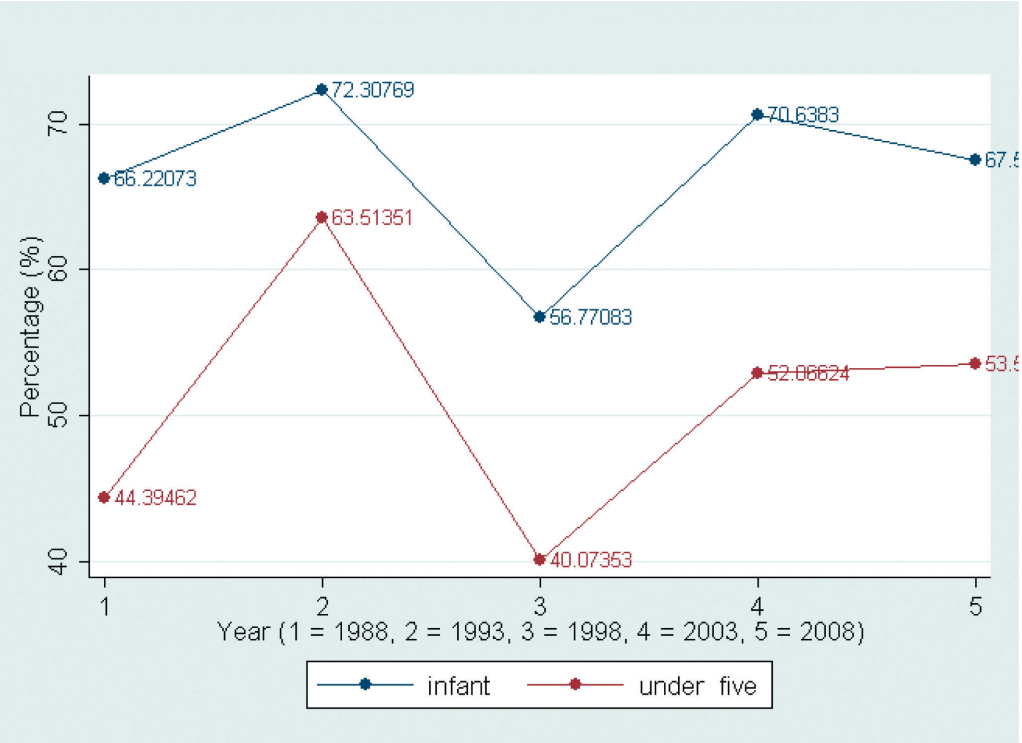


Figure 2. Trends in proportion of infant and under five mortality attributable to neonatal deaths in Ghana from 1988 to 2008

Trends in proportion of infant and under five mortality attributable to neonatal deaths

Figure 2 depicts the trends in the proportion of infant and under five mortality attributable to neonatal deaths. From 1988 to 1998 the percentage of infant and under five mortality attributed to neonatal mortality declined from 66% to 57% and 44% to 40% respectively, whereas from 1998 to 2008 the percentage of infant and under five mortality attributed to neonatal deaths increased by 11% and 13% respectively. Subsequently, trends in the risk of post-neonatal death (death at age 1 month to 11 month) and child death (death at age 12 months to 59 months) were compared to that of neonatal life; results of the Poisson regression analyses are shown in table 3.

In 1988, 1993, 2003 and 2008 GDHS the risk of post-neonatal death (death at age 1 month to 11 month) reduced significantly by 46%, 60%, 56%, and 49% respectively. Similarly, the risk of child death (death at age 12 months to 59 months) declined significantly by 79%, 49% and 60% in 1993, 2003 and 2008, respectively when compared to neonatal life. Due to the low rate of decline in neonatal mortality, the proportion of infant and under five mortality attributed to neonatal mortality has increased. In other words, the relative risk of death in neonatal life compared to post-neonatal

(age 1 month to 11 month) and child stage (age 12 months to 59 months) of life has not improved as expected.

Table 3. Poisson regression analyses of the trend in post-neonatal and under-five mortality compared to neonatal mortality, 1988 to 2008 Ghana DHS

Year	Neonatal phase IRR (95% CI)	Post-neonatal phase IRR (95% CI)	Child phase (1 < 5 yr) IRR (95% CI)
1988 GDHS	1 (reference)	0.54 (0.33 – 0.87)*	0.79 (0.51 – 1.21)
1993 GDHS	1 (reference)	0.40 (0.22 – 0.68)**	0.21 (0.10 – 0.41)***
1998 GDHS	1 (reference)	0.79 (0.47 – 1.31)	0.79 (0.47 – 1.31)
2003 GDHS	1 (reference)	0.44 (0.25 – 0.75)**	0.51 (0.30 – 0.85)*
2008 GDHS	1 (reference)	0.51 (0.29 – 0.90)*	0.40 (0.21 – 0.73)**

IRR: Incidence Risk Ratio; CI: confidence interval; ***P-value > 0.001; **P-value > 0.01; *P-value > 0.05; DHS Ghana Demographic & Health Survey

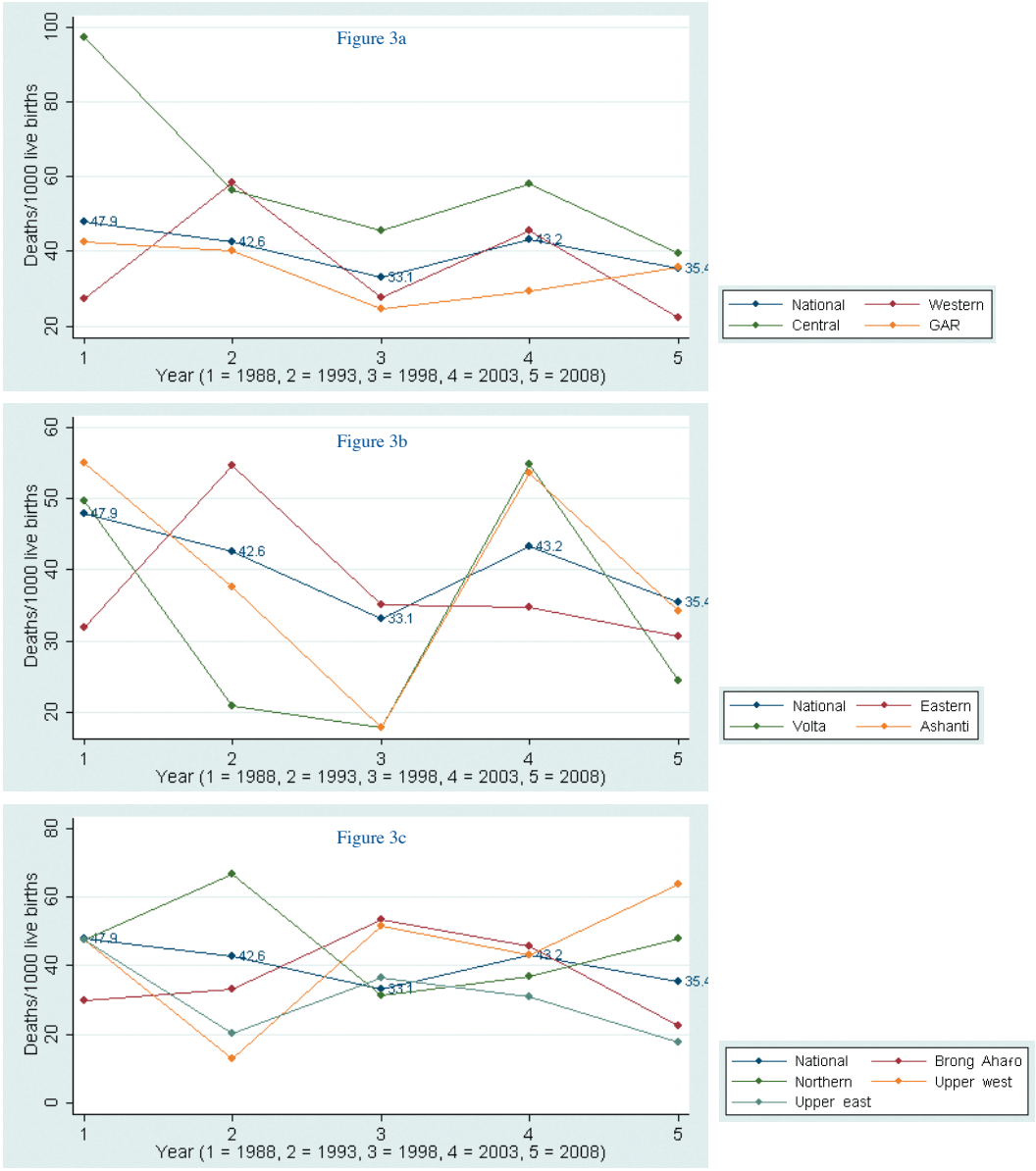


Figure 3. Regional and national trends in neonatal mortality in Ghana, DHS 1988 to 2008

Regional trends in relation to national neonatal mortality

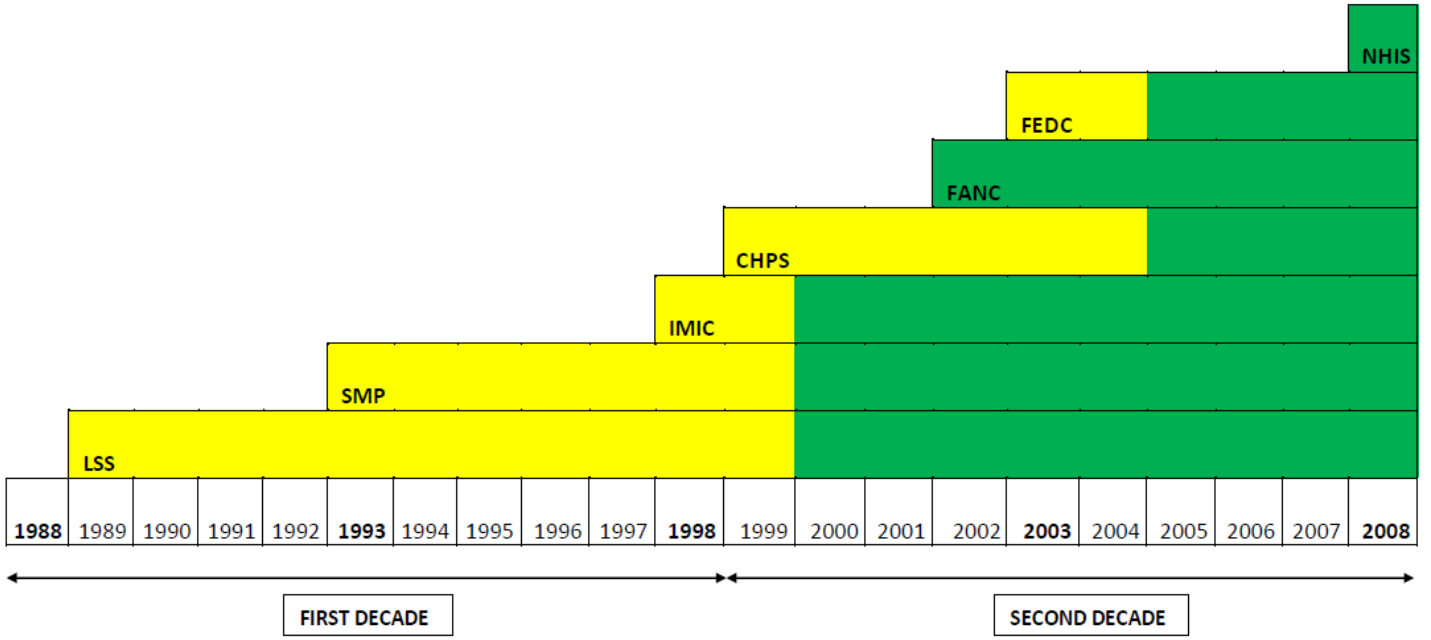
The regional trends of neonatal mortality are shown in figure 3a, 3b, and 3c. In 1988, for three regions (Central, Volta and Ashanti region) neonatal mortality rates were observed to be above the national rate; while in 1998, neonatal mortality rates in five regions (Central, Eastern, Brong Ahafo, Upper East and Upper West region) were observed to have surpassed the national rate. By 2008 three regions (Central, Upper West, and Northern region) exceeded the national neonatal mortality

rate. For the Central region a persistently high neonatal mortality rate above the national average was observed throughout the entire time period (1998-2008) whereas for the Upper West region neonatal mortality rates above the national average was observed from 1998 onwards. For the Greater Accra region neonatal mortality rates stayed below the national average throughout the period of assessment. For other regions, neonatal mortality trends were fluctuating around the national trends.

Impact of implemented health policies and intervention programs on MDG4 in Ghana

Following the adoption of the MGDs in Ghana, the Ghanaian government in collaboration with international donors implemented several intervention programs and health policies aimed at accelerating attainment of MDG 4 and 5 in Ghana. The most important polices were implemented post-adoption of MDG4 until 2008. Findings of studies that have assessed the policies quantitatively or / and qualitatively have been summarized in table 4; corresponding timelines for implementation of the policies and programs, starting from initiation (experimental phase) to scale-up phase are shown in figure 4. On national level, the Life Saving Skills (LSS),[9] Safe Motherhood (SMP),[8] and Integrated Management of Childhood Illness (IMCI)[10] programs were initiated between 1988 and 1998 and subsequently scaled-up thereafter.

Additional interventions such as the Community-Based Health Planning and Services (CHPS),[11] User Fees Exemption for Delivery Care (FEDC),[12] Focused Antenatal Care (FANC),[13] and the National Health Insurance Scheme (NHIS)[14] were implemented from 1999 onwards to complement the impact of the existing programs so as to accelerate attainment MDG 4 and 5. Maternal and child policies reviewed (table 4) showed that most of the policies were directed at maternal, infant and under-five mortality rather than neonatal mortality. Results presented indicate that these policies seem to have a greater effect on maternal healthcare utilization, maternal and childhood mortality and morbidity during the initiation phase than the scale-up phase.[27-30] Factors consistently identified to have a negative impact on the effectiveness of the various interventions were deviation from good standard practice in policy formulation and implementation, erratic funding, insufficient community engagement, inadequate monitoring, and inadequate manpower and equipment.



GDHS datasets were collected in 1988, 1993, 1998, 2003 & 2008; **LSS** Life Saving Skills; **SMP** Safe Motherhood Program; **IMIC** Integrated Management of Childhood Illness; **CHPS** Community-Based Health Planning and Services; FANC Focused Antenatal Care; **FEDC** User Fees Exemption for Delivery Care; **NHIS** National Health Insurance Scheme

Figure 4. Health policies implementation timeline in Ghana from 1988 to 2008

Table 4. Overview of Nation al Health Policies implemented to address childhood mortality in Ghana from 1988 to 2008

National Health policy	Activities	Time of assessment	Findings of studies assessing the effectiveness of National Health Policy Programmes
***Safe Motherhood*[8] *Program* (SMP)**	Ghana SMP entails primary health care, antenatal care, essential obstetric care, clean/safe delivery, family planning and equity for women. (Launched in 1993 and scaled up in 2000)	After scale-up	Okiwelu et al. (2007) and colleagues showed that some donors were implementing other interventions outside the objectives of the SMP, and the authors concluded that such action might dilute the expected effect of the policy.[37]
		After scale-up	Anderson et al. (2007) and colleagues identified migration of care providers (medical doctors) out of Ghana as one of the main factors that hampered the SMP in Ghana.[55]
		After scale-up	Maine et al. (1999) in his review on the SMP, showed that the policy was not well defined and most policy makers believed that most of the components of SMP were already implemented prior to the SMP.[56]
***Community-Based Health Planning and Services*[11] (CHPS)**	Community health officer (CHO) provides the following services: treatment of minor illness, health education, family planning, skilled delivery, antenatal and postnatal care. Community volunteers are trained to carry-out community mobilization. (First piloted in 1999, adopted nationwide in 2005)	Prior to scale-up (experimental phase)	Prior to policy implementation at national level, Phillips et al. (2006) showed that the CHPS program decreased childhood mortality and fertility rate.[27]
		Prior to scale-up	Prior to policy implementation at national level, Debpuur et al. (2002) showed that the CHPS program increased women's knowledge of contraception, willingness for birth spacing and usage of contraception.[57]
		Prior to scale-up	Before the policy was adopted nationally, Pence et al. (2007) showed that the CHPS program decreased childhood mortality.[58]
		Prior to scale-up	Before the CHPS program was adopted, Binka et al. (2007) and colleagues found that the program decreased childhood mortality and improved parental health seeking behavior.[42]

		Prior to scale-up	Philips et al. (2012) observed that CHPS improved contraceptive usage[44] before the policy was adopted nationwide.
		Prior to scale-up	Prior to the adoption of the policy, Awoonor-Williams et al. (2004) showed that CHPS increased usage of contraception, skilled antenatal delivery and postnatal attendants.[41]
		During scale-up,	During scale-up phase, Awoonor-Williams et al. (2013) observed the following challenges: inadequate funding, less preparedness of community health officer, inadequate community engagement , shortage of manpower and equipment and inadequate monitoring.[35]
		After the adoption of the policy	Assessment of the CHPS initiative by Adongo et al. (2013) after its adoption showed that the program improved the acceptance of family planning.[59]
		After the adoption of the policy	Following adoption of the CHPS, Adongo et al. (2014) observed that the implementation of the program in urban areas was difficult due to contextual differences between rural (where the CHPS was tested) and urban areas, suggestion further modification of the implementation strategies.[60]
		Post adoption of CHPS initiative	During post adoption of CHPS, Nyonator et al. (2005) identified the following: inadequate community engagement, lack of funds made health managers to perceive CHPS as an administrative burden.[11]
***User Fees Exemption for Delivery Care* (FEDC)[12]**	Exemption of pregnant women from paying delivery fees in order to increase skilled delivery. Public, private and mission health care providers were receiving	Prior to scale-up	Before the policy was adopted, Asante et al. (2007) reported that the policy decreased catastrophic out-of-pocket payment.[61]

	reimbursement for service rendered (Initiated in 2003, Scaled up in 2005)		
		Prior to scale-up	Before the policy was scaled-up, Bosu et al. (2007) showed that the policy had no statistically significant effect on maternal mortality.[28]
		Prior to scale-up	Before the scaling up the policy, Penfold et al. (2007) observed that the policy increased skilled delivery and reduced inequality in the utilization of maternal healthcare service.[43]
		After scale-up	Witter et al. (2009) reported that the stakeholders believed that the policy was a cost effective initiative that can reduce inequality in the utilization of maternal healthcare service. Insufficient funding, inadequate management, irregular reimbursement, increased workload without any increasing staff strength, subsequently hampered the quality of maternal healthcare[62]
		After scale-up	Witter et al. (2007) reported that the stakeholders believed that the policy was a good initiative to improve skilled delivery. The study showed improvement in early antenatal registrants, but region were not well consulted in terms of reimbursement. Consequently, reimbursement was erratic and insufficient.[38]
		After scale-up	The study conducted by Witter et al. (2007) showed that the policy was well accepted as an effective strategy to improve safe delivery, contents of the policy were clear but insufficient erratic funding, delayed inadequate reimbursement, increased workload without incentive or any corresponding increase in the number of care providers militate against the sustainability of the policy.[39]

		Prior to scale-up	McKinnon et al. (2014) observed that facility-based delivery increased while neonatal mortality decreased.[63]
		After scale-up	Meessen et al. (2011) observed. (1) Agenda setting: It was not clear whether the policy was adopted as a result of pressure from donors or taking the advantage of the offer of being a Highly Indebted Poor Country. (2) Policy formulation: Assessment of this policy based on good practices in policy formulation showed that the objectives of the policy were clear and the stakeholders welcome the policy but its formulation was not free from donor's influence. Important policy formulation good practices such as situation analysis, assessment of different policies options, and stakeholders involvement were not observed. (3) Implementation stage: suffered erratic and insufficient funding.[64]
***Focused Antenatal Care* (FANC)[13]**	Individualized care for pregnant women to improve efficiency and safe delivery. It involves: early detection of complication, pre-exciting morbidity, birth preparedness, health education, and health promotion. For a healthy woman four antenatal visits at < 16wks, 26wks, 32wks, and 36wks were recommended. (Implemented in 2002)	During policy implementation	Increased antenatal registrants, increased early antenatal registrants, improved patient - doctor interaction, reduced waiting time, improved quality of antenatal care, increased health facility delivery, reduced stillbirth, and increased postnatal care utilization were observed by **Deganus et al.**[29] following the implementation of FANC
		During policy	**Nyarko et al.** reported that both patients and healthcare providers accepted the policy. It

		implementation	improved the quality of antenatal care. However there was no difference between the intervention facilities and the control in terms of birth preparedness, complication readiness and postnatal care. In addition, some intervention facilities were unable to implement some of the components of FANC due to lack of equipment.[34]
***National Health Insurance Scheme*[14] (NHIS)**	National health insurance for pregnant women covers: six antenatal visits, delivery (including obstetrics complications), two postnatal visits within six weeks post-delivery, neonatal care up to age 3 months. (Implemented in July 2008)	Following the implementation of NHIS	**Witter et al.** (2013) showed the policy did not learn from the mistake of free delivery policy; NHIS policy formulation was top-down, politically induced by donors, no well-prepared policy guidelines, no proper consultation, poor communication of the policy, no proper costing, no addition fund was made available, no long-time financial plan, erratic and insufficient reimbursement. Sub-optimal implementation, lack of adequate monitoring and evaluation, increased work load with a negative impact on healthcare quality. Despite these limitations the policy increased access to healthcare.[40]
***Integrated Management of Childhood Illness*[10] (IMCI)**	Aims to improve: case management at primary level of care, management of childhood illnesses and family and community childcare practices. It involves antenatal, delivery and postnatal services, treatment and prevention of infectious diseases (pneumonia, diarrhea, malaria, measles, HIV/AIDS), improve nutrition (improve breastfeeding, reduce malnutrition), vaccination, and psychosocial development. (Started in 1998, by 2000 all districts started IMCI)	Following the implementation of IMCI	Baiden et al. (2011) observed that many of the care providers were yet to receive training on IMCI. The study showed a significant level of non-compliance with the IMCI guidelines; all the 11 items in the IMCI checklist were observed in just 1% of the children. 95% of them received antimalarial treatment but only 11% underwent laboratory investigation.[36]

*** Maine et al.** provided assessment was a general assessment of the SMP

DISCUSSION

This study described the trends in childhood mortality and the proportion of infant and under-five mortality attributable to neonatal death over two decades (1988 – 2008) after adoption of the MDGs in Ghana. The risk of dying at different stages of childhood was estimated and studies that assessed the impact of various health policies and programs regarding childhood survival in Ghana were reviewed. Despite the global attention on childhood mortality, we noticed that over the two decades from 1988 to 2008 in Ghana, the decline in childhood mortality was below expectation. Neonatal, infant and under-five mortality only declined by 0.6%, 1.0% and 2.1% per year, respectively. These reductions are far below the expectation of a 4% annual decline to attain MDG 4 globally[31] and less than the 7% annual reduction stipulated to achieve MDG 4 in sub-Saharan Africa.[32] Due to the paltry decline in neonatal mortality, proportion of infant and under-5 mortality attributed to neonatal mortality has increased; this mimicked what has been observed globally and in SSA.[31;33]

Although the observed trends in childhood mortality cannot be attributed to the various policies and programs implemented, we were able to identify policies that coincide with the observed trends in neonatal, infant and under-five mortality. The observed decline in neonatal, infant and under-five mortality rates in the first decade, from 1988 to 1998 coincide with the initial phase of the Safe Motherhood Program (SMP),[8] Life Saving Skills (LSS) for midwives,[9] and Integrated Management of Childhood Illness (IMCI).[10] For the period 1998 to 2008, where infant and under-five mortality declined and neonatal mortality increased by 7%, implementation of maternal and child programs such as the User Fees Exemption for Delivery Care (FEDC),[12] Focus Antenatal Care (FANC),[13] National Health Insurance Scheme (NHIS)[14] and Community based Health Planning and Services (CHPS)[11] were observed, not explaining the differentials identified in neonatal, infant and under-five mortality trends.

Thorough examination of these health policies and trends in childhood in Ghana showed that from 1998 to 2003 (first half of the latter decade) neonatal and infant mortality were observed to have increased while under-five mortality was stationary. This tallies with the scaling-up phase of the programs initiated (1988 to 1998), indicating that the effects observed during the initiation phase of these policies could not be maintained after scaling up to regional and national level from 1998 to 2003.[11;34-40] From 2003 to 2008 neonatal, infant and under-five mortality was observed to have declined and this was in an era when the CHPS, FANC, FEDC, and NHIS were implemented to compliment on-going programs already implemented. Although health policies and programs cannot be fully ascribed to the observed trends, results of the policy review indicate that the observed trends in neonatal, infant, and under-five mortality might have been shaped by the direct and indirect impacts of maternal and child health policies and programs. Even though the health

policies and programs might not primarily targeted all the stages of childhood mortality, their impact tends to influence child survival by modulating the accessibility, affordability, acceptability, utilization and/or quality of health care.[29;30;41-44] In addition, finding emanated from our review showed that factors such as deviation from good standard practice in policy formulation and implementation, erratic funding, insufficient community engagement, inadequate monitoring, and inadequate manpower and equipment are major challenges of health policies and programs that might have influenced the observed trends in childhood mortality.

The observed trends in neonatal mortality are similar to a large extent with what Binka et al.[45] and Engmann et al.[46] observed in Kassena-Nankana district of Northern Ghana. However, the latter part (2003 to 2008) of the trends in neonatal mortality in this district declined faster than what we observed at national level; this might be due to the fact that Navrongo has been used to pilot many health intervention such as Insecticide-Treated Bednet Trial,[47] and Community Health and Family Planning Project.[48] It might be because trends in neonatal mortality were observed at different population level; we observed trends in neonatal mortality at national level while previous study examined it at district level. Both studies were unable to ascribe maternal and child health policies and program to the trends in neonatal mortality.

At regional level we observed some degree of variations in the trends in neonatal mortality. In comparison to national trends in neonatal, infant and under five mortality, the Greater Accra region was consistently below the national rate of neonatal mortality whilst the Central region was persistently above it. These observed variations may partly be explained by differences in implementation of national health policies and programs discussed earlier in combination with the effects of additional regional policies such as the Kybele program in the Greater Accra region,[16;17] Kangaroo Mother Care,[49] UNICEF sponsored Accelerated Child Survival and Development (ACSD)[18] in Northern Ghana, High Impact Rapid Delivery (HIRD),[50] and Project Five Alive.[51;52]

Recommendation

Attainment of MDG 4 will remain elusive in Ghana without a substantial reduction in neonatal mortality. Paucity decline observed in neonatal mortality in Ghana might be due to very few neonatal specific interventions implemented in Ghana.[53]. Thus, government and non-governmental organizations should pay urgent attention to neonatal mortality in addition to on-going efforts addressing childhood morbidity and mortality by implementing cost-effective neonatal-specific interventions such as newborn resuscitation, exclusive breastfeeding, use of partograph, kangaroo mother care, use of micronutrients, tetanus toxoid immunization, just to mention a few of the multifaceted interventions that have been identified.[2;3;54] Findings from this study offer policy makers and health program planners the opportunity to familiarize themselves with the recurrent

defects identified in policy formulation and implementation in order to avoid reoccurrence.[11;35;39] In addition, results generated at the regional level provide policy makers with information to reflect on regional variation in childhood mortality overtime and this may offer the opportunity to learn from other regions.

Study limitations and strengths

Nationally representative data of Ghana was utilized in this study, thus our findings can be generalized. GDHS data are generally regarded as high quality data because of the sampling technique and the excellent household and respondent response rates.[24] We went beyond the traditional graphical description of the mortality trends by applying Poisson regression to estimate the risk of dying at different stages of childhood. Neonatal and infant mortality, may, however be underreported since women that died during labour with their babies will not be captured in the data. Likewise, there is the possibility of misclassifying neonatal death as stillbirth. The observed trends in childhood mortality may be due improvement in data capturing overtime particularly for neonates; although we do not expect this because the same sampling technique was applied overtime. Causality between neonatal mortality and health policy cannot be inferred in the study.

CONCLUSION

This study described the trends in neonatal mortality over two decades in Ghana and showed that the decline rate of neonatal mortality was significantly lower than those of infant and under-five mortality. This could be attributed to health policies and intervention programs focusing more on under-five and infant mortality than neonatal mortality and implementation challenges of these policies on regional or national level. Implementation of a sustainable evidence-based neonatal specific intervention and improving other existing interventions will assist to accelerate the attainment of MDG 4.

COMPETING INTERESTS

The authors declare that they have no competing interests

AUTHORS' CONTRIBUTIONS

Gbenga A. Kayode (GAK), Diederick E. Grobbee (DEG), Han van Dijk (HD) and Kerstin Klipstein-Grobusch (KKG) designed the study. GAK carried out data collection, literature review, data analysis and drafted the first version of the manuscript. All authors (GAK, KKG, DEG, HD, Augustina Koduah (AK), Evelyn Ansah (EA), Mary Amoakoh-Coleman (MAC), and Irene A Agyepong (IAA)) reviewed and approved the final version of the manuscript.

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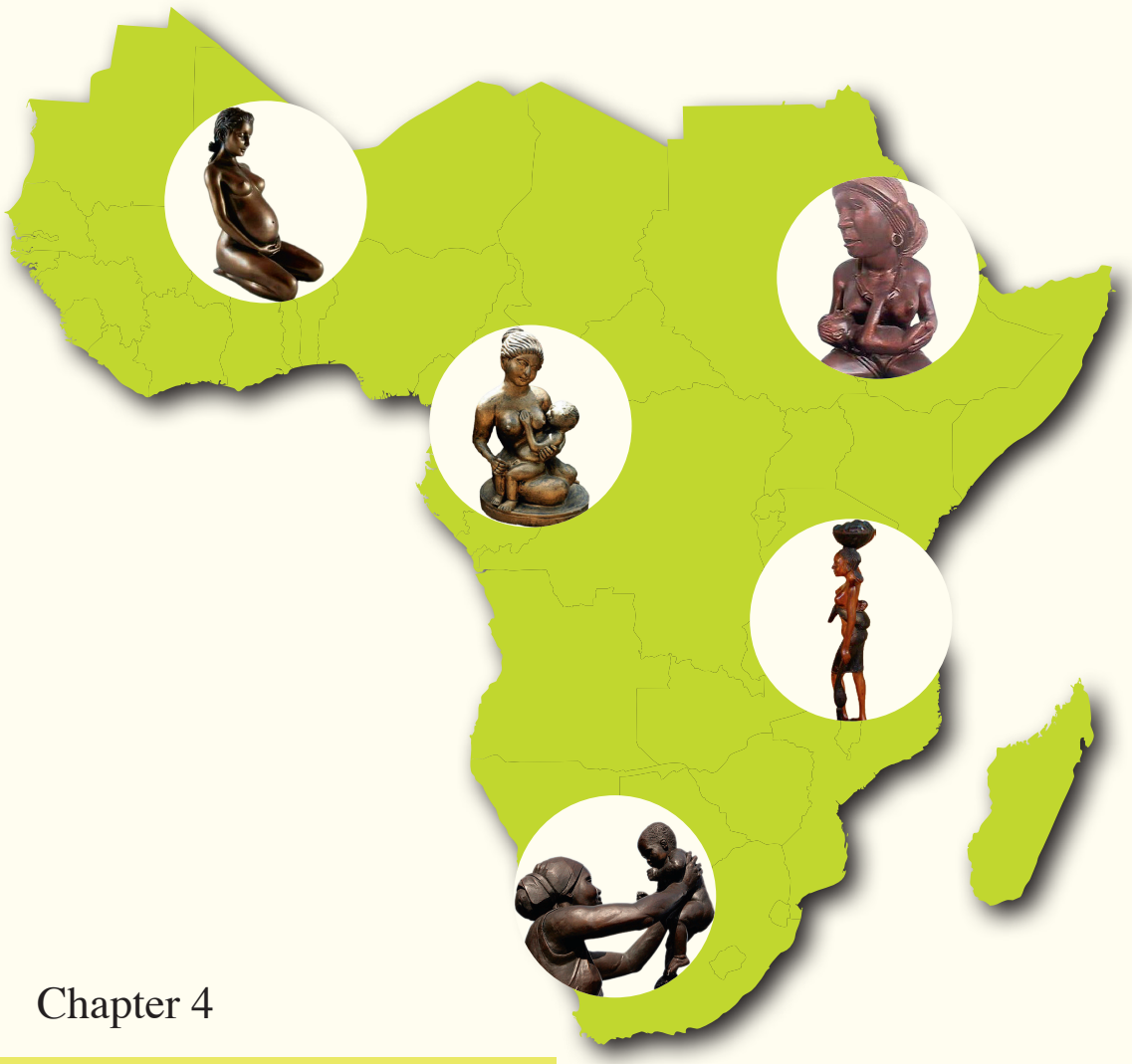
Part 2

Identifying population-based interventions for survival in early life



Chapter 4

Individual and community determinants of neonatal mortality in Ghana: a multilevel analysis

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Abstract

Background

Neonatal mortality is a global challenge; identification of individual and community determinants associated with it are important for targeted interventions. However in most low and middle income countries (LMICs) including Ghana this problem has not been adequately investigated as the impact of contextual factors remains undetermined despite their significant influence on under-five mortality and morbidity.

Methods

Based on a modified conceptual framework for child survival, hierarchical modelling was deployed to examine about 6,900 women, aged 15 – 49 years (level 1), nested within 412 communities (level 2) in Ghana by analysing combined data of the 2003 and 2008 Ghana Demographic and Health Survey. The aim was to identify individual (maternal, paternal, neonatal, antenatal, delivery and postnatal) and community (socioeconomic disadvantage communities) determinants associated with neonatal mortality.

Results

The results showed both individual and community characteristics to be associated with neonatal mortality. Infants of multiple-gestation [OR 5.30; P-value < 0.001; 95% CI 2.81 – 10.00], neonates with inadequate birth spacing [OR 3.47; P-value < 0.01; 95% CI 1.60 – 7.57] and low birth weight [OR 2.01; P-value < 0.01; 95% CI 1.23 – 3.30] had a lower chance of surviving the neonatal period. Similarly, infants of grand multiparous mothers [OR 2.59; P-value < 0.05; 95% CI 1.03 – 6.49] and non-breastfed infants [OR 142.31; P-value < 0.001; 95% CI 80.19 – 252.54] were more likely to die during neonatal life, whereas adequate utilization of antenatal, delivery and postnatal health services [OR 0.25; P-value < 0.001; 95% CI 0.13 – 0.46] reduced the likelihood of neonatal mortality. Dwelling in a neighbourhood with high socioeconomic deprivation was associated with increased neonatal mortality [OR 3.38; P-value < 0.01; 95% CI 1.42 – 8.04].

Conclusion

Both individual and community characteristics show a marked impact on neonatal survival. Implementation of community-based interventions addressing basic education, poverty alleviation, women empowerment and infrastructural development and an increased focus on the continuum-of-care approach in healthcare service will improve neonatal survival.

Background

The first 28 days of life remain the most critical period for an infant to survive during childhood; [1] approximately 10,000 newborns die everyday during this period [2]. As a result of the devastating effects of childhood mortality especially in low and middle income countries (LMICs), 189 United Nations member states unanimously agreed to adopt reduction of under-five mortality by two-thirds between 1990 and 2015 as the Millennium Development Goal 4 (MDG 4) [3]. The deadline for the attainment of MDG 4 target is fast approaching. Yet up to 40 % of under-five mortality occur at neonatal stage even though two-thirds of these deaths are preventable [4]. Worldwide about three million newborns are dying annually [5] before attaining the age of one month and despite repeated "calls for action", [1,2,6,7] this serious public health issue has not received desirable attention [8]. Consequently, in the last two decades, neonatal mortality has shown limited decline globally and in Sub-Saharan Africa (SSA) [1,9]. For instance in 2008 this region only witnessed a 2% decline in neonatal mortality [10]. Low birth weight, prematurity, infections, birth asphyxia and birth trauma have been identified as the leading causes of neonatal deaths worldwide [4], similar to the major causes of neonatal deaths in SSA [11] and Ghana [12-15]. Across the globe, there are great variations in neonatal mortality: 99% of neonatal deaths occur in LMICs [1], whereas until recently 99% of neonatal research publications were conducted in high income countries (HICs). This indicates a gross lack of information and knowledge of neonatal mortality in LMICs.

In Ghana, neonatal mortality is an important public health issue; 30 per 1000 live births are dying within the first 28 days of life [16]. In order to attain MDG 4 neonatal mortality has to reduce substantially because it accounts for more than half of the infant and under-five mortality [16]. Most studies to date mainly examined factors influencing under-five and infant mortality in LMICs [17], whereas only a limited number of studies have specifically identified factors associated with neonatal mortality in SSA. Early initiation of breastfeeding was shown to be inversely associated with neonatal mortality in Ghana [18]. Further in LMICs, neonatal (low birth weight, male infant, multiple pregnancy and prematurity) [19-21], maternal (single, nulliparous mothers and short birth spacing) [19-21], and health service factors (delivery and postnatal services) were reported to have independent associations with neonatal mortality [19,20].

These studies focused on the associations between individual-level factors and neonatal mortality. They typically did not disentangle the influence of individual and community determinants on neonatal mortality even when they analysed population-based data with hierarchical nature. In other words, most of these prior studies disregarded the importance of contextual phenomena because community-level determinants were not appropriately considered in their analyses. Contextual phenomenon is an intuitive core notion of social epidemiology; resting on the observation that

people dwelling in the same neighbourhood tend to resemble each other in terms of their health outcomes more than those living in different areas. Thus, taking contextual factors into account either at the design and/or analytical phase is crucial in understanding individual health outcomes in a population.

In LMICs, neonatal mortality is yet to be adequately examined by multilevel analysis, an analytic method that has the capability of assessing both fixed and random effects in a single model. Application of multilevel analysis allows to disentangle the influence of individual and community characteristics on neonatal survival based on the level at which they shaped child survival. In contrast, the application of single-level analyses (individual or ecological analyses) instead of multilevel analyses will make it difficult to deduce whether community-level factors influence neonatal outcomes regardless of the individual characteristics or whether inter-community variation in neonatal mortality is exclusively due to their individual characteristics without any influence of community-level factors.

In addition, there is increasing evidence of associations between community-level factors and under-five stunting and mortality after considering individual factors [22-24]. The present study aims to identify both individual (biological or proximate) and community (contextual, societal or distal) factors associated with neonatal mortality in Ghana by examining Ghana Demographic and Health Survey (GDHS) data using hierarchical modelling.

Methods

Study design

This is a population-based study which examined the combined dataset of the 2003 and 2008 Ghana Demographic and Health Survey to identify individual and community determinants influencing neonatal mortality in Ghana.

Data collection

Comprehensive information on the sampling techniques and procedures applied for data collection in the Ghana Demographic and Health Survey have been published elsewhere [16,25]. In brief, all women and men in all the selected households, aged 15 to 49 and 15 to 59 respectively were interviewed with the aid of questionnaires (household, women's and men's questionnaires). The questionnaires covered information on socioeconomic, demographic and health indicators. Informed consent was obtained from all the participants before face-to-face interviews were conducted. Information was obtained on under-five deaths in the last five years in both occasions. In both surveys combined, 12,474 households, 11,045 women and 10,114 men were identified for interviews and response rates of 99%, 96% and 94% respectively were observed [16,25].

Ethical consideration

Ethical approval to conduct DHS in Ghana was approved by the Ethics Committee of ICF Macro in Calverton, USA and the Ethics Committee, Ghana Health Service, Accra, Ghana. We obtained ethics approval for analysis of this data from the Ethics Committee of ICF Macro in Calverton, USA.

Variables

Outcome variable

Neonatal mortality was defined during the data collection as the probability of dying within the first month of life.

Determinants

Individual and community characteristics that were examined for possible associations with neonatal mortality were based on an adapted framework of child survival [26] taking into account the available information in the 2003 and 2008 Ghana Demographic and Health Survey. The adapted framework for neonatal survival is depicted in Figure 1.

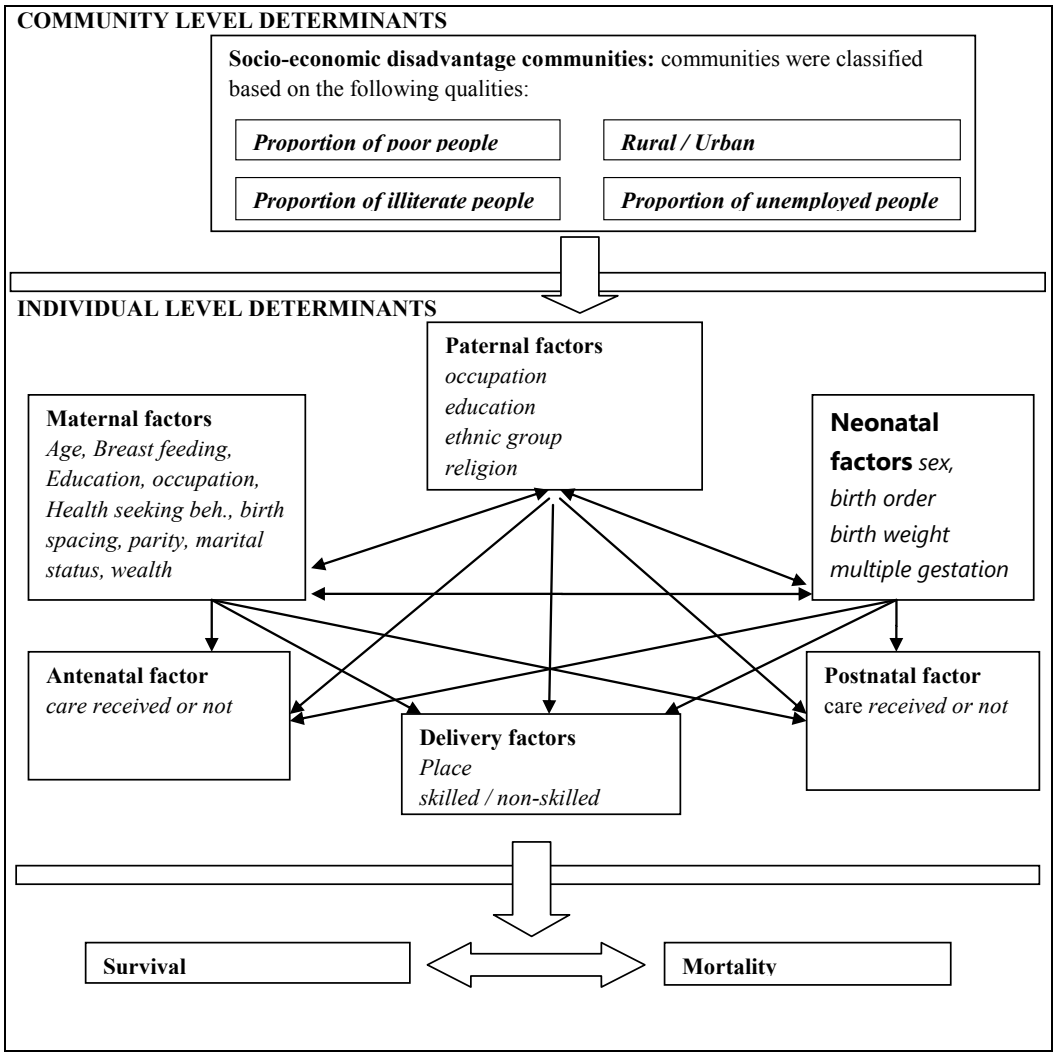

FIGURE 1: Adapted version of the conceptual framework for individual & community-level determinants influencing neonatal mortality [26]

Individual-level determinants

Individual-level factors were categorized into six groups: maternal, neonatal, paternal, antenatal, delivery, and postnatal factors. Maternal factors encompassed maternal age, parity, maternal occupation, maternal education, breastfeeding and preceding birth interval. We examined sex (male/female), birth order, multiple pregnancy and birth weight to assess the effects of neonatal factors while paternal factors entailed paternal occupation and education, ethnic group and household wealth index. Mothers were asked whether the birth weight of their babies were very big, bigger than average, average, smaller than average or very small. We classified smaller birthweight

than average and very small birthweight as small and average, bigger than average and very big as normal birthweight. Maternal uptake of antenatal, delivery and postnatal healthcare services were assessed by considering maternal health seeking behaviour. Maternal health seeking behaviour was operationalized by combining maternal characteristics such as having a health care card, having received tetanus toxoid, having received antenatal care, have delivered in a health facility and having knowledge of oral rehydration solution using Principal Component Analysis (PCA). To evaluate the wealth index of the households an asset based approach was applied by DHS. Household properties such as radio, car, and other features within the house such as water source, toilet facility and roof/floor type were utilized to evaluate the wealth index of the household using PCA [16,25]. Asset-based methods have previously been applied by the World Bank and other studies to estimate wealth status [27-29].

Community-level determinants

The community was used to represent the primary sampling unit (PSU) of the data. Community impact on neonatal mortality was assessed by considering the status of socioeconomic disadvantage of the community in which the participants were dwelling. Community socioeconomic disadvantage was operationalized by combining four factors: place of residence (rural/urban), and the proportion of illiteracy, unemployment and poverty (estimated asset index < 20% poorest quintile). PCA was applied to generate community socioeconomic disadvantage and subsequently classified into low, moderate and high deprivation tertiles. Communities with low socioeconomic disadvantage were the least deprived. A couple of studies have utilised community socioeconomic disadvantage as a community-level determinant [30-33].

Statistical analyses

Descriptive analyses

Descriptive analysis was performed by evaluating the prevalence of neonatal mortality (outcome variable) across the categories of each explanatory variable. Also the frequency and percentage of each of the categories within the explanatory variables were obtained.

Modelling approaches

The hierarchical nature of the Ghana DHS data and the framework for neonatal survival were considered during the analysis. Thus, two-level multivariable multilevel logistic regression was applied. Individual-level determinants were nested within the community-level determinants in which they live. Three models were fitted in the analysis. Model 1 has no determinant variable (empty model). This was fitted to decompose the total variance between individual and community level. We included all the individual-level determinants into model 2 while the model 3 encompassed individual-level and community-level determinants.

Measures of association (fixed effects)

The effects of individual-level and community-level determinants on neonatal mortality were reported in term of odds ratios with their P-values and 95% confidence interval.

Measures of variation (random effects)

Random effects were expressed in terms of Intra-Cluster Correlation (ICC)/Variance Partition Coefficient (VPC) and Median Odds Ratio (MOR).

Model fitness & precision

The loglikelihood and Akaike Information Criterion (AIC) of the models were estimated to assess the fitness of the model relative to the other models. Variance Inflation Factor and Tolerance test were performed to identify the presence of multicollinearity in the model. StataSE 11 software package [34] was used for the analyses and statistical significance of the covariates were determined by two-tailed Wald test at significance level of alpha equal to 5%.

Results

Characteristics of the sample

The general characteristics of the study population are shown in Tables 1 and 2. Approximately 6,900 respondents living in 412 different communities were interviewed in the last decade in Ghana to obtain information on under-5 mortality. Half of the women interviewed were aged 25 to 34 years, 40% of them were illiterate, and about two-thirds of them engaged in manual labour jobs and were residing in rural settlements. More than half of the men were farmers even though more than two-thirds of them had at least a primary school education. About one-third of the communties were classified to be in abject poverty while 90% of the population were unemployed. About 3% of the newborns delivered were not breastfed, 17 % were having LBW and neonatal mortality accounted for more than half of under-five mortality and two-thirds of infant mortality. Neonatal deaths were observed to occur most often in newborns having birth spacing less than 18 months, low birth weight and those that were not breastfed. Similarly, for infants of multiple gestation and those in fifth or higher birth order prevalence of neonatal mortality was higher. Neonatal deaths were reported more often among infants of grand-multiparous women with poor health seeking behaviour. Further details are given in Tables 1 and 2. The time interval between the two subsequent data collection periods was not related to neonatal mortality; its rate has been more or less stationary in the last decade in Ghana [16,25].

Table 1. General characteristics of the study population: individual variables

		Neonatal death		
	Number (%)	Yes	No	
	n (%)	n (%)	n (%)	Total N (%)
INDIVIDUAL-LEVEL DETERMINANTS				
Neonatal factors				
Infant sex				
Male	3,476 (51)	150 (4)	3,326 (96)	3,476 (100)
Female	3,360 (49)	122 (4)	3,238 (96)	3,360 (100)
Birth order				
One	1,518 (22)	66 (4)	1,452 (96)	1,518 (100)
Two	1,342 (20)	37 (3)	1,305 (97)	1,342 (100)
Three	1,090 (16)	37 (3)	1,053 (97)	1,090 (100)
Four	883 (13)	28 (3)	855 (97)	883 (100)
Five	2,003 (29)	104 (5)	1,899 (95)	2,003 (100)
Multiple gestation				
Yes	285 (4)	39 (14)	246 (86)	285 (100)
No	6,551 (96)	233 (4)	6,318 (96)	6,551 (100)
Birth weight				
Small	1,142 (17)	72 (6)	1,070 (94)	1,142 (100)
Normal	5,607 (83)	176 (3)	5,431 (97)	5,607 (100)
Maternal factors				
Maternal Age				
15 – 24 years	1,537 (23)	57 (4)	1,480 (96)	1,537 (100)
25 – 34 years	3,300 (48)	123 (4)	3,177 (96)	3,300 (100)
35 – 49 years	1,999 (29)	92 (5)	1,907 (95)	1,999 (100)
Maternal education				
No education	2,956 (43)	113 (4)	2,843 (96)	2,956 (100)
Primary	1,545 (23)	73 (5)	1,472 (95)	1,545 (100)
Secondary or higher	2,335 (34)	86 (4)	2,249 (96)	2,335 (100)
Maternal occupation				
Unemployed	689 (10)	27 (4)	662 (96)	689 (100)
Manual	4,184 (62)	167 (4)	4,017 (96)	4,184 (100)
White collar job	1,922 (28)	75 (4)	1,847 (96)	1,922 (100)
Parity				
1	1,035 (15)	27 (3)	1,008 (97)	1,035 (100)
2 – 4	3,514 (51)	148 (3)	3,396 (97)	3,514 (100)
≥ 5	2,287 (34)	127 (6)	2,160 (94)	2,287 (100)
Birth interval				
< 18 months	227 (4)	27 (12)	200 (88)	227 (100)
18 – 36 months	2,060 (39)	82 (4)	1,978 (96)	2,060 (100)
> 36 months	3,016 (57)	97 (3)	2,919 (97)	3,016 (100)
Breastfeeding				
Yes	6,647 (97)	138 (2)	6,509 (98)	6,647 (100)
No	189 (3)	134 (71)	55 (29)	77 (100)

Health seeking behaviour				
1 lowest	1,489 (24)	128 (9)	1,361 (91)	1,489 (100)
2	2,231 (35)	64 (3)	2,167 (97)	2,231 (100)
3	1,417 (22)	50 (4)	1,367 (96)	1,417 (100)
4 Highest	1,224 (19)	00 (0)	1,224 (100)	1,224 (100)
Paternal factor				
Paternal occupation				
Farming	3,816 (59)	146 (4)	3,670 (96)	3,816 (100)
Manual	1,481 (23)	52 (4)	1,429 (96)	1,481 (100)
White collar job	1,200 (18)	63 (5)	1,137 (95)	1,200 (100)
Paternal education				
No education	2,331 (38)	93 (4)	2,238 (95)	2,331 (100)
Primary	580 (9)	26 (4)	554 (96)	580 (100)
Secondary or higher	3,329 (53)	125 (4)	3,204 (96)	3,329 (100)
Wealth index				
Poor	3,773 (55)	136 (4)	3,637 (96)	3,773 (100)
Middle	1,186 (17)	61 (5)	1,125 (95)	1,186 (100)
Rich	1,877 (28)	75 (4)	1,802 (96)	1,877 (100)
Ethnicity				
Akan	2,612 (38)	110 (4)	2,502 (96)	2,612 (100)
Ga / Guan	578 (8)	21 (4)	557 (96)	578 (100)
Ewe	791 (12)	26 (3)	765 (97)	791 (100)
Mole-dagbani	1,697 (25)	62 (4)	1,635 (96)	1,697 (100)
Grussi / Gruma	703 (10)	35 (5)	668 (95)	703 (100)
Others	451 (7)	18 (4)	433 (96)	451 (100)

Table 2. General characteristics of the study population: community variables

		Neonatal death		
	Number (%)	Yes	No	
	n (%)	n (%)	n (%)	Total N (%)
COMMUNITY-LEVEL DETERMINANTS				
Place of residence				
Rural	4,793 (70)	198 (4)	4,595 (96)	4,793 (100)
Urban	2,043 (30)	74 (4)	1,969 (96)	2,043 (100)
Illiterate				
No education	3,880 (57)	159 (4)	3,721 (96)	3,880 (100)
Educated	2,956 (43)	113 (4)	2,843 (96)	2,956 (100)
Unemployment				
Employed	689 (10)	27 (4)	662 (96)	689 (100)
Unemployed	6,147 (90)	245 (4)	5,902 (96)	6,147 (100)
Poverty				
lowest 20%	2,174 (33)	84 (4)	2,174 (96)	2,258 (100)
Above 20%	4,578 (67)	188 (4)	4,390 (4)	4,578 (100)

Random effects (Measure of variations)

Table 3 depicts the results of the variance component model which is also referred to as null model or empty model (model 1). This model was applied to estimate the total variance in neonatal mortality that can be attributed to the communities in which the mothers were living; in other words, community-level variance was estimated in order to justify the applicability of multivariable multilevel regression analysis (MMLRA). Community-level variance was statistically significant (P-value < 0.05); it showed that some of the total variance in neonatal mortality can be explained by community-level determinants thus MMLRA was performed to adequately consider community-level factors. The intracluster correlation/intra-community correlation (ICC) or variance partition coefficient (VPC) was estimated at 0.07 which simply means that 7% of the total variance in neonatal mortality in Ghana can be attributed to the communities in which the mothers were residing. This also implies that the correlation between mothers living in the same community

regarding the likelihood of experiencing neonatal mortality was 0.07. The estimated community variance was also expressed as median odds ratios (MOR = 1.58) which means that the likelihood of having neonatal mortality increased by 58% when a woman moved from a community with lower risk to a higher risk community.

Table 3: Associations between neonatal mortality and individual and community level determinants

	Null model	Mode with individual level determinants	Mode with individual & community level determinants
FIXED EFFECT (OR; 95%CI; P-value)			
Individual-level determinants			
Infant sex			
Male		1 (reference)	1 (reference)
Female		0.78 (0.51 – 1.19)	0.79 (0.52 – 1.21)
Birth order			
One		1 (reference)	1 (reference)
Two		---	---
Three		1.58 (0.79 – 3.17)	1.57 (0.78 – 3.16)
Four		0.81 (0.33 – 1.99)	0.77 (0.31 – 1.93)
Five		0.77 (0.25 – 2.42)	0.72 (0.23 – 2.28)
Multiple pregnancy			
Yes		5.30 (2.82 – 9.95)***	5.30 (2.81 – 10.00)***
No		1 (reference)	1 (reference)
Birth weight			
Small (<2.5kg)		2.01 (1.23 – 3.29)**	2.01 (1.23 – 3.30)**
Normal (≥2.5kg)		1 (reference)	1 (reference)
Maternal factors			
Maternal Age			
15 – 24 years		1 (reference)	1 (reference)
25 – 34 years		0.74 (0.34 – 1.59)	0.75 (0.34 – 1.64)
35 – 49 years		0.73 (0.29 – 1.80)	0.74 (0.30 – 1.87)
Maternal education			
No education		0.74 (0.36 – 1.54)	0.88 (0.42 – 1.83)
Primary		1.02 (0.55 – 1.90)	0.99 (0.53 – 1.84)
Secondary or higher		1 (reference)	1 (reference)
Maternal occupation			
Unemployed		1 (reference)	1 (reference)
Manual		1.16 (0.53 – 2.59)	1.24 (0.56 –2.74)
White collar job		0.80 (0.35 – 1.86)	0.79 (0.34 – 1.81)
Parity			
1		1 (reference)	1 (reference)
2 – 4		---	---
≥ 5		2.52 (1.01 – 6.28)*	2.58 (1.03 – 6.49)*
Birth interval			
< 18 months		3.49 (1.60 – 7.59)**	3.47 (1.60 – 7.57)**
18 – 36 months		1.22 (0.77 – 1.93)	1.24 (0.56 – 2.74)
> 36 months		1 (reference)	1 (reference)
Breastfeeding			
Yes		1 (reference)	1 (reference)

No		133.50 (75.89 –234.83)***	142.31 (80.19 –252.54)***
Health seeking behaviour			
Very low (25 %)		1 (reference)	1 (reference)
Low (26-50%)		0.21 (0.13 – 0.36)***	0.21 (0.12 – 0.35)***
Average (50-75%)		0.26 (0.14 – 0.49)***	0.25 (0.13 – 0.46)***
High (76-100%)		---	---
Paternal factor			
Paternal occupation			
Farming		0.75 (0.37 – 1.57)	0.83 (0.40 – 1.73)
Manual		0.95 (0.48 – 1.89)	0.93 (0.46 – 1.85)
White collar job		1 (reference)	1 (reference)
Paternal education			
No education		0.86 (0.43 – 1.70)	0.96 (0.48 – 1.91)
Primary		0.66 (0.29 – 1.50)	0.62 (0.27 – 1.42)
Secondary or higher		1 (reference)	1 (reference)
Wealth index			
Poor		0.55 (0.30 – 1.01)	0.75 (0.39 – 1.43)
Middle		1 (reference)	1 (reference)
Rich		1.54 (0.75 – 3.13)	1.32 (0.64 – 2.76)
Ethnicity			
Akan		1 (reference)	1 (reference)
Ga / Guan		0.77 (0.31 – 1.95)	0.86 (0.34 – 2.18)
Ewe		0.73 (0.33 – 1.62)	0.79 (0.35 – 1.76)
Mole-dagbani		0.99 (0.49 – 1.99)	1.21 (0.60 – 2.47)
Grussi / Gruma		1.22 (0.56 – 2.63)	1.59 (0.71 – 3.57)
Others		0.95 (0.35 – 2.59)	1.14 (0.42 – 3.10)
Community-level determinants			
Community socio-economic disadvantage			
Low deprivation			1 (reference)
Moderate deprivation			2.05 (1.03 – 4.07)*
High deprivation			3.38 (1.42 – 8.04)**
RANDOM EFFECT			
Area Variance	0.235*	1.64 x 10^{-13}	1.02 x 10^{-9}
MOR	1.58	1.000000385	1.000030341
ICC (latent variable method)	0.07	4.98 x 10^{-14}	3.10 x 10^{-10}
AIC	2281.7392	819.77086	816.31818

Model 1 is the null model, contained no explanatory variable
Model 2 adjusted for individual-level characteristics
Model 3 adjusted for both individual-level and community-level characteristics
Abbreviations: OR: odds ratio; 95% CI: 95% confidence interval; MOR: median odds ratio; ICC: intracluster correlation
--- denotes estimate omitted by Stata software
***p < 0.001, **p < 0.01, and *p < 0.05

Following the decomposition of the neonatal variance in model 1, individual-level covariates were introduced into the empty model to form model 2. It was observed that the community-level variance reduced drastically in model 2. This indicated that the composition of the individual characteristics within the communities explained most of the community-level variance observed in

the null model. However, we extended model 2 by introducing community-level covariates to form model 3. Community-level variance was no longer significant after adjusting for both individual and community-level factors. It is important to mention that a random intercept model was constructed rather than the usual single-level model, not only because of the hierarchical nature of the data but also not to have biased associations.

Fixed effects (Measures of associations)

Table 3 also shows the fixed effects for individual and community-level determinants. Fixed effects of model 2 show the associations between neonatal mortality and individual-level determinants when the community-level covariates were not considered while the fixed effects of model 3 show the associations between neonatal mortality and both individual and community-level determinants. After considering both individual and community-level characteristics in model 3, it was noticed that infants of multiple gestation had a five times higher likelihood of dying before attaining the age of one month (OR 5.30; 95% CI 2.81 – 10.00; P-value < 0.001). Similarly, infants with LBW had a twofold increase in the likelihood of dying during the neonatal period compared to their peers with normal birth weight (OR 2.01; 95% CI 1.23 – 3.30; P-value < 0.01). In addition to child factors that were observed to influence neonatal survival, certain maternal factors were shown to be associated with child survival within the first 28 days of life. Infants delivered by grand multiparous women were 3 times more likely to die compared to those delivered by nulliparous women (OR 2.58; 95% CI 1.03 – 6.49; P-value < 0.05). Long birth spacing and breastfeeding had a protective effect on child survival during the neonatal stage. The likelihood of dying during the neonatal life increased 3.5 fold in infants with birth spacing of < 18 months compared to their peers with more than 36 months (OR 3.47; 95% CI 1.60 – 7.57; P-value < 0.01). Not being breastfed was strongly associated with neonatal mortality (OR 142.31; 95% CI 80.19 –252.54; P-value < 0.001). The utilization of antenatal, delivery and postnatal services by women with good health seeking behaviour reduced the likelihood of losing their babies during neonatal life compared to those with the least favourable health seeking behaviour [(OR 0.21; 95% CI 0.12 – 0.35; P-value < 0.001); (OR 0.25; 95% CI 0.13 – 0.46; P-value < 0.001)]. Infants of mothers that were living in communities with high and moderate socioeconomic disadvantage had a 3.4 and 2 fold increase in likelihood of neonatal death respectively (OR 3.38; 95% CI 1.42 – 8.04; P-value < 0.01; OR 2.05; 95% CI 1.03 – 4.07; P-value < 0.05) compared to those residing in areas with the least socioeconomic disadvantage.

Model fit statistics

There was a progressive increase in the loglikelihood observed in model 1 when we fitted model 2 and model 3. More importantly the AIC were decreasing from model 1 to 3. This implies that model 3 explained the determinants better than model 1 and 2.

Discussion

Main findings

The findings from this study shed light beyond the contribution of individual characteristics to neonatal survival. They demonstrated how the communities where the mothers were living shaped the prevalence of neonatal mortality in conjunction with the composition of the individual characteristics. Both individual and community-level characteristics showed significant associations with neonatal survival. Living in a socioeconomic deprived community (rural with a high prevalence of illiteracy, poverty and unemployment) was inversely associated with neonatal survival. These four components of community socioeconomic deprivation coexist together in varying proportions in the communities and the intensity of deprivation depends on them. Prior studies in LMICs have not adequately examined the association between community-level factors and neonatal mortality even though community-level factors have been shown to be associated with under-five mortality and morbidity [22-24]. There are multifaceted plausible explanations for this association. Dwelling in a rural community where illiteracy, poverty, and unemployment are coexisting will influence neonatal survival via multiple channels. People living in the same community with socioeconomic deprivation tend to be similar in terms of health outcome (neonatal mortality) because of the shared community characteristics which may mediate its impact through poor access to health care services, inability to afford health care costs, poor personal and environmental hygiene, poor nutrition, ignorance of the importance of health care services and more. Community factors will impact their effect on the health outcome (neonatal mortality) through the individual-level factors. Although it is not the aim of this study to explain the underlying mechanism of the observed association, we expect that living in a community with low socioeconomic status will mediate its effect on neonatal survival through individual-level factors based on the results of a previous study [26]. Several neonatal, maternal, antenatal, delivery and postnatal characteristics were shown to be associated with neonatal mortality in the present analysis. Being an infant of multiple gestation was negatively associated with neonatal survival as previously reported in studies from LMICs [21,35]. The plausible explanation for this association is that multiple pregnancies/multiple births have a higher risk of prematurity and small-for-gestational age (SGA). These morbid conditions will make the infants more prone to critical medical complications which might not be adequately managed in low-resource settings. Subsequent adjustment for LBW and other determinants did not alter the observed association between multiple pregnancy and neonatal mortality. In addition, LBW showed an independent association with neonatal mortality which is consistent with medical knowledge and outcomes of previous studies. Maternal factors found to be associated with neonatal mortality were breast feeding and birth spacing. Breast feeding

was identified to have the strongest association with neonatal mortality; the odds of this association was observed to be very high (OR = 142.31; 95% CI = 80.19 –252.54), thus it is important to mention that only 3% of the newborns were not breastfed; of these 70% died before attaining the age of one month whereas only 2% of the breastfed babies eventually died in the same period. Breastfeeding has been reported to have a protective effect against hypothermia and hypoglycaemia which are contributors to neonatal deaths [36]. Failure of the newborns to receive colostrum following delivery will make them more susceptible to infections because of their immure immune system. Results of a prior study conducted in Ghana showed that delayed breastfeeding initiation caused an increase in neonatal mortality through infection related diseases; [18] findings from other population-based studies support this notion [36-38].

Adequate birth spacing was another important maternal factor noticed to have a protective effect on neonatal survival. The length of the birth interval was inversely related to neonatal mortality; suggesting that the longer the mothers waited before having the next pregnancy the better their chance of being recuperated well from maternal depletion associated with the prior pregnancy. This will ensure an adequate supply of essential nutritional support for the growth and well-being of a subsequent pregnancy. This is consistent with previous studies [19,35,38,39].

Utilization of antenatal, delivery and postnatal services were inversely related to neonatal mortality. Infants of mothers that utilized these health services were found to have a better neonatal survival. The health of a neonate deteriorates considerably faster than the health of an adult following infection, but neonates also recover very fast if appropriate intervention is received as early as possible. Thus, it is important that mothers seek health intervention promptly in case of illness to save the lives of their infants.

Most of the maternal health indicators that were operationalized to generate maternal health seeking behaviour have been shown to have a similar influence on neonatal mortality. Mothers that possessed good health seeking behaviour such as having tetanus toxoid during pregnancy; and received skilled antenatal, delivery and postnatal care have been shown to reduce the chances of neonatal death among their siblings [19,38,40]. The impact of birth spacing, breast feeding and utilization of antenatal, delivery and postnatal services have clearly demonstrated the possible impact of the continuum-of-care approach [41] from antenatal to postnatal life on the survival and well-being of newborns. Mothers with a good health seeking behaviour will have a better uptake of the components of this approach from antenatal to postnatal care, as they will be more likely to receive tetanus toxoid, breast feeding counselling, birth preparedness, blood supplements, skilled delivery, birth spacing, immediate neonatal care and more.

Study limitations and strengths

Data explored in this study came from two nationally representative surveys with household and individual response rates of 99% and 96% respectively [16,25]. Recall bias in this type of data has been shown to be low [42,43]; and appropriate statistical methods were applied. However, considering the fact that we used secondary data in this study unobserved confouders might be a problem. A high odds ratio was observed among the 3% of infants that were not breastfed. Some babies may have died so early that not being breastfed would not have contributed to their death; the observed association between breastfeeding and neonatal mortality might have been overestimated. Because only surviving mothers had the opportunity to be interviewed, there is a possibility that neonatal deaths might have been underreported. For instance, mothers that died during labour with their babies due to obstetric complications would be omitted in the current analysis, implying that the burden associated with neonatal mortality might even be larger than presented. As information on early neonatal death was not available, we could not assess the effect of removing early neonatal deaths on the observed association between breastfeeding and neonatal mortality, which may have resulted in an overestimation of the true association between breastfeeding and neonatal mortality. With regard to classification in birth weight categories in the current study, we acknowledge that recall of birth weight size by mothers and subsequent classification in low and normal birth weight might have resulted in some misclassification of exposure and loss of information.

Recommendations

This study demonstrated that both individual and community characteristics have a substantial impact on child survival in neonatal life. Thus, a comprehensive approach should be taken in combating neonatal mortality. Provision of universal basic education, creation of job opportunities, poverty alleviation, women empowerment programmes, and abridging the inequality gaps between rural and urban areas are important community-based interventions that will alleviate the impacts of community socioeconomic deprivation.

This cannot be achieved without a strong financial and political commitment of government and non-governmental bodies. Earlier reports showed that neonatal mortality has not received adequate financial attention. Even although it accounted for more than 40% of under-five mortality [44], over 50% of infant mortality and up to the total deaths caused by Acquired Immunodeficiency Syndrome (AIDS) and malaria combined [8], yet neonatal mortality has been receiving inadequate financial attention [45].

In addition to the environment in which women live, individual factors such as neonatal, antenatal, delivery and postnatal factors were important determinants of child survival in neonatal life. Small

babies (preterm, small for gestational age or both) and infants of multiple gestation had a higher likelihood of dying in the neonatal stage indicating needs to provide essential neonatal care to this vulnerable group of neonates. Health system strengthening is needed in order to provide high quality, affordable and accessible health care for them. Integration of neonatal care to the Integrated Management of Childhood Illness (IMCI) programme will fill the observed gap (first seven days of life) between the Safe Motherhood Initiative (SMI) and IMCI [2,8] and this is a critical period when three-quarters of neonatal mortality occur [4].

Infants born to multiparous mothers with short birth spacing intervals were more likely to die in neonatal life while exclusive breastfeeding was found to have a protective effect on neonatal survival implying the importance of effective implementation of family planning programmes, reproductive health education, use of contraceptives and promotion of exclusive breastfeeding. Maternal health seeking behaviour towards antenatal, delivery and postnatal services plays a vital role in neonatal survival, indicating why decision and policy makers and non-governmental bodies should implement the continuum-of-care approach for maternal and newborn healthcare services spanning from antenatal, to delivery, immediate neonatal and postnatal care. The interagration of neonatal care to the IMCI, use of contraceptive, reproductive health education, exclusive breast feeding and other intervention programs can be delivered through a continuum-of-care approach to ensure continuity of healthcare services for infants and their mothers.

Conclusion

This study examined nationally representative data on neonatal mortality over a decade by analysing a combined dataset of the 2003 and 2008 Ghana demographic and health surveys. The outcomes of the study demonstrated both community (community socioeconomic disadvantage) and individual (neonatal, maternal, antenatal, delivery and postnatal) level factors to be significantly associated with infant survival within the first 28 days of life. A comprehensive approach comprising community-based interventions (universal basic education, poverty alleviation, women empowerment and infrastructural development) and the continuum-of-care for maternal-newborn healthcare services is needed to reduce the burden of neonatal mortality in LMICs.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

GAK) and (KKG) conceived the study idea. (GAK) was responsible for the literature review, data extraction and analysis and wrote the first draft of the manuscript. All authors (GAK), (KKG), (DEG), (EA), (MAC), and (IAA) scientifically reviewed and approved the final version of the manuscript.

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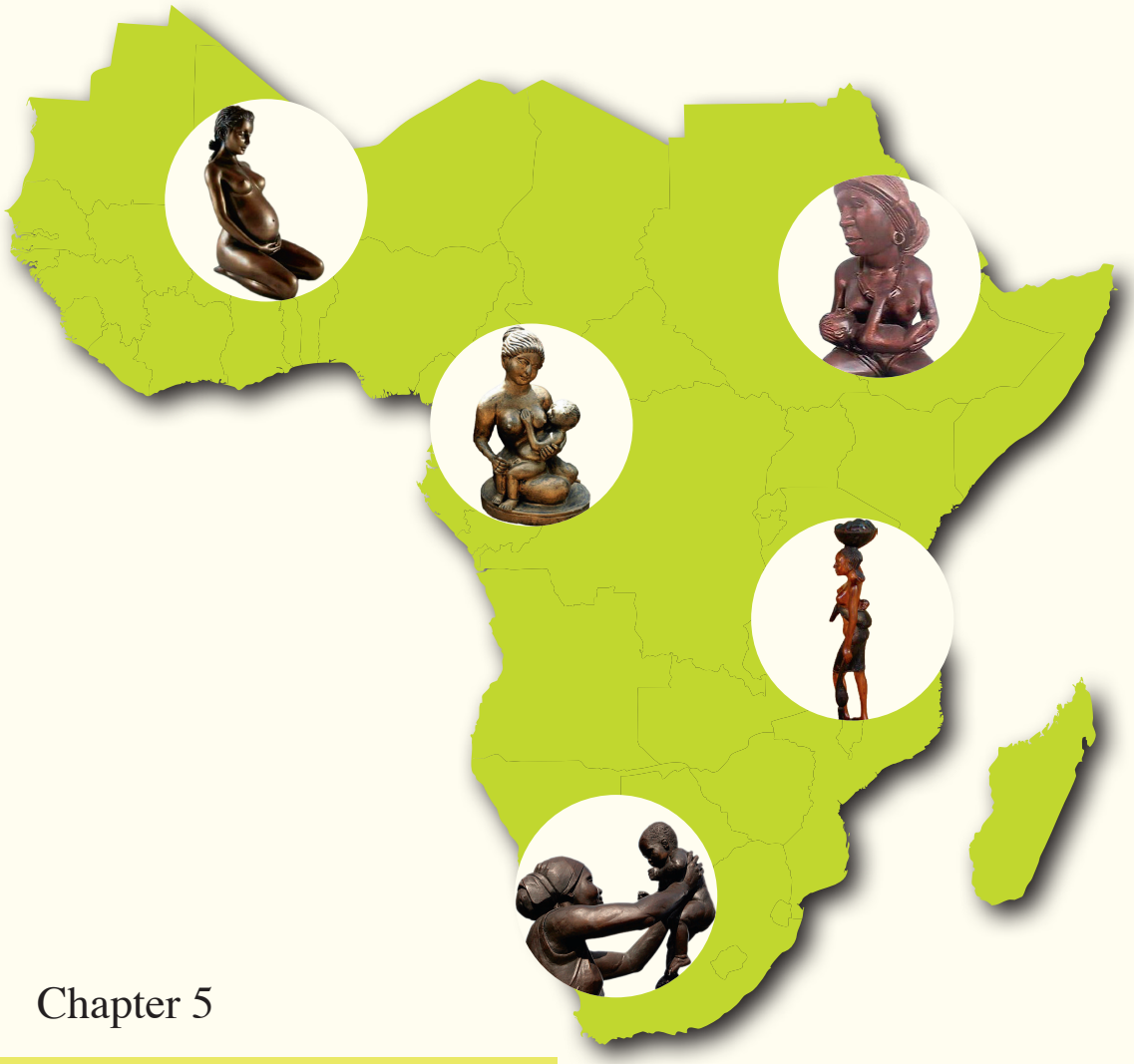

Chapter 5

Contextual risk factors for low birth weight: a multilevel analysis

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Abstract

Background

Low birth weight (LBW) remains to be a leading cause of neonatal death and a major contributor to infant and under-five mortality. Its prevalence has not declined in the last decade in sub-Saharan Africa (SSA) and Asia. Some individual level factors have been identified as risk factors for LBW but knowledge is limited on contextual risk factors for LBW especially in SSA.

Methods

Contextual risk factors for LBW in Ghana were identified by performing multivariable multilevel logistic regression analysis of 6,900 mothers dwelling in 412 communities that participated in the 2003 and 2008 Demographic and Health Surveys in Ghana.

Results

Contextual-level factors were significantly associated with LBW: Being a rural dweller increased the likelihood of having a LBW infant by 43% (OR 1.43; 95% CI 1.01–2.01; P-value <0.05) while living in poverty-concentrated communities increased the risk of having a LBW infant twofold (OR 2.16; 95% CI 1.29–3.61; P-value <0.01). In neighbourhoods with a high coverage of safe water supply the odds of having a LBW infant reduced by 28% (OR 0.74; 95% CI 0.57–0.96; P-value <0.05).

Conclusion

This study showed contextual risk factors to have independent effects on the prevalence of LBW infants. Being a rural dweller, living in a community with a high concentration of poverty and a low coverage of safe water supply were found to increase the prevalence of LBW infants. Implementing appropriate community-based intervention programmes will likely reduce the occurrence of LBW infants.

Background

Deliveries in low and middle income countries are often complicated by adverse birth outcomes such as stillbirth, early neonatal mortality and morbidity. Low birth weight (LBW) remains to be a leading cause of neonatal death [1], and is a major contributor to infant and under-five mortality [2]. Infants weighing less than 2500 grams at birth are regarded as LBW infants. LBW is associated with early and late morbid conditions such as coronary heart disease [3], [4], non-insulin dependent diabetes [5], childhood hypertension [6], behavioural disorders [7], impaired cognitive function [8], [9], psychological disorders [10], and these usually have long-term financial burden [11].

Infants can have LBW either as a result of small-for-gestational-age (SGA) or preterm delivery. An infant is said to be small-for-gestational-age when the gender-specific birth weight is below the 10^{th} percentile for the appropriate gestational age [12], [13]; such a condition could be constitutional or pathological, in the latter case, it is referred to as Intrauterine Growth Retardation (IUGR). Due to the devastating public health implications of LBW, the United Nations incorporated LBW into its action plans and aimed to reduce its incidence by one-third by 2015 [14].

Globally, one out of seven infants is born with LBW. The incidence has not declined in the last decade in Sub-Saharan Africa (SSA) and Asia [15]; even in Europe only very few countries have reduced its incidence [16]. In Ghana, the recent incidence of LBW infants was estimated at 160 per 1000 births and has not witnessed any reduction in the last decade [17]. The aetiology of LBW is yet to be completely understood even though several studies have attempted to unravel the underlying causes. Constitutional factors such as sex [18], maternal height [19] and weight [20] have been identified as risk factors for LBW. Similarly, maternal health, demographic and nutritional factors which include maternal age [21], ethnicity [22], parity [23], [24], birth interval [18], multiple gestation [21], maternal comorbidity [24], skilled antenatal care [21], [25], placenta causes [26], nutritional deficiencies [18], and body mass index [19] have been linked with LBW. In addition, maternal socioeconomic and psychological factors which comprise education [18], alcohol intake [27], smoking [24], use of hard drugs [28], occupation [29], wealth status [18], marital status [22], and domestic violence [30] were also found to be associated with LBW.

However, despite these numerous identified individual-level risk factors for LBW, there is a wide gap in epidemiological knowledge regarding the common effect that the community context has on the incidence of LBW especially in SSA. Studies conducted outside SSA have identified the impact of residential segregation [31], [32], neighbourhood poverty [31], [32] and unemployment on LBW [29] but up to date, the contextual effect on LBW has not been adequately investigated in SSA even though emerging evidence from Nigeria showed that contextual factors have an impact on under-five mortality and morbidity [33]–[35]. Contextual effects can best be revealed by disentangling the

effect of contextual factors from individual factors using a multilevel regression model. It allows the incorporation of contextual factors into the regression model to prevent a residual confounding effect of omitting contextual factors, overestimation of the association, and underestimation of the standard error [36]. Identifying contextual factors for LBW will guide the development of community-based interventions aiming to reduce the occurrence of LBW. Thus, this study aimed to identify contextual risk factors for LBW in Ghana.

Methods

Study design

This is a population-based study that utilized a combined dataset of the 2003 and 2008 Ghana Demographic and Health Survey (GHDS) to identify contextual risk factors for LBW in Ghana.

Data collection

Comprehensive information on the sampling techniques and procedures for the GDHS data collection have been published elsewhere [37], [38]. Detailed information on all under-five children in the last five years was captured in both surveys and 12,474 households, 11,045 women and 10,114 men were identified for interviews. Face-to-face interviews were conducted for all women aged 15 to 49 years and men aged 15 to 59 years in the sampled households by use of questionnaires covering socioeconomic, demographic and health indicators.

Variables

Outcome

Mothers were asked to recall the birth weight of their infants or provide hospital cards to confirm it. In case they could neither recall the birth weight of their infants nor provide a hospital card, they were asked whether the birth weight of their babies was very big, bigger than average, average, smaller than average or very small. For the purpose of the current analysis we classified infants with a birth weight smaller than average and very small as LBW infants [37], [38].

Contextual-level factors (determinants)

We referred to the primary sampling unit (PSU) of the DHS data as a community. The impact of the community context on low birth weight was examined by considering place of residence (rural/urban), proportion of the community that were having access to healthcare and safe water coverage, and proportion of illiterate (those that can neither read nor write in any language) and those living in extreme poverty in the community (estimated asset index <20% poorest quintile) as contextual factors.

Individual-level factors (potential confounders)

Un-confounded effects of contextual risk factors on LBW were estimated after considering potential confounders based on epidemiological knowledge, prior studies, and the available information in

the GDHS. Maternal age, parity, birth interval, unplanned pregnancy, ethnicity, anaemia in pregnancy, use of antenatal care, use of antimalarial or mosquito nets during pregnancy, smoking, body mass index, maternal education, occupation, wealth status and marital status were considered as potential confounders in the analysis. Marital status was classified as currently, formerly and never married. Maternal educational attainment was categorized into no education, primary, and secondary or higher education. The GDHS applied an asset-based approach to estimate household wealth status [39], similar to previous studies conducted [40], [41].

Statistical analysis

Descriptive analyses

In the descriptive analyses, the characteristics of the study population were expressed in terms of numbers and percentages. The prevalences of LBW across the categories of the explanatory variables were estimated in terms of numbers and percentages.

Statistical modeling

We applied a two-level multivariable multilevel logistic regression analysis, fitting three models different models. Model 1 (empty or null model) has no explanatory variable and we used it to decompose the total variance of LBW between the contextual and individual level. Model 2 contained the contextual-level factors and we extended this model to form model 3 by accommodating all the potential confounders (individual-level factors). Sensitivity analysis was conducted to assess whether the results of the analyses were consistent with the group of LBW infants classified to be of very small birth weight. This was necessitated by the potential risk of having a misclassified outcome by maternal self-report.

Measures of association (fixed effects)

Measures of association between the contextual risk factors and LBW were reported in terms of odds ratios (OR) with their P-values and 95% confidence interval (CI) after considering potential confounders.

Measures of variation (random effects)

Random effects were expressed in terms of Area variance (AV), Median Odds Ratio (MOR) and Intra-Cluster Correlation (ICC)/Variance Partition Coefficient (VPC).

Model fitness & precision

The fitness of the model was assessed using Akaike Information Criterion (AIC) while Variance Inflation Factor(VIF) was used to check for multicollinarity in the model. Two-tailed Wald test at significance level of alpha equal to 5% was used to determine the statistical significance of the determinants and all the analyses were performed with StataSE 11 software package, StataCorp LP, Texas, United States.

Ethical approval

Ethical clearance to conduct GDHS was obtained from the Ethics Review Committee, Ghana Health Service, Accra, Ghana and the Ethics Committee of ICF Macro in Calverton, United States. GDHS data are public access data and were made available to us upon request by Measure DHS.

Results

Population characteristics

Table 1 shows the descriptive characteristics of the 6,900 women aged 15–49 years, dwelling in 412 different communities who participated in the Ghana demographic and health survey (GDHS) on child health in the last decade. Characteristics of women between the 2003 and 2008 GHDS did not differ significantly, thus both surveys were combined and analysed. About two-fifths of the women interviewed were illiterate and had an unwanted pregnancy. More than half of them were living in poverty and a quarter of them were either obese or over weight. The majority of the women were non-smokers, cohabiting with their husband and almost one-sixth of them had LBW infants. The prevalence of LBW was estimated at 16.9 percent, and observed to be higher among rural dwellers, and in communities with low coverage of safe water supply, poor access to healthcare, a high proportion of illiterates and those living in extreme poverty.

Table 1. General characteristics of the study population, GDHS 2003 and 2008

INDIVIDUAL-LEVEL DETERMINANTS (POTENTIAL COFOUNDERS)				
		Low Birth Weight		
	Number (%)	Yes	No	
	n (%)	n (%)	n (%)	Total N (%)
Maternal Age				
15 – 24 years	1,537 (23)	300 (20)	1,221 (80)	1,521 (100)
25 – 34 years	3,300 (48)	533 (16)	2,722 (84)	3,255 (100)
35 – 49 years	1,999 (29)	309 (16)	1,664 (84)	1,973 (100)
Marital status				
Never married	227 (3)	42 (19)	185 (81)	227 (100)
Currently married	6,224 (91)	1,027 (17)	5,117 (83)	6,144 (100)
Formerly married	385 (6)	73 (19)	305 (81)	378 (100)
Maternal education				
No education	2,956 (43)	555 (19)	2,353 (81)	2,908 (100)
Primary	1,545 (23)	263 (17)	1,266 (82)	1,529 (100)
Secondary or higher	2,335 (34)	324 (14)	1,988 (86)	2,312 (100)
Maternal occupation				
Unemployed	689 (10)	118 (17)	558 (83)	676 (100)
Manual	4,184 (62)	760 (18)	3,377 (82)	4,137 (100)
White collar job	1,922 (28)	256 (14)	1,640 (86)	1,896 (100)
Parity				
One	1,035 (15)	206 (20)	821 (80)	1,027 (100)
Two – four	3,514 (51)	538 (16)	2,933 (84)	3,471 (100)
Five and above	2,287 (34)	398 (18)	5,607 (83)	6,749 (100)
Birth interval				
< 18 months	227 (4)	40 (18)	181 (82)	221 (100)
18 – 36 months	2,060 (39)	329 (16)	1,706 (84)	2,035 (100)
> 36 months	3,016 (57)	469 (16)	2,508 (84)	2,977 (100)
Skilled antenatal care				
Yes	4,458 (94)	703 (16)	3,741 (84)	4,444 (100)
No	293 (6)	76 (25)	217 (74)	293 (100)
Body mass index (Kg/m^2)				
Underweight	536 (8)	109 (21)	410 (79)	528 (100)
Normal weight	4,545 (67)	794 (18)	3,695 (82)	4,489 (100)
Over weight	1,116 (16)	150 (14)	951 (86)	1,101 (100)
Obese	639 (9)	89 (14)	542 (86)	631 (100)
Maternal smoking				
No	6,825 (99.9)	1,139 (17)	5,600 (83)	6,739 (100)
Yes	8 (0.1)	2 (29)	5 (71)	7 (100)
Use of mosquito net or malaria prophylaxis				
No	2,805 (41)	533 (19)	2,209 (81)	2,742 (100)
Yes	4,031 (59)	609 (15)	3,398 (85)	4,007 (100)
Maternal anaemia				
Severe	81 (1)	12 (15)	68 (85)	80 (100)
Moderate	881 (13)	151 (17)	721 (83)	872 (100)
Mild	2,594 (40)	472 (18)	2,090 (82)	2,562 (100)
Not anaemic	3,012 (46)	457 (15)	2,514 (85)	2,971 (100)
Index pregnancy wanted				
Wanted then	3,978 (58)	637 (16)	3,296 (84)	3,933 (100)
Not wanted	1,752 (26)	195 (18)	885 (82)	1,080 (100)

Wanted later	1,094 (16)	310 (18)	1,426 (82)	1,736 (100)
Wealth index				
Poor	3,773 (55)	683 (18)	3,046 (82)	3,729 (100)
Average	1,186 (18)	206 (18)	962 (82)	1,168 (100)
Rich	1,877 (28)	253 (14)	1,599 (86)	1,852 (100)
Ethnicity				
Akan	2,612 (38.2)	403 (16)	2,181 (84)	2,584 (100)
Ga / Guan	578 (8)	81 (14)	490 (86)	571 (100)
Ewe	791 (12)	113 (14)	671 (86)	784 (100)
Mole-dagbani	1,697 (25)	292 (18)	1,374 (82)	1,666 (100)
Grussi / Gruma	703 (10)	147 (21)	550 (79)	697 (100)
Others	451 (7)	106 (24)	337 (76)	443 (100)
VARIABLES USED TO OPERATIONALISED POPULATION-LEVEL FACTORS				
Residence				
Rural	4,793 (70)	868 (18)	3,863 (82)	4,731 (100)
Urban	2,043 (30)	274 (14)	1,744 (86)	2,018 (100)
Access to healthcare				
Difficult	2,650 (39)	484 (19)	2,129 (81)	2,613 (100)
Not difficult	4,175 (61)	658 (16)	3,469 (84)	4,127 (100)
Water source				
Safe	3,115 (51)	453 (15)	2,618 (85)	3,071 (100)
Not safe	2,992 (49)	554 (19)	2,403 (81)	2,957 (100)
Abject poverty				
Yes	1,353 (20)	295 (22)	1,036 (78)	1,331 (100)
No	5,483 (80)	847 (16)	4,571 (84)	5,418 (100)
Illiterate				
Yes	2,956 (43)	555 (19)	2,353 (81)	2,908 (100)
No	3,880 (57)	587 (15)	3,254 (85)	3,841 (100)

Random effects (measures of variation)

The results of the multivariable multilevel logistic regression (MMLR) are shown in Table 2. In model 1 (null or empty model), variance component analysis was performed to decompose the total variance of LBW and estimate the contextual-level variance which indicates the total variance of LBW that can be attributed to the context of the community in which the mothers were dwelling. The applicability of MMLR in the analysis was justified by the significance of the contextual-level variance [area variance (AV) =0.208; standard error (SE) =0.048; P-value =<0.001], indicating the existence of significant differences between communities with regard to LBW incidence. The AV was expressed as intracluster correlation (ICC) and median odds ratio (MOR); the ICC was 0.060 which implied that 6% of the total variance of LBW in Ghana can be attributed to the context of the community where the mothers were living. The MOR was 1.54 (95% C.I 1.41–1.72) which showed that the likelihood of having a LBW increased by 54% when mothers moved from low to high risk neighbourhoods.

Table 2. Associations between low birth weight and contextual risk factors, GDHS 2003 and 2008

	Null model	Mode with population level factors	Mode with individual & community level determinants
FIXED EFFECT (OR, 95% CI, P-value)			
Contextual-level factors			
Residence			
Rural		1.17 (0.96 – 1.42)	1.43 (1.01 – 2.01)*
Urban		1 (reference)	1 (reference)
Community poverty level			
High		1.61 (1.13 – 2.29)**	2.16 (1.29 – 3.61)**
Low		1 (reference)	1 (reference)
Community Illiteracy level			
High		1.13 (0.83 – 1.54)	1.22 (0.70 – 2.12)
Low		1 (reference)	1 (reference)
Community safe water coverage			
High		0.78 (0.65 – 0.93)**	0.74 (0.57 – 0.96)*
Low		1 (reference)	1 (reference)
Community healthcare access			
Difficult		1.09 (0.84 – 1.42)	1.28 (0.87 – 1.87)
Not difficult		1 (reference)	1 (reference)
RANDOM EFFECT			
Area Variance (SE)	0.208 (0.048)***	0.190 (0.047)***	0.168 (0.081)**
PCV		-8.7%	-12.1%
MOR	1.54 (1.41 – 1.72)	1.51 (1.38 – 1.70)	1.48 (1.28 – 1.87)
ICC (latent variable method)	0.060	0.055	0.049
AIC	6098.007	6059.623	2885.930

Model 1 is the null model, contained no explanatory variable
Model 2 adjusted for contextual-level characteristics
Model 3 adjusted for both population-level and individual-level characteristics
Individual-level characteristics adjusted for: maternal age, marital status, parity, maternal BMI, maternal education, maternal occupation, birth interval, use of mosquito net or malaria prophylactic, anaemia in pregnancy, antenatal care, smoking, unwanted pregnancy, maternal nutritional intake, ethnicity & wealth index
Abbreviations: OR: odds ratio; SE: standard error; PCV: proportional change in variance; 95% CI: 95% confidence interval; MOR: median odds ratio; ICC: intracluster correlation
***p < 0.001, **p < 0.01, and *p < 0.05

After extending Model 1 to form Model 2 by entering the contextual risk factors, AV (AV 0.190; SE 0.047; P-value <0.001), MOR 1.51 (95% CI 1.38–1.70) and ICC (0.055) remained significant but reduced because part of the contextual-level variance was explained by the contextual risk factors in the model. The estimated proportional change in variance (PCV) was −8.7%, indicating that 8.7% of the contextual-level variance was explained by the contextual risk factors entered into the model. Further, in order to estimate an un-confounded effect of the contextual risk factors, we adjusted for the potential confounders (individual-level factors) in Model 3. The AV (AV 0.167; SE 0.081; P-value <0.01), MOR 1.47 (95% CI 1.27–1.70) and ICC (0.048) remained significant but reduced and the PCV was −12.1%, meaning that 12.1% of the contextual-level variance of LBW

can be explained by the compositional characteristics of mothers dwelling in the communities. About 4.8% of the total variance of LBW that can be attributed to the contextual-level factors remained significant even after considering some contextual risk factors for LBW.

Fixed effect (measures of association)

The contextual risk factors for LBW that remained significant after adjusting for the potential confounders (individual-level factors) are shown in Table 2. Being a rural dweller increased the likelihood of having a LBW infant by 43% (OR 1.43; P-value <0.05; 95% CI 1.01–2.01). Similarly, dwelling in a community with a high proportion of people living in extreme poverty increased the likelihood of having a LBW infant by twofold (OR 2.16; P-value <0.01; 95% CI 1.29–3.61) while residing in a community with a high level of safe water coverage reduced the odds of having an infant with LBW by 28% (OR 0.74; P-value <0.05; 95% CI 0.57–0.96).

Model fit statistics

There were progressive reductions in AIC from Model 1 to 3, indicating that the explanatory value of the model increases from Model 1 to 3. In other words Model 3 explained the determinants better than Model 1 and 2.

Sensitivity analysis

To assess the potential effect of misclassification of low birth weight on the association observed between contextual-level factors and low birth weight we limited our analyses to the infants considered to be of very small birth weight (VLBW). Area variance was observed to increase and remained significant (0.534; SE 0.127), the intra-cluster correlation (ICC 0.140) and median odds ratio (MOR 2.00, 95% CI 1.73–2.40) also increased. The odds of having a VLBW infant increased four-fold (OR 4.02; P-value <0.01; 95% CI 1.72–9.38) among mothers living in communities with a high concentration of extreme poverty while mothers living in communities with a high coverage of safe water supply reduced their likelihood of having a LBW infants by 46% (OR 0.54; P-value <0.05; 95% CI 0.40–0.90) compared to their counterparts dwelling in areas with a low coverage of safe water supply. However the statistical significant effect of place of residence on LBW was deattenuated (OR 1.33; P-value >0.1; 95% CI 0.77–2.29).

Discussion

Main findings

This study investigated LBW beyond the traditional method of examining the risk factors for LBW by estimating the association between the context of the community where the mothers were residing, and the prevalence of LBW after controlling for individual characteristics of the mothers. The study showed contextual factors to be significantly associated with LBW. Being a rural dweller increased the likelihood of having a LBW infant and the plausible explanation for this is that living

in rural areas in SSA simply means residing in a deprived community in terms of job opportunities, social amenities and infrastructures which carries an increased risk of LBW. This finding is consistent with a previous study conducted in the United States that found that mothers residing in urban areas tend to be protected from having a LBW infant [42]. However, studies from Brazil reported urbanization to be associated with increased risk of having a LBW infant [43], [44]. Authors have likened this relationship to "low birth weight epidemiological paradox" found in Mexican-America mothers, which to date has not been observed in a SSA context.

Further, residing in wealthier communities was observed to protect women from having LBW infants compared to their counterparts dwelling in neighbourhoods with a high concentration of extreme poverty. Dwelling in such contexts might lead to maternal psychosocial stress which in turn has been implicated to increase the release of catecholamine and cortisol, and subsequent stimulate the release of corticotrophin releasing hormone (CRH) through cortisol. The release of CRH has been hypothesized to initiate the onset of labour [45] via a series biochemical processes while cortisol has been linked with IUGR [46]. This relationship is in line with observations of previous studies [32], [47]. Mothers living in a neighbourhood with a low coverage of safe water were observed to have LBW infants more often than those dwelling in a neighbourhood with a high coverage of safe water supply. The most likely explanation for this is that unsafe water supply will increase episodes of gastrointestinal infections during pregnancy which could impair normal fetal development or initiate preterm labour. This finding is in accordance with a prior study conducted in the United Kingdom that showed that elevated concentrations of disinfection by-product in drinking water increased the risk of LBW [48].

Considering the outcomes of this study, implementation of community-based intervention programs that can bridge the gaps between the rural and urban settlements in terms of infrastructural development are considered to be necessary. In the absence of any intervention, poverty can become an inter-generational problem that may be difficult to address. Thus, both government and non-governmental organizations will need to be more proactive towards implementing sustainable population-based poverty eradication programs coupled with women and youth empowerment programs. Provision of regular safe water supply to the communities will likely reduce the occurrence of LBW. Impact of such programs will go beyond individual-level, population will be its unit of manifestation. It is important to note that 4.8% of the variance in LBW in Ghana that was attributed to contextual factors remained significant even after considering contextual-level factors indicating why it is important for future studies to identify other contextual risk factors for LBW.

Study limitations and strengths

As we used nationally representative data with excellent individual and household response rates

for this study, study findings can easily be generalized for Ghana and beyond. Likewise the application of multilevel analysis in this study, made it possible to disentangle the effects of the individual and contextual factors on LBW. To the best of our knowledge, none of the previous multilevel studies on LBW accounted for haemoglobin concentration status and the desire to be pregnant unlike our study where these factors and other known potential confounders were considered.

However, limitations of this study cannot be overlooked. Alcohol intake was not captured in the GDHS so it was not included as a potential confounder but we believe this will not have any significant impact on the observed contextual effects because smoking and alcohol intake among women in Ghana is rare; for instance this study found that the prevalence of smoking among mothers was 0.1%. Because we examined secondary cross-sectional data, we were unable to evaluate the effect of the duration of living in a poverty-concentrated community on LBW. This study did not examine for possible cross-level interaction effect, thus we suggest that subsequent study should explore this area.

Mothers that neither had any evidence to confirm the birth weight of their children nor were able to recollect the birth weight were asked to specify whether the birth weight of their children was very big, bigger than average, average, smaller than average or very small. We considered smaller than average and very small as LBW in our analysis. Every mother was given the opportunity to specify the birth weight of their baby thus missing data is not an issue in this variable. The main challenge here is the possibility of misclassifying birth weight by mothers that could not provide the birth weight of their children due to their inability to remember the birth weight or the birth weight was not measured at birth; this is different from recall bias. Thus misclassification of birth weight could have occurred, however previous results from demographic and health survey data from Cambodia, Kazakhstan and Malawi assessing whether mother's perception of a baby's birth weight is a good proxy for birth weight noted good agreement between mother's perception of a baby's birth weight and measured birth weight [49], [50]. Comparison of the prevalence of low birth weight in our study (16.9%) to the prevalence of low birth weight in another Ghanaian data source support this notion [17].

Further based on logical reasoning out of the five classes of birth weight (very big, bigger than average, average, smaller than average or very small) the possibility of misclassifying infants with normal birth weight as low birth weight should be minimal among infants classified as “very small infants”. Indeed, the observed difference in the prevalence of “very small infant” among infants that their birth weight was provided and those that were assessed based on mother's perception of a baby's size at birth was less than 1.8%. We thus, examined whether the contextual effects observed

remained significant in the subgroup of infants classified to be very small, i.e. very low birth weight (VLBW). The random effect of the community context increased (AV 0.534, SE 0.127; MOR 2.00, 95% CI 1.73–2.40; ICC 0.140) Likewise the effect of poverty (OR 4.02; P-value <0.01; 95% CI 1.72–9.38) and safe water coverage (OR 0.54; P-value <0.05; 95% CI 0.40–0.90) were more pronounced when VLBW infants were considered; reaffirming the importance of these contextual level factors on the occurrence of LBW.

Conclusions

This study has demonstrated that contextual risk factors have independent effects on the prevalence of LBW infants in Ghanaian communities regardless of individual-level characteristics of the mothers. Being a rural dweller, Living in a community with a high concentration of poverty and a low coverage of safe water supply were found to be associated with a high prevalence LBW while poverty and poor coverage of safe water showed a pronounced impact on the prevalence of VLBW. Implementing community-based intervention programs that will address poverty alleviation, provision of regular safe water supply and the infrastructural development of rural communities will likely reduce the occurrence of LWB.

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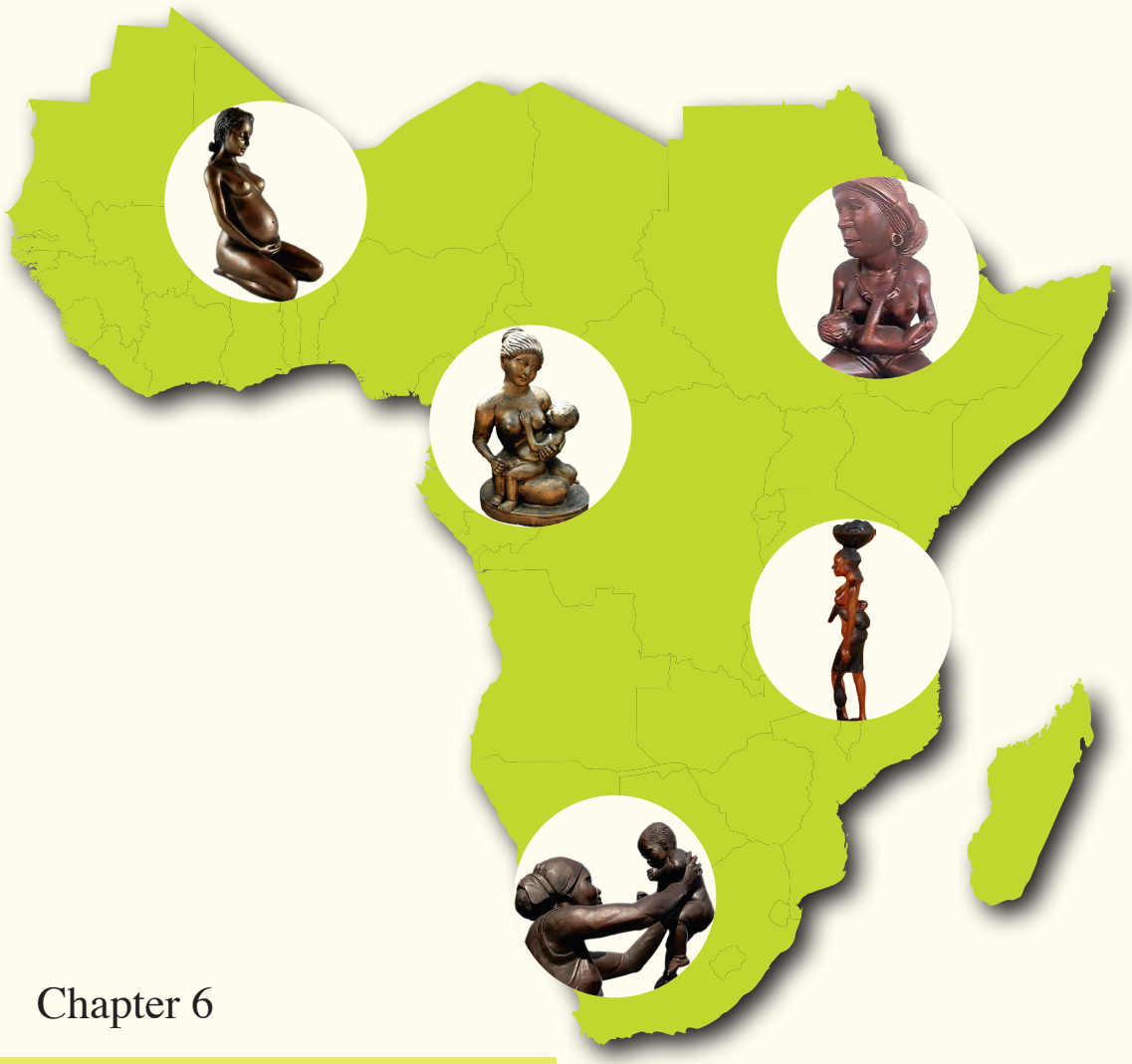

Chapter 6

Variation in neonatal mortality and its relation to country characteristic in 49 sub-Saharan African Countries

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Submitted

Abstract

Background

A substantial reduction in neonatal mortality is the main priority to reduce under-five mortality. A clear understanding of the variation in neonatal mortality and the underlying causes is important for targeted intervention. We aimed to explore variation in neonatal mortality and identify underlying causes of neonatal mortality in sub-Saharan Africa (SSA).

Methods

This ecological study used publicly available data from the World Health Organization, United State Agency for International Development and World Bank. Variation in neonatal mortality across 49 SSA countries was examined using control chart and explanatory spatial data analysis. Associations between country-level characteristics and neonatal mortality were examined using linear regression analysis.

Results

The control chart showed that 57% of SSA countries exhibited special-cause variation, thirteen countries were below the 99.8% control-limits and fourteen countries were above it. The remaining 43% showed common-cause variation. No spatial clustering was observed for neonatal mortality (Global Moran's I statistic -0.10; P-value 0.74). Linear regression analysis showed HIV/AIDS prevalence among the population of reproductive age to be positively associated with neonatal mortality (β 0.463; 95% CI 0.135 to 0.790; P-value < 0.01). Declining socioeconomic deprivation (β -0.234; 95% CI -0.424 to -0.044; P-value < 0.05) and high quality of healthcare governance (β -1.327, 95% CI -2.073 to -0.580; P-value < 0.01) were inversely associated with neonatal mortality.

Conclusion

This study shows a wide in neonatal mortality in SSA. A substantial part of this variation can be explained by differences in the quality of healthcare governance, prevalence of HIV and socioeconomic deprivation.

Background

A substantial reduction in neonatal mortality is the main priority to realize Millennium Development Goal 4 (MDG 4 – aims to reduce under-five mortality by two-thirds between 1990 and 2015) given that neonatal death accounts for 40% of under-five mortality.[1] Globally, about 10,000 neonates are dying daily[2], an estimate that may be significantly higher considering the likelihood of under-reporting[3 4] especially in low- and middle-income countries (LMICs).[5] Sub-Saharan Africa has the highest rate of neonatal mortality worldwide,[6] with some degree of variation across sub-Saharan African countries and witnessed only minor declines over the last two decades.[3] Examining variation in health outcomes across similar settings is an important aspect of epidemiological research to guide assessment of inequality in health outcomes,[7 8] health system performance monitoring,[9-11] and healthcare governance.[12]

Exploring variation in health outcome requires collection of valid data, appropriate application of statistical analyses and adequate knowledge in exploring variation. Several studies have emphasized the approach proposed by Shewhart and Deming on how to investigate and deal with variation[13-15] According to their findings, every system is subjected to both common cause (expected) and special cause (unexpected) variation and variation is a product of multiple factors. This concept has been applied in health system research.[9 16] Both common cause and special cause variations can be observed in health outcome and they are generally shaped by multiple factors.

In common-cause variation, it is expected that the deviation of the estimated health outcome for a particular setting or population should be within 3-standard deviations of the overall average of the estimated health outcome for all settings or populations.[13] In other words, the estimated health outcome should be within so called "control limits".[13] Although such variation is referred to as common-cause variation that does not imply that the causes of variation are identical across the settings within the control limits. It simply means that even though a combination of different multiple factors might have influenced the observed health outcome in these settings, the combined effect of these multiple factors on health outcome for each population is similar considering the fact that their estimated health outcomes are all within the control limits.

In case of special-cause variation, the health outcome of that setting is expected to be outside the 3-standard deviation of the overall average of the estimated health outcomes for all the settings or populations. Factors responsible for such variation usually have an unexpected high impact on the observed health outcome. To thoroughly examine variation in health outcome across different populations, revealing the existence of common-cause and special-cause variation is a key aspect. In addition, it is important to visualize spatial distribution of health outcomes across different populations in order to detect any unusual pattern in the distribution of health outcomes in terms of

spatial clustering and outliers. Findings from such investigations may provide evidence to formulate targeted interventions aimed to improve health outcomes.[17 18]

Beyond the assessment of variation in neonatal mortality across sub-Saharan Africa the current study seeks to identify underlying causes of variation in neonatal mortality by considering country characteristics such as quality of healthcare governance, health financing, human health resources, health service delivery, and the country's socioeconomic status. As sub-Saharan Africa accommodates almost 70 percent of the total number of people living with HIV globally[19] and more than 500,000 newborns are infected annually,[20] we considered the prevalence of HIV among the population of reproductive age as a potential factor to explain variation in neonatal mortality.

Methods

Study design and data collection

This ecological study utilizes 2012 publicly available data from the World Health Organization,[21] United States Agency for International Development [22] and World Bank[23] repositories for 49 sub-Saharan Africa countries. Aggregate data at country level on neonatal mortality, illiteracy rate and HIV prevalence among the population of reproductive age (i.e. 15 to 49 years), health governance, health human resources, health delivery and health financing were extracted. Additional information on country characteristics included poverty rate, percentage of safe water coverage, and improved sanitation facilities.

Outcome

The outcome of interest for this analysis was neonatal deaths per 1000 live births, defined as the number of deaths within the first 28 days of life.

Country-level characteristics (explanatory variables)

Country-level characteristics considered to explain the underlying causes of variation in neonatal mortality were:

(1) Prevalence of HIV infection among the population of reproductive age (i.e. 15 to 49 years)

(2) Health financing based on per capita total expenditure on health at purchasing power parity (PPP) measured in United States dollar, i.e. the ratio of total expenditure on health (private and public) and the total population; expressed in US$ per person per year.

(3) Health service delivery assessed by the average proportion of the population using contraceptive among women aged 15 to 49 years and births attended by skilled health staff.

(4) Health human resources assessed by the average number of physician and nurses per 1000 people.

(5) Health governance: quality of healthcare governance was measured using a large survey that involved both local and international stakeholders in the health sector. Political stability,

government effectiveness, voice and accountability, rule of law, regulatory quality, political stability and control of corruption were the six areas assessed in the survey because of their direct impact on health system operation. Each of the six areas was assessed based on points ranging from -2.5 to +2.5; higher points indicate better quality of health governance. The total health governance performance rating score ranges from -15 to +15; -15 and +15 indicate worst and best quality of health governance respectively. Detailed information on how assessment of health governance was measured has been published elsewhere.[24]

(6) Country's socioeconomic index was measured by use of the average proportion of the population that are literate, live above poverty, and have access to safe water and improved sanitation facilities. Literacy rate was defined as the percentage of people aged 15 years and above who can read or write. Poverty rate was defined as the percentage of the population living below poverty line (less than 1.25 US$/day).[22]

Statistical analysis

Descriptive statistics

Descriptive analyses were performed to determine the range, mean and standard deviation of neonatal mortality and country-level characteristics. In addition, a mixed effect model was applied to estimate the weighted average of neonatal mortality by pooling all the estimates and assign a weight to them using their variance. Statistical analysis was performed using R statistical package.[25]

Control chart

Control chart is a graphical tool used to examine variation across similar settings or within a setting over time. Several variants of control charts have been developed,[26] but an analogue of Shewhart's control chart has been advocated by Spiegelhalter et al.[27] and Mohammed and colleagues to examine variation across similar settings.[28 29] A control chart was constructed by plotting neonatal mortality rates on the y-axis against a measure of their precision, i.e. standard deviation on the x-axis. The chart has five horizontal lines, one central line with two lines below and above it. The central line indicates the overall neonatal mortality rate while the two additional lines at 95% limits (≈ 2 standard deviation) and 99.8% limits (≈ 3 standard deviation) on both sides of the central line represent 95% limits and 99.8% limits of the overall estimate of neonatal mortality rate. Countries with a neonatal mortality rate within the 99.8% control limits (≈ 3 standard deviation) are considered to show common-cause variation while those outside the 99.8% control limits are considered to exhibit special-cause variation. Statistical analysis was performed using Stata statistical package version 11.[30]

Spatial Data Analysis

Pfeiffer et al. and Anselin et al. have described the application of global spatial autocorrelation and

Local Indicators of Spatial Autocorrelation (LISA).[31 32] In this study we used Explanatory Spatial Data Analysis (ESDA) to estimate global spatial autocorrelation that indicates overall clustering or non-randomness, i.e. assessing the degree of overall similarity in the spatial pattern of neonatal mortality across SSA countries. Since global spatial autocorrelation cannot express the degree of similarity between each country and its neighboring countries with regard to neonatal mortality, we applied LISA to determine the presence of significant spatial patterns of neonatal mortality across SSA countries. Non-randomness in the spatial pattern of neonatal mortality was identified in terms of significant spatial clustering or outliers. The estimated Local Moran's I statistic was used to assess the significance of local clusters and outliers. Overall four identifiable categories of local spatial association or local spatial autocorrelation can be observed: two categories indicate clustering while the other two suggest outliers. High-high or hot spot local spatial association (clustering of countries with high incidence of neonatal mortality) and low-low or cold spot local spatial association (clustering of countries with low incidence of neonatal mortality) indicate clustering. High-low local spatial association (a country with high incidence of neonatal mortality surrounded by neighboring countries with low incidence of neonatal mortality) and low-high local spatial association (a country with low incidence of neonatal mortality surrounded by neighboring countries with high incidence of neonatal mortality) indicates outliers.

Associations between country-level characteristics and neonatal mortality

Associations between neonatal mortality and country-level characteristics were visualized by use of bar chart and two-way scatter plot with a prediction line and 95 percent confidence interval. Pairwise correlation tests were used to determine the strength of the relationships between country-level characteristics and neonatal mortality. Based on the observed Moran's I statistic, spatial regression analysis was not considered;[33] instead a linear regression analysis was applied to examine the associations between neonatal mortality and country-level characteristics. Statistical significance of the association was determined by two-tailed Wald test at significance level of alpha equal to 5%.

Ethical approval

For analysis of an anonymous publicly available data no ethical approval is required.[21 23]

Table 1: Descriptive characteristics of 49 Sub-Saharan Africa Countries

Country characteristics	Mean	(Standard deviation; Range)
Neonatal mortality (per 1000 live births)	30.1	(9.8; 8 to 50)
HIV/AIDS prevalence (%)	4.9	(6.5; 0.2 to 26.5)
Health financing (US$ per person)	209.6	(313.4; 17 to 1642.7)
Health human resources (per 1000 people)	0.6	(0.9; 0.2 to 4.7)
Physicians per 1000 people	0.2	(0.28; 0.01 to 1.51)
Nurses and midwives per 1000 people	1.1	(1.46; 0.03 to 7.92)
Health service delivery (%)	43.4	(18.9; 1.8 to 87.6)
contraceptive prevalence (%)	28.1	(19.3; 4 to 75.9)
skilled delivery (%)	59.1	(21.9; 10 to 99.2)
Health governance (score ranged from -15 to +15)	- 4.1	(3.8; - 13.7 to 5.0)
Country socioeconomic status	56.0	(14.9; 29.5 to 95.9)
literacy rate (% of people aged 15 & above)	65.0	(19.1; 27 to 94.2)
poverty rate (%)	47.5	(18.3; 2 to 76.8)
access to improved water source (%)	70.6	(17.0; 29.5 to 99.8)
access to improved sanitation facilities (%)	35.9	(23.0; 8.9 to 97.1)

Results

Descriptive statistics

The summary statistics of the 49 countries included in the analysis are shown in Table 1. Across countries neonatal mortality ranged from 8 per 1000 to 50 per 1000 live births (mean of 30.1 per 1000 live births and standard deviation of 9.8 per 1000). The prevalence of HIV/AIDS among adults of reproductive age ranged from 0.2% to 26.5% (mean of 4.9% and standard deviation of 6.5%). The average literacy and poverty rate were 65% and 47% respectively. For 28% percent of women of reproductive age contraceptive use was reported; on country level 59% of all deliveries were supervised by a skilled healthcare provider. An average of six health professionals cared for a population of 10,000 and 209.6 US$ was spent on health per person per year with a wide disparity ranging from 17 US$ to 1,642 US$ per person per year. Eight countries (Botswana, Equatorial Guinea, Gabon, Mauritius, Seychelles, Swaziland, South Africa and Namibia) spent up to 250 US$ per person per year, the majority of the countries committed less than 100 US$ per person per year. The quality of healthcare governance was generally low with an average of -4.1 and only the Seychelles, Mauritius, Cape Verde, Namibia, Botswana, Ghana and South Africa had a positive score indicating good quality of healthcare governance.

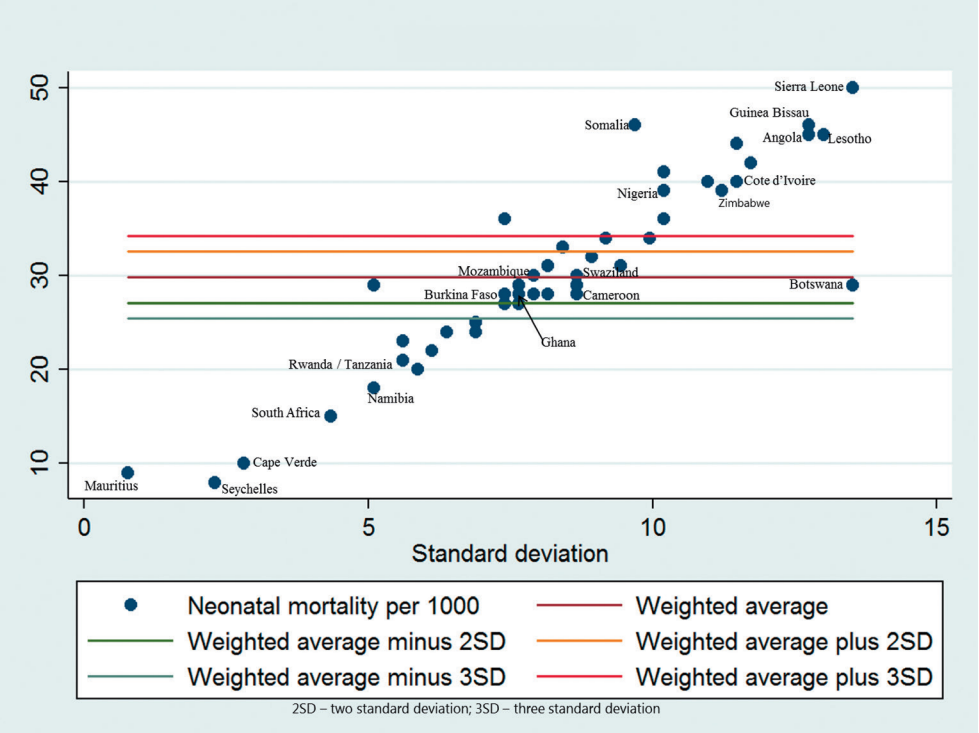

Figure 1. Control chart : Variation in neonatal mortality in sub-Saharan Africa

Special- and common-cause variations in neonatal mortality

Figure 1 shows the results of the control chart that explored variation in neonatal mortality across 49 SSA countries. Neonatal mortality was plotted against its precision, i.e., its standard deviation. The central line represents the weighted mean (29.8 per 1000 live births) of neonatal mortality rates. Neonatal mortality rates in twenty-one SSA countries (43%) were within the 99.8 percent control limits (≈ 3 standard deviations). Variation observed within this limits suggests common-cause variation. Neonatal mortality rates in thirteen SSA countries were below the control limits (≈ 3 standard deviations) while fourteen SSA countries neonatal mortality rates were above it, indicating special-cause variation in twenty-eight (57%) SSA countries.

Geographical variations / clustering in neonatal mortality

Table 2 shows both global and local spatial autocorrelation for neonatal mortality among SSA countries. The global Moran's I statistic (Moran's I statistic = -0.0925; P-value = 0.74) and Geary's C statistic (Geary's C statistic = 1.0640; P-value = 0.71) were not significant indicating absence of spatial clustering of neonatal mortality rates across SSA countries. The local spatial autocorrelation estimates for neonatal mortality in SSA countries were similarly not significant suggesting the

absence of local spatial autocorrelation between any SSA country and neighboring countries for this health outcome.

Table 2. Global and Local Spatial Autocorrelation for Neonatal mortality in Sub-Saharan Africa

Country	Local Moran's Statistic I (P-value)
Angola	-0.2034 (0.6473)
Benin Republic	-0.0077 (0.4859)
Botswana	0.2638 (0.2713)
Burkina Faso	-0.0706 (0.5488)
Burundi	-0.1874 (0.6139)
Cameroon	-0.1784 (0.6588)
Central Africa Republic	0.3505 (0.1849)
Chad	0.1301 (0.3559)
Coast d'Ivoire	-0.0065 (0.4829)
Congo Brazzaville	0.0095 (0.4677)
Congo Democratic Republic	-0.1832 (0.7052)
Djibouti	0.0103 (0.4750)
Equatorial Guinea	-0.1604 (0.5785)
Eritrea	0.4242 (0.2089)
Ethiopia	0.0662 (0.4142)
Gabon	0.0502 (0.4464)
Gambia	0.4236 (0.3243)
Ghana	-0.0975 (0.5525)
Guinea Liberia	0.1890 (0.2854)
Guinea-Bissau	-0.5647 (0.7843)
Kenya	0.1532 (0.3354)
Lesotho	-3.0964 (0.9991)
Liberia	-0.6433 (0.8681)
Malawi	0.5700 (0.1416)
Mali	-0.0743 (0.5527)
Mauritania	0.0342 (0.4660)
Mozambique	0.1434 (0.3279)
Namibia	0.0885 (0.3935)
Niger	-0.1910 (0.6549)
Nigeria	-0.0856 (0.5514)
Rwanda	0.1301 (0.3721)
Senegal	-0.5428 (0.8926)
Sierra Leone	-0.3441 (0.6792)
Somalia	-0.5647 (0.8354)
South Africa	0.0056 (0.4682)
Sudan	0.0057 (0.4651)
Swaziland	0.2429 (0.3486)
Tanzania	0.3956 (0.0925)
Uganda	-0.0616 (0.5268)
Togo	0.4280 (0.1396)
Zambia	0.0242 (0.4390)
Zimbabwe	-0.7644 (0.9617)

Global moran's I statistic = -0.0925; P-value =0.7393; Geary's C statistic = 1.0640; P-value = 0.7116

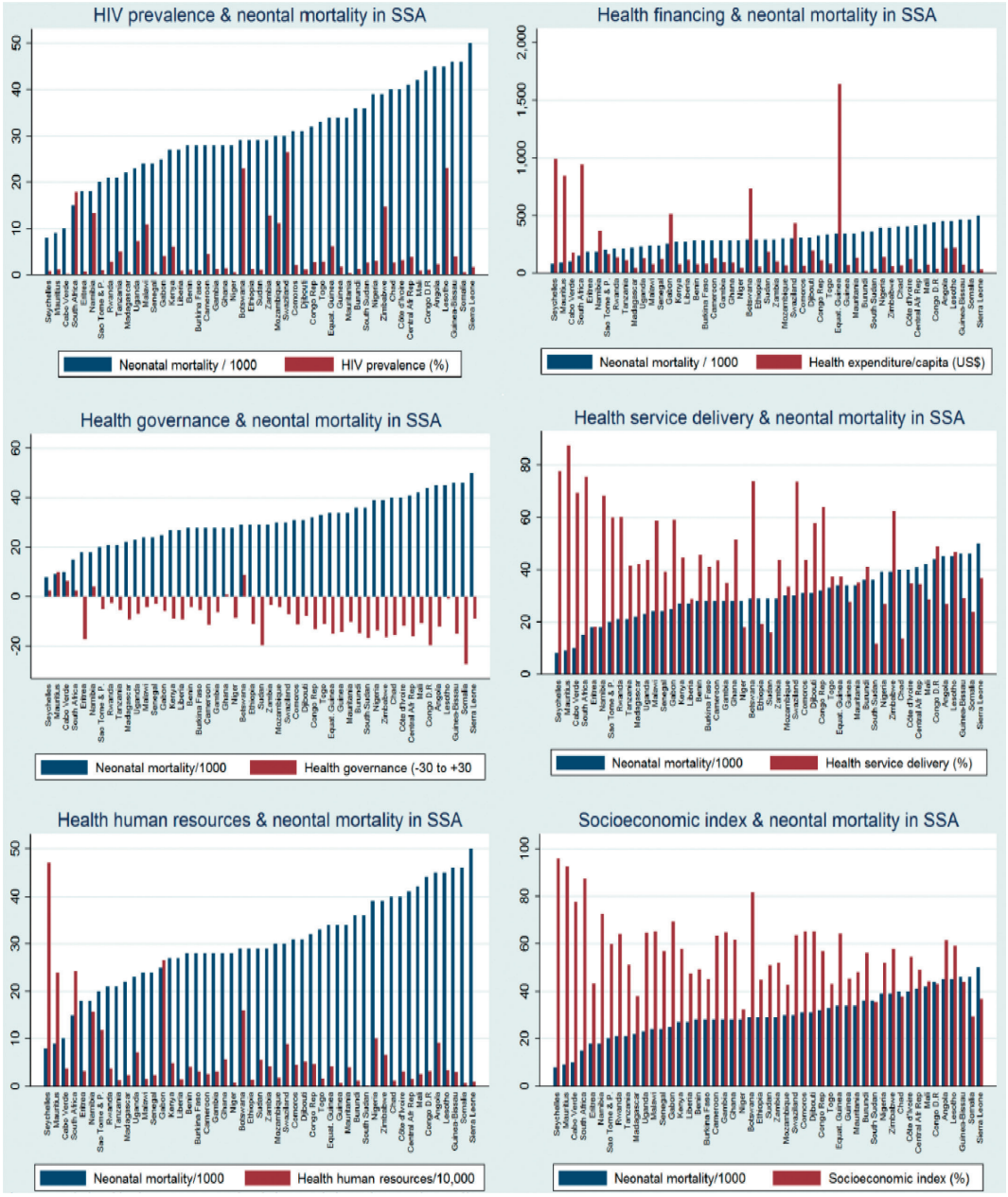

Figure 2. Relationships between country-level characteristics and neonatal mortality in SSA

Associations between country-level characteristic and neonatal mortality

The relationships between country-level characteristics (HIV prevalence, health financing, health human resources, health service delivery, health governance and country socioeconomic status) and neonatal mortality are shown in figure 2 using multiple double-bar charts. No relationship was observed between HIV prevalence among the population of reproductive age and neonatal mortality. The lowest rates of HIV prevalence were found for Cape Verde, Mauritania, Madagascar, Niger, Senegal and Somalia and the highest rates for Swaziland, Lesotho, Botswana, South Africa, Zimbabwe and Namibia. A country's financial investment in health was inversely related with neonatal mortality except for Cape Verde, Eritrea, Gabon, Botswana, Swaziland, Equatorial Guinea, Angola and Lesotho.

Further, figure 2 shows that as country's health human resources capacity increased neonatal mortality decreased with the exception of Cape Verde, Eritrea, Gabon, Botswana, Swaziland, Nigeria, Zimbabwe and Angola. An inverse relationship was observed between the coverage of health service delivery and neonatal mortality except for Eritrea, Botswana, Swaziland, Djibouti, Congo Republic, South Sudan, Zimbabwe, Chad, Congo Democratic Republic and Lesotho. The quality of healthcare governance was generally inversely related to neonatal mortality except for Eritrea, Ghana, Botswana, Sudan, and Lesotho. Likewise, when the average socioeconomic index in a country was higher, neonatal mortality was lower with the exception of Eritrea, Madagascar, Botswana, Swaziland, Comoros, Djibouti, Equatorial Guinea, Zimbabwe, Cote d'Ivoire, Angola and Lesotho.

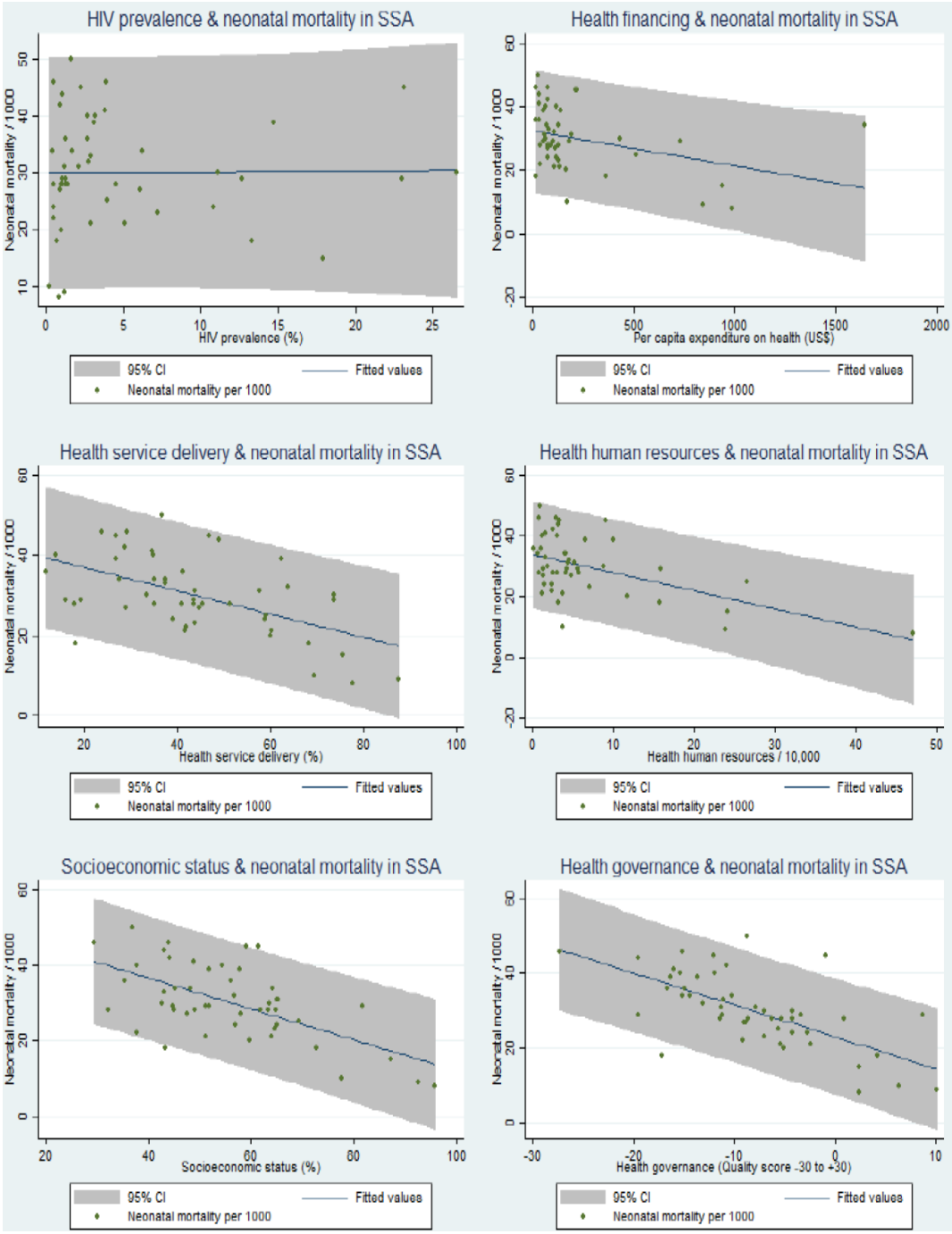

Figure 3. Unadjusted associations between country-level characteristics and neonatal mortality in SSA

For quantitative assessment of relationships between country characteristics and neonatal mortality, two-way scatter plots with a prediction line and 95% confidence interval were constructed (Figure 3). No relationship was observed between HIV prevalence and neonatal mortality. The financial investment in health was inversely related to neonatal mortality with the exception of Sierra Leone, Cape Verde and Equatorial Guinea that were outside or very close to the 95% confidence interval limits of the prediction line (correlation coefficient $r = 0.35$; P-value = 0.01). Similarly, country's health human resources capacity showed an inverse linear relationship with neonatal mortality, although Cape Verde, Angola and Sierra Leone were outside or very close to the 95% confidence interval limits of the prediction line (correlation coefficients $r = 0.52$; P-value < 0.001). An inverse relationship was observed between the population coverage of health service delivery and neonatal mortality. Eritrea, Sierra Leone, Lesotho and Congo Democratic Republic were outside or very close to the 95% confidence interval limits of the prediction line (correlation coefficient $r = 0.54$; P-value < 0.001). As country's quality of healthcare governance increased neonatal mortality decreased (correlation coefficient $r = 0.52$; P-value < 0.001); Eritrea, Sierra Leone, Lesotho and Botswana were outside or very close to the 95% confidence interval limits of the prediction line. Socioeconomic index showed similar relationship with neonatal mortality (correlation coefficient r =0.61; P-value < 0.001); Eritrea, Madagascar, Lesotho and Angola were outside or very close to the 95% confidence interval limits of the prediction line.

The pooled characteristics (HIV prevalence, health financing, health human resources, health service delivery, quality of healthcare governance and country socioeconomic index) of the countries below, within and above the control limits (≈ 3 standard deviation) were compared to average neonatal mortality using multiple double-bar charts as shown in figure 4. The results clearly show linear inverse relationships of the country's health financing, health human resources, health service delivery coverage, health governance performance and socioeconomic index with neonatal mortality. HIV prevalence appeared not to have a significant relationship with neonatal mortality.

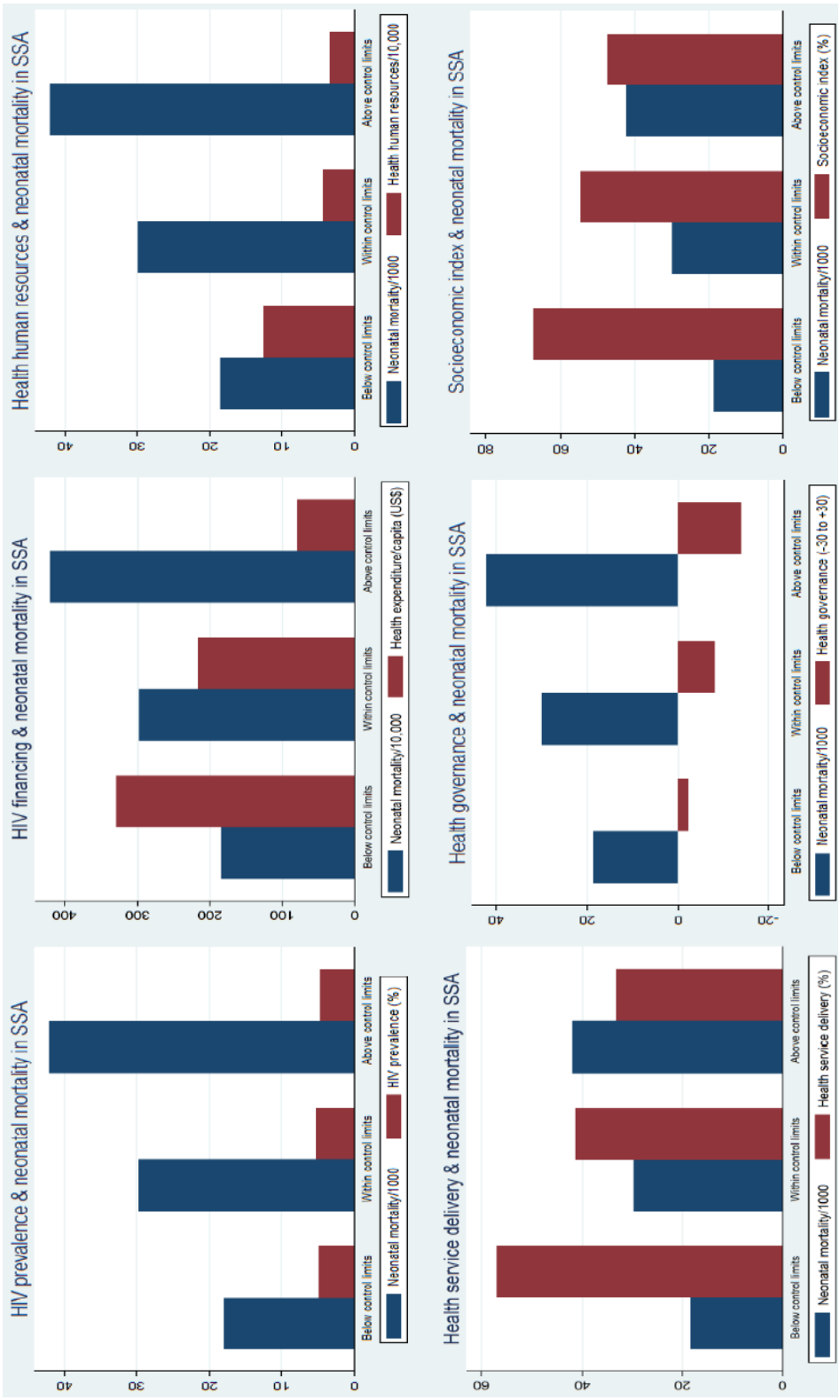

Figure 4: Relationships between country-level characteristics & neonatal mortality for countries below, within, & above the control limits

The results of the linear regression analysis to examine the association between country characteristic and neonatal death are shown in Table 3. In the multivariable regression model, three country characteristics were observed to have a significant independent association with neonatal death. The quality of healthcare governance was the strongest underlying factor for neonatal survival; for every unit increase in country's quality of healthcare governance neonatal mortality declined by -1.327 per 1000 live births (95% CI -2.073 to -0.580; P-value < 0.01). In addition, for every unit decline in the percentage of population under socioeconomic deprivation, neonatal mortality declined by -0.234 per 1000 live births (95% CI -0.424 to -0.044; P-value < 0.05), whereas for every unit increase in the prevalence of HIV/AIDS among the population of reproductive age, neonatal mortality increased by 0.463 per 1000 live births (95% CI 0.135 to 0.790; P-value < 0.01).

Table 3. Association between pre-specified country characteristics and neonatal death

Country characteristics	Univariable model β (95% CI)	Multivariable model β (95% CI)
HIV/AIDS prevalence	0.019 (-0.429 to 0.467)	0.463 (0.135 to 0.790)**
Health financing	-0.011 (-0.020 to -0.002)*	###
Health human resources	-5.962 (-8.870 to -3.055)***	###
Health service delivery	-0.290 (-0.422 to -0.158)***	###
Health governance	-1.707 (-2.282 to -1.133)***	-1.327 (-2.073 to -0.580)**
Country socioeconomic status	-0.408 (-0.562 to -0.254)***	-0.234 (-0.424 to -0.044)*

*****P-value < 0.001; **P-value < 0.01; *P-value < 0.05; β regression coefficient, ### variable omitted in the final model based on adjusted R-squared**

Discussion

This study shows a vast geographical variation in neonatal mortality across 49 SSA countries. A substantial part of this variation could be explained by the differences in quality of healthcare governance, prevalence of HIV/AIDS among the population of reproductive age, and socioeconomic index across SSA countries. Even though we applied the appropriate statistical methods for analysis and the data utilized can be perceived as reliable data considering their sources, our findings could be threatened by ecological fallacy; this seems, however, to be very unlikely for the observed relationship between the quality of healthcare governance and neonatal death. Residual confounding might have influenced the observed relationships as in the data available the individual-level characteristics could not be considered.

In this region, more than half of the residents are living in poverty, one out of 20 people is HIV infected and the scarcity of human and financial resources make it difficult to provide adequate health services and other basic necessities of life such as safe water and education.

Our analyses do not show spatial clustering in neonatal mortality among SSA countries. This spatial randomness might be due to the use of data at a country-level rather than at province or district level as employed in previous studies observing spatial clustering in childhood mortality and morbidity.[7 8]

The control chart analyses showed both common-cause and special-cause variation in neonatal mortality. Further examination of countries located below the control limits may identify factors that explain why these countries perform better than the rest of SSA. Similarly, countries above the control limits (> 3 standard deviation) should be thoroughly assessed to identify factors responsible for their excess incidence of neonatal mortality. While countries within the 99.8% control limits show no evidence of special-cause variation it remains to be explained why they have higher neonatal mortality rate than those below the control limits.

Globally, the leading causes (direct causes) of neonatal deaths are: prematurity / low birth weight, birth asphyxia, neonatal sepsis and birth trauma.[1] Indirect factors contribute to neonatal death by influencing neonatal survival at both individual- and population-level (contextual-level).[34] The present study investigated the associations between neonatal mortality and indirect factors by identifying differences in country characteristics that might be responsible for the observed variations in neonatal mortality in SSA. Quality of health care governance was the strongest determinant of neonatal mortality in this study, though only seven of the 49 SSA countries showed a positive rating in the quality of healthcare governance. To the best of our knowledge prior studies have not linked the quality of healthcare governance with neonatal mortality. Generally, emphasis has been placed on increasing health financing and health service coverage which is commendable, but only in the presence of good healthcare governance can this be fully effective. Without ensuring good quality in healthcare governance, scarce healthcare resources will not be used judiciously as shown by the results of a diagnostic public expenditure tracking survey conducted in Ghana, Uganda and Tanzania that demonstrated extensive leakages of public funds in these three SSA countries.[35] Thus, genuine commitment by governments is required to improve the quality of healthcare governance by ensuring transparency and accountability, government effectiveness, political stability, adherence to the rule of law, high regulatory quality and stiff action against corruption.

HIV prevalence among the population of reproductive age was positively associated with neonatal death, consistent with findings from a previous study that showed that neonates of HIV positive mothers were more likely to die[36] This is yet another argument to promote prevention of mother-to-

child transmission (PMTCT). Neonatal mortality declined as country's socioeconomic index improved, a result in line with previous studies observing that dwelling in a socioeconomically deprived population increases the risk of childhood morbidity and mortality.[34 37 38 39] Similarly, a multi-country study that involved 13 sub-Saharan African countries showed that the likelihood of dying at neonatal stage among the families in the poorest quintile was almost 70% higher than in the richest quintile.[40] Implementing free basic education and poverty alleviation programs in conjunction with expansion of safe water supply and promotion of effective sanitation programs will help to improve neonatal survival.

In conclusion, the results of this study based on data from 49 Sub-Saharan African countries show a marked variation in neonatal mortality. A substantial part of this variation can be explained by differences in health governance performance, prevalence of HIV and socioeconomic deprivation.

Competing interests

The authors declare that they have no competing interests

Authors' contributions

Gbenga A. Kayode (GAK), Klipstein-Grobusch (KKG) and Diederick E. Grobbee (DEG) conceptualized and designed the study. GAK carried out the literature review, data extraction, analysis, result interpretation and drafted the first version of the manuscript. All the authors (GAK, KKG, DEG, Evelyn Ansah (EA), Olalekan A. Uthman (OAU) and Mary Amoakoh-Coleman (MAC) reviewed and approved the final version of the manuscript

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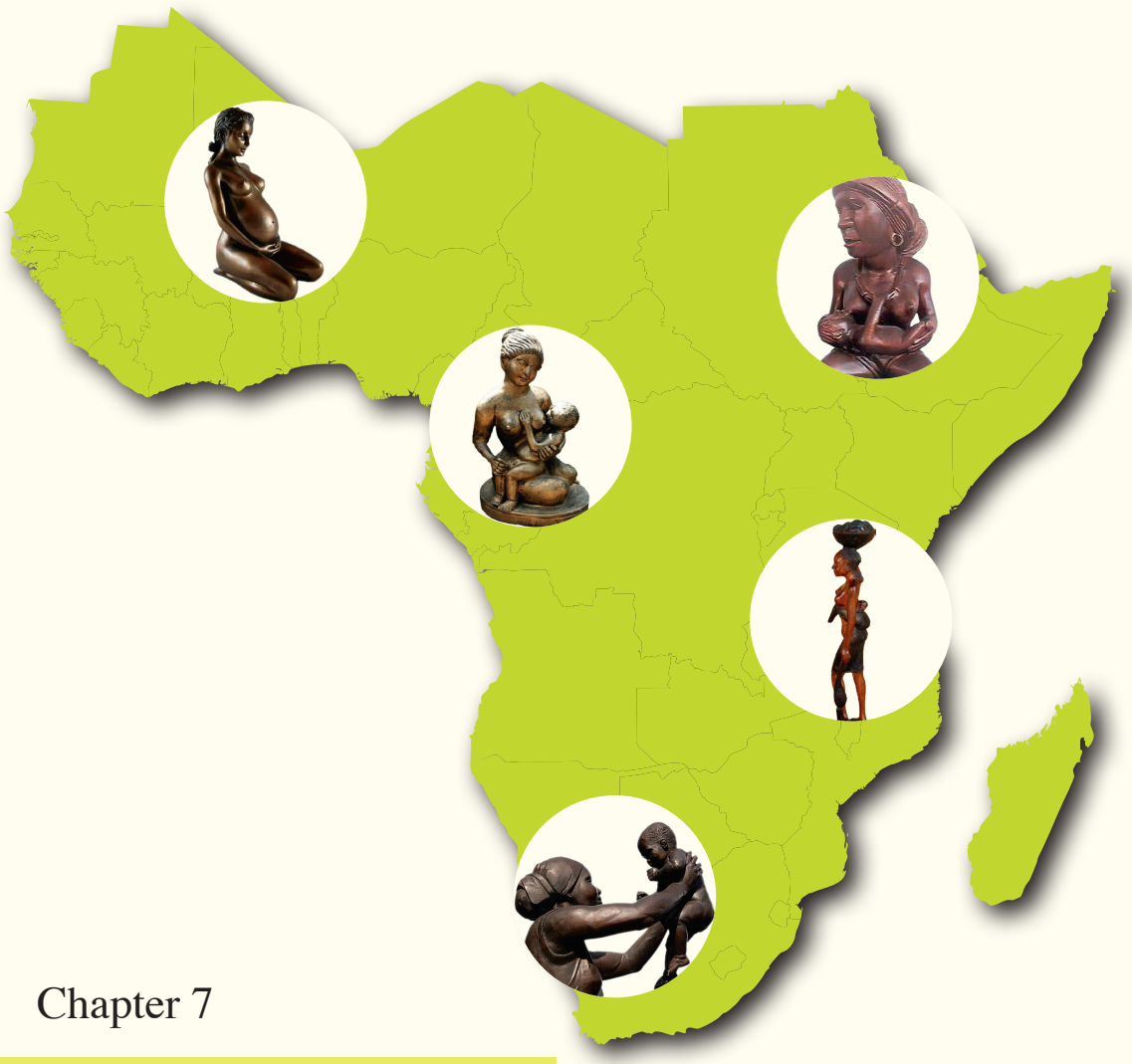

Chapter 7

Impact of maternal insurance on continuum of care services utilization

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Submitted

Abstract

Objective

This study aims to evaluate the effect of maternal health insurance status on the utilization of antenatal, skilled delivery and postnatal care.

Design

A population based cross-sectional study.

Setting and participants

We utilized the 2008 Demographic and Health Survey data of Ghana, which included 2,987 women that provided on information on maternal health insurance status.

Primary outcomes

Utilization of antenatal, skilled delivery and postnatal care.

Results: After adjusting for socioeconomic, demographic and obstetric factors, we observed that among insured woman the likelihood of having antenatal care increased by 96% (OR 1.96; CI 1.52 to 2.52; P-value < 0.001) and of skilled delivery 129% (OR 2.29; CI 1.92 to 2.74; P-value < 0.001), while postnatal care among insured women increased by 61% (OR 1.61; CI 1.17 to 2.21; P-value < 0.01).

Conclusion: This study demonstrated that maternal health insurance status plays a significant role in the uptake of the MNCH continuum of care service.

Background

In the MNCH continuum of care, two dimensions can be identified: first, in time of care provided ranging from preconception, antenatal, childbirth, postnatal and into childhood. Second, in place and approach of provided care, which includes both facility care as well as community-based care or household health practices.[1,2] The continuum of care model is a core principle of maternal, newborn and child healthcare (MNCH), and emphasizes the interconnectivity and shared interests between them.[1–3] With an estimated 292 982 maternal,[4] 2 612 100 neonatal and 3 662 700 total under-five deaths globally,[5] the continuum of care approach provides a valuable tool to identify and evaluate interventions which could reduce preventable mortality.[6,7]

In order to strengthen the continuum of care, strategies are needed to improve access to care and financial protection for women, babies and children. Health insurance coverage has been identified as a critical factor to improve access and quality of maternal and perinatal care,[6,8,9] through protection against unexpected financial setbacks, reduction of illness-associated out-of-pocket expenses, and prevention of loss of employment due to prolonged illness.[10,11] Globally, political commitment has been given for policies to ensure universal health care coverage.[12] In response to the global call to implement universal health insurance coverage, the Ghanaian government established the national health insurance scheme (NHIS) under the Act of 2003.

A systematic review by Comfort et al[11] assessed the effects of health insurance on the use of maternal health services and showed a generally positive association between insurance and antenatal care (ANC) attendance,[13–20] facility-based delivery[15–25] and skilled attendance at birth[15,19,26] in various sub-Saharan African, Asian, South American and Eurasian countries. This association was observed regardless of type of insurance scheme implemented, and particularly pronounced with low baseline service utilization. However, many studies were not based on nationally representative samples that assessed (various combinations of) components of the continuum of MNCH health. In Ghana, two regional studies did not report an effect on receipt[13] of at least four ANC visits,[13,20] though others did report improved attendance.[19] Dixon et al[27] evaluated the association in nationally representative data and assessed ANC care use. We add to that study by including the other components of the continuum of care services. Therefore, we aimed to assess the association between maternal health insurance status and the utilization of MNCH continuum of care service using nationally representative data from the Ghana Demographic and Health Survey (DHS).

Methods

Study design and data collection

This population-based cross sectional study used 2008 Ghana Demographic and Health Survey data (GDHS). Detail information on data collection has been published elsewhere.[28] In summary, a two-stage stratified cluster sampling technique was applied to identify households that were interviewed. All women and men aged 15 to 49 years and 15 to 59 years respectively were interviewed using household, women's and men's questionnaires and information was collected on socioeconomic, household, demographic and health indicators. Individual and household response rates were 96.5% and 98.9%, respectively.[28]

Outcome variables

Three outcomes on the utilization of continuum of care service in MNCH were used to assess the effect of maternal health insurance status : antenatal care, skilled delivery and postnatal care. Antenatal care was defined as care that women receive from their healthcare providers during pregnancy. Skilled delivery was defined as delivery that is performed by healthcare professionals (doctor, midwives, and nurses) while postnatal care was defined as care that women receive from their health providers post-delivery. Skilled delivery and postnatal care were coded "yes/no" based on whether the women received it or not. Similarly, antenatal care was classified into two categories: those that had up to four antenatal visits and others that had less than four.

Determinants

Maternal health insurance status was the main determinant of interest. Based on epidemiological knowledge and prior evidence, we identified as potential demographic, socio-economic and obstetric confounding factors: maternal age, difficulty to reach the facility, maternal education, marital status, maternal occupation, wealth index, parity, and multiple gestation. Wealth index was estimated by Measure DHS using an asset-based approach; household characteristics such as floor/roof type, radio, television, water source, toilet facility were operationalized using Principal Component Analysis (PCA) to generate a wealth index variable.[28] Subsequently, quintiles were re-coded into poor (lowest two quintiles), average (middle two quintiles) and high (highest quintile). Marital status was categorized as: formerly married, currently married and never married while maternal education was classified as: no education, primary, secondary or higher education. Maternal occupation categories comprised of unemployed, manual job or skilled job.

Statistical analysis

First, general descriptive statistics were calculated. Next, multivariable logistic regression analysis was used to examine the association between maternal health insurance status and the utilization of the continuum of care service in MNCH. In the analysis, four models were fitted, Model I determined the crude association between maternal health insurance status and each of the outcomes (antenatal care, skilled delivery and postnatal care) while Model II examined the

association between maternal health insurance status and each of the outcomes when demographic and obstetrics factors (maternal age, distance to health facility, parity and multiple gestation) were considered. Model III estimated the association between maternal health insurance status and each of the outcomes after adjusting for socioeconomic factors (maternal education, marital status, maternal occupation and wealth index). In Model IV all identified possible confounders were incorporated. Statistical significance of the covariate was determined by two-tailed Wald test at significance level of α equal to 0.05. Analyses were performed using STATA version 11.[29]

Ethical consideration

The Ethics Review Committee, Ghana Health Service, Accra, Ghana and the Ethics Committee of ICF Macro in Calverton, United States gave the ethical approval to conduct GDHS. Measure DHS released the data to us upon request.

Results

Characteristics of the study population

General characteristics of the population are shown in table 1. About 3,000 women aged 15 to 49 years were interviewed. More than 90% of the women were co-habiting with their husbands and 60% of them had health insurance coverage. More than half of the women were living in poverty, having two to four children, and were engaged in manual labor. Approximately two-thirds of the women had difficulty to reach the healthcare facility, while two-fifths of them had no education.

Table 1. General characteristics of the study population, GDHS 2008

Characteristics	Frequency (Percentage)
Socioeconomic factors	
Marital status	
Formerly married	150 (5)
Currently married	2,712 (91)
Never married	130 (4)
Maternal occupation	
Unemployed	300 (10)
Manual job	1,650 (55)
Skilled job	1,028 (35)
Maternal education	
No education	1,132 (38)
Primary	722 (24)
Secondary or higher	1,138 (38)
Wealth Index	
Poor	1,629 (54)
Average	504 (17)
Rich	859 (29)
Maternal health insurance	
Yes	1,202 (40)
No	1,785 (60)
Demographic and obstetric factors	
Maternal age (years)	
15 to 24	702 (23)
25 to 34	1,427 (48)
35 to 49	863 (29)
Parity	
1	457 (15)
2 to 4	1,629 (55)
5 and above	906 (30)
Multiple gestation	
No	2,860 (96)
Yes	132 (4)
Distance from facility	
Difficult access	1,003 (34)
Not difficult to access	1,982 (66)

Association between maternal insurance and the continuum of care

Table 2 shows the results of the multivariable logistic regression that examined the association between maternal health insurance status and the utilization of antenatal care, delivery and postnatal care services. The crude association was estimated in Model 1; the likelihood of attending antenatal clinic increased by 2.7 fold (OR 2.71; 95% CI 2.13 to 3.44) among women that were insured. This

Table 2. Association between maternal health insurance status and antenatal, delivery and postnatal care utilization, GDHS 2008.

	Model I	Model II	Model III	Model IV
Antenatal care utilization				
Insured	2.71 (2.13 to 3.44)***	2.40 (1.88 to 3.06)***	2.03 (1.58 to 2.61)***	1.96 (1.52 to 2.52)***
Un insured	1 (reference)	1 (reference)	1 (reference)	1 (reference)
Delivery care utilization				
Insured	3.18 (2.72 to 3.72)***	2.89 (2.45 to 3.40)***	2.37 (1.98 to 2.83)***	2.29 (1.91 to 2.74)***
Not insured	1 (reference)	1 (reference)	1 (reference)	1 (reference)
Postnatal care utilization				
Insured	1.63 (1.20 to 2.23)**	1.59 (1.16 to 2.18)**	1.65 (1.20 to 2.25)**	1.61 (1.17 to 2.21)**
Not insured	1 (reference)	1 (reference)	1 (reference)	1 (reference)

Model I crude associate; Model II adjusted for demographic & obstetric factors maternal age, distance to health facility, parity and multiple gestation, Model III adjusted for socioeconomic factors maternal education, marital status, maternal occupation and wealth index; Model IV adjusted for all confounders.
***p < 0.001; **p < 0.01; *p < 0.05

estimate declined to 2.4 fold (OR 2.40; 95% CI 1.88 to 3.06) and 2.0 fold (OR 2.03; 95% CI 1.58 to 2.61) when adjusted for socioeconomic factors in Model II and demographic and obstetric factors in Model III, respectively. After fully adjusting for socioeconomic, demographic and obstetric factors in Model IV the probability of attending antenatal clinic among women that were insured (OR 1.96; 95% CI 1.52 to 2.52) compared to those that were not insured.

The unadjusted association between maternal health status and skilled delivery was considered in Model I; the odds of having a skilled delivery among women that were insured increased 3.0 fold (OR 3.18; 95% CI 2.72 to 3.72). When socioeconomic factors were accounted for in Model II, and demographic and obstetric factors were considered in Model III, the crude association declined to 2.9 (OR 2.89; 95% CI 2.45 to 3.40) and 2.4 (OR 2.37; 95% CI 1.98 to 2.83) respectively. In model IV, socioeconomic, demographic and obstetric factors were accounted for but the odds of insured pregnant women having a skilled delivery remained statistically significant. The likelihood of having a skilled delivery among pregnant women that were insured was more than doubled (OR 2.29; 95% CI 1.91 to 2.74) compared to those uninsured.

The unadjusted association between maternal health insurance status and the uptake of postnatal care service was evaluated in Model I; the likelihood of attending postnatal clinic increased by 63% (OR 1.63; 95% CI 1.20 to 2.23). After incorporating socioeconomic factors to Model II and adjusted for demographic and obstetric factors in Model III, the probability of attending postnatal clinics declined to 59% (OR 1.59; 1.16 to 2.18) in Model II but increased to 65% (OR 1.65; 1.20 to 2.25) in Model III. Socioeconomic, demographic and obstetric factors were considered in Model IV

showing the probability of attending postnatal clinics among insured women to be 61% higher (OR 1.61; 95% CI 1.17 to 2.21) compared to uninsured women.

Discussion

Main findings

The findings in this study show that maternal health insurance status plays a significant role in the utilization of the MNCH continuum of care services. Insured women had a better uptake of antenatal care, skilled delivery and postnatal care than those who were not insured regardless of differences in socioeconomic, demographic and obstetric characteristics.

Our findings are in line with previous studies reporting that maternal health insurance enhances the continuum of MNCH care utilization.[11] A number of previous studies have explored the association between insurance status and MNCH services utilization in Ghana. Two regional studies by Chankova et al[13] and Smith and Sulzbach [20] did not report an effect on receipt of at least four ANC visits. Dixon et al[27] used nationally representative data of GDHS and observed a higher frequency of ANC care use among NHIS enrolled women, although the timing of the first ANC visit did not differ. We add to the available evidence by including the other components of the continuum of care services. Our findings also generalize the observations by Mensah[19] who found improvement of attendance on the continuum of care in two administrative districts in Ghana, and Dzakpasu,[30] who observed better facility delivery rates after the implementation of free delivery care in 2003/2005 and in 2008 after the NHIS fee exemption scheme had been established. The latter study also suggested that insurance may reduce inequities, as the poor benefited especially. This is of relevance in light of the persistent inequities in maternal health.[31,32]

This DHS study was conducted before the implementation of the broader fee exemption scheme for pregnant women in Ghana. From 1 July 2008 onwards, pregnant women were eligible under the exemption scheme to enroll within the NHIS without registration and premium fees to receive up to six ANC visits, delivery, two postnatal visits within six weeks after delivery, and care of the newborn up to three months.[19] Until then, only delivery was free of charge. [27] Importantly, even during the fee exemption scheme, care is often not completely free of out-of-pocket expenses due to associated costs including transportation or medicines not covered under the scheme. Furthermore, the maternal health insurance package did not include family planning products so although postnatal women may receive counseling as part of the services under the insurance package, any products required had to be secured outside the insurance package. Nevertheless, the reduction of health-associated expenses would most likely further improves the continuum of care services for poor women.[33,34]

The strength of our study is that we use nationally representative data and assessed all components of the continuum of care. The GDHS data is perceived as a reliable data considering its excellent individual and household response rates and robust sampling technique. [28] Limitations include that we do not have information on the quality of care provided. As such, we cannot establish a causal link with health outcomes, which has been previously described as an inherent difficulty of insurance-association studies.[35] Also, most maternal, newborn and child deaths occur at home and may be missed or underreported in the GDHS, requiring to do more to know the magnitude of how births at home impact the continuum of care under maternal health insurance. Utilization of MNCH care in itself does not guarantee a sufficient quality of care, and the evidence by which health insurance affects quality of care is inconclusive.[11] In Ghana, Mensah reported that NHIS members, i.e. those with health insurance were not more likely to have blood pressure measurements or/ and blood and urine analyses during antenatal care.[19] In contrast, in Brazil insurance was associated with a higher likelihood of having routine blood and urine tests, ultrasounds and vitamin and iron prescription. [36] It has been also been reported that insurance does not necessarily improve the timeliness of the essential first ANC visit. [27] An evaluation of the free delivery policy implemented before the maternal health insurance policy in Ghana noted that women's care-seeking behavior in some cases is unlikely to change under the free delivery policy because of negative experiences, perceptions and/or misconceptions about the policy and the fact that the cost of services are clearly not the full story.[37] Efforts to improve the continuum of care require a holistic approach to improve the supply and demand sides of care.

Conclusion

The result of this study using data on a representative sample of 2,987 pregnant women provides strong support that health insurance coverage of pregnant women promotes the uptake of maternal neonatal and child continuum of care service.

Competing interests

The authors declare that they have no competing interests.

Authors' contribution

Joyce L. Browne (JLB), Gbenga A. Kayode (GAK) and Kerstin Klipstein-Grobusch (KKG) conceptualized and designed the study. JBL and GAK carried out the literature review, data extraction and analysis and drafted the first version of the manuscript. All the authors (JBL, GAK, KKG, Daniel Arhinful (DA), Samuel A.J Fidder (SAJF) and Diederick E. Grobbee (DEG) reviewed and approved the final version of the manuscript.

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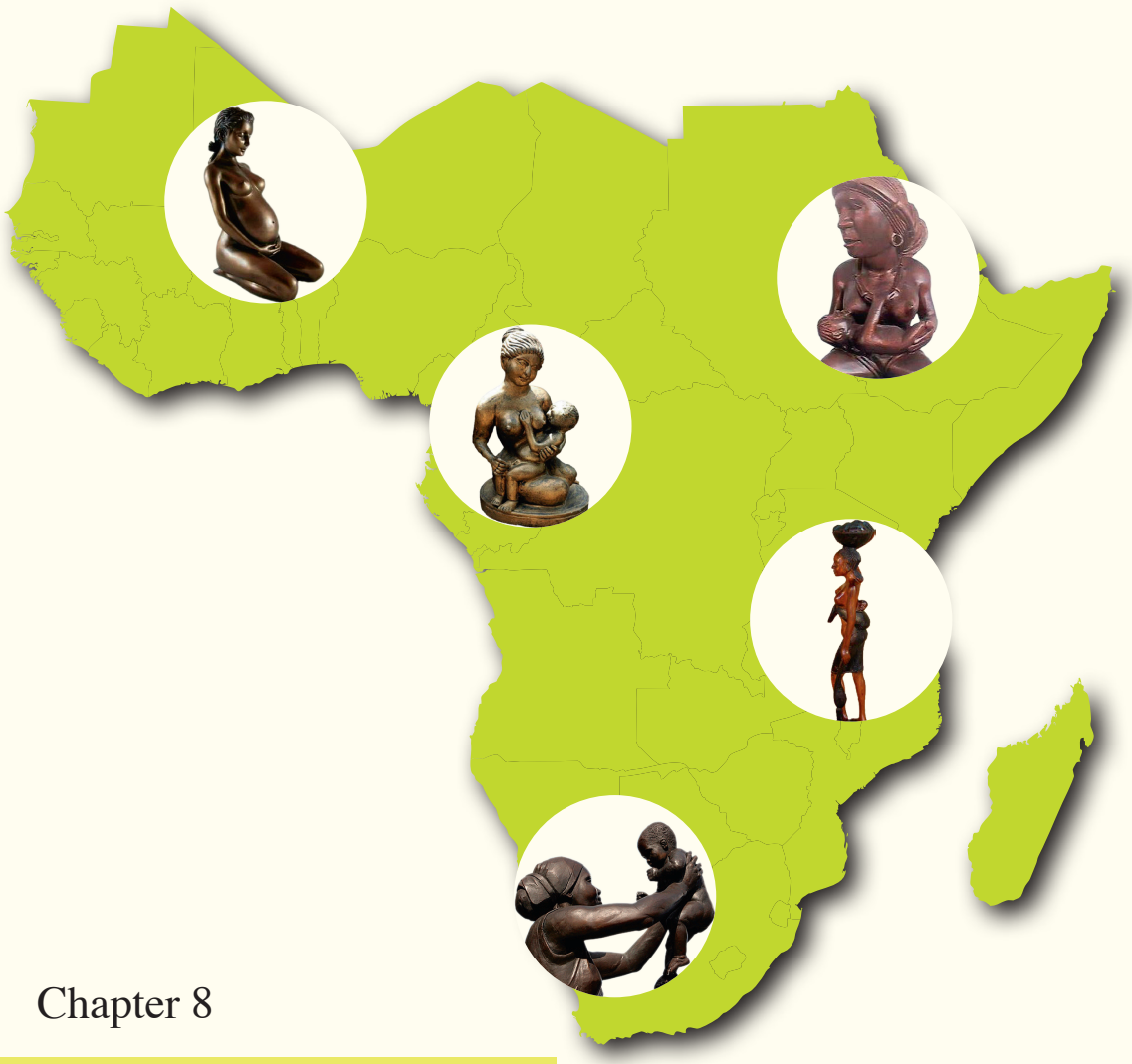
Part 3

Improving healthcare quality through risk-based management



Chapter 8

Predicting stillbirth in a low resource setting

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Submitted

Abstract

Objective

Stillbirth is a major contributor to perinatal mortality and is particularly common in low- and middle-income countries, where annually about three million stillbirths occur in the third trimester. This study aims to develop a prediction model for early detection of pregnancies with a high risk of stillbirth.

Design

Retrospective cohort.

Setting

Federal Medical Centre Bida, a tertiary level of care in Nigeria.

Subjects

6,573 pregnant women that delivered at the center from January 2010 to December 2013.

Statistical analysis

Descriptive statistics were performed and missing data imputed. Multivariable logistic regression was applied to examine the associations between selected candidate predictors and stillbirth. Discrimination and calibration were used to assess the model's performance. The prediction model was validated internally and a shrinkage factor was applied to correct for over-optimism.

Results

We developed a prediction model for stillbirth that comprised maternal comorbidity, place of residence, maternal occupation, parity, bleeding in pregnancy, and fetal presentation. As a secondary analysis we extended the model by including fetal growth rate as a predictor, to examine how beneficial ultrasound parameters would be for the predictive performance of the model. After internal validation, both calibration and discriminative performance of both the basic and extended model were excellent (i.e. C-statistic basic model = 0.80 (95%CI 0.78 – 0.83) and extended model = 0.82 (95%CI 0.80 – 0.83)).

Conclusion

We developed a simple but informative prediction model for early detection of pregnancies with a high risk of stillbirth for early intervention in a low resource setting. Future research should focus on external validation of the performance of this promising model.

Introduction

Stillbirth is a major but silent contributor to perinatal mortality,(1) and about 3 million third-trimester stillbirths(2, 3) occur yearly, mainly in low and middle income countries (LMIC) (98%).(4) Despite several calls for action to reduce the rate of stillbirth,(1, 4-7) stillbirths are yet to be addressed in the Millennium Development Goals, Global Burden of Disease metric,(8, 9) and Sustainable Development Goals.(10) Given that neither vital registration nor national stillbirth registers are adequately provided in low- and middle-income countries,(2, 11) together with the frequent omission from records of stillbirths that occur after twenty-two and before 28 weeks of gestation,(12) the estimated rate of stillbirth has been underestimated. Studies have examined the associations between stillbirths and clinical(13-18) and non-clinical characteristics(19-21) of pregnant women but the knowledge generated is yet to have any positive impact on intrauterine survival in LMIC.(22) This indicates limited application of research findings to clinical settings, notably in low resource settings, due to the inability of healthcare providers to combine these multiple predictors of stillbirth accurately to identify pregnancies with a high risk of stillbirth for early interventions.(5, 6)

It is therefore important to develop an easy to apply clinical decision making tool for early detection of pregnancies with a high risk of stillbirth as recommended by experts in maternal and child health.(11) To date, only few attempts have been made to develop a decision making tool for early detection of pregnancies with a high risk of stillbirth but these models cannot be applied to low-resource settings. For example a prediction model for both stillbirth and neonatal death was developed in the United Kingdom(23) and subsequently validated in the United Kingdom and the Netherlands.(24, 25) This model predicts a different outcome (stillbirth and neonatal death in very preterm babies) and availability of routine data to validate it will be a great challenge in low-resource settings. Likewise, the prediction model developed by Akolekar et al.(26) contains some parameters such as Maternal Serum Pregnancy-Associated Plasma Protein-A and Reversed A-Wave in Ductus Venosus, that are not routinely assessed in low resource settings.(26) In this study we aim to develop a prediction model to be applied in the second trimester of a pregnancy to identify pregnancies with a high risk of stillbirth using routine clinical and non-clinical profiles of pregnant women that received care at a tertiary hospital in a low resource setting.

Methods

Study population

A retrospective cohort of 6,573 pregnant women that delivered at Federal Medical Centre Bida, a tertiary hospital in Niger state, Nigeria, from January 2010 to December 2013 was utilized to

develop a prediction model for stillbirth. Only those that delivered at the hospital after 20 completed weeks of gestation and gave birth to babies with no live-threatening congenital malformation were recruited.

Data collection

Medical records (paper format) of all the included patients were retrieved from the Health Record department of Federal Medical Center Bida. Information was collected on maternal age, parity (number of previous pregnancy carried beyond viability i.e. up to 28 weeks gestational age), maternal education (educated - whether the woman can read and write), maternal occupation, maternal ethnicity, place of residence, previous fetal loss (number of previous pregnancy losses), bleeding in pregnancy (whether the woman has any complaint of vaginal bleeding during the index pregnancy), maternal height, number of previous caesarean section, maternal weight, comorbidity (number of the following medical conditions co-existing with the pregnancy that was diagnosed by a physician: pre-eclampsia, diabetes, sickle cell disease, renal disease, hypertension, thyroid disease and pelvic inflammatory disease), gestational age at birth, multiple gestation, sex, birth weight, fetal presentation (part of the fetus closest the pelvic inlet, was categorized as cephalic, breech, and others), fetal growth rate (birth weight divided by gestational age at birth) and delivery outcome (dead or alive) by the use of data extraction form in an anonymous format.

Outcome

The outcome of the study was stillbirth, defined as fetal death that occurred after 20 completed weeks of gestation.

Candidate predictors

For prediction modelling, the following candidate predictors were considered: maternal age, parity, maternal education, ethnicity, place of residence, maternal occupation, previous fetal loss, bleeding in pregnancy, maternal height, maternal weight, number of comorbid conditions, multiple gestation, number of previous fetal loss, fetal presentation, number of previous caesarean section, and growth rate. All candidate predictors were selected based on availability, clinical experience and medical literature.

Sample size calculation

We expected 2,000 deliveries per year and the incidence of stillbirth was assumed to be 4%,(27, 28). Thus, 320 cases of stillbirths were expected to have occurred among 8,000 pregnant women that delivered at the hospital from 2010 to 2013. We planned to recruit all the 8,000 pregnant women that delivered at the hospital retrospectively. Given that at least 10 events to a potential predictor will be adequate to build a prediction model,(29) we expected to have a sufficient number of events to build a robust prediction model.

Data analysis

Descriptive statistics – Data was inspected and descriptive analyses were performed using the complete dataset. Categorical data were described in terms of numbers and percentages while numerical data were expressed as means and standard deviations; the percentage of missing data in each potential predictor was determined.

Missing data - Multiple imputation technique using fully conditional specification was applied to impute missing data.(30, 31)

Prognostic model – All potential predictors were entered into a multivariable logistic regression model and significant predictors were identified using stepwise backward selection with the Akaike Information Criterion (AIC) stopping rule. Predictors that were consistently retained in the model were selected and entered into a multivariable logistic regression. The best model was identified based on AIC and the results from each imputed dataset were pooled using Rubin's rule.(32) Eventually, a prediction model for stillbirth was developed which we called the basic model. Subsequently, the basic model was extended with the variable fetal growth rate to become the extended model. The extended model was developed for those patients that have information on obstetric ultrasound, a procedure that is not routinely done in low resource settings.

Performance of the model – The predictive performance of the final models was assessed by evaluating calibration and discrimination. Calibration determines the level of agreement between the observed events and model's prediction and was presented by the calibration plot.(33) Discrimination examines how well the model can differentiate between participants with or without event and was expressed as C-statistic (which is equivalent to the area under the receiver operator curve).(34)

Internal validation – A bootstrap re-sampling technique was applied to the whole data to generate 200 testing datasets. The original models were re-fitted in the testing datasets and their shrinkage factors were estimated.

Model shrinkage – The shrinkage factor was used to adjust for over-optimism in each of the original models and the adjusted regression coefficients were calculated. The predictive performance of the final models was then re-assessed. All analyses were performed in R statistical software package.(35)

Ethical clearance

Ethical approval to conduct this research was obtained from the Ethical Review Committee of Federal Medical Centre Bida, Nigeria. Informed consent was obtained from the head of Obstetrics and Gynaecology department before the study commenced.

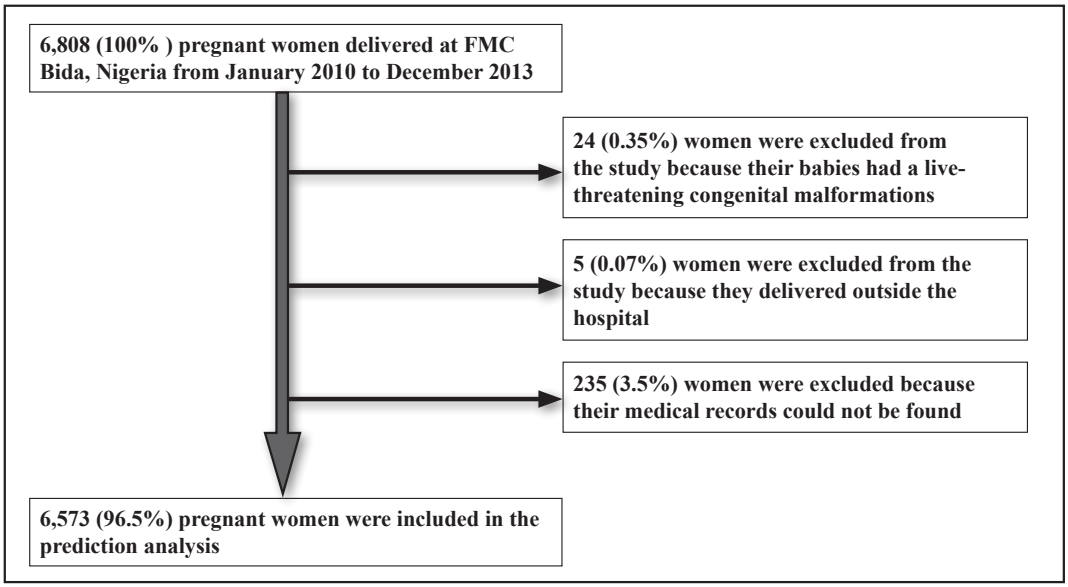

Figure 1. Follow-up of study participants

Results

Patient characteristics – Of 6,808 pregnant women that were recorded to have given birth in the delivery register; 6,573 (96.5%) of them were recruited to this study based on the inclusion criteria as shown in figure 1. A total of 6,956 newborns were delivered, 443 of them were lifeless at birth meaning that six in 100 newborns delivered at this center were lifeless at birth. Table 1 shows the descriptive characteristics of the study population and percentage of missing data in each characteristic of the patients. The mean age of women that delivered at the center was 27.2 years with an average parity of two. About two-thirds of the women had at least primary education; half of them were unemployed. The Nupe ethic group accounted for 72% of the women and they dwelled mainly in the urban areas (89%). Almost 90% of the babies delivered were singleton fetuses in cephalic presentation and 51% were male. The average weight at birth was 3kg and the mean gestational age at birth was 39 weeks. Average percentage of missing data per potential predictor was 11%.

Table 1. General characteristics of the study population

Characteristics	Complete data	Complete data		Missing data
		Stillbirth		
		No(n=6,513; 93.6%)	Yes(n=443; 6.4%)	
	m (sd) n [%]	m (sd) n [%]	m (sd) n [%]	[%]
Maternal age (years)	27.2 (5.1)	27.2 (5.0)	27.7 (5.2)	0.5
Maternal height (centimeters)	156.7 (7.2)	156.8 (7.1)	155.7 (8.1)	32.1
Maternal weight (grams)	67.0 (14.2)	67.0 (14.2)	67.4 (15.4)	30.3
Parity	2.0 (2.0)	1.9 (1.9)	2.8 (2.4)	1.6
Number of previous fetal loss	0.4 (0.8)	0.4 (0.7)	0.5 (1.2)	1.8
Number of previous caesarean section	0.8 (0.3)	0.8 (0.3)	0.9 (0.3)	9.0
Maternal comorbidity	0.2 (0.5)	0.2 (0.4)	0.4 (0.6)	1.5
Birth weight (grams)	3030.7 (596.0)	3058.6 (558.2)	2602.8 (912.4)	4.1
Gestational age at birth (days)	272.4 (18.3)	273.5 (16.7)	248.2 (31.1)	30.8
Maternal education (Educated)	3,284 [63.8]	3,171 [96.6]	113 [3.4]	26.0
Maternal education (Not educated)	1,866 [36.2]	1,747 [96.6]	119 [6.4]	
Sex of the fetus (Male)	3,506 [51.4]	3,287 [93.6]	219 [6.3]	2.0
Sex of the fetus (Female)	3,310 [48.6]	3,113 [94.0]	197 [6.0]	
Bleeding in pregnancy (Yes)	341 [5.1]	220 [64.5]	121 [35.5]	3.0
Bleeding in pregnancy (No)	6,406 [94.9]	6,107 [95.3]	299 [4.8]	
Maternal occupation				16.2
Not employed	2,894 [49.6]	2,650 [91.6]	244 [8.4]	
Self-employed	1,969 [33.8]	1,884 [95.7]	85 [4.3]	
Private/public employee	968 [16.7]	930 [96.1]	38 [3.9]	
Ethnicity				7.7
Nupe	4,611 [71.9]	4,297 [93.2]	314 [6.8]	
Hausa / Fulani	246 [3.8]	220 [89.4]	26 [10.6]	
Yoruba	790 [12.3]	758 [95.9]	32 [4.1]	
Igbo	395 [6.2]	378 [95.7]	17 [4.3]	
Gwari	19 [0.3]	17 [89.5]	2 [10.5]	
Others	356 [5.6]	342 [96.1]	14 [3.9]	
Place of residence (Urban)	5,707 [89.1]	5,449 [95.5]	258 [4.5]	7.9
Place of residence (Rural)	700 [10.9]	552 [78.9]	148 [21.1]	
Multiple gestation				<0.01
Singleton	6,201 [89.2]	5,813 [93.7]	388 [6.3]	
Twins	719 [10.3]	665 [92.5]	54 [7.5]	
Triplets	35 [0.5]	34 [97.1]	1 [2.86]	
Fetal presentation				<0.01
Cephalic	6,506 [93.7]	6,159 [94.7]	347 [5.3]	
Breech	334[4.8]	280 [83.8]	54 [16.2]	
Others	100[1.4]	62 [62.0]	38 [38.0]	

m (sd) mean (standard deviation); n [%] number [percentage]

Multivariable prediction model – The results of the multivariable prediction model for stillbirth (i.e. the basic model) are shown in table 2. The final model comprised maternal comorbidity, place of

residence, maternal occupation, parity, bleeding in pregnancy, and fetal presentation as independent predictors of stillbirth. For every morbid condition co-existing with pregnancy the likelihood of stillbirth increased. Being an unemployed, rural-dwelling woman with a positive history of bleeding in pregnancy increased risk of stillbirth. As parity increased risk of stillbirth increased. Pregnancies in cephalic presentation lowered the risk of stillbirth. Subsequently, the basic model was extended by the variable fetal growth rate and the results of multivariable prediction model (i.e. the extended model) are shown in table 3. All predictors in the extended model showed similar associations as observed in the basic model. For fetal growth rate, the likelihood of stillbirth decreased as growth rate increased.

Table 2. Multivariable prediction model for stillbirth (Basic model)

Predictors	***Unadjusted* β coef.**	**Standard error**	**P-value**	**Adjusted β coef.**
Maternal comorbidity	0.71	0.097	<0.001	0.71
Place of residence (rural)	1.31	0.129	<0.001	1.30
Maternal occupation				
Self employed	-0.30	0.144	0.035	-0.30
Employee	-0.38	0.182	0.037	-0.38
Maternal parity	0.08	0.024	0.001	0.08
Bleeding (yes)	2.18	0.139	<0.001	2.16
Fetal presentation				
Breech	0.96	0.182	<0.001	0.96
Others	2.12	0.240	<0.001	2.06

Unadjusted β coef. denotes β coefficient before penalization; Adjusted β coef. denotes β coefficient after penalization.
C-statistic before and after penalization 0.80 (95%CI 0.78 – 0.83)

Risk of stillbirth = 1 / 1 + exp(-(-3.6486 + 0.7077*(comorbidity) + 1.3047*(rural) – 0.3022*(self-employed) – 0.3788*(employee) +0.0797*(parity) + 2.1579*(bleeding in pregnancy) + 0.9616*(breech presentation) + 2.0588*(other presentations))

For example the risk of a para-7, unemployed, hypertensive, diabetic pregnant woman in compound presentation with a positive history of vaginal bleeding in pregnancy, dwelling in a rural area is:

Risk of stillbirth = 1 / 1 + exp(-(-3.6486 + 0.7077*(2) + 1.3047(1) – 0.3022(1) – 0.3788(0) +0.0797(7) + 2.1579(1) + 0.9616(0) + 2.0588(1))
= 1/1 + exp(-3.5439)
Risk of stillbirth = 0.97

Table 3. Extended multivariable prediction model for stillbirth (Extended model)

Predictors	Unadjusted β coef.	Standard error	P-value	Adjusted β coef.
Maternal comorbidity	0.60	0.100	<0.001	0.60
Place of residence (rural)	1.27	0.129	<0.001	1.26
Maternal occupation				
Self employed	-0.27	0.143	0.07	-0.26
Employee	-0.33	0.183	0.07	-0.33
Maternal parity	0.10	0.024	<0.001	0.10
Bleeding (yes)	2.04	0.142	<0.001	2.01
Fetal presentation				
Breech	0.83	0.181	<0.001	0.83
Others	2.15	0.241	<0.001	2.07
Growth rate	-0.18	0.026	<0.001	-0.18

Unadjusted β coef. denotes β coefficient before penalization; Adjusted β coef. denotes β coefficient after penalization
C-statistic before and after penalization 0.82 (95%CI 0.80 – 0.85)

Risk of stillbirth = 1 / 1 + exp(-(-1.7035 + 0.5965*(comorbidity) + 1.2603*(rural) – 0.2647*(self-employed) – 0.3265*(employee) +0.0959*(parity) + 2.0149*(bleeding in pregnancy) + 0.8342*(breech presentation) + 2.0677*(other presentations) – 0.1810*(fetal growth rate)

For example the risk of a para-five, unemployed, hypertensive pregnant woman in breech presentation with a positive history of vaginal bleeding in pregnancy, dwelling in a rural area and the estimated fetal weight by obstetric scan at 22 weeks was 650 grams.

Risk of stillbirth = 1 / 1 + exp(-(-1.7035 + 0.5965(1) + 1.2603(1) – 0.2647(1) – 0.3265(0) +0.0959(5) + 2.0149(1) + 0.8342(1) + 2.0677(0) – 0.1810(650/22*7))
= 1/1 + exp(-2.4532)
Risk of stillbirth = 0.92

Performance of the model – The discriminative performance of the final basic model was very good with a C-statistic of 0.80 (95%CI 0.78 – 0.83). The extended model (i.e. with obstetric ultrasound variable growth rate added) showed a slightly improved discriminative performance of 0.82 (95%CI 0.80 – 0.85). Calibration for both models was good (figure 2 and 3).

Internal validation – Both models were penalized but the discriminative performance of both model remained unchanged while their calibration improved (figure 2 and 3).

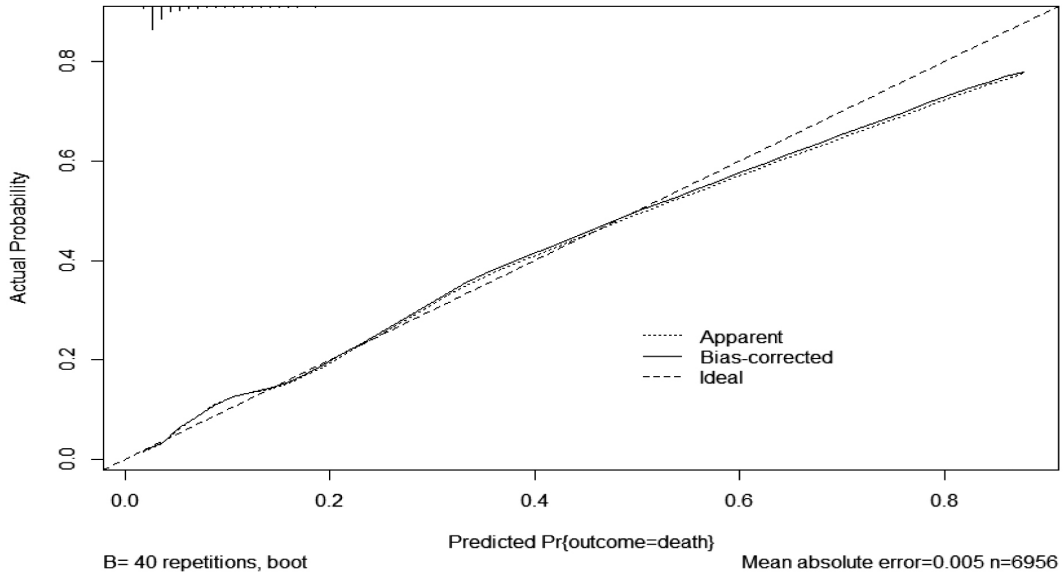

Figure 2. Calibration plot for the basic model

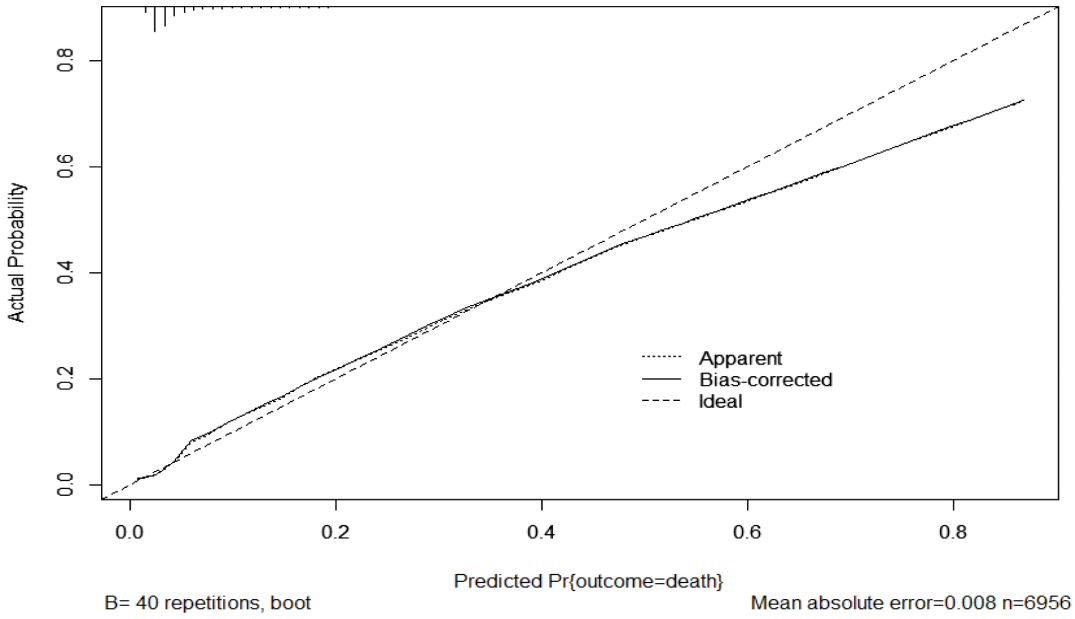

Figure 3. Calibration plot for the extended model

Discussion

In this study we developed an easy to use clinical prediction model to identify pregnancies with a high risk of stillbirth for timely interventions. We also extended this basic model with the variable fetal growth rate (fetal weight divided by gestational age) to see whether this not routinely measured variable (obstetric ultrasound) would improve predictions. This study was reported based on the TRIPOD guidelines(36) and to the best of our knowledge, these are the first prediction models for stillbirth that can easily be applied in the second trimester of pregnancies in low resource settings where 98% of third-trimester stillbirths occur.(4) This study reaffirms stillbirth as an important public health issue; six in every 100 newborns delivered at the center were lifeless at birth, justifying the clinical relevance of an easy to use prediction model to detect high risk pregnancies in an early stage (i.e. the 2nd trimester). The basic prediction model comprised six easy-to-measure, readily available, inexpensive parameters of pregnant women, promoting its easy use during antenatal visits in low-resource settings. A previous model(26) included more predictors, but also used Pregnancy-Associated Plasma Protein-A and Reversed Flow of A-wave in Ductus Venosus that are not routinely measured in low resource settings. Age restriction was not included in the eligibility criteria so as to broaden its application among pregnant women. A large cohort was used to develop the model to increase the power of the study and lower the possibility of overfitting. The predictive performance of the model in terms of discrimination and calibration was very good also after internal validation.

As a secondary analysis we generated fetal growth rate using birth weight and gestational age at birth. This proxy predictor was included in the extended model (table 3) instead of using ultrasound estimated fetal weight and gestational age, because up to 60% of the women did not undergo obstetric ultrasound investigation during antenatal care due to various reasons. To acknowledge the importance of monitoring intrauterine growth retardation in stillbirth, fetal growth rate was included in the extended multivariable model. We preferred to generate fetal growth rate from birth weight and gestational weight at birth instead of using obstetric ultrasound information because based on our knowledge of these data some of the reasons why obstetric ultrasound was not done might be related to the outcome e.g. antenatal visit. Missing data was observed in some of our predictors and multiple imputation was applied to address it instead of performing a complete case analysis which may give biased results. Studies have shown repeatedly that multiple imputation reduces the possibility of bias in the estimates compared to complete case analysis.(37-39) It is important to emphasize that this prediction model has not undergone external validation, and this is planned to be done in a future study; but its predictive performance remained unchanged after internal validation.

Experts have expressed the need to develop a prediction model for stillbirth because of its clinical importance.(11) It allows for early detection of pregnancies with a high risk of stillbirth for timely allocation of targeted interventions and to benefit from closer monitoring throughout the pregnancy. Prioritization of care allocation is particularly relevant in low resource settings. Interventions to improve neonatal, intrauterine and maternal survival have been identified and integrated as a continuum of care because they are related;(5, 6) thus, it is expected that this prediction model may not only improve prevention of stillbirth but may also have a positive collateral effect on maternal and neonatal survival. It is important for future studies to conduct an external validation of this prediction model at all levels of care using prospectively collected data.

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Authors contributions

Gbenga A. Kayode (GAK), Diederick E. Grobbee (DEG), and Kerstin Klipstein-Grobusch (KKG) designed the study. GAK carried out data collection and literature review. Joris A.H. de Groot (JAHG) and GAK performed data analysis; GAK drafted the first version of the manuscript. All authors (GAK, KKG, DEG, JAHG, Taiwo Ibrahim Adeleke (AIT), Evelyn Ansah (EA), and Mary Amoakoh-Coleman (MAC)) reviewed and approved the final version of the manuscript.

Disclosures

The authors declare that they have no competing interests

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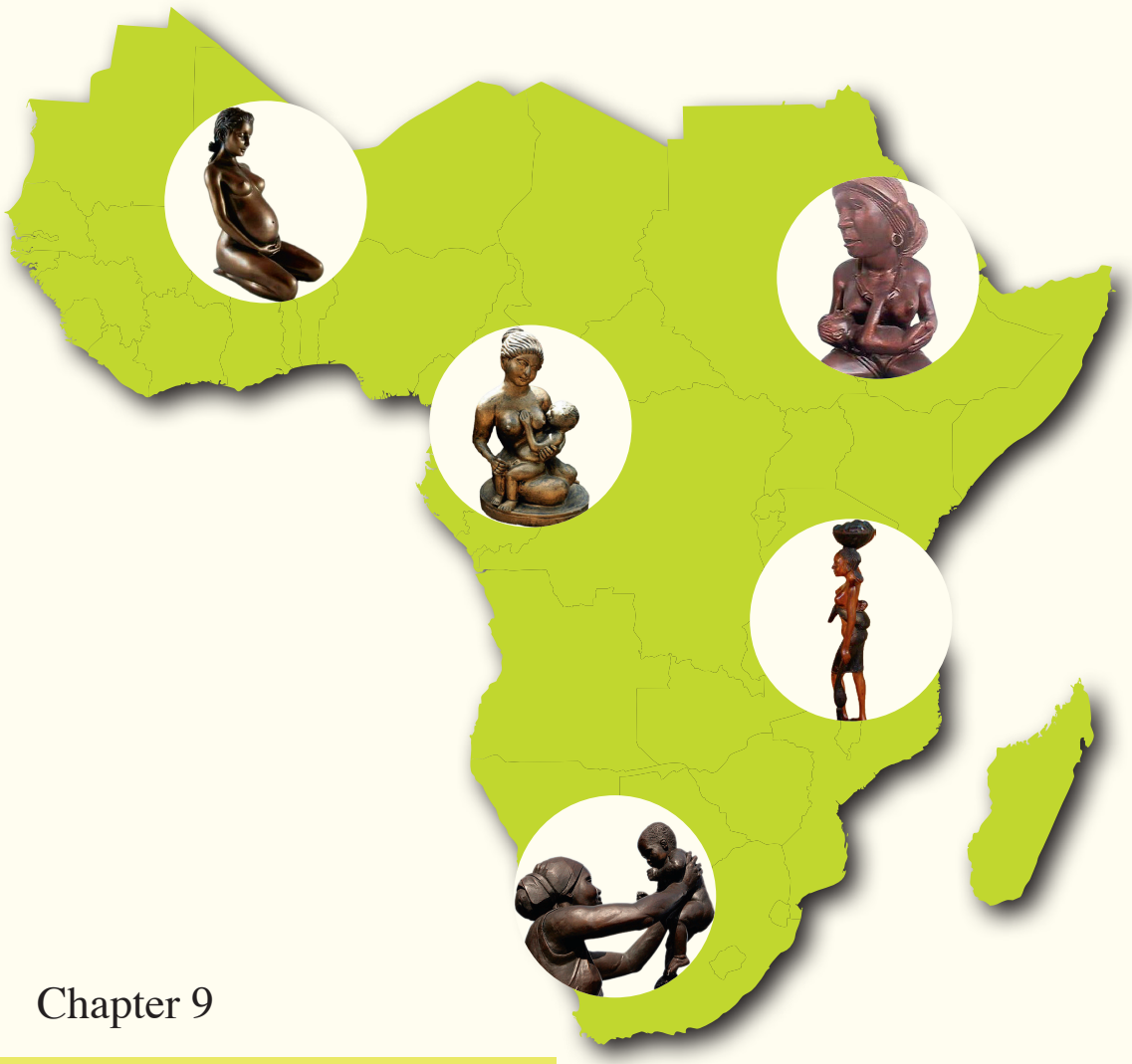

Chapter 9

Discussion

Can we end avoidable neonatal death?

The first 28 days of life are regarded as the most difficult phase in life particularly in sub-Saharan Africa (SSA) that has the highest rate and the least reduction in neonatal mortality.(1-4) Multiple risk factors in the SSA context have created a tense condition for many newborns to survive even before birth. Considering the wide disparity in neonatal survival between low- and high-income countries,(5) it is justifiable to infer that pre-existing factors in SSA have increased risk of dying in early life even before birth. As up to three-quarters of neonatal deaths are preventable,(6, 7) achieving a substantial reduction in neonatal mortality remains a main priority to actualize the Millennium Development Goal 4 (MDG 4 – aims to reduce under-five mortality by two-thirds from 1999 to 2015). As the deadline for the MDGs is fast approaching and MDG 4 has not been achieved in many countries, particularly in Sub-Saharan Africa, it has been incorporated into the newly formulated Sustainable Development Goals (SDG) as SDG 3 sub-section 2 (SDG 3.2) aiming to end preventable neonatal and under-five mortality by 2030.(3)

Given the slow progress to date, a critical question to ask is whether the persistently high occurrence of avoidable neonatal death in SSA can be ended by 2030 as targeted by SDG 3.2. Based on findings emanating from this thesis and previous evidence, ending avoidable neonatal deaths in SSA could be achieved. Experience from high-income countries shows that a substantial decline in neonatal mortality before the advent of high-tech equipment could be realized.(8, 9) Likewise several low-income and middle-income countries in Asia (Vietnam), Latin America (Mexico, El Salvador), Eastern and Central Europe (Belarus, Estonia, Poland) and also in SSA, such as Mauritius and the Seychelles have demonstrated that avoidable neonatal deaths can be reduced substantially,(5) and cost-effective neonatal-specific interventions to achieve such a reduction have been identified.(6, 7)

Thus, if avoidable neonatal death can be ended, why so far is SSA failing to actualize it? The reasons are two-fold. Firstly, before the adoption of the MDGs global attention was mainly targeting efforts to address pneumonia, malaria, and vaccination.(10) Subsequently, after the adoption of the MDGs in 1999, neonatal death, not being explicitly named in MDG 4, was neglected for five years.(11) Since then, neonatal mortality has received some attention following repeated calls by expert in neonatal health and observations that the proportion of neonatal deaths attributed to infant and under-five mortality has increased.(5, 12) Notable neonatal-specific interventions implemented were Kangaroo Mother Care,(13) expansion of Safe Motherhood Program and Integrated Management of Childhood Illness (IMCI) to include neonatal health,(11, 14) and Save Newborn Lives/Save the Children,(15) to name a few of the most important initiatives.

Despite the implementation of such neonatal-specific interventions the decline in neonatal mortality

in sub-Saharan Africa has been observed to remain far below the targeted annual decline rate of 7%.(16) In Ghana, for example the annual decline in neonatal mortality in the last two decades was observed to be 0.6%.(12) Several factors have been identified to explain why the implemented programs were unable to achieve a substantial reduction in neonatal mortality. For Ghana, our findings show that implemented health policy and intervention programs to reduce neonatal mortality seem not to have been properly formulated. Implementations were hampered by insufficient erratic funding, inadequate medical products and equipment, low levels of human resources complicated by continuing brain drain, insufficient community mobilization and engagement and inadequate healthcare quality due to non-adherence to treatment guidelines and high workload for health care professionals.(12); an assessment supported by findings from a multinational study involving African and Asian countries.(17) In the midst of these challenges few SSA countries have been able to ensure low neonatal deaths below two-digits per 1000 live births(18), indicating by best practice example that avoidable neonatal death could be ended in SSA.

Several studies have identified hospital- and community-based intervention packages to reduce neonatal mortality, which is commendable. However, these intervention packages need to be complemented to improve their effectiveness and sustainability; thus we propose a comprehensive three-component intervention package that entails hospital-, community- and health system-based interventions to address neonatal mortality:

Firstly, a comprehensive hospital-based intervention package covering preconception, antenatal, intrapartum, and postnatal periods has been shown to reduce neonatal death by improving the quality of healthcare services to deliver both effective management and prevention of major causes of neonatal death.(6, 7) Considering limited health human resources and high healthcare provider workload in SSA, prioritizing these scare health resources by paying more attention to high-risk patients is of major importance. Thus, implementation of risk-based management in pregnancy using clinical decision making tools to identify high-risk pregnancies for timely intervention will improvement in the quality of health care services.(19) Such a clinical decision making tool to identify high-risk pregnancies in low resource settings where none exists has been developed in this thesis.(19)

Secondly, a comprehensive community-based intervention package covering preconception to postnatal life has been developed(6, 7) with the primary aims (i) to improve acceptability and uptake of healthcare during preconception, antenatal, intrapartum, and postnatal phase, (ii) to engage and mobilize the population to adopt good health practices, and (iii) to improve the early detection of illnesses, community-based management of illness and prompt referral of patients. To

further complement the delivery of this package, community-based interventions need to target high-risk families by using simple population-based risk models to identify families that are not likely to utilize antenatal, delivery and postnatal healthcare for timely interventions. This will then improve effectiveness of interventions and prevent the recurrence of previous observations that showed that implemented maternal and child healthcare interventions were not reaching the deprived families.(20, 21) Beyond targeting vulnerable families, a community-based intervention package should be expanded to accommodate interventions that will target deprived-populations rather than targeting families. Such interventions (population-based interventions) are expected to have a greater impact because a large population of deprived-people will be targeted. Evidence emanating from this thesis shows that implementing population-based interventions such as poverty alleviation programs, improved safe water coverage, universal basic education, infrastructural development in rural areas and increases in maternal health insurance coverage can improve survival in early life.(18, 22-24)

Thirdly, health system strengthening is a key factor for proper formulation, scale-up and monitoring of such comprehensive intervention packages. Apart from improving health human resource capacity, healthcare financing and primary healthcare coverage including prevention of mother-to-child transmission (PMTCT), genuine governmental commitment to ensure transparency and accountability, effectiveness, political stability, adherence to the rule of law, high regulatory quality and fight against corruption will be needed.(18) Without ensuring good quality in healthcare governance, scarce healthcare resources will not be used judiciously as shown by the results of a diagnostic public expenditure tracking survey conducted in Ghana, Uganda and Tanzania that demonstrated extensive leakages of public funds in these three SSA countries.(25)

In conclusion, though neonatal mortality in SSA remained more or less stagnant in the last two decades due to improper implementation of intervention programs, attaining SDG 3.2 in SSA seems to be achievable through thorough implementation of a comprehensive neonatal intervention package that entrains hospital-, community- and health system-based intervention.

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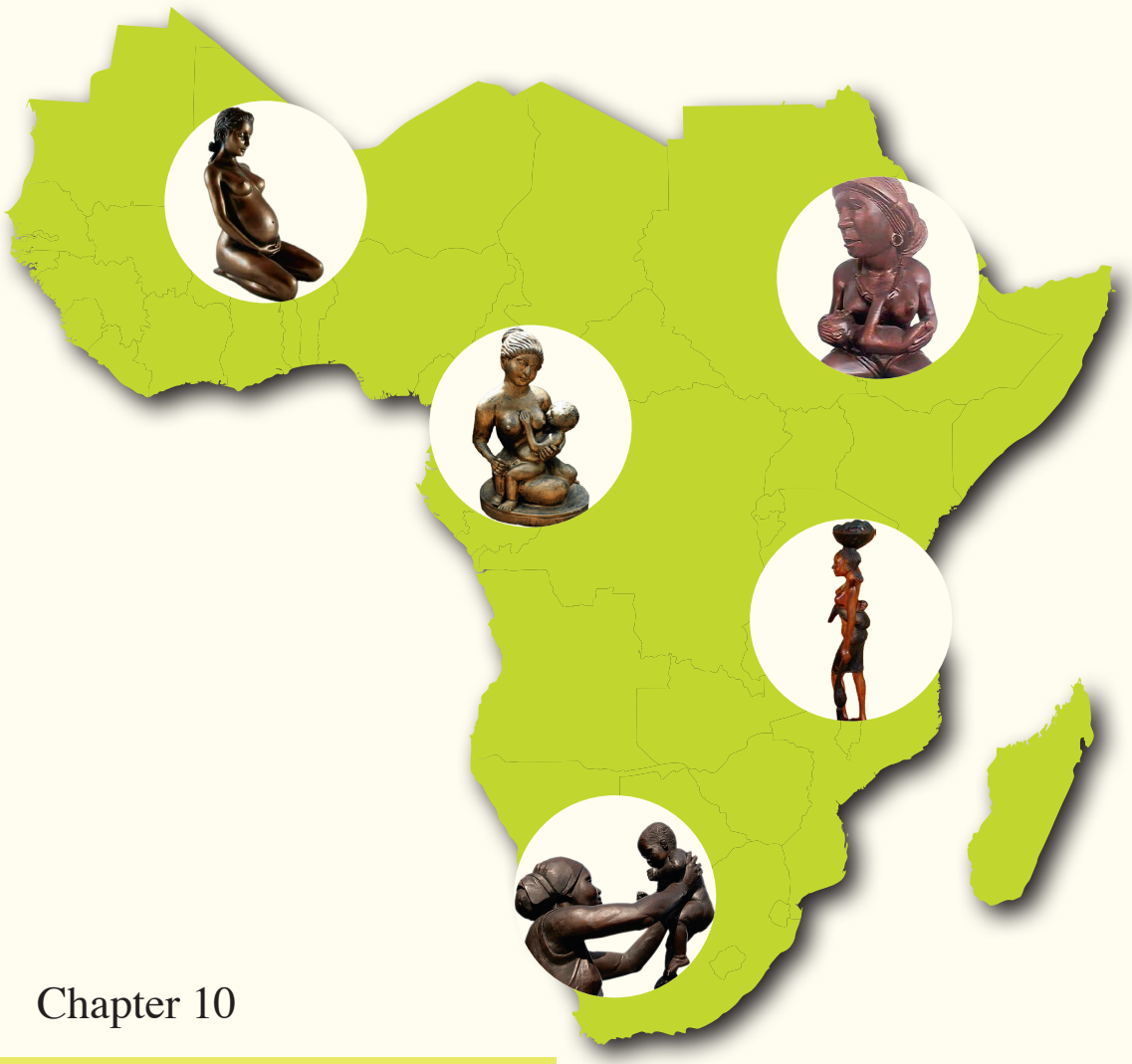

Chapter 10

Summary

Chapter 1 introduces neonatal mortality as a global health issue of important relevance in low- and middle-income countries (LMICs) where high occurrence of neonatal death continues unabated. After twenty-five years of pursuing Millennium Development Goal 4 that aimed to reduce under-five mortality by two-thirds by 2015, it is obvious that survival in early life cannot be improved without paying attention to neonatal death. Following the failure of MDG 4 to achieve its aim in many LMICs particularly in Sub-Saharan Africa (SSA), MDG 4 has been incorporated into the newly formulated Sustainable Development Goal (SDG) as the second objective of SDG 3 that aims to end preventable neonatal death by 2030. For SDG 3 to actualize this goal, it is important to examine why MDG 4 failed to realize its aim largely in SSA and to identify additional interventions to achieve a substantial reduction in neonatal mortality. Thus, it is the aim of this thesis to contribute knowledge directed at prevention of neonatal mortality in SSA.

Chapter 2 describes the validity of routine neonatal healthcare care data being used to monitor neonatal mortality and examine the impact of implemented intervention programs. Seven districts in the Greater Accra Region were randomly sampled and in each district two health facilities were recruited for validation. Seven pre-specified neonatal health indicators were considered for validation: antenatal registrants, deliveries, total number of babies delivered, live birth, stillbirth, low birth weight and neonatal death. Data were extracted on these health indicators from the primary data sources recorded from January to March 2012. The data extracted from the primary data sources were compared to the aggregated data from the facility and District Health Information Management System – 2 (DHIMS–2) database in order to estimate the accuracy and completeness of the DHIMS-2 database. The study demonstrated that the percentage of missing data in the DHIMS-2 database was negligible while its accuracy was closed to the acceptable range for high quality data supporting the use of neonatal health information data for monitoring evaluation, research and decision making.

Chapter 3 describes trends in neonatal, infant and under-5 mortality and highlights the impacts and challenges of health policies and intervention programs implemented since the adoption of Millennium Development Goal 4 in Ghana. Implemented health policies and intervention programs were reviewed and a trend analysis was performed using Ghana Demographic and Health Survey data from 1988 to 2008. Over the two decades, the annual rate of decline in neonatal, infant and under-five mortality in Ghana was below the targeted rate, particularly in neonatal mortality. Consequently, the proportion of infant and under-5 mortality attributed to neonatal death increased. This could be attributed to health policies and intervention programs focusing more on under-five and infant mortality and implementation challenges of these policies on regional or national level. Improving existing interventions and implementation of sustainable evidence-based neonatal

specific interventions will assist to accelerate the attainment of SDG 3 aiming to end preventable neonatal death.

Chapter 4 identifies individual and community determinants associated with neonatal mortality based on analyses of the combined 2003 and 2008 Ghana Demographic and Health Survey data. The study showed both individual and community characteristics to be associated with neonatal mortality. Multiple-gestation, short birth spacing, and low birth weight reduced neonatal survival. Likewise infants that were not breastfed and those delivered by grand-multiparous women were less likely to survival in neonatal life. Adequate utilization of antenatal, delivery and postnatal health services increased neonatal survival. Dwelling in a neighbourhood with high socioeconomic deprivation was associated with increased neonatal mortality. Implementation of community-based interventions addressing basic education, poverty alleviation and infrastructural development and an increased focus on the continuum-of-care approach in healthcare service will improve neonatal survival.

Chapter 5 identifies population-based risk factor for low birth weight (LBW) by analysing combined data of the 2003 and 2008 Ghana Demographic and Health Survey. This study found that being a rural dweller, living in poverty-concentrated community, with a low coverage of safe water supply increased the risk of having a LBW infant and suggest that community-based intervention programs addressing poverty alleviation, provision of regular safe water supple and infrastuctural development of rural communities will likely reduce the occurrence of low birth weight and neonatal mortality.

Chapter 6 describes variation in neonatal mortality across 49 sub-Saharan African countries (SSA) and explains a substantial part of the observed variation using country-level characteristics. This ecological study used publicly available data from the World Health Organization, United States Agency for International Development and World Bank, showing a wide variation in neonatal mortality in SSA. A substantial part of this variation can be explained by differences in the quality of healthcare governance, prevalence of HIV and socioeconomic deprivation across SSA countries.

Chapter 7 evaluates the effect of maternal health insurance status on the utilization of antenatal, skilled delivery and postnatal care. Based on representative 2008 Ghana Demographic and Health Survey data, utilization of antenatal, skilled delivery and postnatal care services were observed to be increased among insured woman. These results provide strong support that health insurance coverage of pregnant women promotes the uptake of maternal, neonatal and child continuum of care service.

Chapter 8 describes the development of a prediction model for early detection of pregnancies with a high risk of stillbirth in a low resource setting. Information on 6,573 pregnant women that

delivered at Federal Medical Centre Bida, a tertiary level of care in Nigeria from January 2010 to December 2013 was analyzed. A prediction model for stillbirth that comprised maternal comorbidity, place of residence, maternal occupation, parity, bleeding in pregnancy, and fetal presentation was developed. For patients that underwent obstetrics ultrasound the basic prediction model was extended by including fetal growth rate as a predictor, to examine how beneficial ultrasound parameters would be for the predictive performance of the model. After internal validation, both calibration and discriminative performance of both the basic and extended model were excellent promoting the use of the prediction models for clinical practice.

Chapter 9 discusses how findings presented in this thesis could contribute towards improvement of existing interventions aiming to prevent neonatal death. To support the achievement of SDG 3, to end preventable neonatal death by 2030, we proposed implementation of a comprehensive three-component intervention package that will comprise hospital-, community-, and health system-based interventions. For the existing hospital-based intervention package to be more efficient, risk-based management of pregnancy should be implemented through the use of clinical decision-making tools to identify high-risk pregnancies for timely interventions. Further, community-based interventions need to target high-risk families by using population-based risk model to identify families that are not likely to utilize antenatal, delivery, and postnatal care for prompt interventions. Community-based intervention package should be expanded to accommodate population-based interventions (poverty eradication programs, universal basic education, safe water supply, and rural infrastructural development programs) that will achieve a greater impact because a large population of deprived-people will be involved. For proper formulation, scale-up and monitoring of these interventions, investments in health system strengthening, namely healthcare governance, health human resource, healthcare financing and primary healthcare coverage are indispensable.

Nederlandse samenvatting

Hoofdstuk 1 begint met de introductie van neonatale sterfte als wereldwijd gezondheidsprobleem. Met name in landen met een laag- en gemiddeld inkomen (LMICs) blijft zuigelingensterfte van groot belang, gezien de onverminderd hoge mortaliteitscijfers. Na vijfentwintig jaar waarin, aan de hand van Millenniumdoel 4 (MD 4), gestreefd werd naar tweederde vermindering van kindersterfte in 2015, is het duidelijk dat overlevingkansen op jonge leeftijd niet kunnen worden verbeterd zonder aandacht te besteden aan neonatale sterfte. Na het mislukken van MD 4 in veel LMICs, in het bijzonder Sub-Sahara Afrika (SSA), is MD 4 opgenomen in de recent geformuleerde Duurzame Ontwikkelingsdoelen (SDG). De tweede doelstelling van SDG 3 heeft als ambitie vermijdbare zuigelingensterfte te beëindigen in 2030. Om SDG 3 te verwezenlijken is het belangrijk om onderzoek te doen naar het falen van MDG 4 in grote delen van SSA, zodataanvullende maatregelen geïdentificeerd kunnen worden welke nodig zijn voor verminderen van sterfte in de neonatale periode. Dit proefschrift heeft als doel om een bijdrage te leveren aan de kennis op het gebied van preventie van zuigelingensterfte in SSA.

Hoofdstuk 2 beschrijft de validiteit voor het gebruik van gegevens uit routine neonatale medische zorg ter bewaking van neonatale sterfte, en onderzoekt de impact van de uitvoering van interventieprogramma's. Zeven districten in de Greater Accra Region werden willekeurig gekozen en in elk district werden twee medische voorzieningen gerekruteerd voor de uitvoering van de validatie. Zeven, vooraf gespecificeerde, indicatoren van neonatale gezondheid werden meegenomen in de validatie: prenatale registratie, bevallingen, het totale aantal geboren baby's, levende geboorte, doodgeboorte, laag geboortegewicht en neonatale sterfte. Gegevens omtrent de indicatoren werden verzameld uit primaire bronnen daterend van januari tot maart 2012. De geëxtraheerde data uit primaire databronnen werden vergeleken met de databank van het District Health Information Management System - 2 (DHIMS-2) voor beoordeling op op nauwkeurigheid en volledigheid. De studie toonde aan dat het percentage ontbrekende gegevens in de DHIMS-2 databank verwaarloosbaar was, terwijl de nauwkeurigheid dichtbij de aanvaardbare norm voor hoogwaardige gegevens lag. Dit ondersteunt het gebruik van neonatale gezondheidsgegevens voor het beoordelen van het gehele proces van evaluatie, onderzoek en besluitvorming

Hoofdstuk 3 beschrijft trends in sterftecijfers onder neonaten, baby’s en kinderen jonger dan vijf jaar. Het wijst op de gevolgen en uitdagingen van gezondheidsbeleid en interventieprogramma's die werden geïmplementeerd sinds de invoering van Millenniumdoel 4 in Ghana. Het gevoerde gezondheidsbeleid en de interventieprogramma's werden beoordeeld en een trendanalyse werd uitgevoerd met behulp van gegevens uit de Ghana Demographic and Health Survey van 1988 tot 2008. In de loop van de twee decennia viel de jaarlijkse daling in neonatale-, baby- en kindersterfte in Ghana onder de beoogde koers, met name in de neonatale sterfte. Als gevolg nam het aandeel

van neonatale sterfte in mortaliteit van zuigelingen en kinderen onder vijf jaar toe. Dit kan worden toegeschreven aan het gezondheidsbeleid en de interventieprogramma's, die zich voornamelijk richten op kindersterfte en de bijbehorende uitdagingen in de uitvoering van dit beleid op regionaal of nationaal niveau. Het verbeteren van bestaande interventies en implementatie van duurzame, evidence-basedinterventies gericht op neonaten zal de verwezenlijking van SDG 3 bevorderen.
Hoofdstuk 4 identificeert individuele- en collectieve determinanten van neonatale sterfte op basis van analyses van de gecombineerde 2003 en 2008 Ghana Demographic and Health Survey data. De studie toonde aan dat er associaties bestaan tussen zuigelingensterfte en zowel individuele- als collectieve determinanten. Meervoudige zwangerschap, korte periode tussen geboortes, en een laag geboortegewicht verminderen neonatale overleving. Eveneens hadden zuigelingen die geen borstvoeding kregen of van wie de moeder een grand-multipara was minder kans om te overleven in de neonatale periode. Voldoende gebruik van prenatale-, natale- en postnatale gezondheidszorg verhoogt neonatale overleving. Wonen in een buurt met een lagere sociaal-economische status werd daarentegen geassocieerd met een verhoogde neonatale sterfte. Neonatale uitkomsten zullen verbeteren als interventies gericht op de gemeenschap zich bezig houden met het aanpakken van basisonderwijs, armoedebestrijding, ontwikkeling van de infrastructuur en als er een grotere focus ligt op het continuüm van zorg.
Hoofdstuk 5 identificeert risicofactoren voor een laag geboortegewicht (LBW) onder de bevolking door het analyseren van gecombineerde gegevens van de 2003 en 2008 Ghana Demographic and Health Survey. Deze studie wees uit dat het risico op het krijgen van een kind met een LBW kind als men leeft op het platteland, in een armoede geconcentreerde gemeenschap of met een lage beschikbaarheid van veilig water. Dit suggereert dat community-based interventieprogramma's gericht op het aanpakken van armoedebestrijding, het verstrekken van veilig water en ontwikkeling van infrastructuur in rurale gemeenschappen het optreden van een laag geboortegewicht en neonatale sterfte waarschijnlijk zullen verminderen.
Hoofdstuk 6 beschrijft de variatie in neonatale sterfte in 49 landen gelegen in SSA en verklaart een groot deel van de waargenomen variatie aan de hand van verschillen op nationaal niveau. Deze ecologische studie gebruikte openbaar beschikbare gegevens van de Wereldgezondheidsorganisatie (WHO), het Amerikaanse Agentschap voor Internationale Ontwikkeling (USAID) en de Wereldbank, om een grote variatie in neonatale sterfte in SSA aan te tonen. Een substantieel deel van deze variatie kan worden verklaard door verschillen in de kwaliteit van de organisatie van de gezondheidszorg, de prevalentie van HIV en sociaal-economische achterstelling in SSA landen.
Hoofdstuk 7 evalueert het effect van het hebben van maternale ziektekostenverzekering op het gebruik van prenatale-, natale- en postnatale zorg. Data uit de Ghana Demographic and Health

Survey uit 2008 toont dat vrouwen met een ziektekostenverzekering meer gebruik maakten van prenatale-, natale -, en postnatale zorg. Deze resultaten leveren krachtig bewijs dat het hebben van een ziektekostenverzekering voor zwangere vrouwen bijdraagt aan het bieden van zorg voor moeders, pasgeborenen en kinderen.

Hoofdstuk 8 beschrijft de ontwikkeling van een prognostisch model voor de vroegtijdige opsporing van zwangerschappen met een verhoogd risico op doodgeboorte in een omgeving met beperkte middelen. Informatie van 6,573 zwangere vrouwen die bevielen tussen januari 2010 tot december 2013 in het Federaal Medisch Centrum Bida, een derdelijns ziekenhuis in Nigeria, werd geanalyseerd. Er werd een prognostisch model voor doodgeboorte ontwikkeld, waarin co-morbiditeit van de moeder, woonplaats, beroep van de moeder, pariteit, bloeding tijdens de zwangerschap, en foetale presentatie geïncludeerd werden. Voor patiënten die een echo ondergingen, werd het model uitgebreid door foetale groeisnelheid mee te nemen. Zodoende was het mogelijk om het nut van echo-metingen te onderzoeken als voorspellende factor voor doodgeboorte. Na interne validatie bleek dat zowel kalibratie en onderscheidend vermogen van beide modellen uitstekend waren. Dit stimuleert het verdere gebruik van de prognostische modellen in de klinische praktijk.

Hoofdstuk 9 bespreekt hoe de bevindingen in dit proefschrift kunnen bijdragen aan verbetering van bestaande interventies ter preventie van neonatale sterfte. Om SDG 3 te bereiken en vermijdbare neonatale sterfte in 2030 te beëindigen, wordt de implementatie van een drietal interventies voorgesteld op het gebied van ziekenhuis, gemeenschap en gezondheidssysteem. Om de bestaande ziekenhuisinterventies efficiënter te maken, moet het beleid in de zwangerschap zich richten op het maken van een risico-inschatting aan de hand van hulpmiddelen in de klinische besluitvorming, zodat hoog risico zwangerschappen kunnen worden geïdentificeerd voor tijdige interventies. De interventies in de gemeenschap zouden zich moeten richten op hoog risico families door gebruik te maken van een populatie-gebaseerd risicomodel dat gezinnen identificeert die geen gebruik maken van prenatale-, natale- en postnatale zorg. Het pakket van interventies gericht op de gemeenschap zouden moeten worden uitgebreid met populatie-gebaseerde interventies (armoedebestrijdingprogramma's, universeel basisonderwijs, veilig water en ontwikkeling van infrastructuur op het platteland). Deze interventies zullen een uitgebreide impact hebben, vanwege het bereik in een grote populatie van sociaal-economisch kwetsbaremensen. Voor de juiste uitwerking, schaalvergroting en monitoring van deze interventies zijn investeringen in de gezondheidszorg onmisbaar, voornamelijk op het gebied van organisatie van gezondheidszorg, human resources, financiering en de universele dekking van ziektekosten.

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Curriculum vitae

Gbenga Ayodele Kayode was born on October 14th, 1976 at Saint Leo's Hospital, Akure, Nigeria. He finished his medical training in 2005 at University of Ilorin, Ilorin, Nigeria. In 2009 he further his study at University of Birmingham, United Kingdom where he obtained Master of Public Health (MPH). He worked briefly at UKBiobank, United Kingdom as a Research Assistant before he commenced his doctoral training at University Medical Centre, Utrecht, Netherlands. From September 2011 till July 2015, Gbenga A. Kayode conducted his PhD research under the supervision of Prof. dr. D.E. Grobbee (Promotor), Dr. K. Klipstein-Grobusch and Dr. E. Ansah (Copromotoren). His research focused on how to identify individual- and population-based interventions to improve survival in early life in low resource settings and the studies were conducted in Ghana and Nigeria. He has special interest in applying epidemiological knowledge to resolve public health challenges especially in low resource settings.