CONTEXTUAL AND INDIVIDUAL FACTORS INFLUENCING CHILD HEALTH

CONTEXTUAL AND INDIVIDUAL LEVEL FACTORS INFLUENCING CHILD HEALTH IN LOW AND MIDDLE INCOME COUNTRIES

By

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ABSTRACT

This thesis examined contextual and individual-level determinants of child health in low and middle income countries, with specific focuses on slum residency, maternal use of cesarean section (CS) during delivery and malaria prevention campaigns. It also examined parental HIV preventive behaviors that could ultimately be associated with child health outcomes (although this was not studied in this thesis). The thesis is presented as four separate projects that examine the following: (1) associations of urban slum residency with infant mortality and child stunting in 45 countries and factors modifying these associations; (2) relations between individual-level CS and neonatal mortality in 46 countries and the moderating influence of country-level CS rates on these relations; (3) determinants of consistent condom use based on the perspectives of both husband and wife where at least one partner is HIV infected and resident in three sub-Saharan African countries with high HIV prevalence; and (4) evaluation of the associations between long-lasting insecticidal nets (LLIN) mass distribution campaigns led by different organizations (the World Bank, UNICEF, or Global Fund) and malaria among children in Nigeria. Data were from nationally representative Demographic and Health Surveys (DHS) for the first three projects and Nigeria Malaria Indicator Survey (NMIS) for the fourth project. The research objectives were addressed using multilevel modeling for projects 1, 3, and 4 and propensity score matching, meta-analysis and meta-regression for project 2.

Results of each separate project of this thesis showed that: (1) after controlling for the socio-economic circumstances of individual families, residency in a slum community

was associated with infant mortality. This association was attenuated among children born to women who had received antenatal care from a health professional. Finally, residency in a slum community exacerbated the risk of stunting among older versus younger children; (2) individual-level CS increased the risk of neonatal mortality and that this risk was the highest in countries with the lowest CS rates; (3) couples were more likely to have used condoms consistently if the husband was HIV positive, and was the only one in the couple who knew his HIV test result. This association was stronger if the HIV-positive husband was aware of his HIV test result and his HIV-negative wife aware of her test result. No corresponding associations were observed for HIV-positive wives; (4) compared with children living in areas with no LLIN mass distribution campaigns, those in the World Bank Booster Project areas were significantly less likely to test positive for malaria but no significant differences in child malaria infections were found between other campaigns and non-campaign areas. Results also showed that community-level wealth, community-level maternal knowledge regarding malaria prevention, and child-level use of insecticidal nets were negatively associated with child malaria.

Taken together, the findings suggest that improving the material circumstances of slum neighborhoods and increasing antenatal care coverage among women living in these neighborhoods could help reduce stunted child growth and infant mortality associated with slum residency. Results also indicate the need of improving the quality of maternal and newborn health care services, especially in countries with low CS rates in order to reduce neonatal mortality associated with CS. In addition to LLIN mass distribution campaigns, improving maternal knowledge on malaria prevention at the community level

might be helpful in preventing child malaria. Finally, results show that increasing HIV testing and awareness of results among husbands could help reduce HIV transmission among couples.

Keywords: contextual influences, slum residency, cesarean section, HIV prevention, long-lasting insecticidal nets, campaigns, child mortality, stunting, malaria

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LIST OF ABBREVIATIONS AND SYMBOLS

ANC: Antenatal care

CS: cesarean section

CI: Confidence interval

DHS: Demographic and Health Survey

GDP: Gross domestic product per capita converted to constant 2005 international dollars based on purchasing power parity

ITN: Insecticide-Treated Nets

LLIN: Long-lasting Insecticidal Nets

MH: Mantel-Haenszel

NDHS: Nigeria Demographic and Health Survey

NMIS: Nigeria Malaria Indicator Survey

OR: Odds ratio

SD: Standard deviation

SES: Socioeconomic status

U5MR: Under-five mortality rate per 1,000 live births

WHO: World Health Organization

DECLARATION OF ACADEMIC ACHIEVEMENT

This thesis includes four projects that were prepared under the guidance of all three members of the thesis committee. The author of this thesis contributed primarily to the following aspects of the studies: conceptualization, developing research questions and objectives, data management and data analysis, interpretation of results, drafting the manuscripts, and revising them according to the comments provided by the thesis committee members. The manuscripts were prepared during the period from January 2010 to August 2012.

CHAPTER 1

General Introduction

About 7.6 million children aged less than 5 years die every year – most of them from low and middle income countries and mainly from preventable causes (United Nations Children's Fund (UNICEF), 2012; World Health Organization (WHO), 2012). On average, children in low income countries are about 18 times more likely to die before the age of five than those in high income countries (WHO, 2012). There is also substantial cross-national variability in the under-five mortality rate per 1,000 live births (U5MR) among low (180 in Somalia versus 48 in Bangladesh) and middle (87 in Pakistan versus 6 in Cuba) income countries (UNICEF, 2012). Living conditions, access to health care services and infections are important determinants of child morbidity and mortality (WHO, 2011a, 2012).

The general objective of this thesis was to examine contextual and individual-level determinants of child health, associated with: living conditions, with a particular focus on slum residency; maternal use of health care services during delivery, with a special focus on cesarean deliveries; and infections, with specific focuses on parental HIV infections and child malaria. The literature review provides an overview of each topic and limitations of previous research. The review is followed by a conceptual framework of the thesis and a discussion of potential mechanisms through which contextual factors could influence child health. The introduction ends with the specific objectives of the thesis and a discussion of important methodological considerations.

Slum residency and child health

Poor living conditions reflected in lack of access to clean water and proper sanitation have been linked to malnutrition, mortality and morbidity worldwide (Fink, Günther, & Hill, 2011; WHO, 2001). More than 800 million people (32.7% of urban population) resided in urban slums in developing countries in 2010 (UN-Habitat, 2010). At its simplest, a slum could be described as "a densely populated usually urban area marked by crowding, dirty run-down housing, poverty, and social disorganization" (Slum, 2012). Over the period from 2000 to 2010, the population living in slums increased by 61 million. This increase mainly occurred in Sub-Saharan Africa, South-Eastern Asia and Western Asia (UN-Habitat, 2010).

Studies have shown that malnutrition and mortality rates of slum children are comparable to or higher than those of rural children (who generally have worse rates than urban children) in some developing countries. For example, in Ahmedabad's slums in India, infant mortality rates were twice the national rural average (Fry, Cousins, & Olivola, 2002). In some countries where malnutrition data on slum children are available (e.g. Bangladesh and Indonesia), the prevalences of underweight, stunting and wasting were higher in slum areas than in rural areas or the overall urban population (Food and Agriculture Organization of the United Nations, 2010). Nevertheless, these are crude estimates unadjusted for characteristics of the slum residents.

Slum dwellers experience considerably higher levels of socio-economic disadvantage than other urban residents. However, not all families living in slums are poor or uneducated. For example, a survey conducted in 211 slums in India reported that the occupations of slum dwellers vary from sweepers and vendors to government employees and small entrepreneurs and there were even a few computer professionals, teachers, nurses and doctors living in some slums (UN-Habitat, 2007). People with reasonable income may choose to live in a slum especially if they have businesses in or around the slum (UN-Habitat, 2007). An important question remained unanswered is whether the increased risk for child malnutrition and mortality in slums reported by previous studies is attributable to the socio-economic status of the slum residents (compositional effect) or the environmental characteristics of the slum neighborhood itself (contextual effect).

Cesarean section and neonatal mortality

The cesarean section (CS) rate, defined as the proportion of all deliveries by CS in a geographical area, has been selected as an indicator of access to life-saving services for both mothers and newborns (WHO, 2009). CS rates have been increasing over the past 30 years with rates varying widely among countries, from 0.4 to 40% of births (Althabe et al., 2006). Both very low and very high CS rates can be harmful (WHO, 2009), because the former reflects women's lack of access to life-saving care while the latter may indicate overuse of the procedure or taking unnecessary surgical risk without any indication (WHO, 1994). The recommended lower and upper limits for CS are 5 and 15% but there is no empirical evidence that these rates are optimal (WHO, 1994, 2009).

CS can be life-saving for the baby in rarely occurring emergency situations that include umbilical cord prolapse and separation of the placenta before birth (Shearer, 1993). However, compared with those delivered vaginally, babies delivered by CS are more likely to have respiratory distress because of failure to remove fetal lung fluid at birth. Fetal lungs are filled with fluid which needs to be cleared immediately to allow for gas exchange. Normally, labor stimulates the release of fetal catecholamines which helps remove fetal lung fluid, stimulates breathing and enhances postnatal lung adaptation (Coad, Dunstall, & McCandlish, 2005). The disruption of this process in infants delivered by CS may result in failure to remove fetal lung fluid and respiratory distress. Several studies have shown that infants delivered by CS before the onset of spontaneous labor were more likely to develop respiratory distress and be admitted to neonatal intensive care units (Hansen, Wisborg, Uldbjerg, & Henriksen, 2007; Jain & Eaton, 2006; Ramachandrappa & Jain, 2008).

Some recent studies using individual-level data have reported that CS may be (Lumbiganon et al., 2010; MacDorman, Declercq, Menacker, & Malloy, 2006, 2008; Villar et al., 2007) or may not be (Kallen & Olausson, 2007) associated with neonatal mortality. Two ecological studies using country-level data have reported negative, positive or no association between country-level CS rates and neonatal mortality (Althabe et al., 2006; Betran et al., 2007). No study has attempted to understand these conflicting findings using both country and individual-level data. This left open important questions: is there any between-country variation in the association between individual-level CS and neonatal mortality? Is the variation (if there is any) explained by country-level factor(s)?

Parental HIV infections and child health

About 1.8 million adults and children were newly infected with HIV in sub-Saharan Africa in 2009 (Joint United Nations Programme on HIV/AIDS (UNAIDS), 2010). As many as one in three infants born to and breastfed by HIV-infected mothers are at risk for being infected with HIV unless preventive measures are taken (UNAIDS, 2010). Furthermore, from 2005 to 2009, the total number of children aged 0–17 years orphaned by AIDS increased from 14.6 to 16.6 million with about 90% of these children resident in sub-Saharan Africa (UNAIDS, 2010). According to a review by Cluver and Gardner (2007), children orphaned by AIDS are at increased risk for problems associated with anxiety and depression (internalizing problems) in 10 (eight in Africa, two in the US) out of 13 studies included in the review. (The control groups in these studies included non-orphaned children or those orphaned for other reasons). A study among children and adolescents (N=1025) in Cape Town, South Africa also reported that compared with non-orphaned children, those orphaned by AIDS had more peer problems and post-traumatic stress while no such association was found for children orphaned by other causes (Cluver, Gardner, & Operario, 2009). Parental HIV infection invariably places children at risk for being infected and/or having mental health problems associated with being orphaned by AIDS.

The majority of new HIV infections in sub-Saharan Africa now occur in married and cohabiting couples (Matovu, 2010), and most of these couples are HIV discordant (i.e., only one partner is HIV positive) (De Walque, 2007). Regular use of condoms among married couples remains very low: according to a study in eight African countries, the estimated probability of condom use at last sex among women in stable relationships is less than 5% (Glick & Sahn, 2008). Men's resistance to the use of condoms and unequal decision-making powers between men and women often result in high vulnerability of women to HIV infection (UNAIDS, 2009) but this could also lead to an increased risk of HIV infection in men if the wife is HIV positive but the husband is not. Only one previous study has been conducted among HIV-infected couples (Wagner et al., 2010) but this study used data collected from only one partner (i.e., either husband or wife) but not both. Given the male dominance in decision making, it is conceivable that among couples at risk of HIV infection, husband's knowledge or husband's awareness of his HIV status could have a stronger effect on condom use than wife's knowledge or wife's awareness of her status but this question has not been studied using information collected from both husbands and wives.

Malaria infections among children and LLIN mass distribution campaigns

Malaria is a disease transmitted from person to person by the bite of *Anopheles* mosquitoes that carry the Plasmodium parasite. Malaria caused an estimated 655,000 malaria deaths worldwide in 2010 and more than 90% of these deaths occurred in Africa (WHO, 2011b). Nigeria, a country located in West Africa, carries the greatest malaria burden among countries in the world with over 300,000 malarial deaths each year - most of them occurring in children less than 5 years of age (The World Bank, 2009; United States Embassy in Nigeria, 2011).

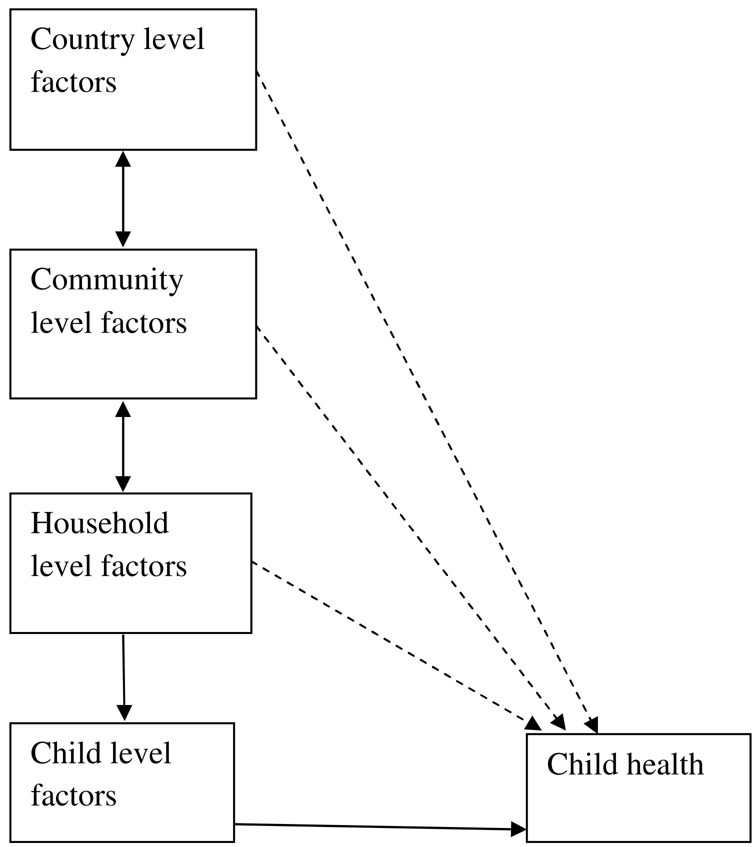
A systematic review of randomized trials reported protective effects of Insecticide-Treated Nets (ITNs) on a variety of outcomes including anemia, splenomegaly and prevalence of malaria infection (Lengeler, 2004). One randomized trial (conducted after the publication of the systematic review) among children aged 6 months to 5 years (N=100) in a rural community in Nigeria also reported that febrile episodes and parasitemia were significantly lower in the ITN group compared with the traditional bed net group (Osondu & Jerome, 2009). Although there is evidence that ITNs are efficacious in preventing malaria in randomized trials (under optimal conditions), limited evidence exists as to their effectiveness (under real world conditions) when distributed for free in the general population.

More than 24 million long-lasting insecticidal nets (LLINs) were distributed in 14 of the 37 states of Nigeria between May 2009 and August 2010 as part of the National Malaria Control Strategic Plan to adopt a universal coverage campaign approach (The U.S. Global Malaria Coordinator, 2010). The recently available data from the Nigeria malaria indicator survey (NMIS) which was carried out from October to December 2010 on a nationally representative sample of households (National Population Commission (NPC) [Nigeria], National Malaria Control Programme (NMCP) [Nigeria], & ICF International, 2012), provide a unique opportunity to evaluate the association between the presence versus absence of LLIN distribution campaigns in a community and child malaria. An important question left unanswered is: using secondary data analysis, is it possible to demonstrate the effectiveness of such programs when implemented in the general population?

Conceptual framework of the thesis

In this thesis, the influence of compositional (i.e., characteristics of individuals within natural groupings including countries, communities and households) and contextual effects (i.e., group level variables) (Diez Roux, 2002) on child health is examined using the conceptual model adapted from the general theoretical model put forth by Bronfenbrenner (1979). The relationship among contexts is portrayed as a nested hierarchy of levels (Fig 1). This figure was taken from the study of Boyle and colleagues (2007), looking at contextual influences on child health and functioning. Children are nested in households which are nested in communities which are in turn nested in countries. The flow of contextual influences on child health is directed downward from distal to proximal variables. (The terms distal and proximal variables are used to refer to the “ecological closeness of influences” on child health). These contextual variables may: (1) exert direct, cross level effects on child health (dashed lines), (2) exert indirect, cross-level effects mediated through more proximal variables (solid lines), and (3) modify the associations between independent and dependent variables operating within or across levels in a hierarchy (e.g., country level factors modifying the effects of child level factors on child health). The correlations between variables at different levels (double headed arrows) make it difficult to disaggregate country, community and household-level influences on child health.

Fig. 1. Conceptual framework of the thesis



Mechanisms through which contextual factors could influence child health

Country level factors and child health

Country-level factors (e.g. economic development) can be beneficial to child health directly or indirectly by: improving material circumstances such as quality of food and shelter; increasing work opportunities and income of adults (or parents); and increasing investment in public and private infrastructure (Boyle et al., 2006). Several studies have shown that child mortality and malnutrition are strongly associated with economic indicators such as gross national product (GNP) and gross domestic product (GDP) per capita in developing countries (Filmer & Pritchett, 1999; Pritchett & Summers, 1996; Shen & Williamson, 2001; Smith & Haddad, 2001; Wang, 2003). A study using Demographic and Health Surveys (DHS) conducted in 42 developing countries found that between-country variation in child weight and height for age is 13.4% and 7.3%, respectively and that GDP at the country level accounts for larger amount of unique variability in both outcomes than household wealth and maternal education at the household and individual levels, respectively. The amount of unique variation attributable to GDP-Purchasing Power Parity is 31.7% (4.251/13.41) of weight for age and 27.1% (1.991/7.34) of height for age (Boyle et al., 2006).

Community level factors and child health

Community wealth could improve child health by improving material circumstances and infrastructure in a similar way that economic development can improve child health at the country level. On the other hand, living in disadvantaged communities can undermine child health in several ways. Available evidence has shown that residents in disadvantaged communities are less likely to have usual sources of care and preventive services, and more likely to have unmet medical needs (Kirby & Kaneda, 2005). Unsanitary environmental conditions in a community can also have harmful effects on child health. Feachem et al. (1983) suggested that a household’s access to water and sanitation facilities may have limited health benefits if the household is located in a community with high level of fecal contamination.

Household/Family level factors and child health

Many studies of urban populations in developing countries have shown that household access to safe drinking water/piped water, toilet and/or housing conditions are strongly associated with child mortality (e.g. Crook & Malaker, 1992; Pant, 1991; Victora et al., 1988; Woldemicael, 2000). Household wealth can improve child health by improving the material circumstances of the family and the ability to purchase goods and services that are beneficial to health (Boyle et al., 2006). Higher level of maternal education can influence child survival through better health care practices regarding nutrition, hygiene, and prevention and treatment of diseases (Mosley & Chen, 1984). One may therefore expect that the effect of contextual factors (e.g. residing in a slum community and/or a slum household) on child health can be largely accounted for by household wealth and maternal education. Moreover, these socio-economic characteristics could also modify the association between contextual factors and child health (e.g. maternal education may attenuate the unwholesome effect of slum residency on child health through better health care practices).

Quantifying individual and contextual effects – Multilevel modeling

In multilevel studies (e.g. households within communities), information collected from respondents will be correlated because of shared characteristics and this violates the assumption of independence. Accordingly, statistical analyses that fail to consider the multilevel nature of the data are vulnerable to underestimating the "standard error of ecological effects" (Blakely & Woodward, 2000). Unbiased estimates of standard errors may be obtained by specifying random error terms for each level of analysis (Blakely &

Woodward, 2000). Multilevel modeling (e.g. multilevel regression) allows one to do such analysis by yielding two types of effects. One, fixed effects are regression estimates which are interpreted in the same way as coefficients derived in ordinary least square regression. Two, random effects provide estimates of variation in the outcome between countries, communities, etc. In addition, one can test for between-country differences in the association between the study variable of interest and the outcome of interest (e.g. between-country variation in the association between slum residency and infant mortality) using multilevel modeling. Demographic and Health Surveys (www.measuredhs.com) integrate macro (e.g. country- and community-level) and micro (individual-level) information, allowing one to study contextual effects and to distinguish between population-level effects and individual-level effects.

Specific objectives of the thesis

This thesis involves four conceptually linked projects – each one addresses limitations of previous research and/or gaps in the literature regarding specific determinants of child health as outlined in the introduction. These determinants operate at different levels: child, family, community or country. The objectives of the first project were to: 1) study the associations between slum residency and infant mortality and child stunting in 45 low and middle income countries, and 2) examine factors that might modify these associations. The second project aimed at: 1) using propensity score matching to estimate the association between individual-level cesarean section (CS) and neonatal mortality in 46 countries; 2) conducting a meta-analysis of the associations between individual-level CS and neonatal mortality across countries; and 3) performing a meta-regression to examine if the association between individual-level CS and neonatal mortality across countries varies depending on country-level CS rates and GDP. The third project aimed to examine the determinants of consistent condom use based on the perspectives of both husband and wife where one or both partners are HIV infected and resident in Swaziland, Zambia or Zimbabwe. This project is linked to child health by way of their vulnerability to HIV infection from their parents and/or to mental health problems associated with being orphaned by AIDS. The objectives of the fourth project were to: (1) assess the between-community and between-household variations in malaria among children (in terms of presence of malaria parasites in blood samples) in Nigeria; (2) examine the association between LLIN distribution campaigns and child malaria after adjusting for geographic characteristics; and (3) examine if the campaign effects are explained by other community and individual-level characteristics.

Method

Data were from nationally representative Demographic and Health Surveys (DHS) (http://www.measuredhs.com/) for the first three projects and the Nigeria Malaria Indicator Survey (National Population Commission (NPC) [Nigeria] et al., 2012) for the last project. The DHS project was funded by the United States Agency for International Development (USAID) to conduct nationally representative cross-sectional surveys of socio-demographic characteristics and health status in low- and middle-income countries using standardized methodology. DHS supports other standardized data collection options (e.g. Malaria Indicator Surveys that collect data focusing on malaria prevention and treatment and conduct blood testing for malaria parasites among children in countries where malaria is endemic) depending on specific requirements of countries (MEASURE DHS, n.d). DHS were approved by the ORC Macro Institutional Review Board in Calverton, USA as well as by an ethical review board from each participating country (http://www.measuredhs.com/).

The countries included in the first and second projects were the same except for 13 countries which did not overlap the two projects. The first project used data from the household files and children files in 45 DHS countries and the second project from children files in 46 DHS countries. GDP data for the included countries were obtained from the World Bank's World Development Indicators online (The World Bank, n.d.). The third project used data from the DHS couple files and HIV data files from Swaziland, Zambia, and Zimbabwe. Table (1) presents the total number of countries, clusters, households and children contributing to each study and the overall survey response rates.

Table 1. Total number of countries, clusters, households and children contributing to each study and the overall survey response rates

	Project 1	**Project 2**	**Project 3**	**Project 4**
Countries (N)	45	46	3	1
Clusters (N)	13 056	-	601	233
Households (N)	84 918	-	1173	2549
Couples (N)	-	-	1177	-
Men (N)	-	-	-	-
Children (N)	119 988	392 883	-	4082
Overall survey response rate	>90%	>90%	89% (men), >90% (women)	>90%

Data management and data analysis

DHS have separate datasets for households, women, children and HIV data for each participating country. It was necessary to explore and merge the datasets and ensure proper linkages to compute aggregates and conduct the analyses. It was also necessary to ensure that the variables and how they were measured were comparable across countries.

Multilevel modeling was conducted to address the research objectives of the first, second and fourth projects. For the second project, propensity score matching, meta-analysis, and meta-regression were performed.

Sources and control of error in estimating individual and contextual effects

Observational studies are prone to bias. Grimes and Schulz (2002) suggested that researchers look for the presence of three biases: selection bias, information bias (also known as classification or measurement bias) and confounding. In the presence of selection bias, the relation between exposure and outcome among those who are selected into the study is different from the relation among the target population (Hernan, Hernandez-Diaz, & Robins, 2004). For example, studies using registry data are prone to selection bias because patients enrolled in the registry may differ from the general population (European Commission, n.d; Krumholz, 2009). The potential problem with selection bias is less likely in population-based health surveys as long as the survey design uses strict probability sampling and response rate is high (European Commission, n.d). The DHS studies use probability sampling and the participation rate of respondents is usually more than 90% (www.measuredhs.com).

Information bias is likely if information has been gathered in a different way in the exposed and unexposed groups (Grimes & Schulz, 2002). DHS use a standardized approach for data collection within and across countries to minimize information bias. In multilevel studies, the lag time between an ecological exposure and individual level health outcome is also considered as information bias. For example, studies using cross-sectional survey data to examine the associations between ecological socioeconomic exposures and individual level health outcome are prone to information bias because it might imply “a zero lag time” between exposure and outcome unless the exposure is stable over time (Blakely & Woodward, 2000). To minimize this bias, GDP in the year before the DHS survey was used in the analyses in this thesis although GDP is quite stable over time.

Confounding is present if a variable: is associated with exposure; is related to the outcome; does not lie in the causal pathway between the exposure and the outcome and is extraneous to the analysis. In multilevel studies, it may be difficult to differentiate whether an individual level covariate is a confounder or an “intermediary variable”: in the latter case, controlling for that covariate may lead to overlooking an “indirect cross level effect” (Blakely & Woodward, 2000). Effect estimates with and without the adjustment of individual level covariates were therefore presented in this thesis as suggested by Blakely and Woodward (2000).

If the results of a study cannot be explained by any of the above three biases, then chance might be another explanation (Grimes & Schulz, 2002). However, a small difference between two samples can be statistically significant if sample size is sufficiently large while a large difference between groups might be statistically non-significant if sample size is sufficiently small (Morgan, 2003). Small p values or statistically significant results do not necessarily mean that results are of practical importance (Gliner, Morgan, Leech, & Harmon, 2001; Thompson, 1999). The use of a relative risk ratio or an odds ratio can better identify treatment effects given the limitations of null hypothesis significance testing (Morgan, 2003). These measures of associations should be presented with confidence intervals in preference to p-values (Grimes & Schulz, 2002) and this thesis did so.

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CHAPTER 2

Association of Urban Slum Residency with Infant Mortality and Child Stunting in Low and Middle Income Countries

Abstract

This study aimed to: (i) examine the incremental risk of urban slum residency on infant mortality and child stunting after controlling for national and individual level factors, and (ii) identify factors that exacerbate or attenuate any adverse effects. Data were from Demographic and Health Surveys conducted in 45 countries. The respondents were women (15–49 years) and their children (0-59 months). Results showed that living in a slum neighborhood was associated with infant mortality after adjusting for all covariates and this risk was attenuated among children born to women who had received antenatal care from a health professional. We also found that increasing child age exacerbated the risk for stunting associated with residing in a slum neighborhood and a slum household. Improving the material circumstances of slum neighborhoods as well as increasing antenatal care coverage among women living in these neighborhoods could help reduce infant mortality and stunted child growth.

Key words: urban slum residency; infant mortality; child stunting; multilevel modeling

Introduction

More than 800 million people (32.7% of urban populations) resided in urban slums in developing countries in 2010 (UN-Habitat, 2010). A slum household is defined as "a household lacking one or more of the following conditions: improved water; improved sanitation; sufficient living area; durable housing; and secure tenure" (UN-Habitat, 2010, p.16). Mortality rates of children living in urban slums are comparable to or higher than those of children residing in rural areas in some developing countries. For example, in Ahmedabad's slums in India, infant mortality rates are twice the national rural average (Fry, Cousins, & Olivola, 2002). In some countries where malnutrition data on children living in urban slums are available (e.g. Bangladesh and Indonesia), the prevalence of underweight, stunting and wasting were higher in slum areas compared to rural areas or the overall urban population (Food and Agriculture Organization of the United Nations (FAO), 2010).

The Millennium Development Goal No.7 Target 11 is "to achieve a significant improvement in the lives of 100 million slum dwellers by 2020" (United Nations, 2004). Although earlier studies have established that risk for mortality or malnutrition is elevated among children living in urban slums, precise estimates of this risk in comparison with children living in non-slum urban areas are unavailable. Furthermore, the extent to which this elevated risk is attributable to the characteristics of families who reside in slums (compositional effects) versus the environmental features of slum residency (contextual effects) is unknown. Slum dwellers experience considerably higher levels of socio-economic disadvantage than other urban residents. However, not all families living in slums are poor (UN-Habitat, 2007). The association between slum residency and child mortality or malnutrition will be confounded, at least in part, by the low socio-economic status of slum residents. This leaves open the important question of the extent to which the characteristics of slums exert adverse effects on child health over and above socio-economic status and other characteristics of inhabitants. If an incremental adverse effect associated with slum residency exists after adjusting for characteristics of inhabitants, the next step is to identify factors that could attenuate or exacerbate this effect on child health.

Child health and poor living conditions in households and neighborhoods

Many studies of urban populations in developing countries have shown that a household's lack of access to safe drinking water/piped water and toilet facilities and/or housing conditions are strongly associated with child mortality (e.g. Woldemicael, 2000; Pant, 1991; Victoria et al., 1988; Crok and Malaker, 1992). However, a household's access to water and sanitation facilities may have few health benefits if the household is located in a neighborhood with high level of fecal contamination (Feachem et al., 1983). Timaeus and Lush (1995) examined the influence of neighborhood level environmental conditions on child health after adjusting for household level characteristics in four countries (Ghana, Thailand, Egypt and Brazil). Using the Demographic and Health Survey urban data, the authors constructed an environmental index based on drinking water source, toilet facility, and type of floor (the index was based only on toilet facility in Brazil). They then categorized all families in each neighborhood into one of 4 groups on this environmental index (1 = low to 4 = high – a higher number indicating better conditions). After controlling for household level socio-economic status, the results showed that compared with high category neighborhoods, children in low category neighborhoods were at elevated risk for moderate or severe stunting in Ghana (OR=2.5, p<0.05) and Egypt (OR=2.2, p<0.05), and diarrhea in Thailand (OR=1.9, p<0.05) and Brazil (OR=2.1, p<0.01). The effects for the environmental index in Ghana and Thailand were no longer statistically significant after controlling for household level water and toilet facilities. The authors commented that the between-country variation in intra-urban differentials in child health may be related to economic and urban development in those countries (Timaeus and Lush, 1995).

Other factors implicated in slum residency effects on child health

Economic development

Country-level factors (e.g. economic development) can be beneficial to child health directly or indirectly by; improving material circumstances such as quality of food and shelter; increasing work opportunities and income of adults (or parents); and increasing investment in public and private infrastructure (Boyle et al., 2006). Several studies have shown that child mortality and malnutrition are strongly associated with economic indicators such as gross national product (GNP) and gross domestic product (GDP) per capita in developing countries (Filmer & Pritchett, 1999a; Pritchett & Summers, 1996; Shen & Williamson, 2001; Smith & Haddad, 2001; Wang, 2003). One may therefore expect that the effect of urban slum residency on child health can be partly accounted for by the economic status of a country.

Family and individual level factors

Household wealth can improve child health within countries by providing an opportunity to improve the material circumstances of the family and to purchase goods and services that are beneficial to health (Boyle et al., 2006). Higher levels of maternal education can influence child survival through better health care practices regarding nutrition, hygiene, and prevention and treatment of diseases (Mosley & Chen, 1984). The effect of residing in a slum neighborhood and/or a slum household on child health can therefore be largely accounted for by household wealth and maternal education.

Timaeus and Lush (1995) reported statistically significant interactions between socio-economic status and environmental conditions on child mortality in unadjusted analyses. In Egypt, better-off children living in good neighborhoods had lower mortality rates; while in Brazil, poor children living in bad neighborhoods had higher mortality rates (Timaeus & Lush, 1995). However, these results did not adjust for covariates, leaving open the question of attribution – the extent to which these effects might be attributable to important covariates. A study based on the Malaysian Family Life Survey (1976– 1977) showed that among infants from households with no access to toilet/piped water, those born to mothers who were illiterate were twice as likely to die as those born to mothers who are literate (Esrey & Habicht, 1988).

While the studies cited above have shown that neighborhood or household level environmental effects on child health may be conditional on socio-economic status and maternal literacy, interventions during the earliest periods of life (e.g., prenatal period or infancy) may also modify these associations. According to the World Health Organization, these early interventions (e.g. supplementary feeding of pregnant women, intervention to control diseases) can have the largest influence on physical growth of children less than five years of age (WHO, 1999). Antenatal care may provide such health benefits because it identifies and treats conditions that are harmful to the health of the newborn and/or the mother and by educating pregnant women on safe motherhood (WHO, 2011a). Studies have shown that antenatal care is negatively associated with pre-term labour (Orvos et al., 2002) and perinatal death (Kapoor, Reddaiah & Lobo, 1985; McCaw-Binns et al., 1994) and positively associated with delivery of a healthy weight baby (Brown et al., 2008). Under the conditions of excessive risk found in slums, the protective effects of antenatal care could exert a differentially beneficial effect on child mortality but this has not been studied. Furthermore, among children living past infancy, it is reasonable to expect that continued exposure to the adverse environmental conditions associated with slum residency would differentially increase the risk for poor health outcomes in these same children.

Measuring slum household and slum neighborhood

The availability of Demographic and Health Surveys (DHS) for many developing countries provides a unique opportunity to examine the strength of association between slum residency (at the neighborhood and household levels) and child health and factors that may modify this association across countries. A prerequisite for studying slum effects cross-nationally is to use a common measure of slum residency. There are some challenges to this. Available evidence suggests that two components of the UN slum definition may be unsuitable indicators in a cross-national study. ‘Secure tenure’ is not easy to measure or monitor because it carries a legal meaning (UN-Habitat, 2010), and information on this is not available for most countries (United Nations, 2011). Furthermore, sufficient living area, defined as not more than 3 household members sharing the same room (UN-Habitat, 2010), could misclassify a non-slum household as a slum household in many cultures where ‘co-sleeping’ with children is the norm (McKenna, n.d).

Slum neighborhoods have been defined differently across countries using various methods. The development of satellite imagery and geographic information systems has made it possible to identify and incorporate slums into censuses and surveys but this technique is not yet available for measurement and comparison of slums worldwide (UN-Habitat, 2008/2009). A different approach recommended by UN-Habitat is to use enumeration areas to localize slum neighborhoods as these areas represent the ‘smallest household aggregation’ in many countries and are relatively homogeneous (UN-Habitat, 2008/2009). In DHS, enumeration areas are usually selected from Census files (Measure DHS, 2011), making it possible to aggregate household level survey data up to comparably defined geographic areas.

Mechanisms through which slum residency could influence child mortality and stunting

Nationally representative data on causes of death in slum children are unavailable. According to studies conducted in urban slums in selected cities and towns in some developing countries, causes of death in slum children include poor neonatal care (Fry, Cousins, & Olivola, 2002), neonatal tetanus (Awasthi & Pande, 1998; Hussain et al., 1999), diarrhea (Fry, Cousins, & Olivola, 2002; Vaid et al., 2007) and respiratory infections (Fry, Cousins, & Olivola, 2002; Vaid et al., 2007). The majority of women in urban slums usually deliver at home, mostly assisted by non-health professionals (e.g. traditional birth attendants or relatives) (Aziz et al., 2010; Khan et al., 2009). For babies born in unsanitary conditions, spores of Clostridium tetani bacteria can enter the umbilical cord stump, causing neonatal tetanus which is fatal in more than 70% of cases (UNICEF, 2004). Moreover, lack of access to clean water and sanitation facilities could create a fecally contaminated environment (e.g. Ahmedabad slums in India) (Fry, Cousins, & Olivola, 2002). Diarrhea, associated with unclean water and lack of sanitation, is causing an estimated 1.5 million child deaths every year (UNICEF/WHO, 2009). Children who survive frequent episodes of diarrhea usually become malnourished. A study using data from nine cohort studies in five countries found that 25% of stunting among 24-month old children is attributable to experiencing five or more episodes of diarrhoea prior to 24 months of age (Checkley et al., 2008). Stunting or low height-for-age is an indicator of long-term malnutrition in children and is the best measure of ‘cumulative growth retardation’ (Jamison et al., 2006). Malnourished children have increased risk of acute respiratory infection (Cunha, 2000; Tupasi et al., 1990), one of the leading causes of child death in developing countries. Housing conditions in slums often potentiate the spread of infection. For example, an earth floor (a characteristic of many slum households) can be a breeding ground for various infectious agents (e.g. eggs and larvae of intestinal worms) (Shrivastava, 2004). Living in earth floor houses (compared with cement floors) has been linked to increased risk of diarrhea (Woldemicael, 2001) and being a carrier of Streptococcus pneumoniae (Nyandiko et al., 2007), a bacteria that commonly causes acute respiratory infections in children. In addition, the use of poor quality building materials in slums, for example, a "leaky" house can cause dampness and mould which in turn may result in respiratory problems. The common use of flammable or non-durable construction materials in slums (e.g. wood planks, cardboard) may increase risks of various injuries (WHO, 2002). While not all people living in urban slums are poor and not all households in a slum neighborhood are slum households, it is reasonable to expect that a child living in a non-slum household located in an infectious or fecally contaminated slum neighborhood can have increased risk of repeated infections and malnutrition. One may also expect that the longer a child lives in a slum neighborhood, the worse it is for child growth among those children who survive the infectious diseases.

Rationale and Study objectives

The extent to which the elevated risk of slum residency on child health is attributable to the characteristics of families who reside within a slum neighborhood versus the contextual effects or environmental features of a slum neighborhood has not been studied.

The objectives of this study were: (i) to examine the incremental risk associated with residing in an urban slum neighborhood and a slum household on infant mortality and child stunting after controlling for national and individual level factors in low and middle income countries, and (ii) to study if the adverse effects of urban slum residency on the outcomes were modified by household wealth, maternal education, antenatal care, place of delivery and child age in those countries.

Method

Data come from nationally representative Demographic Health Surveys (DHS) conducted in 45 low and middle income countries between 2001 and 2009 (child height data are available only in 43 countries). Study details are available at the DHS website (http://www.measuredhs.com/aboutdhs/) and we provide a brief outline here. The sampling frame is a list of non-overlapping area units (enumeration areas) that cover the entire country and serve as the primary sampling units or clusters. In the selected clusters, all households are listed and a fixed proportion is chosen by systematic sampling. All eligible persons in selected households are included in the final sample. DHS conducts interviews with all women aged 15–49 years in these households, assesses their children

(0–59 months), and measures maternal and child heights using a standardized approach. In some countries, height data are collected in a random subset (33 or 50%) of the sample. The response rates vary from 92% in Ukraine to 98% in Cambodia.

Concepts and measures

Dependent variables

Infant Mortality. This measures whether a child survived up to 12 months of age and is a binary outcome variable. For all biological children born in the previous 5 years, DHS collected information from mothers about the timing of these births and the survival status of these children at the time of interview (alive or dead). If alive, mothers were asked the age of their child; if dead, mothers were asked the child's age at death. The survival status of the child between birth and one year of age was determined from this information.

Stunting. Height measurements for children (0–59 months) of sampled women were performed using a standardized measuring board. Children younger than 24 months were measured lying down on the board, whereas standing height was measured for older children. The height measures were converted to standard deviation units (z scores) using the World Health Organization (WHO) Child Growth Standards (WHO, 2011b). They were then classified as no stunting [$z \geq -2$ standard deviation(SD)] and stunting ($z <-2$ SD) (WHO, 2012).

Independent variables

Slum household

In this study a slum household was defined as a household lacking *at least two* of the conditions identified below. [We eliminated the contentious elements (i.e., secure tenure and sufficient living area), focused on the core elements and conducted sensitivity analyses by using a lower threshold definition (i.e., one or more of the conditions below)].

Access to improved water. Improved drinking water sources (United Nations, n.d) include: piped connection to house or plot, public tap/stand pipe, tube well/bore hole, protected dug well, protected spring, and rain water collection while unimproved drinking water sources (United Nations, n.d) include: unprotected dug well/spring, cart with small tank/drum, bottled water, tanker-truck, and surface water.

Access to improved sanitation. Improved sanitation (United Nations, n.d) includes availability of: flush or pour-flush to piped sewer system, septic tank or pit latrine, ventilated improved pit latrine, pit latrine with slab, and composting toilet. Unimproved sanitation facilities (United Nations, n.d) include: flush or pour–flush to elsewhere, pit latrine without slab or open pit, bucket, hanging toilet or hanging latrine, and no facilities or bush or field.

Structural quality/durability of dwellings. DHS includes the following standard categories for describing the floor, wall and roof of a household: natural, rudimentary and finished. Information concerning wall and roof is not available for many countries. In this study a house is considered not durable if the floor of the house was made of natural or rudimentary materials (i.e., earth, mud, sand, wood planks, palm and bamboo).

Slum neighborhood

To construct the slum neighborhood variable for this study, slum households were aggregated up to the enumeration area or cluster level. Using the threshold of 50% recommended by UN-Habitat (2008/2009), a cluster is defined as a slum neighborhood if it includes 50% or more slum households.

Covariates

We selected covariates to adjust for possible confounding in the analyses (control variables) and to examine the potential of selected variables to modify associations between slum residency and infant mortality and child stunting [i.e., household wealth, maternal education, antenatal care and place of delivery for infant mortality, with the addition of child age for stunting)]. The following variables served as covariates: GDP, household wealth (wealth index), antenatal care, place of delivery, maternal height-for-age, maternal age at birth of child, mother's education, child gender, multiple births, birth order, previous birth interval, child age in months (rescaled for the purposes of the analyses so that one unit increase represents one year) and duration of residence.

GDP. At the national level, GDP is gross domestic product per capita converted to constant 2005 international dollars based on purchasing power parity (World Bank, 2007). It has been rescaled for the purposes of analyses so that one unit increase in GDP represents 1000 international dollars.

We used the *wealth index* (Gwatkin et al., 2000; Filmer & Pritchett, 2001) variable already available in each DHS dataset. It has been shown to be a good proxy for long-run household wealth (Filmer & Pritchett, 1999b, 2001). It was derived from an index (generated through principal component analysis) of household assets ranging from televisions to bicycles and characteristics of the dwelling (e.g electricity for lighting, quality of building materials, number of rooms in the dwelling, type of fuel used for cooking, kitchen in a separate room, water and toilet facilities) depending on the specific questions asked in each country. The index was standardized to a mean of 0 and a standard deviation of 1 and higher scores refer to greater wealth.

Antenatal care (ANC). Women were asked whether they had received antenatal consultation from a health professional (doctor, nurse, or midwife) during the antenatal period. They were also asked the total number of antenatal visits during pregnancy. For women who had received at least one antenatal consultation from a health professional, two dummy variables were created and coded 1 if applicable ‘1-3 antenatal visits’ and ‘4 or more antenatal visits’. The reference group coded 0 was women who did not receive any antenatal consultation from a health professional.

Place of delivery. For each child born in the previous 5 years before the survey, respondents were asked whether (1) a health professional (doctor, nurse or midwife) was present at delivery and (2) the birth occurred at home or in a health facility. Two dummy variables were created and coded as 1 if applicable: ‘assisted delivery by a health professional at home’ and ‘delivery at a health facility’. The reference category coded 0 was delivery at home with no skilled assistance.

Maternal height-for-age. DHS measured maternal heights using a standardized measuring board and calculated height for age standard deviations from the reference median based on the CDC Standard Deviation-derived Growth Reference Curves (DHS recode manual, 2008). For all women aged 18 years and over, the value of 215 months (17 years, 11 months) was used for their age, assuming that women have grown fully by the age of 18.

Maternal age at birth of child was calculated by subtracting the date of birth of the mother from the date of birth of the child, and was converted into years. [Dates of birth were expressed in the form of century month codes (CMCs) which are number of months since the start of the century (DHS recode manual, 2008)].

Maternal education was measured based on total years of schooling.

Child gender was coded as 0=female and 1=male.

Multiple birth was coded as 0=singleton and 1=multiple birth.

Birth order of the child referred to the order in which a child was born. Three dummy variables were created and coded as 1 if applicable: ‘2-3 born’, ‘4-5 born’ and ‘6+ born’. The reference category coded 0 was 'first born'.

Previous birth interval was the interval (in months) between the previous birth and the current birth. Two dummy variables were created and coded as 1 if applicable: ‘<19 months’ and ‘≥35 months’. The reference category coded 0 was '19-35 months'. (First born children do not have a preceding birth interval. A dummy variable representing first born children was therefore included in the analyses).

Duration of residence (based on maternal report) was categorized as: <4 years, 5-14 years, and ≥15 years (reference group).

Sample for Analysis

For this study, we found DHS were conducted in 53 countries between 2000 and 2009. Eight out of the 53 countries were excluded for the following reasons: information on duration of stay at the current place of residence was not available (4 countries); specific information on toilet facility was not available to differentiate between improved and unimproved sanitation (2 countries); and the possibility of a non-representative sample because of massive slum clearance (2 countries). The following 45 countries with requisite data were included: Armenia, Albania, Azerbaijan, Bangladesh, Benin, Bolivia , Burkina Faso, Cambodia, Cameroon, Congo (Brazzaville) , Congo DR, Colombia, Dominican Republic , Ethiopia, Gabon, Ghana, Guinea, Haiti ,Honduras, India, Jordan, Kenya, Lesotho, Liberia, Madagascar, Mali, Malawi, Moldova, Namibia, Nepal, Nicaragua, Niger, Nigeria, Philippines, Rwanda, Sao Tome and Principe, Senegal, Sierra Leone, Swaziland, Tanzania, Timor-Leste, Turkey, Uganda, Ukraine, and Zambia.

Only the usual residents (not visitors) of the households located in urban areas of the 45 countries were eligible to be included in this study. The sample for analysis included 119,988 children from 45 countries for the outcome infant mortality, and 83,956 children from 43 countries for the outcome stunting (child height data were not available in Philippines and Ukraine).

Data Analysis

In our descriptive analyses, country-specific sample weights were used to ensure that the findings are nationally representative. We used multi-level logistic regression and the statistical software MLwiN version 2.24 (Rasbash et al., 2009) to conduct a three-level regression analysis of the DHS data with children, nested in clusters which are nested in countries. All continuous variables were grand-mean centered. Household-level variables were treated as child-level variables because the average number of children (aged 0-59 months) clustered in households (1.4) was too small to have a separate level.

Information regarding antenatal care was available only for the most recent birth in 43 countries (75% of total sample) and maternal height data were collected in only 42 countries. For the analyses, we created two dummy variables to indicate if information on these variables were available (1, missing; 0, not missing).

The models begin by examining the effects of living in a slum neighborhood and a slum household (adjusting for each other) on the outcome variables. Next, we included all covariates and one interaction term at a time into the model because the interaction terms were highly correlated. In Model 2, slum variables, all covariates and significant interaction terms were included.

We conducted a sensitivity analysis by defining a slum household using a lower threshold (i.e., lacking one or more of the following indicators: improved water, sanitation or durable housing).

Results

There were 119,988 children living in 13,056 clusters in urban areas from 45 countries (Table 1). The average numbers of children and households per cluster were 9.2 and 6.5, respectively. About 12% of neighborhoods were slum neighborhoods and about 18% of children lived in slum households. Infant mortality was 3.4% [5% in slum neighborhood versus 3.1% in non-slum neighborhood (not shown)]. Child stunting was 26% [36.9% slum neighborhood versus 24.1% in non-slum neighborhood (not shown)]. About 7.3% of mothers of the children did not receive any antenatal consultation from a health professional: residents of slum neighborhoods were about three times more likely to report not having any antenatal care compared with non-slum residents (18.1% versus 6.0%). There was substantial between-country variation in the proportion of women who did not receive antenatal care (0.8% in Ukraine versus 30.4% in Ethiopia) (overall sample) and even more variation among women living in slum neighborhoods (0% in Ukraine versus 52.9% in Mali) (not shown in table).

Table 2 presents odds ratios (OR) for infant mortality associated with slum residency after adjusting for covariates. In Model 1, both residing in a slum neighborhood and a slum household were associated with infant mortality: OR =1.32 (95%CI=1.19-1.46) and OR=1.26 (95%CI=1.15-1.38), respectively. In Model 2, the slum neighborhood effect was still statistically significant (OR=1.24, 95% CI=1.09-1.41) but the slum household effect was not. There was a significant interaction between slum neighborhood and 1-3 antenatal visits: the risk for infant mortality associated with residing in a slum neighborhood was muted among children born to women who had 1-3 antenatal visits (OR=0.79, 95%CI=0.63-0.99) (see also Fig. 1). However, there were no statistically significant interactions involving household wealth, maternal education or place of delivery. To determine if there was between-country variation in the association between slum neighborhood and infant mortality, we specified slum neighborhood to have a random slope. The test for random slope was not statistically significant, suggesting that the slum neighborhood effect on infant mortality was consistent across countries.

Table 3 presents ORs for child stunting associated with slum residency. In Model 1, both residing in a slum neighborhood and a slum household were associated with stunting: OR=1.28 (95% CI=1.20-1.37) and OR = 1.49 (95% CI=1.42-1.57), respectively. In Model 2, when the covariates and interaction terms were included, increasing child age exacerbated the risk for stunting associated with residing in a slum neighborhood (OR=1.12, 95% CI=1.08-1.16) and a slum household (OR=1.10, 95% CI=1.06-1.14) (see also Fig. 2 & Fig. 3). There were no statistically significant interactions involving household wealth or maternal education or place of delivery.

The sensitivity analysis (not shown in table) using a lower threshold slum definition (i.e., one or more indicators) yielded the following adjusted estimates (Model 2) for the associations between stunting and slum neighborhood (OR=1.09, 95%CI=1.03-1.15) and slum household (OR=1.08, 95%CI=1.03-1.13). Similar to the primary analysis, there was a significant interaction between child age and slum neighborhood (OR=1.07, 95%CI=1.04-1.11) and slum household (OR=1.06, 95% CI=1.03-1.10). The sensitivity analyses for the outcomes infant mortality showed similar directions of associations to those of the primary analysis but the associations were not statistically significant.

Discussion

In this study, residing in a slum neighborhood was significantly associated with infant mortality after controlling for national, household and individual level factors. This risk was attenuated among children born to women who had received antenatal care from a health professional. Increasing child age exacerbated the risk for stunting associated with residing in a slum neighborhood and a slum household. These findings indicate the importance of contextual or environmental effects of slum residency on child health. To our knowledge, this is the first cross-national study to provide an overall estimate of the effect of slum residency on child health using a multi-level approach and controlling for an extensive array of covariates.

The results of this study show that about 12% of neighborhoods were slum neighborhoods and about 18% of children lived in slum households. When using a lower threshold definition, the corresponding prevalence estimates for slum neighborhood and children lived in slum households are 56% and 55% respectively. These estimates may not be directly comparable to those of the United Nations because the latter reports the overall slum population as a percentage of urban residents: it does not specifically report the percentage of slum neighborhoods or children living in slum households. In addition, the United Nations' estimates are not based on a uniform number of indicators: only two indicators (e.g. water and sanitation only) in some countries and three or four indicators in others (UNdata, 2011). In this study, we selected countries based on the availability of information on all three indicators: water, sanitation and housing condition and used a standardized approach to define a slum household and a slum neighborhood.

Our study adds to concerns raised by Timaeus and Lush (1995) about the harmful effects of poor environmental conditions on child health. We also found that increasing child age elevated the adverse effects of residing in a slum neighborhood and a slum household on child stunting. Prolonged exposure might account for this in older children although we cannot be sure due to the cross-sectional nature of the study. While the first priority intervention needs to be improving the material circumstances of people living in slum conditions, our findings also indicate that antenatal care does attenuate the adverse effects of slum residency on infant mortality – a beneficial effect not observed for household wealth or maternal education. This may be because antenatal care is a more proximal determinant of child health than household wealth and maternal education. Socio-economic factors rarely cause poor/good health directly and are therefore called 'distal determinants' (Victora et al., 1997). These distal determinants may influence maternal risk factors (e.g. maternal age at child birth and birth intervals) and protective factors (e.g. antenatal care), which, in turn, affect more proximal determinants (e.g. low birth weight) for neonatal death (Victora et al., 1997).

Rose and colleagues (2004) have distinguished between protective factors and resource factors – the former exerting beneficial effects under conditions of risk and the latter exerting beneficial effects generally. In our study, antenatal care would be a 'protective factor', if its beneficial effects were observed *only* among slum residents (i.e., there was a statistical interaction between antenatal care and residency). However, if the beneficial effects of antenatal care were observed equally among slum residents and non-residents, it would be a 'resource factor'. Because there are different levels of antenatal care (e.g., frequency of visits), it is possible for antenatal care to serve as both a protective factor and a resource factor if these different levels of care serve different functions (i.e., at one level, reducing child health problems only for those residing in urban slums; and at another level, reducing child health problems in all children regardless of their residency risk (living in slums versus non-slums). In this study, we classified antenatal care as no visits, 1-3 visits and 4 or more visits. The World Health Organization (WHO, 2008) recommended that women have at least four antenatal visits but the results of our study show that even 1-3 antenatal visits may be a protective factor for infant mortality under conditions of risk. Receiving 4 or more antenatal visits appears to reduce the risk of infant mortality equally among slum residents and non-residents and may therefore be regarded as a resource factor. However, for the outcome child stunting, there were no significant interactions between slum neighborhood and both categories of antenatal visits: they are therefore more likely to be resource factors for preventing stunted growth.

This study has some limitations. First, newly emerging slum neighborhoods excluded in the Census enumeration might have been omitted during DHS data collection. If that was the case, our findings may not be representative of all slum settlements in the included countries. Second, because countries may vary in their approach to defining slums, a uniform definition may not capture all slums across countries given the wide disparities of socio-economic and physical environmental conditions. However, most slum definitions (Centre for Urban Studies (CUS), National Institute of Population Research and Training (NIPORT) and MEASURE Evaluation., 2006; Jadhav, 2010) share common characteristics (i.e., water, sanitation and housing conditions) that were used to construct the slum variable in this study. In this study, a lower threshold definition of slums leads to weaker infant mortality effects in the same direction. Given that some slum indicators are not stand-alone, using the lower threshold definition may produce an overestimation of slum households as well as the observed weaker association between slum residency and infant mortality. Third, there appears to be some overlap in the items (e.g water and sanitation facilities) used to define a slum household and those used to define the household wealth variable. However, since the purposes of constructing the two variables are different, the way the items are defined is not the same. For example, for the purposes of constructing the household wealth variable, toilet facility is classified as having a flush toilet (yes, no) or a pit toilet (yes, no). For the purposes of constructing a slum household variable, a flush toilet is defined as improved or unimproved depending on whether it is connected to a sewer system. Similarly, a pit toilet can be improved or unimproved depending on whether it has a slab or not. The point-biserial correlation between the two variables (slum household and household wealth) is -0.206 ($p<0.001$). This conservative approach allocates maximal weight for the effect of household wealth. Although controlling for household wealth reduced the slum effects, there was still a statistically significant and meaningful adverse effect on child mortality. Fourth, the exact duration of residence in slum neighborhoods was not known but 95% of the respondents reported to have lived at their current places of residence for at least one year at the time of the survey. Finally, although cross-sectional studies are always vulnerable to residual confounding and omitted variable biases, we believe that our study has established adequate control for important distal and proximal variables associated with infant mortality and child growth.

The large diverse sample, representing 45 low and middle income countries, is a strength of this study, making it possible to estimate the association between slum residency and child health cross-nationally. The consistency of the adverse effects of residing in a slum neighborhood on both outcomes and the consistent direction of adverse effects in the sensitivity analysis support the robustness of our findings.

In conclusion, the results of our study indicate that the physical conditions associated with slum housing and areas exert independent effects on child health over and above the socioeconomic status and other characteristics of residents. We also found that the risk of stunting in slum neighborhoods was greater for older children. Maternal use of antenatal care services might attenuate the harmful effect of slum residency on infant mortality but antenatal care coverage among slum women remains relatively low. Improving the material circumstances of slum neighborhoods as well as increasing antenatal care coverage among slum women could help reduce stunted child growth and infant mortality associated with slum residency.

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Table 1. Sample characteristics in 45 countries

Level 3, countries (n)	45
GDP *Mean* (SD)	2658 (2713)
Mean number of clusters per country (SD)	290 (426)
Mean number of children per country (SD)	2666 (2885)
Level 2, clusters (n)	13,056
Mean number of children per cluster (SD)	9.2 (7.7)
Slum neighborhood (at least two components) (%) (min, max)	12.1 (0.2-61.3)
Slum neighborhood (at least one component) (%) (min, max)	55.8 (13.7-94.2)
Level 1, children (n)	119,988
Infant mortality (%)	3.4
% Stunting (N=83956, 43 countries)	26.0
Slum household (at least two components) (%) (min, max)	17.7 (0.1, 50.5)
Slum household (at least one component) (%) (min, max)	54.8 (23.4, 89.0)
Household wealth *Mean* (SD)	0.7(2.5)
Maternal education (yrs)	7.3 (4.9)
Maternal height-for-age (N=91538) *Mean* (SD)	-1.2(1.2)
Missing data for maternal height (%)	25.4
Antenatal care (Overall sample) (%) None	7.3
1-3 visits	19.0
4 or more visits	73.7
Missing data for antenatal care (%)	24.6
Antenatal care (residents of slum neighborhood only) (%) None	18.1
1-3 visits	27.9
4 or more visits	54.0
Antenatal care (residents of non-slum urban areas only) (%) None	6.0
1-3 visits	17.5
4 or more visits	76.5
Place of delivery (%) At home and no skilled assistance	15.5
At home with skilled assistance	3.9
At health facility	80.6
Birth order (%) First born	30.6
2-3 born	41.1
4-5 born	17.1
6+ born	11.3

Table 1. (continued)

Previous birth interval (%) <19 mths	7.2
19-35 mths	27.3
≥35 mths	34.9
Maternal age at child birth (%) <20 yrs	15.6
20-24 yrs	30.8
25-29 yrs	26.1
30-34 yrs	16.5
≥35 yrs	11.0
Male child (%)	51.4
Multiple births (%)	2.3
Child age (yrs) *Mean* (SD)	2.4(1.4)
Duration of residence <4 yrs	26.0
5-14 yrs	28.6
15 yrs or more	45.5

Table 2. Odds ratios and 95%CIs for infant mortality associated with slum residency after adjusting for covariates

	Model 1 OR (95%CI)	Model 2 OR (95%CI)
Fixed effects Intercept (SE)	-3.49(0.07)***	-3.50(0.11)***
Study variables Level 2 (Cluster) Slum neighborhood	1.32(1.19-1.46)***	1.24(1.09-1.41)**
Level 1 (Child) Slum household	1.26(1.15-1.38)***	1.04(0.94-1.15)
Covariates Level 3 (country) GDP rescale		0.94(0.89-0.99)*
Level 1 (child) Household wealth		0.96(0.94-0.98)**
Maternal education (yrs)		0.97(0.96-0.98)***
Maternal height		0.93(0.90-0.97)***
Maternal height (missing data)		1.17(1.04-1.31)**
Antenatal care No		Ref.
1 to 3 visits		0.82(0.70-0.97)*
4 or more visits		0.69(0.60-0.80)***
Antenatal care (missing) No		Ref.
Yes		1.67(1.46-1.90)***
Place of delivery At home and no skilled assistance		Ref.
At home with skilled assistance		0.90(0.75-1.07)
At health facility		0.95(0.86-1.05)
Birth order First born		Ref.
2-3 born		0.80(0.72-0.89)***
4-5 born		0.90(0.79-1.03)
6+ born		0.94(0.80-1.10)
Previous birth interval 19-35 mths		Ref.
<19 mths		1.85(1.65-2.08)***
≥35 mths		0.93(0.85-1.02)

Table 2. (continued)

	Model 1 OR (95%CI)	Model 2 OR (95%CI)
Maternal age at child birth <20 yrs		Ref.
20-24 yrs		0.88(0.78-0.98)*
25-29 yrs		0.89(0.79-1.01)
30-34 yrs		0.99(0.85-1.14)
≥35 yrs		1.24(1.05-1.47)**
Male child No		Ref.
Yes		1.24(1.16-1.32)***
Multiple birth Singleton		Ref.
Multiple birth		3.59(3.16-4.08)***
Duration of residence ≥15 yrs		Ref.
<4 yrs		0.54(0.49-0.60)***
5-14 yrs		0.93(0.86-1.01)
Interactions Slum neighborhood*ANC 1 to 3 visits		0.79(0.63-0.99)*
Slum neighborhood*ANC ≥4 visits		0.88(0.73-1.07)
Random effects		
Level 3 (country) Variance intercept (SE)	0.22(0.05)***	0.17(0.04)***
Level 2 (cluster) Variance intercept (SE)	0.27(0.03)***	0.37(0.04)***

*p<0.05, **p<0.01, ***p<0.001

Table 3. Odds ratios and 95%CIs for child stunting associated with slum residency after adjusting for covariates

	Model 1 Coefficient (95%CI)	Model 2 Coefficient (95%CI)
Fixed effects Intercept (SE)	-1.25(0.08)***	-1.19(0.09)***
Study variables Level 2 (Cluster) Slum neighborhood	1.28(1.20-1.37)***	1.04(0.97-1.11)
Level 1 (Child) Slum household	1.49(1.42-1.57)***	1.13(1.07-1.19)***
Covariates Level 3 (country) GDP rescale		0.91(0.87-0.96)***
Level 1 (child) Household wealth		0.91(0.90-0.92)***
Maternal education (yrs)		0.96(0.96-0.96)***
Maternal height		0.70(0.69-0.71)***
Maternal height (missing data)		1.35(1.14-1.60)***
Antenatal care No		Ref.
1 to 3 visits		0.86(0.80-0.93)***
4 or more visits		0.79(0.74-0.85)***
Antenatal care (missing data) No		Ref.
Yes		0.77(0.71-0.83)***
Place of delivery At home and no skilled assistance		Ref.
At home with skilled assistance		0.93(0.84-1.02)
At health facility		0.82(0.78-0.87)***
Birth order First born		Ref.
2-3 born		1.34(1.27-1.41)***
4-5 born		1.53(1.43-1.64)***
6+ born		1.77(1.62-1.93)***
Previous birth interval		
19-35 mths		Ref.
<19 mths		1.19(1.11-1.27)***
≥35 mths		0.79(0.76-0.83)***

Table 3. (continued)

	Model 1 Coefficient (95%CI)	Model 2 Coefficient (95%CI)
Maternal age at child birth <20 yrs		Ref.
20-24 yrs		0.82(0.78-0.87)***
25-29 yrs		0.72(0.68-0.77)***
30-34 yrs		0.66(0.61-0.71)***
≥35 yrs		0.62(0.56-0.67)***
Male child No		
Yes		1.24(1.20-1.29)***
Multiple birth Singleton		
Multiple birth		1.88(1.68-2.11)***
Duration of residence ≥15 yrs		Ref.
<4 yrs		1.00(0.95-1.04)
5-14 yrs		0.97(0.93-1.01)
Child age (yrs)		1.08(1.07-1.10)***
Interactions Slum neighborhood*child age		1.12(1.08-1.16)***
Slum household*child age		1.10(1.06-1.14)***
Random effects Level 3 (country) Variance intercept (SE)	0.28(0.06)***	0.22(0.05)***
Level 2 (cluster) Variance intercept (SE)	0.34(0.02)***	0.23(0.01)***

*p<0.05, **p<0.01, ***p<0.001

Fig.1. Interaction between slum neighborhood and antenatal care (1-3 visits) on infant mortality

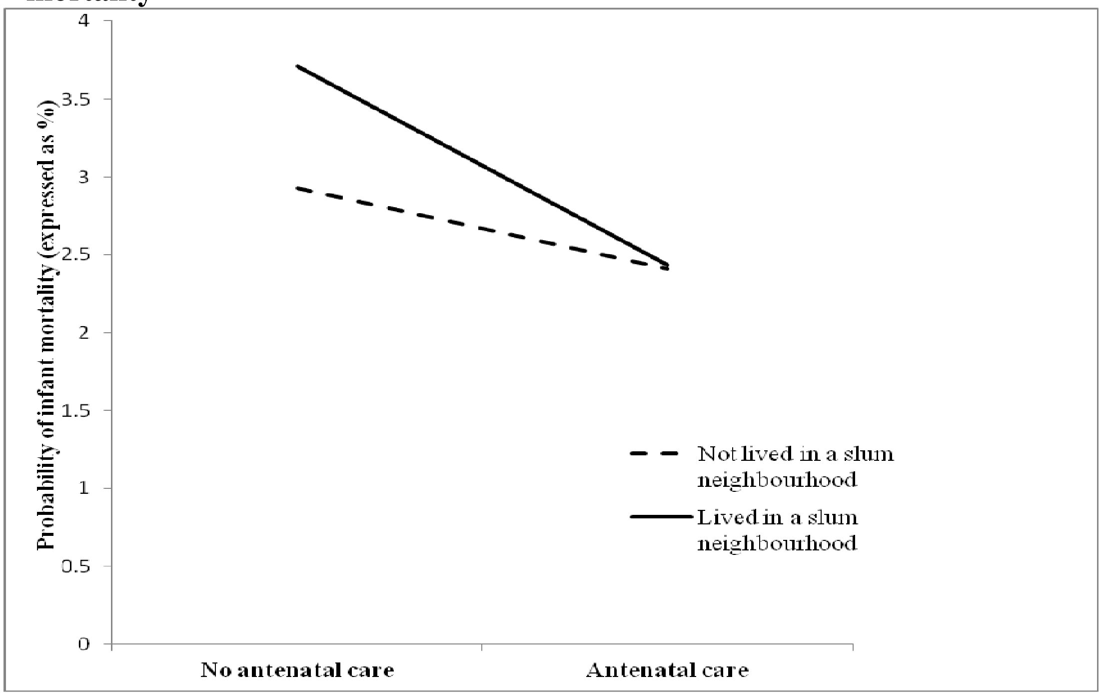


Fig. 2. Interaction between slum neighborhood and child age on stunting

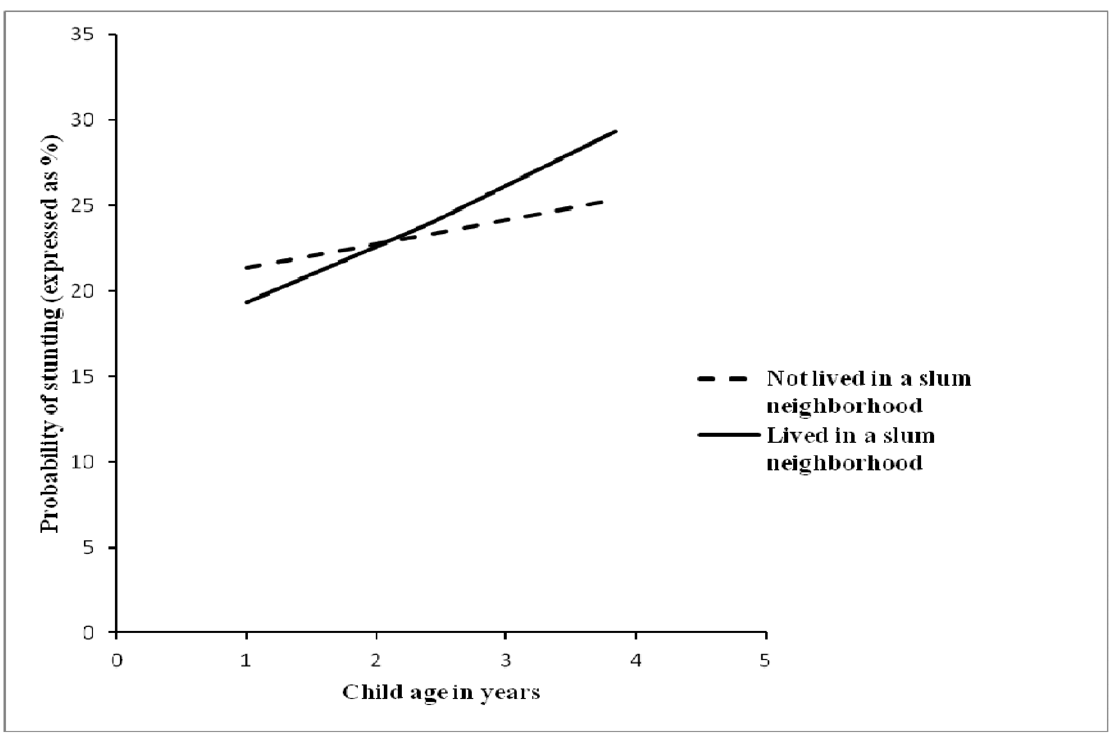
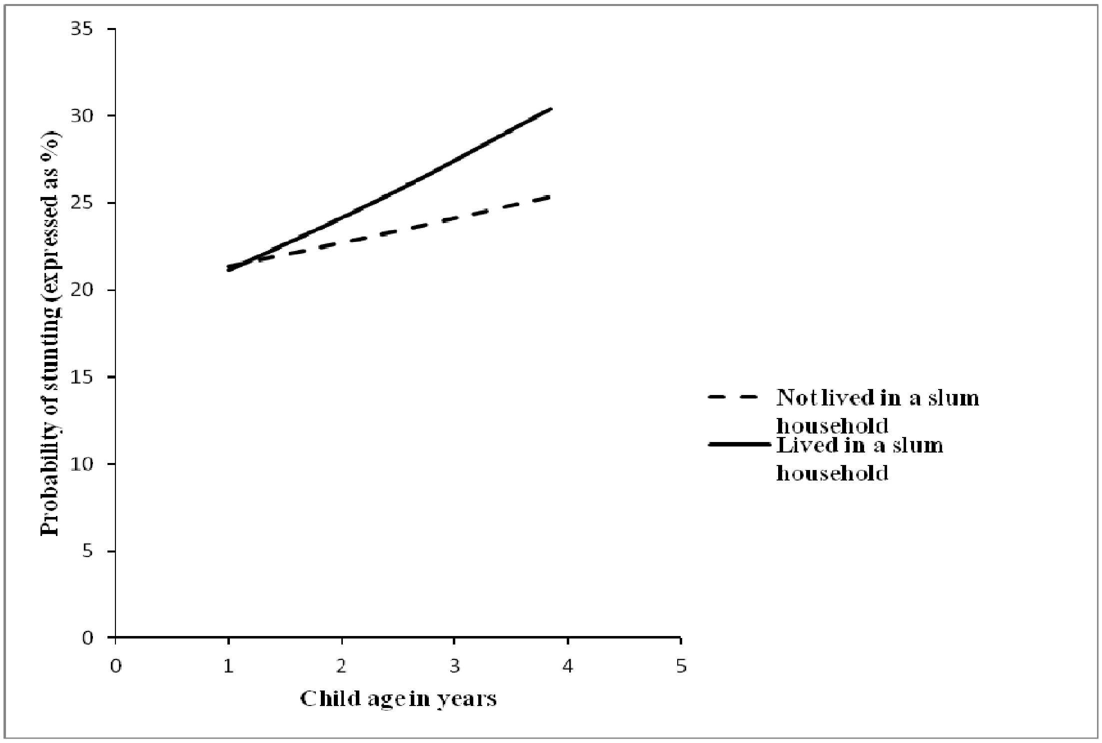


Fig. 3. Interaction between slum household and child age on stunting



CHAPTER 3

Cesarean Section and Neonatal Mortality in 46 Low and Middle Income Countries

Abstract

Background: The rationale for this study arises from the conflicting results and methodological weaknesses of previous research examining the association between cesarean section (CS) and neonatal mortality. The objectives of this study were: (1) to use propensity score matching to estimate the association between individual-level CS and neonatal mortality in 46 countries; (2) to conduct a meta-analysis of the associations between individual-level CS and neonatal mortality across countries; (3) to perform a meta-regression to examine if the association between individual-level CS and neonatal mortality across countries varies depending on country-level CS rates and gross domestic product per capita (GDP).

Methods and Findings: Data were from nationally representative Demographic and Health Surveys. Participants were women aged 15-49 years and their children (0-59 months) (N=392883). The main outcome measure was neonatal mortality based on maternal report. Results showed that the pooled odds ratio (OR) for the association between individual level CS and neonatal mortality in 46 countries was 1.67 (95%CI=1.48-1.89) with moderate heterogeneity (I^2=39%). Sub-group meta-analysis results indicated that individual-level CS was associated with neonatal mortality in countries with low (OR=1.99, 95%CI=1.71-2.33, I^2=8.5%) and medium (OR=1.53, 95%CI=1.29-1.82, I^2=24%) CS rates while the association for high CS rate countries (OR=1.31, 95%CI=0.97-1.76, I^2=63%) verged on statistical significance. Meta-regression results showed that the association between individual-level CS and neonatal mortality depends on country-level CS rates. Compared with high CS rate countries, the odds ratio of neonatal mortality associated with individual-level CS was estimated to increase by a factor of 1.48 (95% CI=1.09, 1.97) in low CS-rate countries.

Conclusions: Further studies are necessary to explore possible reasons for the elevated risk of neonatal mortality associated with individual-level CS in low and medium CS rate countries. Studies to evaluate the quality of maternal and newborn health care services are also needed in those countries.

Introduction

The cesarean section (CS) rate, defined as the proportion of all deliveries by CS in a geographical area, has been selected as an indicator of access to life-saving services for both mothers and newborns (World Health Organization, 2009). CS rates vary widely among countries in the world, ranging from 0.4 to 40% of births (Althabe et al., 2006). Both very low and very high CS rates can be harmful (World Health Organization, 2009): the former may reflect women's lack of access to life-saving care while the latter may indicate overuse of the procedure with attendant unnecessary surgical risk (World Health Organization, 1994). The recommended lower and upper limits for CS are 5 and 15% but there is no empirical evidence that these rates are optimal (World Health Organization, 1994, 2009).

The rationale for this study arises from the conflicting results and methodological weaknesses of previous research. For example, the two ecological studies (Althabe et al., 2006; Betran et al., 2007) available for review generated different findings for countries with relatively high CS rates: one study (Althabe et al., 2006) reported that there was no association between CS rates and neonatal mortality in medium and high income countries where CS rates are mostly >10% while another study (Betran et al., 2007) found that CS rates were positively associated with neonatal mortality in countries with CS rates >15%. Ecological studies contain" only marginal observations on the joint distribution of individually defined confounders and outcomes, and so identify neither contextual nor individual-level effects" (Greenland, 2001). This limitation can be addressed by multilevel study designs which integrate individual and group-level data

(Greenland, 2001). Studies based on individual-level data (Kallen & Olausson, 2007; Lumbiganon et al., 2010; MacDorman, Declercq, Menacker, & Malloy, 2006, 2008; Villar et al., 2007) have also reported conflicting results on the association between individual-level CS and neonatal mortality. Among individual-level studies that sampled from multiple countries (Lumbiganon et al., 2010; Villar et al., 2007), there was no attempt to account for country-level factors even though the association between individual-level CS and neonatal mortality maybe conditional on country-level CS rate or country-level income (i.e., cross-level interaction). In countries with very low CS rates, poverty and clinical inexperience might exacerbate the risk of neonatal mortality associated with individual-level CS while in countries with higher CS rates, this risk might be attenuated by expertise, affluence and resources.

In observational studies, factors which influence exposure may also influence the outcome of interest. Women with high risk pregnancies are more likely to undergo CS and these risks, in turn, may affect the probability of neonatal mortality. The use of propensity score matching is one approach to addressing this potential problem of unequal chances of receiving the procedure (Braitman & Rosenbaum, 2002). The propensity score (Rosenbaum & Rubin, 1983, 1985) is the conditional probability of assignment to a particular group given a set of observed covariates: it is intended to mimic the allocation of subjects in a randomized trial so that the groups being contrasted (eg. CS versus vaginal delivery) are comparable on important observed prognostic characteristics.

There are a number of prognostic factors that could help identify women who are more likely to undergo CS and/or at high risk for neonatal death. For example, short maternal stature (height <150-155 cm) is associated with CS delivery (Kirchengast & Hartmann, 2007; Sheiner, Levy, Katz, & Mazor, 2005) and increases the risk for obstructed labour (Sheiner et al., 2005; World Health Organization, 2006), intrauterine growth restriction, premature rupture of membranes, failed induction, labor dystocia and mal-presentations (Sheiner et al., 2005). Increasing maternal age has been found to be associated with a longer duration of labour (Smith et al., 2008) and an increased risk for cesarean delivery (Khawaja & Al-Nsour, 2007; Scioscia et al., 2008; Smith et al., 2008) as a result of impaired uterine function (Smith et al., 2008). Inter-pregnancy intervals (birth intervals) shorter than 18 months and longer than 59 months have been associated with increased risk of adverse perinatal outcomes (e.g. preterm birth, low birth weight and small for gestational age) according to a meta-analysis of studies from both developed and developing countries (Conde-Agudelo, Rosas-Bermudez, & Kafury-Goeta, 2006). The same study reported that birth intervals shorter than 6 months and longer than 50 months are associated with increased risk of early neonatal death (Conde-Agudelo et al., 2006). Short birth intervals have also been associated with uteroplacental bleeding disorders (placental abruption and placenta previa) (Conde-Agudelo, Rosas-Bermudez, & Kafury-Goeta, 2007), which are obstetrical emergencies of pregnancy while long birth intervals have been linked to an increased risk of pre-eclampsia and labor dystocia (Conde-Agudelo et al., 2007), which are common indications of CS (Penn & Ghaem-Maghami, 2001; Villar et al., 2007).

Although a randomized controlled trial would address concerns about comparability of the groups on observed and unobserved prognostic features, randomizing women into CS and vaginal delivery groups would face strong ethical objections, insurmountable barriers to enlistment and concerns about cross-country generalizability. Given these challenges, secondary analyses of existing nationally representative databases such as Demographic and Health Surveys provide a viable option for studying the effects of CS if the issue of comparability – a general weakness of observational studies – can be addressed analytically and properly evaluated using sensitivity analyses. The objectives of this study are thus: (1) to use propensity score matching to estimate the association between individual-level cesarean section (CS) and neonatal mortality in 46 countries; (2) to conduct a meta-analysis of the associations between individual-level CS and neonatal mortality across countries; (3) to perform a meta-regression to examine if the association between individual-level CS and neonatal mortality across countries varies depending on country-level CS rates and gross domestic product per capita (GDP).

Methods

Data were from nationally representative DHS conducted in 46 developing countries between 2001 and 2008 and having the requisite data (see Table 2 for the countries). We briefly outline the DHS methodology here. Study details are available at (http://www.measuredhs.com/What-We-Do/methodology.cfm) (Measure DHS, n.d) . The DHS sampling frame is a list of non-overlapping area units (enumeration areas) that cover the entire country and serve as the primary sampling units or clusters. In the selected clusters, all households are listed and a fixed proportion is selected by systematic sampling. Eligible persons include all women aged 15-49 years in selected households and their children (0-59 months) and interviews are conducted with these women about maternal and child health. The response rates went from 90% in Zimbabwe to 98% in Cambodia.

Concepts and measures

Dependent variable

Neonatal Mortality. This measure indicates whether a child survived his or her first 30 days of life and is a binary outcome variable. DHS collected information from mothers about all of their biological children's months and years of birth and whether a child born in the 5 years before the survey was alive or dead at the time of interview. Mothers reported the age of the child if s/he was alive and age at death if applicable. The survival status of each child between birth and 1 month of age was determined from this information.

Independent variable

Cesarean section. Respondents were asked whether a child born in the five years before the survey was born by CS. This variable was coded as (0, vaginal delivery versus 1, CS).

Selecting covariates for the propensity score model

There is no consensus on whether to include variables that are highly associated with treatment assignment or the outcome in propensity score models (Austin, 2007; Brookhart et al., 2006; Lunceford & Davidian, 2004; Rubin & Thomas, 1996). Millimet and Tchernis (2009) suggested that overfitting propensity score models may have little negative impact on treatment effect estimates or may even result in more efficient estimates.

In this study we selected the covariates that are likely associated with the CS or neonatal mortality or both. These include: household wealth (wealth index), number of antenatal visits, mother's education in years, maternal age at birth of child in years, maternal height-for-age, birth order of the child, previous birth interval, birth size, child gender and urban/rural residence.

We used the *wealth index* (Filmer & Pritchett, 2001; Gwatkin, Rutstein, Johnson, Pande, & Wagstaff, 2000) variable already available in each DHS dataset. It has been shown to be a good proxy for long-run household wealth (Filmer & Pritchett, 1999; Filmer & Pritchett, 2001). It was derived from an index (generated through principal component analysis) of household assets that included televisions, bicycles, type of fuel used for cooking, type of material used for flooring, and water and sanitation facilities, etc. depending on the specific questions asked in each country. The index was standardized to a mean of 0 and a standard deviation of 1 and higher scores refer to greater wealth.

Number of antenatal visits. Women were asked whether they had received antenatal consultation from a health professional (doctor, nurse, or midwife) during the antenatal period. They were also asked the total number of antenatal visits during pregnancy. The variable used in this study reflects the number of visits reported by women who had received at least one antenatal consultation from a health professional. If women received antenatal care from a non-health professional, it was coded as zero in the 'number of antenatal visits' variable.

Maternal height-for-age. DHS measured maternal heights using a standardized measuring board and calculated height for age standard deviations from the reference median based on the CDC Standard Deviation-derived Growth Reference Curves (DHS recode manual, 2008). For all women aged 18 years and over, the value of 215 months (17 years, 11 months) was used for their age, assuming that women have grown fully by the age of 18.

Birth size. The mother's recall of the child's size at birth was used as a substitute for the child's birth weight in this study because 53% of data for the latter were missing. The child's estimated birth size and birth weight in the included DHS countries were correlated at $r=0.58$, $p<0.001$. Birth size was categorized as: smaller than average, average and larger than average.

Country-level variables

GDP. At the national level, GDP is gross domestic product per capita converted to constant 2005 international dollars based on purchasing power parity (The World Bank, n.d.).

CS-Rates. The country-level CS rates were obtained by aggregating individual-level CS up to the country level. They were then stratified as low (<5%), medium (5-15%), and high (>15%) CS rates.

Data Analysis

The analysis was restricted to singleton births representing 97.5% of all births. We excluded multiple births to improve the comparability of groups. Birth size data were not collected in Bangladesh and Colombia: the birth size variable was therefore not included in estimation of propensity scores in these two countries. Antenatal care data were collected only for the most recent birth (27.8% of data were missing for older children). For the analyses, we created a dummy variable to indicate if information on the antenatal care variable was available (1=missing; 0=not missing). In our descriptive analyses, country-specific sample weights were used for all estimates (except for the aggregated ones) to ensure that the findings are nationally representative.

In our inferential analyses, first, propensity score matching was performed in each country to estimate the odds ratios of neonatal mortality associated with individual-level CS. Second, meta-analysis was conducted to obtain summary odds ratios of the association. Third, meta-regression was carried out to examine if the effect of individual-level CS on neonatal mortality depends on country-level CS rates and GDP.

Propensity score matching

Propensity scores were estimated from a logistic regression model that included all covariates and quadratic terms for continuous covariates. A propensity score for each infant in the dataset represents that particular infant's conditional probability of being delivered by CS given the observed covariates. The PSMATCH2 Stata module (Leuven & Sianesi, 2003) was used to conduct radius matching within caliper distance of 0.01 on the probability scale. Rosenbaum and Rubin (1985) suggested using a caliper distance of ≤0.25 standard deviation (SD) of the estimated propensity scores of the sample. (In this study, the SD of the propensity score was 0.12 and the chosen caliper distance 0.01 was less than a quarter of the SD.) All comparison infants within the caliper distance from CS infants were considered a match.

Matching with replacement was used because it minimizes the propensity score distance between the matched comparison units and the treatment unit and is beneficial in bias reduction (Dehejia & Wahba, 2002). Unmatched cases (N=202) and unmatched controls (N=19153) were dropped from the analyses. The final sample for analysis includes 392,883 children.

The effect of individual-level CS on neonatal mortality was estimated for each country using a logistic regression model, adjusting for the covariates (Stuart & Green,

2008) to control for the remaining minor differences in the matched sample and adjusting for clustering within matched pairs (Austin, 2009).

Assessing the quality of matching

The "pstest" command (Leuven & Sianesi, 2003) in Stata was used to check covariate balance after propensity score matching in each country. It provides t-tests for equality of means in the individual-level CS and vaginal delivery groups, both before (unweighted) and after (weighted using the matching weight) matching. In the matched sample, there were no significant differences in any covariate between the two groups in each country. A sample checking of quality of matching in one of the included countries (Cameroon) is presented in Supplemental Material, Table S-1.

Meta-analysis

Meta-analysis and subgroup meta-analyses were conducted in STATA IC (version 12) using the 'meta' command (Sharp & Sterne, 1997, 1998a, 1998b). Random effects models were chosen to allow for between-country variation of odds ratios.

Meta-regression

In meta-regression, the country is the unit of analysis and the outcomes are log odds ratios of neonatal mortality based on individual-level data in 46 countries. The independent variables are country-level CS rates and GDP. A significant association between an independent variable (e.g. country-level CS rates) and the outcome indicates that the treatment effect depends on country-level CS rates. Meta-regression was conducted in STATA by using the 'metareg' command (Harbord & Higgins, 2008; Sharp, 1998).

Sensitivity Analyses

We checked the sensitivity of our results to hidden bias using the bounding approach suggested by Rosenbaum (2002) and the mhbounds package developed by Becker and Caliendo (2007). The sensitivity analysis does not indicate the existence of hidden bias but it shows how large the bias would need to be to cancel out the observed CS effect by providing a test statistic called gamma, which is the "odds ratio of differential treatment assignment due to unobserved factors". In this approach, the threshold value of gamma was calculated at the point where hidden bias would render the estimated CS effect statistically non-significant. The closer the threshold value of gamma is to 1 (e.g. <1.05), the more likely it is that the effect can be explained away by an unobserved factor (Minnesota Department of Corrections, 2010). A threshold value of gamma between 1.25 and 1.30 can be considered relatively robust to bias due to unobserved factors (Caliendo et al., 2005). A threshold value of gamma=1.50 could be considered very robust, particularly when a study is able to match on many important observed covariates. In addition, the effect of the unobserved variable (that causes a 50% difference in the odds of receiving CS) on the outcome (i.e., neonatal mortality) would need to be so strong that it almost predicts the outcome perfectly in each pair of matched cases in the data (Caliendo et al., 2005).

Results

Table 1 presents the sample characteristics. The number of countries that fall within the low, median and high CS-rates groupings were 27, 13 and 6 respectively. Among all children, 7.7% were delivered by CS and 3% died during the neonatal period.

Table 2 presents the odds ratios and 95% CIs for neonatal mortality associated with CS in each of the 46 countries, grouped by CS rate. The pooled odds ratio (OR) for the association between individual-level CS and neonatal mortality in 46 countries was 1.67 (95%CI=1.48-1.89) with moderate heterogeneity (I^2=39.4%, p=0.004) (not shown). The subgroup meta-analysis results (Table 2 and Figures 1-3) showed that individual-level CS was positively associated with neonatal mortality in countries with low (pooled OR= 1.99, 95%CI=1.71-2.33, I^2=8.5%) and medium (pooled OR=1.53, 95%CI=1.29-1.82, I^2=24%) CS rates but the association for high CS rate countries (pooled OR=1.31, 95% CI=0.97-1.76, I^2=63%) verged on statistical significance. There was significant heterogeneity in ORs among high CS rate countries ranging from 0.53(95% CI=0.20-1.38) in Turkey to 2.40(95% CI=1.56-3.71) in Jordan.

Table 3 presents the meta-regression results. Model 1 shows that the association between individual-level CS and neonatal mortality depends on country-level CS rates: the log odds ratio of neonatal mortality associated with individual-level CS was estimated to increase by 0.39 units (95% CI= 0.09, 0.68) (equivalent to an odds ratio of 1.48 (95% CI=1.09, 1.97) in low CS rate countries compared with high CS rate countries. When GDP was included in Model 2, there was no significant association between GDP and log odds ratios of neonatal mortality. The association between low country-level CS rate and log odds ratios was still significant after including GDP.

Sensitivity analysis results showed the following gamma threshold values for countries with low (gamma=1.80), medium (gamma=1.15), and high (gamma=1.00) CS rates. In countries with low CS rates, inference about the association between individual-level CS and neonatal mortality would not be changed even if there is a hidden bias up to a degree that two matched individuals differ in their odds of receiving CS by 80% due to hidden bias, while in countries with medium CS rates, the association was more sensitive to hidden bias. In countries with high CS rates, even under the assumption of no hidden bias, the association between CS and neonatal mortality would be statistically non-significant.

Discussion

This study found positive associations between individual-level CS and neonatal mortality in countries with low, medium and high CS rates. These associations were statistically significant in low and medium CS-rate countries, and insensitive to hidden bias in low CS-rate countries. In high CS-rate countries, the association verged on statistical significance. In addition to evidence that the association between individual-level CS and neonatal mortality depended on country-level CS-rates, there was substantial cross-country heterogeneity in the associations between individual-level CS and neonatal mortality, particularly among countries with higher CS rates.

This study is the first of its kind to: (1) estimate the strength of association between CS and neonatal mortality using integrated country and individual-level data, (2) mimic randomization using propensity score matching based on observed prognostic variables, (3) perform sensitivity analysis to estimate the boundary where unobserved factors could account for the findings, and (4) test the moderating influence of country-level CS rates on the relationship between individual-level CS and neonatal mortality. Although the large diverse sample representing 46 countries is an important strength of this study, we have only six countries in the high CS rate category. These six countries exhibited significant heterogeneity in the association between individual CS and neonatal mortality and their pooled estimate should be interpreted with caution. Although propensity score matching provides a rigorous approach to ensure group equivalence on observed prognostic variables, limited information on specific maternal and neonatal risk factors in DHS forced us to restrict the analyses to singleton births and to use proxy variables (e.g. short maternal stature, maternal age at child birth, inter-pregnancy intervals, and birth order of the child) to develop propensity scores. One or more of these proxy variables have been linked to an extensive array of risk factors for CS and/or neonatal mortality ranging from obstetrical emergencies of pregnancy (placental abruption and placenta previa) to common indications for CS (obstructed labor, pre-eclampsia, labor dystocia, and malpresentations) and adverse perinatal outcomes (preterm birth, low birth weight, small for gestational age and early neonatal death) (Conde-Agudelo et al., 2006, 2007; Gubhaju, 1985; Khawaja & Al-Nsour, 2007; Khawaja, Kabakian-Khasholian, & Jurdi, 2004; Scioscia et al., 2008; Sheiner et al., 2005; Smith et al., 2008; World Health Organization, 2006). Other variables included in our propensity score model (e.g. household wealth, antenatal care, mother's education, and urban/rural residence) have also been reported by previous studies as important determinants of CS (Arrieta, 2011; Khawaja & Al-Nsour, 2007; Khawaja et al., 2004). Based on our 'reasonable' confidence in the proxy variables, our successful matching and the results of our sensitivity analysis, we believe that the CS effects observed in low CS-rate countries are very robust.

Previous population-based studies on CS effects (Althabe et al., 2006; Betran et al., 2007; Kallen & Olausson, 2007; Lumbiganon et al., 2010; MacDorman et al., 2006, 2008; Villar et al., 2007) are limited in number, scope and methodology. In estimating CS effects, the integration of both country and individual-level data combined with propensity score matching to control for selection factors are strengths of the present study not reflected in previous research. Ecological studies have suggested that country-level CS rates or country-level income may condition risk for neonatal mortality (Althabe et al., 2006; Betran et al., 2007). Our study shows that the association between individual-level CS and neonatal mortality does depend on country-level CS rates but not GDP. Compared with high CS rate countries, the odds ratio of neonatal mortality associated with individual-level CS was estimated to increase by a factor of 1.48 in low CS-rate countries. In attempting to understand CS effects at the individual level, it is important to consider overall practice levels within countries and to be aware of between-country heterogeneity in risks for neonatal mortality associated with CS. Indeed, the inconclusive findings from previous studies based on individual-level data (Kallen & Olausson, 2007; Lumbiganon et al., 2010; MacDorman et al., 2006, 2008; Villar et al., 2007) are most likely a reflection of the between-country differences in CS effects observed here.

Our study has important implications. In countries with very low CS rates, it is likely that many women who could benefit from a CS did not receive one (Althabe et al., 2006) while those who underwent the procedure may have placed their newborn at elevated risk of death. About 78% of countries with low CS rates in our study were from sub-Saharan Africa. In many sub-Saharan African countries, coverage in the provision of maternal and newborn health care services is inadequate and of poor quality (Bryce et al., 2008; Kinney et al., 2010). There are also inadequacies in the monitoring of pregnancy and labour, identifying complications, and providing timely life-saving interventions (Hofmeyr et al., 2009). Strategies are needed to increase the coverage of maternal and newborn health care services and improve the quality of those services. Although the risk of neonatal death associated with CS is lessened among countries with higher CS rates, the associations remained positive and retained statistical significance among countries with CS rates in the recommended range between 5-15%. Programs to evaluate the quality of maternal and newborn health care services are needed in countries with CS rates both below and within the recommended range. The striking between-country heterogeneity in the strength of association between CS and neonatal mortality in high CS-rate countries should focus the attention of health policy analysts on this issue within their own country. In some high CS-rate countries, practices associated with CS can not only increase the risk of neonatal death but also add to the burden of health care costs. In those countries, in addition to improving the quality of health care services, it is imperative to define and abide by the clinical indications for CS to avoid exposing mothers and their babies to unnecessary risk. Available evidence suggests that physicians might use looser diagnostic criteria for common indications of CS rather than following recommended criteria. For example, a study conducted among patients who underwent CS in four hospitals in Colombia reported that about 84% of patients diagnosed with dystocia and 63% with breech presentations did not meet the criteria of justified CS (Gomez & Carrasquilla, 1999). In the World Health Report (2010), it was estimated that 6.2 million unnecessary CS were carried out in middle and high income countries during 2008 if 15% was used as a threshold rate of CS overuse. The estimated cost of this global "excess" CS was approximately U$ 2.32 billion (Gibbons et al., 2010).

Our study raises several unanswered questions. What are the factors associated with CS that increase risk for neonatal death especially in low and medium CS-rate countries? In low CS-rate countries, to what extent are women who would benefit from a CS being denied this procedure? Are there national-level phenomena that explain cross-country differences in the strength of association between CS and neonatal death especially in high CS rate countries? The CS 'problem' is an important, poorly understood multifaceted challenge to address. The high cost, increased reliance on and potential adverse effects associated with CS provide a strong rationale for addressing these questions in future studies.

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Table 1. Sample characteristics in 46 countries

Countries (n)	46
CS rates *n* (%)	
Low (<5%)	27 (58.7)
Medium (5-15%)	13 (28.3)
High (>15%)	6 (13.0)
GDP *Mean* (SD)	2478 (2626)
Children (n)	392883
Neonatal death (%)	3.0
CS (%)	7.7
Urban (%)	33.6
Birth size (%)	
Smaller than average	17.6
Average	44.9
Larger than average	33.7
Male child (%)	51.4
Number of antenatal visits *Mean* (SD)	2.9(3.5)
Missing data for antenatal care (%)	28.7
Household wealth *Mean* (SD)	-0.2(0.01)
Maternal education (years) *Mean* (SD)	4.4(4.6)
Maternal height *Mean* (SD)	-1.0 (1.2)
Maternal age at child birth *Mean* (SD)	26.2 (6.6)
Birth order *Mean* (SD)	3.3(2.3)
Previous birth interval in years *Mean* (SD)	2.4 (2.3)

Table 2. Odds ratios (OR) and 95%CIs for neonatal mortality associated with CS in 46 countries

Countries	OR (95% CI)
Low CS rate countries	
Azerbaijan	1.00 (0.29- 3.50)
Benin	2.40 (1.50- 3.84)
Burkina Faso	1.74 (0.55- 5.48)
Cambodia	2.36 (0.89- 6.28)
Cameroon	0.49 (0.12- 2.02)
Chad	2.01 (0.59- 9.37)
Congo-Brazzaville	3.08 (1.49- 6.36)
Congo DR	1.69 (1.04-2.77)
Ethiopia	0.71 (0.21-2.42)
Gabon	1.78 (0.74- 4.27)
Guinea	1.39 (0.48- 4.00)
Haiti	2.28 (0.90- 5.74)
Liberia	1.51 (0.60-3.82)
Madagascar	0.90 (0.27- 2.96)
Malawi	1.29 (0.66- 2.49)
Mali	1.27 (0.60- 2.71)
Mozambique	1.94 (0.89- 4.24)
Nepal	0.45 (0.05- 3.76)
Niger	4.41 (2.07- 9.39)
Nigeria	2.73 (1.78- 4.21)
Rwanda	2.23 (1.24- 3.99)
Senegal	2.66 (1.47- 4.79)
Sierra Leone	1.74 (0.62- 4.91)
Tanzania	1.56 (0.78- 3.09)
Uganda	2.93 (1.57- 5.49)
Zambia	2.49 (1.29- 4.81)
Zimbabwe	1.33 (0.54- 3.29)
Pooled OR (95% CI)	**1.99 (1.71-2.33)**
Cochran heterogeneity statistic, p value	**28.43, p=0.34**
I^2 (%)[a]	**8.5**
Medium CS rate countries	
Bangladesh	1.50 (0.78- 2.88)
Ghana	1.26 (0.52- 3.10)
Honduras	2.16 (1.30- 3.60)
India	1.10 (0.90-1.35)
Indonesia	1.99 (1.30-3.06)

Table 2. (cont,)

Countries	Odds Ratios (95% CI)
Medium CS rate countries (cont.)	
Kenya	1.76 (0.95-3.27)
Lesotho	0.93 (0.39-2.27)
Morocco	1.67 (0.75- 3.70)
Namibia	1.34 (0.66- 2.72)
Nicaragua	1.84 (1.02- 3.31)
Pakistan	1.48 (0.98- 2.22)
Philippines	1.69 (0.74- 3.84)
Swaziland	2.45 (1.21- 4.98)
Pooled OR (95% CI)	**1.53 (1.29-1.82)**
Cochran heterogeneity statistic, p value	**15.85, p=0.20**
I^2 (%)[a]	**24.3**
High CS rate countries	
Bolivia	0.94 (0.59-1.50)
Colombia	1.51 (1.06- 2.16)
Dominican Republic	1.32 (0.92 -1.90)
Egypt	1.18 (0.80-1.74)
Jordan	2.40 (1.56-3.71)
Turkey	0.53(0.20- 1.38)
Pooled OR (95% CI)	**1.31 (0.97-1.76)**
Cochran heterogeneity statistic, p value	**13.61, p=0.02**
I^2 (%)[a]	**63.2**

[a] I^2 describes the percentage of total variation in ORs across countries that is due to heterogeneity rather than chance. It was calculated as $I^2 = 100\% * (Q\text{-}df)/Q$ where Q is the Cochran heterogeneity statistic (Higgins, Thompson, Deeks & Altman, 2003).

Table 3. Meta-regression with log odds ratios of neonatal mortality as dependent variable and country- level CS rates and GDP as independent variables

	Model 1 Coefficient (95% CI)	Model 2 Coefficient (95% CI)
Intercept	0.29 (0.05, 0.53)	0.26 (-0.05, 0.57)
Country-level CS rate Low	0.39 (0.09, 0.68)*	0.42 (0.03, 0.81)*
Medium	0.15 (-0.16, 0.46)	0.17 (-0.19, 0.54)
High	Ref.	Ref.
GDP (rescale)		0.01 (-0.05, 0.07)
Residual variation due to heterogeneity, I^2 (%)	25.70	26.84

*p<0.05

Figure 1. Forest plot showing odds ratios and 95% CIs of neonatal mortality in CS versus vaginal delivery groups in 27 low CS rate countries

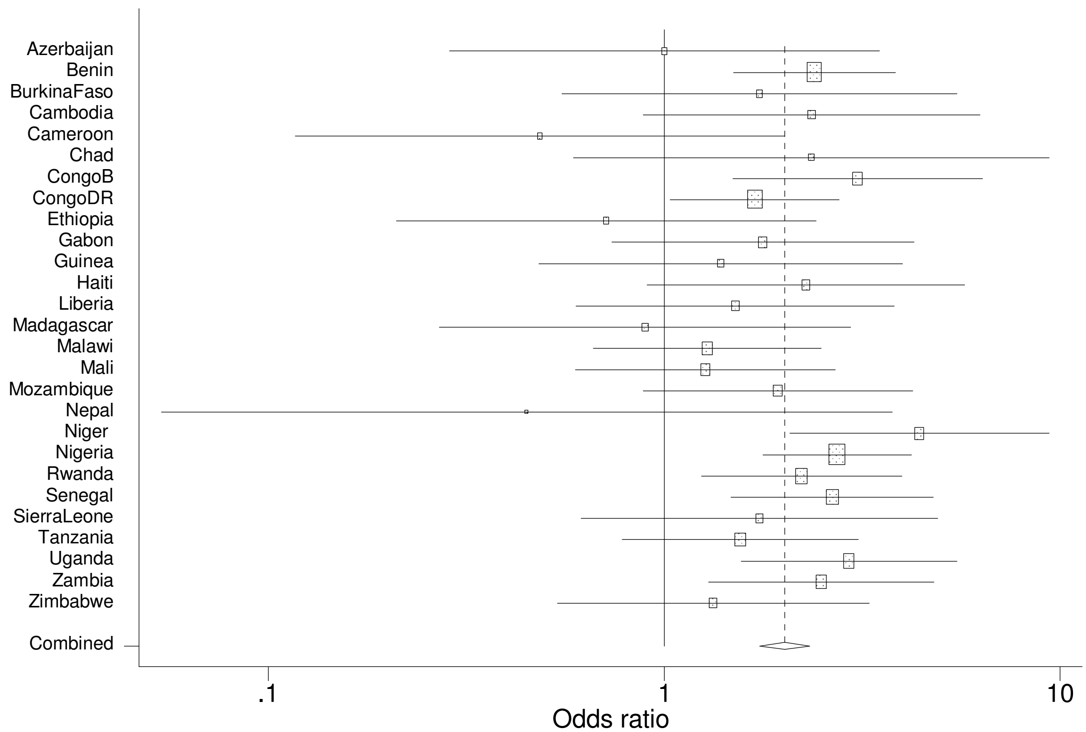


Figure 2. **Forest plot showing odds ratios and 95% CIs of neonatal mortality in CS versus vaginal delivery groups in 13 medium CS rate countries**

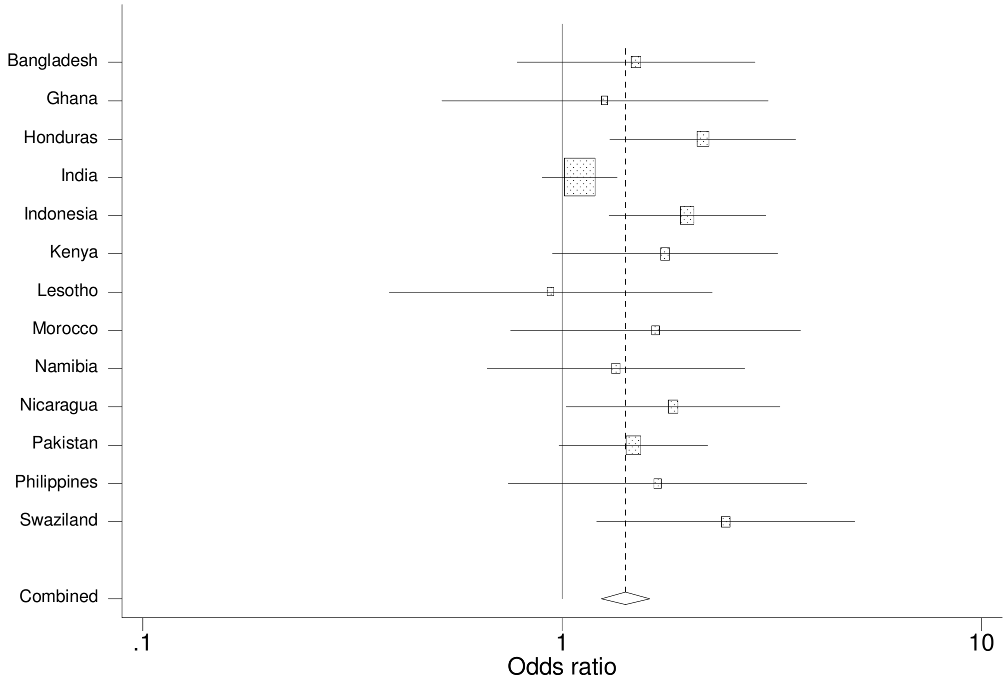
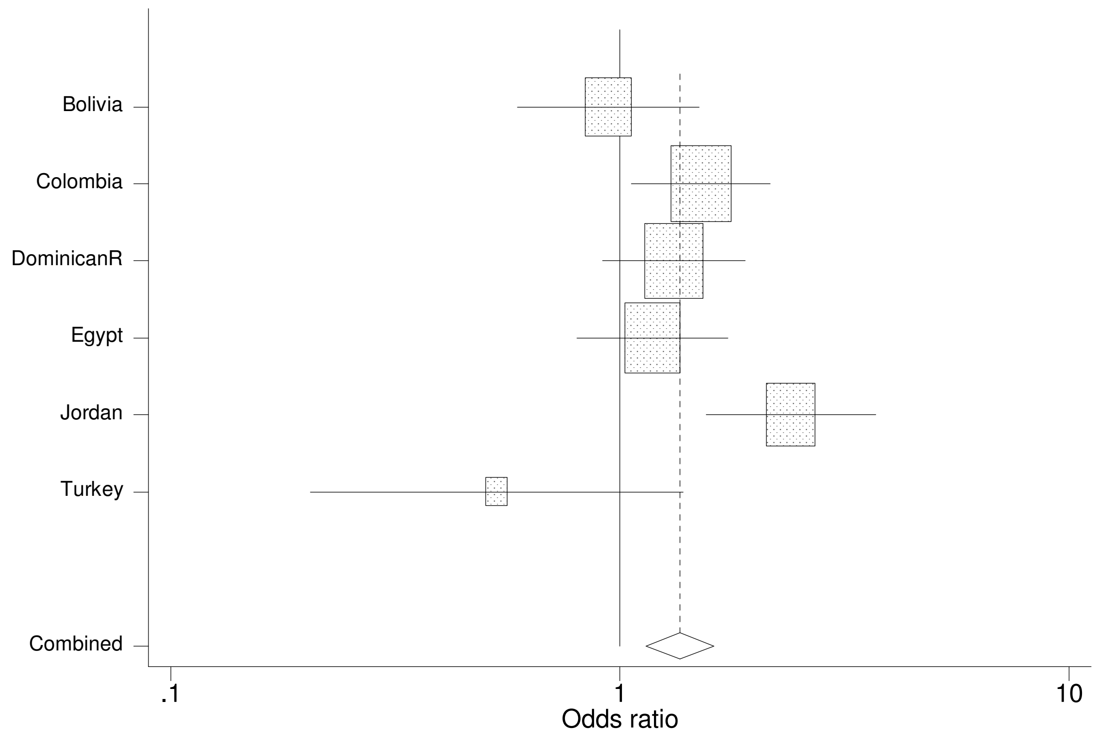


Figure 3. Forest plot showing odds ratios and 95% CIs of neonatal mortality in CS versus vaginal delivery groups in 6 high CS rate countries



Supplemental Material

Table S-1. Reduction in covariate imbalance after matching on the propensity score in one of the included countries, Cameroon[1]

Variable	Sample	CS (Mean)	VD (Mean)	% bias reduction	t
Wealth	Unmatched	0.55	-0.23		9.73***
	Matched	0.54	0.52	97.4	0.16
Wealth sq	Unmatched	1.37	0.89		4.67***
	Matched	1.33	1.34	98.2	-0.04
Urban	Unmatched	0.74	0.38		8.59***
	Matched	0.74	0.73	97.3	0.18
Maternal education	Unmatched	7.84	4.74		9.51***
	Matched	7.81	7.67	95.3	0.35
Maternal education sq	Unmatched	22.13	14.02		5.61***
	Matched	21.88	21.01	89.2	0.26
Maternal HFA	Unmatched	-0.37	-0.31		-0.84
	Matched	-0.37	-0.34	35.7	-0.35
Maternal HFA sq	Unmatched	0.95	0.74		1.50
	Matched	0.96	0.80	26.8	0.68
Maternal age	Unmatched	25.82	25.57		0.43
	Matched	25.72	25.78	86.4	0.04
Maternal age sq	Unmatched	43.42	46.03		-0.54
	Matched	42.43	42.11	87.9	0.05
Birth order	Unmatched	2.72	3.59		-4.00***
	Matched	2.73	2.78	94.1	-0.19
Birth order sq	Unmatched	5.23	6.39		-1.21
	Matched	5.26	5.34	93.4	-0.06
Number of antenatal visit	Unmatched	4.63	2.65		.66***
	Matched	4.61	4.55	97.2	0.12
Number antenatal visit sq	Unmatched	15.80	8.81		5.89***
	Matched	15.80	16.16	94.9	-0.09
Previous birth interval	Unmatched	2.54	2.34		1.10
	Matched	2.46	2.45	92.0	0.04
Previous birth interval sq	Unmatched	9.82	4.18		5.48***
	Matched	9.20	7.72	73.7	0.63
Birth size small	Unmatched	0.09	0.17		-2.48*
	Matched	0.09	.09	96.9	-0.07
Birth size large	Unmatched	0.49	0.41		1.97*
	Matched	0.49	0.49	92.2	0.11
Male child	Unmatched	0.59	0.49		2.32*
	Matched	0.59	0.59	97.0	0.05

*p<0.05, **p<0.01, ***p<0.001

[1]Quality of matching was similar for all other countries

CHAPTER 4

Factors influencing Consistent Condom Use among HIV-infected Married and Cohabiting Couples in Swaziland, Zambia and Zimbabwe

Abstract

Background: Most new HIV infections in sub-Saharan Africa now occur in married and cohabiting couples where the prevalence of condom use to protect against the infection is low. The objective of this study was to examine the determinants of consistent condom use among HIV-concordant and discordant couples in Swaziland, Zambia and Zimbabwe.

Methods: Data were from Demographic and Health Surveys (2005-2007) of women aged 15-49 and their husbands/cohabiting partners in the three countries.

Results: Couples were more likely to have used condoms consistently (OR=3.47, 95% CI=1.45-8.34) if the husband was HIV positive, and the only one in the couple who knew his HIV test result. This association was stronger (OR=5.92, 95% CI=2.23-15.68) if the HIV-positive husband was aware of his HIV test result and his HIV-negative wife aware of her test result. No corresponding associations were observed for HIV-positive wives. Results also showed that couples using modern contraceptive methods other than condoms were less likely to have used condoms consistently (OR=0.34, 95% CI=0.20-0.56).

Conclusions: The subordinate role of women in decision-making over condom use, and the use of modern contraceptive methods other than condoms, may both contribute to new HIV infections, especially among discordant couples. Strategies to deal with these issues are necessary, in addition to the need to promote HIV-testing among men.

Introduction

About 1.8 million adults and children were newly infected with HIV in sub-Saharan Africa in 2009 (Joint United Nations Programme on HIV/AIDS, 2010). Most new HIV infections in sub-Saharan Africa now occur in married and cohabiting couples (Matovu, 2010) and most of these couples are sero-discordant (i.e., only one partner is HIV positive) (de Walque, 2007). In Rwanda and Zambia, it was estimated that between 55 and 93% of new infections occurred within sero-discordant marital or cohabitating relationships (Dunkle et al., 2008). There is also substantial variation in HIV prevalence in sub-Saharan Africa: adult HIV prevalence goes from <1% in Niger and Senegal to about 14% in Zambia and Zimbabwe, and about 26% in Swaziland (Joint United Nations Programme on HIV/AIDS, 2010).

Condom use is the main preventive method for HIV infection (Joint United Nations Programme on HIV/AIDS, 2009). Regular use of condoms among married couples remains very low but condom use is essential for sero-discordant couples unless abstinence is a feasible option (Glick & Sahn, 2008). Couples are more likely to use condoms after couple-centered HIV voluntary counseling and testing programs through which both become aware of their own status and their partner's status (Desgrees-du-Lou & Orne-Gliemann, 2008). In general, women are more likely to get tested for HIV usually during antenatal care but, for men, HIV testing opportunities are few (Desgrees-du-Lou & Orne-Gliemann, 2008). After the woman's antenatal testing and awareness of her HIV-positive status, condom use within the couple does not increase (Nebié et al., 2001) unless the husband is aware of the wife's status (Desgrées-Du-Loû et al., 2009). Two studies in sub-Saharan Africa reported that more than 75% of HIV-positive pregnant women did not disclose their results to their husbands (Kilewo et al., 2001; Gaillard et al., 2000). Barriers to disclosure reported by HIV positive women include fear of accusations of infidelity, abandonment, loss of financial support, and violence (Medley, Garcia-Moreno, McGill, & Maman, 2004). Little is known as to the association between awareness of HIV status by the husband only and condom use with their wives (Desgrees-du-Lou & Orne-Gliemann, 2008).

Determinants of condom use among HIV infected couples

In sub-Saharan Africa, other than the couple-centered voluntary counseling and testing studies (Desgrees-du-Lou & Orne-Gliemann, 2008), only one study has examined the determinants of condom use among HIV discordant and concordant couples: Wagner and colleagues (2010) examined the factors influencing consistent condom use among 272 HIV clients in stable relationships with HIV positive, negative or unknown-status partners at two HIV clinics in Uganda and reported that the only predictor of condom use was condom use self-efficacy (the level of confidence in being able to use condoms). They found no association between condom use and other factors (e.g. male gender, Church attendance, and peer support).

Role of modern contraceptive methods other than condoms on condom use

Research has shown that women using contraceptive methods other than condoms are at increased risk of sexually transmitted infections, although they may be well-protected against pregnancy (Centers for Disease Control and Prevention, 1996). A study among women at risk for sexually transmitted infections in selected sites in the United States showed that compared with women who reported using condoms as a contraceptive method, those using hormonal contraception were 4.2 and 2.2 times more likely to report not using condoms at last intercourse with their main partner and casual partner respectively (Centers for Disease Control and Prevention, 1996). A general population study in Zambia also showed that respondents (unmarried or married men and women) who reported using a contraceptive method other than condoms were less likely to report using condoms consistently (OR=0.098, $p<0.01$) (Benefo, 2010). This behavior could arise for at least two reasons: women may be less motivated to use condoms as an additional contraceptive to prevent sexually transmitted infections(Centers for Disease Control and Prevention, 1996) or women using a particular contraceptive method (e.g. contraceptive pill) may incorrectly believe that it will not only prevent pregnancy but also prevent sexually transmitted infections (Galavotti & Schnell, 1994). Among sero-discordant couples in whom consistent condom use is essential, little is known whether the use of contraceptive methods other than condoms results in less consistent use of condoms.

Role of health education and gender norms

A previous study among HIV infected adults in Uganda did not find any association between knowledge of HIV transmission and condom use at last sex (Bunnell et al., 2008) but a study among the general population in Zambia found that having the knowledge that condoms prevent HIV transmission increased the likelihood of consistent condom use (Benefo, 2010). A recent qualitative study in Nigeria revealed that misbeliefs and concerns about the effectiveness and adverse effects of condoms (e.g. condoms provide little protection against pregnancy and sexually transmitted infections; condoms can cause disease, etc) are common reasons for not using condoms, highlighting the need for increasing awareness among the population (Adejoh & Uchenna, 2011). A national family planning education campaign targeting men (married or unmarried) in Zimbabwe (1988-89) demonstrated that men exposed versus not-exposed to the campaign were 1.7 times more likely to use condoms (Kim, Marangwanda, & Kols, 1996).

Gender norms may also play an important role in condom use. Men's resistance to the use of condoms and unequal decision-making powers between men and women often result in high vulnerability of women to HIV infection (Joint United Nations Programme on HIV/AIDS, 2009). Given the male dominance in decision making, it is conceivable that among couples at risk of HIV infection, husband's knowledge of HIV prevention or awareness of HIV status could have a stronger effect on condom use than wife's knowledge or awareness but this question has never been studied using information collected from *both* husbands and wives.

Rationale and study objective

The only previous study (Wagner et al., 2010) among HIV concordant and discordant couples used data collected from only one partner (i.e., either husband or wife). To our knowledge, no published studies have examined comprehensively the determinants of consistent condom use based on the perspectives of both husband and wife in this population in sub-Saharan African countries. Accordingly, the objective of this study is to examine the determinants of consistent condom use based on the perspectives of *both* husband and wife (i.e., husband's and wife's exposure to family planning information, HIV preventive knowledge of husband and wife, woman's perceived ability to request condom use, HIV testing and awareness of status, and contraceptive choice) among couples where either one or both partners are HIV infected in Swaziland, Zambia and Zimbabwe.

Methods

Data

The data came from cross-sectional Demographic and Health Surveys (DHS) conducted between 2005 and 2007 in Swaziland, Zambia, and Zimbabwe. DHS collected HIV data in 20 countries between 2001 and 2008, of which 16 countries had all the relevant data on study variables. Of those 16 countries, 13 countries had low prevalence of HIV (0.5 to 3%) and were excluded due to very low statistical power. HIV prevalence in the three included countries ranges from 14% in Zambia to 26% in Swaziland (Central Statistical Office (CSO), Ministry of Health (MOH), Tropical Diseases Research Centre (TDRC), University of Zambia, and Macro International Inc., 2009; Central Statistical Office (CSO) [Swaziland], and Macro International Inc., 2008).

The detailed methodology of DHS is available at (http://www.measuredhs.com/What-We-Do/Survey-Types/DHS-Methodology.cfm). DHS uses a two-stage survey design (clusters, households) to identify a probability sample representative of each country. Eligible women aged 15-49 and men aged 15-59 were interviewed. The response of women went from 90% in Zimbabwe to 97% in Zambia while those of men went from 82% in Zimbabwe to 91% in Zambia (Central Statistical Office (CSO) [Zimbabwe] and Macro International Inc. 2007; Central Statistical Office (CSO), Ministry of Health (MOH), Tropical Diseases Research Centre (TDRC), University of Zambia, and Macro International Inc., 2009).

HIV testing in the DHS is an informed, voluntary, confidential standard procedure in which blood spots are collected on filter paper from a finger prick for testing in a central laboratory. An initial ELISA test is conducted at the laboratory followed by retesting of all positive tests using a second ELISA. If there are discordant results on the two ELISA tests, a new ELISA or a Western Blot is performed. HIV testing of men varied from 63% (Zimbabwe) to 78% (Swaziland); and of women, 76% (Zimbabwe) to 87% (Swaziland) (Central Statistical Office (CSO) [Zimbabwe] and Macro International Inc. 2007; Central Statistical Office (CSO) [Swaziland], and Macro International Inc., 2008). An analysis of non-response bias in DHS HIV testing did not show a significant effect on national estimates of HIV prevalence (Mishra et al., 2006).

Concepts and measures

Dependent variable

Consistent condom use. Men were asked “the last time you had sexual intercourse, was a condom used?”. For those who answer ‘yes’, a subsequent question asked “did you use a condom every time you had sexual intercourse with this person in the last 12 months?” (To be included in the analyses, the sexual partner of the man in the most recent sexual activity had to be his wife or live-in partner – 98.6% of the sample. We excluded couples in which men last had sex with a non-marital partner (1.4% of the sample) because women's reports were not available in those couples). A response of “yes” to the latter question was coded as 1; otherwise coded as 0. (Information on *consistent condom use* was not collected from women in Zimbabwe).

Independent variables

Perceived inability of a wife to request her husband uses a condom. Women were asked: “Could you ask your husband to use a condom if you wanted him to?” There were 3 response categories: yes, no, and don't know/not sure/it depends. Responses of “no” and “don't know” to this question were classified as *inability to request* and coded as 1 [the results were the same after excluding those who answered don’t know (3% of the sample)]. A response of ‘yes’ was coded as 0 used as the reference category.

HIV preventive knowledge regarding condom use. Men and women were asked: “Can people reduce their chances of getting the AIDS virus by using a condom every time they have sex?" The response categories include: yes, no, and don't know. Separate variables were created for men versus women. A response of "yes" to this question was coded as 1, while responses of "no" and "don't know" were coded as 0. For the analyses, two dummy variables were created: "only husband had the knowledge" and "both partners had the knowledge". The reference category was "neither partner or only the wife had the knowledge". (Only a small percentage of couples was in the "neither partner" category and there was no significant difference between "neither partner" and "only the wife had the knowledge" on consistent condom use and therefore these two were collapsed into a single category).

Exposure to family planning information. Men and women were asked if they ever heard about family planning information from the following sources in the last few months prior to the survey: radio, television, newspaper and health worker/health facility. Three dummy variables were created as to whether one or both partners had been exposed to family planning information: "husband only", "wife only", and "both partners" while the reference category was "neither of the partners exposed".

*Previous HIV testing (prior to the DHS) and awareness of HIV status***.** Men and women were asked if they had ever been tested for HIV. For those who answered 'yes', they were asked if they had received results for the most recent HIV test. Four dummy variables were created based on the reports of both men and women: "one or both tested: both unaware of the result", "one or both tested: only husband knew his result", "one or both tested: only wife knew her result" and "both tested: both knew their results" while the reference category was "both partners have never been tested".

*Use of modern contraceptive methods other than condoms***.** Modern contraceptive methods include oral hormonal pills, intra-uterine device, injectables, condoms, implant (including Norplant), sterilization, vaginal barrier methods, and emergency contraception. The variable was coded as 1 if the women reported that the couple was using any modern contraceptive method other than condoms and coded as 0 otherwise [We use women's reports to create this variable because wives use these methods except for male sterilization (only 0.5% of men were sterilized)].

Covariates

Covariates were the following variables which are likely influencing condom use.

Extra-marital partners. Husbands and wives were asked separately to report the number of women/men other than their spouses/cohabiting partners that they had sex with in the last 12 months. The responses were coded as (0, no extra-marital partner; 1, one or more extra-marital partners).

Wealth index. We used the *wealth index* (Gwatkin, Rutstein, Johnson, Pande & Wagstaff, 2000; Filmer & Pritchett, 2001) variable already available in each DHS dataset. It has been shown to be a good proxy for long-run household wealth (Filmer & Pritchett, 2001; Filmer & Pritchett, 1999). It was derived from an index (generated through principal component analysis) of household assets (e.g. televisions, bicycles, water and sanitation facilities). The index was standardized to a mean of 0 and a standard deviation of 1 and higher scores refer to greater wealth.

Desire for more children. Based on men's and women's reports relating to desire for future children, two dummy variables were created separately for men and women: "wants in 2 yrs" and "wants after 2 yrs/wants but unsure timing" while the reference category was "wants no more or undecided or sterilized" (there was substantial overlap in men's and women's reports and including them one at a time or both in the analyses did not change the results of the study variables: therefore only husband's report was included in the regression analysis).

Other covariates include: country of residence, place of residence (0, rural; 1, urban), and for each partner, age in years, and education in total years of schooling.

Sample for analysis

To be included in the analysis, couples had to be married or in a cohabiting monogamous relationship, sexually active and report having sex with their spouses at the most recent sexual activity in the year before the survey, and at least one partner (either the woman or her spouse) was HIV positive based on the DHS HIV test results. We identified a total of 1260 couples in monogamous unions in which at least one partner tested HIV positive. Eighteen couples (1.4%) were excluded because the sexual partner of the man in the most recent sexual activity was not his wife or live-in partner and women's report were not available in those couples. Another 5% of the couples (N=65) had missing information on the dependent variable, independent variables or covariates and were excluded. In about 15% of couples (after the exclusions), the tested partner was HIV positive while his/her spouse's DHS HIV test result was missing. We included these 15% of couples in the main analysis which involved a total sample of 1177 couples. (Analyses excluding the 15% of couples were also conducted and described in the data analysis section).

Data Analysis

In our descriptive analyses, sample weights were used to ensure the representativeness of the sample selected. This study uses binomial logistic regressions and the statistical software MLwiN version 2.24 (Rasbash, Charlton, Browne, Healy, & Cameron, 2009) to conduct a two-level regression analysis of the DHS data with couples nested in clusters. Regression analyses were conducted in the overall sample (including and excluding the 15% of couples with missing DHS HIV test results in one partner). In addition, we conducted separate analyses in two sub-samples, one restricted to HIV-positive husbands and their wives (excluding HIV-positive wives who knew their previous HIV test results) (n=584); and the other, restricted to HIV-positive wives and their husbands (excluding HIV-positive husbands who were aware of their previous HIV test results) (n=593). In both sub-samples, the 15% of couples with a missing DHS HIV test result in one partner were excluded.

All estimates were derived by the use of second-order penalized quasi-likelihood and iterative generalized least squares estimation.

Results

Sample characteristics are presented in Table 1. The prevalence of consistent condom use was 10.1% among the overall sample, 7.5% among sero-discordant couples (49% of the sample) and 12.1% among sero-concordant couples (51% of the sample). Fewer than half the couples had been tested previously for HIV, and only 15.2% reported that both had been tested and knew their results. The use of modern contraceptive methods other than condoms applied to 38% of couples.

Table 2 presents the adjusted odds ratios (ORs) in the overall sample and the two sub-samples. (Because the proportion of wives having extra-marital partners is very small, this variable was not included in the regression analysis). In the overall sample (Table 2, column 1), couples were more likely to have used condoms consistently if the husband (OR=3.77, 95% CI=1.48-9.59) or both partners (OR=2.38, 95% CI=1.11-5.13) had the knowledge of HIV prevention compared with those where only the wife or neither partner had the knowledge. Both partners' exposure to family planning information (OR=3.25, 95% CI=1.13-9.34) was associated with consistent condom use compared with those who were both unexposed. Compared with couples never tested previously for HIV, couples were more likely to have used condoms consistently if husbands (OR=2.49, 95% CI=1.24-5.01) or if both partners (OR=4.46, 95% CI= 2.53-7.88) had been tested before and knew their test results. Couples using modern contraceptive methods other than condoms (OR=0.34, 95% CI=0.20-0.56) were less likely to have used condoms consistently.

The results of the sensitivity analysis (i.e., excluding the 15% of couples with missing DHS HIV test result in one partner) were similar to those of the main analysis (not shown).

Table 2, column 2, presents the results in the sub-sample restricted to HIV-positive husbands and their wives (excluding HIV-positive wives who were aware of their HIV test results). In this sub-sample, a wife's perceived inability to request condom use was negatively associated with consistent condom use (OR=0.34, 95% CI=0.15-0.79). Couples were more likely to have used condoms consistently if the HIV-positive husband knew his test result (OR=3.47, 95%CI=1.45-8.34) or knew his test result in combination with his HIV-negative wife knowing her test result (OR=5.92, 95%CI=2.23-15.68).

Table 2, column 3, presents the results in the sub-sample restricted to HIV-positive wives and their husbands (excluding HIV-positive husbands who were aware of their HIV test results). In this sub-sample, no significant associations were observed between consistent condom use and the HIV-positive wife’s awareness of her test result (OR=0.56, 95%CI=0.23-1.32) or the combination of the HIV-positive wife's awareness of her test result and the HIV-negative husband knowing his test result (OR=1.20, 95%CI=0.32-4.55).

Discussion

This is the first study to examine the determinants of consistent condom use among discordant and concordant couples based on the perspectives of *both* husband and wife in sub-Saharan African countries. The prevalence of consistent condom use among couples was very low: only 7.5% among sero-discordant couples, indicating a very high risk of heterosexual HIV transmission. The findings suggest a pattern of male dominance in the decision to use condoms consistently as evidenced by differentials in husbands and wives with respect to the associations between condom use and awareness of HIV test results and knowledge of HIV prevention. The wife's inability to request condom use tended to associate negatively with actual consistent condom use, and this association was statistically significant among HIV positive husbands and their wives, excluding HIV-positive wives who knew their test results.

Previous couple-based intervention studies focusing on HIV voluntary counseling and testing have reported substantial increase in condom use rates among discordant couples after the interventions (Desgrees-du-Lou, A & Orne-Gliemann, 2008). However, in routine circumstances (i.e., without the interventions), women are more likely to get tested for HIV usually during antenatal care but, for men, HIV testing opportunities are rare (Desgrees-du-Lou & Orne-Gliemann, 2008). Little is known about the association between awareness of HIV status by the husband only and condom use with their wives (Desgrees-du-Lou & Orne-Gliemann, 2008). This study contributes to this knowledge gap by showing that couples were more likely to have used condoms consistently if the husband was HIV positive and knew his test result. This effect was even stronger if the HIV-positive husband was aware of his test result and his HIV-negative wife aware of her test result. No corresponding associations were observed for HIV-positive wives. This finding was consistent with the results of previous studies which have reported low rates of disclosure and condom use after women's antenatal HIV testing and awareness of their HIV-positive status (Nebié et al., 2001; Kilewo et al., 2001; Gaillard et al., 2000). It is noteworthy that a larger proportion of women than men had been tested for HIV and knew their results (about 40% versus 26% - not shown in table) in this study. These findings attest to the perverse elevation in risk among husbands for HIV because their wives may fear retribution arising from disclosure.

Results of this study also suggest an increased risk among wives for HIV as evidenced by the negative association between a woman's inability to request condom use and actual condom use (Table 2, column 2) despite the fact that husbands were HIV positive and wives were either unaware of their status or those who knew their status were HIV negative in this sub-sample. In these couples, consistent condom use was unlikely unless the HIV-positive husband had been tested and knew his test result. In addition to the need to increase HIV testing among husbands, women should be empowered to have a role in decision making over condom use to protect themselves from HIV infection or to avoid transmitting the infection to their husbands.

In this study, couples using modern contraceptive methods other than condoms were less likely to have used condoms consistently in the overall sample and in the sub-samples. This finding is consistent with the results of previous studies conducted among different populations (Centers for Disease Control and Prevention, 1996; Benefo, 2010). Those using modern contraceptives may be well-protected from unwanted pregnancy but not from transmitting HIV infection to the uninfected spouse in discordant couples.

Further studies are therefore necessary to examine the HIV risk perceptions related to contraceptive choice among high risk couples.

There are some limitations of this study. First, the self-reported measures may be subject to some bias. The tendency of over-reporting (e.g. after exposure to HIV prevention information) or under-reporting (e.g. reluctant to admit condom use because of shyness) the use of condoms has been reported by previous studies (Ahmed, Schellstede, & Williamson, 1984; Cordero-Coma & Breen, 2012). These reporting biases (if there were any) may either attenuate or inflate the associations between the determinants and condom use. Second, no information is available as to whether the husband has told his wife about his HIV status (or vice versa). Third, there could be changes in sero-status between previous HIV-testing and the DHS HIV-testing. For example, a person might be tested HIV-negative during the previous HIV testing but became HIV-positive during the DHS testing. If that was the case, this could result in under-estimation of the association between the husband's awareness of his HIV status and condom use, especially in Table 2, column 2. Fourth, a causal relation between independent and dependent variables cannot be established because of the cross-sectional nature of the study. Finally, unmeasured covariates may have contributed to residual confounding in this study.

In conclusion, results suggest that a large proportion of men not being tested for HIV, the inability of HIV-positive women who aware of their HIV status to act on that knowledge to reduce risk of infection in their husbands, the subordinate role of wives in the decision making to use condoms, and the use of modern contraceptive methods other than condoms, especially among discordant couples may contribute to new HIV infections which are now mainly occurring among married and cohabiting couples. Results clearly indicate the need to increase HIV testing and awareness of results among men. Strategies that could enable women to have a role in decision making over condom use are also necessary. Sero-discordant couples using modern contraceptives other than condoms are less likely to use condoms consistently and thus are at increased risk of transmitting HIV infection to their uninfected spouses. It is important to inform husbands and wives through appropriate channels that modern contraceptives other than condoms cannot prevent HIV infection and that condom use alone well serves the dual objectives of contraception and prevention if they are used correctly and consistently. Since the effectiveness of male condoms in preventing pregnancy ranges from 82% to 98% (Centers for Disease Control and Prevention, 2012), couples should also be informed that dual method use (i.e., condoms plus another modern contraceptive) can better prevent pregnancy (World Health Organization, 2009). Further studies are also necessary to find out why the high risk couples using other contraceptive methods did not use condoms for prevention of HIV infection.

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Table 1. Sample characteristics of HIV discordant and concordant couples in Swaziland, Zambia and Zimbabwe (2005-2007)

Countries (n)	3
Level 2, clusters (n)	601
Mean number of couples per cluster (min/max)	2.0 (1/9)
% Urban residence	39.9
Level 1, couples (n)	1177
Husband's age (years) *Mean*(SD)	35.8 (7.5)
Wife's age (years) *Mean* (SD)	29.6 (6.9)
Husband's education (years) *Mean*(SD)	8.4 (3.7)
Wife's education (years) *Mean*(SD)	7.5 (3.3)
Wealth index *Mean* (SD)	0.2(1.0)
% Husband having extra-marital sexual partner(s)	14.1
% Wife having extra-marital sexual partner(s)	0.5
Desire for more children %Wants no more or undecided	 43.4
%Wants in 2 yrs	20.5
%Wants after 2 yrs/wants but unsure timing	36.2
Condom use % Using condom consistently - overall	 10.1
% Using condom consistently among discordant couples	7.5
% Using condom consistently among concordant couples	12.1
%Wife cannot request condom use	22.5
HIV preventive knowledge % None	 3.9
% Husband only	14.2
% Wife only	14.5
% Both partners	67.4
Exposure to family planning information % None	 20.2
% Husband only	19.9
% Wife only	16.0
% Both partners	43.8
Ever been tested for HIV and Knew the result	
% Both have never been tested	44.8
% Tested: both unaware of the result	5.8
% Tested: only husband knew his result	10.3
% Tested: only wife knew her result	23.8
% Tested: both knew their results	15.2
% Using modern contraceptive method	38.4

Table 1 (cont.)

HIV status[a]	
% Only one partner HIV tested positive	48.7
% Both partners HIV tested positive	51.3
Tested partner was HIV positive but spouse's test result missing	
% Yes	15.1
% No missing	84.9

Notes: Husband and wife refer to partners in married or cohabiting relationships.
[a] Based on N=1003 after excluding 15.1% of couples in which spouse's test result were missing

Table 2. Odds Ratios and 95% CIs of consistent condom use among HIV infected couples after adjusting for country of residence and covariates[a]

	Overall sample (N=1177)	Restricted to couples where husbands were HIV positive[b] (N=584)	Restricted to couples where wives were HIV positive[c] (N=593)
Fixed Effects Intercept coef. (SE)	-4.07(0.69)	-4.08(0.91)	-3.19(0.94)
Study Variables Ability to Request condom use Can request	Ref	Ref	Ref
Cannot request	0.51(0.25-1.05)	**0.31(0.10-0.94)**	0.37(0.10-1.43)
HIV preventive knowledge Neither or wife only	Ref	Ref	Ref
Husband only	**3.77(1.48-9.59)**	3.63(0.92-14.27)	3.80(0.74-19.35)
Both husband & wife	**2.38(1.11-5.13)**	2.35(0.72-7.63)	2.69(0.73-9.88)
Exposure to family planning information None	Ref	Ref	Ref
Husband only	1.79(0.59-5.47)	2.06(0.55-7.74)	0.54(0.11-2.54)
Wife only	1.33(0.41-4.33)	1.43(0.35-5.89)	0.63(0.14-2.85)
Both husband & wife	**3.25(1.13-9.34)**	2.03(0.58-7.16)	1.41(0.38-5.25)
Ever been tested for HIV and awareness of result Never been tested	Ref	Ref	Ref
Tested: both unaware of the result	0.67(0.18-2.47)	0.71(0.15-3.46)	0.26(0.03-2.19)
Tested: husband knew his result	**2.49(1.24-5.01)**	**3.47(1.45-8.34)**	1.35(0.33-5.61)
Tested: wife knew her result	1.13(0.59-2.16)	2.72(0.91-8.07)	0.56(0.23-1.32)
Tested: both knew their results	**4.46(2.53-7.88)**	**5.92(2.23-15.68)**	1.20(0.32-4.55)
Modern contraceptive method No	Ref	Ref	Ref
Yes	**0.34(0.20-0.56)**	**0.34(0.15-0.79)**	**0.18(0.07-0.47)**

Notes: Husband and wife refer to partners in married or cohabiting relationships.

[a] Adjusted for country of residence, age, education of husband and wife, household wealth, husband's having extramarital partner, desire for more children and urban/rural residence

[b] HIV-positive husbands and their wives, excluding HIV-positive wives who were aware of their HIV test results

[c] HIV-positive wives and their husbands, excluding HIV-positive husbands who knew their HIV test results

CHAPTER 5

Evaluation of the association between Long-lasting Insecticidal Nets Mass Distribution Campaigns and Child Malaria in Nigeria

Abstract

Background: Nigeria carries the greatest malaria burden among countries in the world. As part of the National Malaria Control Strategic Plan, free long-lasting insecticidal nets (LLINs) were distributed in 14 states of Nigeria through mass campaigns led by different organizations (the World Bank, UNICEF, or Global Fund) between May 2009 and August 2010. The objective of this study was to evaluate the association between LLIN distribution campaigns and child malaria in Nigeria.

Methods: Data were from the Nigeria Malaria Indicator Survey which was carried out from October to December 2010 on a nationally representative sample of households. Participants were women aged 15-49 years and their children aged less than five years (N=4082). The main outcome measure was the presence or absence of malaria parasites in blood samples of children (6-59 months).

Results: Compared with children living in communities with no campaigns, those in the World Bank Booster Project areas were less likely to test positive for malaria (OR=0.50, 95% CI=0.28-0.89) after adjusting for geographic locations, community- and individual-level characteristics including child-level use of Insecticide-Treated Nets (ITNs). No significant differences in child malaria infections were found between other campaigns and non-campaign areas. Results also showed that community-level wealth (OR=0.53, 95% CI=0.36-0.78), community-level maternal knowledge regarding malaria prevention

(OR=0.67, 95% CI=0.49-0.91), and child-level use of ITNs (OR=0.79, 95% CI=0.63-0.99) were negatively associated with child malaria.

Conclusions: The observed protective effect of the World Bank Booster Project on child malaria, needs to be corroborated by future studies given the lack of associations between other campaign areas and malaria in children, which also need to be explored further. Results also show that improving community-level maternal knowledge through appropriate channels might be helpful in preventing child malaria in Nigeria.

Keywords: child malaria; insecticide-treated nets, campaigns, evaluation

Background

Malaria caused an estimated 655,000 deaths worldwide in 2010 and more than 90% of these deaths occurred in Africa (World Health Organization (WHO), 2011). Nigeria carries the greatest malaria burden among countries in the world with over 300,000 malarial deaths each year - most of them occurring in children under 5 years of age (The World Bank, 2009; United States Embassy in Nigeria, 2011). Malaria is transmitted from person to person by the bite of *Anopheles* mosquitoes. Symptoms appear 7 to 30 days after biting by the mosquito that carries the malaria parasite (Centers for disease control and prevention, 2010). According to the Nigeria Malaria Indicator Survey (National Population Commission (NPC) [Nigeria], National Malaria Control Programme (NMCP) [Nigeria], & ICF International, 2012), almost everyone in the country is at risk for malaria transmission except the minority (3%) located at an altitude 1,200 to 1,400 metres, where the transmission risk is relatively low. The duration of the malaria transmission season decreases from the South to the North (National Population Commission (NPC) [Nigeria] et al., 2012).

There has been a rapid scale-up of Insecticide-Treated Net (ITN) or Long-lasting Insecticidal Net (LLIN) distribution in African countries in the recent years (WHO, 2011), fuelled by randomized controlled trials (efficacy studies) of ITN on a variety of outcomes. A systematic review of randomized trials reported protective effects of ITN on all-cause mortality in children less than 5 years of age, anemia, splenomegaly and prevalence of malaria infection (Lengeler, 2004). One randomized trial (conducted after the publication of the systematic review) among children aged 6 months to 5 years

(N=100) in a rural community in Nigeria also reported that febrile episodes and parasitemia were significantly lower in the ITN group compared with the traditional bed net group (Osondu & Jerome, 2009). While there is evidence on the efficacy of using ITNs to prevent malaria (under optimal conditions), limited evidence exists as to the effectiveness of ITN when distributed in the general population (under real-world conditions). In the scale-up of ITN interventions at the national level, using randomized controlled trials to evaluate the effectiveness of the programs would be unethical since these study designs require withholding of an intervention of proven efficacy (Rowe et al., 2007). According to Habicht and colleagues (1999), one might assume that reduction in disease burdens (e.g. malaria prevalence) are attributable to the interventions (e.g. scale-up of ITNs) after one has attempted to rule out external factors (e.g. improved socioeconomic status, the presence of ancillary projects in the intervention areas, etc) using non-randomized control groups, which may be either cross-sectional (i.e., comparing intervention and control groups at the end of the programme) or longitudinal (i.e., comparing intervention and control groups both at the beginning and end of the program) (Habicht, Victora, & Vaughan, 1999). One evaluation study (Terlouw et al., 2010) has been conducted in three districts of Togo, comparing changes in malaria morbidity among children before and after an integrated LLIN-measles campaign. This study found protective effects of campaigns in two of the three districts but the lack of program effects in the remaining district could not be explained.

Malaria preventive interventions in Nigeria

The National Malaria Control Strategic Plan (2009-2013) in Nigeria includes universal access to LLINs, increased indoor residual spraying, and environmental management to decrease mosquito breeding places (The U.S. Global Malaria Coordinator, 2010). The LLIN distribution strategy in Nigeria included a "scale-up phase"(2009-2010) of free LLIN distributions through mass campaigns (≥2 LLINs per household); and a "keep-up phase" of replacing "torn or worn out nets" and providing LLINs to new household members and new families (The U.S. Global Malaria Coordinator, 2010). By August 2010, more than 24 million LLINs were distributed in 14 of the 37 states in Nigeria (The U.S. Global Malaria Coordinator, 2010). Mass distribution of LLINs started in Kano (as a pilot state) in May 2009 where households were visited "door-to-door", registered and provided with "net cards" (to exchange for LLINs) (Boakye, Scott, & Smyth, 2010). RapidSMS (a short message service (SMS) based data collection and communication tool) was used to monitor the distribution of LLINs in all states (RapidSMS, n.d). The World Bank was responsible for LLIN distribution in 7 states (Akwa Ibom, Anambra, Bauchi, Gombe, Jigawa, Kano, and Rivers), UNICEF in 4 states (Adamawa, Sokoto, Kaduna, Kebbi) and Global Fund in 3 states (Niger, Ogun and Ekiti) (National Population Commission (NPC) [Nigeria] et al., 2012; The U.S. Global Malaria Coordinator, 2010; World Health Organization, 2010) (See also Figure 1). The campaigns led by UNICEF were not standalones but integrated with child health days (The U.S. Global Malaria Coordinator, 2010) where children received immunizations, vitamin A supplements, etc. and LLINs. Campaigns were completed in 11 states by March 2010 (World Health Organization, 2010) and in the remaining 3 states (Adamawa, Kaduna and Gombe) by August 2010 (The U.S. Global Malaria Coordinator, 2010). In a separate initiative just before the start of the universal mass distribution campaigns in 14 states, USAID and the Canadian Red Cross delivered 676,877 LLINs to children aged less than 5 years in Cross River State in late 2008 and early 2009. An evaluation report of the Cross River State campaign showed that 81% of households received an LLIN (The U.S. Global Malaria Coordinator, 2010).

The World Bank selected the seven states based on the following criteria (National Population Commission (NPC) [Nigeria] et al., 2012): high mortality rates among children aged less than five years (>260 deaths per 1,000 live births); high prevalence of drug-resistant *Plasmodium falciparum* malaria (>85%); demonstrated commitment by the states to implement the campaigns; and a lack of substantial aid from other donors to control malaria in the states. No information was available as to the selection of states for campaigns led by UNICEF and Global Fund.

According to the Nigeria Malaria Indicator Survey (NMIS) conducted between October and December 2010, 42% of households reported owning at least one ITN compared with 8% in the 2008 Demographic and Health Survey (National Population Commission (NPC) [Nigeria] & ICF Macro, 2009; National Population Commission (NPC) [Nigeria] et al., 2012). The percentage of households owning at least one ITN in the 14 campaign states (72 to 75%) was more than three times that of households in areas with no campaigns (22%) (National Population Commission (NPC) [Nigeria] et al., 2012). Less than 1% of the households were reported to have been sprayed indoors in the past 12 months prior to the survey (National Population Commission (NPC) [Nigeria] et al., 2012).

Individual- and community-level influences on malaria infection

Failure to use available nets and lack of knowledge about malaria prevention are important determinants of risk. Despite the ownership of an ITN in households, the NMIS (2010) reported that only 49% of people used them the night before the survey and that use extended to only 59% of children (National Population Commission (NPC) [Nigeria] et al., 2012). When asked about various ways to avoid getting malaria, only 17% of women answered "using an ITN or LLIN" while 20% and 8% of women cited "using insecticide spray" and "eliminating stagnant water around living areas", respectively (National Population Commission (NPC) [Nigeria] et al., 2012). Lack of knowledge at the individual and community levels about the effectiveness of preventive interventions may result in refusal to: use an ITN, spray indoors, or participate in neighborhood clean-up activities to remove mosquito breeding sites, since people may not understand or know the importance of these preventive activities.

In addition to malaria preventive knowledge, other community and individual-level factors may influence risk of malaria infection. According to a study in the Democratic Republic of Congo (Messina et al., 2011), both community and individual-level wealth were protective against malaria infections among adults. The exact mechanism through which wealth could reduce risk of malaria is not clear but it might be attributable to better housing conditions, and better access to health care services. In general, higher levels of education are related to wealth and also to knowledge of prevention measures which could in turn be linked to reduced risk of malaria. The same study (Messina et al., 2011) found that increased community use of bed nets was protective against malaria at the community-level but the effect of individual-level bed net use was not statistically significant. Malaria infection has also been associated with proxies for crowding including household size in rural Benin (Mensah & Kumaranayake, 2004) and the number of persons per sleeping room in a peri-urban area of the Gambia (Koram, Bennett, Adiamah, & Greenwood, 1995). A study among Nigerian children using the Nigeria Demographic and Health Survey (2008) found that fever (as a proxy for malaria) was associated positively with the child's age, being male and living in a rural area (Yusuf, Adeoye, Oladepo, Peters, & Bishai, 2010). Malaria studies have confirmed the elevated risk of infection associated with rural residency (Coene, 1993; Robert et al., 2003) and reported a negative association between geographic elevation and the human biting rate of Anopheles mosquitoes (Bodker et al., 2003).

Rationale and study objectives

The previous study in Togo (Terlouw et al., 2010) evaluated the impact of integrated LLIN campaigns on malaria morbidity among children less than 5 years old in three districts of Togo using a before-after design. Adjustment for confounding is crucial in such an approach since there is no external comparison group (Habicht et al., 1999). The Togo study controlled for age and sex of the child, household socio-economic status (SES), and the education level of the caretaker but there were no attempts to take into account community-level characteristics (e.g. community SES). In Nigeria, although LLINs have been freely distributed on a large scale among the general population either through standalone or integrated campaigns, no study has attempted to evaluate the impact of these campaigns on malaria infections among children. The availability of the NMIS (2010) data provides an opportunity to conduct a low-cost secondary data analysis to evaluate the impact of LLIN campaigns on child malaria, using an external comparison group (i.e., states that have not been covered by the campaigns) and adjusting for an extensive array of control variables both at the individual- and community-levels. Although this secondary data analysis study can contribute to our understanding of malaria control, dependence on one cross-sectional study to assess 'outcome' (parasitological test results for malaria in children) poses a significant challenge, namely, to establish comparability of risk at baseline among the study areas – those selected and not selected for LLIN campaigns. We attempted to achieve comparability by statistically controlling for population differences in levels of risk using: fever data from the 2008 Nigeria Demographic and Health Survey (NDHS) (National Population Commission (NPC) [Nigeria] & ICF Macro, 2009).

The objectives of this study were: (1) to assess the between-community and between-household variations in malaria among children (in terms of presence of malaria parasites in blood samples) in Nigeria; (2) to examine the association between LLIN distribution campaigns and child malaria after adjusting for geographic characteristics; and (3) to examine if campaign effects are explained by other community and individual-level characteristics.

Method

The 2010 Nigeria Malaria Indicator Survey (NMIS) was carried out from October to December, 2010 on a nationally representative sample of households. The objectives of NMIS include (but are not limited to): measuring the ownership and use of bed nets, measuring malaria prevalence among children, and assessing malaria related knowledge, attitude and practices among women. The detailed methodology is available elsewhere (National Population Commission (NPC) [Nigeria] et al., 2012), and we provide a brief outline here. The sampling frame was a list of census enumeration areas (EAs) from the 2006 Population and Housing Census of the Federal Republic of Nigeria. EAs formed the primary sampling units or clusters. The sample was selected using a stratified, two-stage cluster design consisting of 240 clusters, 83 in the urban areas and 157 in the rural areas. (One cluster was inaccessible resulting in 239 clusters in the final sample.) In each cluster, all households were listed and an average of 26 households was selected by equal probability systematic sampling. All women aged 15-49 years in the selected households were eligible to be interviewed. The response rate was 97%. During the interviews, women were asked questions on topics including socio-demographic characteristics and knowledge of malaria symptoms, causes, prevention and treatment. In addition, all children aged 6-59 months in selected households were eligible to be tested for malaria. Of the children eligible for testing, 91% were tested for malaria using blood smears collected for malaria microscopy (the detailed procedure will follow). Verbal and written informed consents were obtained from each participant and from parents or guardians for testing of children. The NMIS was approved by the Nigeria Health Research Ethics Committee of the Federal Ministry of Health.

Concepts and Measures

Dependent variable

The outcome is the presence or absence of malaria parasites in blood samples of children (6-59 months). Trained laboratory scientists obtained finger (or heel) prick blood samples from eligible children and prepared a thick blood smear and thin blood film for each child to be examined in the Department of Medical Microbiology and Parasitology Laboratory at the University of Lagos. The laboratory had ten experienced malaria microscope specialists and each blood slide was examined by two independent specialists. All discordant results were read and adjudicated by a third specialist.

Individual-level variables

Maternal knowledge of malaria prevention. A knowledge score was based on a count of correct responses coded 1, yes or 0, no to 8 items following the stem question: "What are the ways to avoid getting malaria?" Sample items include: sleep under an ITN/LLIN, use insecticide spray, use mosquito coils, and eliminate stagnant water around living area.

Other individual-level variables included: maternal education in total years of schooling, whether the child slept under an ITN the night before the survey, whether the child was treated with anti-malarial drugs for fever during the past two weeks before the survey, child gender and child age in months (rescaled for the purposes of data analyses so that one unit increase represents one year).

Household-level variables

Household wealth. We used the wealth index (Gwatkin, Rutstein, Johnson, Pande, & Wagstaff, 2000) variable already available in the NMIS dataset. It was derived from an index (generated through principal component analysis) of household assets ranging from televisions to bicycles, characteristics of the dwelling, source of drinking water and sanitation facilities. The index was standardized to a mean of 0 and a standard deviation of 1 and higher scores refer to greater wealth.

Average number of people per sleeping room. This variable was calculated by dividing the number of household members by the number of rooms used for sleeping in the household.

Community-level variables

Wealth, maternal knowledge of malaria prevention, *proportion of children using ITN,* and *proportion of febrile children treated with anti-malarial drugs* at the *community level* were calculated by aggregating the corresponding household and individual-level variables (i.e., wealth index, maternal knowledge, whether a child slept under an ITN the night before the survey, and whether a child with fever was being treated with anti-malarial drugs) up to the cluster levels.

Areas for long-lasting insecticidal nets (LLINs) distribution campaigns. Three dummy variables were created based on the main lead partners of the campaigns: "the World Bank Booster Project" "UNICEF", and "Global Fund". [Note: In Kaduna State, Global Fund and UNICEF were responsible for distributing 477,649 and 2,253,539 LLINs respectively (World Health Organization, 2010). Since the former only distributed

17% of total LLINs in Kaduna, this state was classified into the UNICEF group for the purposes of the analyses.]

Geographic variables

Regions include: north-central, north-east, north-west (reference), south-east, south, south-west.

Urban/rural residence was coded as 0, rural and 1, urban.

Cluster (EA) altitude in meters was classified as 200 m or less (reference), 201 to 400m, 401 to 600m, and 601 to < 800m, and more than 1000m. (There were no clusters at the altitudes between 800 and 1000 meters).

State-level differences in risk of fever: prevalence of fever among children 6-59 months in 2008 estimated from NDHS, 2008 (National Population Commission (NPC) [Nigeria] & ICF Macro, 2009). In the absence of baseline information on differences between campaign areas in levels of risk for child malaria, we obtained state-level estimates of child fever in 2008. In young children, the proportion of fever attributable to malaria is very high during the rainy season in malaria endemic areas (Bisoffi et al., 2010; Dicko et al., 2005; McGuinness et al., 1998). The NDHS (2008) was conducted during the rainy season (June to October, 2008), enabling us to: (1) estimate campaign-area differences in risk for malaria just before the programs were launched; and (2) evaluate our ability to control for these differences statistically (i.e., using state-level differences in risk for fever as a control variable to adjust for campaign-area differences in risk for malaria prior to the programs).

Using the 2008 NDHS to model risk of child fever at the individual level as a function of the campaign areas indicated that there were significant differences between them in fever (as a proxy for malaria risk) compared with non-campaign areas. For example, areas served by the World Bank campaign exhibited elevated risk (OR=1.56, 95% CI=1.33-1.82) while the campaigns served by UNICEF (OR=0.64, 95% CI=0.52-0.79) and the Global Fund (OR=0.74, 95% CI=0.57-0.96) exhibited lower risk compared with non-campaign areas. Controlling for the prevalence of child fever at the state-level explained all these differences: the World Bank Booster areas (OR=0.97, 95% CI=0.85-1.11), UNICEF (OR=1.01, 95% CI=0.85-1.21) and Global Fund (OR=1.00, 95% CI=0.81-1.25).

Data Analysis

We used multi-level modeling and the statistical software MLwiN version 2.24 (Rasbash, Charlton, Browne, Healy, & Cameron, 2009) to conduct a three-level regression analysis of the NMIS data with children nested in households nested in clusters. All estimates were derived by the use of second-order penalized quasi-likelihood and iterative generalized least squares estimation. Residual variation at level 1 is assumed to have a standard logistic distribution with mean zero and variance $\pi^2/3 = 3.29$ (Goldstein, Browne, & Rasbash, 2002). At subsequent levels (households, clusters), the intra-class correlation coefficient is given by the estimated residual variation at each level divided by total residual variation.

Sample for analysis

Of the 4901 children (6-59 months) whose mothers were interviewed, 4345 children were tested for malaria and had blood test results available. Of the 4345 children, 175 children (4.0%) were either visitors or had missing data on covariates and were excluded. Because the sample size of children (N=88) in Cross River State (where USAID and the Canadian Red Cross delivered 676,877 LLINs to children aged less than 5 years in late 2008 and early 2009) was too small to be included as a separate independent variable, we excluded these children from the analysis. The final sample for analysis included 4082 children.

We also conducted a sensitivity analysis by excluding Sokoto, Jigawa and Kebbi States which were reported to be seriously affected by heavy flooding (as a result of rainfall, overflow of rivers and release of water from dams) in Northern Nigeria in August and September (2010) (International Federation of Red Cross and Red Crescent Societies, 2011). Since malaria outbreaks following flooding are not uncommon (World Health Organization, 2012), we compared the results of sensitivity analysis (where these three states were excluded) with that of the main analysis (where these states were included) to see if the results were still similar.

Results

Table 1 compares sample characteristics by campaign areas. The overall sample comprised of 4082 children living in 2549 households in 233 clusters. About 42% of children tested positive for malaria parasites overall: the lowest rate was associated with the World Bank Booster Project (34.4%), and the highest rate, with the Global Fund

(62.5%) compared to 41.8% in areas with no campaigns. Among the campaign areas, the Global Fund had the smallest sample of children and the lowest levels of ITN use: 40.2% at the child level, and 34.9% at the community level.

Between-community/cluster and between-household variations in malaria among children were 2.025 and 0.241 - the corresponding percentages were 36.5% [2.025/(2.025+0.241+3.29)] and 4.3% [0.241/(2.025+0.241+3.29)] respectively (not shown). Table 2 summarizes the results in two models, each one adding a new group of variables. In Model 1, compared with areas having no campaigns, children living in areas covered by the World Bank Booster Project (OR=0.58, 95% CI=0.38-0.98) were less likely to have tested positive for malaria after adjusting for geographic variables and state-level fever rates prior to the start of the campaigns. In Model 2, after including the community- and individual-level variables, the World Bank effect became stronger (OR=0.50, 95% CI=0.28-0.89). No significant differences in child malaria infections were found between non-campaign areas and the campaign areas led by UNICEF and Global Fund in both models. Community-level wealth (OR=0.53, 95% CI=0.36-0.78), community-level maternal knowledge regarding malaria prevention (OR=0.67, 95% CI=0.49-0.91), and child-level use of ITNs (OR=0.79, 95% CI=0.63-0.99) were negatively associated with child malaria.

A sensitivity analysis excluding the three states seriously affected by heavy flooding yielded similar results (Model 2, not shown): the World Bank (OR=0.53, 95% CI=0.29-0.94); UNICEF (OR=0.45, 95% CI=0.18-1.09); and Global Fund (OR=1.83, 95% CI=0.80-4.18). The UNICEF effect in the sensitivity analysis was stronger compared with that of the main analysis (OR=0.65, 95% CI=0.30-1.41) in Table 2.

Discussion

In this study, compared with children living in areas with no campaigns, those in the World Bank Booster project areas were less likely to test positive for malaria after adjusting for numerous variables measured at the region, state, community and individual levels. No significant differences in malaria risk between other campaigns and non-campaign areas were observed. Community-level wealth, community-level maternal knowledge regarding malaria prevention, and child-level use of insecticide treated nets were negatively associated with child malaria.

The largest validity threats to this study come from baseline differences (non-comparability) between campaign and non-campaign areas in child malaria risk, the relatively small sample coverage in the Global Fund and UNICEF campaign areas and the problems of co-intervention (ancillary programs operating in campaign areas - e.g. indoor residual spraying campaigns in the World Bank Booster areas (The U.S. Global Malaria Coordinator, 2010)) and contamination (program elements being implemented in non-campaign areas - e.g. ITNs may be obtained from a primary health center or purchased from markets (National Population Commission (NPC) [Nigeria] et al., 2012)). In addition to accounting for geographic variation in risk associated with regional differences and location (urban-rural residency and altitude), we controlled for state-level differences in child fever in 2008 before the campaigns began. We can show that controlling for fever at the state level made the campaign areas comparable in 2008 but cannot be sure that similar conditions of area risk applied in 2009 and 2010: malaria risk varies not only from place-to-place but from one year to the next (National Bureau of Statistics (NBS), 2009).

The estimated reduction in risk associated with the UNICEF campaign (OR=0.65, p=0.27) became stronger (OR=0.45, p=0.08) after excluding states affected by heavy flooding in the sensitivity analysis. (Of the three excluded states, Sokoto and Kebbi were from the UNICEF campaign area and Jigawa from the World Bank area.) However, a larger sample would be needed to demonstrate that these effects were statistically significant in comparison with non-campaign areas. Small sample size is an even greater concern for the Global Fund campaign area. Although a previous study in Togo (Terlouw et al., 2010) found a lack of program effects in Tone which is consistent with the absence of effect in the Global Fund area in the present study, the take-up of ITNs in these two places were different. Children in Tone (88.6%) were more likely to sleep under an ITN the night before the survey than in Ogou (62.7%) or Yoto (57.1%) and thus the lack of program effect was difficult to explain (Terlouw et al., 2010). In the present study, the take-up of bed-nets is lower in the Global Fund areas (34.9%) than the campaign areas led by UNICEF (60.7%) and the World Bank (51.6%). The observed increase in risk in the Global Fund area compared with non-campaign areas (although not statistically significant) is counter-intuitive, although a finding of no appreciable effect is possible if there were problems with program implementation and take-up.

Overall, it appears that the campaigns were implemented fairly well. Between 2008 and 2010, households' ownerships of ITNs increased considerably from 8 to 42%

(National Population Commission (NPC) [Nigeria] & ICF Macro, 2009; National Population Commission (NPC) [Nigeria] et al., 2012). Households in the 14 states with an LLIN campaign were about three times more likely to have at least one ITN than households in states without any LLIN campaign (72 to 75% in campaign areas versus 22% in areas with no campaigns) (National Population Commission (NPC) [Nigeria] et al., 2012). The NMIS (2010) also reported an increase in the proportion of children with fever being treated with anti-malarial drugs from 33% in 2008 to 49% in 2010. Given that the proportions of children receiving anti-malarial treatment in the World Bank Booster areas (52.4%) and non-campaign areas (50%) (Table 1) were quite similar, the observed protective effect against malaria in the World Bank Booster areas was unlikely a consequence of treatment effect. The reduced risk for malaria in these areas may also be attributable to indoor residual spraying but less than 1% of households reported being sprayed in the 12 months prior to the survey (1.7% in the World Bank Booster areas versus 0.4% in non-campaign areas) (National Population Commission (NPC) [Nigeria] et al., 2012). When we conducted a separate analysis by restricting the analysis to children who lived in households that were not sprayed, the results were not affected. The observed reduced risk of malaria among children in the World Bank Booster areas could therefore be attributable to the increased use of LLINs in the project areas after the campaigns. Nevertheless, the campaign effects in other campaign areas were less clear cut despite a dramatic increase in households' net ownerships.

Failure to use ITNs as planned is a challenge to malaria prevention programs. According to a survey of 160 randomly selected households in two local government areas in Cross River State conducted by International Federation of the Red Cross in July and August, 2010, 32% of respondents reported that they no longer had the LLINs distributed by the campaigns. Reasons provided include: torn nets; nets had been given out; or nets were used for other purposes (e.g. door screens or bed sheets). Focus group discussions following the household survey found that a majority of respondents thought the LLINs were no longer effective after one year or the net was not usable after washing twice (Cross River Qualitative Survey, 2011; The U.S. Global Malaria Coordinator, 2011). Despite the net ownership, misperceptions and lack of awareness about proper maintenance might attenuate the campaign effect. It would be helpful to conduct similar qualitative studies in other campaign areas to better understand why the effects of LLINs were inconsistent across different campaigns areas.

In this study, children living in communities with higher levels of maternal knowledge were less likely to have malaria but the association for individual-level maternal knowledge did not reach statistical significance. This finding is plausible if community-level knowledge motivates participation in community-based malaria prevention activities including elimination of mosquito breeding sites in the neighborhood. We also found that children living in wealthier communities were less likely to have malaria. This finding is consistent with the result of a previous study conducted among adults in the Democratic Republic of Congo (Messina et al., 2011). Individual-level child ITN use was negatively associated with malaria which is in line with the increased use of ITNs and reduced risk of malaria in the World Bank Booster areas.

The NMIS (2010) is the first of its kind to be conducted in all 36 states and the Federal Capital Territory of Nigeria, and included testing for malaria among children (6-59 months). Because this is a one-time cross-sectional study, we were unable to assess change and had to rely on statistically controlling for differences between campaign areas in malaria risk that could confound the results. Furthermore, information on program implementation was limited to maternal report on ITN use. Although these are important methodological limitations, attempting to control for baseline differences, using an extensive array of control variables, incorporating different campaigns into the analysis as well as having an external control group, and the low cost of secondary data analysis are strengths of the present study. We believe that our analysis provides some insights into effectiveness questions bearing on the prevention of malaria infections among children in the general population.

Conclusions

The findings of this study show that children living in the World Bank Booster Project areas were less likely to have tested positive for malaria. There was also an observed but statistically non-significant reduction in risk associated with the UNICEF campaign. These beneficial effects need to be corroborated by future studies, using stronger designs and larger samples. Although the increased risk associated with the Global Fund campaign was non-significant, it does raise the possibility that efficacious interventions may not always be effective when introduced into the general population. Program efficacy and effectiveness studies address two very different research questions. The former examines the effect of an intervention under optimal conditions; and the latter, under "real-world" conditions (Flay, 1986). Both types of studies are central to understanding program effects. Finally, it is very clear that community level wealth and knowledge exhibit strong negative associations with malaria risk. Results also suggest that improving community-level maternal knowledge through appropriate channels might be helpful in preventing child malaria in Nigeria.

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Table 1. Sample Characteristics

	World Bank Booster Project	UNICEF	Global Fund	Areas with no campaigns	Overall sample
Level 3, clusters (n)	54	23	15	141	233
Average number of households per cluster (SD)	12.1(3.9)	13.2(3.4)	10.7(4.7)	10.2(4.6)	10.9 (4.4)
Average number of children per cluster (SD)	20.2(7.7)	21.6(7.1)	17.6(9.6)	15.8(8.0)	17.5 (8.2)
Regions (%)					
North Central	0	0	46.7	23.4	17.2
North East	25.9	30.4	0	13.5	17.2
North West	25.9	69.6	0	7.1	17.2
South East	16.7	0	0	22.0	17.2
South	31.5	0	0	12.8	15.0
South West	0	0	53.3	21.3	16.3
Urban (%)	29.6	26.1	26.7	37.6	33.9
Cluster altitude (%)					
≤ 200 meter	44.4	4.3	46.7	47.5	42.5
201-400 meter	16.7	47.8	20.0	31.9	29.2
401-600 meter	37.0	17.4	33.3	13.5	20.6
601 to 800 meter	1.9	30.4	0	2.8	5.2
> 1000 meter	0	0	0	4.3	2.6
State-level fever rate (DHS 2008) *Mean* (SD)	23.1(10.5)	11.0(1.8)	12.9(4.5)	16.5(8.9)	16.9(9.0)
LLINs distribution campaigns (%)					
World Bank Booster Project	100	0	0	0	23.2
UNICEF	0	100	0	0	9.9
Global Fund	0	0	100	0	6.4
No campaigns	0	0	0	100	60.5

Table 1. (cont.)

	World Bank Booster Project	UNICEF	Global Fund	Areas with no campaigns	Overall sample
Community-level wealth *Mean* (SD)	-0.1(0.9)	-0.5(0.6)	0.3(0.9)	0.2(0.9)	0.1 (0.9)
Community-level maternal knowledge *Mean* (SD)	1.7(0.7)	2.1(0.9)	1.2(0.7)	1.5(0.7)	1.6 (0.8)
Proportion of community-level child ITN use *Mean* (SD)	51.6(21.5)	60.7(19.3)	34.9(25.7)	13.7(20.4)	28.5 (28.2)
Proportion of children with fever treated with anti-malarial drugs *Mean* (SD)	52.4(34.2)	54.7(34.9)	59.9(36.7)	50.0(35.3)	51.6(35.0)
Level 2, households (n)	653	304	161	1431	2549
Average number of children per household (SD)	1.7(0.8)	1.6(0.8)	1.7(0.9)	1.6(0.8)	1.6 (0.8)
Household wealth *Mean* (SD)	-0.3(0.9)	-0.6(0.5)	-0.1(1.0)	-0.1(1.00)	-0.2(1.0)
Average number of people per sleeping room (SD)	3.1(1.4)	3.3(1.6)	2.7(1.3)	3.0(1.4)	3.0 (1.5)
Level 1, children (n)	1092	497	264	2229	4082
Child slept under an ITN (%)	53.0	58.7	40.2	14.3	31.0
Maternal education (yrs) *Mean* (SD)	3.6(5.2)	1.7(3.8)	3.7(5.3)	5.0(5.1)	4.2 (5.1)
Maternal knowledge *Mean* (SD)	1.8(1.3)	1.8(1.2)	1.1(0.8)	1.4(1.2)	1.5(1.2)
Child age (yrs)	2.6(1.3)	2.6(1.3)	2.6(1.3)	2.7(1.3)	2.6 (1.3)
Male child (%)	53.1	50.8	48.2	50.5	51.0
Malaria (%)	34.4	40.9	62.5	41.8	41.6

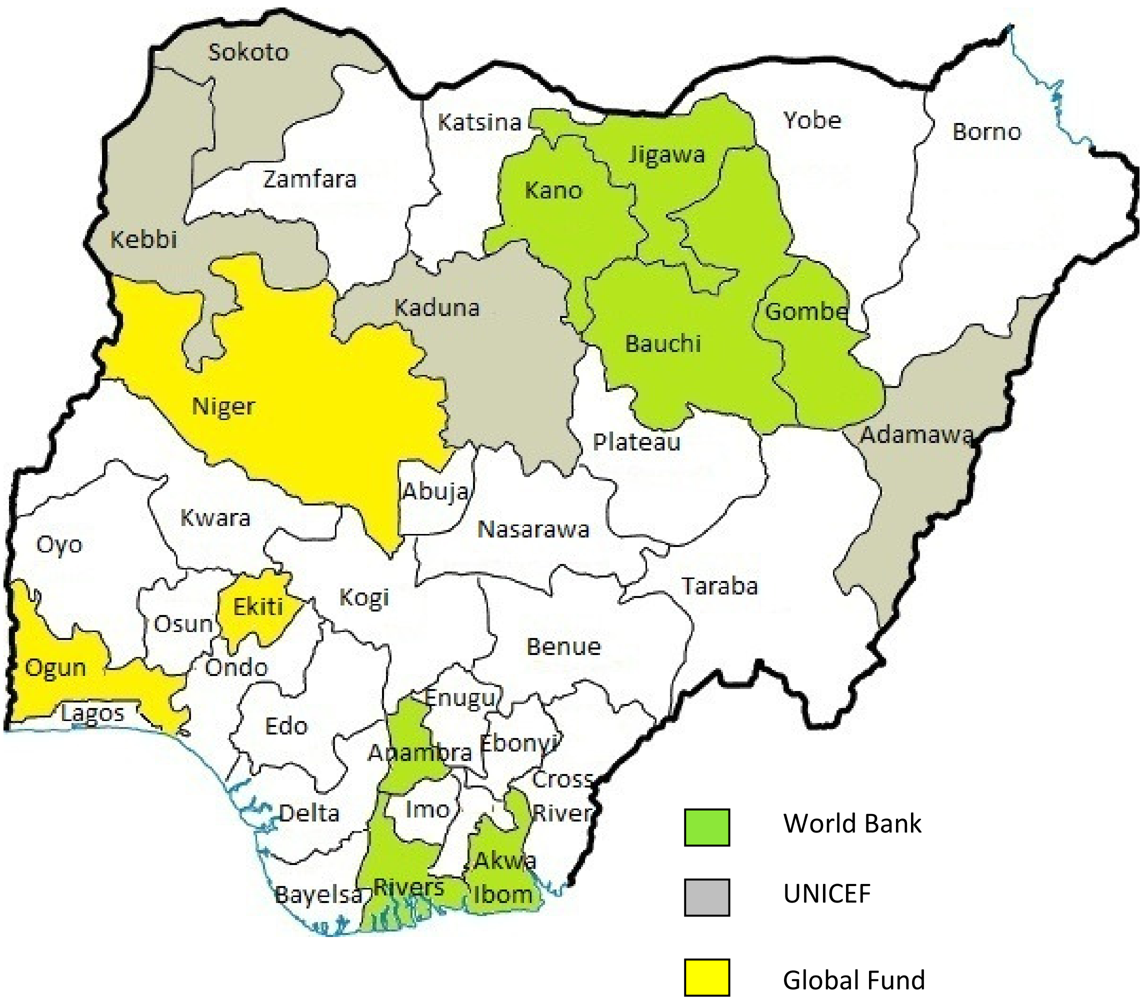
Table 2. Multilevel logistic regressions of child malaria on study variables and covariates

	Model 1 OR (95%CI)	Model 2 OR (95%CI)
Fixed effects Intercept (SE)	-0.003(0.41)	-0.49(0.41)
Level 3 (Cluster) Regions North Central	1.01(0.44-2.31)	1.30(0.59-2.85)
North East	**0.36(0.19-0.69)**	**0.36(0.19-0.66)**
North West	Ref.	Ref.
South East	0.36(0.15-0.85)	1.03(0.44-2.46)
South	0.54(0.23-1.25)	1.68(0.73-3.87)
South West	0.68(0.28-1.66)	1.46(0.57-3.70)
Urban	0.25(0.17-0.38)	0.67(0.42-1.06)
Cluster altitude ≤ 200 meter	Ref.	Ref.
201-400 meter	1.58(0.90-2.77)	1.28(0.76-2.15)
401-600 meter	1.42(0.75-2.67)	1.67(0.92-3.06)
601 to 800 meter	0.97(0.36-2.61)	0.96(0.39-2.38)
> 1000 meter	0.37(0.08-1.60)	**0.22(0.05-0.87)**
State-level fever rates (DHS 2008)	1.22(0.89-1.67)	0.98(0.73-1.32)
LLIN distribution campaigns World Bank Booster Project	**0.58(0.34-0.98)**	**0.50(0.28-0.89)**
UNICEF	0.67(0.30-1.49)	0.65(0.30-1.41)
Global Fund	2.11(0.92-4.86)	1.79(0.77-4.17)
No campaigns	Ref.	Ref.
Community-level wealth		**0.53(0.36-0.78)**
Community-level maternal knowledge		**0.67(0.49-0.91)**
% Children using ITN		1.07(0.97-1.18)
% Children with fever treated with anti-malarials		1.00(0.94-1.05)
Level 2 (Household) Household wealth		0.81(0.66-1.00)
Number of people per sleeping room		0.98(0.92-1.04)
Level 1 (Child) Maternal knowledge		0.97(0.88-1.06)
Maternal education		0.98(0.95-1.01)
Child slept under an ITN		**0.79(0.63-0.99)**

Table 2. (cont.)

	Model 1 OR (95%CI)	Model 2 OR (95%CI)
Treated with anti-malarial drugs Child with fever not being treated		Ref.
Child with fever being treated		0.97(0.74-1.28)
No fever		**0.66(0.53-0.83)**
Child age		**1.30(1.23-1.38)**
Male child		1.14(0.97-1.34)
Random effects (SE) Level 3, cluster	1.34(0.18)	1.02(0.15)
Level 2, household	0.52(0.11)	0.54 (0.12)

Figure 1. Map of LLIN Distribution Coverage in Nigeria



CHAPTER 6

General Discussion

"Equity" is critical when dealing with child mortality globally and nationally (Hypher, 2011). There is substantial variation in child mortality both between and within countries. In general, children from the poorest countries are most likely to die before their fifth birthdays, mainly from preventable causes. There is also considerable within-country variation (e.g. intra-urban differentials) in child mortality in low and middle income countries. While the negative impact of residing in urban slum settlements on child health remains poorly understood, knowledge is also limited as to the understanding of several other factors that could play a crucial role in tackling child mortality across countries. For example, rising cesarean section (CS) rates, an indication of unjustified use of scarce resources, has been a concern for many countries but empirical evidence is lacking as to the optimal CS rates. Moreover, despite the fact that HIV/AIDS is one of the leading causes of death among African children infected from their parents and that new HIV infections in sub-Saharan Africa now mainly occur in married couples, the prevalence of condom use to prevent HIV transmission remains very low even among couples where only one partner is HIV positive. Limited knowledge exists as to the determinants of consistent condom use among such couples. Prevention and control of malaria, another major child-killer disease in sub-Saharan Africa, has received much attention in recent years. Enormous resources have been invested in free mass LLIN distribution campaigns in this region, but the effectiveness of LLINs in reducing child malaria is still poorly understood. The preceding chapters (Projects 1,2,3,4 described in chapters 2,3,4 and 5) attempted to contribute to the understanding of these issues.

This chapter presents a general discussion of the important findings and implications, followed by limitations and future directions.

Important findings and implications

The findings of project 1 add to the existing knowledge of slum residency and child health by showing that living in a slum neighborhood was associated with infant mortality beyond the socio-economic status and other characteristics of the families. In other words, children from better-off households located in a slum neighborhood could also have an increased risk for infant mortality. Results also showed that the longer a child lived in a slum neighborhood, the worse it was for child growth. The findings of project 1 thus highlight the importance of contextual or environmental effects of slum residency on child health. There have been slum upgrading projects on infrastructure improvement that include water, sanitation and housing (Field & Kremer, n.d) but there are also challenges to these projects. For example, low income households may not be able to repay housing loans provided by the projects and thus choose not to participate (Merrill & Suri, 2007). Results of project 1 suggest that slum upgrading projects should be community-based rather than household-based.

Results of project 2 add to the existing knowledge of the association between CS and neonatal mortality by indicating that in countries with low and medium CS rates, CS was associated with an elevated risk of neonatal death and this association was particularly robust to sensitivity analysis in low CS rate countries. Studies to evaluate the quality of maternal and newborn health care services are necessary in those countries. Project 2 also found that there was substantial between-country variation in the associations between individual-level CS and neonatal mortality (i.e., positive associations in some countries and no associations in others). This suggests a double burden for some high CS-rate countries, where CS can not only increase the risk of neonatal death but also add to the burden of health care costs. In those countries, in addition to evaluating the quality of health care services, it is important to find out how many CS performed are due to need (i.e., clinical indications) versus preference (i.e., no indications but physician's preference or maternal request) to avoid exposing mothers and their babies to unnecessary risks.

Using data collected from both husband and wife, project 3 adds to the existing knowledge of the determinants of condom use among HIV-infected married couples by revealing that there is a pattern of male dominance with regard to the associations between consistent condom use and: awareness of HIV test result and HIV preventive knowledge. If only the husband knew his HIV test result or had the preventive knowledge, the couple was more likely to have used condoms. However, no corresponding associations were found for the wife. These findings suggest that the subordinate roles of wives in decision-making with respect to condom use could result in elevation in HIV risks among themselves or their husbands (especially if one partner is HIV positive and the other negative). This further implies that for women, improving HIV preventive knowledge or increased HIV testing alone may be inadequate. Strategies to empower women are necessary so that they could have a role in decision-making over condom use and protect themselves from getting the infection or avoid transmitting the infection to their husbands.

In the absence of nationally representative evaluation studies on the effectiveness of LLINs, project 4, using secondary data, showed that the association between LLIN mass distribution campaigns and child malaria were inconsistent (i.e., showing either protective or no effect) across different campaign areas in Nigeria. These findings imply that although LLINs were efficacious in well-controlled randomized trials where high coverage and use were ensured (Lengeler, 2004), they could turn out to be ineffective in real world settings where the actual or proper use could not be controlled. This study also shed light on the contextual factors influencing child malaria. Results suggest that improving community-level maternal knowledge through appropriate channels might be helpful in preventing child malaria in Nigeria.

Limitations of the projects

Despite the novel findings and rigorous analytical approaches used in this thesis, there are also limitations. First, countries are not a random sample from all low and middle income countries but only those that participate in the DHS program. The findings of projects 1 and 2 may therefore be restricted to the countries included. Second, of the countries that participated in DHS, some had to be dropped because of the lack of the required data. For example, in project 1 duration of stay at the current place of residence was not available in 4 countries which were excluded. This decreases both the number of countries being compared and the scope of the comparative analysis. Third, in secondary data analysis where the primary objectives of data collection were different from those of the dissertation, proxy variables or proxy baseline data had to be used when information was unavailable. For example, in project 2, proxy variables were used to estimate risk factors for CS and/or neonatal mortality and there could be residual confounding as a result of unmeasured factors. We therefore performed sensitivity analysis to estimate the boundary where unobserved factors could account for the findings and found that the association between individual-level CS and neonatal mortality was the most robust in low CS rate countries. In project 4, only post-program data were available on malarial infection. To ensure that campaign and non-campaign areas were comparable in terms of malaria risk, fever data from the 2008 DHS (which were collected during the rainy season) were used as a proxy baseline. Although fever is not a reliable proxy for malaria in the dry season, research evidence has consistently shown that the proportion of fever attributable to malaria was very high during the rainy season (Bisoffi et al., 2010; Dicko et al., 2005; McGuinness et al., 1998). Finally, all four projects used cross-sectional data and thus causal relations between the variables could not be established.

Future research directions

Despite the limitations of secondary data analysis, using available nationally representative data such as Demographic and Health Surveys is a great, low-cost starting point for studying important un-answered research questions and providing direction for further studies based on the findings.

Project 1 has shown that residing in a slum neighborhood was associated with infant mortality and child stunting. Further studies should corroborate these findings by looking at these associations longitudinally to establish causal relations. Project 1 found that the risk for infant mortality associated with residing in a slum neighborhood was attenuated among children born to women who had received antenatal care (ANC) from a health professional. There was substantial between-country variation in the proportion of women who did not receive ANC (0.8% in Ukraine versus 30.4% in Ethiopia) (overall sample) and even more variation among women living in slum neighborhoods (0% in Ukraine versus 52.9% in Mali). Studies are needed to examine barriers to access to ANC services in slum neighborhoods in countries where ANC coverage in these neighborhoods remains low.

Project 2 showed that the odds of neonatal mortality associated with CS in low CS-rate countries were about 48% higher and statistically different from those observed in high CS rate countries. Studies are necessary to examine possible factors associated with these elevated risks (e.g. poor infrastructure in health facilities, inadequate expertise, or poor neonatal care). There is considerable cross-country variability in the distribution of operating theatres: the estimated number varies from 1.0 (95% CI 0.9-1.2) per 100,000 people in west sub-Saharan Africa to 25.1 (20.9-30.1) per 100,000 in eastern Europe (Funk et al., 2010). In Afghanistan, for example, it is not uncommon for many health facilities to have a single operating table in the theatre to perform both general surgery and obstetric operations including CS (Kim et al., 2012). This could interfere with performing a timely CS. In addition, proper sterilization of the operating theatre could be a challenge in low resource settings, which could lead to an increased risk for nosocomial infections in both the mother and the newborn. Moreover, in 'low-volume settings' where rates of performing CS are very low, maintenance of clinical expertise and confidence to perform the procedure could also be a challenge (Kim et al., 2012). Finally, although babies delivered by CS are more likely to have respiratory distress as a result of failure to remove fetal lung fluid at birth and increased admission to neonatal intensive care units (Hansen, Wisborg, Uldbjerg, & Henriksen, 2007; Jain & Eaton, 2006; Ramachandrappa & Jain, 2008) , intensive care services in developing countries, especially in sub-Saharan Africa, are underdeveloped. In fact, neonatal intensive care units are 'a novel concept' in these countries (Okafor, 2009). While there are several factors possibly related to the increased risk of neonatal mortality associated with individual-level CS in low CS rate countries, future studies are necessary to identify specific factors contributing to this increased risk.

In project 3, about half of the respondents mentioned a desire for more children in the near future. Although "harm-reduction strategies" have been proposed for discordant couples who have a desire to conceive, the effectiveness of these strategies has not been established (Beyeza-Kashesya et al., 2010). There are at least 2 issues associated with having a child in HIV-infected couples: (1) risk of mother to child transmission of HIV and (2) risk of HIV transmission to the uninfected partner in sero-discordant couples. Studies looking at reasons for desiring or not desiring more children are needed to better understand this issue so that appropriate counselling and care can be provided to high risk couples.

Project 4 found that the associations between the presence of LLIN mass distribution campaigns in a community and child malaria were inconsistent. Studies are necessary to find out possible reasons for these findings. Qualitative techniques that include observation of ITN use, key informant interviews and focus group discussions could be helpful in understanding the observed differences in program outcomes.

Recommendations for DHS

The secondary data used in this thesis helped address several important novel research questions, yet they were limited in some ways to address these questions. Recommendations arising from the thesis projects are presented below. They are expected to be helpful to the DHS in improving their surveys.

***Recommendation #1*:** Future DHS should include questions as to whether a neighborhood is located in hazardous sites (UN-Habitat, 2010) that include rubbish dump sites and industrial areas with high pollution. While not all slums are located in hazardous sites (UN-Habitat, 2010), little is known regarding the association between the location of slums and child health. Adding this information to future DHS could allow studies to examine the contextual effects of slum residency on child health in more detail.

Recommendation #2: In the future rounds of DHS, questions should be included regarding complications during pregnancy and delivery in all women irrespective of mode of deliveries (vaginal or CS), and reasons for having CS (e.g. clinical indications or maternal request without any indications). Future studies could use these more specific indicators and replicate the findings of project 2. For those answering maternal request as a reason for CS, further questions should be asked to specify the reason (e.g. fear of child birth, cultural reason, etc). Tokophobia or fear of childbirth that occurs in about 6 to 10% women is one of the main reasons for maternal request (Nama & Wilcock, 2011).

Cultural factors may also play a role. For example, in Taiwan, CS were more likely to be performed on ‘auspicious days’ and less likely to be conducted on non-auspicious days compared with normal days (those days were calculated based on traditional Chinese cosmology/astrology and recorded in the lunar calendar) (Lo, 2003). As such, including questions on specific reasons for having CS in DHS could help one better understand the considerable between-country variation in CS rates and also shed light on how many CS are due to need versus preference in these countries.

Recommendation #3: To help better understand the association between awareness of HIV status by husband only and condom use (and the lack of corresponding association for wife) as shown in project 3, future DHS should ask questions as to whether the respondents tested positive for HIV, have disclosed their HIV status to their spouses, and experienced barriers and motivating factors for disclosure. From the results, effective counseling strategies could be developed. For those who have disclosed, questions related to the consequences of disclosure should also be asked. Since few studies have examined these questions based on the perspectives of both partners among high risk couples, asking these questions in future rounds of DHS could be very helpful in advancing knowledge on this topic.

Recommendation #4**:** The beneficial effects of LLIN campaigns observed in project 4 need to be corroborated by future studies, using stronger designs and larger samples. More robust evaluation studies could be conducted by cooperation between future campaigns and MIS. For example, staggered interventions that start at different times in different places could be conducted to have historical controls as well as external comparison groups (Habicht, Victora, & Vaughan, 1999). Plausibility of program effects on outcomes could be improved by using both types of controls (Habicht et al., 1999).

***Recommendation #5*:** Adding a longitudinal component to the DHS for some countries could be very helpful. Not only would it allow for a more complete understanding of the long term impact of certain exposures (e.g. slum residency or already established LLIN campaigns) on child health, but it would provide valuable data for use in future studies with different objectives.

Conclusions

The findings of this thesis indicate the importance of contextual influences which could either be harmful or beneficial to child health. Residing in a slum community increased the risk for infant mortality or stunted growth but living in a community with certain LLIN campaigns, higher levels of wealth or maternal knowledge were protective against child malaria. The harmful effects of slum residency was alleviated by maternal use of ANC services and aggravated by increasing child age. Results also showed the moderating influence of contextual factors, as evidenced by country-level CS rates modifying the association between individual-level CS and neonatal mortality. Results also shed light on the understanding of parental HIV preventive behaviors, where a pattern of male dominance was observed in the decision to use condoms consistently among couples.

Taken together, these findings suggest that improving the material circumstances of slum neighborhoods and increasing ANC coverage among women living in urban slums could help reduce intra-urban differentials in child health. Results also indicate the need of improving the quality of maternal and newborn health care services in countries with low and medium CS rates in order to reduce neonatal mortality associated with CS. In addition to LLIN mass distribution campaigns, promoting maternal knowledge on malaria prevention at the community level could help reduce the burden of child malaria. In the case of HIV prevention, improving HIV preventive knowledge or increased HIV testing alone among women may be inadequate. Strategies to empower women are necessary so that they could have a role in decision-making over condom use and protect themselves from getting the infection or avoid transmitting the infection to their husbands.

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