

**Supplement** - Promoting health  
research in Africa: research from  
emerging African scholars



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## About this Special Issue

This special issue of the Pan-African Medical Journal showcases research conducted by some of the fellows of the African Doctoral Dissertation Research Fellowship (ADDRF) Program. The ADDRf Program was established in 2008 by the African Population and Health Research Center (APHRC) in partnership with the International Development Research Centre (IDRC). The goal of the ADDRf is to nurture a critical mass of the next generation of locally well-trained and skilled African researchers and scholars who are committed to the reconstruction of the African academy and to facilitate rigorous policy-relevant research on health systems, governance, equity, and population-related issues in the region.

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## Editorial

# Strengthening local health research capacity in Africa: The African Doctoral Dissertation Research Fellowship Program

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## Introduction

Unlike many other regions of the world, sub-Saharan Africa still suffers massive deficits in doctorates. Yet, PhD training is key to building mastery of specific subject-matters and equipping researchers with the high-level skills needed to design, implement and evaluate development interventions and activities. Tetley [1] argues that the lack of PhDs in Africa is a major impediment to development in the continent. African universities which are expected to provide doctoral training face myriad challenges that impede their capacity to produce high quality PhD graduates to meet local development needs. These gaps in post-graduate training have resulted in numerous initiatives to enhance research capacity on the continent.

The African Population and Health Research Center (APHRC), a Nairobi-based regional research institute that conducts high-quality research on urbanization, population, health and education issues facing sub-Saharan Africa, has developed two complementary programs to address the research capacity gaps that plague the continent, particularly with respect to graduate training in population and public health as well as health systems research. The first, the Consortium for Advanced Research Training in Africa (CARTA) [2] brings together nine universities and four research institutions from West, East, Central, and Southern Africa and selected northern partners to build multidisciplinary research capacity in the broad fields of public and population health. CARTA offers a collaborative four-year doctoral training program in public and population health for junior faculty and researchers at participating African institutions. CARTA also has a strong institutional capacity building component that includes training workshops for faculty and staff and infrastructural investments. While CARTA addresses the important challenge of the scarcity of a robust research and training infrastructure capable of offering the type of vibrant and sustained doctoral training necessary to attract, train and retain the continent's brightest minds; the relatively small number of institutions involved in CARTA raises the urgent need for other innovative strategies to achieve greater reach in

strengthening doctoral training in Africa. The second, the African Doctoral Dissertation Research Fellowship (ADDRF) Program, responds to this need and provides doctoral fellowships and targeted training workshops to facilitate rigorous research addressing governance, equity, health and population-related issues in Africa. The ADDRf Program provides a means to reach a wider number of PhD students from across the region (including both Anglophone and Francophone Africa) providing them the requisite guidance and transferable skills that will prepare them for academic and research positions. This supplemental issue of the Pan-African Medical Journal showcases some of the research conducted by fellows of the ADDRf Program.

## About the African Doctoral Dissertation Research Fellowship (ADDRF) Program

The ADDRf Program was initiated in 2008 by APHRC in partnership with the International Development Research Centre (IDRC). The Program aims to build a critical mass of the next generation of scholars committed to the reconstruction of the African academy and to facilitate rigorous research addressing health systems, governance, equity, and population-related issues in Africa. The Program achieves these objectives through the provision of PhD fellowships and targeted training workshops for fellows on critical research skills. Central to the ADDRf are methodology and advanced writing workshops designed to steadily enhance skills and knowledge, guide and propel the fellows through the research process, and provide a foundation for building networks of researchers, peers, and mentors. A detailed description of the rationale for and structure of the ADDRf Program is provided elsewhere [3]. The Program has supported 133 doctoral students from 20 Anglophone and Francophone sub-Saharan African countries. At the writing of this editorial, 61 (46%) of the fellows had completed their doctoral studies.

The bulk of ADDRF graduates also continue to staff research and higher education institutions on the continent. Findings from a 2012 evaluation of the Program demonstrate several key successes in strengthening beneficiaries' research capacity and enhancing retention. The evaluation covered 55 of 68 fellows in the first three cohorts who completed an electronic questionnaire. Out of these, 28 (51%) had graduated when the study took place. Results showed that 25 of the 28 graduates were working in their countries of origin; suggesting minimal 'brain drain.' Fellowships awarded to PhD students studying in sub-Saharan Africa-based universities—often in fellows' countries of origin—can therefore be effective in reducing brain drain and enhancing retention. Almost all of the ADDRF graduates continue to work on health systems, governance, equity, and population-related issues and are making a contribution to knowledge production—22 out of the 28 graduates had publications in peer-reviewed journals within three years of receiving the award, several had undertaken policy-related consultancies since the completion of their studies, and 18 were involved in higher education teaching. Altogether, ADDRF fellows have published over 150 peer-reviewed papers in the last six years. Several of these papers are co-authored by more than one ADDRF fellow, sometimes from different countries. This is in tandem with ADDRF's commitment to promote scientific networking among Africans, break national barriers, and facilitate collaboration among fellows and across countries. Evaluation results also show that the training workshops have had an impact with about nine in ten fellows noting that the Program had improved their research methodology and scientific writing skills, as well as the quality of their dissertations. The evaluation also showed that the fellows felt that the Program had expanded their access to networking opportunities. Fellows largely rated the ADDRF Program's contribution to their educational experience in terms of access to networking opportunities/connections as excellent or very good. Other reported benefits of the Program included financial support for personal expenses, increased technical knowledge in one's field, improved communication skills, and personal development.

Managing the ADDRF Program over these years, we have realized the enormity of the need to support African doctoral students, an issue highlighted by other capacity building initiatives in the region [4]. For instance, the initial call attracted 118 applications from 19 countries in East, West, South, and Central Africa. However, less than a fifth of these were funded. In the first five years, over 750 applications were received, but less than one fifth of these were funded. Importantly, initial outcomes underscore the need for further investments to reach fellows from Francophone and Lusophone Africa. Since 2008, the number of applicants from Anglophone Africa has far exceeded the number from Francophone Africa. Currently, 17% (22 fellows) are from Francophone Africa. Over the years, the Program has made deliberate steps to reach potential applicants and to support fellows from Francophone Africa including wider dissemination of the call for application in French to research and academic institutions based in Francophone-Africa, the option to submit applications in French, the use of bilingual reviewers during selection, and the involvement of bilingual instructors in the training workshops.

ADDRF's initial vision of training and retaining a critical mass of scholars in the region remains as vital and relevant today as in 2008 when it was established. While several aspects of the African higher education environment are improving, the local production of quality PhDs continues to progress very slowly. Although universities in Africa face enormous constraints, they remain central to the creation of intellectual capital. Longer-term investment is thus needed to support and sustain the emergence of a critical mass of the next generation of scholars. The initial funding from IDRC has been critical in expanding the reach of the Program and has enabled the Center to leverage additional funding to support PhD training in the region. The additional funding has also expanded the scope of funded-research to areas beyond health systems research, such as sexual and reproductive health, giving APHRC the opportunity to leverage synergies between the ADDRF Program and its other research and research capacity strengthening programs, including CARTA. In the years ahead, the ADDRF will seek to sustain the momentum of its efforts to build a critical mass of the next generation of scholars as well as find innovative ways to secure the future of its graduates, primarily, by investing in their transition from PhD studentships to postdoctoral positions and beyond. In the long-run, however, the sustainability of the ADDRF and indeed, other research and training fellowship programs on the continent, will depend on investments from African governments and foundations.

## About the supplement

This supplement of the Pan-African Medical Journal showcases research conducted by 14 ADDRF fellows. The supplement is intended to promote fellows' emergence as confident scholars and as internationally-recognized academics and researchers. Two papers by Saban and colleagues draw on nationally-representative data to examine the links between substance use and mental health among adolescents in South Africa. These papers draw attention to the mental health challenges faced by adolescents—an important, but often-understudied, aspect of health and wellbeing.

Sub-Saharan Africa has high levels of maternal and child morbidity and mortality [5]. Seven papers in this supplement are based on research on various aspects of maternal and child health (MCH). Ononokpono and Odimegwu draw on Demographic and Health Survey (DHS) data to describe the determinants of maternal health care utilization in Nigeria. Stephens and colleagues, examine the association between peripheral malaria parasitaemia and maternal anaemia and infant birthweight in Ghana. The paper on Barriers to antenatal syphilis screening in Burkina Faso examines barriers at facility- and community-levels that impede the uptake of antenatal syphilis screening. Echoka and colleagues report on the barriers that women face in accessing emergency obstetrics care services in a Kenyan coastal district with a large rural population. Kiondo and colleagues assess adverse neonatal outcomes in women with pre-eclampsia in Uganda. Two of the seven MCH-related articles highlight child health issues. The first paper, Anaemia among school children older than five years in the Volta Region of Ghana, shows that malaria parasitaemia, ferritin concentration and child's sex are associated with anemia in children. The second paper by Wado and colleagues investigates child vaccination status in rural Ethiopia and shows low overall levels of completion of child vaccination series. The authors also underscore the association between child vaccination status, parity and women's autonomy within the household. The authors call for interventions to enhance women's empowerment and access to family planning.

Although the majority of ADDRF fellows are engaged in health systems or public health research, the Program has also funded fellows conducting laboratory-based studies that have critical implications for health. For example, the paper by Ngure and colleagues examines the therapeutic properties of the East African greenheart (*Canellaceae*) in treating leishmaniasis, a neglected tropical disease currently treated through extensive hospitalization and the use of highly toxic and expensive drugs.

The remaining five papers report on various distal or proximate determinants of health. Okidu investigates HIV/AIDS communication in four Nigerian newspapers and argues that newspaper editors can do more to nurture an environment in which HIV/AIDS is discussed openly. Orem and colleagues, examine the role of research in informing health policy development in Uganda. Kretchy and colleagues assess adherence to anti-hypertensive medication among patients in two hospitals in Ghana and evaluate the extent to which an individual's locus of control is associated with adherence. Finally, two papers by Obembe and colleagues, and Mbada and colleagues report new and important research on the physical rehabilitation of patients with stroke and low back pain, respectively.

Overall, this collection of papers serves to demonstrate the wide range of topics that ADDRF fellows are researching. Each paper highlights programmatic and policy issues and it is our expectation that beyond showcasing the work of ADDRF fellows, this supplement will add to the body of research that can inform the formulation of programs and policies to improve health outcomes in sub-Saharan Africa.

## Competing interests

The African Doctoral Dissertation Research Fellowship Program is managed by the African Population and Health Research Center, where the authors currently work.

## Authors' contributions

CWK, COI, JW and DA are involved in coordinating the ADDRDF program. CWK, COI, and ACE contributed to development of grant proposals for funding to support the ADDRDF program. CWK prepared the initial manuscript draft. All authors critically reviewed and edited the manuscript. All authors read and approved the final manuscript.

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## Research

# Determinants of Maternal Health Care Utilization in Nigeria: a multilevel approach

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**Introduction:** Fourteen percent of maternal deaths globally occur in Nigeria. Low utilization of maternal health services for delivery may partially explain the high maternal mortality. The aim of this study was to examine the contribution of community factors in explaining variations in the use of health facilities for delivery in Nigeria.

**Methods:** Our sample consisted of 17,542 women aged 15-49 years drawn from 2008 Nigeria Demographic and Health Survey, who had had their last birth in the five years before the survey. We employed multilevel analysis to identify community factors related to the use of delivery care.

**Results:** In addition to several individual factors, region of residence was significantly associated with facility delivery. Women who lived in Northern Nigeria were less likely to deliver in a health facility than those who resided in the Southern part of the country. Residence in communities with a high proportion of women who had secondary and higher education significantly increased the odds of facility delivery whereas ethnic diversity was negatively associated with health facility delivery.

**Conclusion:** Interventions aimed at promoting the use of health facility for childbirth should not only be implemented at the individual level but also tailored to the community level as interventions conceived without consideration for community context are likely to have limited impact. Increasing women's education in disadvantaged communities and region-specific interventions that increase access to health facilities are likely to have far-reaching impacts in reducing maternal mortality.

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## Introduction

The increasing attention given to maternal health globally has concentrated on the reduction of maternal mortality. Although there has been a 47% decline in maternal deaths globally, the maternal mortality ratio is still unacceptably high. In high income countries, delivery is often a positive and fulfilling experience, but for many women in low-resource countries, delivery is associated with suffering, morbidity and in many cases maternal death [1]. With an estimated maternal mortality ratio of 500 per 100,000 live births, sub-Saharan Africa accounts for 56% of all maternal deaths globally [2]. Nigeria contributes 14% of global maternal deaths with a maternal mortality ratio of 630 per 100,000 live births [3]. Although maternal mortality declined by 41% between 1990 and 2010 [2], Nigeria still ranks high in the list of countries with high maternal mortality rates. The high maternity rate has been attributed to inadequate use of maternal health care services [4].

Delivery in a health facility is associated with lower maternal and

newborn mortality and morbidity rates compared with home delivery [5]. However, the 2008 Nigeria Demographic and Health Survey (NDHS) showed that only 38 % of women delivered in a health facility [6]. Community perceptions of the quality of maternity health care, community beliefs about the importance of delivery in a health facility, knowledge of the benefits of having deliveries assisted by skilled health attendants, and place of last birth have been found to be associated with delivery in a health facility [7, 8]. Socioeconomic factors including husband's occupation, wealth status, and financial difficulty have been found to influence the utilization of maternity services both in Nigeria and elsewhere [9-12]. Adamu and Salihu also identified several socio-cultural factors, including illiteracy, husband's permission to use health services and purdah restrictions as barriers to women's use of hospital delivery in rural Kano, North west Nigeria [13]. Other studies in Nigeria found that region of residence, perceived quality of care, income, ethnicity and possession of health insurance were significantly associated with the use of delivery care service [14-17]. The decision to deliver in a particular health facility is also associated with proximity to the facility, cost and quality of care [18].

Several studies have identified individual and familial factors associated with the use of delivery care. However, most of these studies have shown an inconsistent pattern of association between the use of facility delivery and individual and household factors. For example, whereas Mpembeni and colleagues [19] found that delivery care is positively associated with maternal age, Aremu et al reported that maternal age was not significantly related to health facility delivery [17]. Further, although some studies have documented a positive effect of education on health facility delivery, some researchers have questioned the strong independent effects of education on the utilization of maternal health care services and have argued that factors such as place of residence and socioeconomic status interact to confound the strong effect of education on maternal health care behaviour [20].

As decisions to seek maternal health care are not solely dependent on individual characteristics, it is imperative to examine community conditions, such as social factors and the location of services [21], that can interact with individual preferences or choices to influence delivery care utilization. Researchers have argued that health promotion emphasizes the role of enabling environments and individual behaviour, therefore it is important to broaden the scope to other determinants of health, including community conditions [22]. The review of extant literature has shown that very few studies on maternal health care have examined factors at the community level. Most previous studies have rarely considered all the domains of the community. Examining community level factors related to place of delivery, for example ethnic diversity, may help in understanding aspects of communities that are important for policy manipulation. To address the identified research gaps, this study examined the relationship between community level factors and the use of health facility for childbirth in Nigeria.

## Methods

The data analyzed in this study were derived from the 2008 NDHS, a cross-sectional survey designed to provide information on population and health indicators at the national and state levels. The survey covered all 36 states and the Federal Capital Territory (Abuja). The sample frame for the survey was the list of Enumeration Areas (EAs) developed from the 2006 population census. The primary sampling units (PSU), which are referred to clusters, were selected from the lists of (EAs). The sample survey was selected using a stratified two-stage cluster design, made up of 888 (286 urban and 602 rural) clusters. Details about the sampling have been provided elsewhere [6]. In all, 33,385 women aged 15-49 years participated in the survey. The analysis reported in this study was limited to 17,542 women who had had their last delivery in the five years preceding the survey. Women who had more than one birth in the reference period were excluded from the analysis. Our choice of last birth is based on the assumption that information on maternal health care for the most recent birth is less subject to recall bias.

The dependent variable was place of delivery and was coded 1 if a woman delivered in a health facility and 0 if she delivered at home. We examined a number of individual/household variables including maternal age at last birth, education, religion, ethnic origin, occupation, women's autonomy, parity and socioeconomic status. Maternal age was calculated by subtracting the century month code (CMC) of the child's date of birth from the CMC of the date of birth reported by the respondent and categorized as: 15-24, 25-34 and 35-49. Education was categorized as: no education, primary, and secondary or higher. Religion was classified as Muslim, Christian and Traditional religion/others. Ethnic origin was categorized as Hausa (a merger of Hausa, Fulani and Kanuri based on geographical location and small number of Kanuri women in the sample), Igbo, Yoruba and Others (all the minority ethnic groups). Occupation was re-grouped into formal employment (professional/ technical/ managerial/ clerical/ sales/ services/ skilled manual workers), agricultural employment, unskilled manual workers and unemployed. Woman's autonomy was measured using a single variable assessing whether the respondent makes decisions on her own health care independently, jointly with her partner, or whether the partner or others make the decision. Parity was measured as the number of live births and categorized as 1-2, 3-4, 5 or more. Socioeconomic status was assessed using a household wealth index generated through Principal Component Analysis (from Factor Analysis) and based on household assets and amenities (e.g., type of flooring, water supply, electricity, radio, television, refrigerator and type of vehicle) [23].

We assessed four community level variables; place of residence (urban and rural), region of residence, community level education and ethnic diversity. Region of residence was categorized as: North Central, North East, North West, South East, South-South and South West. Community level education was measured as the proportion of women with secondary and higher education in the PSU. The measure was divided into three tertiles and categorized as low, medium and high. Ethnic diversity was defined as the proportion of women from different ethnic groups in the PSU [24]. The measure was divided into tertiles and categorized as low, medium and high. The community level variables were constructed by aggregating individual characteristics (educational attainment and ethnic origin) at the cluster level. The index woman was excluded while constructing the community level variables to reduce collinearity. A total of 886 clusters were represented in the study and each cluster or PSU was made up of a minimum of 80 households.

Bivariate tabulations were computed to identify the distributions of the outcome variables by selected background characteristics. The chi square test of association was used to test the statistical significance of these bivariate distributions. We estimated a multilevel model that assessed the relation of individual and community level factors (fixed effects) as well as community level random effects using Stata 11.1 software. Individual and household variables were considered as 'individual level' variables in the study. The average number of women in a household was 1.7; thus, the household was not large enough to be specified as a level of analysis.

Multilevel analysis was used to account for the hierarchical nature of the DHS data [25]. A two-level multilevel logistic regression model was estimated. The model consisted of two sub models at level 1 and level 2 (i.e., individuals (level 1) were nested within communities (level 2)). A two-level multilevel model for a dichotomous outcome uses a binomial sampling and a logit link [26]. In level 1 model, the outcome variable  $Y_{ij}$  for individual  $i$  living in community  $j$  is written as follows:

$$\text{Probability}(Y_{ij}=1|B) = \Phi_{ij}$$

$$\text{Level 1 variance} = [\Phi_{ij}(1 - \Phi_{ij})]$$

$$\text{Predicted log odds } \eta_{ij} = \log [\Phi_{ij} / (1 - \Phi_{ij})]$$

$$\eta_{ij} = \beta_{qj} + \sum \beta_{qij} X_{qij} \quad (1)$$

$$q=1$$

Where:  $\Phi_{ij}$  is the probability that the  $i$ th individual in the  $j$ th community take value "1" ("1" indicates that the event will occur);  $\beta_{qj}$  is the level 1 intercept;  $\beta_{qij}$  is level 1

coefficients.  $X_{qij}$  is level 1 predictor  $q$  for  $i$ th individual within  $j$ th community

The level 2 model, and can be expressed as follows:

$$\beta_{qj} = \gamma_{q0} + \gamma_{q1} W_{1j} + \gamma_{q2} W_{2j} + \dots + \gamma_{qsq} W_{sqj} + u_{qj} S_q$$

$$= \gamma_{q0} + \sum \gamma_{qs} W_{sj} + u_{qj} \quad (2)$$

$$s=1$$

Where

$\gamma_{qs}$  ( $q = 0, 1, \dots, S_q$ ) are level 2 coefficients;  $W_{sj}$  are level 2 predictors and  $u_{qj}$  is level

2 random effects.

We estimated four models. The first model was an empty model containing no covariates, but decomposed the total variance into individual and community components. The second model included individual characteristics. The third model contained only the community characteristics and this allowed the assessment of the relation of the community variables to the outcome variable. The final model contained explanatory variables at both the individual and community levels and allowed the assessment of the net effect of community variables over and above the individual variables. The variables were retained in each of the models if the variance component was significant ( $p < 0.05$ ) or if they were important demographic variables.

In all the estimated models, fixed effects were expressed as odds ratios (OR), while the random effects were expressed as variance partition coefficient (VPC) and proportional change in variance (PCV). The precision was measured by the standard error (SE). The VPC was calculated based on the linear threshold model method which converts the individual level variance from the probability scale to the logistic scale, on which the community level variance is expressed [27]. In this case, the individual level variance  $\sigma^2_e$  is equal to  $n^2/3$  (i.e., 3.29). The maximum likelihood was evaluated by integrating the random effects using the adaptive Gaussian quadrature (AGQ) [28] available in Stata; while the significance of the random effects were evaluated using the likelihood ratio (LR) statistics. AIC (Akaike information criterion) and the BIC (Bayesian information criterion) were used to test the goodness of fit of the models.

## Results

### Descriptive analyses

Forty-five percent of the sample was aged 25-34 years (Table 1).

Characteristics	All women	
	%	n
<b>Maternal age at birth</b>		
15-24	36.9	6476
25-34	44.7	7847
35-49	18.4	3238
<b>Educational attainment</b>		
No education	45.4	7969
Primary	22.8	4004
Secondary	25.9	4542
Higher	5.9	1045
<b>Occupation</b>		
Unemployed	30.4	5312
Formal employment	41.4	7235
Agricultural employment	17.2	3005
Manual workers	10.9	1910
<b>Religion</b>		
Muslims	54.3	9482
Christians	44.0	7685
Traditional/Others	1.7	297
<b>Ethnic origin</b>		
Hausa/Fulani/Kanuri	39.6	6924
Igbo	11.6	2033
Yoruba	15.0	2627
Others	33.7	5887
<b>Women's autonomy (decisions over own health)</b>		
Wife alone	8.8	1450
Wife/husband	33.1	5477
Husband alone/Others	58.2	9634
<b>Parity</b>		
1-2	40.7	7144
3-4	32.7	5740
5 or more	26.6	4677
<b>Household wealth index</b>		
Poorest	23.1	4059
Poor	22.2	3898
Middle	19.0	3332
Rich	18.2	3187
Richest	17.6	3084
<b>Type of place of residence</b>		
Urban	30.2	5308
Rural	69.8	12253
<b>Region of residence</b>		
North Central	14.3	2516
North East	15.6	2745
North West	30.4	5337
South East	9.1	1599
South South	13.1	2303
South West	17.4	3061
<b>Community women's education</b>		
Low	42.6	7487
Medium	29.0	5097
High	28.3	4976
<b>Ethnic diversity</b>		
Low	41.1	7223
Medium	28.4	4984
High	30.5	5354

Forty-five percent of women had no education, while 31% had a secondary or higher level of education. Fifty-four percent of the women were Muslims and 44% were Christians. Almost a third (30%) of the women were unemployed. Forty percent of the women were Hausa/

Fulani/Kanuri, 12% Igbo, and 15% Yoruba. More than half of the women (58%) reported that their husbands or other people have a final say over their own health. Fifty-nine percent of the women had given birth to more than two children. Seventy percent of the women lived in a rural area. About two in five (43%) women lived in communities with a low proportion of educated women and high ethnic diversity communities.

Characteristics	Place of delivery		P-value
	Health facility		
<b>Maternal age at birth</b>			0.001
15-24	32.5		
25-34	44.4		
35-49	37.0		
<b>Educational attainment</b>			0.001
No education	10.9		
Primary	43.6		
Secondary	70.7		
Higher	91.4		
<b>Occupation</b>			0.001
Unemployed	28.1		
Formal employment	50.4		
Agricultural employment	31.9		
Manual workers	34.0		
<b>Religion</b>			0.001
Muslims	21.3		
Christians	60.9		
Traditional/Others	19.3		
<b>Ethnic origin</b>			0.001
Hausa/Fulani/Kanuri	9.3		
Igbo	79.7		
Yoruba	79.3		
Others	40.8		
<b>Women's autonomy (decisions over own health)</b>			0.001
Wife alone	59.3		
Wife/husband	53.6		
Husband alone/Others	26.3		
<b>Parity</b>			0.001
1-2	43.8		
3-4	39.3		
5 or more	30.1		
<b>Household wealth index</b>			0.001
Poorest	8.4		
Poor	17.5		
Middle	36.1		
Rich	61.9		
Richest	85.1		
<b>Type of place of residence</b>			0.001
Urban	65.3		
Rural	27.1		
<b>Region of residence</b>			0.001
North Central	43.2		
North East	14.0		
North West	9.3		
South East	77.8		
South South	51.8		
South West	77.7		
<b>Community women's education</b>			0.001
Low	9.3		
Medium	48.1		
High	73.2		
<b>Ethnic diversity</b>			0.001
Low	19.1		
Medium	59.6		
High	45.5		

All explanatory variables were significantly associated with place of delivery at bivariate level. The bivariate results (Table 2) showed that a greater proportion of women aged 25-34 years (44%) delivered in a health facility than those aged 15-24 years (33%). While over 70% of women with secondary or higher education delivered in health facility only 11% of women with no education did so. A higher proportion of women in formal employment and Christian women delivered in a health facility compared with the unemployed and Muslims respectively. A lower proportion of women who had five or more live births and those who reported that their husbands or others make decisions on their own health care delivered in a health facility compared with women who had 1-2 live births and those who make decisions alone respectively. A key observation was the wide variation in health facility delivery observed among women from different ethnic groups. The proportion of women reporting that the most recent birth occurred in a health facility was higher for women of Igbo, Yoruba and minority ethnic origin compared with Hausa/Fulani/Kanuri women. Delivery in a health facility was higher for women who were in the richest wealth quintile. A lower proportion of rural than urban women delivered in a health facility. The use health facility for child delivery varied across regions, with a lower proportion of women from North West and North East delivering in a health facility. Women who lived in communities with a high proportion of educated women and a high proportion of women from different ethnic groups were more likely to deliver in a health facility compared with women who resided in disadvantaged communities.

## Multilevel analysis

The variation in health facility delivery across communities was significant ( $\tau = 7.467$ ,  $p = 0.001$ ) (Table 3, model 1).

Characteristics	Model 1	Model 2	Model 3	Model 4
	Empty model	Individual variables	Community variables	Individual/Community variables
		Odds Ratio	Odds Ratio	Odds Ratio
<b>Fixed effects</b>				
<b>Individual characteristics</b>				
<b>Maternal age at last birth</b>				
15-24		1.000		1.000
25-34		1.142		1.093
35-49		1.394**	-	1.274*
<b>Educational attainment</b>				
No education		1.000		1.000
Primary		1.889***	-	1.518***
Secondary/Higher		4.133***		2.826***
<b>Religion</b>				
Muslims		1.000	-	1.000
Christians		1.243		0.955
Traditional/Others		0.445**		0.455***
<b>Ethnic Origin</b>				
Hausa/Fulani/Kanuri		1.000	-	1.000
Igbo		21.091***		4.699***
Yoruba		13.588***		2.920***
Others		3.871***		2.083***
<b>Occupation</b>				
Unemployed		1.000	-	1.000
Formal employment		1.220*		1.171*
Agric employment		1.034		1.044
Manual workers		1.021		1.058
<b>Women's autonomy (decisions over own health)</b>				
Wife alone		1.000		1.000
Wife/Husband		1.230		1.215*
Husband alone/Others		0.948		1.044
<b>Household wealth index</b>				
Poorest		1.000		1.000
Poorer		1.829***	-	1.478***
Middle		3.548***		2.121***
Richer		8.558***		3.599***
Richest		23.897***		7.222***
<b>Parity</b>				
1-2		1.000	-	1.000
3-4		0.683***		0.732***
5 or more		0.646***		0.707***
<b>Place of residence</b>				
Urban		-	1.000	1.000
Rural		-	0.385***	0.639***
<b>Region of residence</b>				
North Central		-	1.000	1.000
North East		-	0.178***	0.362***
North West		-	0.107***	0.215***
South East		-	2.200***	0.923
South South		-	0.611**	0.492***
South West		-	2.456***	1.451*
<b>Community women's education</b>				
Low			1.000	1.000
Medium			6.603***	2.710***
High			17.955***	4.012***
<b>Ethnic diversity</b>				
Low			1.000	1.000
Medium			0.727*	0.710*
High			0.544***	0.597**
<b>Random effects</b>				
	Empty	Individual	Community	Individual/Community
Variance (SE)	7.467*** (0.492)	1.933*** (0.774)	1.442*** (0.113)	1.118*** (0.097)
(VPC) = ICC (%)	69.4	37	31	25.4
(PCV) (%)	Reference	74.1	80.7	85
Log-likelihood	-7376.9092	-5957.9257	-6844.3507	-5830.1125
<b>Model fit statistics</b>				
AIC	14759.8	11961.9	13714.7	11726.2
BIC	14783.2	12139.4	13816	11980.9

Note: Only variables with a significant ( $p < 0.5$ ) variance component were included in the models. The empty model contains no variables but partitions the variance into two component parts. SE = Standard error, VPC = Variance Partition Coefficient, PCV = Proportional Change in Variance. AIC = Akaike Information Criterion, BIC = Bayesian Information Criterion. Significance level \*\*\* $p < 0.001$  \*\* $p < 0.01$  \* $p < 0.5$

The variance partition coefficient as shown by the estimated intercept component variance was 69.4%. This is the variability in the outcome variable attributed to the community level.

Model 2 contained only the individual level variables. Results showed that maternal age was significantly associated with health facility delivery, with older women (35-49 years) having higher odds of delivering in a health facility compared with younger women aged 15-24 years. There was no statistical significant association between a woman's autonomy and delivery in a health facility. Women with secondary/higher education had 4 times greater odds of delivery in a health facility than women with no education. There was no significant difference between Muslims and Christians in place of delivery. Women from Igbo, Yoruba and others (minority ethnic groups) were more likely to deliver in a health facility compared with Hausa/Fulani/Kanuri women. Similarly, compared with the unemployed, women in formal employment had higher odds of delivering in a health facility. Increasing socioeconomic status was associated with greater odds of having a delivery in a health facility. Parity was negatively associated with delivery care. As parity level increased, women were less likely to deliver in a health facility compared with low parity women (women with 1-2 live births). Compared to the empty model, the variation in health facility delivery was significant across communities ( $\tau = 1.933$ ,  $p < 0.001$ ). The intra-community correlation was 37% indicating the variability in the outcome variable.

In model 3, all the community variables were significantly associated with delivery care. Rural women had 61% lower odds of delivering their baby in a health facility compared with urban women. Interestingly, the odds of delivering a child in a health facility were 2.5 times and 2.2 times higher for women from South West and South East respectively, compared with those from North Central. However, women from North East and North West had lower odds of delivery in a health facility than those from the North Central region. Women who lived in communities with a high proportion of educated women were more likely to use delivery care compared with women who resided in disadvantaged communities. However, living in communities with a high proportion of women from different ethnic groups was associated with lower odds of delivery in a health facility. In comparison to model 2, the variance in health facility delivery across communities was significant ( $\tau = 1.442$ ,  $p < 0.001$ ). The intra-community correlation estimate reduced to 31%. The inclusion of the community level factors reduced the community level variance from 1.933 to 1.442 ( $p < 0.001$ ).

Controlling for individual/household and community variables in the final model (model 4), maternal age at last birth, education, religion, occupation, ethnic origin, woman's autonomy, parity and household wealth index were found to be significantly associated with health facility delivery. The pattern of association remained the same as in model 2. However, the inclusion of the community variables attenuated the odds for educational attainment, ethnic origin and household wealth index. Interestingly, women's autonomy was significantly associated with health facility delivery unlike in the model without the community level variables.

The association between delivery care and community variables yielded interesting results. The odds of having a health facility delivery were lower for women in South west and South east compared with women in North Central, although the association was no longer statistically significant for South east. Further, inclusion of individual factors attenuated the odds for community women's education compared with the model that included only community level variables. The community level variance was significant ( $\tau = 1.118$ ,  $p < 0.001$ ). The intra-community correlation decreased to 25.4% suggesting that the inclusion of the community variables improved the overall explained variance in the use of delivery care compared with model 3. Moreover, the smaller values of AIC and BIC indicated that model 4 was a better explanatory model.

## Discussion

Study findings demonstrated the significant association between community level factors and delivery in a health facility. Importantly, we found a strong association between community level education and delivery in a health facility. The finding that the likelihood of delivering a baby in a health facility was higher for women from communities with a high proportion of women with secondary/higher education compares well with findings elsewhere [5,29]. These results suggest that in communities where educational attainment is high, women may have more material resources and autonomy to access health care services. The strong association of community women's education points to the need to increase women's education particularly in disadvantaged communities.

Surprisingly, ethnic diversity showed a negative significant association with delivery care. Women in communities with a high proportion of women from different ethnic groups had a lower likelihood of delivering their baby in a health facility. The nature of this relationship is unclear, but could reflect "the heterogeneity and social and ecological settings in Africa" [30], which are barriers to utilization of maternal health care services. Furthermore, the negative association between ethnic diversity and poor health outcomes could be explained in relation to the problems of collective action faced by many heterogeneous communities in Africa [31].

Region of residence was significantly associated with facility delivery. Women from the North East and North West were less likely to deliver in a health facility. Regional differences in the use of maternal health care could reflect disparities in socio-economic development, as more health care services are located in the Southern regions of Nigeria than in the Northern regions [6]. The finding that women from Igbo, Yoruba, and Northern/Southern minority ethnic groups had a higher likelihood

of using health facility for childbirth compared with Hausa/Fulani/Kanuri women, underscores the complexity of forces in operation among the different ethnic groups in a culturally-diverse society like Nigeria [25].

With respect to individual level variables, educational attainment, occupation, ethnic origin, a woman's autonomy, household wealth index, parity and religion were significantly associated with delivery care. These results are consistent with studies other studies in developing countries [2, 32, 33]. Educational attainment, occupation and household wealth are markers of economic resources which empower women to take control of their own health and facilitate easy access to quality maternal health care [25] Results indicate that women who reported making joint decisions with their partners were more likely to deliver in a health facility. This finding suggests the need for programmes to improve women's status and autonomy, and also involve women's partners in maternal health programmes so as to educate them on issues regarding appropriate health care seeking during delivery [29].

The likelihood of having a delivery in a health facility decreased consistently as number of children ever born increased. Presumably, this may reflect the assumption that women of higher parity are less likely to deliver in a health facility either because of their maternity experiences or because having a large family size means having fewer resources (both time and money) available to seek maternal health care [2, 34]. Therefore there is need for policy that encourages small family sizes or women to access delivery care services for every pregnancy.

Study findings should be interpreted in light of some limitations. First, the study used primary sampling units as a proxy for the community. As observed, using the DHS PSU as the community may bias results because of selection effects [35]. Second, some important factors known to influence delivery care service utilization (e.g., distance to a health facility) were not included in our analyses due to data limitation. The omission of these important confounders may have biased the estimates of the measured variables in this study. Third, the community variables were constructed by aggregating the individual level characteristics at the community level and this may be associated with problem of making inferences at a higher level based on information from data collected at the individual level [35]. Fourth, the 2008 NDHS data were collected retrospectively and may be associated with recall bias. Finally, the cross-sectional nature of the survey does not allow for cause-effect inferences. However, the study remains significant. The study is based on a large nationally-representative population-based survey whose findings are relevant for comprehensive national policy initiatives. The study is also relevant in identifying aspects of the community that are important for interventions. However, qualitative research is needed to adequately understand the association between the cultural identity factors (ethnic origin and region of residence) and place of delivery.

## Conclusion

Community factors were significantly associated with the use of maternal health care. Interventions aimed at promoting the use of health facilities for childbirth should not only be implemented at the individual level but tailored to the community level as interventions conceived without consideration for community context are likely to have limited impact. To close the gap in facility delivery, community and regional specific interventions that allow equitable distribution of maternal health care services should be implemented. Importantly, there is need for interventions that explore the most effective ways to raise women's status in terms of education and socio-economic status in disadvantaged communities.

## Competing interests

The authors declare no competing interests.

## Authors' contributions

DNO is the principal author and analyzed the data, interpreted the results and participated in the writing of the paper. COO Participated in the

conception of the methodology, supervised the statistical analysis and edited the manuscript.

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## Research

# Prevalence of peripheral blood parasitaemia, anaemia and low birthweight among pregnant women in a suburban area in coastal Ghana

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**Introduction:** Malaria and anaemia have adverse effects in pregnant women and on the birth weight of infants in malaria endemic areas. *P. falciparum* malaria, the most virulent species continues to be a major health problem in sub-Saharan Africa. This study was carried out to establish the prevalence of pregnancy-associated malaria and its associated consequences including maternal anaemia and low birthweight (LBW) deliveries and placental malaria among pregnant women in a sub-urban area in coastal Ghana.

**Methods:** A facility-based investigation was carried out among 320 pregnant women seeking antenatal care in a hospital in suburban coastal Ghana. Information on the use of Insecticide Treated Nets (ITNs) and Intermittent Preventive Treatment in pregnancy (IPTp) were collected using a structured questionnaire at enrolment. Venous blood was collected for microscopy and screening for Glucose 6-phosphate dehydrogenase (G6PD) deficiency. Haemoglobin concentration was obtained from an automatic blood analyzer. Placental smears and birth weight measurements were taken at delivery.

**Results:** The prevalence of *Plasmodium falciparum* parasitaemia was 5%. The mean haemoglobin (Hb) level at registration was 11.44g/dL (95% CI 11.29 – 11.80). Placental blood parasitaemia and low birthweight were 2.5% and 3% respectively. ITN possession was 31.6% with 5.4% usage. The IPTp coverage was 55%.

**Conclusion:** The prevalence of malaria and anaemia among the pregnant women were low at enrolment. Placental blood parasitaemia and LBW at delivery were also low. These are clear indications of the high coverage of the IPTp. Increase in ITN use will further improve birthweight outcomes and reduce placental malaria.

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**Key words:** Malaria prevalence, pregnancy, anaemia, birthweight, ITNs, IPTp

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## Introduction

Malaria, which is transmitted by female anopheles mosquitoes, results in peripheral blood parasitaemia which may be asymptomatic in adults living in malaria endemic areas. Among pregnant women, however, peripheral blood parasites may accumulate in the placenta resulting in malaria-associated pregnancy (PAM) with adverse consequences such as maternal anaemia and low birthweight infants [1]. Interventions such as Intermittent Preventive Treatment in pregnancy (IPTp) and Insecticide Treated Nets (ITNs) prevent PAM by eliminating peripheral parasitaemia or minimizing the exposure to the vector.

Malaria is the main determinant of anaemia among women who are pregnant for the first time in endemic regions [2] whereas iron deficiency contributes more to anaemia among pregnant women who have been pregnant before and are semi-immune to placental malaria. A haemoglobin (Hb) concentration below 11.0g/dl or packed cell volume (PVC) of less than 33.0% is regarded as anaemia [3]. A low Hb has also

been identified as a clinical indicator of placental infection with malaria parasites [4]. A significant reduction in mean Haemocrit (Hct) and Hb levels and a higher incidence of anaemia have also been observed among afebrile pregnant women with malaria parasitaemia [2, 5]. It is estimated that about 400,000 pregnant women living in malaria endemic areas in sub-Saharan Africa are at risk for developing severe anaemia (Hb<5.0g/dL) from infection with malaria [6].

Low birthweight (LBW) is a significant risk attributable to malaria in pregnancy. It is estimated that in malaria endemic areas 19% of infant LBW is due to malaria and also that 6% of infant deaths are due to LBW caused by malaria. These estimates imply that around 100,000 infant deaths each year could be due to LBW caused by malaria during pregnancy in malaria endemic areas in Africa [7]. The infants of primigravidae are at greatest risk, especially those of older primigravidae [8].

Most studies on the risk of anaemia in pregnancy have examined associations with micronutrient deficiencies [9, 10] or with parity, age, urban/rural disparities and hookworm infection [11]. The present study

examined the association between malaria parasitaemia and maternal anaemia and the incidence placental blood parasitaemia and low birth weight of infants among a group of pregnant women making their initial visit for antenatal attendance at a suburban hospital in a low malaria transmission setting in coastal Ghana.

## Methods

### Study setting

The study was conducted at the Alpha Medical Centre (AMC) in Madina town. Madina is situated in the Ga-East District of the Greater Accra Region about 13.5 kilometres from Accra, the capital of Ghana. It is densely populated with an estimated 2007 population of 112,888 from the 2000 census report [12]. The District experiences two distinct rainy seasons from April to June and from September to November with average temperature of about 26°C. Malaria transmission is low to moderate and perennial with considerable seasonal variations and peaks after the rains, between May-October. It is estimated that there are an estimated 20 infective bites per person year [13]. *Plasmodium falciparum* accounts for 98% of all infections reported in the hospital.

### Sample

The number of pregnancies expected in the study area was 20,000 within the year, with an expected prevalence of pregnancy malaria of about 20% in Southern Ghana [1]. The minimum sample size to assess differences by malaria parasitemia status was estimated at 243 (Epi Info 3.4, 95% confidence level). To compensate for losses to follow-up three hundred and twenty (320) pregnant women were enrolled.

Pregnant women living in Madina and its environs making initial attendance to seek antenatal care at the maternity unit of the AMC for the current pregnancy who had not received IPTp and planned to deliver at the AMC were enrolled for the study from July to August 2008 and followed to delivery. The infants were also followed at monthly intervals at the Child Healthcare Clinics for six months.

### Ethical considerations

Ethical clearance was received from the Institutional Review Board (IRB) of the Noguchi Memorial Institute for Medical Research (NMIMR), College of Health Sciences, University of Ghana, Legon. All participants provided informed consent prior to data collection.

### Procedures

Demographic survey details as well as information on knowledge, possession and use of Insecticide Treated Nets (ITNs) were collected using a structured questionnaire. Venous blood was collected from each participant into a 5ml ethylene diamine tetra-acetic acid (K3EDTA) vacutainer tubes (Becton Dickinson vacutainer systems, UK). Each tube was labelled with the participant's unique identification number and was stored in a cold box, which was immediately transported to the laboratories of the NMIMR. Haematological, parasitological and clinical chemistry analyses including the Glucose-6-phosphate dehydrogenase (G6PD) deficiency test were run for each blood sample. An automatic blood analyzer (sysmex, Germany) was used to obtain the haemoglobin concentration.

To determine asexual *P. falciparum* malaria parasitaemia, two sets of thick and thin blood films per blood sample were prepared on glass slides and allowed to dry on a rack. The thin films were fixed in absolute methanol and stained with 2% giemsa (BDH Laboratory Supplies Poole bh15 ITD, England) for ten minutes. The slides were then washed, left to dry and later examined in immersion oil under the microscope (Olympus BH2 Microscope, Japan) at X6 eyepiece and X100 oil immersion objective lens [14]. The number of parasites per microlitre of blood in a thick film was determined in comparison with a standard number of leukocytes as described in the WHO Basic Malaria microscopy. Part I. Learner's guide [15]. The asexual forms and gametocytes of *P. falciparum* were counted and recorded separately. All the slides were double-checked blindly by an independent microscopist for quality control. Placental blood smears were collected at delivery onto labelled microscopic glass slides. The slides were air dried and transferred to the laboratory for staining and examination of malaria parasites.

Infants were weighed at delivery using a previously calibrated scale at the labour ward and weights recorded on record sheets provided with the mother's unique identification number. The infants born to study participants were followed at monthly intervals for six months. The infants' body temperature was determined at each visit.

Eligible women received Intermittent Preventive Treatment (IPTp) for malaria from hospital staff by direct observed therapy (DOT) at monthly intervals. Information about IPTp administration was initially entered by the hospital staff into the ANC attendance record booklets and was transferred onto the record forms provided for the study.

### Data analysis

The mean values for various parameters such as haemoglobin levels, and gestation were compared for the various categories of the pregnant women using standard statistical methods. Pair wise and three-way comparisons of mean Hb, proportion of low birthweight and prevalence of parasitaemia and parasite densities were done by Students't-test, ANOVA, and Fishers' test. A value  $p < 0.05$  was considered significant.

## Results

The characteristics of the pregnant women are shown as Table 1.

Characteristic	Mean	95% Confidence interval
<b>Age (Years)</b>		
Age of pregnant women	28.42	27.8-29.04
Age at first pregnancy	23.95	23.03-24.88
<b>Gestation (weeks)</b>		
Gestation at registration	18.5	17.12-19.05
Gestation at first dose IPTp	23.53	22.91-24.15
<b>Level of Parasitaemia</b>		
Parasite density (µl blood)	1990.80	213.53-4195.13
<b>Haemoglobin concentration (g/dL) at registration</b>		
All pregnant women	11.44	11.29-11.8
Parasitaemic	10.74	9.79-11.67
Non parasitaemic	11.45	11.29-11.61
Primigravidae	11.38	11.08-11.67
Secundigravidae	11.56	10.91-12.21
Multigravidae	11.40	11.20-11.60

A significant proportion (46.6%) of participants lived outside Madina but within a 20 kilometer radius. Gestation at registration or first booking ranged from 2 weeks to as late as 39 weeks with a mean of 18.5 weeks (95% CI: 17.12 – 19.05). The prevalence of peripheral blood asexual *P. falciparum* parasitaemia on enrolment was 5% (n=15).

The mean haemoglobin level at registration for all the women was 11.44 g/dL (95% CI 11.29 – 11.80). Thirty-two percent of women had mild to moderate anaemia based on Hb<11g/dL as a cut-off. The lowest Hb recorded was 8.4g/dL among two women (Table1) The mean Hb level of women who were diagnosed with peripheral blood parasitaemia (10.73g/dL) was significantly lower than that among women without parasitaemia (11.45g/dL). The mean Hb levels at first ANC visit did not differ significantly by parity (Table 1). Eleven percent (n=35) of women were found to have G6PD deficiency (data not shown).

Three percent of babies were of low birth weight. There was no significant association between the weight of babies and the number if IPTp doses received. None of the women who delivered infants with LBW had peripheral parasitaemia or anaemia at the time of first ANC registration but were among those who did not receive any IPTp during pregnancy. Microscopic examinations of the placental smears showed a 2.5% (n=3) prevalence of placental malaria at delivery. There was no association between placental parasitaemia and the incidence of LBW.

Knowledge of bed nets was high (97.3%). Sixty one percent of the women had ever slept in a net, however only 5% had slept under an ITN the night preceding the interview. ITN coverage was 31.6 %. Fifty-five percent of women received IPT during pregnancy. Of those who received IPTp, 38% received three doses (Table 2).

**Table 2:** Summary results of use of ITNs and IPTp among pregnant women (n=320) attending ANC in Madina, Accra

Variable	Proportion
<b>Gravid status</b>	
Primigravidae	31.2%
Secundigravidae	3.7%
Multigravidae	64.0%
Unknown gravid status	0.6%
<b>ITNs</b>	
Awareness	97.3%
Ever slept in a net	60.5%
Have a bed net (treated + non treated)	41.2%
Have a treated net during pregnancy	31.6%
Slept in treated net the previous night	5.4%
<b>IPTp</b>	
Received IPT during pregnancy	55.0%
<b>IPTp doses (n=175)</b>	
First IPTp dose during 1st trimester	1.1%
First IPTp dose during the second trimester	74.8%
First IPTp dose during third trimester	24.0%
One dose of IPTp	28.0%
Two doses of IPTp	33.7%
Three doses of IPTp	38.3%
<b>Birth-weight (n=121)</b>	
Birthweight < 2.5 kg	3.3%
Birthweight ≥ 2.5kg	96.7%

## Discussion

The present study examined the prevalence of pregnancy associated malaria and its associated consequences including maternal anaemia and the incidence of low birth weight of infants and placental malaria among a group of pregnant women in a low malaria transmission setting in coastal Ghana. The prevalence of malaria parasitaemia on enrolment was much lower than what is reported in other studies in Ghana [1, 11].

Although, the absence of peripheral blood malaria parasites might reflect low rates of transmission of malaria in the study area (as indicated by relatively high Hb levels) or wide spread use of antimalarials as a result of the improved education on malaria during pregnancy in Ghana, in general, it is plausible that many women may have had submicroscopic peripheral blood parasites undetected by microscopy but detectable by the more sensitive PCR method [16, 17]. The low prevalence of peripheral blood parasitaemia may also have stemmed from the general affinity of the placenta to accumulate *P. falciparum* parasites [18-22] as was observed in 2.5% of the women. In addition, G6PD deficiency was higher among women in this study compared with levels observed in a cross-sectional study among pregnant women in the Ashanti region of Ghana [23]. Red blood cells with low G6PD activity offer a hostile environment to parasite growth and are thus protective for malaria infection. However, this protective effect also may lead to haemolysis from sulphonamides including antimalarials [24] like sulphadoxine pyrimethamine (SP) used in IPTp. With a relatively high prevalence of G6PD deficiency in Madina, testing for G6PD should be an important pre-requisite for antimalarial treatment including IPTp.

Pregnant women with anaemia may have an increased risk for poor pregnancy outcomes, particularly if they are anaemic in the first trimester. Although women in the present study had a relatively low prevalence of anaemia compared with other studies in Ghana [1, 11] almost one in three women had mild to moderate anaemia and women with *P. falciparum* infection had lower haemoglobin levels. These findings highlight the need for policies aimed at treating anaemia and limiting malaria infection in pregnant women in Madina.

Low birth weight attributable to malaria is associated with infant mortality. Only 3% of infants in this study had low birth weight. IPTp has been shown to improve birth weight [25, 26] hence most women in the study who were on IPTp had infants with birth weight equal or greater than 2500 kilograms.

Although malaria transmission in Madina is low to moderate, use of ITN was low despite high awareness levels. Low utilization of insecticide-treated nets was also observed in a malaria endemic area in Burkina Faso [27] where usage was limited due in part to community perceptions of the effectiveness of ITNs. The low usage may account for the parasitaemia detected albeit very low, in spite of IPTp administration

during pregnancy [17]. These results suggest the need for public health education to encourage both the ownership and use of bed nets among pregnant women.

Some limitations must be acknowledged. First, helminthiasis and nutritional deficiencies are important causes of maternal anaemia in pregnancy. These factors were not investigated in the present study. Second, we were unable to examine the association between malaria parasitaemia and maternal anaemia and birth weight due to the small number of women who tested positive for *P. falciparum* infection. Third, although malaria transmission is seasonal with a peak during the rainy season (July to September), the very low prevalence of malaria among the pregnant women limited our ability to assess seasonality effects.

## Conclusion

The malaria prevalence on enrolment among the pregnant women was very low and was mostly asymptomatic. None of the women who delivered infants with LBW had peripheral parasitaemia or anaemia at the time of first ANC registration in their second to third trimesters. A high coverage of IPTp showed a reduced risk in maternal anaemia and LBW. Post partum studies need to be carried out on women who take IPTp. Although three of the women in the present study with G6PD deficiency had malaria infection at first presentation at ANC, the number was too low to make any meaningful conclusion about its protective effect. High knowledge of ITNs has not translated into use and even the few women who had ITNs were not sleeping in them. The non-use of ITNs has implications for malaria infection. The absence of clinical symptoms in the infants does not rule out infection especially with the low rate of use of ITNs.

## Competing interests

The authors declare no competing interests.

## Authors' contributions

JKS was responsible for conceptualization, study design, data collection, data analysis and interpretation, drafting and revision of the manuscript. MKO was involved in data collection, laboratory analysis, and interpretation of results and critical revision of the manuscript. MLW participated in conceptualization, analysis, interpretation and critical revision of the manuscript. IAQ contributed to the documentation for ethical clearance, field site selection and critical revision of the manuscript. BDA was instrumental in the design, study site and laboratory selection and provision and implementation of the field study for data collection, laboratory analysis, data interpretation and critical review of the manuscript. All authors read and approved the final version.

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## Research

# Barriers to emergency obstetric care services: accounts of survivors of life threatening obstetric complications in Malindi District, Kenya

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**Introduction:** Pregnancy-related mortality and morbidity in most low and middle income countries can be reduced through early recognition of complications, prompt access to care and appropriate medical interventions following obstetric emergencies. We used the three delays framework to explore barriers to emergency obstetric care (EmOC) services by women who experienced life threatening obstetric complications in Malindi District, Kenya.

**Methods:** A facility-based qualitative study was conducted between November and December 2010. In-depth interviews were conducted with 30 women who experienced obstetric "near miss" at the only public hospital with capacity to provide comprehensive EmOC services in the district.

**Results:** Findings indicate that pregnant women experienced delays in making decision to seek care and in reaching an appropriate care facility. The "first" delay was due to lack of birth preparedness, including failure to identify a health facility for delivery services regardless of antenatal care and to seek care promptly despite recognition of danger signs. The "second" delay was influenced by long distance and inconvenient transport to hospital. These two delays resulted in some women arriving at the hospital too late to save the life of the unborn baby.

**Conclusion:** Delays in making the decision to seek care when obstetric complications occur, combined with delays in reaching the hospital, contribute to ineffective treatment upon arrival at the hospital. Interventions to reduce maternal mortality and morbidity must adequately consider the pre-hospital challenges faced by pregnant women in order to influence decision making towards addressing the three delays.

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## Introduction

Existing evidence suggests that in any population, 1-2 percent of pregnant women will develop life-threatening obstetric conditions during childbirth [1,2]. If they fail to receive rapid medical interventions, it is likely to result in a maternal death. While complications responsible for most maternal deaths are often unpredictable [3,4], even in well-nourished and well-educated women who receive sufficient prenatal and delivery care [5], there is evidence that many maternal deaths can be avoided, even in countries with limited resources [6]. That is if women deliver in a setting where skilled attendants can provide emergency obstetric care (EmOC) [3,7-12].

While sub-Saharan Africa accounts for more than half of the global burden of maternal mortality [13,14], many women still face challenges in accessing life-saving obstetric interventions [15,16]. In Kenya, over 50 percent of deliveries are attended to by unskilled persons and/or outside a health facility [17], exposing mothers and babies to poor

health outcomes should a complication arise during delivery or postnatal period. The low ratio of EmOC facilities to population size (2.7/500,000) [18], which is below the recommended minimum of 5/500,000 [10], and inequitable access to health services across the country [18,19] suggests that high maternal mortality in Kenya may result from limited access to life saving interventions for most pregnant women. Maternal mortality is only the tip of an iceberg, the bulk of which is made up of severe morbidity that may lead to long term disability.

The three delays model suggests that pregnancy-related morbidity and mortality stems from delays in (a) making the decision to seek appropriate care, (b) reaching an appropriate facility and (c) receiving adequate and appropriate care once at a health facility [5]. This model provides a valuable theoretical framework for studying the underlying causes of maternal mortality in resource-limited settings. We used this framework to explore the barriers to EmOC services by women who experienced life-threatening obstetric complications or "near miss" in Malindi District, Kenya. According to the district bureau of statistics, Malindi has an estimated maternal mortality ratio of 625 maternal deaths

per 100,000 live births compared to 488 deaths per 100,000 live births, nationally [18].

This qualitative paper documents the barriers to EmOC services in Malindi District, from the users' perspective. It is based on data from a larger study that examined the existence and functionality of EmOC services from a health system perspective in the district [20].

## Methods

### Study setting

This study was conducted in Malindi District (currently Malindi and Magarini Districts) in Kenya. Malindi is located in the southern coastal region and covers an area of 7,792 km<sup>2</sup>. The total population in the district was 400,514 people in 2009, with an urban/rural distribution of 140,739 and 259,739 persons respectively [21]. The district has a total of 105 public and private health facilities [22], of which 42 (40%) offer maternity services. Among these, there are three hospitals and six health centres, which offer 24 hour/7 days maternity services. The average distance to the nearest health facility is 1 km for urban and 3 km for rural areas. Therefore, the majority of the population is considered to have relatively good access to health facilities. However, the distribution of health facilities is unequal and much of the rural area has poor road infrastructure and limited public transportation, which prevent people from accessing health facilities [23].

The three hospitals provide comprehensive EmOC. Although the coverage of EmOC services (6.2/500,000) is meets the minimum recommended coverage of 5/500,000 rural-urban inequities in geographical distribution of EmOC facilities exist [20]. According to a 2007 population based survey, 84 percent of women in the district deliver at home (REACT project, unpublished).

The study was conducted in the maternity ward of Malindi District Hospital in November-December 2010. The hospital is the only public referral hospital in the district with capacity to provide comprehensive EmOC services (blood transfusion and caesarean section). The hospital has a full time specialist obstetrician/ gynaecologist. In 2010, the hospital recorded a total of 2893 annual deliveries out of 5901 institutional deliveries in the district [20]. The hospital has a 250 bed capacity and a maternity shelter for women with high risk pregnancies. However, the hospital administration notes that the maternity shelter is underutilised as a result of competing demands for women and disruption of household responsibilities as a result of hospital confinement.

### Study population

The participants in this study were female residents of Malindi District, who experienced an obstetric "near miss" or severe acute maternal morbidity and were treated at the district hospital. Near miss is defined as an acute obstetric complication that immediately threatens a woman's survival but does not result directly in her death whether by chance or because of the hospital care she receives during pregnancy, labor or within six weeks after termination of pregnancy or delivery [24]. Since the objective was to understand and give meaning to a social process, rather than quantify and generalize to a wider population, 30 women with were purposively sampled to represent a variety of "near miss" conditions. The sample was deemed adequate to reveal the full range (or nearly the full range) of potentially important insights on pre-hospital and hospital barriers pregnant women with life-threatening obstetric complications experience [25,26].

The criteria for selecting women who had experienced near miss conditions was based on five categories of obstetric emergencies defined according to disease-specific criteria, based on management and/ or clinical signs and symptoms [24]. These included: haemorrhage at any pregnancy state (leading to transfusion, caesarean section or hysterectomy), hypertensive disorders of pregnancy (eclampsia or severe pre-eclampsia with a minimum diastolic pressure of 110 mmHg), puerperal sepsis (peritonitis, septicemia, offensive vaginal discharge), dystocia resulting from prolonged labor, obstructed labor or malpresentation (leading to ruptured uterus or impending uterine rupture, caesarean section, instrumental delivery or perineal lacerations) and severe anemia (hemoglobin < 6 g/dl).

### Interview guide

An in-depth interview guide was developed based on the three delays framework [5]. The guide focused on knowledge on danger signs during pregnancy, delivery and post partum; antenatal care (ANC) attendance; birth preparedness including choice on where to deliver, identification of health facility for delivery services and saving money; distance and mode of transport to nearest health facility and/ or referral to district hospital; and the woman's experience from onset of complication, arrival at hospital and receiving definitive treatment. Perceptions on quality of care received were also explored. The interview tool was translated from English into Kiswahili, and back-translated to ensure validity of findings.

### Procedure

The women were recruited at the maternity ward on a daily basis over a 4-week period. An attempt was made to interview women with a variety of life-threatening complications from both urban and rural settings. Two female nurse-midwives were trained to recruit the women in the study. Records of all women admitted following an obstetric complication were scrutinised to determine whether the women met the near-miss criteria at admission. If a woman met the criteria, she was approached and informed about the purpose of the study and invited to participate. After obtaining written consent, each woman was interviewed in Kiswahili by a female interviewer at the hospital after the woman had recovered from the life threatening condition. Women who did not speak Kiswahili were interviewed in Kigiriyama, which is the local language. The interviews were semi-structured, open ended and included probing to allow women to respond freely. The interviews were audio-recorded and lasted between 30 to 45 minutes. Additionally, a form was used to extract data on age, residence, obstetric complication and intervention performed from the admission records of the participants.

### Data analysis

The qualitative data were analysed thematically using NVivo 9. The recorded interviews were transcribed verbatim and translated from Kiswahili or Kigiriyama to English. Transcripts were coded into themes around pertinent issues relating to healthcare seeking and the process of obtaining care. Interview reports were supplemented by information on the type of obstetric condition experienced and management extracted from patient personal case files, theatre and ward daily report books. Attempts were made to identify possible, plausible barriers to the use of EmOC services by the respondents.

### Informed consent and ethical clearance

Ethical approval for this study was granted by the Kenya Medical Research Institute's Ethical Review Committee. Written permission was obtained from the Medical Officer of Health in the district prior to conducting the study. Informed consent was sought from the women and participation was fully voluntary. All information presented in this paper is anonymised.

## Results

### Characteristics of women

All the 30 women interviewed were treated at the hospital, upon arrival in a critical obstetric condition, therefore fulfilling the near miss criteria. Table 1 shows characteristics of the women who were interviewed. The mean age of the women was 25.7 years, ranging from 18 to 39 years. Seventeen women were rural residents. All the women had at least one ANC attendance, with over half having attained the minimum recommended four visits. The most common intervention was caesarean section, indicated by obstructed labour. Severe pre-eclampsia was the second common complication. The first delay was observed for 16 women, the second delay in 8 women, and the third in 6 women. Table 2 shows a summary of residence of and type of delay experienced.

### Delays in deciding to seek care

Knowledge of danger signs during pregnancy, delivery and post partum is considered a first step towards initiating appropriate and timely care seeking in the event of an obstetric emergency. A majority of the women mentioned at least two of the following danger signs during pregnancy; heavy vaginal bleeding before the expected delivery date, unpleasant vaginal discharge, water breaking before the due date, abnormal presentation, abdominal pains and dizziness. Common danger signs

**Table 1:** Characteristics of women admitted at Malindi District Hospital in near miss condition

ID	Age	Area	No. of ANC	Delivery preference	Complication	Intervention	Outcome of baby
01	30	Urban	3	Hospital	OL, FD	CS	Born alive
02	37	Urban	1	Hospital	severe PET	MgSO <sub>4</sub>	N/A*
03	30	Urban	4	Hospital	severe PET	MgSO <sub>4</sub>	N/A*
04	32	Urban	4	Hospital	severe PET	MgSO <sub>4</sub>	N/A*
05	23	Urban	5	Hospital	Primid, OL	CS	Born alive
06	18	Rural	3	Home	OL, Sepsis	CS, antibiotics	Born dead
07	32	Urban	1	Hospital	severe PET	MgSO <sub>4</sub>	N/A*
08	20	Urban	1	Hospital	OL	CS	Born alive
09	20	Rural	3	Hospital	OL	CS	Born alive
10	19	Rural	1	Home	OL, CPD	CS	Born alive
11	22	Rural	5	Home	OL, CPD, FD	CS	Born alive
12	23	Rural	4	Home	PET, FD	CS	Born alive
13	28	Rural	5	Hospital	OL, FD	CS	Born alive
14	23	Rural	1	Home	APH, severe PET	BT, MgSO <sub>4</sub>	Born dead
15	24	Rural	4	Home	OL, CPD	CS	Born alive
16	39	Rural	3	Hospital	Severe PET	MgSO <sub>4</sub>	N/A*
17	32	Rural	2	Hospital	Ruptured uterus	CS	Born alive
18	18	Rural	1	Home	OL, CPD, FD	CS	Born alive
19	17	Urban	5	Hospital	Severe eclampsia, FD	CS	Born dead
20	23	Rural	3	Hospital	OL, FD	CS	Born alive
21	25	Urban	5	Hospital	OL, FD	CS	Born alive
22	31	Urban	2	Hospital	severe PET	MgSO <sub>4</sub>	N/A*
23	29	Rural	2	Home	OL, FD	CS	Born dead
24	23	Rural	4	Home	severe PET	MgSO <sub>4</sub>	N/A*
25	26	Urban	5	Hospital	OL	CS	Born alive
26	18	Rural	1	Home	OL	CS	Born alive
27	26	Rural	1	Home	severe PET	MgSO <sub>4</sub>	N/A*
28	37	Urban	4	Hospital	severe PET	MgSO <sub>4</sub>	Born alive
29	18	Rural	4	Home	OL, fully dilated	CS	Born alive
30	29	Urban	5	Hospital	OL, severe PET	CS	Born alive

APH (ante partum haemorrhage); CPD (cephalo pelvic disproportion); PPH (postpartum haemorrhage); PS (puerperal sepsis); PP (placenta praevia); FD (foetal distress); PET (Pre-eclampsia); OL (obstructed labor); CS (Caesarean section); MgSO<sub>4</sub> (magnesium sulphate).  
N/A\*- condition managed, awaiting delivery.

**Table 2:** Distribution of women who experienced near miss by type of delay and residence

Type of delay	Residence		
	Rural	Urban	Total
First: Delays in making decision to seek care	9	7	16
Second: Delays in reaching care facility	6	2	8
Third: Delays in receiving care at facility	2	4	6
<b>Total</b>	<b>17</b>	<b>13</b>	<b>30</b>

during child birth were typically described in respondent wording as pushing without the baby coming out, abnormal presentation, the birth canal being too small or failing to open, high blood pressure and too much bleeding. Heavy bleeding was commonly mentioned as a danger sign after delivery.

The women recollected their personal experiences during the near miss episode. It is interesting to note that some women perceived the danger signs to be normal during pregnancy and would not seek medical care immediately. A 19 year old woman who underwent a caesarean section delivery arising from obstructed labor (OL) and cephalo pelvic disproportion (CPD) reported severe pains and only went to hospital because she "was so tired and could not withstand the pain anymore" after several hours of labor. Perceived severity of the illness also seemed to influence decision to seek care. For example, a woman who underwent blood transfusion following severe pre-eclampsia (PET) and ante-partum haemorrhage (APH), but lost the baby described her ordeal:

*"My expected delivery date had not reached. I started having abdominal pains, feeling of fatigued and dizzy in the morning. I dismissed it as normal problems related to pregnancy and would pass. By noon, the pain became severe and I started bleeding heavily. I cannot say much about what happened afterwards because I passed out. My mother in law and other women carried me on a stretcher and brought me to Madunguni Dispensary"* (23 year-old rural resident with APH, severe PET)

Pregnant women are advised to attend ANC and make certain preparations prior to birth. This includes identification of health facility to deliver. All the women interviewed had attended ANC at least once. A majority of the women had attained the recommended four visits, a marker of birth preparedness. However, some still preferred to deliver at home, perceiving the pregnancy as normal often based on previous uncomplicated pregnancies, but ignoring the fact that most complications occur suddenly and are unpredictable. A woman who developed severe

PET and ante-partum haemorrhage narrated.

*"Yes I attended ANC four times...I had planned to deliver at home, the same way I did with my two children. I did not have any problem through out this pregnancy. When I started feeling dizzy, I knew it would pass"* (23 year-old rural resident with APH and severe PET)

The women also narrated how lack of money influenced choice of place of delivery. In some instances, the women had already made advance arrangements to deliver at home with the help of a TBA to cut on costs, as illustrated by the statement below:

*"I had planned to deliver at home with the help of a TBA, so as to reduce on the expenses. When the pain started, I called the TBA, she examined me and advised me to go to the dispensary. At the dispensary, the doctor informed me that they could not assist me because the baby was too big and referred me to Malindi. I came in a Bajaj from Gede to Malindi. We paid KSh 700"* (22 year-old rural resident with obstructed labor and CPD)

### Delays in reaching care facility

Delays in reaching an appropriate obstetric facility once the decision to seek care has been made constitute the second delay. A majority of the participants from the rural areas first sought care in a dispensary or health centre, from where they were referred to the district hospital. This often meant that women had to organise their own public transport because the ambulances from the district hospital were often unavailable. Poor road infrastructure and transportation contributed to the second delay, particularly for rural women. This is exemplified by narrations of several women.

*"I was first brought to Madunguni dispensary on a stretcher. We had to cross the river. I could not get into the boat because it was too small. They had to carry me on a stretcher and walk across the river because I had passed out...the doctor examined me and immediately called for the ambulance"* (23 year-old rural resident with APH, severe PET)

*"I was brought to Gongoni health center in a Bajaj (three wheeled cabin cycle). It was at night and I was in so much pain...they called for an ambulance, but were informed that it had gone to pick another patient. At 2pm, the ambulance arrived. We arrived here at around 4pm"* (18 year-old rural resident with obstructed labor and bandl's ring)

*"I started having pains in the morning. I called the TBA to accompany me to the health centre, where I had planned to deliver. When we arrived at around 8 am, I continued to push the whole day. Later at around 6.30pm, the baby's head could be seen but I did not have any more energy to push. I started to bleed. The doctor examined me and informed (us) that he was referring me to Malindi District Hospital. They called for the ambulance from the District Hospital only to be informed that the vehicle had gone to pick a patient at Chakama and would delay because the connecting road from Chakama to Marafa was in bad condition. Later, we hired a Nissan from Marafa and paid 4000 Kenyan shillings. The labor pains were then very intense. We reached Malindi Hospital at 10pm"* (23 year-old rural resident with OL and FD)

### Delays in receiving treatment at care facility

Delays experienced at the health care facility contributed to the third delay. These delays included long queues at the facility and doctor unavailability. The women arrived at the hospital with complications, having delayed at home and on the way. The additional delays at the hospital before an intervention was performed added to the first two delays. A woman who had severe PET had to wait for several hours to receive treatment because of a long queue, while another who had OL and FD had to wait for the doctor to be called.

*"We arrived at the hospital around 8pm. I was received well, examined and admitted to the labor ward. But there were so many women waiting to be seen by the doctor. I had to wait until midnight to be given treatment... I am happy about the care I received. My pressure is back to normal"* (39 year-old rural resident with severe PET)

*"We reached the hospital around 10.00pm. The pains were very intense. I was examined and referred to theatre immediately, but the doctor arrived at around 1.00 am...I waited for so long"* (23 year-old rural resident with OL and FD)

For some women, travel delays meant that they arrived at the hospital too late, compromising survival of the unborn baby as narrated below.

*"I was in my uncle's house when the pains started at around 11pm. They brought me to Gongoni Dispensary in a Bajaj immediately because I had been advised to deliver in a hospital since I did not have enough blood. When we arrived, I was examined and encourage to walk because the baby was still far. I was in pain the whole night. The next morning they took me to the delivery room, but I could not push any more. At around noon, the doctor called for an ambulance from district hospital, but they were informed that it had gone to pick another patient. I was in pain until around 2 pm, when the ambulance finally arrived. When we reached the District hospital, I was still kept waiting for about 1 hour, because doctor had to be called. The nurses examined me several times, only to tell me later that the baby was dead... I was operated on later to remove the dead baby". (18 year-old rural resident with OL)*

*"When we arrived at Madunguni Dispensary, the doctor had left. He was called as he lives nearby. He examined me and remarked that the problem was beyond him and that he was referring me to the district hospital. He called for an ambulance. When we arrived here, a nurse examined and gave me some medication. I was bleeding heavily. Later, I delivered but the baby was dead". (23 year-old rural resident with APH due to placenta abruption and severe PET)*

## Discussion

This paper documents the findings from a study whose main objective was to assess barriers to EmOC services by women who experienced life-threatening obstetric complications or "near miss" in Malindi District, Kenya. Studies investigating barriers to safe motherhood interventions in low-income countries have mainly focused on verbal autopsies and maternal mortality reviews to provide evidence of underlying causes of maternal mortality [27,28]. However, maternal mortality represents the tip of the iceberg and capturing near-miss morbidity provides a more comprehensive picture of maternal health outcomes [24]. In this study, interviewing women who experienced life threatening obstetric complications before discharge from hospital provided the advantage of obtaining firsthand information, not prone to recall bias from onset of the complication to when the survivors received treatment.

Findings from this study reveal that a combination of delays occurred for the majority of near-miss participants. Many women delayed seeking care, and on reaching the nearest facility, which often was a dispensary or health centre, their conditions necessitated referral to the district hospital. Additional delays occurred at the initial health facility because there were no available ambulances, the lack of regular commuter transport and the long distance to the district hospital, particularly for rural women. When women eventually arrived at the district hospital, there were further delays because of long queues and unavailability of doctors. These findings support the classical three delays framework [5] and are similar to those observed in other resource-limited settings [29-33].

Knowledge about the risks of childbirth and the benefits of skilled attendance should increase preventive care-seeking, while recognition of danger signs and knowledge about available beneficial interventions should increase care-seeking for complications [4,5]. Although the women in this study generally had good knowledge of the danger signs during pregnancy, this knowledge did not translate into timely care seeking in the advent of a complication. Women who did not experience obstetric complications in previous pregnancies tended to believe that the index pregnancy would also be without problems. Using experience of a previous pregnancy as a risk predicting tool has been reported elsewhere [29,31]. Birth preparedness, which is an essential part of ANC, not only entails preventive care seeking, but also identification of a health facility with delivery services, making transportation plans and saving money [33]. This practice was not a norm in this setting, partly because a pregnancy was viewed as a normal and natural process, and therefore not planned for. The contribution of financial limitation in hindering access to maternal health services and consequently to the first delay are well documented [4,16,29,32,34,35].

While it is expected that women who attend ANC would be more likely to deliver in a health facility [5], we observed that ANC attendance was not linked to a desire to deliver in a health facility. It is however not

surprising given that despite high ANC coverage (90 percent) in Kenya, over 50 percent of women are attended by unskilled persons and/or outside a health facility during delivery [17]. While it is acknowledged that multiple factors may influence a woman or families' choice about whether to deliver at home or health facility [5], planning for facility delivery beforehand and following the plan is likely to influence a positive outcome from the pregnancy. Hypothetically, appropriate care may be provided should a complication arise during delivery, thus preventing the first two delays substantially [33]. The lack of a strong association between ANC attendance and preference to deliver in a health facility has also been observed in rural Uganda [36].

Although women and families may make timely decisions to seek care, they can still experience delays in reaching appropriate care facilities [4,5]. Delays in reaching appropriate care facilities when women experience life-threatening obstetric complications is reported as a major factor contributing to high maternal mortality and in developing countries [16,31,37]. In many situations, access to care for a woman experiencing a life threatening complication is limited to nearby lower level facilities, which are not equipped to handle obstetric complications [5]. In this study we noted that rural women often had to first visit a dispensary or health centre, which meant that they experienced further delays because health workers in these health facilities had to refer them to the district hospital.

Testimonies of rural women in this study also attest to lack of regular commuter transport, long distances and poor road network. Distance is reported to play an important role in the first and second delays because it influences travel time to access EmOC services [5,16,31]. Distance plays two roles in influencing use of services; as a discouragement to seek care in the first place and as an actual barrier to reaching a facility after a decision has been made to seek care [5]. An assessment of existence and functionality of EmOC services in this setting revealed geographical inequities in distribution of comprehensive EmOC services with rural women having to travel longer distances to access services [20].

Near miss upon arrival in hospital is an indication of delays in reaching the hospital, either because of a failed referral chain or because women and their caretakers are late in deciding to seek care [38]. These two aspects are strongly evident in our findings. Nevertheless, the findings provide useful insights into the barriers women experiencing life threatening obstetric conditions face in accessing EmOC, which is vital for maternal mortality reduction in Kenya.

The findings confirm a well known need to prioritise the promotion of birth preparedness, by strengthening knowledge of danger signs and skilled birth attendance as a direct responsibility of health services. This study further documents the importance of saving money and making transportation plans during antenatal services or other preventive or health promotion activities as part of birth preparedness. Increasing actual access to EmOC services in underserved areas and/or compensation through an effective referral infrastructure requires a broader involvement of health sector. A broader involvement of other sectors, local administration and communities in overall priority setting will assist in getting consensus and thus support for decreasing all three delays including better roads, communication and emergency transport availability as part of local development. Such broader involvement for health improvement is referred to in a previous paper [20] as part of a multi country study [39] carried out in Malindi district.

### Study limitations

This study had several limitations. First, we only captured information from women who managed to reach hospital. It is quite likely that many women with similar obstetric problems never get to reach hospital and either die at home or survive with serious morbidities. Thus, a comprehensive appraisal of the barriers women with obstetric complications face cannot be provided in this study. Second, although we note delays in obtaining treatment at the health facility as a barrier, these delays are also related to the quality of care and responsiveness of the hospital in treating obstetric emergencies. Quality of care is influenced by multiple health service factors such as availability of supplies, presence of qualified staff, staff attitude, organization of care and efficiency [5]. A comprehensive examination of these factors is beyond the scope of our study.

## Conclusion

The various delays rarely operate in isolation and are likely to be linked. As demonstrated, pregnant women make an attempt to obtain care when an emergency complication occurs. However, delays in making the decision to seek this care, combined with delays in reaching care facilities means that many arrive too ill to be effectively treated. Although factors at the health care facilities contribute to maternal morbidity and mortality, it is important to underscore the role of the first and second delays, which greatly influence the eventual outcome of both mother and unborn baby. Interventions to reduce maternal mortality and morbidity should therefore adequately address pre-hospital barriers in order to have the greatest effect. Findings in this study highlight the need to prioritise and promote birth preparedness, including knowledge of danger signs, identification of skilled care for childbirth, saving money and making transportation plans. Increasing actual access to EmOC services in underserved areas and/or compensation through an effective referral infrastructure that includes adequate good roads, communication and emergency transport is also necessary.

## Competing interests

The authors declare no competing interests.

## Authors' contributions

JKS was responsible for conceptualization, study design, data collection, data analysis and interpretation, drafting and revision of the manuscript. MKO was involved in data collection, laboratory analysis, and interpretation of results and critical revision of the manuscript. MLW participated in conceptualization, analysis, interpretation and critical revision of the manuscript. IAQ contributed to the documentation for ethical clearance, field site selection and critical revision of the manuscript. BDA was instrumental in the design, study site and laboratory selection and provision and implementation of the field study for data collection, laboratory analysis, data interpretation and critical review of the manuscript. All authors read and approved the final version.

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## Research

# Influence of Mckenzie protocol and two modes of endurance exercises on health-related quality of life of patients with long-term mechanical low-back pain

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**Introduction:** Long-term Mechanical Low-Back Pain (LMLBP) negatively impacts on patients' physical capacity and quality of life. This study investigated the relationship between Health-Related Quality of Life (HRQoL) and pain intensity, and the influence of static and dynamic back extensors' endurance exercises on HRQoL in Nigerian patients with LMLBP treated with the McKenzie Protocol (MP).

**Methods:** A single-blind controlled trial involving 84 patients who received treatment thrice weekly for eight weeks was conducted. Participants were assigned to the MP Group (MPG), MP plus Static Back Endurance Exercise Group (MPSBEEG) or MP plus Dynamic Endurance Exercise Group (MPDBEEG) using permuted randomization. HRQoL and pain was assessed using the Short-Form (SF-36) questionnaire and Quadruple Visual Analogue Scale respectively.

**Results:** Sixty seven participants aged  $51.8 \pm 7.35$  years completed the study. A total drop-out rate of 20.2% was observed in the study. Within-group comparison across weeks 0-4, 4-8 and 0-8 of the study revealed significant differences in HRQoL scores ( $p < 0.05$ ). Treatment Effect Scores (TES) across the groups were significantly different ( $p = 0.001$ ). MPSBEEG and MPDBEEG were comparable in TES on General Health Perception (GHP) at week 4; and GHP and Physical Functioning at week 8 respectively ( $p > 0.05$ ). However, MPDEEG had significantly higher TES in the other domains of the SF-36 ( $p = 0.001$ ).

**Conclusion:** HRQoL in patients with LMLBP decreases with pain severity. Each of MP, static and dynamic back extensors endurance exercises significantly improved HRQoL in LMLBP. However, the addition of dynamic back extensors endurance exercise to MP led to greater improvement in HRQoL.

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## Background

Low-Back Pain (LBP) is described as the constellation of symptoms of pain or discomfort originating from impairments in the structures in the low back [1-2]. LBP is one of the most common ailments afflicting mankind [3]. It is a complicated condition which affects the physiological and psychosocial aspects of the patient [4, 5]. Epidemiological reports indicate that 70 to 85 % of all people have LBP at some time in their life [1, 6]. The World Health Organization predicted that the greatest increases in LBP prevalence in the next decade will be in developing nations [7]. In line with this, a systematic review by Louw et al [8] concluded that the global burden and prevalence of LBP among Africans is rising.

It is estimated that 80-90% of patients with LBP will recover within six weeks, regardless of treatment [9]. However, 5-15% of all people that have LBP will develop long-term LBP (i.e. LBP of 12 weeks and longer) [10, 11]. The patient subgroup with long-term LBP accounts for 75-90%

of the socioeconomic cost of LBP [12] and over 30% of these patients with long-term LBP seek healthcare for their back complaints. Long-term LBP significantly impacts on patients' physical [13], psychological and social functioning [14] and can affect well-being and quality of life [15]. Reduced quality of life in patients with long-term LBP is associated with poor prognosis [16], intermittent or recurrent episodes of LBP [17], disability [18] and psychosocial dysfunction [19, 20].

Assessment of Health-Related Quality of Life (HRQoL) in relation to LBP has been recommended in LBP management [21, 22]. Several HRQoL instruments have been developed to assess self-perceived general health status [21, 22]. The SF-36 Health Status Questionnaire, though a generic instrument, has been recommended in the assessment of HRQoL of patients with long-term LBP [22] and it assesses eight domains such as physical functioning, role limitations due to physical problems, bodily pain, general health perceptions, vitality, social functioning, role limitation due to emotional problems and general mental health [23, 24].

Consequent to the foregoing, treatment intervention that may help

improve the HRQoL of patients with long-term LBP has been advocated. Although, physiotherapy plays an important role in the management of patients with LBP, the traditional approach based on biomedical model, which is centered on the treatment of impairments and pathophysiological variables, may not fully address the wider range of factors including psychosocial impairments associated with long-term LBP [25, 26]. However, long-term LBP is considered to be a multi-factorial bio-psychosocial problem which has an impact on both social life [27, 28] and quality of life [29] and thus requires a multi-dimensional approach based on a bio-psychosocial model (a model that includes physical, psychological and social elements) in its assessment and treatment [30, 31].

Based on empirical recommendations from research, recent decades have witnessed tremendous advances in preventive, pharmacological and physiotherapy management for a limited number of patients with LBP especially in developed countries. However, the improvement in health outcomes observed in most Western countries over the past few decades has not been achieved in Africa [32] and therefore, the health of Africans is of global concern [8]. Compared with Australians [33], Europeans [34] and North Americans [35], the use of exercise as medicine in Africans is poor. Exercise is the central element in the physical therapy management of patients with long-term LBP [9, 36]. Exercise often does not require expensive instruments and probably the cheapest intervention and one in which the patient has some measure of direct control [37]. Nonetheless, it remains inconclusive which exercise regimen will significantly influence the quality of life of patients with long-term LBP. The McKenzie Protocol (MP) is one of the most commonly used physical therapy interventions in long-term mechanical LBP with documented effectiveness [38-41]. However, there is a dearth of studies that have investigated the influence of the MP on HRQoL in patients with long-term mechanical LBP. Therefore, this study was intended to answer the following questions: (1) Will pain intensity significantly influence HRQoL? (2) Will static and dynamic back extensors' endurance exercises significantly influence HRQoL in Nigerian patients with long-term mechanical LBP (LMLBP) treated with the MP?

## Methods

Eighty four patients with LMLBP participated in this single-blind randomized trial. The participants were consecutively recruited from the physiotherapy department, Obafemi Awolowo University (OAU) Teaching Hospitals Complex and the OAU Health Centre, Ile-Ife, Nigeria. The McKenzie Institute's Lumbar Spine Assessment Format (MILSAF) [3] was used to determine eligibility to participate in the study. Based on the MILSAF, patients who demonstrated Directional Preference (DP) for extension only were recruited to ensure homogeneity of samples. DP is described as the posture or movement that reduces or centralizes radiating pain that emanates from the spine. Exclusion criteria were red flags indicative of serious spinal pathology with signs and symptoms of nerve root compromise (with at least two of dermatomal sensory loss, myotomal muscle weakness and reduced lower limb reflexes), individuals with any obvious spinal deformity or neurological disease; pregnancy; previous spinal surgery; previous experience of static and dynamic endurance exercise and having DP for flexion, lateral or no DP. Long-term low-back pain was defined as a history of LBP of not less than 3 months [42].

Based on the sample size table by Cohen [43] with alpha level set at 0.05, degree of freedom at 2, effect size at 0.25, and power at 80, the study found a minimum sample size of 52. However, in order to accommodate for possible attrition or loss during the study, a total of 75 patients (25 per group) was included. The participants were randomly assigned to one of three treatment groups using permuted block randomization; the McKenzie Protocol (MP) Group (MPG) (n=29), MP plus Static Back Endurance Exercise Group (MPSBEEG) (n=27) and MP plus Dynamic Back Endurance Exercise Group (MPDBEEG) (n=28). Sixty seven (32 males (47.8%) and 35 females (52.2%)) participants completed the eight week study. Twenty five participants completed the study in MPG, 22 in MPSBEEG and 20 in MPDBEEG. A total drop-out rate of 20.2% was observed in the study. Fourteen percent of participants in MPG were lost to follow-up. Nineteen percent of the participants in MPSBEEG dropped out (out of these, 40% were lost to follow-up while 60% absconded due to improvement in their health condition). In the MPDBEEG, 28.6% of the participants dropped out (37.5% were lost to follow-up while 62.5%

absconded due to improvement in their health condition).

Treatment was given thrice weekly for eight weeks and outcomes were assessed at the end of the fourth and eighth week of study. Ethics and Research Committee of the Obafemi Awolowo University Teaching Hospitals Complex and the joint University of Ibadan /University College Hospital Institutional Review Committee respectively gave approval for the study.

## Instruments

A height meter calibrated from 0-200cm was used to measure the height of each participant to the nearest 0.1cm. A weighing scale was used to measure the body weight of participants in kilograms to the nearest 1.0Kg. It is calibrated from 0 - 120kg. A metronome (Wittner Metronom system Maelzel, Made in Germany) was used to set a uniform tempo for dynamic back endurance muscles endurance test, which involves repeated contraction or movements over a period of time performed synchronously to the metronome beat. Patients lay on a plinth for the MP, static and dynamic back endurance exercise respectively.

General Health Status Questionnaire - Short Form -36 (SF-36) was used to assess the quality of life of the participants. The SF-36 has been recommended in the assessment of patients with long-term LBP [24, 44, 45]. A Yoruba translated version of the Health Status Questionnaire (SF-36) was used for participants who were literate in the Yoruba language and preferred the Yoruba version. The translation was done at the department of linguistics and African languages of Obafemi Awolowo University, Ile Ife. Pearson product moment correlation coefficient (r) of 0.84 was obtained for the criterion validity of the back translation of the Yoruba version. Quadruple Visual Analogue Scale (QVAS) was used to assess pain intensity of participants. QVAS is a reliable and valid method for pain measurement [46, 47]. A Yoruba translated version of the QVAS was used for participants who were literate in the Yoruba language and prefers the Yoruba version. The translation was done at the department of linguistics and African languages of Obafemi Awolowo University, Ile Ife. Pearson product moment correlation coefficient (r) of 0.88 was obtained for the criterion validity of the back translation of the Yoruba version.

## Treatment

Treatment for the different groups (MPG, MPSBEEG and MPDBEEG) comprised three phases including warm up, main exercise and cool down. Prior to treatment, the participants were instructed in details on the study procedures. This was followed by a low intensity warm-up phase of five minutes duration comprising active stretching of the upper extremities and low back and strolling at self-determined pace around the research venue. Treatment also ended with a cool-down phase comprising of the same low intensity exercise as the warm-up for about five minutes.

The McKenzie Protocol (MP) involved a course of specific lumbosacral repeated movements in extension that cause the symptoms to centralize, decrease or abolish. The determination of the direction preference for extension was followed by the main MP activities including "Extension lying prone", "Extension In Prone" and "Extension in standing". The MP also included a set of back care education instructions which comprised a 9 item instructional guide on standing, sitting, lifting and other activities of daily living for home exercise for all the participants (Appendix).

In addition to completing the MP (i.e., back extension exercises plus the back care education), static back extensors endurance exercise which included five different static exercises differentiated by the alteration of the positions of the upper and lower limbs with the patient in prone lying on a plinth was carried out [48]. The participants began the exercise training programme with the first exercise position, but progressed to the next exercises at their own pace when they could hold a given position for 10 seconds. On reaching the fifth progression, they continued with the fifth progression until the end of the exercise programme [48, 49]. The following were the five exercise progressions:

- 1) Participant lay in prone position with both arms by the sides of the body and lifting the head and trunk off the plinth from neutral to extension;
- 2) Participant lay in prone position with the hands interlocked at the occiput so that shoulders were abducted to 90° and the elbows flexed, and lifting the head and trunk off the plinth from neutral to extension;
- 3) Participant lay in prone position with both arms elevated forwards,

and lifting the head, trunk and elevated arms off the plinth from neutral to extension;

- 4) Participant lay in prone position and lifting the head, trunk and contralateral arm and leg off the plinth from neutral to extension; and
- 5) Participant lay in prone position with both shoulders abducted and elbows flexed to 90°, and lifting the head, trunk and both legs (with knees extended) off the plinth.

If pain was aggravated during the exercise, the participant was asked to stop. If the pain diminished within 5 minutes after the exercise, he/she was asked to continue the exercise but to hold the exercise position for only 5 seconds. The participant was asked to progress to 10 seconds if there was no adverse response. Each exercise was repeated 9 times. After 10 repetitions, the participant was instructed to rest for between 30 seconds to 1 minute. Static holding time in the exercise position was gradually increased to 20 seconds to provide a greater training stimulus [50, 51]. The dosage of series of 10 repetitions was adopted from a previous protocol for participants with sub-acute LBP [52].

In addition to completing the MP, dynamic back extensors endurance exercise which included five different isokinetic exercises differentiated by the alteration of the positions of the upper and lower limbs with the patient in prone lying on a plinth was carried out. The dynamic back endurance exercise was an exact replica of the static back extensors endurance exercise protocol in terms of exercise positions, progressions and duration. However, instead of static posturing of the trunk in the prone lying position and holding the positions of the upper and lower limbs suspended in the air during all the five exercise progressions for the 10 seconds, the participant was asked to move the trunk and the suspended limbs 10 times.

If pain was aggravated during the exercise, participant was asked to stop. If the pain diminished within 5 minutes after the exercise, the participant was asked to continue the exercise but to carry out only 5 movements in the exercise position. The participant was asked to progress to 10 movements if there is no adverse response. Each exercise was repeated 9 times. After 10 repetitions, the participants were instructed to rest for between 30 seconds to 1 minute. The number of movements of the trunk in the exercise position was gradually increased to 20 seconds to provide a greater training stimulus.

In order to achieve adequate training effect based on recommendation of previous studies, a 30 to 45 minute exercise duration, thrice weekly and eight weeks exercise; and training load of 10 seconds static hold or 10 repetitions per exercise position was adopted [53, 54].

The researchers (CEM and OA) were credentialed in the McKenzie method and supervised the exercises. The researchers were blinded to the recruitment, randomization and assessment procedures which were carried out by an assistant who was blinded to the treatment protocols of the different groups. The research assistant was also credentialed in McKenzie method. The questionnaires used in this study were self-administered.

### Data analysis

Data were analyzed using descriptive of mean and standard deviation; and inferential statistics. One-way ANOVA was used to compare the participants' general characteristics and pain intensity by treatment groups. Pearson's Product Moment Correlation Analysis was used to test the relationship between HRQoL and intensity of pain. The Kruskal Wallis test was used to compare the treatment outcomes (mean change) on HRQoL across group at week four and eight of the study respectively. Friedman's ANOVA and Wilcoxon signed ranked tests for multiple comparisons were used to compare within group changes in across the three study time points Alpha level was set at  $p=0.05$ . The data analyses were carried out using SPSS 13.0 version software (SPSS Inc., Chicago, Illinois, USA).

## Results

The mean age, height, weight and BMI of all the participants was  $51.8 \pm 7.35$  years,  $1.66 \pm 0.04$ m,  $76.2 \pm 11.2$  Kg and  $27.2 \pm 4.43$  kg/m<sup>2</sup> respectively. Comparison of the participants' general characteristics by treatment groups revealed that the participants in the different groups

were comparable in their general characteristics ( $p>0.05$ ) (Table 1).

	MPG (n = 25)	MPSBEEG (n = 22)	MPDBEEG (n = 20)		
	$\bar{x} \pm SD$	$\bar{x} \pm SD$	$\bar{x} \pm SD$	F-ratio	p-value
Age (yr)	$50.6 \pm 7.57$	$51.2 \pm 7.50$	$53.8 \pm 6.83$	1.106	0.339
Height (m)	$1.67 \pm 0.04$	$1.66 \pm 0.04$	$1.68 \pm 0.04$	2.185	0.331
Weight (Kg)	$76.3 \pm 9.95$	$75.2 \pm 13.2$	$77.2 \pm 10.8$	0.156	0.856
BMI (Kg/m <sup>2</sup> )	$27.5 \pm 4.20$	$27.3 \pm 5.25$	$26.9 \pm 3.89$	0.093	0.912
VAS	$6.56 \pm 1.83$	$6.50 \pm 1.71$	$6.60 \pm 1.79$	0.017	0.983

Alpha level was set at  $p < 0.05$   
 Key: MPG = McKenzie Protocol Group; MPSBEEG = McKenzie Protocol plus Static Back Endurance Exercise Group; MPDBEEG = McKenzie Protocol plus Dynamic Back Endurance Exercise Group;  $\bar{x}$  = Mean; SD = Standard deviation; VAS = Visual Analogue Scale

The mean pain intensity score (VAS) reported by the participants was  $6.55 \pm 1.75$ . The relationship between each of the eight domains of HRQoL and intensity of pain (VAS score) is presented in Table 2.

Domain	r	p-value
GH	-0.603	0.001
PF	-0.772	0.001
RP	-0.759	0.001
RE	-0.755	0.001
SF	-0.878	0.001
MH	-0.86	0.001
BP	-0.874	0.001
EV	-0.857	0.001

From the result, correlation co-efficient (r) ranged between -0.603 to -0.878 at  $p = 0.001$ .

Table 3 shows the comparison of the participants' baseline measure of HRQoL.

	Mean Rank				
Outcome	MPG (n=25)	MPSBEEG (n=22)	MPDBEEG (n=20)	H	p-value
GH	33.3	32.9	36.2	0.364	0.839
PF	33.0	36.3	32.8	0.442	0.802
RP	35.9	32.3	33.0	0.387	0.824
RE	34.2	34.7	33.0	0.083	0.96
SF	33.4	36.0	32.6	0.351	0.839
MH	32.5	35.2	34.5	0.246	0.884
BP	36.7	31.6	33.2	0.867	0.648
EV	31.7	35.6	35.1	0.597	0.742

The results indicate that the participants in the different treatment groups were comparable in all the domains of HRQoL ( $p>0.05$ ). Within-group comparison of HRQoL in MPG, MPSBEEG and MPDBEEG across the 3 time points (weeks 0-4, 4-8 and 0-8) of the study showed that there were significant improvements ( $p<0.05$ ) (Table 4). Comparison of treatment outcomes (mean change score (MCS)) at week four and eight of the study are presented in Table 5. There were significant differences in SF-36 scores across the group ( $p>0.05$ ) at the end of the 4th and 8th week of the study respectively. The Tukey multiple comparisons post-hoc analysis was used to elucidate where the differences within between groups lie. The result indicated that MPSBEEG and MPDBEEG had significantly higher MCS on all domains of SF-36 compared with MPG at week four and eight respectively ( $p<0.05$ ). There was no significant difference between the MPSBEEG and MPDBEEG in the MCS of General Health Perception domain of SF-36 at week four; and on General Health Perception and Physical Functioning Domains of SF-36 at week eight respectively. However, MPDBEE had significantly higher treatment effects on other domains of HRQoL ( $p=0.001$ ).

**Table 4:** Friedman's ANOVA and Wilcoxon signed ranked test multiple comparisons of HRQoL among MPG, MPSBEEG and MPDBEEG across the 3 time points of the study

Outcome	Mean Rank			$\chi^2$	p-value
	Baseline	4th week	8th week		
<b>MPG (n=25)</b>					
GH	33.3 <sup>a</sup>	59.3 <sup>b</sup>	69.2 <sup>c</sup>	50.00	0.001
PF	33.0 <sup>a</sup>	57.8 <sup>b</sup>	66.8 <sup>c</sup>	48.08	0.001
RP	35.9 <sup>a</sup>	38.5 <sup>b</sup>	48.4 <sup>c</sup>	45.96	0.001
RE	34.2 <sup>a</sup>	43.8 <sup>b</sup>	52.7 <sup>c</sup>	40.735	0.001
SF	33.4 <sup>a</sup>	64.8 <sup>b</sup>	72.6 <sup>c</sup>	48.91	0.001
MH	32.5 <sup>a</sup>	56.4 <sup>b</sup>	63.1 <sup>b</sup>	47.446	0.001
BP	36.7 <sup>a</sup>	54.4 <sup>b</sup>	66.2 <sup>c</sup>	52.108	0.001
EV	31.7 <sup>a</sup>	57.7 <sup>b</sup>	64.8 <sup>c</sup>	47.265	0.001
<b>MPSBEEG (n=22)</b>					
GH	32.9 <sup>a</sup>	64.4 <sup>b</sup>	72.5 <sup>c</sup>	42.34	0.001
PF	36.3 <sup>a</sup>	65.0 <sup>b</sup>	74.0 <sup>c</sup>	44.5	0.001
RP	32.3 <sup>a</sup>	48.4 <sup>b</sup>	59.2 <sup>c</sup>	41.4	0.001
RE	34.7 <sup>a</sup>	49.6 <sup>b</sup>	57.3 <sup>c</sup>	39.321	0.001
SF	36.0 <sup>a</sup>	72.3 <sup>b</sup>	81.2 <sup>c</sup>	43.517	0.001
MH	35.2 <sup>a</sup>	59.9 <sup>b</sup>	68.1 <sup>c</sup>	42.091	0.001
BP	31.6 <sup>a</sup>	61.3 <sup>b</sup>	70.2 <sup>c</sup>	44.12	0.001
EV	35.6 <sup>a</sup>	60.7 <sup>b</sup>	71.2 <sup>c</sup>	38.273	0.001
<b>MPDBEEG (n=20)</b>					
GH	36.2 <sup>a</sup>	67.6 <sup>b</sup>	77.4 <sup>c</sup>	38.4	0.001
PF	32.8 <sup>a</sup>	72.8 <sup>b</sup>	80.4 <sup>c</sup>	40.22	0.001
RP	33.0 <sup>a</sup>	55.2 <sup>b</sup>	65.0 <sup>c</sup>	44.11	0.001
RE	33.0 <sup>a</sup>	53.4 <sup>b</sup>	62.1 <sup>c</sup>	42.34	0.001
SF	32.6 <sup>a</sup>	72.7 <sup>b</sup>	81.6 <sup>c</sup>	39.519	0.001
MH	34.5 <sup>a</sup>	67.5 <sup>b</sup>	76.4 <sup>c</sup>	43.124	0.001
BP	33.2 <sup>a</sup>	65.0 <sup>b</sup>	71.2 <sup>c</sup>	42.645	0.001
EV	35.1 <sup>a</sup>	66.2 <sup>b</sup>	78.4 <sup>c</sup>	45.6	0.001

**Table 5:** Kruskal Wallis comparison of the participants' treatment outcomes (mean change) at week four of the study

	Mean rank			H	p-value
	MPG (n=25)	MPSBEEG (n=22)	MPDBEEG (n=20)		
<b>Week 4</b>					
GH	19.0 <sup>a</sup>	41.7 <sup>b</sup>	44.3 <sup>b</sup>	24.06	0.001
PF	18.1 <sup>a</sup>	37.1 <sup>b</sup>	50.5 <sup>c</sup>	31.887	0.001
RP	14.8 <sup>a</sup>	40.1 <sup>b</sup>	51.3 <sup>c</sup>	42.277	0.001
RE	22.5 <sup>a</sup>	36.7 <sup>b</sup>	45.4 <sup>c</sup>	16.702	0.001
SF	22.4 <sup>a</sup>	39.5 <sup>b</sup>	42.4 <sup>c</sup>	14.397	0.001
MH	21.7 <sup>a</sup>	30.5 <sup>b</sup>	53.3 <sup>c</sup>	30.639	0.001
BP	18.9 <sup>a</sup>	38.4 <sup>b</sup>	48.1 <sup>c</sup>	26.813	0.001
EV	23.4 <sup>a</sup>	36.0 <sup>b</sup>	45.1 <sup>b</sup>	14.193	0.001
<b>Week 8</b>					
GH	22.1 <sup>a</sup>	43.2 <sup>b</sup>	44.1 <sup>b</sup>	27.01	0.001
PF	19.2 <sup>a</sup>	40.1 <sup>b</sup>	52.3 <sup>b</sup>	33.122	0.001
RP	16.4 <sup>a</sup>	41.2 <sup>b</sup>	51.7 <sup>c</sup>	46.108	0.001
RE	23.7 <sup>a</sup>	38.2 <sup>b</sup>	46.3 <sup>c</sup>	22.112	0.001
SF	24.2 <sup>a</sup>	40.4 <sup>b</sup>	44.0 <sup>c</sup>	16.014	0.001
MH	23.4 <sup>a</sup>	36.2 <sup>b</sup>	53.1 <sup>c</sup>	36.114	0.001
BP	21.3 <sup>a</sup>	40.3 <sup>b</sup>	49.2 <sup>c</sup>	28.612	0.001
EV	24.7 <sup>a</sup>	38.2 <sup>b</sup>	47.0 <sup>b</sup>	15.018	0.001

## Discussion

This study evaluated the relationship between HRQoL and pain intensity, and the influence of static and dynamic back extensors' endurance exercises on HRQoL in Nigerian patients with LMLBP treated with the MP. The mean age of the patients in this study was  $51.8 \pm 7.35$  years. This age falls within the age bracket during which LBP is reported to be a more common problem [55]. From the result of this study, no significant difference in physical characteristics and pain intensity was found in the different treatment groups at baseline. Baseline characteristics are believed to be predictors of response to treatment in clinical trials for LBP [56]. Comparability in baseline measure in clinical trials is reported to reduce the chances of co-founders other than the intervention in predicting outcomes. Therefore, it is implied that the results obtained at different point in the course of this study could have been largely due to the effects of the various treatment regimens.

This study investigated the relationship between HRQoL and the intensity of pain. From the result, significant moderate to high inverse relationships were found between pain intensity and the different domains of HRQoL. General health perception showed the least correlation ( $r=-0.603$ ;  $p=0.001$ ) while social functioning had the highest correlation with pain intensity ( $r=-0.878$ ;  $p=0.001$ ). It is inferred from the study's result that HRQoL of patients with long-term LBP decreases with severity of pain. Previous studies have reported an association between LBP and psychosocial factors [26, 57]. Specifically, significant inverse correlation has been reported between severity of pain and quality of life in patients with chronic LBP [57-59]. Pain is believed to have a profound effect on HRQoL [59] and the degree, to which the patients believe that they are disabled by it, is a powerful factor in the extent of their quality of life impairments [60]. Therefore, quality of life is an indicator of the level of endurance of people to pain [61].

Within-group comparison of each of MP, MP plus Static Back Endurance Exercise (MPSBEE) and MP plus Dynamic Back Endurance Exercise (MPDBEE) across the 3 time-points (weeks 0-4, 4-8 and 0-8) of the study revealed that each treatment regimen led to significant improvement in HRQoL. Patients in this study displayed baseline values of the SF-36 comparable to those described in other studies on chronic LBP [62]. The baseline values of all domains of the SF-36 observed in this study were lower than those of adult normative data reported by Jenkinson et al [63] leaving room for any improvement accruable to treatment regimens to be assessed. From this study, all the eight domains of the SF-36 significantly improved at the 4th and 8th week assessment. However, on the final assessment, social functioning, general health perception and bodily pain improved more than the other domains of SF-36 in the MPG. General health perception, physical functioning, social functioning, bodily pain and energy vitality improved more than the other domains of SF-36 in the MPSBEE while general health perception, physical functioning, social functioning, bodily pain and energy vitality improved more than the other domains of SF-36 in the MPDBEE. Role physical, role emotional and mental health were the least improved domains of the SF-36 among the treatment groups. Though significant improvements were observed in the different domains by treatment groups on final assessment, the values were still lower than the adult normative data for general health status assessed using the SF-36 questionnaire [63]. A previous study by Smeets and colleagues [64] found that active physical therapy regimen primarily designed to improve physiological aspects of LBP such as aerobic fitness level, low back muscle strength and endurance can also reduce the impact of psychosocial factors that it did not deliberately target. In view of current evidence, Hill and Fritz [57] suggest that it may not necessarily follow that a psychologist is better placed to improve treatment outcomes than a physical therapist, even when a goal of treatment is the mediation of a psychosocial factor. Hill and Fritz [57] also argue that psychosocial factors including fear of movement, anxiety, a faulty coping strategy and quality of life have a strong influence on the success of treatment for patients with back pain at a group level. Literature suggests that exercise generally has a potential benefit on psychosocial aspect of patient with long-term LBP. Long-term LBP leads to deconditioning [65] and many problems associated with deconditioning are believed to be reversible through general and specific exercise regimens [66]. Harding and Watson [66] note that improvement in overall physical function is linked with improvement in psychosocial function. Unfortunately, there is a dearth of studies on the effect of the MP and back extensors endurance exercises on HRQoL in patients with long-term mechanical LBP.

From the result of this study, comparison of the different treatment regimens indicate that MPSBEE and MPDBEE had significantly higher treatment effect on all domains of HRQoL compared with MP at week four and eight respectively. MPSBEE and MPDBEE were comparable in their effect on general health perception domain at week four; and on health perception and physical functioning domains of the HRQoL at week eight. However, MPDBEE had significantly higher treatment effects on other domains of HRQoL. Generally, exercise seems to lead to improved wellness and quality of life. Still, there does not appear to be a consensus of opinion on the most effective programme designed to maintain exercise benefits. The McKenzie method is a popular and promising classification-based treatment for LBP among physical therapists [3] in addition to delivering theoretical information in order to educate patients about their condition, so that patients are better able to understand their condition and how to change their behaviour towards an episode of LBP [67]. However, few studies have investigated the effect of the MP on HRQoL in patients with LMLBP. Udermann et al [68] found significant improvements

in HRQoL measures in chronic LBP patients treated with MP but reported that the addition of resistance training for the lumbar extensors provided no additional benefit. In recent times, endurance training of the low-back extensors aimed at improving physical performance and psychosocial health in patients with LBP has increased in popularity [69,48, 52, 70], yet their effectiveness in enhancing quality of life remains unclear [71].

The observed efficacy of the MP, MPSBEE and MPDBEE in this study could be as a result of the fact that each of the regimen contained active exercise carried out in extension positions. Active exercise can be described as functional exercise performed by the patient or client. Previous studies have shown that active exercise, irrespective of the type is more effective in the management of patients with long-term LBP than passive therapy [72, 73]. The MP utilizes a system of patient self generated force to mobilize or manipulate the spine through a series of active repeated movements or static positioning and it is based on the patient's pain response to certain movements and postures during assessment [3]. Similarly, endurance exercises are active exercises that require static posturing or repeated movements in order to initiate overload stimuli on the musculature. The different treatment regimen in this study had movement components, either from the MP which is the baseline treatment for all the groups or from the back extensors endurance exercise protocols. It is postulated from the results of this study that the significant higher treatment outcome of MPDBEE might be due to the combined effects of movements and overload stimulus on the back extensor muscles. MPDBEE seems to contain movement ingredients, firstly, from the MP which is the baseline treatment for this group and it involved a series of active repeated movements. Secondly, the dynamic back extensors endurance exercise also involved repeated movements of the trunk and limbs in the sagittal plane. It seems that extension exercise with movement elements carried out in patterns similar to the daily tasks motions might help to improve psychosocial aspects of long-term LBP as observed in this study.

#### Limitations of the study

The generalizability of the findings of this study is limited by the fact that a generic quality of life tool was employed because of the scarcity of standard HRQoL tools with documented psychometric properties specific for patients with LBP. Theoretically, specific HRQoL measures are opined to be more responsive than generic HRQL measures [74]. Like all other self-reported assessment, it is possible that the patients in this study might have given exaggerated responses or overestimated the effect of exercise on their HRQoL. Furthermore, individuals' perception of psychosocial construct such as HRQoL is believed to be influenced by subjective interpretation and cultural bias [75, 76]. The high drop-out rate observed in this study is also a potential limitation and source of bias which may limit the interpretation and generalizability of study results. Finally, the treatment outcomes of the different regimens were only measured over such a short period of time of eight weeks.

## Conclusion

Health-related quality of life of patients with long-term LBP decreases with severity of pain. The McKenzie Protocol, static and dynamic back extensors endurance exercises had significant therapeutic effect on HRQoL in patients with LMLBP. However, the addition of dynamic back extensors endurance exercise to MP led to higher improvement on HRQoL. It is recommended that static or dynamic endurance exercise be combined with MP in patients with LMLBP to derive maximum improvement in general health status.

## Competing interests

The authors declare no competing interests.

## Authors' contributions

All the authors have contributed in this study in ways that comply to the ICMJE authorship criteria. All the authors have read and approved the final version of the manuscript.

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## Research

# Gait and balance performance of stroke survivors in South-Western Nigeria - A cross-sectional study

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**Introduction:** Stroke survivors are often left with neurological and functional deficits, which impair their ability to walk and affect their balance. This study assessed gait parameters and balance performance among stroke survivors and examined the relationship between these two factors.

**Methods:** Seventy stroke survivors (65.7% males) who were 6 months or more post stroke participated in this study. Using Observational Gait Analysis, the gait of participants was assessed by gait speed and cadence. Balance performance was assessed using the Activities-specific Balance Confidence scale for balance self-efficacy and Functional Reach Test for standing balance.

**Results:** Participants had a mean age of 53.5±10.4 years. Forty five (64.3%) stroke survivors had haemorrhagic stroke while 25 (35.7%) had ischaemic stroke. The mean gait speed and cadence were 0.6±0.3m/s and 69.1±38.1 steps/min, respectively. The mean balance self-efficacy score was 66.5±17.7 and mean functional reach distance was 18.7±2.6cm. There were significant relationships between gait speed and balance self-efficacy ( $r = 0.461$ ,  $p = 0.001$ ) and between cadence and functional reach distance ( $r = 0.247$ ,  $p = 0.020$ ).

**Conclusion:** This study concluded that stroke survivors with higher cadences had higher functional reach distances, and those with higher gait speeds had better balance self-efficacy. Gait speed and cadence are factors related to balance performance. These factors should be considered during gait and balance retraining and should go *pariparsu* in the rehabilitation of stroke survivors.

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**Key words:** Stroke, gait, balance, stroke survivors, rehabilitation, cadence, gait speed, Nigeria

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## Introduction

The most significant physical impact on stroke survivors is long term disability. Ambulation is a significant part of the functional recovery following stroke and this function depends on several factors including the size and location of the infarct and the premorbid health of the stroke survivor [1]. Dependence in mobility is one of the primary reasons of admission for inpatient rehabilitation after stroke. Much effort goes into helping these patients regain the ability to walk, at least in the home, prior to discharge. In spite of these efforts, approximately 35% of survivors with initial paralysis of the leg do not regain useful walking function, and 25% of all survivors are unable to walk without full physical assistance [2]. The result of this disability is a significant impact on the independence, quality of life and productivity of the survivors [3].

Gait is a major determinant of independent living. Therefore, it is not surprising that improvement of walking function is the most commonly stated priority of stroke survivors [4]. Approximately 80% of stroke

survivors achieve this goal [5] though the quality of walking performance often limits endurance and quality of life [6]. A lot of time and resources are invested into rehabilitation to restore walking ability following stroke and reduce functional dependence.

Balance dysfunctions in stroke survivors are common and have significant impact on functional independence and overall recovery of the patient. Patients who have suffered a stroke, present with abnormal and delayed postural responses in the lower extremity muscles during standing displacements and distorted proprioception. They also demonstrate postural control problems such as loss of anticipatory activation during voluntary movements, increased sway during quiet standing, especially on the affected side, and decreased area of stability during weight shifting while standing. All these could result in clinical presentations such as loss of static and dynamic stability and reduced functional abilities [7].

Balance problems have been implicated in the poor recovery of activities of daily living (ADL) and mobility and an increased risk of falls [8]. Studies on balance impairments have shown that stroke survivors have

greater postural sway than age-matched volunteers who are healthy [9-11]. They also have altered weight distribution patterns, so that less weight is taken through the weak leg, and they have smaller excursions when moving their weight around the base of support, especially in the direction of the weaker leg [12]. This pattern is seen in all aspects of balance—static, dynamic, or responses to external perturbations—and even in people with stroke with high levels of function, such as those who are ambulatory in the community.

Postural balance is closely related to gait ability [13]. A strong relationship has been reported between gait velocity and dynamic balance in the acute rehabilitation period among patients with first time ever stroke [14]. In a study of balance rehabilitation programs in which outcome measures consisted of gait velocity, timed stair climbing, self-assessment of ease of gait and balance under six sensory conditions, improvements in gait measures were correlated with improved balance [15]. Balance and gait impairments increase the risk of falls in older people [16]. During gait and balance retraining of stroke survivors, treatment goals are usually determined by analysing patients' gait parameters and assessing the balance performance.

The incidence and prevalence of stroke have not been established in Nigeria. However, the frequency of stroke in hospital populations has varied from 0.9% to 4.0%, whereas among neurological admissions, stroke accounted for 0.5% to 45% of admissions [17]. There has been an increase in the incidence of stroke in Nigeria [18] and due to improved medical care many stroke victims now survive. Many patients will therefore need long term rehabilitation. Thus, assessing gait and balance is critical to stroke rehabilitation. Previous studies have separately reported gait [19-21] and balance performance [22, 23] in Nigerian stroke survivors, but the relationship between these attributes has rarely been studied. This study therefore assessed gait parameters and balance performance of stroke survivors to investigate the relationship between them.

## Methods

### Study setting

This was a cross sectional study of stroke survivors with hemiparesis attending outpatient physiotherapy clinics in the two teaching hospitals in Osun State, Nigeria. Using the sample size computation used by Eng [24] for descriptive clinical studies, we calculated a minimum sample size of 61 patients. Seventy stroke survivors were recruited from Obafemi Awolowo University Teaching Hospitals Complex (OAUTHC), Ile-Ife and Ilesa units; and Ladoke Akintola University of Technology Teaching Hospital (LAUTTH), Osogbo. Obafemi Awolowo University Teaching Hospitals Complex is one of the first generation teaching hospitals established by the federal government, while LAUTTH is jointly owned by the state governments of Osun and Oyo. These two tertiary hospitals are urban health centres that provide medical services and training for medical and other health students. By virtue of their locations and the scarcity of health care facilities in neighbouring areas, patients that are seen in these hospitals come from all areas of Osun State and south-western states in Nigeria -Oyo, Ondo, Ekiti, Kwara, Kogi, Lagos and Edo States.

### Participants

Fifty-two (74.3%) stroke survivors were recruited from OAUTHC and 18 (25.7%) from LAUTTH. The participants met the following criteria for inclusion in the study: a diagnosis of first episode of unilateral stroke by a neurologist; experienced stroke more than six months prior to the study; ability to understand and follow simple verbal instructions; ambulant before stroke; and ability to walk 10 metres in 1 minute or less without the physical assistance of a therapist or carer. This criterion corresponds to Functional Ambulation Categories (FAC) level 3 [25]. A patient was excluded if he or she had a history of other neurological pathology, conditions affecting balance (dementia, impaired conscious levels) and musculoskeletal conditions affecting the lower limbs. Stroke survivors who scored 0 to 2 on the FAC classification or who were dependent on a walker were also excluded from the study.

Twenty four (34.3%) women and 46 (65.7%) men participated in this study. Their ages ranged from 31-83 years with a mean of 53.5±10.4 years. Based on the heterogeneous nature of the study sample considering their ages and because most stroke survivors in Nigeria

are between 50-70 years [17,26], participants were classified into three age categories; less than 50 years, 50 to 70 years and more than 70 years. Twenty three (32.9%) participants had FAC of 3 (they could walk independently with supervision), while 43 (61.4%) had FAC of 4 (they could walk independently on level ground) and only 4 (5.7%) had FAC of 5 (they could walk independently).

### Ethical considerations

The protocol was approved by the Ethics and Research Committee of the Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife. All the participants received an explanation of the procedure of the study and gave informed consent prior to enrolment for assessment and data collection.

### Procedures

Demographic and clinical information were obtained directly from the participants and from their case records. From neurologists' diagnosis which included radiological investigations, and our clinical findings, patients' strokes were classified as haemorrhagic or ischaemic. Physical measurements were conducted in the gymnasias and walkways of the physiotherapy clinics of the selected hospitals on 15-metre walkways created on smooth floors for the purpose of the study.

The Functional Ambulation Categories test was used to assess walking ability by providing information on the level of physical support needed by patients to ambulate. Standing height and body weight of all the participants were measured using standardized protocols. Gait of participants were assessed with their gait speed and cadence by observational gait analysis (OGA). Balance performance was assessed using the Activities-specific Balance Confidence (ABC) scale and Functional Reach Test (FRT).

The gait parameters measured were gait speed and cadence. Measurements were taken by OGA. The measurement of gait speed was taken with the participant walking 10m without physical assistance while under the supervision of a physiotherapist. Distances of 2.5m were allowed before and after the 10m mark to allow for acceleration and deceleration respectively. Walking devices were allowed during the measurements. Five of the stroke survivors used quadripods during assessment.

Gait speed was assessed at comfortable self-paced walking speeds using a standard approach of observational gait analysis [27]. During each session, the participant walked 10m at a comfortable and at a self-paced walking speed. Timing with a digital stopwatch that registers time in seconds was manually initiated after the "go" instruction when the participant crossed the beginning of the 10m mark and stopped when the participant crossed the end of the 10m mark. Each participant rested for about one minute between each test [28]. Normal comfortable gait speed ranges from 1.3 to 2.5m/s [27]. Speed was calculated in metres per second by dividing the distance walked by the time required. This was recorded as the actual gait speed. Higher scores indicated faster gait speeds. To reduce measurement error of timed walking test, the mean of three repeated measurements was used.

Step length relates to body height and body height relates to gait speed in normal persons. Considering this relationship between height and gait speed and the established usefulness of height for reducing inter-individual variability in gait speed [29], gait speed was normalized by dividing speed by height. Height normalized speed (HNS) was determined by the formula;

Height-normalized speed = Actual speed (m/s)/Height (m) [27]

Cadence was recorded as the number of steps taken per minute. Higher scores indicated better cadence. Normal walking cadence is 90 - 120 steps/minute [30]. No encouragement to facilitate performance during walking session was permitted.

The Functional Reach Test (FRT) [31] was used to measure the maximum distance that the stroke survivors could reach forward horizontally beyond arm's length while maintaining a fixed base of support in standing with comfortable stance width [32]. Using a yardstick calibrated in centimetres (cm), mounted on the wall at shoulder height, each participant was asked to position the body close to, but not touching the wall with

feet at a comfortable distance apart, the non-paretic arm outstretched and hand fist. The starting position was noted by determining what number the metacarpophalangeal (MCP) joints lined up with on the ruler. Each participant was asked to reach as far forward as possible with the unaffected arm, without losing his or her balance or taking a step. The start and end measurements were recorded. The functional reach distance was the difference between the two measurements. Each participant was given two practice trials then the performance on an additional three trials was recorded and averaged. A 15 second rest break was allowed between trials. The participants were guided in case of loss of balance. The functional reach distance was recorded in centimetres (cm). Scores of 6-7 inches (15.2 - 17.8 cm) indicate a frail person with limited ability to perform ADLs and increased risk of falls [31]. Patients were classified as fallers (FRT distance < 17.8cm) and non-fallers (FRT distance > 17.8cm) using their FRT distances [33]. The use of assistive devices was not allowed during this test.

Perceived balance self-efficacy was assessed using the Activities-specific Balance Confidence (ABC) scale [34]. The Activities-specific Balance Scale which has been shown to be valid and reliable for people with stroke, is a self-efficacy scale that evaluates confidence in 16 functional activities, 9 of them outside the home [35]. The ratings are based on an 11-point scale ranging from 0% ("no confidence at all") to 100% ("completely confident"). Participants were asked to rate their confidence that they will lose their balance or become unsteady in the course of completing 16 activities of daily living. The mean of the total score was recorded. A total score out of 100 was computed by taking the average of the item scores. The higher the ABC score, the higher the level of balance confidence. It took 10 - 20 minutes to administer the scale for each participant. Lajoie and Gallagher [36] reported that with an ABC Scale cut-off score of 67%, one can accurately classify people who fall 84% of the time. Patients in this study were classified as fallers (ABC score < 67%) and non-fallers (ABC score > 67%) using their ABC scale scores.

#### Data Analysis

Data were analysed using both descriptive and inferential statistics. Descriptive statistics of mean, standard deviation, percentage, frequency, minimum and maximum values were determined for characteristics of the participants. Pearson product-moment correlation coefficient was used to determine the relationship between the gait parameters and balance performance. Independent samples t-test was used to determine the difference between fallers and non-fallers (risk of falls) and one way analysis of variance (ANOVA) was used to determine the difference among the age categories. Significance was set at 0.05  $\alpha$ -level. All statistical analyses were carried out using Statistical Package for Social Sciences (SPSS) 16.0 (SPSS Inc. Chicago, USA)

## Results

Table 1 shows the frequency values and percentages of the demographic (gender and age) and stroke (side of paresis, type of stroke and balance performance) characteristics of the stroke survivors. Twenty three (32.9%) stroke survivors had left-side paresis while 47 (67.1%) had right side paresis. Of the 70 stroke survivors, 45 (64.3%) had haemorrhagic type of stroke while 25 (35.7%) had ischaemic type.

The range, mean and standard deviation of the physical (weight and height) and stroke (stroke duration, gait and balance performance) characteristics of the participants are presented in Table 2. The stroke durations ranged from six months to twenty four months (mean=18.3±8.8 months); Activities-specific Balance Confidence scale scores ranged from 21.4% to 97.9% (mean = 66.5±17.7%); functional reach test distances ranged from 7.6 cm to 39.4 cm (mean = 18.7±4.6cm); gait speeds ranged from 0.11 m/s to 1.12 m/s (mean= 0.6±0.3m/s); and cadence ranged from 13.4 to 136.8 steps/minute (mean =69.1±38.1 steps/minute).

The result of the Pearson product-moment correlation analysis showed a weak positive correlation between cadence and FRT distance ( $r = 0.247$ ,  $p = 0.020$ ); and a moderate positive correlation between gait speed and balance self-efficacy ( $r = .461$ ,  $p = 0.001$ ). But there was no significant relationship ( $p > 0.05$ ) between FRT distance and balance self-efficacy (Table 3).

There were significant differences in the FRT distance ( $p = 0.016$ ) and

Variable	Frequency	Percentage (%)
<b>Demographics</b>		
<b>Age categories (years)</b>		
less than 50	24	34.3
50- 70	44	62.9
Above 70	2	2.9
<b>Gender</b>		
Female	24	34.3
Male	46	65.7
<b>Stroke characteristics</b>		
<b>Side of paresis</b>		
Left	23	32.9
Right	47	67.1
<b>Type of stroke</b>		
Haemorrhagic	45	64.3
Ischaemic	25	35.7
<b>FAC Score</b>		
3	23	32.9
4	43	61.4
5	4	5.7
<b>ABC score category</b>		
Fallers ( $\leq 67$ )	31	44.3
Non fallers ( $> 67$ )	39	55.7
<b>FRT distance category</b>		
Fallers ( $\leq 16$ cm)	27	38.6
Non fallers ( $> 16$ cm)	43	61.4

FAC- Functional Ambulation Categories, FRT- Functional Reach Test, ABC- Activities-specific Balance Confidence, FAC 3 - Patient could walk independently with supervision, FAC 4 - Patient could walk independently on level ground, FAC 5 - Patient could walk independently.

Variable (N=70)	Minimum-maximum		Mean±SD
Age (Years)	31.0 -	83.0	53.5±10.4
Height (m)	1.7 -	1.9	1.7±0.8
Weight (Kg)	44.0 -	94.0	67.4±9.2
Stroke duration (Months)	6.0 -	24.0	18.3±8.8
Body mass index (Kg/m <sup>2</sup> )	16.8 -	33.7	24.3±2.8
FAC score	3.0 -	5.0	3.7±0.6
ABC scale score (%)	21.4 -	97.9	66.5±17.7
FRT distance (cm)	7.6 -	39.4	18.7±4.6
Gait speed (m/s)	0.1 -	1.1	0.6±0.3
Height normalized speed	0.1 -	0.7	0.3±0.2
Cadence (steps/min)	13.4 -	136.8	69.1±38.1

FAC- Functional Ambulation Categories, FRT- Functional Reach Test, ABC- Activities-specific Balance Confidence

Variable	ABC Scale score (r)	FRT distance (r)
Gait speed (m/s)	0.461**	0.115
Height normalized speed	0.069	0.107
Cadence (steps/min)	0.116	0.247*

\*Correlation is significant at  $p < 0.05$ , \*\*Correlation is significant at  $p < 0.01$ , ABC- Activities-specific Balance Confidence, FRT- Functional Reach Test.

ABC scores ( $p = 0.001$ ) between fallers and non-fallers, when the stroke survivors were categorized according to risk of falls. However, there were no significant differences between fallers and non-fallers using both the ABC score and FRT distance categories in the following variables; gait speed, HNS and cadence. The result of the one way ANOVA showed no significant difference in gait speed ( $F = 0.230$ ,  $p = 0.796$ ), cadence ( $F = 0.442$ ,  $p = 0.644$ ), balance confidence ( $F = 1.137$ ,  $p = 0.327$ ) and functional reach distance ( $F = 0.338$ ,  $p = 0.715$ ) among the three age categories considered.

## Discussion

This study assessed the gait characteristics and the balance performance of stroke survivors and also explored the relationship between them. The gait speed observed was within the range reported by Olney and Richards [37] who observed that the average gait speed in stroke survivors ranged from 0.23m/s to 0.73m/s depending on the severity of the hemiparesis. These mean values are below the values reported for normal subjects in self-paced walking [27]. Our results therefore demonstrate the impact of stroke on the ambulatory capability of stroke survivors. Although it is known that stroke survivors typically have reduced gait speed and cadence and present with abnormal and delayed postural responses, attempt to improve these parameters without compromising static and dynamic balances should be strongly considered in their walking re-education.

Mean ABC scale scores are similar to findings in previous studies of people living in the community after stroke [23,38]. In a Canadian study by Miller and Yiu [38] the mean balance confidence for the mostly male (71%) older adult sample (mean age  $67.7 \pm 1$  years) was  $62 \pm 2$ . They found balance confidence to be an independent predictor of physical function, participation and stroke recovery. Their study provided support for Bandura's premise that self-efficacy is more important than skill in predicting behaviour [39]. Balance confidence is a remedial condition; however, it is seldom addressed in rehabilitation [38]. The mean ABC score for stroke survivors in our study is lower than that of documented healthy community-dwelling elderly people [40]. The lower mean ABC Scale score for stroke survivors observed in our study indicates that stroke has a major effect on balance self-efficacy despite independent walking function. People with reduced balance confidence may therefore try to avoid falls by limiting their participation in activities.

The risk of falls is high among stroke survivors and falling is one of the most frequent complications these patients present with in rehabilitation. According to Lamb et al [8], approximately 40% of people fall within the first year of a stroke. Falls therefore remain a common feature in the life of people with stroke after discharge from hospital. Lajoie and Gallagher [36] have suggested that with an ABC Scale cut-off score of 67%, people who fall 84% of the time can be accurately classified. Functional reach distance has also been associated with an increased risk of falls and frailty in elderly people who are unable to reach more than 15 cm [32]. We did not find significant differences in the gait speed, HNS and cadence between fallers and non-fallers, though the non-fallers had higher gait speed and cadence values. The reason for this result may be because all our participants could ambulate independently and therefore had similar gait speeds and balance performance.

The mean ABC score of stroke survivors in our study is also lower than that of stroke survivors in the study by Pang et al [41] among older adults with chronic stroke ( $>1$  year). But higher than that of stroke patients in the study by Salbach et al [42] who included patients with more than one occurrence of stroke (11%) in their study. The higher scores obtained by Pang et al [41] probably occurred because all their participants were independent in walking. Whereas the lower mean score obtained in the study by Salbach et al [42] may be because a considerable proportion of people in their study required either supervision or physical assistance to walk. Salbach et al also included patients with less than 1 year post stroke and those with recurrent stroke, while our study included participants who were more than 6 months post stroke and did not include those with recurrent stroke. The difference in these results suggests that longer period of walking re-education (and balance retraining) of stroke survivors will be beneficial to their balance self-efficacy.

The moderate positive correlation between balance confidence and

gait speed is similar to the findings in the study by Botner et al [43]. Guimaraes, and Issacs [44] also reported that gait speed is related to fall risk. This implies that stroke survivors with slower gait speeds have poorer balance confidence and vice versa. Findings from experimental studies have indicated that gait training enhances balance self-efficacy and that depression, age, sex, comorbidity, time post stroke, and functional mobility predict improvement in self-efficacy [42]. The findings in our study therefore suggest that slow gait speed is a potential risk factor for falls in chronic stroke survivors. Reports of previous studies have suggested that walking ability is a factor in falls because many reported cases of falls occurred during walking [45, 46]. Gait retraining will improve gait ability and balance self-efficacy and reduce the risk of falls in stroke survivors.

The mean FRT distance for the stroke survivors in this study is lower than that observed by Wolf et al [47] and Takatori et al [48]. Many participants in the Wolf study used assistive devices (canes and ankle-foot orthoses), while none of the participants in our study used any assistive device to carry out this test. This implies that assistive devices can improve balance performance in stroke survivors by improving mobility and allowing for independence in the performance of mobility-related tasks. In the Takatori et al [48] study patients were receiving intensive rehabilitation. The stroke survivors in our study were community-dwelling chronic stroke survivors who were not receiving intensive rehabilitation. Intensity of rehabilitation may enhance standing balance, thereby reducing the risk of falls in all categories of ambulatory stroke survivors. The evidence of the relationship between gait speed and balance performance has some implications for the rehabilitation of chronic stroke survivors. Reduced gait can negatively affect their balance ability and reduced balance may contribute to higher risk of falls. Ambulatory activities and balance retraining should be promoted during the rehabilitation of chronic stroke survivors.

Apart from a weak positive correlation with cadence, functional reach distance had no significant correlation with gait speed in our study similar to findings by Wolf et al [47], who found no significant relationship between gait speeds of stroke survivors assessed with a timed 10-metre walk test and functional reach distance. Winstein et al [49] also found no association between gait function and standing balance. In evaluating the physical impairment and functional limitations of patients, it is clinically useful to assess walking capacity and monitor the recovery of gait performance. The findings of this study support the suggestions by van de Port et al [50] who argue that the ability to walk in the community requires more than gait speed alone. They showed in their study that improvement in balance control was the most important driver for improvement in hemiplegic gait. Balance control is therefore an important independent compensatory factor enabling patients to walk in the community despite lower gait speeds, suggesting that patients with a slow walking speed seem to be able to compensate by an appropriate use of walking aids and sufficient control of balance walker.

There are several study limitations that warrant acknowledgment. First, because the stroke survivors in our study could ambulate independently, the findings of this study may not be generalized to stroke survivors who cannot do so. Second, we used convenience sampling and therefore findings may not be generalizable. Further research with a more representative sample is therefore necessary to explore other factors that may affect gait and balance in Nigerian stroke survivors with varying degrees of recovery.

## Conclusion

Stroke survivors with higher cadences had higher functional reach distances, and those with higher gait speeds had better balance self-efficacy. This implies that gait speed and cadence are factors related to balance performance and should be considered during balance and gait retraining and should go *pari per su* in the rehabilitation of stroke survivors. Rehabilitation should focus not only on improving gait speed and balance performance, but also on other factors that are conditional for becoming an independent community.

## Competing interests

The authors declare no competing interests.

## Authors' contributions

Obembe and Olaogun jointly conceived and designed this study, Obembe analysed the data and interpreted same; all the authors jointly took part in data collection, drafting the article, and finally approved this version for submission.

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## Research

# Adverse neonatal outcomes in women with pre-eclampsia in Mulago Hospital, Kampala, Uganda: a cross-sectional study

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**Introduction:** Pre-eclampsia, which is more prevalent in resource-limited settings, contributes significantly to maternal, fetal and neonatal morbidity and mortality. However, the factors associated with these adverse outcomes are poorly understood in low resource settings. In this paper we examine the risk factors for adverse neonatal outcomes among women with pre-eclampsia at Mulago Hospital in Kampala, Uganda.

**Methods:** Pre-eclampsia, which is more prevalent in resource-limited settings, contributes significantly to maternal, fetal and neonatal morbidity and mortality. However, the factors associated with these adverse outcomes are poorly understood in low resource settings. In this paper we examine the risk factors for adverse neonatal outcomes among women with pre-eclampsia at Mulago Hospital in Kampala, Uganda.

**Results:** Predictors of adverse neonatal outcomes were: preterm delivery (OR 5.97, 95% CI: 2.97-12.7) and severe pre-eclampsia (OR 5.17, 95% CI: 2.36-11.3).

**Conclusion:** Predictors of adverse neonatal outcomes among women with pre-eclampsia were preterm delivery and severe pre-eclampsia. Health workers need to identify women at risk, offer them counseling and, refer them if necessary to a hospital where they can be managed successfully. This may in turn reduce the neonatal morbidity and mortality associated with pre-eclampsia.

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**Key words:** Risk factors, pre-eclampsia, adverse neonatal outcomes, Mulago hospital, Uganda

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## Introduction

Pre-eclampsia is a multisystem disorder of pregnancy characterized by hypertension and proteinuria in the second half of pregnancy [1]. It complicates 5-10% of all pregnancies [2, 3], but may be higher in resource-limited settings [4, 5]. Together with other hypertensive diseases of pregnancy, it is one of the leading cause of maternal, fetal and neonatal mortality and morbidity especially in resource limited-settings [4, 6, 7] where diagnosis and obstetric management are deficient [8, 9]. In a study conducted in three hospitals in Uganda, severe pre-eclampsia/eclampsia comprised 8% of cases of severe maternal morbidity [10] and in another study in Mulago Hospital, Uganda, severe pre-eclampsia/eclampsia accounted for 12% of maternal deaths among women with severe maternal morbidity [11].

The perinatal outcomes in women with pre-eclampsia are poor, especially if pre-eclampsia is of early onset and is severe. Haddad and colleagues [12], for example, studied maternal and perinatal outcomes among

239 severe pre-eclamptic women at 24 and 34 weeks of gestation and observed a perinatal mortality of 5.4% although the neonatal morbidities were high especially in early gestation. Similarly, Jantasing and Tanawattnacharoen [7] reported perinatal outcomes in 99 severe pre-eclamptic women between 24 and 34 weeks gestation. The perinatal mortality was 11% and the perinatal morbidity was high especially in lower gestational age mothers.

The etiology of pre-eclampsia is elusive [13] and management depends on early detection, antihypertensive treatment, seizure prophylaxis and rapid delivery in severe cases [1]. Pre-eclampsia is a leading cause of iatrogenic premature delivery [14-15]. Because pre-eclampsia is a progressive disorder, delivery minimizes severe maternal morbidity although it increases neonatal morbidity and mortality because of prematurity [16]. Neonatal survival depends on gestational age at delivery and is low in small-for-gestational age babies [17].

It is difficult to identify mothers with pre-eclampsia whose neonates will develop adverse outcomes [18]. However, previous studies in high-

resource settings have highlighted possible factors that may lead to adverse neonatal outcomes. These include recurrent pre-eclampsia [19-20], preexisting hypertension [21-22] and severe hypertension [21-23].

Women with recurrent pre-eclampsia have increased adverse neonatal outcomes because recurrent pre-eclampsia develops early and is severe [19, 20]. Therefore, they are more likely to deliver preterm and small-for-gestation age babies. These infants are prone to have respiratory distress syndrome, have low 5 minute apgar score, and need surfactant, ventilators and admission to the neonatal intensive care unit [21]. Severe hypertension, a feature of severe pre-eclampsia and preexisting hypertension [19-20], and advanced maternal age [24] are associated with adverse neonatal outcomes because these mothers are prone to abruptio placenta, preterm delivery and neonatal deaths.

Previous studies [21, 25], have examined maternal and neonatal outcomes mainly in high-resource countries where the prevalence of pre-eclampsia is low. The purpose of this study was to assess the maternal characteristics that are associated with adverse neonatal outcomes among women with pre-eclampsia in a resource-limited-setting with a high prevalence of pre-eclampsia.

## Methods

**Design:** A cross-sectional study of pregnant women with pre-eclampsia was carried out from May 2008 to May 2009.

### Setting

The study was conducted in Mulago Hospital's labor wards. Mulago Hospital is Uganda's National Referral Hospital and serves as the teaching hospital for Makerere University College of Health Sciences. Many women with complications of pregnancy, including pre-eclampsia, are referred to Mulago Hospital for management. The hospital carries out approximately 70 deliveries per day and on average six women with pre-eclampsia present to the hospital each day.

### Study population

The study population consisted of 171 women aged 15-39 years who had been diagnosed with pre-eclampsia in Mulago Hospital, Department of Obstetrics and Gynaecology between May 2008 and May 2009. Among women who were enrolled, we identified women who developed adverse neonatal outcomes and compared their socio-demographic characteristics, past medical and obstetric history with those of women who had good outcomes.

Pre-eclampsia was defined according the criteria of the International Society for the Study of Hypertension in Pregnancy [26]. Under this classification, hypertension was defined as a blood pressure of  $\geq 140/90$ mmHg. The blood pressure was taken with a woman in sitting position using a mercury sphygmomanometer (DT-S101) after 10 minutes of rest. The blood pressure measurement was repeated after four hours. Significant proteinuria was defined as  $\geq 2+$  protein by dipstick on two urine samples taken 4 hours or more apart. This was confirmed by a 24hr urine collection of  $>300$ mg of protein. Pre-eclampsia was defined as hypertension and significant proteinuria developing after 20 weeks of pregnancy.

Pre-eclampsia was defined as severe if a woman had one or more of the following symptoms: a blood pressure of  $\geq 160$ mmHg systolic or  $\geq 110$ mmHg diastolic,  $\geq 3+$  protein by dipstick on two urine samples taken four hours or more apart or 5g of protein in a 24hr urine sample, epigastric or right upper-quadrant pain, blurring of vision, cerebral disturbances, abnormal liver function, pulmonary edema or cyanosis, fetal growth restriction, low platelets and oliguria of less than 500 ml in 24 hours [1].

### Selection of participants

Pregnant women were eligible for inclusion if they were diagnosed with pre-eclampsia and were at least 20 weeks pregnant. Women were excluded if they had serious medical conditions like pre-existing renal diseases, hypertension, diabetes mellitus, and eclampsia or if they were carrying multiple pregnancies. Women carrying multiple pregnancies were excluded because multiple pregnancies are typically associated with

low birth weight (one measure of adverse neonatal outcomes).

Women with pre-eclampsia were selected daily using systematic sampling in which every third mother with pre-eclampsia was selected if she satisfied the inclusion criteria. A sample of 171 women was selected by research assistants who were trained midwives. Sample size was calculated using a formula for cross-sectional studies [27]. We assumed the expected proportion of still births to be 23% as was found in a study by Kharb [28] among Indian women, with 95% confidence interval, power of 80%, with an odds ratio of at least two.

### Explanatory variables

At recruitment, women's socio-demographic characteristics, past medical and obstetric histories were collected through an interviewer administered questionnaire. Blood was drawn at the time of recruitment for complete blood counts, renal and liver function tests. Mid - stream urine samples were taken from the women for random urine protein estimation by dipstick and urine was collected for a 24hr urine protein measurement. All women in this hospital undergo routine counseling and testing for HIV and information about the women's HIV status was collected.

The socio-demographic characteristics included women's age, marital status, education level and socio-economic status. Socioeconomic status was assessed using a household asset index derived using principal components analysis [29]. Measures assessed in the household asset index included type of house (e.g., wall material, floor material and the roofing material), household ownership of assets (e.g., fridge, radio, bicycle, car, motorcycle, and vehicle) and amenities (e.g., water source, electricity and the toilet facility). We also collected data on the women's medical history including previous diagnosis of diabetes mellitus and hypertension, as well as family history of hypertension and renal disease. Obstetric history included information on previous pregnancies and their outcomes and the first day of the last normal menstrual period.

### Outcome measures

Adverse neonatal outcomes were recorded during the women's stay at the hospital. An adverse neonatal outcome included one or more of the following: delivery of a stillborn baby, an early neonatal death, a need to admit the baby to the special care unit, a baby who needed oxygen resuscitation and, a baby weighing less than 2500gm. A still birth was defined as delivery of a baby that died in the uterus after 24 weeks of gestation. An early neonatal death was defined as death of a baby in the first seven days after delivery. Oxygen resuscitation was defined as infants whose partial oxygen pressures were low and who needed oxygen resuscitation. In Mulago Hospital, the period of viability is at least 24 weeks of gestation. Therefore, in this study, delivery of a dead fetus aged less than 24 weeks was not classified as an adverse outcome.

### Statistical analysis

The data collected were coded and entered in Epi Data 3.1 software package. It was transferred to Stata version 10 for analysis. The frequency distributions of the maternal socio-demographic, medical and obstetric characteristics were examined and presented. Bivariate analyses were conducted to assess the association between adverse neonatal outcomes and the maternal socio-demographic, medical and obstetric factors. A p-value less than 0.05 was considered statistically significant.

To control for confounding, we employed multivariable logistic regression analysis. We included all the socio-demographic factors, medical factors and obstetric factors with a p-value of 0.1 or less in the bivariate analysis (e.g, maternal age, parity, systolic blood pressure and diastolic blood pressure) and factors which we thought a priori might be associated with adverse neonatal outcomes (e.g., marital status, educational level, socio economic status, HIV status, and family history of hypertension and plasma vitamin C). Factors with large p-values were eliminated until a stable model was obtained. The results are reported as adjusted odds ratios with their corresponding 95% confidence intervals.

### Ethical consideration

This study was approved by the Makerere University College of Health Sciences Ethics Committee, the Mulago Hospital Ethics Committee and the Uganda National Council for Science and Technology. Written informed consent was obtained from the participants.

# Results

There were 171 women with pre-eclampsia who delivered singleton babies. Most women were married (79.5%), 59.5% had secondary level of education or higher, 50.8% stayed 5km or more from hospital, 1.6% were smokers, 16.3% consumed alcohol and 8.0% were HIV positive.

The neonatal outcomes are shown in Table 1.

Characteristic	n (%)
<b>Birth weight</b>	
<1500	18(10.6)
1500-2400	59(34.9)
≥2500	92(54.4)
<b>Mode of delivery</b>	
Normal	74(43.8)
Emergency Caesarean Section	95(56.2)
<b>Birth Outcome</b>	
Still births	22(13.1)
Early neonatal deaths	15(8.9)
Live births	1316(77.9)
<b>Admission to neonatal intensive unit</b>	
Yes	54(32.1)
No	114(66.9)
<b>Apgar score</b>	
0	22(12.9)
1-6	15(8.8)
7-10	133(78.2)

Characteristic	Adverse neonatal outcomes		Crude Odds Ratio	P Value
	No n (%)	Yes n (%)		
<b>Age in years</b>				
≤24	52(27.2)	56(56.6)	-	-
≥25	20(27.8)	43(43.4)	1.99(1.04-3.82)	0.037
<b>Marital Status</b>				
Married	55(76.4)	80(80.8)	-	-
Single	17(23.6)	19(19.2)	0.76(0.36-1.61)	0.48
<b>Educational level</b>				
Primary or less	34(47.2)	38(38.4)	-	-
Secondary or more	38(52.7)	61(61.6)	1.43(0.77-2.65)	0.24
<b>Socio economic</b>				
Low	21(29.2)	36(36.7)	-	-
Middle income	26(36.1)	29(29.5)	0.65(0.30-1.38)	0.26
High	25(34.7)	33(33.7)	0.77(0.36-1.62)	0.49
<b>HIV</b>				
Positive	04(5.6)	08(6.3)	0.65(0.18-2.26)	0.5
Negative	68(94.4)	89(91.8)	-	-
<b>Hypertension in family</b>				
Yes	30(41.7)	45(58.3)	-	-
No	42(58.3)	54(54.6)	0.85(0.46-1.58)	0.62
<b>Parity</b>				
1	51(71.8)	47(47.5)	-	-
≥ 2	20(28.2)	52(52.5)	2.82(1.47-5.41)	0.002
<b>Delivery</b>				
Normal	35(48.6)	39(39.4)	-	-
Caesarean	37(51.4)	60(60.6)	1.45(0.78-2.68)	0.23
<b>Pre-eclampsia</b>				
Mild-Moderate	41(56.9)	24(24.2)	-	-
Severe	31(43.1)	75(75.8)	4.13(2.14-7.95)	0.001
<b>Gestational age</b>				
≤36 weeks	19(26.4)	66(66.7)	5.57(2.85-10.9)	0.001
≥37 weeks	53(73.6)	33(33.3)	-	-
<b>Pre-eclampsia history</b>				
Yes	01(1.4)	10(10.1)	0.12(0.15-1.00)	0.05
No	71(98.6)	89(89.9)	-	-
<b>Vitamin C</b>				
<0.11	09(12.5)	12(12.1)	-	-
0.11-0.2	47(65.3)	57(57.6)	0.90(0.35-2.34)	0.84
>0.2	16(22.2)	30(30.3)	1.40(0.48-4.04)	0.52
<b>ANC attendance</b>				
≤2 times	41(56.9)	60(60.6)	-	-
≥3 times	31(43.1)	39(39.4)	0.86(0.46-1.59)	0.6
<b>Smoking</b>				
Yes	01(1.39)	02(2.0)	-	-
No	71(98.6)	97(98.0)	0.68(0.06-7.68)	0.75
<b>Alcohol</b>				
Yes	07(9.7)	22(22.2)	-	-
No	65(90.3)	77(77.8)	0.37(0.15-0.94)	0.03
<b>Total</b>				
(N=171)	72(42.1)	99(57.9)		

Low birth weight (<2500gm) constituted 45.5%, still birth delivery was 13.1% and early neonatal deaths were 8.9% of the deliveries among women with pre-eclampsia.

Ninety nine out of the 171 women with pre-eclampsia with singleton

Characteristic	Crude Odds Ratio	Adjusted Odds ratio
<b>Age in years</b>		
≤24	1.99(1.04-3.82)	Ref
≥25	-	1.69(0.69-4.1)
<b>Educational level</b>		
Primary or less	-	Ref
Secondary or more	1.43(0.77-2.65)	1.5(0.72-3.41)
<b>Parity</b>		
1	-	Ref
≥2	2.82(1.47-5.41)	1.71(0.69-4.22)
<b>Pre-eclampsia</b>		
Severe	4.13(2.14-7.95)	5.17(2.36-11.3)
Mild-Moderate	-	Ref
<b>Gestational age</b>		
≤36 weeks	5.57(2.85-10.9)	5.97(2.79-12.7)
≥37 weeks	-	Ref
<b>Pre-eclampsia history</b>		
Yes	0.12(0.15-1.00)	0.12(0.01-1.28)
No	-	Ref

babies (57.9%) had adverse neonatal outcomes. At the bivariate level, women who were multiparous (p=0.002), women who had severe pre-eclampsia (p=0.001), and women who delivered preterm (p=0.001) were more likely to experience adverse neonatal outcomes (Table 2). After adjusting for other variables, women who had severe pre-eclampsia had 5.2 higher odds of developing adverse neonatal outcomes than women who had mild or moderate pre-eclampsia. Similarly, women who delivered preterm had 5.9 higher odds of developing adverse neonatal outcomes than women who delivered at term (Table 3).

## Discussion

Pre-eclampsia is one of the leading causes of adverse maternal and child outcomes. The risk factors associated with adverse neonatal outcomes in women with pre-eclampsia in resource-limited settings are poorly understood. In this paper we examined the risk factors associated with adverse neonatal outcomes in women with pre-eclampsia.

The risk factors for adverse neonatal outcomes were severe pre-eclampsia and preterm delivery. In this study women with severe pre-eclampsia were at an increased risk of delivering an infant which developed an adverse outcome. This is similar to what was found by other researchers [12,30, 31]. Buchibinder and colleagues [30], in Ohio in the United States reported that the perinatal mortality in women with severe pre-eclampsia was 8.9% and there was a high perinatal morbidity. Jenkins and colleagues [31] studied maternal and neonatal outcomes in women with severe pre-eclampsia before 25 weeks gestation and observed that only 10% of the neonates survived with major morbidities. Haddad and colleagues [12] studied the maternal and perinatal outcomes during expectant management of women with severe pre-eclampsia between 24 and 33 weeks gestation. The still birth rate was 2.5% and neonatal rate was 3% but with high neonatal morbidity. Perinatal mortality and morbidity were highest in women who developed severe pre-eclampsia at an earlier gestational age and improved with increasing gestational age and where mothers were managed conservatively with prolongation of the pregnancy. Women with severe pre-eclampsia have decreased uteroplacental blood flow and ischemia which compromises blood flow to the fetus [32]. These increases the chances that a mother with severe pre-eclampsia will deliver a baby that will develop an adverse outcome.

In our study, women who delivered preterm were at an increased risk of adverse neonatal outcomes. This is similar to what has been found by other researchers. Khashu and colleagues [33] studied perinatal outcomes associated with preterm birth at 33 to 36 weeks? gestation and found perinatal mortality rate to be 8 times higher, neonatal mortality rate to be 5.5 times higher and, respiratory morbidity to be 4.4 times higher in the pre-term babies than in term babies. Similarly, Young and colleagues [34] studied mortality in late preterm new born babies and found the neonatal mortality rate to be higher in preterm babies than babies born at term.

Pre-eclampsia is a progressive disorder and the only definitive management is the delivery of the fetus [1] to minimize the maternal morbidity and mortality. However, this increases the chance of premature delivery with low odds of child survival [35]. As noted, preterm babies are more likely to be admitted to the neonatal intensive care unit, have assisted ventilation, to be of low birth weight and small for gestational age, and to develop respiratory distress syndrome than term infants

[36,37]. This undoubtedly increases the cost of hospital stay. Given the resource-constraints within the health system, early detection of pre-eclampsia is critical. This can be achieved by ensuring that all maternity facilities are able to provide basic emergency obstetric care. At minimum, maternity facilities should have a functioning blood pressure machine and urine sticks for measuring proteinuria.

Study findings should be interpreted in light of several limitations. In particular, the study sample was relatively small and some predictors had small numbers, therefore the results interpreted with caution as they may not be representative of the general population. In addition, the study was conducted in the national referral hospital and findings may not be generalizable to all women presenting with pre-eclampsia in Uganda. However, this study has enabled us to identify predictors for adverse neonatal outcomes in our setting which can be used to predict and prevent them in resource limited settings

## Conclusion

In this study, the predictors of adverse neonatal outcomes in pre-eclamptic women were severe pre-eclampsia and preterm delivery. Health workers need to identify mothers at risk, offer them counseling and refer them to a hospital where pre-eclampsia can be managed. This is expected to reduce the perinatal morbidity and mortality associated with pre-eclampsia in resource-limited settings.

## Competing interests

The authors declare no competing interests.

## Authors' contributions

PK conceived, designed the study, participated in the data collection and analysis, and drafted the manuscript. NMT participated in the study design, analysis and reviewed the manuscript. GW, PO and GSB participated in the study conception and design and critically reviewed the manuscript. JW participated in the study design, data management and critically reviewed the manuscript. All the authors read and approved the final version of the manuscript.

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## Research

# The association between psychopathology and substance use: adolescent and young adult substance users in inpatient treatment in Cape Town, South Africa

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**Introduction:** Evidence suggests that comorbid psychopathology can negatively affect treatment outcomes in substance users. In South Africa, limited information exists regarding the prevalence, nature and role of psychiatric comorbidity in substance users. This study examined psychiatric comorbidity and its association with specific substance use, and young adult substance users in treatment for substance use.

**Methods:** Male and female inpatient substance users (n=95; ages 17-30 years) were sampled consecutively in order of admission from three clinics in Cape Town. An interview schedule was administered to elicit patients' sociodemographic and substance use history details. The computer-assisted Diagnostic Interview Schedule DSM IV (C-DIS IV) was administered to screen patients for current psychiatric disorders.

**Results:** The sample was largely male, Coloured, Muslim and single. Cannabis (51.6%) and crystal methamphetamine (17.9%) were the most common first substances of use. Heroin (53.7%) and crystal methamphetamine (33.7%) were the most common substances for which treatment was sought (primary substances). The most common comorbid psychopathologies were anti-social personality disorder (ASPD 87.4%) and conduct disorder (CD 67.4%). Regression analyses showed a marginally significant association between specific phobia and first use of cannabis, but indicated no statistically significant associations between psychopathology and substance use.

**Conclusion:** The results demonstrated a high proportion of previously unidentified comorbid psychopathology in inpatient substance users. Further research is needed to investigate psychiatric comorbidity in inpatient substance users.

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**Key words:** Comorbidity, psychopathology, substance use treatment

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## Introduction

In psychiatry, non-substance use psychopathology and problematic substance use are a common form of comorbidity [1]. The comorbid conditions may co-exist simultaneously (concurrent), in tandem (sequential) or separately at any time in the patient's life (lifetime) [2]. Comorbidity is sometimes referred to as 'dual diagnosis' or 'co-occurring disorders', and can involve the co-occurrence of two or more disorders. [3,4]. The comorbidity might involve pathology that meets the criteria for diagnosis of a disorder, or might refer to the presence of symptoms of a disorder [5]

Various suggestions have been proposed to explain relationships between comorbid psychopathology and substance. These include i) that people with psychiatric illness attempt to alleviate their discomfort by self-medicating with substances, leading to problematic use of the substances or to substance use-related disorders [2], ii) that the substance use could lead to mental illness [2], iii) that certain individuals might be genetically

predisposed to either psychiatric illness and/or substance use resulting in comorbid conditions [2], iv) that either condition could influence, or effect a change in, the course of the other [2], and v) that the substance use and psychopathology share a common neural substrate [4].

Community and hospital-based studies have provided evidence for an increased likelihood of comorbid psychiatric disorder in substance users [5], with a greater likelihood of such comorbidity as the severity of the substance use increases [6]. Psychological and psychiatric problems associated with substance use include cognitive impairment, poor scholastic performance, personal and relationship problems [7], depression, anxiety [8] and PTSD [9]. Disruptive behaviour disorders like antisocial personality disorder [10] and conduct disorder [11] have been found to be very common in patients who receive treatment for substance use [12].

However, the evidence for associations between specific forms of psychopathology and the use of specific substances has not been clear or consistent. For example, the review of community studies by Armstrong

and Costello [6] indicated that, except for cannabis, associations between psychiatric disorders and the use of specific substances was not specific to either the psychiatric disorders or the substances of use. In the National Comorbidity Survey (NCS), anxiety disorders and conduct disorder/adult anti-social behaviour disorder were found to precede and predict later alcohol dependence, but such consistency in chronicity was not duplicated with the same certainty with regards to other mental disorders or substances of use [13].

In treatment populations, co-morbidity is known to be characterised by heterogeneity [14]. For example, co-occurring substance use and psychopathology differ with respect to the types of substances and psychiatric problems, the temporality of the comorbid conditions [14], and the possible influence of socio-demographic factors such as age [15], gender or race/ethnicity in the associations [6].

Comorbid substance use and psychiatric disorder has also been associated with poor treatment outcomes for either or both conditions, including increase in substance use and psychosocial impairment, compared with outcomes of treatment when either substance use or psychiatric disorder occur individually [5,16]. The diagnosis of psychiatric comorbidity in substance users, and of substance use disorders in psychiatric patients, is thus an important component in the development of strategies for treatment [17].

More information is available on comorbid psychiatric disorders and substance use in adults than in children, adolescents and young adults [6,18]. In South Africa, the prevalence of substance use is a cause for concern, with an increase in the use of substances such as crystal methamphetamine (locally known as 'tik') and diacetyl morphine (heroin) [19], and evidence for increased use of substances in general, and cannabis in particular, in adolescents and young adults [20]. Globally, substance use and psychiatric disorders are managed largely independently. Reasons for this include treatment facilities being historically specialised as either substance use treatment centres, or centres for the treatment of psychiatric disorders, with limited numbers of suitably-trained professionals to treat comorbidity [21]. The trend is similar in South Africa. Consequently, patients with comorbid psychopathology and problematic substance use usually attend either a psychiatric or a substance use treatment facility depending on the problem deemed by the patient or his/her family as the one most urgently in need of attention.

In many substance use treatment centres comorbid psychopathology might be suspected in patients, but not assessed or addressed because of a lack of expertise, capacity, time or opportunity at the treatment centres [21]. Consequently, if the substance use treatment results in the patient behaving more socially-appropriately, concurrent psychopathology will receive little attention unless the patient's behaviour becomes disruptive or dysfunctional. Since these behavioural problems are often accompanied by substance use [22], the cycle can be repeated endlessly. Individuals with comorbid psychopathology and substance use can thus repeatedly enter and exit either psychopathology and/or substance use treatment depending on which problem is regarded as the "most problematic" at any one time.

The examination of comorbid psychopathology and substance use in both clinical and community populations of substance users is important particularly because these groups may differ with respect to the nature of the comorbidity [6]. For example, morbidity might be more severe, and comorbidity rates might be higher, in clinical samples compared with community samples. Patients might be more likely to seek treatment for certain disorders (for example, disruptive behaviour disorders) than for others (for example, depression), resulting in clinical samples having a predominance of disorders that are more likely to precipitate admission to treatment [6]. Results from clinical samples might thus not be generalisable to community samples and, conversely, the information obtained from community samples might not apply to clinical populations. Examination of both community and clinical samples is, therefore, needed to ascertain the prevalence of comorbidity in general, and to determine the likelihood of associations between co-morbid conditions.

Information from the South African Stress and Health (SASH) study provides evidence for high prevalence rates of mental disorders in particularly the urban areas of South Africa [22]. However, there has been only limited investigation of the occurrence and nature of comorbid

psychiatric diagnoses in substance users in South Africa, and the factors that impact on this comorbidity, for both community [20] and treatment samples [23] of substance users.

This study aimed to assess the frequency and nature of non-substance psychopathology in adolescent and young adult substance users who were receiving inpatient treatment for their substance use, and to examine the association between psychopathology and substance use in these patients, adjusting for social and demographic factors.

## Methods

**Sample:** Ninety-five inpatient substance users were sampled from three privately-funded inpatient substance use treatment centres in Cape Town, South Africa. The treatment centres were selected from the list of Cape Town substance use inpatient treatment centres affiliated to the South African Community Epidemiology Network on Drug Use (SACENDU) [23]. The inpatient treatment centres that had the largest number of admissions over the previous six months were shortlisted as potential study sites. Since the Cape Town area is geographically still largely divided in terms of racially classified social groups (RCSGs, as defined by the Population Registration Act of 1950, and consisting of the categories White, Coloured, Black and Indian/Asian) and economic class, three clinic study sites were selected (from the shortlist of treatment centres) from three different suburbs of Cape Town, in an attempt to gain information from as broad a racial and economic spectrum of inpatients within the research period. These were i) a predominantly White upmarket residential-cum-commercial area, and followed a medical model of treatment ii) a middle-class residential area of largely White, Coloured and Indian communities, and followed a treatment modality that included homeopathy, spirituality and Ayurvedic medicine, and iii) an area which included largely Coloured and Black communities, brick homes, informal dwellings, smallholdings and farmland, and provided custodial care, and encouraged spirituality, accompanied by administration of vitamins, massage, periods in a sauna, motivational talks and group therapy.

Sampling of patients was completed over the period December 2008 to December 2009. A minimum sample size of 46 would be required for logistic regression analyses with 6 predictor variables (excluding the constant), a precision of 0.05, 80% power, and a large effect ( $f^2=0.35$  or model  $r^2=0.26$ ), while a minimal sample size of 97 would be required for a medium anticipated effect ( $f^2=0.15$ , or model  $r^2=0.13$ ). We assumed the latter effect being most likely in this study, given previous findings in the literature. A total of 95 young people, constituting all admissions aged 30 years and younger, and admitted for inpatient treatment of problematic substance use.

**Instruments:** An Interview Schedule was used to elicit demographic, social, substance use history and recent substance use information. Demographic and social information included age, gender, racially classified social group (RCSG), religious denomination, highest educational level, referral source, marital status, living arrangements and employment status. Substance use information included age of onset, the first substance of use (other than tobacco), the most frequently used substance, the substance for which treatment was sought, the frequency and quantity of substance use, and previous treatment for substance use. The most frequently used substance (the primary substance of use) was invariably the substance for which treatment was sought.

The computer-assisted Diagnostic Interview Schedule (DIS) for Diagnostic and Statistical Manual (DSM) IV (C-DIS IV) [24] was administered to screen for any current (12-month) psychiatric disorders. Although the C-DIS had not been standardized for a South African population because of the absence of suitable benchmarks against which to measure the instrument, it is one of few available recognized diagnostic instruments that are regarded as sufficiently reliable for use by lay interviewers [25], that shows high concordance with clinically-derived diagnoses [25], and provides the opportunity to screen for current diagnoses when the interviewing time is limited [24]. The C-DIS can be administered by trained, non-clinically experienced examiners, and does not need corroborating details from alternative sources, such as hospital records, to make diagnoses. The C-DIS is considered to be more accurate than the pencil-and-paper version because it automatically counts symptoms for diagnostic criteria, checks dates to ensure accuracy of onset and

remission of symptoms. The C-DIS can be used in both treatment and community settings, has the option of being used in either a limited screening version or full version, with the screen version providing information about the presence or absence of a disorder without details regarding the symptoms, course or severity of the disorder.

The full versions of the instrument are recommended to assess disorders with early onset (such as attention deficit hyperactivity disorder, separation anxiety, oppositional disorder and conduct disorder) since these disorders might be risk factors for disorders of later onset. However, the study team felt that the study would not be compromised by use of the screening version with respect to early onset diagnoses because the study sample consisted largely of young adults. To ensure parity in the mode of administration throughout the study, the screened version of the instrument was used for all interviews. All the interviews were conducted by a trained DIS interviewer (primary author).

**Procedure:** Potential study participants were approached after completing a detoxification programme (a period ranging from one to two weeks) offered at each clinic. This was done to ensure that patients had largely overcome the discomfort and agitation associated with withdrawal from substance use, and were more amenable to interviewing. This delay also allowed for the symptoms of substance-induced psychiatric symptoms to be minimized, where present. Each potential study participant was approached to obtain written informed consent. One patient under the age of 18 completed assent forms, and written parental consent was obtained before interviewing this patient. All interviews were conducted by the primary author, at the clinics, and in private. Each interview was completed in one session, with the duration of each session approximating 90 to 120 minutes. The study was approved by the Research Ethics Committee of the University of Cape Town.

## Data analyses

The data were analysed using STATA Version 10 [26]. Percentages were estimated for demographic factors, substance use, and psychiatric diagnoses.

Bivariate associations were assessed using Fisher's Exact tests or chi-squared tests to compare the distribution of patients across the clinics socio-demographically by substance use and by current psychopathology. The percentage of psychopathology and first and primary substances of use and the percentage of first and primary substance use with respect to the most commonly-occurring forms of psychopathology were calculated. Bivariate associations between psychopathology and substance use were calculated using Fisher's Exact and chi-squared analyses. Multiple logistic regression analyses were conducted to determine associations between type of psychiatric disorder (selected from the most commonly-occurring psychiatric diagnoses) and a) the first substances of use, and b) the most frequently used (primary) substances. First substance of use was coded as either cannabis, crystal methamphetamine, or other, based on the most common substances first used; most common primary substance of use was coded as crystal methamphetamine, heroin or other, based on the most common substances for which patients were admitted for treatment. For these, odds ratios and 95% confidence intervals were calculated, unadjusted and adjusted for the treatment centres, and socio-demographic factors including age, gender, religious denomination, racially classified social group and treatment centre. In all the relevant analyses, substance use (in the form of first and primary substances of use) was the dependent variable, and the socio-demographic characteristics and psychopathology diagnoses were the independent variables. Forced statistical modelling was used for the logistic regression.

## Results

Table 1 summarises the characteristics of the sample at the three treatment centres. The total sample consisted of 95 inpatients (ages 17-30 years, with a mean age of 23 years (SD = 2.9)). The sample was predominantly male (89.5%), Coloured (88.4%), and Muslim (68.4%). Eighty-six percent of the patients had some secondary school education, 77.9% had never been married, 91.6% lived with immediate family, and 61.1% had entered treatment on their own volition. More than half the sample (54.7%) was unemployed, while nearly a third had fulltime employment, at the time of entering treatment. The proportions of patients at the three clinics differed with respect to two demographic

**Table 1:** Demographic, behavioural and psychopathological characteristics of study participant in the three treatment centres (n; %)

	Clinic 1 n = 17	Clinic 2 n = 30	Clinic 3 n = 48	Total n = 95	p-value
Mean Age (SD)	21.7 (3.5)	23.2 (3.0)	23.4 (3.6)	23.0 (2.9)	0.111 <sup>†</sup>
Gender Male	16 (94.1)	24 (80.0)	45 (93.8)	85 (89.5)	0.151 <sup>††</sup>
Racially Classified Social Group					0.066 <sup>††</sup>
White	3 (17.7)	1 (3.3)	0	4 (4.2)	
Coloured	13 (76.5)	27 (90.0)	44 (91.7)	84 (88.4)	
Indian	1 (5.9)	2 (6.7)	4 (8.3)	7 (7.4)	
Religion					<0.001 <sup>††</sup>
Muslim	2 (11.8)	27 (90.0)	36 (75.0)	65 (68.4)	
Christian	15 (88.2)	3 (10.0)	11 (22.9)	29 (30.5)	
None	0	0	1 (2.1)	1 (1.1)	
Highest educational level					0.176 <sup>††</sup>
Primary school	1 (5.9)	0	2 (4.2)	3 (3.2)	
Secondary school	16 (94.1)	24 (80.0)	42 (87.5)	82 (86.3)	
Tertiary	0	6 (20.0)	4 (8.3)	10 (10.5)	
Referral source					0.250 <sup>††</sup>
Self	10 (58.8)	18 (60.0)	30 (62.5)	58 (61.1)	
Family	3 (17.6)	11 (36.7)	13 (27.1)	27 (28.4)	
Other	4 (23.5)	1 (3.3)	5 (10.4)	10 (10.5)	
Marital status					0.488 <sup>††</sup>
Never married	15 (88.2)	22 (73.3)	37 (77.1)	74 (77.9)	
Other	2 (11.8)	8 (26.7)	11 (22.9)	21 (22.1)	
Living arrangements					0.819 <sup>††</sup>
Live alone	0	0	2 (4.2)	2 (2.1)	
Live with immediate family	16 (94.1)	29 (96.7)	42 (87.5)	87 (91.6)	
Other	1 (5.9)	1 (3.3)	4 (8.3)	6 (6.3)	
Employment status					0.186 <sup>††</sup>
Unemployed	7 (41.2)	18 (60.0)	27 (56.3)	52 (54.7)	
Casually employed	1 (5.9)	2 (6.7)	4 (8.3)	7 (7.4)	
Permanently employed	7 (41.2)	7 (23.3)	17 (35.4)	31 (32.6)	
Other	2 (11.8)	3 (10.0)	0	5 (5.3)	
Usual employment					0.635 <sup>††</sup>
Professional	0	0	1 (2.1)	1 (1.1)	
Skilled	6 (35.3)	10 (33.3)	18 (37.5)	34 (35.8)	
Unskilled	4 (23.5)	10 (33.3)	16 (33.3)	30 (31.6)	
None/student/scholar	7 (41.2)	8 (26.7)	9 (18.7)	23 (24.2)	
Other	0	2 (6.7)	5 (10.4)	7 (7.4)	
Age of first substance use (years)					0.127 <sup>††</sup>
10 - 14	13 (76.5)	13 (43.3)	23 (47.9)	49 (51.6)	
15 - 17	3 (17.6)	11 (36.7)	18 (37.5)	32 (33.7)	
18 - 20	0	5 (16.7)	7 (14.6)	12 (12.6)	
21 - 24	1 (5.9)	1 (3.3)	0	2 (2.1)	
Mean (SD)	13.6 (2.4)	15.1 (2.6)	14.8 (2.3)	14.7 (2.4)	
First substance of use					0.163 <sup>††</sup>
Alcohol	4 (23.5)	0	3 (6.3)	7 (7.4)	
Cannabis	8 (47.1)	16 (53.3)	25 (52.1)	49 (51.6)	
Ecstasy	0	5 (16.7)	4 (8.3)	9 (9.5)	
Heroin	1 (5.9)	2 (6.7)	3 (6.3)	6 (6.3)	
Methqualone (mandrax)	0	2 (6.7)	0	2 (2.1)	
Crystal methamphetamine (tik)	4 (23.5)	3 (10.0)	10 (20.8)	17 (17.9)	
Multiple	0	2 (6.7)	3 (6.3)	5 (5.3)	
Primary substance of use					<0.001 <sup>††</sup>
Alcohol	3 (17.6)	0	0	3 (3.2)	
Cannabis	4 (23.5)	0	1 (2.1)	5 (5.3)	
Heroin	2 (11.8)	20 (66.7)	29 (60.4)	51 (53.7)	
Crystal methamphetamine (tik)	7 (41.2)	8 (26.7)	17 (35.4)	32 (33.7)	
Methqualone (mandrax)	1 (5.9)	1 (3.3)	0	2 (2.1)	
Multiple	1 (5.9)	0	1 (2.1)	2 (2.1)	
Frequency of use of primary substance					0.844 <sup>††</sup>
Daily	15 (88.2)	28 (93.3)	43 (89.6)	86 (90.5)	
Few times a week	1 (5.9)	2 (6.7)	3 (6.3)	6 (6.3)	
Sometimes	1 (5.9)	0	2 (4.2)	3 (3.2)	
Intensity/Volume of primary substance use					0.509 <sup>††</sup>
As much as I can obtain	11 (64.7)	14 (46.7)	31 (64.6)	56 (58.9)	
As much as I can afford to buy	6 (35.3)	15 (50.0)	16 (33.3)	37 (38.9)	
Other	0	1 (3.3)	1 (2.1)	2 (2.1)	
Previous treatment for substance use					0.081 <sup>††</sup>
None	11 (64.7)	12 (40.0)	19 (39.6)	42 (44.2)	
Once in past year	3 (17.6)	2 (6.7)	8 (16.7)	13 (13.7)	
More than once in past year	0	5 (16.7)	12 (25.0)	17 (17.9)	
More than a year ago	3 (17.6)	11 (36.7)	9 (18.8)	23 (24.2)	
Age of first treatment for substance use (years)					0.139 <sup>††</sup>
10 - 14	1 (16.7)	2 (11.1)	0	3 (5.7)	
15 - 17	0	4 (22.2)	7 (14.6)	11 (20.9)	
18 - 20	5 (83.3)	7 (38.9)	13 (46.8)	25 (47.2)	
21 - 24	0	3 (16.7)	9 (31.0)	12 (22.6)	
>24	0	2 (11.1)	0	2 (3.8)	
Mean age of first treatment for substance use (SD)	17.5 (3.3)	18.9 (3.9)	19.3 (2.6)	19 (3.1)	0.454 <sup>†</sup>
Psychopathology					
No previous diagnosis of psychopathology	15 (88.2)	29 (96.7)	47 (97.9)	91 (95.8)	0.298
Generalised anxiety disorder	3 (17.6)	1 (3.3)	1 (2.1)	5 (5.3)	0.059
Post-traumatic stress disorder (PTSD)	3 (17.6)	5 (16.7)	6 (12.5)	14 (14.7)	0.065
Depression	6 (35.3)	9 (30.0)	9 (18.8)	24 (25.3)	0.291
Mania	6 (35.3)	1 (3.3)	5 (10.4)	12 (12.6)	0.007
Schizophrenia	0	2 (6.7)	0	2 (2.1)	0.128
Obsessive Compulsive Disorder (OCD)	2 (11.8)	1 (3.3)	1 (2.1)	4 (4.2)	0.298
Eating disorder	0	2 (6.7)	2 (4.2)	4 (4.2)	0.656
Separation anxiety	1 (5.9)	2 (6.7)	2 (4.2)	5 (5.3)	0.848
Oppositional defiant disorder	7 (41.2)	10 (33.3)	15 (31.1)	32 (33.7)	0.771
Conduct disorder	10 (58.8)	18 (60.0)	36 (75.0)	64 (67.4)	0.263
Antisocial personality disorder	14 (82.4)	26 (86.7)	43 (89.6)	83 (87.4)	0.657
Pain disorder	3 (17.6)	4 (13.3)	3 (6.3)	10 (10.5)	0.330
Specific phobia	4 (23.5)	5 (16.7)	6 (12.5)	15 (15.8)	0.565
Substance dependence	12 (70.6)	29 (96.7)	46 (95.8)	87 (91.6)	0.007
Substance abuse	4 (23.5)	5 (16.7)	6 (12.5)	15 (15.8)	0.606

<sup>†</sup> Comparisons between clinics based on Kruskal-Wallis testing for age, and on chi-squared test for other sociodemographic variables

<sup>††</sup> Fisher's Exact testing for expected frequencies <5

**Table 2:** Frequency of most common first and primary substances of use by most common psychopathology diagnoses

Psychopathology	First substance of use			
	Cannabis	p-value <sup>†</sup>	Crystal Methamphetamine	p-value <sup>†</sup>
Conduct disorder	38 (59.3)	0.048	11 (17.2)	0.782
Anti-social personality disorder	46 (55.4)	0.065	14 (16.9)	0.445
Major depression	14 (58.3)	0.486	2 (8.3)	0.223
Oppositional defiant disorder	20 (62.5)	0.192	4 (12.5)	0.405
Most common primary substance of use				
	Heroin	p-value <sup>†</sup>	Crystal Methamphetamine	p-value <sup>†</sup>
Conduct disorder	19 (29.7)	0.170	15 (23.4)	0.592
Anti-social personality disorder	29 (34.9)	1.000	16 (19.3)	0.271
Major depression	8 (33.3)	1.000	3 (12.5)	0.385
Oppositional defiant disorder	9 (28.1)	0.371	10 (31.1)	0.111

<sup>†</sup> Chi-squared testing when expected frequencies ≥5 and Fisher's Exact testing when expected frequencies <5

variables - religious denomination (p <0.001), with Clinics 2 and 3 having 90% and 75% Muslim patients respectively, while Clinic 1 had 88.2% Christian patients, and RCSG (p=0.066), with Clinics 2 and 3 having more

**Table 4:** Association between psychopathology and substance use (OR, 95% CI and p-value)<sup>†</sup>

Psychopathology		First substance of use				Most common primary substance of use			
		Cannabis		Crystal methamphetamine		Heroin		Crystal methamphetamine	
		Unadjusted	Adjusted	Unadjusted	Adjusted	Unadjusted	Adjusted	Unadjusted	Adjusted
<b>Anti-social personality</b>	<b>OR</b>	3.730	3.228	0.609	0.644	1.074	1.496	0.478	0.424
	<b>95% CI</b>	0.942-	0.745-	0.146-	0.136-	0.298-	0.326-	0.128-	0.100-
	<b>p-value</b>	14.773	13.975	2.537	3.047	3.872	6.857	1.785	1.800
		0.061	0.117	0.495	0.579	0.913	0.604	0.272	0.245
<b>Conduct disorder</b>	<b>OR</b>	2.657	2.256	0.865	0.722	0.513	0.413	1.592	1.895
	<b>95% CI</b>	1.092-	0.847-	0.287-	0.213-	0.211-	0.139-	0.520-	0.553-
	<b>p-value</b>	6.464	6.006	2.605	2.443	1.246	1.229	4.870	6.493
		0.031	0.103	0.796	0.600	0.140	0.112	0.415	0.309
<b>Oppositional defiant</b>	<b>OR</b>	1.954	1.920	0.549	0.503	0.636	0.670	2.409	2.192
	<b>95% CI</b>	0.818-	0.749-	0.163-	0.139-	0.253-	0.232-	0.879-	0.752-
	<b>p-value</b>	4.666	4.917	1.847	1.824	1.601	1.939	6.599	6.385
		0.131	0.174	0.333	0.296	0.336	0.460	0.087	0.150
<b>PTSD</b>	<b>OR</b>	0.929	1.571	0.313	0.334	2.115	2.207	0.251	0.245
	<b>95% CI</b>	0.299-	0.388-	0.038-	0.030-	0.672-	0.482-	0.031-	0.025-
	<b>p-value</b>	2.888	6.363	2.568	3.753	6.659	10.116	2.045	2.385
		0.898	0.527	0.279	0.375	0.200	0.308	0.197	0.226
<b>Major depression</b>	<b>OR</b>	1.440	1.669	0.339	0.586	0.920	1.014	0.454	0.569
	<b>95% CI</b>	0.565-	0.537-	0.072-	0.111-	0.346-	0.296-	0.120-	0.131-
	<b>p-value</b>	3.670	5.183	1.608	3.083	2.448	3.467	1.710	2.479
		0.445	0.376	0.173	0.528	0.867	0.983	0.243	0.453
<b>Specific phobia</b>	<b>OR</b>	1.500	4.739	0.286	0.417	1.309	1.665	0.926	1.098
	<b>95% CI</b>	0.488-	0.990-	0.035-	0.045-	0.422-	0.382-	0.235-	0.230-
	<b>p-value</b>	4.607	22.677	2.337	3.857	4.060	7.249	3.660	5.237
		0.479	0.051	0.243	0.441	0.641	0.497	0.913	0.906
<b>Pain disorder</b>	<b>OR</b>	1.144	1.077	1.022	1.609	0.675	0.677	1.478	1.812
	<b>95% CI</b>	0.324-	0.276-	0.200-	0.269-	0.166-	0.124-	0.354-	0.354-
	<b>p-value</b>	4.040	4.199	5.221	9.634	2.737	3.699	6.174	9.263
		0.834	0.915	0.979	0.602	0.582	0.652	0.592	0.475

<sup>†</sup> Adjusted for age, gender, racially classified social group, religion and treatment centre

**Table 3:** Prevalence of most common substance use by most common psychopathology\*

First substance of use n (%)				
Most common psychopathology (n)	Cannabis (Total = 49)	p	Crystal Methamphetamine (Total = 17)	p
<b>Conduct disorder</b>				0.796
Present: 64	38 (59.4)	0.049	11 (17.2)	
Absent: 31	11 (35.5)		6 (19.4)	
<b>Oppositional defiant disorder</b>				0.405
Present: 32	20 (62.5)	0.193	4 (12.5)	
Absent: 63	29 (46.0)		13 (20.6)	
<b>Major depression</b>				0.223
Present: 24	14 (58.3)	0.596	2 (8.3)	
Absent: 71	35 (49.3)		15 (21.1)	
<b>Anti-social personality disorder</b>				0.445
Present: 83	46 (55.4)	0.064	14 (16.9)	
Absent: 12	3 (25.0)		3 (25.0)	
Primary substance of use n (%)				
Most common psychopathology (n)	Heroin (Total = 33)	p	Crystal Methamphetamine (Total = 20)	p
<b>Conduct disorder</b>				0.587
Present: 64	19 (29.7)	0.209	15 (23.4)	
Absent: 31	14 (45.2)		5 (16.1)	
<b>Oppositional defiant disorder</b>				0.141
Present: 32	9 (28.1)	0.461	10 (50.0)	
Absent: 63	24 (38.1)		10 (15.9)	
<b>Major depression</b>				0.385
Present: 24	8 (57.1)	0.867	3 (21.4)	
Absent: 71	25 (35.2)		17 (23.9)	
<b>Anti-social personality disorder</b>				0.271
Present: 83	29 (34.9)	1.000	16 (34.8)	
Absent: 12	4 (33.3)		4 (33.3)	

\*Chi squared tests were used to calculate p-values when cell sizes were >5 and Fisher's Exact was used when cell sizes were <5

Approximately 52% of the sample had commenced substance use between the ages of 10 and 14 years while 85.3% (n=81) had started using substances by age 17 years, with a mean age of substance use onset of 14.7 years (SD=2.4). The most common first substances of use were cannabis (51.6%) and crystal methamphetamine (tik) (17.9%). The most common substances for which treatment was sought (i.e. primary substances of use) were heroin (53.7%) and crystal methamphetamine (33.7%). The large majority of patients used substances every day (90.5%), and used as much as they could obtain (58.9%) or afford to buy (38.9%). All but two participants smoked cigarettes daily, did not count how many cigarettes they smoked, and did not regard their cigarette smoking as a problem (not shown). There was a statistically significant difference in the proportion of patients at the three clinics with respect to the primary substance of use. Heroin was the primary substance of use in more than 60% of the patients at Clinics 2 and 3, compared with 11.8% at Clinic 1. At Clinic 1, more than 40% of the patients had crystal methamphetamine as their primary substance of use compared with 26.7% and 35.4% at Clinics 2 and 3 respectively. Forty-four percent of the patients were in substance use treatment for the first time at the time of the study. Of those who had had previous treatment for their substance use (n=53), 68% (n=36) had been between the ages of 15 and 20 years when they had their first treatment. However, the proportion of patients at each clinic was marginally different with respect to their previous history of substance use treatment (p=0.081), with the majority of patients at Clinic 1 (64.7%) being in substance use treatment for the first time.

Table 2 lists the proportions of patients at each of the clinics with respect to their diagnosis of current psychopathology. In the study all the C-DIS IV modules were administered, but only the most common psychiatric diagnoses are listed in Table 2. Ninety-six percent (Table 1) of patients had some form of psychopathology; only three patients had no non-substance use psychiatric diagnosis. Some patients had more than one current psychiatric disorder. Sixty patients (63.2%) had at least two non-substance use psychopathology diagnoses, and 27 patients (28.4%) had at least three non-substance use psychopathology diagnoses. Of the 92 patients with psychopathology, only four patients had previously been diagnosed with a non-substance use psychiatric disorder (Table 2). There was no statistically significant difference in the proportions of patients at each clinic who had never previously been diagnosed with a psychiatric

than 90% Coloured patients while 17.7% of the patients at Clinic 1 were White.

disorder. The most common current psychiatric diagnoses were substance dependence (91.6%), anti-social personality disorder (ASPD) (87.4%), conduct disorder (CD) (67.4%), oppositional defiant disorder (33.7%) and major depression (25.3%). The proportion of patients differed significantly at the three clinics with respect to mania ( $p=0.007$ ), with one patient at Clinic 2 having had a manic episode in the last 12 months compared with six and five patients at Clinics 1 and 3 respectively. The numbers of patients diagnosed with substance dependence differed significantly across the treatment centres ( $p=0.007$ ), with Clinics 2 and 3 having more than 95% of patients dependent on substances compared with 70.6% of patients with substance dependence at Clinic 1. The clinics also differed marginally with respect to generalised anxiety disorder ( $p=0.059$ ) and post-traumatic stress disorder (PTSD) ( $p=0.065$ ) although the numbers of patients with these diagnoses were generally relatively small.

There was no statistically significant difference in the proportions of any psychopathology by either first substance of use or by primary substance of use (results not shown). Table 3 presents the percentage of patients with the most common first and primary substances of use in terms of the most commonly-occurring non-substance use psychopathology. These results indicate that a statistically significant proportion of those who were positive for conduct disorder had started out using cannabis ( $p=0.048$ ) compared with those who were not positive for conduct disorder. The proportion of patients who had anti-social personality disorder and had used cannabis as their first substance was marginally higher than the proportion of patients who were positive for the other commonly-occurring disorders and used cannabis as their first substance of use. The difference in the proportions of the other psychopathologies by substance use were not statistically significant.

Table 2 lists the percentage of the most common first and primary substances of use by the most common psychopathology. Significantly more patients ( $p=0.049$ ) who were found to be positive for conduct disorder, compared with those who were not diagnosed with conduct disorder, had used cannabis as their first substance. Marginally more patients ( $p=0.0654$ ) who were found to be positive for antisocial personality disorder, compared with those who were not positive for antisocial personality disorder, had their substance use debut with cannabis.

Table 4 documents the results of the regression analyses which were conducted to determine associations between different forms of non-substance use psychopathology and different forms of first substance used and primary substance use at bivariate level. Anti-social personality disorder was marginally associated with cannabis as the first substance of use ( $p=0.061$ ). However, this association was no longer significant after adjusting for demographic factors ( $p=0.117$ ). Similarly, the significant association between conduct disorder and cannabis as the first substance of use ( $p=0.031$ ) was no longer significant after adjusting for demographic factors ( $p=0.103$ ).

The unadjusted odds ratio for the association between specific phobia and cannabis as the first substance of use was not statistically significant ( $p=0.479$ ) but approached statistical significance on adjustment (OR=4.74; 95% CI 0.99-22.66,  $p=0.051$ ). The association between oppositional defiant disorder and crystal methamphetamine as the primary substance of use was only marginally significant ( $p=0.087$ ) at bivariate level.

## Discussion

This study examined the frequency and nature of non-substance use psychopathology in young adult substance users in inpatient treatment for their substance use, and to identify demographic, social and substance use factors that influenced the association between psychopathology and substance use.

The results obtained indicate a large proportion of inpatient substance users who had not previously been diagnosed with a psychiatric disorder, while a large number of patients was diagnosed with a current (12-month) non-substance psychiatric disorder in this study, demonstrating a high percentage of comorbid psychopathology in these inpatients in Cape

Town, with a percentage that exceeds the prevalence of these psychiatric diagnoses reported for the general adult community but using a different instrument, namely the Composite International Diagnostic Interview (CIDI) which also provides DSM IV diagnoses [22].

The high percentage of previously-undiagnosed psychopathology in these inpatient substance users, despite many of the patients having been in treatment for their problematic substance use previously, suggests a need for substance users to be assessed for co-occurring psychopathology as part of treatment and rehabilitation. It might also be necessary to recognize the demographic and social heterogeneity of these patients, and to tailor their treatment according to their individual needs.

It is likely that the study sample was vulnerable to Berkson's Bias [27] in that there would be an increased likelihood of patients seeking treatment for their substance use problems because they experienced a co-existing non-substance use psychiatric disorder. The presence of disruptive behavior disorders (noted by the high prevalence of diagnoses such as anti-social personality disorder, conduct disorder and oppositional defiant disorder) could also have played a role in treatment-seeking by causing social conflict in the lives of the substance users [7], precipitating admission for substance use treatment. It is also possible that the percentage of psychopathology in this substance use treatment group differed from that in community substance users because of differences in the severity of the extant conditions in the two groups [6]. In other words, substance users in the community might experience symptoms related to the same psychiatric diagnoses as those of patients in this study, but these psychiatric symptoms might be less severe and not yet meet the criteria for diagnoses and hence might not yet play a role in treatment-seeking behavior.

While there is debate on whether substance use (in the form of problematic substance use, or abuse or dependence) may be regarded as a dysfunctional or antisocial behaviour, constituting part of a psychiatric disorder, or a psychiatric disorder itself [8], there is little doubt about the predominance of disruptive behavior disorders in clinical samples of substance users compared with the prevalence of other non-substance use psychopathology [7], and the role that disruptive behaviour disorders might play in treatment-seeking.

The presence of a comorbid disruptive behavior disorder might also be more likely to precipitate treatment-seeking for substance use problems than would a co-occurring anxiety disorder [6], possibly accounting for the low proportions, or absence, in the present study, of those comorbid psychiatric diagnoses (for example, depression [8] anxiety [7] and posttraumatic stress disorder [6]) that have commonly been associated with substance use, abuse or dependence in the community [7, 8] and in patients who receive treatment for their substance use [5].

The proportions of patients with the most common psychiatric diagnoses did not show statistically significant differences by either the first or primary substances of use. However, a significantly greater proportion of patients who were diagnosed with conduct disorder and anti-social personality disorder had also initiated their substance use with cannabis. It is thus possible that cannabis was a notable first substance of use in those who were diagnosed with conduct disorder or antisocial personality disorder. The the marginal results obtained in this study, however, must be interpreted with caution.

There might be other factors that also play a role in the nature, prevalence and associated substance use of psychopathology amongst inpatient substance users. For example, when examining the psychiatric symptoms of patients in the National Treatment Outcome Research Study, Marsden et al. [7], found that the relationship between psychiatric symptoms and substance use was not a direct relationship but rather a relationship that was conditional on the types of substance use. For example, these authors reported that depressive symptoms were less likely or less severe in opiate users in treatment, than in users of stimulants who were in treatment. They also found that, in substance users who receive treatment, the frequency and severity of psychiatric symptoms were predicted by poor physical health, previous psychiatric treatment, gender, and personal relationships characterized by high levels of conflict. It is thus possible that factors such as these, of which physical health, previous psychiatric treatment and personal relationships were not assessed in relation to comorbidity in the present study, contributed to the findings of the present study by influencing psychiatric symptoms

and disorders, and, indirectly, the association between psychopathology and substance use.

The distribution of the Western Cape province (of which Cape Town is the capital city) treatment population during the study period, in terms of racially classified social grouping, indicates that Coloured patients who presented for substance use treatment constituted the majority of the treatment population [28]. The study sample thus reflects the population preponderance of Coloured substance use patients relative to White and Indian patients. The complete absence of Black patients from this sample is, however, surprising, particularly considering the close proximity to Clinic 3 of a largely Black informal settlement. This finding could possibly be a result of a combination of factors that involved financial constraints and/or the nature of the treatment offered at the treatment centres selected for sampling.

The sample contained few females. The proportion of males (90%) is consistent with the gender distribution of the substance using population that sought treatment, from which the sample was drawn [28], and with samples of similar studies [29, 30]. On examining possible reasons for the uneven gender distribution of substance use inpatients, Green et al. [31] found that in females, a comorbid psychiatric diagnosis predicted a failure of treatment initiation, while in males a low educational level predicted a failure of treatment initiation. It is possible that comorbid psychopathology might have played a role in the treatment initiation of some females, but this association was beyond the design of the present study, as was the role of low educational level in potential male substance use inpatients in treatment initiation.

However, the paucity of females in this study sample could also be indicative of females possibly facing more obstacles to entering inpatient treatment. For example, women may face more social stigma and treatment beliefs [31], or financial constraints [32] compared with males.

Further investigations could be geared at identifying and minimizing the obstacles that females face with regards to attending inpatient treatment facilities. Based on the findings of Green et al. [33], it might thus be useful to emphasise assessment of females for psychiatric disorder prior to suggesting inpatient admission. Such assessment, coupled with treatment for psychiatric disorder and counseling, might aid admission of females where this is deemed appropriate and potentially beneficial. Similar support for males with low educational levels might also prove helpful in aiding initiation of treatment for substance use.

The high percentage of cigarette smoking amongst this group of substance users in treatment might be cause for concern. Most participants viewed their cigarette smoking as more socially acceptable and with a smaller impact on their lives than their use of other substances. Cigarette smokers who receive treatment for use of other substances could potentially face a future of compromised health as a result of their cigarette smoking, irrespective of whether or not they attain abstinence from their other substance use.

It is noteworthy that few of the patients were in treatment for problem-drinking of alcohol when alcohol is still the most common substance of abuse for which treatment is sought in the area [28]. The preponderance of Muslim patients in this sample could have accounted for this result since alcohol consumption is forbidden in Islam and is considered a social taboo in Muslim communities, even among users of other substances. However, alcohol generally appears to be an unlikely substance of use for which treatment is sought in young people, particularly when there are other (usually illicit) substances of use available [34]. The most likely reason for the small number of patients in treatment for alcohol use in this sample might thus be that patients in treatment for alcohol use were usually older [28] and thus not eligible for selection in the study.

The present study did not elicit information regarding the mode of substance use. Injecting substances like heroin is known to be associated with increased Severity of Dependence scores compared with smoking heroin [35], while increased severity of dependence on substances has been associated with increased risk of psychopathology [13]. In the absence of information regarding mode of drug administration, its relevance for associations between substance use, substance use severity and psychopathology cannot be commented on. However, smoking appears to be the most common means of non-alcohol substance

administration in this community [28] so it would be appropriate to assume that, where relevant, substances in this sample were smoked rather than injected.

Study findings should be interpreted in light of potential study limitations. Firstly, because of the small sample size, the multiple comparisons could have produced differences between groups that might be chance findings, and real differences between groups might have been missed. Secondly, the lack of a representative sample precludes generalisability of the results beyond the study sample. Lastly, the cross-sectional design of the study limits inferences regarding temporality, causality, and gateway pathways to comorbid substance use and psychopathology, even in those cases where statistically significant associations emerged. Further investigations in the form of longitudinal studies that assess the risk for substance use in individuals diagnosed with psychiatric disorder and the risk for psychiatric disorder in substance users are needed to provide information regarding temporal associations between the psychopathology and substance use. Further investigations of both treatment and community samples might provide additional insights, particularly as regards differences in comorbid non-substance use psychopathology.

## Conclusion

This study has highlighted that psychopathology is common in substance using young people who receive inpatient treatment for their substance use. The study has illustrated the need for psychiatric assessment of comorbid psychopathology in substance users who receive treatment for their substance use in Cape Town, South Africa, with the suggestion that integrated service models be developed for the treatment of mental illness and substance use.

## Competing interests

The authors declare no competing interests.

## Authors' contributions

Authors AS and AF were responsible for the conceptualization, development and design of the study. Author AS was responsible for drafting the entire manuscript, and author RL completed all the data analyses. All the authors participated in the preparation and revision of the manuscript. All the authors approved the final manuscript, except AF, who sadly passed away before the manuscript was completed.

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## Research

# Childhood vaccination in rural southwestern Ethiopia: the nexus with demographic factors and women's autonomy

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**Introduction:** Vaccination can reduce child mortality significantly and is a cost effective way to improve child health. Worldwide, more than 22 million children do not receive the basic recommended vaccinations. Vaccination coverage in Ethiopia remains low. Research on child health has focused on socio-economic factors such as maternal education and access to health care, but little attention has been given to demographic factors and women's autonomy within the household. The purpose of this study was to examine the influences of demographic factors and women's autonomy on the completion of childhood vaccination in rural Ethiopia.

**Methods:** A cross-sectional community-based study was conducted in a Health and Demographic Surveillance System (HDSS) in southwestern Ethiopia. Data were drawn from a random sample of women with children aged 12-24 months (n=889). Information on maternal socio-demographic characteristics and household variables were collected using an interviewer-administered structured questionnaire. Vaccination data were obtained from vaccination cards or mother's recall. Multivariate logistic regression was used to assess the association of independent variables with completion of childhood vaccination.

**Results:** Of 889 children aged 12-24 months, 690 (78%) had received at least one vaccination. Only 37% (95% CI, 33.5-39.9) were fully vaccinated. Women's decision making autonomy, number of under-five children in the household, mother's education, use of antenatal care services and proximity to health facility were the main factors associated with full vaccination status.

**Conclusion:** Completion of basic vaccination series is very low in the study area. Initiatives that enhance women's autonomy within the household and that promote healthy timing and spacing of pregnancies may help in improving child health through vaccination.

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## Introduction

The fourth Millennium Development Goal (MDG 4) calls for efforts to reduce child mortality by two-thirds by 2015. Although there has been a decline in child mortality in recent decades in many regions of the world, about 7 million child deaths occur annually in the world [1]. The highest rates of child mortality occur in sub-Saharan Africa - where 1 in 9 children die before age five. The rate of decline in the region is also slower and most countries are unlikely to meet MDG 4 [1]. Ethiopia, one of the countries with high child mortality, has shown a remarkable decline in child mortality in the last decade. The under-five mortality rate declined from 166 deaths per 1000 live births in 2000 to 88 deaths per 1000 live births in 2011 [2, 3]. However, the majority of deaths are still caused by infectious diseases that can be prevented through cost-effective prevention efforts [4].

Childhood vaccination can reduce child mortality significantly and is a cost effective way to improve child health [5-7]. According to the World Health

Organization (WHO), vaccination averts an estimated 2 to 3 million deaths every year from diphtheria, tetanus, pertussis, and measles [8]. In 2011, about 83 percent of infants worldwide were vaccinated with three doses of diphtheria-tetanus-pertussis (DTP3) vaccine, and 162 countries have reached DTP3 coverage of 80 percent. Globally, in 2011, 22.4 million children under one year of age did not receive DTP3 vaccination. Ethiopia is one of ten countries with large proportions of children without DTP3 vaccination [8].

The Ethiopian Health Policy emphasizes prevention and control of major communicable diseases [9]. Strengthening the Extended Program on Immunization (EPI) is therefore one of the core activities in the recent Health Sector Development Program (HSDP) to reduce child mortality. The EPI policy calls for BCG vaccine at birth, three doses of DTP-HepB-Hib vaccine at approximately 4, 8, and 12 weeks of age, four doses of oral Polio vaccine at 0-2, 4, 8, and 12 weeks of age, and measles vaccine at or soon after reaching 9 months of age. A child is said to be fully vaccinated if all eight vaccinations have been received. Although the EPI was initiated in 1980 with the goal of universal coverage by 1990 [10],

achievements are still far below the international standard. According to the 2011 Ethiopian Demographic and Health Survey (EDHS), only 24% of children age 12-23 months were fully vaccinated. The coverage of measles vaccination was 56% [3] although service statistics by the Ministry of Health and a national EPI coverage survey conducted in 2006 showed a higher coverage than the DHS reports. The 2006 national EPI coverage survey showed that 50% of children age 12-23 months were fully vaccinated [11]. In addition to the low coverage, rural-urban and regional disparities in vaccination coverage are substantial [3]. The 2011 EDHS also showed that urban children were more than two times as likely as rural children to have all basic vaccinations.

Previous studies have documented several maternal, social and health care provision factors that influence completion of child vaccination in low and middle income countries. Maternal education and use of antenatal care services are consistently associated with completion of childhood vaccinations [12-16]. In studies from Ethiopia and other low and middle income countries, low access to services and inadequate awareness of the roles of vaccinations were found to be barriers to completion of child vaccination series [10,14,17-19]. While the association between mother's age and parity and completion of childhood vaccination has been less consistent [14, 19, 20], two recent studies from Africa (Kenya and Nigeria) found that younger maternal age and lower parity are associated with completion of child vaccination series [15,19]. Gender differences in vaccination coverage have been reported in studies from India [21], Bangladesh [22] and Nigeria [23] but not in previous studies from Ethiopia [14,20].

Few studies in Sub-Saharan Africa have examined associations between vaccination rates and factors such as pregnancy intention, the number of under-five children in a family and women's autonomy within the household. However, these demographic factors are likely to be implicated in the coverage and completion of childhood vaccination. For instance, a large body of research highlights the negative consequences of unintended pregnancy on maternal health behavior. These studies have shown that unintended pregnancies are associated with delayed initiation and inadequate use of antenatal care services [24-26], maternal depression and anxiety during pregnancy [27,28], and a shorter duration of breast feeding [29,30]. On the other hand, studies that assessed the association between pregnancy intention and child preventive and curative care in high income countries found no effects [31,32]. A study by Marston and Cleland (2003) that used DHS data from five low and middle income countries showed significantly higher risk of incomplete childhood vaccination for unintended births in three (Egypt, Kenya and Peru) of the five countries studied [33]. Another study that assessed the effects of unwantedness on curative care using DHS data from Indonesia showed that unwanted children were less likely to receive treatment for illness compared with wanted children [34]. Overall, there are few studies on the subject from low income countries and existing ones have shown mixed results.

Although some studies have examined the association between women's autonomy and maternal health care [35-37], few have examined whether a similar relationship exists in the utilization of child health services including vaccination. In the only study from Ethiopia that used the 2005 EDHS data to assess the associations of women's autonomy with maternal and child health care, women's participation in decision making was found to be significantly associated with completion of childhood vaccination [37]. Another study that assessed the associations of women's autonomy with under-five mortality from Central Ethiopia found that women's involvement in household decision making was significantly associated with under-five mortality [38]. This study examined the association between childhood vaccination and demographic factors including pregnancy intention, women's autonomy and the number of under-five children in a family in southwestern Ethiopia.

## Methods

### Study setting

A cross-sectional survey was conducted in the Gilgel Gibe Health and Demographic Surveillance System (HDSS) which is located 260 kilometers to the southwest of Addis Ababa (the capital) in southwestern Ethiopia. The Gilgel Gibe HDSS, which is run by Jimma University, is used to collect vital events data. The HDSS covers more than 10,000 households and a

population of over 55,000 people.

### Sample

Women residing in the demographic surveillance area who had a live birth in the two years before the survey served as a sampling frame for the present study. The data used for this study were collected as part of a larger study on the effects of unintended pregnancy and related socio-demographic factors on maternal and child health in the HDSS. A sample size of 1,456 women was estimated for the study. Participants were drawn from eleven kebeles (smallest administrative unit in Ethiopia) in the HDSS area using simple random sampling. There were 1,370 women interviewed in the main study who gave birth to 1,382 children in the two years before the survey. A sub-sample of 889 children of age 12-24 months were eligible for the present analysis.

### Procedures

Data collection took place from March to May 2012. Data were collected by ten trained female data collectors who had a diploma-level training and data collection experience. They were closely supervised by supervisors who had similar or higher level of education and experience in supervision of data collection. The data collectors and supervisors participated in 5 days of training focusing on questionnaire administration and ethical considerations. After the training, a pre-test of the questionnaire was conducted. Information from the pre-test was used to finalize the questionnaire.

Data were collected using a structured questionnaire originally developed in English and translated to Oromo. Vaccination data were recorded from cards if the mother was able to present a card or reported verbally. All study participants were interviewed at their home in private area. Ethical approval was obtained from the College of Health Sciences, Addis Ababa University. Support letters were obtained from regional and district health offices. Local (kebele) administrations were informed about the study. Participants were briefed on the study and provided informed consent.

### Measures

The main outcome variable was full vaccination coverage of children age 12-24 months. We used the WHO definition of full vaccination which states that children are considered to be fully vaccinated when they have received a vaccination against tuberculosis (BCG), three doses each of DPT-HepB-Hib vaccine and polio vaccines, and a measles vaccination by the age of 12 months.

The main explanatory variables were women's pregnancy intention for the index child, number of under-five children in the household and women's participation in household decision making. Pregnancy intention was measured using the standard DHS approach, which asks women to recall their feelings at the time they became pregnant; "At the time you became pregnant, did you want to become pregnant then, did you want to wait until later, or did you not want to have any (more) children at all?" Women's participation in decision making was measured by asking the following questions; "who makes decisions in your household about: (1) obtaining health care for yourself; (2) large household purchases; (3) household purchases for daily needs; and (4) visits to family or relatives?" The responses were: (1) respondent alone, (2) respondent and husband/partner, (3) husband/partner alone, (4) someone else. Women were considered to participate in a decision if they usually make that decision alone or jointly with their husbands. A composite index was constructed by grouping women into two categories: women who participate in all four household decisions, indicating a higher level of autonomy, and women who do not have any say in one or more decisions. The internal consistency of the scale, as assessed using Cronbach's alpha, was 0.82. Socio-economic status was measured using a household assets index derived using principal components analysis. Maternal health seeking behaviour included antenatal care, place of delivery and postnatal check up. We also included several control variables including education, wealth index, parity, and distance from health facility.

Data analysis Data were analyzed using STATA software version 11. Bivariate associations between child vaccination and the explanatory and control variables were assessed using Chi-square analyses. At the multivariate level, two logistic regression models were run to identify factors associated with complete versus incomplete vaccination and receipt of at least one vaccination versus no vaccination. Variables were entered into the models based on their association in the bivariate

analysis (at  $p < 0.20$ ). Adjusted odds ratio and 95% confidence intervals are reported.

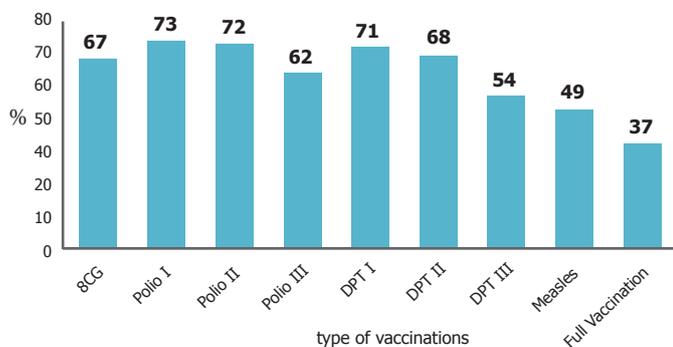
## Results

Sixty percent of mothers were aged 25-34 years, with a mean age of 27.5 years ( $SD \pm 5.4$ ) (Table 1).

Socio-demographic Variables	Percent	Number of women
<b>Mother's age</b>		
15-24	24.6	219
25-34	59.5	529
35+	15.9	141
<b>Mother's marital status</b>		
Married	97.8	869
Divorced or widowed	2.3	20
<b>Religion</b>		
Muslim	92.5	822
Christian	7.5	67
<b>Mother's Educational status</b>		
No formal education	75.8	674
Primary	21.2	188
Secondary and above	3.0	27
<b>Residence</b>		
Rural	75.9	675
Urban	24.1	214
<b>Use of ANC during pregnancy</b>		
No ANC Visit	57.7	513
1-3 ANC visits	24.2	215
4 or more ANC visits	18.1	161
<b>Place of delivery for last birth</b>		
Home	88.6	788
Health facility	11.4	101
<b>Pregnancy Intention</b>		
Intended	65.0	574
Unintended	35.0	311
<b>Participation in decision making</b>		
Low	44.9	400
High	55.1	489
Mean number of living children	3.83	889

Almost all mothers were married (98%), most had no formal education (76%), were Muslim (93%), and lived in rural areas (76%). Women reported an average of four living children. Forty two percent of mothers made at least one antenatal care visit during their last pregnancy, but only 18% reported the recommended number of four or more antenatal care visits. Nearly nine in ten women delivered their last child at home. For 35% of the births, the pregnancy was reported as unintended. Fifty-five percent of women said they participated in all household decisions and were categorized as having high participation in household decisions.

Seventy-eight percent ( $n=690$ ) of children had ever been vaccinated. However, only 37% (95% CI, 33.5-39.9) of children age 12-24 months had received all basic recommended vaccinations (Figure 1).



**Figure 1**  
Percentage of children age 12-24 months who received different vaccinations series and full vaccination in Gilgel Gibe SW Ethiopia, 2012

Among the 690 children who had ever received vaccination, 86% received

BCG, 92% received DPT1, 88% received DPT2, 70% received DPT3, and 63% received measles vaccinations (Table 2).

Variable	Frequency	Percentage
Any vaccination (n=889)	689	77.6
BCG	596	86.4
DPT1	634	91.9
DPT2	604	87.5
DPT3	480	69.6
Measles	433	62.8
Vaccination card	283	40.9

Note: Percentages for the vaccinations and vaccination card variables are based on the number of those who had at least one vaccination

Almost half (48%) of those who had at least one vaccination received all basic vaccinations. Vaccination cards were produced for only 283 (41%) of children with at least one vaccination.

Table 3 shows bivariate associations between demographic and social factors and child vaccination (receiving at least one vaccination and full vaccination).

Socio-demographic Variables	Received at least one vaccination	p-value	Fully vaccinated	p-value
<b>Mother's Age</b>				
15-24	78.5	0.714	48.8	0.896
25-34	78.7		46.7	
35+	72.5		47.0	
<b>Sex of the child</b>				
Female	76.0	0.128	49.4	0.150
Male	79.3		45.1	
<b>Educational status</b>				
No formal education	75.9	0.010	45.1	0.012
Primary	81.4		52.9	
Secondary and above	96.3		57.7	
<b>Father's education</b>				
No formal education	75.0	0.003	42.1	0.01
Some education	84.0		55.8	
<b>Wealth tertile</b>				
Low	74.8	0.257	46.5	0.328
Middle	78.7		44.3	
Upper	79.4		51.1	
<b>Pregnancy Intention</b>				
Intended	78.2	0.180	49.0	0.219
Unintended	76.6		44.1	
<b>Participation in household decision making</b>				
Low	72.7	0.007	43.9	0.013
High	81.7		49.8	
<b>Number of under-five children</b>				
1	79.5	0.008	52.5	0.023
2	77.1		45.0	
3+	70.4		31.6	
<b>ANC use</b>				
None	68.8	0.001	42.3	0.008
1-3 visits	87.0		48.7	
4 or more visits	93.7		57.4	
<b>Place of delivery</b>				
Home	76.1	0.001	45.7	0.033
Health facility	90.0		57.8	
<b>Walking distance from health facility</b>				
≤ 60 minutes	84.9	0.001	53.7	0.001
> 60 minutes	70.1		39.3	

The analysis showed that both receiving at least one vaccination and completion of vaccination varied by mother's education, women's participation in household decision making, number of under-five children in a family, antenatal care use, place of delivery and distance from health facility ( $p < 0.05$ ). However, there was no variation in immunization (both completion and receipt of at least one) by mother's age, child's sex, wealth tertile and pregnancy intention.

Table 4 summarizes the results of the logistic regression analyses. Mother's age, wealth index and pregnancy intention were not significantly associated with vaccination status.

Male children were more likely than female children to be fully vaccinated. Among demographic factors, the number of under-five children in a family

**Table 4:** Odds ratio from logistic regression predicting factors associated with child vaccination in Gilgel Gibe, southwestern Ethiopia, 2012

Variables	Receiving at least one vaccination <sup>1</sup> , OR (95% CI)	Completing all vaccinations <sup>1</sup> OR (95% CI)
<b>Sex of the child</b>		
Female	Ref	Ref
Male	1.32 (0.94-1.88)	1.35 (1.00-1.82)*
<b>Mothers age</b>		
15-24	Ref	Ref
25-34	0.82 (0.54-1.24)	0.93 (0.61-1.44)
35+	0.57 (0.28-1.14)	0.97 (0.52-1.78)
<b>Mothers educational status</b>		
No education	Ref	Ref
Primary	1.23 (0.86-1.69)	1.22 (0.87-1.55)
Secondary and above	2.74 (1.34-5.80)*	1.77 (1.04-3.59)*
<b>Wealth tertile</b>		
Poor	Ref	Ref
Middle	0.82 (0.54-1.24)	0.75 (0.51-1.11)
Rich	1.18 (0.71-1.95)	1.08 (0.72-1.63)
<b>Pregnancy intention</b>		
Intended	Ref	Ref
Unintended	0.81 (0.61-1.07)	0.93 (0.67-1.28)
<b>Number of under-five children</b>		
1	Ref	Ref
2	0.98 (0.64-1.51)	0.97 (0.68-1.39)
3+	0.70 (0.33-1.46)	0.45 (0.21-0.93)*
<b>Father's education</b>		
Illiterate	Ref	Ref
Literate	1.20 (0.79-1.82)	1.38 (0.98-1.92)
<b>Participation in decisions</b>		
Low	Ref	Ref
High	1.63 (1.15-2.31)**	1.35 (1.01-1.80)*
<b>Distance from health facility</b>		
≤ 60 minutes	Ref	Ref
> 60 minutes	0.55 (0.38-0.80)**	0.58 (0.41-0.81)**
<b>Antenatal care visits</b>		
None	Ref	Ref
1-3 visits	2.79 (1.72-4.55)**	1.50 (1.06-2.13)*
4 or more visits	5.73 (2.77-11.84)**	2.27 (1.53-3.36)**
<b>Place of delivery</b>		
Home	Ref	Ref
Health institution	1.37 (0.63-2.98)	1.28 (0.80-2.03)

\*significant at P<0.05 \*\* significant at P<0.01  
<sup>1</sup>Adjusted for mother's age, education, wealth index, father's education, place of delivery, antenatal care use and distance from health facility

was significantly associated with completion of vaccination. Children are less likely to be fully vaccinated if there were three or more under-five children in the household (OR; 0.45, 95% CI, 0.21-0.96) compared with children living in households with only one under-five child. Women's participation in household decision making, maternal education, use of antenatal care services, and distance from the nearest health facility were associated with both completion of childhood vaccination and receiving at least one vaccination. Children were 1.35 times more likely to be fully vaccinated if their mothers participated in all household decisions than if they did not participate in all household decisions. Children with mothers who had completed secondary education were 1.77 times more likely to be fully immunized compared with children whose mothers had no formal education. Children were more likely to be fully vaccinated if their mother received any antenatal care during pregnancy. Children were 2.27 times more likely to be fully vaccinated if their mother reported four or more antenatal care visits than those whose mothers reported no antenatal visits while children whose mothers reported one to three visits were 1.5 times more likely to be fully vaccinated compared with those reporting no antenatal care visits.

Proximity to health facility, measured by the time taken to reach to the nearest health facility, was associated with full vaccination. Children from households living within a 60-minute walking distance from any health facility were more likely to complete vaccination schedules than those located farther than a 60-minute walking distance.

## Discussion

This study examined associations between childhood vaccination and demographic factors such as pregnancy intention, women's autonomy and the number of under-five children in a family in rural southwestern Ethiopia. We found that 78% of children age 12-24 months have received at least one of the vaccination series, although only 37% completed

all basic vaccinations. The proportion of children age 12-24 months who were vaccinated with DPT3 was 54%. Considering the fact that DPT3 is an indicator of the global Universal Childhood Immunization initiative, this level of DPT vaccination in the study site is quite low compared with the global average of 83% coverage [8]. The 2011 EDHS also showed that only 24% of children 12-23 months received all basic vaccinations and 37% received DPT3 vaccine [3]. These results show that the coverage and completion of basic vaccinations in Ethiopia is low, particularly in rural areas where the majority of the population lives.

We found that children from families with more than one under-five child were less likely to be fully vaccinated. This may be because women with many under-five children face a higher burden of care and may not be able to take their younger child(ren) for vaccination services. Other studies from low and middle countries have also found an association between parity and vaccination status [15, 19]. Pregnancy intention was not associated with vaccination status in this study showing that children from unintended pregnancies are no different from intended births in receiving full vaccination. Studies that assessed the association between pregnancy intention and child preventive and curative care in high income countries also found no effects [31, 32]. However, in a study by Marston and Cleland that used DHS data of five developing countries, unintended pregnancy was associated with incomplete childhood vaccination [33].

Child's sex was associated with fully vaccinated status with male children being more likely to be fully vaccinated than female children. Although previous studies on child vaccination did not report significant differences by gender in Ethiopia [14, 20], other studies have reported that significant gender differences exist in food consumption and schooling [39], and food insecurity and morbidity in Ethiopia [40]. There is a tradition of son preference in Ethiopia (44) and the current finding may thus reflect this tradition of sex preference in providing proper care for male children including the decision to immunize a child.

In Ethiopia, women are considered to be subordinate to men as evidenced by attitudes towards wife beating, women's participation in decision making, and women's financial autonomy [3]. We found that women's participation in household decision making was associated with complete vaccination. Participation in decision making on health care use (a dimension of women's autonomy) may enable women to independently or jointly decide to have their child vaccinated. Previous studies from Ethiopia [21] and Nigeria [23] also found that women's autonomy is important in the utilization of child vaccination services.

Our results show that other variables such as maternal education and use of antenatal care during pregnancy were significantly associated with full vaccination status. Children with mothers who have at least secondary level of education were more likely to complete the recommended vaccination series than children with mothers with no formal education. Education increases awareness on the role of vaccination services, and such awareness is important in influencing use of vaccination services. This association is consistent with findings of several previous studies on maternal education and completion of vaccination series [12, 13, 15, 16, 20].

As observed in previous studies [13, 14, 20], use of antenatal care during pregnancy was significantly associated with completing childhood vaccination. Importantly, completing the recommended ANC visits (four or more visits) was strongly associated with full vaccination. The use of antenatal care encourages the use of subsequent maternal and child health services including vaccination [41, 42]. The use of delivery care was not significant in this study probably because the small number of women who delivered in health facilities meant the study was insufficiently powered for this analysis. Proximity to health facility, however, was associated with completion of the recommended vaccination series. This finding is consistent with previous studies from Ethiopia and other low and middle income countries, indicating that access to health facilities is an important factor for the utilization of child vaccination services [17, 43].

Study findings should be interpreted in light of several limitations. First, because this was a cross-sectional study, we cannot make causal inferences. In addition, although we sought to obtain vaccination data from actual records, not all women had vaccination cards for their children. As such, we had to rely on mothers' reports which are subject to recall bias.

## Conclusion

Our study adds to the existing body of literature regarding the factors that influence childhood vaccination in low and middle income countries. Study findings highlight several potential avenues to improve childhood vaccination rates. First, the association between women's decision making autonomy and vaccination highlights the need for initiatives that improve women's autonomy in order to attain both gender equality and improved child health service utilization. In addition, in contexts characterized by low literacy levels, providing information and education about the benefits of childhood vaccination may be important. Antenatal care provides provide a good opportunity to provide mothers with information about vaccination and other maternal and child health services. Finally, improving access to family planning information and services is also important because healthy timing and spacing of pregnancies may ease the burden of care and hence promote health care use including vaccination.

## Competing interests

The authors declare no competing interests.

## Authors' contributions

YDW, designed the study, monitored the data collection, analyzed the data, and wrote the first draft of the manuscript. MFA and MJH participated in the design of the study, supervised the whole process and reviewed and modified the drafts of the manuscript. All the authors have read and approved the final version of the manuscript.

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## Research

# Anaemia among school children older than five years in the Volta Region of Ghana

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**Introduction:** Anaemia among children is a public health issue in Ghana. The Ghana School Feeding Programme (GSFP) was instituted on pilot basis in an effort to provide nutritious lunch to school children. Evidence on the nutritional status of pupils is needed to inform the expansion of GSFP. This study sought to assess anaemia among Ghanaian pupils

**Methods:** This cross-sectional study involved a random sample of 143 pupils aged 6 to 12 years. Blood samples were collected and analysed for serum-ferritin (SF), C-reactive protein (CRP), haemoglobin and malaria-parasitaemia (MP). Stool samples were examined for soil-transmitted helminthes. Dietary data were collected using the 24 hour-recall method on three non-consecutive days and a food frequency questionnaire. The Student's t-test was used to compare mean values between sexes. Binary logistic regression was performed to identify factors associated with anaemia. Statistical significance was set at  $p < 0.05$

**Results:** SF and haemoglobin concentrations were  $23.9 \pm 15 \text{ ng/ml}$  and  $120 \pm 11 \text{ g/L}$  respectively. The prevalence of anaemia was 30.8%. More females (41.5%) than males (21.8%) had anaemia ( $p < 0.005$ ). Seventy-one percent of pupils had low SF levels. MP prevalence was 67.8%. Hookworm infestation was only observed in males (18.0%). Dietary iron and vitamin C intakes were  $18.98 \pm 8.8 \text{ mg}$  and  $23.7 \pm 6.7 \text{ mg}$ , respectively. Child's sex, SF and MP were associated with anaemia. Males had a lower likelihood of being anaemic (OR=0.2, CI 0.1-0.5,  $p = 0.002$ )

**Conclusion:** The study findings underscore the need for multi-pronged approaches that address both malaria control and nutrition in order to reduce anaemia among pupils.

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## Introduction

Micronutrient deficiencies impose substantial health, economic, and social burdens worldwide [1]. Iron deficiency (ID) is the most prevalent haematologic disorder during childhood, globally [2]. One major consequence of ID is anaemia, which affects a large proportion of the world's population [3-7]. Anaemia has a range of adverse consequences including; poor cognitive performance, poor growth of infants, preschool and school-aged children; impairment of physical capacity and work performance of adolescents and adults; reduction in immune competence; and increased morbidity from infections in all age groups [8]. Severe anaemia is a common condition causing significant morbidity and mortality in children in Africa [9]. Severe anaemia carries a high "hidden" morbidity and mortality occurring in the months after initial diagnosis and treatment [9].

Anaemia in children is a public health issue in Ghana. It has been reported that 76% of Ghanaian children below five years of age [10],

73% of children aged 2-10 years [11], and 63% of school children aged 5-12 years suffer from anaemia [12]. Anaemia has multiple causes and associated risk factors which often work in tandem. They include various nutritional deficiencies, infections and infestations, as well as genetic defects including glucose-6-phosphate dehydrogenase (G6PD) deficiency, and haemoglobinopathies [13-15]. Studies in Kenya, India and Bangladesh have shown multiple coexisting causes of anaemia in individuals [16-18]. These causes include iron deficiency, vitamin A deficiency, malaria parasitaemia and other parasitic infestations. Traditionally, haemoglobin level has been used to estimate iron deficiency and iron deficiency anaemia even though haemoglobin estimates are neither specific nor sensitive as a screening test for iron [19].

Across the spectrum of anaemia, iron deficiency anaemia (IDA) is the most prevalent nutritional disorder worldwide accounting for about 75%-80% of the total burden of anaemia [4, 5]. IDA is partly induced by plant-based diets containing low bioavailable non-haeme iron [20]. Blood losses within the gastrointestinal tract due to intestinal parasites or inflammatory bowel disease may also contribute to IDA [20]. However,

the major correlates of anaemia among Ghanaian children are largely understudied. Existing studies on anaemia focus primarily on preschool children (< 5 years) and little is known about anaemia in school-aged children in rural Ghana. The objective of the present study was to assess dietary intakes, iron status, and anaemia prevalence and its associated factors among Ghanaian school children aged 6-12 years. Study findings are expected to inform intervention strategies to reduce iron deficiency and anaemia among Ghanaian children. Method

## Methods

### Study setting

The study was conducted in the Kodzobi community of the Adaklu-Anyigbe district of the Volta Region of Ghana. Adaklu-Anyigbe is one of the newly created districts in the middle belt of the Volta Region. The study was cross-sectional in design and involved school children aged 6 to 12 years.

### Study sample

Using a power of 80% with a two-sided test significance level of 5% and mean difference in ferritin level and standard deviation from a recent work [21], a minimum sample size of 143 was estimated. To account for refusals (estimated at 13%) the desired sample size was increased to 162; 81 females and 81 males. A sampling frame of public basic schools not benefitting from the Ghana School Feeding Programme was constructed and Adaklu Kodzobi basic school was selected at random. Pupils in lower and upper primary as well as junior high school aged 6-12 years were randomly selected after stratification based on sex. Of 162 children approached, 143 provided assent and subsequently blood samples for biochemical analysis. Others refused citing religious and customary reasons.

### Ethical consideration

Ethical approval was obtained from the Institutional Review Board (IRB) of Noguchi Memorial Institute for Medical Research, College of Health Sciences, University of Ghana, Legon. Permission was obtained from the District Director of Education, the local chief and elders and the head of the school sampled. Written informed consent was also obtained from the parents/guardians of pupils.

### Procedures

Data were collected over a 4-week period in July 2010. Biological samples (blood and stool) were collected from each participant. Five millilitres of fasting venous blood were collected by a phlebotomist into eppendorf tubes without anticoagulants from a sub sample of participants (40 children in the morning of each day) before they had their breakfast meal. The blood sample collection was done in a private setting. Haemoglobin concentrations were determined immediately in the field using a Hemocue Hemoglobinometer (Hemocue AB, Angelhom, Sweden). The blood samples were transported on ice-chips to Noguchi Memorial Institute for Medical Research (NMIMR). Each blood sample was centrifuged at 3000g for 15 minutes in the laboratory and serum aliquots were prepared and stored at -80°C until they were analysed.

Serum ferritin levels were measured using the Enzyme-Linked Immunosorbent Assay Alpha Diagnostics Inc. (ADI), (ADI's Ferritin ELISA kit, Cat No. 1810, San Antonio, USA). Human C-Reactive Protein (CRP) levels, which indicate presence of inflammation, were determined with ADI's CRP ELISA kit (Cat No. 1000, San Antonio, USA). The age specific cut-off values for haemoglobin concentrations used to define anaemia were 115g/L for those aged 5-11 years and 120g/L for those aged 12 years [22]. Iron deficiency was defined as ferritin concentration  $\leq$  30ng/ml due to high prevalence of malaria [23]. Malaria parasitaemia was assessed using the Giemsa staining technique [24]. Soil-transmitted helminthes were identified in stool using the Standard Kato-Katz technique [24]. The stool and blood examinations were carried out at the Parasitology Department of NMIMR by a parasitologist. Dietary data were collected using the 24 hour-recall method on three non-consecutive days and a food frequency questionnaire [25, 26]. Dietary data were used to calculate (estimate) amount of nutrients consumed using Eish FPRO software Version 6.5 and the Ghana Food Composition Table [27].

## Data analysis

All data collected were analysed with SPSS (version 16.0). Variables were checked for normality. Haematological indices and dietary data were normally distributed so their summary values are presented as means plus standard deviations. The Mann-Whitney test was used to determine whether there was a significant difference between males and females for prevalence of low iron store and anaemia. Student's t-test was used to compare means of dietary data and haematological indices of sexes. Correlations between age, haemoglobin levels, ferritin levels, C-reactive protein concentrations and malaria parasitaemia were determined using the Pearson product-moment correlation test. Binary logistic regression was performed to identify factors associated with anaemia among the children. Statistical significance was set at  $p < 0.05$  for all analyses.

## Results

The study comprised 65 females and 78 males aged 6-12 years. Participants' mean age was  $9.2 \pm 2.3$  years. Twenty-eight percent (31% females and 26% males) of the participants were aged 12 years (Table 1).

Factor	Females (n=65)	Males (n=78)	P-value	Sexes combined (n=143)
<b>Age distribution</b>	n(%)	n(%)		
6 years	13(20)	14(18)		27(19)
7 years	4(6)	11(14)		15(10)
8 years	9(14)	10(13)		19(13)
9 years	5(8)	8(10)		13(9)
10 years	5(8)	8(10)		13(9)
11 years	9(14)	7(9)		16(11)
12 years	20(31)	20(26)		40(28)
Serum ferritin concentration (ng/ml) mean $\pm$ SD	25.3 $\pm$ 16.3	22.6 $\pm$ 13.8	0.28	23.9 $\pm$ 15.0
Prevalence of low iron store (serum ferritin concentration <30ng/ml) (%)	67.7	74.4	0.32	71.3
Haemoglobin concentration (g/L) mean $\pm$ SD	118 $\pm$ 9	121 $\pm$ 12	0.9	120 $\pm$ 11
Prevalence of anaemia (haemoglobin concentration <120g/L) (%)	41.5	21.8	0.01*	30.8
CRP concentration (ng/ml) mean $\pm$ SD	44.6 $\pm$ 27.1	48.5 $\pm$ 29.0	0.51	46.7 $\pm$ 28.0
Prevalence of high CRP levels >10ng/ml (%)	100.0	91.8		95.7
Prevalence of malaria (%)	66.2	69.2		67.8
Prevalence of hookworm (%)		18.0		9.8
Cut off values: ferritin <30ng/ml, haemoglobin <115g/L for children below 12 years and 120g/L for children 12years and above; CRP = C-reactive protein. P-values obtained from independent t-test analysis. *Significant at $p < 0.05$ .				

The mean serum ferritin concentration for both sexes was  $23.9 \pm 15.0$  ng/ml. The mean serum ferritin concentration for females ( $25.3 \pm 16.3$  ng/ml) was higher than that for the males ( $22.6 \pm 13.8$  ng/ml). The mean haemoglobin concentration of the participants was  $120 \pm 11$  g/L. No statistically significant difference was observed in the mean haemoglobin concentrations for females and males.

The prevalence of low iron store (serum ferritin concentration  $\leq$  30ng/ml) among the study participants was 71.3% (Table 2).

Factor	Females (n=65)			Males (n=78)			P-value
	Mean $\pm$ SD	NAR >1 n(%)	NAR <1 n(%)	Mean $\pm$ SD	NAR >1 n(%)	NAR <1 n(%)	
<b>Energy (kcal)</b>	939.50 $\pm$ 244.36	ND	ND	1018.61 $\pm$ 261.27	ND	ND	.06
<b>Protein (g)</b>	32.73 $\pm$ 10.46	59(91)	6(9)	31.12 $\pm$ 6.16	71(91)	7(9)	.26
<b>Fat (g)</b>	34.33 $\pm$ 7.53	ND	ND	32.83 $\pm$ 6.84	ND	ND	.22
<b>Iron (mg)</b>	19.49 $\pm$ 8.72	65(100)	-	18.55 $\pm$ 8.98	78(100)	-	.53
<b>Vitamin C (mg)</b>	23.0 $\pm$ 7.0	15(23)	50(77)	24.26 $\pm$ 6.54	22(28)	56(72)	.27
Nutrient Adequacy Ratio = NAR RDA sources: 1 Food and Nutrition Board, Institute of Medicine, National Academy of Sciences. Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids (2000). 2 Food and Nutrition Board, Institute of Medicine, National Academy of Sciences. Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc (2001). 3 Food and Nutrition Board, Institute of Medicine, National Academy of Sciences. Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids (2002/2005); and Dietary Reference Intakes for Calcium and Vitamin D (2011). P-values for nutrients intakes obtained from independent t test analysis and significance level set at 0.05.							

The prevalence was 68% for the females and 74% in the males ( $p > 0.05$ , Mann-Whitney test). Females had higher prevalence of anaemia (41.5%) compared with males (21.8%), ( $p < 0.005$ , Mann-Whitney test). All females had CRP levels above the cut off (10.0ng/ml) in this study. The total prevalence of malaria parasitaemia among the children was (67.8%); females (66.2%) and males (69.2%). Hookworm infestation was 18.0% and was only observed among male participants. The mean caloric (energy) intakes of male participants ( $1018.61 \pm 261.27$  kcal) was higher than that of females ( $939.50 \pm 244.36$  kcal) even though the mean difference was not statistically significant ( $p > .05$ ) (Table 2). No child had a Nutrient Adequacy Ratio (NAR)  $< 1$  for dietary iron intake. Nine-percent of males and females had NAR <1 for protein; 77% females and 72% males, respectively, had NAR <1 for vitamin C.

Age was correlated with malaria parasitaemia ( $r=-.223$ ;  $p=0.035$ ), haemoglobin concentration ( $r=.374$ ;  $p=0.001$ ) and C-reactive protein levels ( $r=-.278$ ;  $p=0.007$ ) (Table 3).

**Table 3:** Correlation between haematological, inflammation variables and age of study participants

	Haemoglobin	Ferritin	CRP	MP	Child age
Haemoglobin	1				
Ferritin	-.022	1			
CRP	-.285**	.288*	1		
MP	-.175	.005	.319*	1	
Child age	.374**	.140	-.278**	-.223*	1

\*Correlation is significant at 0.05 level. \*\*Correlation is significant at 0.01 level.  
CRP = C-reactive protein; MP = Malaria Parasitaemia.

Similarly C-reactive protein levels were found to be correlated with malaria parasitaemia (.319,  $p=0.012$ ), haemoglobin concentration ( $r=-.285$ ;  $p=0.006$ ) and ferritin levels ( $r=.288$ ;  $p=0.026$ ).

Child's sex and C-reactive protein levels were associated with anaemia in the multivariable analysis (Table 4).

**Table 4:** Factors associated with anaemia among the study participants

Factor	Odds Ratio	95% CI	P-value
<b>Child age</b>			
< 9years	0.805	0.26 – 2.54	.711
≥ 9 years	1.0	Reference	
<b>Gender</b>			
Males	0.172	0.06– 0.54	.002
Females	1.0	Reference	
<b>Ferritin concentration (ng/ml)</b>			
14.2 – 25.3	0.305	0.08 – 1.160	.081
≥ 25.4	1.0	Reference	
<b>Malaria/inflammation</b>			
Malaria absent	0.529	0.21 – 1.11	.170
Malaria present	1.0	Reference	
C-reactive protein level ≥ 10 ng/ml	.977	0.957 – 0.998	.031
C-reactive protein level < 10 ng/ml	1	Reference	

Statistical significance  $p<0.05$ , OR (Odds Ratio), Hosmer and Lemeshow test of significance ( $P = .192$ ), Nagelkerke  $R^2 = .259$ , adjusting for child age and C-reactive protein level.

Sex was significantly associated with anaemia. Males were less likely than females to be anaemic after adjusting for age and C-reactive protein levels (OR=0.2, CI 0.1-0.5,  $p=0.002$ ). Ferritin concentration and presence of malaria parasitaemia were not associated with anaemia ( $p>0.05$ ).

## Discussion

The aim of this study was to assess the prevalence of anaemia and examine its associated factors among Ghanaian school children aged 6-12 years. We observed a high prevalence of anaemia, particularly among females, and low iron stores. The results are similar to findings from studies conducted in Ghana, Kenya, India and Bangladesh [11, 16-18] where multiple causes of anaemia were found to co-exist. We found that the prevalence of anaemia and low iron store among the children in the current study corroborates earlier studies [11, 23, 28] that anaemia is a public health issue in the West African sub region.

The prevalence of anaemia among the female participants was in excess of 40%, the level used to indicate a public health problem [22]. Previous studies have also found a higher prevalence of anaemia among females [29]. Caloric intake was slightly lower in females and Vitamin C, (known enhancer of iron bioavailability and absorption) inadequacy was also slightly higher in females. These factors may partially explain

the higher rate of anaemia in females. The increased iron requirements related to rapid growth and development of females may also account for the difference in anaemia prevalence [30, 31]. The high prevalence of anaemia among females may have implications for their development [32].

Interestingly, the findings showed that both male and female participants consumed higher levels of iron than the recommended daily requirements [33]. This suggests that other factors such as the presence of iron absorption inhibitors such as phytic acid, tannins and polyphenols (not investigated in this study) in addition to infection (malaria parasitaemia), infestation (hookworm), and probably low bioavailability of non-haeme iron might have produced adverse nutritional effects among study participants. Few participants met the Estimated Average Requirement for Vitamin C [34], a known enhancer of non-haeme iron bioavailability [35-37] which may also explain the high prevalence of anaemia and low iron stores. Further research is warranted on factors that may affect iron bioavailability. Malaria parasitaemia destroys red blood cells and therefore its presence in the participants leads to low haemoglobin levels that puts infected children at higher risk of anaemia.

Hookworm infestation was only observed in males in the study. Since hookworm is a soil transmitted helminthes (human and animal faeces are major vehicles for spreading soil transmitted helminthes) it is probable that the males might have come into contact with hookworm-infested faecal matter through outdoor activities.

## Limitations of the study

There are several limitations to the present study that warrant acknowledgement. First, the study involved pupils (aged 6-12 years) from public schools not benefiting from Ghana School Feeding Programme (GSFP) at Adaklu-Kodzobi. Study findings may therefore not be generalized to out-of-school children and those in schools benefiting from the GSFP. Secondly, the use of 24-hour recall alone for nutrients intake assessment may not reflect the actual nutrient intake. Thirdly, due to the high prevalence of malaria coupled with high CRP concentrations, the cut-off point for serum ferritin concentration was raised to 30.0ng/ml instead of the normal cut off point of 12.0ng/ml to cater for the effect of infection or inflammation that would result in elevated ferritin levels. The few participants without malaria parasitaemia but with normal ferritin levels between 12.0ng/ml and 30.0ng/ml were considered as having low iron store which may have resulted in an over estimation of prevalence of low iron store among the study participants. Finally, the cross-sectional nature of the study means that we cannot make causal inferences.

## Conclusion

Study findings demonstrate a high prevalence of anaemia among children aged 6-12 years attending a school not benefiting from the Ghana School Feeding Programme. Females, in particular, were more likely to be anaemic and therefore vulnerable to adverse consequences of anaemia and iron deficiency. Study findings underscore the need for multi-pronged approaches that address both malaria control and nutrition in order to reduce anaemia among pupils.

## Competing interests

The authors declare no competing interests.

## Authors' contributions

Godfred Egbi: Data collection, statistical analysis, data presentation, drafting of paper and paper review. Matilda Steiner-Asiedu: Data presentation and Paper review. Faribu Saalia Kwesi: Statistical analysis and data presentation. Irene Ayi: Data presentation and paper review. Winfred Ofori: Drafting of paper and paper review. Jacob Setorglo: Drafting of paper and Paper review. Seth Selorm Klobodu: Statistical analysis. Margaret Armar-Klimesu: Paper review. All the authors have read and approved the final version of the manuscript.

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## Research

# The association between substance use and common mental disorders in young adults: results from the South African Stress and Health (SASH) Survey

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**Introduction:** Although substance use is commonly associated with mental disorders, limited data on this association are available from low and middle income countries such as South Africa. The aims of the study were i) to determine patterns of substance use in young adults, ii) to identify trends of common psychiatric disorders in relation to use of specific substances, and iii) to determine whether specific psychiatric disorders were associated with use of specific substances in the South African population.

**Methods:** Data were drawn from the South African Stress and Health (SASH) study, a nationally-representative, cross-sectional survey of South African households that forms part of a World Health Organisation (WHO) World Mental Health (WMH) initiative to standardise information on the global burden of mental illness and its correlates. Data from a subset (n=1766; aged 18 to 30 years) of the SASH sample of 4351 individuals were analysed. The Composite International Diagnostic Interview Version 3 (CIDI 3.0) was used to elicit basic demographic details and information regarding mental illness and substance use. Multiple regression analyses, adjusted for age and gender, were used to identify associations between mental disorders and substance use.

**Results:** Significant associations were found between substance use and mood and anxiety disorders, with a particularly strong relationship between cannabis use and mental disorder.

**Conclusion:** The results are consistent with those from previous studies, and reinforce the argument that comorbid substance use and mental disorders constitute a major public health burden.

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**Key words:** SASH, comorbidity, mental disorders, substance use

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## Introduction

Debilitating mental illness often places a burden on society [1]. Mental illness can result in reduced economic productivity in affected individuals [2], and can influence the quality of life for individuals and their families as a result of the disabling effects of the mental illness [3]. Mental illness can also increase the load on service providers [4]. Similarly, problematic substance use poses a challenge to society because of its effects on the psychosocial functioning, productivity and general health of the affected individuals [5,6]. It has been argued that individuals who suffer from mental illnesses are more likely to be or become dependent on substances than are individuals who do not have mental disorders [4]. Conversely, individuals who abuse substances appear to be more likely to develop or suffer from mental illnesses than are those who do not abuse substances [7]. Thus, when mental illness and problematic substance use or abuse co-occur, the resulting problems are often compounded and more complex [8], increasing the challenges posed to the management and treatment of the affected individuals [4].

Although many studies have examined comorbid psychopathology and substance use globally, more details on comorbidity are generally available for older individuals, and less regarding children, adolescents and young adults [6]. Furthermore, most of these studies have examined samples in treatment for either substance use or psychiatric disorders [9], resulting in less published information on comorbidity in communities.

Armstrong and Costello [9] described six important reasons for examining comorbid psychopathology and substance use in representative community samples. Firstly, since individuals with more than one disorder are more likely to seek treatment for either disorder than are individuals with only one disorder, clinical samples are more likely than community samples to contain comorbid individuals. Secondly, the nature of some disorders might be more likely to precipitate treatment seeking. Hence, for example, a disruptive behaviour disorder (such as conduct or antisocial personality disorder) that co-occurs with substance use might be more likely to elicit treatment seeking than would an internalising disorder (such as depression), resulting in clinical samples possibly having a higher percentage of comorbid disruptive behaviour disorders than is

commonly prevalent in communities. Thirdly, community and clinical samples might differ with respect to the severity of occurring symptoms. Fourthly, community and clinical samples might differ with respect to the temporality of comorbidity. Fifthly, clinic and community samples might differ with respect to the risk factors for comorbid psychopathology and substance use. These differences can usually be assessed for diseases where most cases are treated. However, since not all comorbid substance users receive treatment, it would be inappropriate to assume that risk factors for comorbidity are the same in both treatment and community samples. Lastly, substance use treatment samples might reflect a different patient economic profile compared with community samples by containing mainly individuals who have access to finances for treatment, and thus excluding those individuals who might need treatment but cannot afford it.

In South Africa, as in other developing countries, information regarding comorbid psychopathology and substance use, its consequences, and the implications for society, is limited by a paucity of published studies [10, 11]. Evidence has indicated that sociodemographic factors can play a significant role in comorbidity and its effects [12-20]. Findings from non-South African studies have included evidence for associations between conduct disorder and substance use within specific developmental stages [21,22], and differing associations between psychopathology and substance use in males and females [23, 16]. While some findings included evidence for associations between depression and smoking [17,24,25] between depression and alcohol use [26], and between psychopathology in general and cannabis use [19], other findings have not indicated definitive associations between psychopathology and substance use [18, 27, 28]. For example, Boyle et al. [27] found associations between conduct disorder and cannabis use, but not between conduct disorder and use of tobacco or alcohol, while Costello et al. [18] found no evidence for associations between anxiety and substance use. Though these findings play a significant role in the understanding of associations between psychopathology and substance use, their generalisability to the South African population cannot be assumed. In particular, these studies had not always used similar psychopathology assessment tools, had differing measurements of substance use, and subscribed to different conceptual frameworks, suggesting that over-arching conclusions about the nature of comorbid psychopathology and substance use be drawn with caution.

The current study focussed on the nature of associated psychopathology and substance use in a previously unexamined sample of young South African adults aged 18 to 30 years. The study advances knowledge about comorbidity in general, and particularly in South Africa, by using a nationally-representative community sample. The aim of the study was threefold. Firstly, the prevalence of substance use was calculated with respect to selected demographic factors to determine substance use patterns in young adults. Secondly, the prevalence of psychopathology (namely mood and anxiety disorders) amongst younger users of various selected substances was calculated, to determine percentage of psychopathology in relation to specific substances of use. Thirdly, the current study calculated associations between selected lifetime and 12-month psychopathology (namely mood and anxiety disorders) and substance use, adjusted for age and gender to determine whether specific psychopathology was associated with use of specific substances of use in young South African adults.

## Methods

This study draws on the nationally-representative South African Stress and Health (SASH) survey, the South African arm of the World Health Organisation's (WHO) World Mental Health (WMH) initiative, aimed at providing standardised information on the global burden of mental disorders and its correlates in 28 countries [29,30]. The SASH study was conducted between January 2002 and June 2004 [31]. The study protocol was approved by the Institutional Review Board of the University of Stellenbosch. All sampled individuals provided written informed consent for participation in the study.

### Sample

The SASH study randomly sampled adult males and females, aged 18 years and older, from all the South African racially classified social groups

(RCSGs). RCSGs are defined according to the Population Registration Act of 1950 that classified citizens in terms of skin colour, and still reflect social disparities in South Africa [32]. The RCSGs were Asian/Indian, White, Coloured and Black, with Coloured referring to individuals of mixed racial origin. A three-stage probability sample design was used. The primary stage involved stratification by census enumerator areas (EA). A probability sample of households (that excluded prisons, hospitals and military barracks) and hostel quarters (single-sex migrant labour accommodation) was selected from each EA. One adult was randomly selected from each household included in the sample. Of these, questionnaires were adequately completed for 98.1% of the interviewed individuals, resulting in a sample size of 4351 participants. The present study extracted data regarding those individuals who were aged 18 to 30 years (inclusive), to address comorbid psychopathology and substance use in young adults (sub-sample size of 1766).

### Instruments

The mental health of each selected individual was assessed using the lay-administered World Mental Health (WMH) Composite International Diagnostic Interview Version 3 (CIDI 3.0) [33], providing both Diagnostic and Statistical Manual-Version IV (DSM IV) and International Classification of Diseases-Version 10 (ICD-10) psychiatric diagnoses for lifetime and the last 12-months. Since the CIDI had not previously been used in a South African population sample, parallel validation interviews were conducted by a clinician who was blind to the CIDI diagnoses, on 100 study participants [31]. The interview questions were translated from English into six of the 11 official languages in South Africa, to enable respondents to communicate in their mother tongue. Iterative back-translation was conducted by panels of bilingual and multilingual experts following WHO recommendations and discrepancies resolved by an expert consensus panel.

### Procedure

Interviewers were trained to use the CIDI and become fieldworkers, operating in conjunction with fieldwork supervisors to identify and select potential subjects. The scheduled face-to-face interview was completed by the fieldworker, usually at the home of the participant, after informed consent had been obtained from the subject. Interviews were conducted in seven of the 11 official languages of South Africa, namely English, Afrikaans, isiXhosa, isiZulu, seSotho, Northern Sotho and seTswana. The duration of interviews averaged three hours. In the event of an interview not being completed in one sitting, a second interview was scheduled and conducted.

### Measures

The pencil-and paper version of the CIDI was administered to all study participants. It elicited lifetime and 12-month occurrence for major depression (MD), panic disorder, social phobia, agoraphobia, generalised anxiety disorder (GAD), intermittent explosive disorder (IED), suicidality, substance use and post-traumatic stress disorder (PTSD), while personality disorders and psychoses were screened for. Anxiety disorders included panic disorder, generalised anxiety disorder (GAD) with hierarchy, social phobia, agoraphobia, and PTSD. A summary category was created 'any anxiety disorder or mood disorder. Diagnoses of mood (namely, major depression) and anxiety disorders were selected for analyses in the present study (Table 1, Table 2, Table 3, Table 4), thus excluding intermittent explosive disorder, suicidality and those disorders that were screened for (personality disorders and psychoses).

Basic sociodemographic information was elicited, including both time-fixed (age, gender and RCSG) and time-varying factors (highest educational level, marital status, employment, income and area of residence). Income was defined as the participant's personal earnings from employment in the past 12 months, before taxes, and excluded income from investments or pensions. Participants also answered questions regarding their own substance use, including use of tobacco; alcohol; cannabis; cocaine; LSD; heroin; opium; glue; and non-medical use of sedatives, tranquilisers, stimulants, analgesics, or any other psychoactive over-the-counter compounds. Tobacco smokers were defined as those who reported having smoked more than 100 cigarettes in their lifetime. Alcohol use was defined as ever having had a drink of alcohol. Use of other drugs was defined as ever having used the specific drug.

## Data analyses

Data were analysed using Stata Version 11.0 [34], and considered the survey design based on person-level weights, and incorporated sample selection, non-response and post-stratification factors. All statistical tests were two-sided at  $\alpha=0.05$ .

Descriptive statistics were generated, providing mean age, and proportions for categorical data. The prevalence of the demographic and socioeconomic variables was examined and stratified, and presented by substance use categories (tobacco, alcohol, cannabis, other drugs, extra-medical drugs). Differences between the proportions were tested with the chi-squared test, and p-values reported to compare demographic and socioeconomic characteristics by substance use. The prevalence and 95% confidence intervals of lifetime and 12-month DSM-IV disorders were stratified by substance use and p-values from chi-squared tests for proportions were reported, with prevalence of comorbidity reported for specific forms of psychopathology in relation to specific substances of use. To examine associations between DSM-IV disorders (both lifetime and 12-month) and substance use, regression analyses were conducted, including adjustment for age (as a continuous variable) and gender.

## Results

The study sample consisted of 1766 males and females, comprising a subset of the SASH survey sample ( $n=4351$ ), and consisting of all the SASH survey participants aged 18 to 30 years (Mean age 23.6 years; 95% CI 23.4-23.8).

Table 1 summarises the prevalence of substance use for the selected

proportion of cannabis users differed significantly by gender ( $p<0.001$ ), RCSG ( $p<0.001$ ), educational level ( $p=0.020$ ), employment status ( $p=0.003$ ) and residential area ( $p<0.001$ ). Significantly more males than females used cannabis ( $p<0.001$ ). A larger proportion of Whites had ever used cannabis compared with the other RCSGs. The highest proportions of cannabis users were reported for those who had no formal education (21.6%) and those who had tertiary education (16.8%), suggesting a bimodal distribution. A significantly larger proportion of cannabis users were unemployed and lived in rural areas.

A larger proportion of males had ever used other drugs ( $p<0.001$ ) while the proportion of Blacks who used these substances was significantly smaller than the proportions of other RCSGs who used these substances ( $p=0.004$ ). A significantly larger proportion of individuals who reported non-medical use of prescription drugs lived in urban areas ( $p=0.010$ ) compared with the proportion who lived in rural areas.

Overall comorbidity rates in the SASH sample were as follows (percentages adjusted for survey weighting with 95% CIs): For any lifetime substance use and any DSM IV disorder 21.3% (CI 18.8-23.9); for any lifetime substance use disorder and any anxiety or depression disorder 4.0% (CI 2.6-6.1); for any 12-month substance use and any DSM IV disorder 11.5% (CI 9.2-14.2); for any 12-month substance use disorder and any anxiety or depression disorder 1.6% (CI 1.0-2.7).

Table 2 lists the odds ratios for mental disorders by substance of use compared with absence of the particular substance of use. In the total sample, the odds of any lifetime anxiety disorder were 14.7, and 19.7 for any lifetime anxiety or mood disorder. The odds of any 12-month anxiety or mood disorder were 10.3 while for the total sample, the odds of having any 12-month anxiety disorder was 7.1. The odds ratios of lifetime

**Table 1:** Prevalence of substance use by demographics

		Tobacco		Alcohol		Cannabis		Other substances <sup>a</sup>		Non-medical use of prescription drugs <sup>b</sup>	
		100+ cigarettes (%)	p-value	Ever (%)	p-value	Ever (%)	p-value	Ever (%)	p-value	Ever (%)	p-value
<b>Total sample</b>		27.4 (24.9-30.1)		38.7 (35.5-41.9)		10.7 (9.0-12.8)		2.7 (1.8-4.0)		20.6 (17.5-24.1)	
<b>Gender</b>	Males	44.9 (40.2-49.8)	<0.001	54.0 (49.8-58.1)	<0.001	17.7 (14.5-21.6)	<0.001	4.2 (2.5-7.0)	0.001	21.4 (17.2-26.4)	0.497
	Females	9.8 (7.5-12.6)		22.7 (19.4-26.4)		3.6 (2.5-5.2)		1.1 (0.6-1.9)		19.8 (16.7-23.4)	
<b>RCSG</b>	Black	23.7 (21.2-26.3)	<0.001	34.0 (30.5-37.7)	<0.001	9.3 (7.5-11.4)	<0.001	2.1 (1.3-3.4)	0.004	21.2 (18.2-24.5)	0.416
	White	47.7 (39.4-56.2)		67.4 (57.2-76.2)		25.4 (19.7-32.0)		6.7 (3.3-13.4)		13.8 (6.8-26.2)	
	Coloured	44.0 (30.1-58.9)		59.3 (46.9-70.6)		11.2 (4.4-25.8)		5.1 (2.6-9.5)		25.6 (11.4-48.0)	
	Indian/Asian	32.0 (21.9-44.2)		26.1 (19.1-34.6)		6.5 (3.9-10.6)		0		13.4 (5.6-28.7)	
<b>Education</b>	None	40.8 (21.9-62.8)	0.152	55.9 (34.5-75.3)	0.574	21.6 (5.6-56.4)	0.020	0	0.094	11.6 (4.0-29.4)	0.482
	Grade 1-7	35.8 (28.3-44.2)		37.7 (29.7-46.5)		11.9 (7.0-19.4)		2.0 (0.6-6.8)		19.7 (12.3-29.9)	
	Grade 8-11	26.9 (23.2-31.0)		38.2 (33.8-42.8)		10.4 (7.9-13.6)		3.5 (1.9-6.5)		18.8 (14.7-23.6)	
	Matric	25.1 (20.7-30.0)		37.9 (33.3-41.8)		7.6 (5.3-10.7)		1.1 (0.5-2.7)		21.3 (16.5-27.1)	
	Matric +	29.5 (23.0-37.1)		40.3 (33.1-48.1)		16.8 (12.4-22.5)		4.3 (2.4-7.8)		24.3 (18.2-31.6)	
<b>Marital status</b>	Not married	25.9 (23.0-29.1)	0.073	38.8 (34.5-42.8)	0.684	10.0 (8.0-12.5)	0.289	2.7 (1.7-4.2)	0.978	19.8 (16.6-23.4)	0.241
	Married	31.9 (26.6-37.7)		37.3 (31.4-43.5)		12.8 (8.8-18.2)		2.6 (1.3-5.4)		23.1 (17.7-29.6)	
<b>Employment</b>	Employed	40.9 (33.8-48.4)	<0.001	56.1 (49.6-62.4)	<0.001	16.9 (12.5-22.4)	0.003	4.1 (2.4-7.1)	0.120	25.9 (19.3-33.9)	0.061
	Unemployed	23.9 (21.2-26.8)		33.8 (30.3-37.5)		9.1 (7.1-11.5)		2.3 (1.4-3.8)		19.2 (16.1-22.8)	
<b>Income<sup>c</sup></b>	Zero	23.2 (19.3-32.1)	0.912	39.9 (31.9-48.5)	0.715	12.3 (7.7-19.2)	0.167	3.7 (1.2-11.2)	0.401	19.4 (13.5-27.2)	0.404
	Low	26.6 (31.7-32.1)		36.1 (31.7-40.6)		8.4 (6.0-11.7)		3.3 (1.7-6.6)		21.6 (17.6-26.3)	
	Low-average	28.5 (23.2-34.6)		42.5 (35.6-49.6)		7.3 (4.5-11.7)		0.6 (0.1-4.4)		15.8 (11.1-22.1)	
	High-average	28.7 (23.2-34.9)		37.6 (31.1-44.6)		12.4 (8.7-17.4)		3.5 (1.6-7.8)		20.5 (15.4-26.8)	
	High	28.2 (22.4-34.8)		38.3 (31.4-45.8)		13.0 (9.3-17.9)		1.8 (0.7-4.4)		23.1 (17.7-29.6)	
<b>Area of residence</b>	Rural	22.3 (17.9-27.4)	0.006	31.8 (26.5-37.7)	0.003	13.6 (11.0-16.8)	<0.001	1.7 (0.8-3.6)	0.133	15.8 (12.3-20.1)	0.010
	Urban	30.8 (27.9-33.8)		42.7 (38.9-46.6)		6.2 (4.7-8.2)		3.3 (2.2-5.2)		23.8 (19.5-28.7)	

<sup>a</sup> cocaine, heroin, opium, glue, LSD, peyote <sup>b</sup> non-medical use of sedatives, tranquilisers, stimulants, analgesics <sup>c</sup> personal earnings from employment in the past 12 months, before taxes, excluding pensions and investments

demographic factors. This table indicates that 27.4% of the sample had smoked 100 or more cigarettes in their lifetime, 38.7% had ever used alcohol, 10.7% had ever used cannabis, 2.7% had used other substances such as cocaine, heroin, opium, glue, LSD or peyote, and 20.6% had used sedatives, tranquilisers, stimulants or analgesics for non-medical use. Significantly more males than females smoked cigarettes ( $p<0.001$ ) and significantly fewer Blacks smoked cigarettes compared with other RCSGs ( $p<0.001$ ). Smokers were also more likely to be employed ( $p<0.001$ ) and to live in urban areas ( $p=0.006$ ).

A larger proportion of males used alcohol compared with females ( $p<0.001$ ). A significantly smaller proportion of Indians/Asians used alcohol compared with the other RCSGs ( $p<0.001$ ). Significantly more alcohol users were employed ( $p<0.001$ ), and lived in urban areas ( $p=0.003$ ). The

anxiety disorders was lowest for panic disorder (0.7) and highest for agoraphobia (11.1), while the odds ratios of 12-month anxiety disorders was lowest for PTSD (0.3) and highest for agoraphobia (5.1). The odds ratios were 8.6 for lifetime major depression, and 4.3 for 12-month major depression.

Compared with non-tobacco users, tobacco users had a significantly higher likelihood of lifetime social phobia (OR=5.1;  $p=0.011$ ), and major depression (OR=12.1;  $p=0.027$ ), and had significantly higher odds of 12-month generalised anxiety disorder (OR=1.6;  $p=0.005$ ), major depression (OR=7.0;  $p=0.037$ ) and any anxiety or mood disorder (OR=14.7;  $p=0.004$ ). Alcohol users differed significantly from non-alcohol users with respect to the prevalence of lifetime social phobia, PTSD, major depression and any anxiety or mood disorder. Alcohol users also differed

**Table 2:** Prevalence of anxiety and mood disorders by substance use

		TOTAL		Tobacco Use		Alcohol Use		Cannabis		Other substances <sup>a</sup>		Non-medical use of prescription drugs <sup>b</sup>	
		Prevalence (95% CI)		100+ cigarettes % (CI)	p-value	Ever % (CI)	p-value	Ever % (CI)	p-value	Ever % (CI)	p-value	Ever % (CI)	p-value
<b>Lifetime DSM-IV Disorders</b>													
Anxiety Disorders	Panic Disorder	0.7 (0.3-1.3)		1.1 (0.4-2.8)	0.211	1.0 (0.4-2.3)	0.287	0.8 (0.1-5.8)	0.815	1.8 (0.2-12.1)	0.321	2.2 (1.0-5.1)	<0.001
	GAD with hierarchy	1.1 (0.7-1.7)		1.7 (0.9-3.5)	0.102	1.3 (0.6-2.5)	0.485	2.4 (0.9-6.4)	0.080	1.9 (0.3-13.3)	0.536	1.7 (0.7-4.0)	0.189
	Social Phobia	2.8 (2.0-4.1)		5.1 (2.7-9.6)	0.011	4.4 (2.4-8.1)	0.044	5.9 (2.7-12.5)	0.021	5.8 (0.8-33.4)	0.438	4.1 (2.0-8.3)	0.120
	Agoraphobia	11.1 (9.2-13.4)		10.0 (6.8-14.5)	0.498	12.2 (9.1-16.1)	0.387	8.8 (5.5-13.7)	0.276	4.0 (0.9-16.5)	0.142	10.8 (8.1-14.3)	0.816
	PTSD	4.5 (1.0-2.2)		2.1 (1.0-4.4)	0.230	2.6 (1.5-4.5)	0.004	5.1 (2.0-12.2)	0.003	10.6 (3.9-26.1)	<0.001	1.3 (0.4-3.6)	0.758
	Any anxiety disorder	14.7 (12.5-17.2)		16.4 (11.8-22.2)	0.388	17.7 (13.5-22.9)	0.063	17.7 (10.9-27.4)	0.405	24.1 (9.9-48.1)	0.219	16.4 (12.7-20.9)	0.312
Mood Disorders	Major Depression	8.6 (7.1-10.3)		12.1 (8.4-17.1)	0.027	11.8 (9.0-15.5)	0.001	15.4 (10.1-22.7)	0.003	27.2 (10.8-53.6)	0.009	12.8 (9.1-17.7)	0.010
	Any anxiety or mood disorder	19.7 (17.3-22.3)		23.3 (18.0-29.8)	0.092	24.1 (19.7-19.1)	0.007	26.8 (19.4-35.8)	0.054	42.5 (21.0-67.3)	0.021	24.4 (19.8-19.6)	0.027
<b>12-month DSM-IV Disorders</b>													
Anxiety Disorders	Panic Disorder	0.5 (0.2-1.1)		1.1 (0.4-2.8)	0.068	0.7 (0.3-1.9)	0.415	0.8 (0.1-5.8)	0.594	1.8 (0.2-12.1)	0.199	2.2 (1.0-5.1)	<0.001
	GAD with hierarchy	0.7 (0.4-1.3)		1.6 (0.8-3.4)	0.005	1.2 (0.6-2.5)	0.062	2.4 (0.9-6.4)	0.007	1.9 (0.3-13.3)	0.295	0.9 (0.3-2.8)	0.691
	Social Phobia	1.9 (1.3-2.8)		2.9 (1.2-6.5)	0.192	2.7 (1.3-5.3)	0.189	4.3 (1.6-10.5)	0.042	4.8 (0.5-35.8)	0.361	3.3 (1.5-7.1)	0.067
	Agoraphobia	5.1 (3.9-6.6)		4.9 (2.9-8.2)	0.872	4.9 (3.1-7.9)	0.898	5.0 (2.5-9.8)	0.958	0	-	4.1 (2.8-6.0)	0.259
	PTSD	0.3 (0.2-0.7)		5.4 (0.2-1.9)	0.296	0.6 (0.2-1.6)	0.030	1.4 (0.4-4.9)	0.006	1.9 (0.3-12.8)	0.055	0	-
	Any anxiety disorder	7.1 (5.5-9.0)		8.8 (5.8-13.2)	0.102	8.1 (5.3-12.3)	0.340	10.1 (5.5-17.9)	0.181	10.4 (2.5-34.3)	0.532	8.1 (5.3-12.1)	0.384
Mood Disorders	Major Depression	4.3 (3.3-5.6)		7.0 (4.4-10.9)	0.037	6.1 (4.3-8.7)	0.012	11.0 (6.9-17.2)	<0.001	21.0 (7.2-47.5)	0.002	6.7 (4.2-40.7)	0.059
	Any anxiety or mood disorder	10.3 (8.5-12.5)		14.7 (10.7-19.8)	0.004	12.9 (9.9-16.8)	0.019	19.6 (13.3-27.7)	0.001	26.6 (10.5-52.6)	0.025	12.9 (9.6-17.2)	0.086

<sup>a</sup> cocaine, heroin, opium, glue, LSD, peyote; <sup>b</sup> non-medical use of sedatives, tranquilisers, stimulants, analgesics; Note: GAD= generalised anxiety disorder; PTSD= post-traumatic stress disorder

**Table 3:** Crude associations between anxiety and mood disorders, and substance use, using regression analyses

		Tobacco Use		Alcohol Use		Cannabis		Other substances <sup>a</sup>		Non-medical use of prescription drugs <sup>b</sup>	
		OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
<b>Lifetime DSM-IV Disorders</b>											
Anxiety Disorders	Panic Disorder	2.5 (0.6-8.4)	0.223	2.1 (0.5-8.3)	0.298	1.3 (0.2-11.0)	0.815	2.8 (0.3-25.1)	0.342	9.3 (2.4-35.5)	0.001
	GAD with hierarchy	2.2 (0.8-5.8)	0.110	1.4 (0.6-3.4)	0.487	2.7 (0.8-8.9)	0.093	1.9 (0.2-15.6)	0.543	1.9 (0.7-5.2)	0.196
	Social Phobia	2.7 (1.2-5.8)	0.014	2.5 (1.0-6.0)	0.050	2.5 (1.1-5.4)	0.025	2.2 (0.3-16.5)	0.449	1.7 (0.9-3.2)	0.124
	Agoraphobia	0.9 (0.5-1.4)	0.499	1.2 (0.8-1.8)	0.388	0.7 (0.4-1.3)	0.278	0.3 (0.1-1.6)	0.162	1.0 (0.7-1.4)	0.816
	PTSD	1.8 (0.7-4.6)	0.236	3.8 (1.5-9.7)	0.007	5.2 (1.6-16.8)	0.006	9.8 (2.9-32.5)	<0.001	0.8 (0.2-2.8)	0.758
		Any anxiety disorder	1.2 (0.8-1.8)	0.388	1.5 (1.0-2.2)	0.064	1.3 (0.7-2.3)	0.406	1.9 (0.7-5.3)	0.226	1.2 (0.9-1.6)
Mood Disorders	Major Depression	1.8 (1.1-2.9)	0.029	1.9 (1.3-2.8)	0.001	2.2 (1.3-3.6)	0.003	4.3 (1.3-13.7)	0.016	1.8 (1.2-2.9)	0.011
	Any anxiety or mood disorder	1.4 (0.9-1.9)	0.092	1.6 (1.1-2.1)	0.008	1.6 (1.0-2.5)	0.056	3.2 (1.1-8.7)	0.028	1.4 (1.0-1.9)	0.027
<b>12-month DSM-IV Disorders</b>											
Anxiety Disorders	Panic Disorder	4.1 (0.8-20.8)	0.091	1.9 (0.4-9.2)	0.423	1.8 (0.2-16.1)	0.599	3.8 (0.4-35.7)	0.232	49.5 (9.4-259.4)	<0.001
	GAD with hierarchy	4.5 (1.4-13.8)	0.010	2.9 (0.9-9.0)	0.074	4.9 (1.4-17.3)	0.015	2.9 (0.3-24.8)	0.318	1.3 (0.3-5.2)	0.691
	Social Phobia	1.9 (0.7-5.0)	0.199	1.9 (0.7-5.0)	0.196	2.7 (1.0-7.4)	0.050	2.7 (0.3-26.6)	0.381	2.2 (0.9-5.0)	0.073
	Agoraphobia	1.0 (0.6-1.6)	0.872	1.0 (0.5-1.8)	0.898	1.0 (0.6-2.1)	0.958	-	-	0.8 (0.5-1.2)	0.260
	PTSD	2.3 (0.5-11.3)	0.309	4.6 (1.0-20.7)	0.047	7.2 (1.4-36.3)	0.017	6.8 (0.7-64.5)	0.096	-	-
		Any anxiety disorder	1.4 (0.9-2.2)	0.104	1.3 (0.7-2.3)	0.341	1.6 (0.8-3.1)	0.184	1.6 (0.4-6.4)	0.535	1.2 (0.8-1.9)
Mood Disorders	Major Depression	2.2 (1.1-4.6)	0.034	2.0 (1.2-3.5)	0.013	3.4 (1.9-6.4)	<0.001	6.7 (1.7-25.6)	0.007	1.9 (1.0-3.8)	0.063
	Any anxiety or mood disorder	1.8 (1.2-2.7)	0.004	1.6 (1.1-2.3)	0.019	2.4 (1.4-4.0)	0.001	3.3 (1.1-9.8)	0.033	1.9 (1.0-2.0)	0.087

<sup>a</sup> cocaine, heroin, opium, glue, LSD, peyote; <sup>b</sup> non-medical use of sedatives, tranquilisers, stimulants, analgesics; Note: GAD= generalised anxiety disorder; PTSD= post-traumatic stress disorder

**Table 4:** Adjusted associations between anxiety and mood disorders and substance use using regression analyses

		Tobacco Use		Alcohol Use		Cannabis		Other substances <sup>a</sup>		Non-medical use of prescription drugs <sup>b</sup>	
		OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
<b>Lifetime DSM-IV Disorders</b>											
Anxiety Disorders	Panic Disorder	3.1 (0.7-13.7)	0.129	2.5 (0.8-7.8)	0.0124	1.4 (0.2-11.3)	0.731	3.1 (0.3-33.5)	0.349	9.5 (2.5-36.5)	0.001
	GAD with hierarchy	3.0 (1.0-9.4)	0.061	1.5 (0.6-3.8)	0.373	3.2 (0.9-12.2)	0.082	2.0 (0.2-17.6)	0.516	1.67 (0.7-5.1)	0.214
	Social Phobia	3.9 (1.5-10.1)	0.006	3.0 (1.1-7.9)	0.030	2.9 (1.1-7.5)	0.025	2.3 (0.3-21.6)	0.460	1.7 (0.9-3.4)	0.113
	Agoraphobia	1.2 (0.8-2.1)	0.390	1.6 (1.0-2.5)	0.044	1.0 (0.6-1.8)	0.997	0.4 (0.1-2.0)	0.266	1.0 (0.7-1.4)	0.966
	PTSD	2.7 (0.8-9.1)	0.119	5.2 (2.0-13.4)	0.001	8.1 (2.3-29.2)	0.002	12.5 (3.9-40.6)	<0.001	0.8 (0.2-2.8)	0.712
		Any anxiety disorder	1.8 (1.1-2.9)	0.011	2.0 (1.3-3.2)	0.004	1.7 (0.9-3.3)	0.087	2.4 (0.8-6.8)	0.108	1.2 (0.9-1.7)
Mood Disorders	Major Depression	3.0 (1.7-5.4)	<0.001	2.7 (1.8-3.9)	<0.001	3.1 (1.8-5.5)	<0.001	5.6 (1.7-18.1)	0.005	1.8 (1.2-2.0)	0.011
	Any anxiety or mood disorder	2.2 (1.4-3.2)	<0.001	2.1 (1.5-3.1)	<0.001	2.2 (1.3-3.6)	0.003	4.0 (1.5-11.1)	0.008	1.5 (1.1-2.0)	0.020
<b>12-month DSM-IV Disorders</b>											
Anxiety Disorders	Panic Disorder	6.9 (1.5-31.7)	0.014	2.3 (0.8-6.5)	0.215	2.1 (0.3-16.3)	0.471	4.3 (0.4-52.8)	0.247	50.5 (9.5-268.4)	<0.001
	GAD with hierarchy	6.2 (1.5-25.7)	0.012	3.1 (0.9-10.3)	0.065	5.5 (1.2-25.4)	0.028	2.9 (0.3-27.6)	0.356	1.3 (0.3-5.1)	0.723
	Social Phobia	3.5 (1.0-12.9)	0.059	2.7 (0.9-8.0)	0.066	4.4 (1.5-13.0)	0.009	3.7 (0.3-42.6)	0.296	2.2 (1.0-5.1)	0.063
	Agoraphobia	1.9 (1.1-3.1)	0.016	1.5 (0.7-3.0)	0.289	1.7 (0.7-3.8)	0.216	-	-	0.8 (0.5-1.3)	0.356
	PTSD	3.1 (0.4-24.2)	0.276	5.9 (1.3-27.6)	0.025	10.4 (1.5-70.1)	0.017	7.5 (0.7-75.2)	0.086	-	-
		Any anxiety disorder	2.9 (1.8-4.6)	<0.001	2.0 (1.0-3.8)	0.043	2.6 (1.2-5.6)	0.012	2.2 (0.5-9.9)	0.284	1.3 (0.8-2.0)
Mood Disorders	Major Depression	4.7 (2.2-10.0)	<0.001	3.0 (1.7-5.4)	<0.001	6.3 (3.0-13.2)	<0.001	10.2 (2.8-37.0)	0.001	1.9 (1.0-3.8)	0.060
	Any anxiety or mood disorder	3.8 (2.5-5.8)	<0.001	2.4 (1.5-3.7)	<0.001	4.1 (2.3-7.4)	<0.001	4.7 (1.6-14.4)	0.006	1.4 (1.0-2.1)	0.058

<sup>a</sup> Adjusted for age and gender; <sup>b</sup> cocaine, heroin, opium, glue, LSD, peyote; <sup>c</sup> non-medical use of sedatives, tranquilisers, stimulants, analgesics; Note: GAD= generalised anxiety disorder; PTSD= post-traumatic stress disorder

significantly from non-alcohol users with respect to the prevalence of 12-month PTSD, major depression and any anxiety or mood disorder. Those who had ever used cannabis differed significantly from those who had never used cannabis with respect to the prevalence of lifetime social phobia, PTSD, major depression, and 12-month generalised anxiety disorder, PTSD, major depression and any anxiety or mood disorder. Users of other drugs differed significantly from non-users with respect to the prevalence of lifetime PTSD, major depression and any anxiety or mood disorder, and to 12-month major depression and any anxiety or mood disorder. The proportion of individuals who reported non-medical use of prescription drugs differed significantly from non-users with respect to the prevalence of lifetime panic disorder, major depression and any anxiety or mood disorder, and 12-month panic disorder.

Table 3 presents associations between any anxiety or mood disorders

and substance, while Table 4 presents associations adjusted for age and gender. It is evident from Table 3 and Table 4 that the odds of comorbid psychopathology are increased in the presence of substance use compared with the odds of psychopathology in the absence of substance use. For example, the odds of having any lifetime anxiety or mood disorder was 1.4 with use of tobacco and non-medical use of prescription drugs, 1.6 with use of alcohol or cannabis, and 3.2 with use of other substances (Table 3). The equivalent odds on adjustment for age and gender were 2.2 and 1.5 for tobacco use and non-medical use of prescription drugs respectively, 2.1 and 2.2 for alcohol and cannabis use, and 4.0 for other substance use (Table 4). Similarly, the odds of a 12-month mood or anxiety disorder, on adjustment for age and gender, were 1.4 for non-medical use of prescription drugs, 2.4 for alcohol use, 3.8 for tobacco use, and 4.1 and 4.7 for cannabis and other substance use respectively (Table 4).

On adjustment for age and gender, there was approximately a twofold increased likelihood of lifetime psychopathology, and a threefold increased likelihood of 12-month psychopathology in tobacco users versus non-tobacco users. Tobacco users had a six- sevenfold increased likelihood of 12-month panic or generalised anxiety disorder over non-tobacco users, and a 5-fold increased likelihood of 12-month major depression. The increased likelihood of lifetime and 12-month PTSD in alcohol, cannabis and other drug users, the increased likelihood of 12-month major depression in cannabis and other drug users, and the increased likelihood of lifetime and 12-month panic disorder in individuals who reported non-medical use of prescription drugs, were significant.

On adjustment for age and gender, lifetime generalised anxiety disorder (GAD) was not significantly associated with any of the substances of use examined, while lifetime agoraphobia, panic disorder, PTSD and social phobia were associated with only some of the selected substances of use. Similarly, with regards to 12-month disorders, the specific disorders were significantly associated with certain, and not all, the selected substances of use. Both lifetime and 12-month major depression were significantly associated with all (barring one) the selected substances of use.

## Discussion

The main findings of the study were that, in young adults 1) substance users were more likely than non-substance users to be male, White, employed and living in urban environments, 2) lifetime and 12-month anxiety or mood disorder was more likely to occur in substance users than in non-users of substances, and 3) strengths of association between psychopathology and substances of use were higher in relation to specific psychopathology (for example PTSD) and specific substances of use (for example, cannabis and alcohol) .

Overall, the results obtained concur with previous findings that males were more likely than females to smoke [19], and to have been regular users of alcohol [35] and other drugs. These results possibly reflect the stereotypical norms of male socialisation with regards to cigarette smoking and alcohol use. However, recent evidence suggests that, as traditional gender roles start to equalise, prevalence of female substance use might approach that of males, with potentially similar consequences regarding substance-related morbidity [36].

Employed individuals were more likely to use substances, possibly reflecting greater access to disposable income, compared with unemployed individuals. However, substance users did not differ significantly from non-substance users with respect to income, thus suggesting that factors other than economic resources and linked to employment status, such as access to particular social networks, may also be operative.

Blacks were the least likely of the RCSGs to smoke cigarettes, potentially suggesting a protective factor(s) against cigarette smoking among the Blacks in this sample, or an increased rate of cigarette smoking in the non-Black population, or a link between being Black and being unemployed. Similarly, individuals of Indian or Asian origin were the least likely to use alcohol, cannabis or any substances other than cigarettes. These findings concur with that of studies reported by Rodriguez et al. [37] who found associations between unemployment and substance abuse, but also demonstrated differences between population groups in terms of the impact that factors such as gender, marital status, employment status, job satisfaction and educational level had on health and wellbeing. Other reports from the SASH study showed that there were marked racial differences on all indicators of economic status including education, income, employment, and ownership of material resources [38]. The latter authors suggested that it might be important to distinguish between minority status and racial-ethnic groups when assessing the impact of sociodemographic factors on the mental health of individuals in South Africa.

Substance users in the SASH sample were more likely than non-substance users to have had lifetime or 12-month anxiety disorders or major depression, irrespective of the choice of substance use. In addition, the results in the current study indicated statistically significant associations between psychopathology and substance use, irrespective of the substances of use. These findings echo those of several earlier studies reviewed by Saban and Flisher [11] that indicated increased

risk of psychiatric disorder with substance use [11]. The trends in this younger adult sample are also similar to those in the National Comorbidity Survey- Replication (NCS-R), with the prevalence of the anxiety disorders exceeding that of the mood disorders [39]. Further, these results similarly concur with the findings of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) [40].

The results also indicate that illicit substances such as cannabis have a manifold increased risk of psychopathology with adjustment for age and gender. The Australian National Survey of Mental Health and Well-being (NSMHWB) reported similar findings in relation to adult anxiety disorders [28]. It is thus important that the risks of psychopathology with cannabis use be emphasised, particularly in communities where exposure to cannabis use is high. It is also important that the factors that place individuals at risk of cannabis use are identified and addressed, both to protect against cannabis use, and to decrease the risk of associated psychopathology.

The results indicated relatively high increased odds of lifetime and 12-month PTSD, particularly when PTSD was comorbid with alcohol or cannabis. Earlier studies with substance-using inpatients and war veterans also provided evidence for a strong association between PTSD and substance use and related disorders [41,42]. However, these studies have cautioned that the associations be considered with particular reference to the role of trauma in more general family or social dysfunction. Thus, it might be necessary to identify the factors that predispose individuals with PTSD diagnoses to substance use, and particularly alcohol and cannabis use, and to identify the factors that increase the risk of PTSD in substance users [43].

Several limitations of the SASH study should be recognised when interpreting these results. Firstly, the SASH sample excluded individuals who were in prison, hospital or mental institutions, or who lived on military bases. Thus psychiatric disorders or substance use pertinent to these categories of individuals would have been underestimated or excluded from the sample. These include, for example, antisocial personality disorders and available substances of use in the prison population, psychiatric or substance use diagnoses that might have precipitated admission in hospital or mental institution patients, and PTSD that might have been more prevalent in soldiers than in the non-military community. Secondly, the SASH survey assumed equal chance of representation of mentally ill and healthy subjects in the sample, even though individuals with psychopathology are known to be less likely than those without psychopathology to be willing participants in surveys, particularly when those surveys relate to mental illness [44] (citing Kessler, Wittchen and Abelson, 1998). These are factors that might have skewed the prevalence of psychopathology in favour of mentally-healthy individuals, and provided an under-estimate of substance use. Thirdly, the SASH data excluded psychiatric diagnoses such as bipolar disorder, oppositional defiant disorder, conduct disorder, attention deficit hyperactivity disorder, obsessive compulsive disorder, specific phobia and separation anxiety disorder, thus limiting the associations between psychopathology and substance use that could be examined. Fourthly, the cross-sectional nature of the sample did not permit identification of causative factors in the associations, or the temporal order of co-occurring psychopathology and substance use. Fifthly, the SASH data relied on self-reports. The reliability of the information obtained might thus have been compromised if, for example, use of substances was under- or over-reported, particularly since this information was not verified with biomarkers. Lastly, the statistical analyses for this study involved multiple comparisons between variables, suggesting that the statistically significant results might have been chance findings and, thus, subject to error. This error could have benefitted from adjustment using the Dunn-Bonferroni correction. However, this correction was not applied here since an inherent limitation of the method is to increase the probability of false negative results, thus reducing statistical power in the study.

## Conclusion

The results obtained highlight the prevalence of substance use in young adults, with particular reference to sociodemographic factors and the most commonly-occurring psychiatric diagnoses, and have provided compelling evidence for an association between psychopathology and substance use.

## Competing interests

The authors declare no competing interests.

## Authors' contributions

All the authors participated in the development of the study and/or the preparation of the manuscript. All the authors have approved the final manuscript. Authors DJS and DW were the PIs for the SASH study, author AS was responsible for drafting the manuscript, authors DJS, NM, LL and DW were involved with revisions of the manuscript, and author AG was responsible for the data analyses. Alan Flisher sadly passed away before completion of the final draft of the manuscript. All the authors have read and approved the final version of the manuscript.

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## Research

# Barriers to antenatal syphilis screening in Burkina Faso

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**Introduction:** Despite advances in treatment and management, syphilis remains a major public health problem in Burkina Faso. Syphilis in pregnancy poses major health risks for the mother and the fetus and also increases the risk for HIV transmission. Despite its potential benefits, antenatal syphilis screening is often poorly implemented in many sub-Saharan African countries. The purpose of the study is to identify and understand barriers affecting health system performance for syphilis screening among pregnant women in Burkina Faso.

**Methods:** We conducted in-depth interviews and observations in the Kaya health district, Burkina Faso. Participants were purposively selected to capture a range of perspectives across different actors with different roles and responsibilities. Seventy-five interviews were conducted with health providers, district managers, facility managers, traditional healers, pregnant women, community health workers, and Non-Governmental Organizations (NGO) managers. Interviews were transcribed and organized into codes and categories using NVivo software.

**Results:** Participants identified multiple barriers at health providers and community levels. Key barriers at provider level included fragmentation of services, poor communication, low motivation for prescription, and low awareness of syphilis burden. Cost of testing, distance to laboratory and lack of knowledge about syphilis were identified as barriers at community level.

**Conclusion:** The study highlights barriers such as distance, cost of testing, and knowledge about syphilis. The introduction of point of care testing for syphilis could be an entry point for improving coverage of antenatal syphilis screening.

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## Introduction

Despite several advances in treatment and management, syphilis remains a major public health problem. The World Health Organization (WHO) estimates that there are twelve million new cases of syphilis worldwide each year [1]. Ninety percent of syphilis cases occur in low income countries [1] and the prevalence ranges from less than 1% to 10%. African studies show prevalence during pregnancy of 2% in Mali [2], 3% in Nigeria [3], 5% in Botswana [4], and 7.3% in Tanzania [5]. In Burkina Faso, Kirakoya-Samadoulougou et al found a low prevalence of syphilis during pregnancy at national level but with important regional variations [6]. For instance, in Kaya District the prevalence was 7.5 in 2009 whereas in Ouagadougou it was 1% [7].

Syphilis in pregnancy poses major health risks for the mother and the fetus and also increases the risk for HIV transmission [8]. The World Health Organization (WHO) estimates that two million pregnant women each year are infected with syphilis globally [2]. The risk of vertical transmission could be up to 80% in early latent syphilis [2]. Approximately 1.2 million pregnant women with syphilis transmit the infection to their

newborn every year [9]. It is estimated that 492 000 infants in sub-Saharan Africa die annually from congenital syphilis [10]. In Tanzania, a clinic-based study found that a quarter of women with high-titer active syphilis infection had stillbirths compared with 1% among seronegative women [11].

Maternal syphilis is detectable by serological screening and entirely treatable with penicillin. Therefore, screening and treatment for syphilis has been recommended as a routine part of antenatal care [12,13]. In Burkina Faso, syphilis screening is recommended for premarital tests and during pregnancy [14]. Unfortunately, antenatal syphilis screening is often poorly implemented in many sub-Saharan African countries [15]. Currently, only 30% of women with syphilis are screened and treated in developing countries [16]. The influence of health systems issues on timely prenatal syphilis screening has been observed in several countries, including Bolivia, Kenya and South Africa [17]. In West African countries such as Burkina Faso, barriers to syphilis screening are understudied.

In this study, we sought to identify and understand barriers affecting health system performance for syphilis screening among pregnant

women in Burkina Faso. Existing literature on syphilis screening among pregnant women suggests that antenatal care (ANC) is the cornerstone for the control of maternal syphilis. Thus, factors affecting attendance to ANC are likely to affect syphilis screening for pregnant women. We therefore explored various factors at policy, health provider, patient, and community levels that are likely to drive syphilis screening levels.

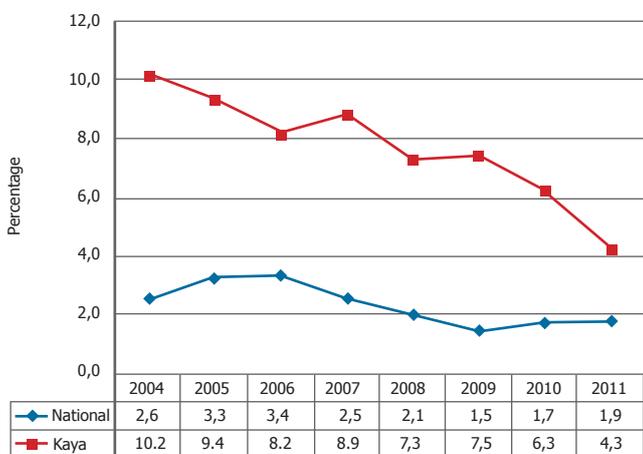
## Methods

### Study design

We conducted a Multilevel Assessment (MLA) [18] comprising of qualitative interviews and observations, as well as a review of existing data. For the latter, we assessed health information systems records, policy documents, service provider guidelines, training manuals, monitoring and evaluation reports and other relevant research reports and published literature. These data enabled us to investigate how the syphilis screening policy was implemented at facility level, the available indicators of its health outcomes, and any documented barriers to its implementation to date. The in-depth interviews were held with health providers, district managers, facility managers, traditional healers, pregnant women, community health workers, and representatives of national and international Non Governmental Organizations (NGOs) which work on maternal and child health issues to explore barriers and constraints which affect the effective delivery of maternal syphilis screening. During data collection, the first author also observed interactions between health workers and clients in selected health facilities.

### Study setting

The study was conducted in the Kaya health district, based in the central north region of Burkina Faso. Kaya district has 484 932 inhabitants, 40 primary health facilities and is a sentinel site for the national AIDS and STI control program. We conducted this research in Kaya District because of the high syphilis prevalence relative to the national average. Figure 1



**Figure 1**  
Trends in syphilis prevalence from 2004 to 2011 in Burkina Faso. Source: report CMLS/Santé, 2010, 2011

presents the trend of syphilis prevalence among pregnant women from 2004 to 2009 in Kaya district and nationally. The study was nested in the Kaya Health and Demographic Surveillance System (Kaya HDSS), which was launched in 2007 by the Health Sciences Research Institute (IRSS). Kaya HDSS covers seven semi-urban areas and 18 villages of the district with a population of 48,131 inhabitants. In 2011, there were seven public primary health facilities that offered ANC, one faith-based health center and one regional hospital. The faith-based facility and the hospital did not offer ANC but their laboratories offer the venereal diseases research laboratory (VDRL) test and Treponema pallidum haemagglutination assay (TPHA). One pharmacy offered a rapid test for syphilis. The health facilities selected for the study were all located within Kaya HDSS area.

### Study population and sampling

The study population consisted of health providers, district managers,

Group	Number and position
District managers	1 pharmacist
	1 information systems specialist
	1 reproductive health specialist
	Head of District
	Head of regional laboratory
Health workers	2 lab technicians
	4 midwives
	6 auxiliary midwives
Community health workers	4 community care workers
	7 drug shop managers
NGO and private	2 NGO managers
	1 midwife
	1 lab technician
	1 pharmacist
Facility manager	7 (Primary health care center)
Community	35 pregnant women
	4 traditional healers

facility managers, traditional healers, pregnant women, community health workers, and NGO managers (Table 1).

The healthcare providers included doctors, midwives, nurses, laboratory personnel, and pharmacists. Participants were purposively selected to capture a range of perspectives across different actors with varying roles and responsibilities. In each health facility, five pregnant women were approached as they queued to receive antenatal services and informed about the study. For those who consented, the interview was held at the end of their visit. Although we initially planned to have focus group discussions (FGDs) with pregnant women, the number of women available for the FGDs was too small because data collection occurred during the rainy season.

### Data collection

Data were collected using interview guides that were adapted for each profile of respondent. The interview with pregnant women explored experiences of ANC, satisfaction with ANC, knowledge and perceptions of sexually transmitted infections (STIs) including syphilis, perceptions of existing point-of-care tests, opinion on the introduction of additional test. We sought to find out key informants' perception of ANC, management of STI during pregnancy, knowledge and perceptions of syphilis, barriers and constraints which affect the effective delivery of maternal syphilis screening, organizational and managerial issues, experience with point-of-care tests, and introduction of a rapid diagnostic test (RDT) for syphilis screening.

Data tools were pre-tested and appropriate modifications made before the final data collection. Data collection was conducted by the first author and two research assistants who are familiar with qualitative studies and have a social sciences background. Research assistants were trained on the study objectives, data collection tools, and processes before embarking on field data collection. Interviews with health providers, district managers, facility managers, and NGO managers were conducted in French while those with pregnant women, traditional healers and community workers were conducted in Mooré the local language. Appointments were made with community health workers, traditional healers, health providers, district managers, facility managers and NGO managers. All interviews were recorded using a digital recorder and files downloaded to a laptop the same day. Transcription was done by two transcribers. Interviews in Mooré were translated into French and transcribed.

### Data analysis

Interviews were transcribed into a text program and then uploaded on Nvivo software. An analytical grid of key themes was developed based on the list of possible barriers in our conceptual framework, the objectives of the research and familiarization with the first few transcripts. Additional themes that emerged during the process of re-reading of transcripts were coded. Thematic content analysis was employed to systematically analyze the content of each theme.

### Ethical issues

Ethical clearance was obtained from the University of Western Cape, the National Ethics Committee for Health in Burkina Faso and the Ethics Committee Review of the WHO. In addition, the study team obtained permission to conduct the research from the District authorities. Written informed consent was obtained from all participants.

## Results

Although the guidelines on the management of STIs recommend syphilis screening for all pregnant women, we found no information on the proportion of pregnant women routinely tested for syphilis at district, regional and national level. Our study findings highlight considerable weaknesses within operational systems for syphilis screening. In tracking a woman's journey from antenatal care (ANC) through to laboratory, the study documented several barriers at health provider and community levels.

### Barriers at health provider level

The first barrier to routine syphilis screening among pregnant women was related to providers' perception that syphilis in pregnancy was not an important issue relative to other diseases. In addition, health workers also felt that syphilis prevalence was low because most women who undertook the test were seronegative. As one auxiliary midwife who had worked in an urban facility since 2009 stated, "I have never found a positive test, all were negative." Related to this, some health workers felt that syphilis was more prevalent in urban areas and thus, screening was more systematic in urban-based facilities. One district manager noted "For syphilis screening it is not really systematic and I know that in urban facilities health workers prescribe it to all women but at rural facilities it is not systematic." Overall, we noted an absence of interventions and information on maternal syphilis in the district.

The second barrier to routine syphilis screening among pregnant women was related to the availability of screening equipment, which was particularly a challenge for rural facilities. One facility manager in a rural-based facility noted that, "I do not systematically prescribe syphilis test because we have no laboratory here." A mapping of the facilities in the district indicated that three facilities (one public and two private) offered the syphilis test. All three facilities were urban-based. The public facility hosts the laboratory of the regional hospital and performs rapid plasma reagin (RPR) and *Treponema pallidum* particle agglutination assay (TPHA) tests. Between August 2011 and August 2012, this facility had performed 279 RPR tests and 260 TPHA tests. Among the two private that offered screening, one was a pharmacy offering a point of care test, while the second was a faith based facility offering the RPR and TPHA test. At the private pharmacy, only four clients had requested a syphilis test between June 2011 and June 2012. At the faith based facility, 50 RPR tests and 10 TPHA tests were performed between August 2011 and August 2012. The third barrier was related to health workers' inability to communicate the need for syphilis screening to pregnant women. Health workers noted that it was difficult to convince women about the importance of screening for syphilis. This challenge was partly related to the need to collect multiple blood samples from women for an HIV test, as part of the PMTCT program, as well as for the syphilis test. According to one health worker, women did not understand the need for multiple blood tests: "when we do an HIV test, you get a blood sample. We said that they need to go to the laboratory and have another blood test to know if they have other diseases, they said no, it is the same blood you got here and tested it is not necessary to have another sample." Health workers acknowledged that they did not explain the importance of some of the examinations. For example, one manager in an urban-based facility noted that "Most of the time it is a lack of communication at our level, we do not tell to the women the importance of some exams, why this prescription..." The narratives from pregnant women corroborated this observation. One pregnant woman in a rural area stated "One day the health worker took blood from my left finger but I did not know if it is HIV test or not ...) I don't know because until now they have said nothing." The poor communication between health workers and pregnant woman may be related to the lack of routine training as the health workers stated that they had no specific training, except for a course on syphilis management during their professional training.

A fourth barrier was the fragmentation of services in a setting where geographic distance was already a barrier. Often women have to be referred to an external laboratory for the syphilis screening. According to health workers, many women live in rural areas and have to travel long distances to health facilities that offer screening services. One health worker commented, "we observe that most women are from villages around Kaya, they walk from their house to our facility and we ask them to do the test the day after. The distance from their house to the laboratory is same to our facility. Thus the majority do not go." We observed that

traveling from the nearest urban primary health facilities to the public laboratory would take about 1 hour by foot or 20 minutes by bicycle. Due to this situation, one urban health center had a lab technician who came to the facility to collect blood samples, but few women did the test.

### Barriers at community level

The cost of the syphilis test was reported to be a barrier for many women. At the public laboratory, RPR and TPHA cost the equivalent of USD 2-3. The point of care test cost more in the pharmacy (USD 3) compared with the faith based facility (USD 2). Although the cost of syphilis tests in the public sector is subsidized by the government, many women are not screened because of the cost of the test. One auxiliary nurse stated "There are women who keep the exam prescription until delivery because they said that they have no money for the exams."

Our findings also indicate that a pregnant woman's husband or partner plays a key role in the decision to be screened for syphilis. Due to exemption of fees, women do not carry a lot of money when they go for their ANC visit. When they receive a prescription for additional medical examinations, such as the syphilis test, they have to go back home and get money from their husband. Sometimes, women need approval from their husbands as illustrated by this quote from a midwife in an urban facility, "sometimes, until the delivery they (women) kept the prescription in their health card, when you ask them why, they explain that they gave it to the head of the family but he did nothing."

Findings also show that poor knowledge about syphilis was also a potential barrier to testing. For example, although many women could describe the symptoms of sexually transmitted infections (STIs) (itches, pimples, and vaginal discharge), many were unaware about syphilis or the consequences of untreated syphilis for the mother and child.

Finally, perceptions about syphilis also affected screening rates. In particular, the stigma surrounding sexually transmitted diseases was noted as a barrier to screening particularly in certain settings like pharmacies. One facility manager noted "the pharmacy advertised and gave the prices but you know women, it is difficult for them to go to the pharmacy and do an exam related to sex. They prefer to go to the laboratory of the hospital if they have money because it is a public service."

## Discussion

Syphilis screening is recommended for premarital tests and during pregnancy [14]. Although a policy that promotes syphilis screening in pregnant women exists in Burkina Faso, screening is very limited. Our findings identified several barriers to the uptake of syphilis screening among pregnant women in Burkina Faso.

Syphilis testing is largely dependent on the availability of adequate laboratory facilities [19]. However, our results suggest that the fragmentation of services is key barrier to the uptake of syphilis screening. Health workers often have to refer women to external laboratories and many women, particularly those living in rural areas, have to travel long distances to access these laboratories. Other studies have also reported that long distances to screening facilities are associated with delay or failure to screen [20, 21]. Our findings suggest the need to introduce a "one-stop" service point that including ANC, PMTCT and syphilis testing.

As highlighted in previous studies [22, 23], we found that low motivation of healthcare workers to prescribe syphilis screening also contributes to low screening. Although the need for continued antenatal screening for syphilis may be questionable in areas with low prevalence [24], health workers in the current study were not aware about the relatively high prevalence of syphilis in their district. Consequently, some health workers failed to prescribe the test. Treпка et al [25] also found that a lack of provider awareness of the prevalence of syphilis was associated with inadequate provision of screening test in the United States. The absence of interventions to increase syphilis screening and the lack of information on maternal syphilis in the district shows also the low prioritization of the problem. Efforts to increase awareness about syphilis are therefore warranted in order to enhance syphilis screening levels.

The relatively high cost of screening, despite government subsidies, also prevents pregnant women from being screened for syphilis. The cost for

testing was observed to range between \$2 and \$3 USD, a prohibitive cost in a country where 73% of population lives on less than \$2 a day [26]. The cost of screening is, therefore, a significant deterrent for many women particularly those who are financially dependent on their husband or partner. Women's financial dependency means that pregnant women's husbands or partners play a key role in the decision to be screened. Similar findings have been highlighted in previous studies [27-28] and underscore the need for male involvement in efforts to increase the uptake of syphilis screening among pregnant women.

Lack of knowledge about syphilis in the community was identified as a reason for not being screened. Most respondents at community level do not know the symptoms of syphilis nor its serious consequences for the unborn and born child. This misperception may be due to the lack of differentiation between STIs [29]. Most of STIs are recognized through symptoms and respondents do not realize that a STI could be asymptomatic. Community may also not perceive syphilis to be a problem because of its lack of visibility [30]. Low knowledge about syphilis might therefore pose a barrier to screening since pregnant women do not perceive the benefit of testing particularly for asymptomatic infections. As reported in a recent meta synthesis, many pregnant women did not feel the need to seek professional care when there is nothing wrong with their pregnancy [31]. Efforts to enhance awareness of syphilis and other STIs are therefore recommended.

Our study findings should be interpreted in light of several limitations. First, because of the exploratory nature of the study, we relied on qualitative methods and therefore our findings cannot be generalized to the larger population. Second, community's perceptions reflected mostly health services users. However, study findings highlight potential barriers to the uptake of syphilis screening. Further research using a more representative sample is warranted.

## Conclusion

Our study suggests that barriers such as distance to health facilities, cost of testing, and knowledge about syphilis among health workers and communities may limit screening levels and hinder the implementation of syphilis screening during pregnancy as recommended in national guidelines. Pregnant women often weigh the benefits of syphilis screening against the high direct and opportunity costs. Our results have several implications for efforts to improve screening levels. First, communication between health workers and clients needs to be improved in order to facilitate the acceptability of the test. Second, the introduction of point of care testing for syphilis during ANC may improve coverage of antenatal syphilis screening.

## Competing interests

The authors declare no competing interests.

## Authors' contributions

All the authors have contributed to this study in ways that comply to ICMJE authorship criteria. All the authors have read and approved the final version of this manuscript.

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## Research

# Locus of control and anti-hypertensive medication adherence in Ghana

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**Introduction:** Medication non-adherence is a major public health problem in Ghana. Locus of control (LoC) may influence adherence to medication. In this study we examine the association between locus orientation and adherence to hypertensive medication among adult patients. We also take into account the role of medication side effects.

**Methods:** We conducted a hospital-based cross-sectional study involving two tertiary hospitals in southern and northern Ghana. Data were collected from 400 hypertensive patients using a structured questionnaire. We gathered information on patient's sociodemographic characteristics, health LoC, side effects of anti-hypertensive medication and adherence to anti-hypertensive medication.

**Results:** Participants exhibited features of mixed LoC (both internal and external) usually referred to as bi-local expectancy. However, orientation was skewed towards external LoC. Females were marginally more likely than males to have an internal LoC. Education was associated with a greater likelihood of internal LoC. While most patients (93.3%) poorly adhered to antihypertensive medications, logistic regression model revealed that non-adherence was significantly associated with low internal LoC, medication side effects and the combined effect of medication side effects and external LoC.

**Conclusion:** Medication non-adherence, experiences of medication side effects and LoC are associated. Multifaceted intervention programmes highlighting personality characteristics like LoC may improve anti-hypertensive medication adherence.

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**Key words:** Locus of control, personality, bi-local expectancy, medication side effects, medication non-adherence, hypertension, individualism, collectivism, culture, Ghana

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## Introduction

As the global disease burden shifts from communicable to non-communicable diseases, hypertension has become a key public health problem. Hypertension is the leading risk factor for cardiovascular diseases and is a major cause of death globally [1]. Hypertension affects approximately 11% - 42% of Africans [2-5]. Twagirumukiza and colleagues [3] have projected that by 2025, 125.5 million people in sub-Saharan Africa will be affected. The prevalence of hypertension in Ghana has been estimated at 25% in urban and 20% in rural populations [6].

Hypertension requires long term management and follow-up. Adherence to therapy is a key component of management. Both pharmacologic (medications) and non-pharmacologic (psychotherapy, lifestyle) therapies are prescribed for hypertensive patients with the expectation that patients will be adherent [7-9]. However, many patients fail to adhere to treatment recommendations resulting in less than optimal treatment [10, 11]. The WHO estimates that adherence rate to pharmacotherapy

for hypertension is 50% [12]. According to Buabeng and colleagues [13], the level of non-adherence to anti-hypertensive medication in Ghana is about 93%. Medication side effects are often cited as the main barrier to adherence [10-12, 14-16].

Personality constructs like the locus of control (LoC) can influence health behavior and impact on illness and treatment [17]. The LoC concept stems from Rotter's social learning theory [18] which posits that individuals can be differentiated in terms of their internal or external source of control. People with an internal LoC take responsibility and decisions without any form of influence from the external world. Studies have shown that internally-driven people are more likely to adhere to prescribed treatment regimens because they believe in their ability to influence their health [19, 20]. Conversely, individuals with external LoC assign their experiences to forces in the outer world such as chance, fate or other people. Externally-driven people are thought to be less likely to adhere to therapy because of the belief that their actions may not appreciably affect health outcomes [21, 22]. Studies have shown that internal LoC is associated with adherence to daily peak expiratory

flow rate monitoring recommended for asthma management [19, 21], maintaining a gluten-free diet in the control of celiac disease [23], diabetic management [24], and use of antipsychotic medications in the management of schizophrenia [22].

Some studies have demonstrated that individuals are not entirely internal or external in their LoC; rather they consider different sources of control [18]. This leads to an exhibition of a mixed LoC also referred to as "bilocal" LoC [3] or "responsible internal" [25]. In addition, although LoC is often thought to be stable particularly in adulthood [26, 27], there is evidence suggesting that LoC may change over time [28]. Internal health LoC is associated with knowledge and attitude, psychological state, health behaviour, and better health conditions. External health LoC, on the other hand, is linked with negative health behaviours and weak psychological state [29]. High internal LoC has been found to be beneficial when barriers to medication adherence (e.g., side-effects, forgetting to take medication, and keeping track of pills) are low.

Although differences in locus orientation have been shown to be associated with health behaviour, differences in adherence behaviour in relation to LoC may be due to differences in the cultures of particular groups of people. Culture often drives societal values and distinguishes different groups of people [30]. Contrary to many studies conducted in the West that have found an association between a high internal LoC and positive health behaviours, studies conducted in other parts of the world have found different associations. Azlin and colleagues [31] observed, for example, that Malaysians with high internal LoC reported poor adherence to medications. This observation underscores cultural variability in locus orientation. Unlike western cultures which are more individualistic encouraging internal LoC, Eastern cultures tend to value collectivism, thus promoting external LoC [32, 33]. In individualistic cultures, individuals have greater personal autonomy and value the pursuance of individual goals of health and well-being to a large extent. In collectivist cultures however, individuals may not feel personally responsible for their health seeking behaviours due to greater social influence from the external world. Thus, an individual with an internal LoC in an individualistic culture may take great responsibility for his or her successes and failures about health whereas an individual with an internal LoC in a collectivist culture may take responsibility for successes and failures while placing emphasis on external factors. Although in South Africa one study showed a preponderance of bi-local expectancies [34], information regarding having this mixed LoC in view of the African cultural belief and medication adherence is inadequate. Additionally, cultural orientations may affect the responses of hypertensive patients towards their experiences with side effects. In general, however, there is a paucity of information regarding LoC, side effects and hypertensive medication adherence among Africans [20].

This study sought to examine the association between LoC and adherence to medications among hypertensive patients in Ghana. In addition, we assessed the possible influence of LoC on the association between medication side effects and adherence behaviour. We postulated that hypertensive patients with high internal LoC would be more adherent than those with external LoC. We also hypothesized that medication side effects would be associated with non-adherence, but that the association will be moderated by LoC.

## Methods

### Study setting

This cross-sectional study was conducted in two tertiary hospitals in southern and northern Ghana between May and July 2012. Korle-Bu Teaching Hospital (KBTH) is the premier and largest teaching hospital. KBTH serves the Greater Accra Region and surrounding areas. Komfo Anokye Teaching Hospital (KATH) is located in Kumasi, the Regional Capital of Ashanti Region. KATH is the second-largest hospital in the country. The hospital serves as the main referral facility for the Ashanti, Brong Ahafo, Northern, Upper East and Upper West Regions. Ashanti and Greater Accra are predominantly urban and are estimated to be home to over one-third of Ghanaians [35]. Both hospitals serve patients from diverse socio-cultural backgrounds.

### Study population

Study participants consisted of 400 hypertensive patients attending KBTH (n=200) and KATH (n=200). The minimum total sample size was determined using the statistical formula below where N is the required sample size, Z is the critical value corresponding to a 95% confidence interval (1.96), P is the estimated prevalence of hypertension (28.7%), and d is the desired level of precision taken here as 0.05 [36]:

$$N = Z^2 P (1-P) = 315/d^2$$

Participants were selected through a simple random process using a random number table [37]. Participants were adult male and female patients (above 18 years), diagnosed with hypertension or who were comorbid with other health conditions and reported having a prescription for at least one anti-hypertensive medication. Newly diagnosed, or patients who were not on any form of prescribed anti-hypertensive medications as well as in-patients, pregnant women and the incapacitated were excluded from this study.

### Study instrument

Data were collected using a researcher-administered semi-structured interview. Each interview lasted about 30 minutes. Measures included socio-demographic characteristics, health locus of control, adherence to medication, and side effects experienced. Health locus of control was assessed using the Multidimensional Health Locus of Control (MHLC) form C [38]. The MHLC scale measures variations in LoC beliefs in relation to health conditions [39] and assesses the extent to which a person believes that health status is influenced by one's actions, 'chance' and 'powerful others' (specifically 'doctors' and 'others') [40]. The MHLC Form C included 18 items assessing whether the respondents agreed or disagreed with belief statements about hypertension (Cronbach's alpha= 0.90).

Medication adherence was measured using the Morisky Medication Adherence Scale (MMAS) [41] which comprises 8 items (Cronbach's alpha = 0.79). MMAS scores can range from zero to eight with higher scores reflecting higher adherence. Participants were categorized as having low adherence, medium adherence and high adherence based on the number of positive responses obtained. Patients who scored low and moderate were eventually grouped in one category for analysis purposes [42].

The frequency at which patients experience various side effects associated with different anti-hypertensive medications was assessed with the 18-item Hypertensive Medication Side Effect Experience Scale (HMSEES) (Cronbach's alpha = 0.80). Responses were scored on a 5-point frequency response scale that ranged from never (0), rarely (1), sometimes (2), very often (3), and always (4). Item scores were added and responses categorized as low (score of 0-24), moderate (25-48) and high (49-72) experience of side effects.

### Data analysis

Data were analyzed using the Statistical Package for Social Sciences (SPSS) version 20 and R version 2.15.2. Descriptive statistics were computed to summarize the characteristics of study participants. The chi-square test was used to assess the bivariate association between health LoC and socio-demographic characteristics. Logistic regression analysis was used to assess the association between health LoC, side effects and medication adherence while adjusting for socio-demographic characteristics.

### Ethical issues

The Institutional Review Boards at the Noguchi Memorial Institute for Medical Research, Accra, and Committee of Human Research, Publications and Ethics, Kumasi approved all procedures used in this study. All participants provided informed consent from prior to data collection.

## Results

Four hundred hypertensive patients participated in the study (Table 1). The majority of study participants were 50- 59 years old, female (62.7%), and married (63.5%). Fifty-four percent had attained a minimum of secondary school education and 89.5% were Christians. Eighty-three

**Table 1: Descriptive characteristics of participants (N=400)**

Variable	Percentage
<b>Sex (%)</b>	
Male	37.3
Female	62.7
<b>Age (%)</b>	
< 20	0.3
20 – 29	3.0
30 – 39	5.0
40 – 49	17.8
50 – 59	32.5
60 – 69	26.3
≥ 70	15.3
<b>Marital status (%)</b>	
Single	9.8
Married	63.5
Widowed	18.3
Divorced/ Separated	6.3
Co-habiting	2.3
<b>Education Level (%)</b>	
No formal	12.0
Primary	8.3
Secondary	54.3
Tertiary	25.5
<b>Religious affiliation (%)</b>	
Christian (spiritual)	4.5
Christian (Charismatic/Pentecostal)	41.5
(Orthodox)	43.5
Muslim	5.0
African Traditional Religion	1.0
Other	4.5
<b>LoC (Mean/ standard deviation)</b>	
Internal LoC	1.54/ 0.499
External LoC	1.50/ 0.501
<b>Experience of medication side effects (%)</b>	
Low	39.8
Moderate	53.0
High	7.2
<b>Medication adherence (%)</b>	
Poor	93.3
High	6.7

**Table 3: Logistic regression model for LoC and side effects in relation to medication non-adherence behaviour**

Variable	Odds ratio	95% confidence interval	p value
High Internal LoC (Ref: Low internal LoC)	0.32	0.11 – 0.95	0.039
Low external LoC (Ref: High external LoC)	0.64	0.20 – 2.11	0.468
Low internal LoC(Ref: Low external LoC)	5.64	1.14 – 27.87	0.034
Low external "others"(Ref: high "others")	0.19	0.06 – 0.57	0.003
Low external "doctors"(Ref: high "doctors")	0.64	0.27 – 1.50	0.304
Low external "chance"(Ref: high "chance")	1.61	0.66 – 3.92	0.296
Moderate to high side effects (Ref: low side effects)	4.84	1.07 – 1.85	0.04
Side effects and external LoC (Ref: side effects and internal LoC)	2.4	0.35 – 16.31	<0.001

p < 0.05

side effects were more likely to be non-adherent than those who had low experiences of side effects (OR = 4.84 (1.07 – 21.85), p = 0.04). Participants reporting both medication side effects and external LoC had 2.4 times greater odds of non-adherence than participants with side effects and internal LoC (OR = 2.4 (0.35 – 16.31), p <0.001).

## Discussion

This study examined the association between personality characteristics (LoC) and medication adherence behaviour while taking into account medication side effects. We found that a very high proportion of patients (93%) did not adhere to their medications. The low level of adherence is similar to that reported by Buabeng and colleagues among hypertensive patients in Ghana [13]. These results underscore the need for interventions to improve adherence levels.

The health LoC construct has been one of the most widely considered predictors of health-related behaviour of patients. Previous research on medication adherence provides evidence linking internal LoC with adherence [20] and non-adherence [31]. The HLoC results from this study showed that hypertensive patients exhibited a blend of LoC. However, it is worth noting that though patients responded highly for both internal and external orientations, the pattern was skewed towards externality particularly, "doctors". It is possible that although patients feel that they are responsible for their health they also attribute health-related outcomes to doctors. This leads to the belief that the health of hypertensive patients is controllable, either by themselves or doctors, and is not as a result of chance, fate or luck [25]. Patients who are internally-driven have a sense of self-responsibility in following recommendations made by health professionals. According to Wallston and Wallston [25], mixed LoC could be a helpful coping mechanism for patients with chronic conditions and successful management of hypertension may mean patients encouraging themselves to adhere to their doctors' recommended regimen. In general, there is a paucity of information on the relationship between bilocal LoC and medication adherence behaviour although the general evidence from other studies predominantly associate bilocal LoC with positive attributes and behaviours [43, 44].

The presence of characteristics associated with low internal LoC and high external "others" accounted for the non-adherence observed. That is, patients with low internal LoC are less likely to take full responsibility for their illness and health behaviours. Additionally, having a high external LoC makes patients more likely to attribute their health actions to external forces instead of taking personal responsibility. Therefore observing a significant relationship between the variables and non-adherence confirmed that patients had a reduced tendency to adhere to prescribed treatment regimen, because they believe they cannot affect their own health behaviours. These findings are similar to studies by Omeje and Nebo (2011) [20] and Combes and Feral (2011) [22].

Though only marginally significant, results showed that women were more inclined towards internal LoC than males. This result contradicts the belief that females are less likely to possess internal LoC than males [45,46] while corroborating findings by Hamedoglu et al, 2012 [47] as well as Sariçam et al [48]. Internality was also associated with higher education.

Medication side effects were observed to be a potential factor that could repress adherence. The majority of hypertensive patients pointed out that they experienced moderate to high side effects which included difficulty sleeping, erectile dysfunction, reduced sexual drive, constipation, chest pain, depressed mood, headaches, cough, fatigue and dizziness. This

percent of participants resided in urban communities. Eighty percent had been diagnosed with hypertension for 10 years or less.

Variations in internal and external LoC were minimal indicating a mixed LoC (Table 1). Though patients demonstrated a mixed internal and external LoC orientation, responses were skewed towards externality. Chi square test results are shown in Table 2.

**Table 2: Comparing LoC with sex and educational level**

LoC	Sex		Educational level	
	Male (%)	Female (%)	Higher (%)	Lower (%)
High internal	13.5	34.8	25.0	23.3
Low internal	23.8	28.0	27.5	24.3
Chi square	$X^2 = 12.9574, p = 0.0003$		$X^2 = 4.5526, p = 0.0329$	
High external	13.5	32.8	21.5	24.8
Low external	23.8	30.0	31.0	22.8
Chi square	$X^2 = 8.9369, p = 0.0028$		$X^2 = 0.0273, p = 0.8687$	

Sex was significantly associated with internal LoC ( $X^2 = 12.9574, p = 0.0003$ ) and external LoC ( $X^2 = 8.9369, p = 0.0028$ ). Education was significantly associated with external LoC ( $X^2 = 4.5526, p = 0.0329$ ) but not internal LoC ( $X^2 = 0.0273, p = 0.8687$ ). The MMAS scores showed that majority (93.3%) of hypertensive patients poorly adhered to their medications (Table 1). Participants cut back or stopped taking their medication without telling the doctor because they felt worse when they took it, or stopped taking the medicine when they felt their blood pressure was under control. About 60% of patients experienced moderate to severe side effects associated with anti-hypertensive medications (Table 1). These side effects included difficulty sleeping, erectile dysfunction, reduced sexual drive, constipation, chest pain, depressed mood, headaches, cough, fatigue, and dizziness.

The logistic regression model results are presented in Table 3. Participants with high internal LoC had 68% lower odds of non-adherence than those with low internal LoC (OR = 0.32 (95% CI 0.11 – 0.95), p = 0.039). Likewise, participants exhibiting low internal LoC had 5.64 times greater odds of being non-adherent than participants with low external LoC (OR = 5.64 (1.14 – 27.87), p = 0.034). Participants scoring low on the "others" subscale of external LoC, had 81% lower odds of non-adherence than their counterparts with high "others" (OR = 0.19 (0.06 – 0.57), p = 0.003) Additionally, participants who experienced moderate to high

corroborates well-documented evidence on medication side effects being a major cause of non-adherence to therapy [12,14]. External LoC did not considerably influence medication adherence yet when employed, external LoC significantly moderated the relationship between side effects and adherence. The study shows that, external LoC on its own may not be a true predictor of adherence behaviour, but, in the presence of barriers to medication intake such as side effects, the role of external LoC is highly important, contrary to what has been reported in a prior study [49]. However, the possibility of patients managing high external LoC and employing an enhanced internality as an underlining preserve in managing experiences of side effects associated with medications can still be suggested. With the existence of barriers to medication intake, intervention programmes for non-adherence can be directed towards a greater involvement of personality characteristics such as LoC.

Some limitations must be acknowledged. First, although we selected participants from tertiary institutions that serve a diverse population, results may not be widely generalizable. Second, we included patients with co-morbid health conditions, which might have affected the outcomes we observed.

## Conclusion

Medication non-adherence dominates as a major health problem. The results of this study bring to bear a persistent problem of non-adherence to anti-hypertensive medication among the Ghanaian population, hence, highlighting the need for intervention programmes to enhance adherence to pharmacotherapy. The LoC construct has been one of the most widely considered predictors of health-related behaviour among patients. This study showed that hypertensive patients exhibited a mixed LoC referred to as "bilocal" LoC. Yet this mixed orientation was skewed towards externality. Experiences of medication side effects and medication non-adherence behaviour appear to be linked. Multifaceted intervention programmes that take into account factors like LoC may improve anti-hypertensive medication adherence.

## Competing interests

The authors declare no competing interests.

## Authors' contributions

Irene Kretchy: Data collection, analysis and interpretation of results, writing of manuscript; Frances Owusu-Daaku: contributed to development of concept, study design and review of manuscript; Samuel Danquah: contributed to development of concept, study design and review of manuscript.

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## Research

# Improving knowledge translation in Uganda: more needs to be done

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**Introduction:** Meeting the health-related Millennium Development Goals in Africa calls for better access to and higher utilisation of quality evidence. The mechanisms through which research evidence can effectively guide public health policy and implementation of health programmes are not fully understood. Challenges to the use of evidence to inform policy and practice include the lack of a common understanding of what constitutes evidence and limited insight on the effectiveness of different research uptake activities. Available Knowledge Translation (KT) models have mainly been developed in high income countries and may not be directly applicable in resource-limited settings. In this study we examine the uptake of evidence in public health policy making in Uganda.

**Methods:** We conducted a cross-sectional qualitative study consisting of in-depth interviews with 17 purposively-selected health policy makers and researchers. The study explored respondents' perceptions of the role of evidence in public health policy development, their understanding of KT and their views on the appropriateness of different KT activities that are currently implemented in Uganda.

**Results:** Although all respondents stated that evidence should inform health policies and programmes, they noted that this occurred infrequently. We noted a lack of conceptual clarity about KT and what precisely constitutes evidence. Respondents reported having been involved in different KT activities, including partnerships and platforms created for knowledge sharing between researchers and end users, but with very mixed results.

**Conclusion:** There is need for conceptual clarity on the notion of KT and an understanding of the most appropriate KT strategies in low-income settings.

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## Introduction

Most African countries are unlikely to meet the health-related Millennium Development Goals' (MDGs) targets by 2015 [1,2]. Accelerated progress can only be realised if the coverage of effective health interventions is scaled up. However, this remains a challenge partly as a result of weak health systems [3]. Existing evidence on validated interventions to strengthen the health system rarely informs health policy development and programming. Uptake of evidence in public health policy development and programme implementation has been a subject of research, mainly in high income countries. Several facilitating factors for knowledge translation (KT) have been documented including timely availability of good quality evidence, credibility of researchers, effective interactions between researchers and policy makers', availability of funding to implement research recommendations, and effective dissemination of evidence, among others [4,5].

Efforts to improve research uptake have involved the development of

models that can explain interactions between stakeholders and the evidence generated, and relationships between evidence and policy processes. Armstrong and colleagues [6] defined several models among which is the linear model which posits that evidence will lead to action. They argued that evidence that responds to identified knowledge gaps will guide policy [6]. The linearity model, however, does not take into consideration other factors that influence policy development, such as the political context and external influence. Enlightenment models highlight the importance of gradual sedimentation of ideas which over time may lead to change [7, 8]. Enlightenment models assume that policymakers stay in office for a fairly long time to allow for sedimentation; however, frequent turn-over of staff in policy making positions limits this model. Political and tactical models, where research is used by policy makers to justify government positions or to reduce the pressure to respond to a given problem, have been criticised for putting emphasis on research processes as opposed to getting evidence into policy [9]. Other KT models have focused on linkages between stakeholders, dissemination modalities of evidence and structures for decision making without adequate attention to the peculiar context of LIC [10,11]. These

peculiarities as pointed out by Young [12] include the chaotic policy making process characterised by donor influence, exaggerated role of civil society, and limited supply of good quality research.

Among the frameworks specifically proposed for low-income countries (LIC) is the Council on Health Research for Development (COHRED) framework encompassing five components namely; 1) research generation and decision making; 2) stakeholders involvement; 3) the mediators who help to link research and policy processes; 4) the research products – consideration for a series of different outputs beyond the research report; and 5) the larger context within which the decision-making and research processes take place [13]. This framework, however, does not specify capacity and institutional requirements for the framework to be applied. The Regional East African Community Health (REACH) policy initiative was established as a knowledge broker to bridge the gap between research and health policy decision making in East African countries. Efforts under REACH focused more on brokering between researchers and policy makers [13,14]. However, we note that uptake of evidence takes more than dissemination and linkage. Several KT activities have been tried in LIC including putting in place platforms bringing together researchers and policy makers, dissemination in various forms, use of policy entrepreneurs, building capacity of implementers to implement research recommendation but with varying results [5,13,15,16]. Several terminologies have been used to describe the research to action process among which is research application, getting evidence into policy and practice, evidence application, and 'making that leap between what we know and what we do'. The lack of appreciation of the role of evidence [4] and the lack of common terminology to describe the research to action processes have been cited in literature as possible hindrances to KT [17]. In this paper, we adopt the Canadian Institute for Health Research's (CIHR) definition of KT as "a dynamic and iterative process that includes synthesis, dissemination, exchange and ethically sound application of knowledge to improve health, provide more effective health services and products and strengthen the health care system"[18] This implies that KT is a process spanning the pre-evidence generation stage, evidence generation, synthesis, dissemination to application. Although this definition is widely accepted, there is a lack of clarity of the conceptualization of KT and multiple definitions still exists [17, 19]. Lack of conceptual clarity not only poses a challenge to putting in place mechanisms and activities to promote KT, but also monitoring the extent to which evidence is taken up into policy. Tetroe and colleagues underscored the need to understand the effectiveness of different KT activities [20].

Improving uptake of evidence in public health policy development and programming in low-income settings requires the generation of context-specific evidence on effective KT activities. Understanding stakeholders' perspectives of the KT process is a starting point. This study investigates the importance of evidence in public health policy making and programming in Uganda, and assesses stakeholders' conceptualization of KT and involvement in different KT activities.

## Methods

**Study design:** We conducted a cross-sectional qualitative study comprising in-depth interviews with key informants (KI) to explore their perceptions on the importance of evidence in public health policy development and programming, their understanding of KT, and their involvement in different KT activities.

**Participants:** Respondents included 15 health policy makers and two researchers who were purposively-selected on the basis of their day-to-day involvement in policymaking or research in health systems. All policy makers were members of the Health Policy Advisory Committee (HPAC), the policy advisory body for the health sector. The HPAC comprises of senior government officials from the central and district levels, and representatives of donor agencies, civil society organisation (CSOs), private not for profit (PNFP) organizations and the private-for-profit sector (PFP). Details of selected respondents are shown in Table 1.

**Procedures:** Interviews followed a guide that included probes on the informants' perception of the role of evidence in health policy development and programme design, their conceptualization of KT, and their involvement in various KT activities. The interview guide was pilot

Sector		No. in HPAC	No. selected
Public	Ministry of Health (5)		
	Central level	9	4
	District level	1	1
	Researcher from School of Public Health*	-	1
Private	Private not for profit (Civil society) (4)		
	Facility based	2	2
	Non facility based	2	2
	Researcher*	-	1
	Private for profit	1	1
Donors	Bilateral	4	2
	Multilateral	3	3
Total			17

HPAC: Health Policy Advisory Committee; \*Researchers are not members of HPAC

tested and revised accordingly. KI were initially contacted by email or telephone and invited to participate in the study. All interviews were conducted face-to-face by the first author. All interviews were audio-recorded and transcribed verbatim. The interviewer also took notes during the interviews.

**Analysis:** Data were manually analysed following the precepts of content analysis. Key stages in analysis included all authors independently identifying codes from which emergent views were developed and refined. Efforts were made to determine adequacy, credibility, usefulness and consistency of data in relation to the general objective of the study. Where interpretation differed, consensus was achieved through revisiting the raw data and discussions

**Ethical considerations:** This study was approved by the Institutional Review Board of the Institute of Tropical Medicine, Antwerp (Belgium) and the Uganda National Council for Science and Technology. All respondents provided informed consent prior to the interviews.

## Results

**Role of evidence:** Almost all respondents noted that evidence is important in guiding health policy and programming decisions because it shows what can and cannot work. However, several respondents stated that the use of evidence in policy development was limited and that politics and previous experience played a greater role in policy making. A Ministry of Health (MoH) official noted, "Currently there is little or no use of evidence, we are relying more on previous experience, politics and previous views on issues. We are developing so many policies that are not evidence based." A donor similarly remarked that "...policy in Uganda is guided by political influence not research evidence".

Some respondents raised a concern of a limited understanding of what evidence is as one of the hindrances to its uptake as elaborated in the following quotes:

*"The challenge is the narrow view of what evidence is. People think that evidence is what has been published in peer reviewed journals and this in a way limits the evidence that goes into our policy process. Evidence could be in a report that was done following a systematic approach"* Donor respondent

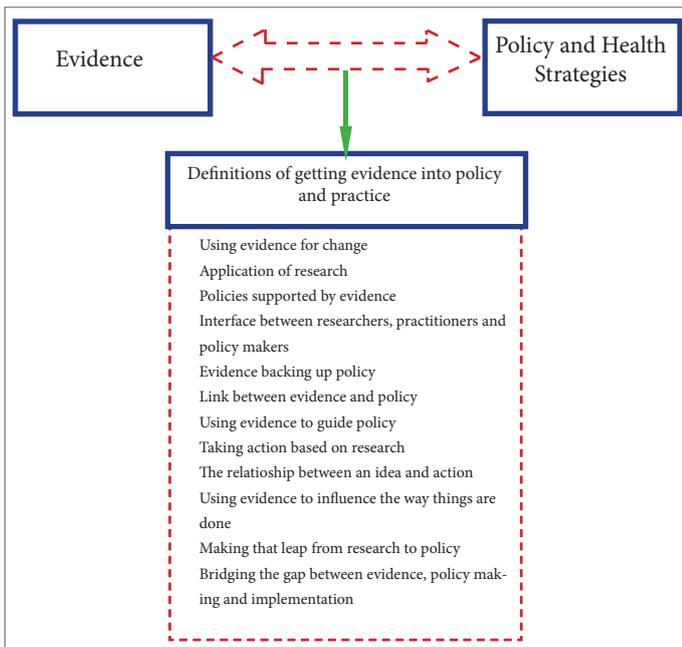
*"Evidence is very important for practice but also we need to define what is called evidence. Sometimes evidence to one is not evidence to another. Is it empirical or scientific? We need to know that policy development is sometimes driven by people who even do not sit to formulate the policy so what evidence do you give them?"* CSO respondent.

### Definition of KT

We noted significant variations in respondents' conceptualization of KT. The study identified 14 definitions of KT from our respondents (Figure 1). Some respondents defined KT as a relationship between stakeholders, between an idea documented in available evidence and action. Others referred to KT as taking action based on research while others defined it as having policies supported by evidence.

### Involvement in KT activities

Respondents reported having been involved in several KT activities as shown in Table 2. Majority of respondents reported involvement



**Figure 1:** Definitions of getting evidence into policy given by policy actors in Uganda

**Table 2:** Number of respondents who reported trying the different KT activities in Uganda

	MoH	Donors	CSO/PNFP	PFP	Researchers
Building partnerships/participation in partnerships	2	2	4	0	1
Putting platforms in place including researchers, policy makers, CSOs	4	1	2	0	0
Ensuring that Prioritized/commissioned research undertaken/supported	4	1	2		1
Dissemination	0	3	3	1	2
Ensuring MoH leadership in the KT process	1	0	0	0	0
Building capacity of implementers to implement research results	1	1	0	0	0
Demonstration that a given intervention works	0	1	4	0	0
Involving communities in research processes	0	1	0	0	0
Hiring independent credible researchers	0	1	0	0	0
Building basic research skills among stakeholders	0	0	1	0	0

MoH: Ministry of Health; CSO: civil society organization; PNFP: private not for profit; PFP: private-for profit sector

in partnerships at several stages including, research priority setting, undertaking research and policy development where they advocate for the adoption of evidence-based decisions. Partnerships in KT were described by some as difficult to define and implement. A donor respondent remarked that *“What is the best way to involve all stakeholders through the whole process? Should it be through regular updates, should it be in analysis? But how do you ensure independence of researchers?”*

Some respondents reported having put in place platforms for stakeholder engagement; however, the participation in and life span of these platforms varied considerably. Many platforms were implemented as a one off to follow a certain research process through, while one had been in place for a longer duration (up to four years). Platforms for KT were in most cases between two categories of stakeholders for example, civil society and policy makers, civil society and researchers, researchers and policy makers, or donors and policy makers. No respondent reported a platform purposively for KT involving more than two categories of stakeholders. A MoH focal person explained that interactions between researchers and policy makers were often limited to presentations by researchers to an audience of policy makers. Respondents emphasised the need to evaluate the effectiveness of these platforms as illustrated in the following quote by a researcher, *“Previous exercises of bringing policy makers and researchers together have not been reviewed, even WHO has not done any systematic evaluation on effectiveness of KT platforms”*

Undertaking or supporting commissioned research was identified as an

activity that facilitated KT because this ensured that research undertaken was addressing information gaps highlighted by policy makers. For example, the MoH had commissioned research on priority areas that had resulted in changes in the logistics systems as highlighted in the quote below from a MoH official:

*“Efforts undertaken include commissioning research. We as policy makers perceived the need for evidence and commissioned studies. We discussed results in technical fora that bring together researchers and policy makers specifically in the technical working groups (TWG). Here I have several examples where actually research has influenced policy. For example, the study on tracking medicines, we commissioned the research, good quality research was undertaken which was then discussed in the technical working group. This informed development of the medicines logistics system and quantification of medicines requirements”*

Dissemination took several modalities including meetings to present research reports, sharing policy briefs with senior health officials, publication in peer-reviewed journals and on websites, and face-to-face discussions with policy makers. Respondents reported that none of these methods worked consistently.

KIs from the CSOs mentioned sharing of evidence from their implementation research where they have demonstrated that a given intervention works. A CSO KI stated that *“In the case of TB/HIV integration, we noted that the programmes were running parallel and thought of ways we could gain from integration. We then decided to pilot integration to see what benefit it has and how it actually works and we got good results. We shared this with policy makers and it was easy to convince them”*

A donor respondent reported successful KT following implementation research stating, *“An example is the community HIV/AIDS programme. We demonstrated that it works through implementation research. Although global evidence was available that it was successful, people here were not convinced that it works. We undertook implementation research and we kept addressing problems as they arose, eventually people were convinced that it works.”* Similarly, an MoH official reported, *“We piloted injectable depo-provera at the community level, finalised the implementation research process and it is now policy”*

However, in some instances, despite demonstration that a certain intervention works through implementation research, KT has not been successful. For example, a respondent from a CSO stated that although there was evidence demonstrating the feasibility of task shifting to address the human resources for health challenges in Uganda, there has been little success in developing a task shifting policy. Additional efforts to influence the development of a task shifting policy were also unsuccessful as highlighted in the quote below by a researcher: *“We produced policy briefs on task shifting, we went ahead and disseminated them to policy makers and parliamentarians and they were discussed in these fora. This may not have been used as expected at country level (Uganda), but has been taken up by WHO and the global guidelines are being developed on task shifting”*

## Discussion

Our study aim was to increase our understanding of the utilization of evidence in health policy making and programming in Uganda, and to assess stakeholders’ conceptualization of KT and involvement in different KT activities. Majority of respondents agreed that although policies should be informed by evidence, this was not always the case in Uganda.

We noted that respondents had multiple, often limited, definitions of KT. The multiplicity and limited nature of definitions of KT may be a hindrance to KT in Uganda. None of the definitions provided showed an appreciation of understanding of KT as a prolonged process starting with the generation of evidence, synthesis, interpretation and subsequently application. Some respondents defined KT as a link between evidence and policy which infers a notion of a linear model. Previous studies have shown that linear models are not effective [2]. Most definitions were limited to one step in the research generation and application process and in most cases, when results were available [13]. Cordero et al, in their survey of funding agencies supporting KT in low-income settings, also noted a multiplicity of definitions [17].

Although respondents had been involved in several KT activities, the

outcomes of these activities varied. Partnerships between stakeholders were frequently mentioned. However, majority of partnerships were short lived and largely involved researchers and policy makers. In contrast to Armstrong et al [6] who emphasised the importance of a two way participation involving translation and exchange amongst stakeholders, we noted that knowledge sharing in these partnerships was mostly uni-directional with researchers sharing their results to an audience of policy makers.

The limited success of partnership may stem from several factors. First, it may imply presence of a very bureaucratic policy making process where the issue of providing evidence and policy development is restricted to a few stakeholders. Indeed, in an earlier study on use of evidence in policy development in Uganda, CSO respondents highlighted the bureaucratic policy making process as a hindrance, citing government restrictions on who participates in certain processes [21]. Second, the limited nature of partnerships could reflect people's understanding of who qualifies to be a stakeholder in KT. For example, a study carried out in Uganda by the COHRED revealed the limited involvement of civil society in health research [22]. Donors, on the other hand, have been shown to have un-due influence [12] and have in some instances required the undertaking of research as a pre-requisite to providing funding [23]. Third, the limited success of partnerships may stem from the challenges of engaging some of the stakeholders. Partnerships are more complex than perceived by the respondents in this study. Successful partnerships take into account varied capacity of stakeholders and the need to invest both time and resources [7]. Bergstrom et al, in their study on the relevance of the Promoting Action on Research Implementation in Health Services (PARIHS) framework in Uganda, identified the importance of community involvement [24] but noted that modalities of engaging the community effectively were not in place [24, 25]. The need to map out all relevant stakeholders and tailored modalities of engaging them has been emphasised in literature [26]. Theobald et al elaborated the need to develop partnerships at multiple levels and with multiple layers within the health system [26].

Respondents identified instances where evidence has informed policy and strategy development, for example, in cases of commissioned research. In the case of demonstration through implementation research, we see a mixed picture. On one hand, evidence demonstrating that a given intervention works may fail to lead to change because of the implementation costs, for example in the case of task shifting [27]. On the other hand, where there is extensive support, successful evidence uptake may occur following implementation research as happened with the community HIV programme. Donor influence may have played a role here, although we did not assess this specifically.

Dissemination of research findings took several forms and was not always systematic and audience-tailored. This could be explained by the nature of partnerships reported in this study which may not allow mapping relevant stakeholders and developing tailored messages. The importance of using several modalities for disseminating evidence that are audience-specific has been emphasised [17]. Ineffective dissemination may also stem from the lack of an institutional set up for dissemination of evidence. An earlier study in Uganda highlighted the need to establish a unit within the MoH that would be charged with the responsibility of disseminating evidence [21].

Overall, the effectiveness of KT strategies is highly variable and dependent on the setting. Success hinges on whether the strategies have been sufficiently tailored to target audiences. The effectiveness of the different KT strategies is not known and Cordero et al pointed the need for further research in this area specifically to evaluate KT activities to learn what works, why and in what context [17]. Working through government institutions has been emphasised as a way of ensuring that government takes ownership of the KT process [21]; but, relevant government institutions must be strengthened. In the case of Uganda, the Uganda National Health Research Organization is legally mandated to coordinate KT efforts. However, the institution is not sufficiently resourced to play that role effectively. Inadequate investment in improving KT may partly stem from the low prioritisation of research. Although Uganda recognises the importance of evidence as a critical factor in public health policy development, there is no system in place to track research undertaken and over 90% of health research is funded by external sources whose priorities may not align with country priorities [22]. Use of evidence in public health policy development in resource-constrained settings is of

paramount importance because meagre resources must be invested wisely to ensure maximum return. In light of this, investment in KT needs more emphasis.

Study findings should be interpreted in light of the following limitation. The study reported respondents' perspectives about KT in general and not in reference to on-going specific policies or research project activities. Therefore, responses provided in this study did not refer to a specific research and policy. We note that different KT activities may work for different policies and the generalised responses may not clearly highlight this fact. In this regard, generalised application of our findings may be limited. We however provide a basis for further research on this subject.

## Conclusion

Strategies to improve KT are context-specific. Although a lot of work has been done on KT in high income countries, LIC, where the use of evidence would help countries use limited resources in more effective ways, still face a dearth of context-specific literature on this subject. There is need for conceptual clarity on KT, adoption of a systematic KT framework and, further understanding of the effectiveness of the different KT strategies in low-income settings.

## Competing interests

The authors declare no competing interests.

## Authors' contributions

JNO participated in the conceptualisation of the study, data collection, data analysis and interpretation and led the drafting of the manuscript. DKM participated data analysis, interpretation and in the drafting of the manuscript. HN participated in data analysis and interpretation and in the drafting of the manuscript. BC participated in the conceptualisation of the study, data analysis and interpretation. All authors reviewed and approved the final manuscript.

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## Research

# Immunostimulatory responses to crude extracts of *Warburgia ugandensis* (sprague) subsp *ugandensis* (canellaceae) by Balb/c mice infected with *Leishmania major*

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**Introduction:** To determine the immunostimulatory potential of crude extracts of *Warburgia ugandensis* subsp. *ugandensis* with a soluble leishmanial antigen in vaccinating BALB/c mice.

**Methods:** Seventy two female BALB/c mice were randomly assigned into six groups. The mice were vaccinated with soluble *leishmania* antigens (SLA) alone, hexane, ethyl acetate, and dichloromethane extract co-administered with SLA. Unvaccinated mice formed the control group. The induction of cell-mediated immunity following vaccination was determined by measuring in vitro lymphocyte proliferation and the production of interleukin (IL)-4 and gamma interferon (IFN- $\gamma$ ) determined by flow cytometry. Protection against *L. major* was determined by quantifying parasite burdens in *L. major* infected footpads using a limiting dilution assay and by measuring lesion sizes of the infected footpad compared to the contralateral uninfected footpad.

**Results:** On vaccination with extracts of *W. ugandensis* subsp. *ugandensis* alone or as adjuvants when used in combination with *Leishmania* antigens, the hexane extract and the dichloromethane extract plus SLA stimulated moderate production of IFN- $\gamma$  and low levels of IL-4. These mice were partially protected from cutaneous leishmaniasis as shown by the slow development of lesions and comparatively less parasite burdens.

**Conclusion:** These data suggest that extracts of *W. ugandensis* subsp. *ugandensis* are suitable adjuvants for *Leishmania* vaccines. However, since *W. ugandensis* subsp. *ugandensis* has been shown to be effective against *Leishmania* parasites in vitro and in vivo, further studies ought to be conducted to determine its immunochemotherapeutic potential when co-administered with a soluble leishmanial antigen in vaccinating BALB/c mice.

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**Key words:** Leishmaniasis, immunostimulatory responses, *Warburgia ugandensis*, cytokines

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## Introduction

Leishmaniasis is a parasitic disease caused by protozoa of the genus *Leishmania* transmitted by the bite of infected phlebotomine sand flies. It encompasses a wide spectrum of clinical manifestations ranging from chronic cutaneous ulcers to fatal visceral infection. The World Health Organization estimates that at least 350 million people are at risk of the disease worldwide, 12 million people are infected with *Leishmania* parasites, and two million new cases of leishmaniasis occur each year in 88 countries in parts of Africa, India, the Middle East, southern Europe, and Central and South America [1].

The primary challenge associated with the treatment of leishmaniasis is that the drugs of choice are highly toxic, expensive and require hospitalization for more than three weeks. They include pentostam, pentamidine, miltefosine, and paromomycin. There are efforts towards the development of drugs based on natural products which are deemed to be safe. In this regard, medicinal plants offer prospects for discovering

new compounds with therapeutic properties.

*Warburgia ugandensis* subsp *ugandensis* Sprague, the East African greenheart(Canellaceae) is one of the most highly utilized medicinal plants in tropical and subtropical Africa and is now highly endangered in the wild [2-3]The dried bark of the tree is commonly chewed and the juice swallowed as a remedy for stomach ache, constipation, toothache, venereal diseases, cough, fever, muscle pains, weak joints and general body pains. The leaf decoction baths are used as a cure for skin diseases while the bark, roots or leaves can be boiled in water and drunk to treat malaria, although this causes violent vomiting. *Warburgia ugandensis* subsp *ugandensis* which is known as "soket" in Tugen tribe is used by traditional healers to treat VL (W. Tonui, personal communication). The stem barks are taken orally in boiled water or soup. Previous studies on *W. ugandensis* subsp *ugandensis* have shown good antibacterial, antifungal, antiviral activity and trypanocidal effects. For example, crude extracts and purified compounds of *W. ugandensis* subsp *ugandensis* showed activity against Mycobacterium tuberculosis H37Rv and M. Bovis BCG Pasteur [4], *Candida albicans* and measles virus [5]. Similarly, the

activity of *W. ugandensis* subsp *ugandensis* against trypanosomes has been demonstrated [5-6]. However, there is limited information on the immunostimulatory effects of the plant. The objective of the present study was to determine the immunostimulatory effects of extracts of *W. ugandensis* subsp *ugandensis* against *Leishmania major* and *L. donovani* in BALB/c.

## Methods

### Collection of *W. Ugandensis* subsp. *ugandensis* plant materials

*Warburgia ugandensis* subsp *ugandensis* stem barks were collected from Sesia village in Kabarnet, Baringo District, in the Rift Valley Province in Kenya. Sesia village is located 265 km northwest of Nairobi on the Tugen Hills on the western edge of the Rift Valley (Grid Reference 056 547 on the 1:50,000 sheet 104/1 Kipkabus). Botanical identification was carried out by botanists from the National Museum of Kenya.

### Preparation and extraction of *W. Ugandensis* subsp *ugandensis* extracts

The stem barks were cut into small pieces and air-dried for three weeks. The dried specimens were shredded using an electrical mill in readiness for extraction. The sample preparation and extraction was carried out as described by Harborne [7]. Successive extraction was carried out on the plant material with distilled organic solvents of increasing polarity, which included n-hexane, dichloromethane, ethyl acetate and methanol. Three hundred grams of the shredded stem barks were weighed and put in 1 litre conical flasks. Six hundred millilitres of n-hexane was added and soaked for 48 hours. The residue was filtered using a Buchner funnel under vacuum until the sample dried. The sample was soaked further with 600ml of n-hexane for 24 hours until the filtrate remained clear. The filtrate was then concentrated under vacuum by rotary evaporation at 30-35°C to yield a brown residue [7]. The brown residue was transferred to a sample bottle and dried under vacuum; the weight of the dry extract was recorded and stored at -20°C until required for bioassay. The process was repeated sequentially for dichloromethane, ethyl acetate and methanol.

### Bioassays

Six week-old BALB/c mice were obtained from KEMRI'S animal house facility and used for the in vivo studies. These experiments were carried out in compliance with all relevant KEMRI institutional policies.

### In Vitro parasite culture for *L. Major*

Metacyclic promastigotes of *L. Major* strain (Strain IDU/KE/83 =NLB-144) and *L. Donovani* strain (NLB-065) were used. Parasites were maintained as previously described by Titus et al. 1984 [8] and metacyclics were isolated from stationary phase cultures by negative selection using peanut agglutinin [9]. Stationary-phase promastigotes were obtained from 5 to 7-day-old cultures. The cultures were made in T25 sterile disposable culture flasks (25 ml) and incubated at 25°C as recommended by Evans et al. 1989 [10] to stationary metacyclic stage.

### Preparation of extracts for bioassays

Stock solutions of the extracts were made in culture media for anti-leishmanial assay and re-sterilized by passing through 0.22 µm micro-filters under sterile conditions in a laminar flow hood. The extracts that were insoluble in water or media were first dissolved in 1% DMSO to avoid solvent carry over [11]. All the extracts were stored at 4°C until use.

### Preparation of soluble *Leishmania* antigens

Soluble *Leishmania* antigens (SLA) were produced as previously described by Scott and colleagues [12]. Promastigotes ( $1 \times 10^9$ ) were harvested from culture and washed four times in cold phosphate-buffered saline (PBS) and resuspended in PBS containing a protease inhibitors cocktail of 100 mM Tris-HCl, 1mM EDTA (pH 8) supplemented with 50 µg/ml leupeptin, 50 µg/ml antipain, 50 µg/ml aprotinin and 1.6 mM phenylmethylsulfonyl fluoride (PMSF) (Sigma Chemicals Co.). The suspension was incubated for 10 min on ice and sonicated for 10 periods of 30 seconds each (separated by an interval of 1 min) at medium amplitude. The sonicate was left at 4°C for complete extraction of soluble antigen for 18 h. After incubation, sonicated suspension was centrifuged at 4000g for 30 min at 4°C. The supernatant obtained was finally ultra-centrifuged at 40000 g for half an hour. After assessing the protein content of the supernatant by Lowry method, it was distributed in small aliquots and stored at -70°C

until use [13].

### Infection of mice, treatment and determination of parasite numbers in cutaneous lesions

Female BALB/c mice were infected in the hind footpad with  $1 \times 10^6$  *L. major* metacyclic promastigotes. In all experiments, treatment was initiated 4 or 5 weeks after infection had established as determined by the presence of lesions [12]. Lesion development was followed by measuring the thickness of the infected footpad as compared to the thickness of the same footpad prior to infection using a vernier caliper. Disease progression in mice was evaluated by measuring lesion sizes for a period of eight weeks on a week-to-week basis. At 1, 2 and 4-weeks post infection, duplicate mice were sacrificed to estimate the parasite burden in the footpads using a limiting dilution assay (LDA) [14]. Mice that were not vaccinated formed the control groups.

The extracts were injected intraperitoneally. The untreated group received phosphate buffered saline. Lesion development was followed by measuring thickness of the infected footpad as compared to the thickness of the contralateral footpad prior to infection using a vernier caliper. All mice were sacrificed during the 12th week, spleens weighed and impression smears made. These were fixed in absolute methanol and stained with Giemsa before examination for parasites to determine whether or not visceralization of the parasite had taken place.

### Immunostimulatory effects of crude extracts derived from *W. Ugandensis* subsp. *Ugandensis*

To test the immunostimulatory effects of the crude extracts, soluble *Leishmania* antigens (SLA) were used. Female BALB/c mice in groups of ten were vaccinated by subcutaneous (s.c) injections of 100 µg of SLA alone, 100 µg of test sample alone or with 100 µg of SLA plus 100 µg of test sample [9].

### Cell cultures, proliferation of cytokine producing cells and measurement of cytokines

Spleens from mice infected with *L. Major* were harvested in each experimental group on day 0 and at days 7, and 21 post-infection. Mononuclear cells were purified with Ficol-Paque ingredients [9]. Spleen cells were adjusted to 106/ml in complete RPMI 1640 medium supplemented with 10% fetal bovine serum (FBS), 2 mM L-glutamine, 100 units of penicillin per ml, and 100 µg of streptomycin per ml then stimulated with SLA for six days at 37°C and 5% CO<sub>2</sub>. Negative control cultures consisted of unstimulated splenocytes. Viability of splenocytes was tested by stimulating the cells with a known mitogen, concanavalin A (con A). Colorimetric microassay was used to determine cell proliferation as previously described by Hay and Westwood [15]. The cytometric bead array (CBA) kit was used to measure levels of IFN-γ and IL-4 as previously described by Hodge et al. [16].

### Ethical and biosafety considerations

Approval for the study was sought from Kenya Medical Research Institute (KEMRI) ethical review committee. The experiments were done in compliance with KEMRI'S Animal Care and Use Committee (ACUC).

### Statistical analysis

Data were recorded in Microsoft Excel and imported into SPSS 13.0 for analysis. All experiments were carried out in triplicate. The mean and standard deviation of at least three experiments were determined. Statistical analysis of the differences between mean values obtained for the experimental groups were done by Student's t test. P values of ≤0.05 or less were considered significant.

## Results

### Lymphoproliferative responses of splenocyte cultures before and after infection with *L. major*

The proliferative responses of splenocyte cultures to SLA obtained from mice that had been vaccinated with SLA, hexane, dichloromethane and ethyl acetate was significantly higher ( $P < 0.05$ ) to the unvaccinated control (Table 1). Combination of SLA and extracts yielded similar results. There was marked increase in the proliferative response to SLA for the groups vaccinated with SLA, hexane extract and dichloromethane extract plus SLA

**Table 1:** Mean optical density (OD) readings (540 nm) of in vitro proliferative responses of splenocytes one week and four weeks post vaccination

Treatment groups	Proliferative responses one week after vaccination			Proliferative responses four weeks after vaccination		
	Mean OD readings ( 540 nm) ± S.E			Mean OD readings (540 nm) ± S.E		
	LA	Medium	P value compared to the unvaccinated control	SLA	Medium	P value compared to the unvaccinated control
SLA	0.636 ± 0.02	0.355± 0.037	0.002	1.069± 0.072	0.378 ± 0.007	< 0.001
HEX	0.540± 0.013	0.335 ± 0.07	0.002	0.953± 0.004	0.365 ± 0.05	0.118
DCM	0.511± 0.028	0.393± 0.007	0.009	0.597± 0.023	0.403 ± 0.011	0.002
ETAC	0.536± 0.003	0.258± 0.003	< 0.001	0.598± 0.024	0.298 ± 0.008	0.023
HEX/SLA	0.737± 0.027	0.278± 0.007	0.004	0.328± 0.024	0.279 ± 0.008	0.02
ETAC/SLA	0.868± 0.067	0.340± 0.011	0.014	0.304± 0.004	0.347 ± 0.002	0.006
DCM/SLA	0.587± 0.010	0.289± 0.014	0.002	0.746± 0.009	0.307 ± 0.09	0.042
PBS	0.268± 0.005	0.230± 0.003	-	0.268± 0.005	0.256 ± 0.006	-

SLA=Soluble *Leishmania* antigen; HEX=Hexane; DCM=Dichloromethane; ETAC=Ethyl acetate; HEX/SLA=Hexane/SLA; ETAC/SLA=Ethyl acetate/SLA; DCM/SLA=Dichloromethane/SLA; PBS=Phosphate Buffered Saline

**Table 2:** In vitro IFN-γ production (mean ± SE) one week and four weeks after vaccination

Treatment groups	Mean production of IFN-γ one week after vaccination			Mean IFN-γ production four weeks after vaccination		
	Mean OD readings ( 540 nm) ± S.E			Mean OD readings (540 nm) ± S.E		
	Mean Production of IFN-γ (pg/ml) induced by SLA	Mean production of IFN-γ (pg/ml) by cells in medium	P value compared to the unvaccinated control	Mean production of IFN-γ (pg/ml) induced by SLA	Mean production of IFN-γ (pg/ml) by cells in medium	P value compared to the unvaccinated control
SLA	349.1± 9.825	6.0 ± 1.971	0.002	123.2± 2.730	5.6 ± 0.345	0.002
HEX	134.3± 7.549	7.07±0.368	0.005	141.8± 1.205	6.7 ± 0.211	0.005
DCM	142.0± 3.132	7.8 ± 0.988	0.006	142.9± 5.775	7.0 ± 0.548	0.032
ETAC	116.1± 2.119	5.6 ± 0.731	<0.001	112.9± 2.905	6.4 ± 0.706	< 0.001
HEX/SLA	111.2± 4.932	6.7 ± 0.575	0.028	135.4± 5.084	6.1 ± 1.977	0.012
ETAC/SLA	138.2± 1.376	5.8 ± 0.309	< 0.001	109.2± 2.960	6.3 ± 0.367	0.017
DCM/SLA	167.3± 4.350	6.2 ± 0.889	0.005	120.6± .684	5.8 ± 0.506	0.005
PBS	65.8± 2.892	5.3 ± 0.070	-	63.5 ± 6.612	5.7 ± 0.172	-

SLA=Soluble *Leishmania* antigen; HEX=Hexane; DCM=Dichloromethane; ETAC=Ethyl acetate; HEX/SLA=Hexane/SLA; ETAC/SLA=Ethyl acetate/SLA; DCM/SLA=Dichloromethane/SLA; PBS=Phosphate Buffered Saline

**Table 3:** In vitro IL-4 production (mean ± SE) one week and four weeks after vaccination

Treatment groups	Mean production of IL-4 one week after vaccination			Mean IL-4 production four weeks after vaccination		
	Mean OD readings ( 540 nm) ± S.E			Mean OD readings (540 nm) ± S.E		
	Mean Production of IL-4 (pg/ml) induced by SLA	Mean production of IL-4 (pg/ml) by cells in medium	P value compared to the unvaccinated control	Mean production of IL-4 (pg/ml) induced by SLA	Mean production of IL-4 (pg/ml) by cells in medium	P value compared to the unvaccinated control
SLA	39.3 ± 2.563	6.2 ± 0.642	0.002	71.6 ± 0.329	7.5 ± 0.384	< 0.001
HEX	33.9 ± 2.237	6.4 ± 0.656	0.005	36.9 ± 0.525	7.1 ± 0.379	0.001
DCM	34.8 ± 3.303	7.3 ± 0.464	0.004	32.1 ± 0.414	6.9 ± 0.312	< 0.001
ETAC	29.5 ± 1.424	7.4 ± 0.327	0.022	31.2 ± 0.476	7.4 ± 0.658	< 0.001
HEX/SLA	22.9 ± 0.983	7.9 ± 0.543	0.245	65.4 ± 1.762	7.4 ± 0.312	0.915
ETAC/SLA	33.4 ± 1.688	7.7 ± 0.719	0.003	74.0 ± 0.732	7.3 ± 0.478	< 0.001
DCM/SLA	36.3 ± 1.227	7.8 ± 0.503	0.036	32.9 ± 0.492	8.4 ± 0.251	< 0.001
PBS	21.1 ± 2.115	6.7 ± 0.165	-	65.7 ± 0.541	6.7 ± 0.175	-

SLA=Soluble *Leishmania* antigen; HEX=Hexane; DCM=Dichloromethane; ETAC=Ethyl acetate; HEX/SLA=Hexane/SLA; ETAC/SLA=Ethyl acetate/SLA; DCM/SLA=Dichloromethane/SLA; PBS=Phosphate Buffered Saline

**Table 4:** Parasite burden in the infected footpads of mice treated with BCG, SLA, hexane extract, dichloromethane extract, ethyl acetate extract and control (PBS) group alone during the course of infection

Day	Experimental groups (No. of <i>L. major</i> (10 <sup>6</sup> )/footpad (95% confidence limits))				
	Control	SLA	Hexane extract	Dichloromethane extract	Ethyl acetate extract
14	10.5 (28.9-2.67)	11.4 (18.31-3.16)	6.99 (13.6-1.71)	12.6 (17.8-9.61)	14.3 (16.1-5.28)
35	20.4 (37.35-13.83)	18.4 (27.7-12.25)	8.27 (21.01-3.38)*	25.8 (31.74-17.2)	23.6 (32.78-16.9)
56	69.8 (98.1-38.44)	52.3 (72.37-19.4)*	9.33 (7.20-0.93)*	53.5 (82.5-21.37)*	48.8 (62.1-39.04)

\*P<0.05 Parasite burden is significantly different from that of the unvaccinated control.

**Table 5:** Parasite burden in the infected footpads of mice treated with hexane/SLA, dichloromethane/SLA, ethyl acetate/SLA and control (PBS) group alone during the course of infection

Day	Experimental groups (No. of <i>L. major</i> (10 <sup>6</sup> )/footpad (95% confidence limits))			
	Control	Hexane/SLA extract	Ethyl acetate/ SLA extract	Dichloromethane/SLA extract
14	10.5(28.9-2.67)	9.25(24.7-3.39)	11.7(19.62-6.94)	9.25(10.7-1.12)*
35	20.4(37.35-13.83)	19.03(31.62-14.56)	20.97(26.8-15.72)	8.11(10.16-1.37)*
56	69.8(98.1-38.44)	48.83(87.21-29.73)*	63.7(88.9-38.7)	6.78(7.39-0.96)*

\*P<0.05 Parasite burden is significantly different from that of the unvaccinated control.

compared to the proliferation before infection (P<0.05).

#### Interferon gamma production by splenocyte cultures before and after infection with *L. major*

The mean production of IFN-γ by splenocytes of mice vaccinated with SLA, hexane extract, dichloromethane extract, ethyl acetate, hexane plus SLA, ethyl acetate plus SLA, and dichloromethane plus SLA in response to in vitro stimulation with SLA before challenge was significantly higher (P<0.05) compared to the control unvaccinated group (Table 2). The mean production of IFN-γ by splenocytes of mice vaccinated with SLA, hexane extract, dichloromethane extract, ethyl acetate, hexane plus SLA, ethyl acetate plus SLA, and dichloromethane plus SLA, in response to in vitro stimulation with SLA after challenge was significantly higher (P<0.05) compared to the control unvaccinated group.

#### Interleukin - 4 production by splenocyte cultures before and after infection with *L. major*

The mean production of IL-4 by splenocytes of mice vaccinated with SLA, hexane extract, dichloromethane extract, ethyl acetate, ethyl acetate plus SLA, and dichloromethane plus SLA in response to in vitro stimulation with SLA after challenge was significantly higher (P<0.05) compared to the control unvaccinated group. The mean production of IL-4 by splenocytes of mice vaccinated with hexane extract, dichloromethane extract, ethyl acetate and dichloromethane plus SLA in response to in vitro stimulation with SLA after challenge was significantly lower (P<0.05) compared to the control unvaccinated group.

The production of IL-4 by splenocytes from mice vaccinated with hexane plus SLA was not significantly different (P=0.245) from that of the unvaccinated control (Table 3), while the levels of production of IL-4 for mice vaccinated with ethyl acetate extract plus SLA and SLA, were significantly higher (P< 0.001) compared to that of the unvaccinated control.

#### Lesion size measurements for BALB/c mice vaccinated before infection with *L. major*

For mice vaccinated with hexane extract, the size of lesions were

significantly smaller (P<0.05) than those of the unvaccinated controls from week 2 to week 8. For mice vaccinated with dichloromethane extract, ethyl extract, hexane extract plus SLA and ethyl acetate extract plus SLA there was no significant difference (P>0.05) between the lesion sizes of these mice compared to those of the unvaccinated controls from week 2 to week 8 (Table 4).

Mice in the control unvaccinated and *L. major* challenged group developed large progressive footpad lesions reaching a peak at week (mean ± S.E., 0.947 ± 0.022) mm. Unvaccinated control groups were euthanized if they reached a predetermined level of lesion severity and/or displayed clinical signs of distress or pain.

#### Quantification of *L. major* in infected footpads of BALB/c mice vaccinated before and after infection with *L. major*

The number of *L. major* parasites present in the infected footpads was quantified at 14, 35 and 56 days post infection using a limiting dilution assay (LDA) [15]. The results were analyzed using the ELIDA statistical package (2001-2005). In the first LDA done at 14 days post infection, *L. major* parasites were detected in both the vaccinated and unvaccinated groups of mice. The number of *L. major* in the footpads from mice vaccinated with dichloromethane extract plus SLA (9.25 × 10<sup>6</sup>) was significantly lower (P<0.05) than that of the controls (10.5 × 10<sup>6</sup>) at 14 days post infection. However, there was no significant difference (P<0.05) in the number of parasites for the rest of the groups compared to the unvaccinated control (Table 5).

The parasite burdens in the mice vaccinated with hexane extract (8.27 × 10<sup>6</sup>) and dichloromethane extract plus SLA (8.11 × 10<sup>6</sup>) were significantly lower (P< 0.05) from those of the control unvaccinated mice as the disease progressed as quantified at day 35. On the 14th day, there was no significant difference (P<0.05) in the number of parasites for the rest of the groups compared to the unvaccinated control (Table 5).

By the 56th day, parasite burdens for the mice vaccinated with hexane extract group (9.33 × 10<sup>6</sup>) and the dichloromethane plus SLA group (6.78 × 10<sup>6</sup>) reduced significantly (P<0.005) compared to those of the unvaccinated control group (69.8 × 10<sup>6</sup>). Similarly, parasite burdens for

the SLA group ( $52.3 \times 10^6$ ), dichloromethane group ( $53.5 \times 10^6$ ), ethyl acetate group ( $48.8 \times 10^6$ ), hexane plus SLA group ( $48.8 \times 10^6$ ) and ethyl acetate plus SLA group ( $63.7 \times 10^6$ ) reduced significantly ( $P < 0.05$ ) compared to the unvaccinated controls ( $69.8 \times 10^6$ ). The parasite burdens of the dichloromethane, and the dichloromethane plus SLA were significantly lower ( $P < 0.005$ ) compared to those of the SLA group, dichloromethane group, ethyl acetate group, hexane plus SLA group and ethyl acetate plus SLA group.

## Discussion

The study focused on the immunostimulatory activities of the crude extracts of a native medicinal plant used by traditional healers in Kenya. The limitation of the study is that the active principles responsible for the immunostimulatory responses observed were not identified. Further, the mechanisms of the immunostimulatory activities were not elucidated.

Our results show that organic extracts of *W. ugandensis* subsp *ugandensis* can induce lymphocyte proliferation to SLA on their own or enhance such response if co-administered with SLA in a vaccine. Lymphocyte proliferation is a crucial event in the activation of both cellular and humoral responses [17]. Proliferative responses of splenocytes to SLA have previously been used as a measure of exposure to the parasites, as well as a measure of protection [18]. Our results are consistent with previous studies that suggest that some plant products, such as artemisinin, induce proliferation of T-cells in vitro [19]. The enhanced proliferative responses for extracts co-administered with SLA in this study is consistent with findings of a previous study where mice vaccinated with SLA and Th1 promoting adjuvant had significantly higher stimulation indices compared to those vaccinated with SLA alone [18]. Thirty days post infection with *L. major* there was marked increase in the proliferative response to SLA for the groups vaccinated with SLA, hexane extract and dichloromethane extract plus SLA compared to the proliferation before infection indicating a recall proliferative response. For mice vaccinated with hexane extract plus SLA and the group vaccinated with ethyl acetate plus SLA, the proliferative responses of the splenocyte cultures to SLA was significantly lower. The reduction in the proliferative responses is probably an indication of immunosuppression caused by the combination of SLA with the plant extracts.

Extensive studies with experimental mouse models infected with *L. major* have shown that the outcome of infection with *Leishmania* parasites is critically dependent on the activation of one of the two subsets of CD4 T cells, Th1 and Th2 [20,21]. In the present study, IFN- $\gamma$  was expressed in splenocytes, which is in agreement with the findings of other authors who have shown that this cytokine is important in the development of protective immune responses in experimental Leishmaniasis [22, 23]. Gamma interferon secreted by Th1 cells, is the most potent macrophage-activating cytokine leading to host resistance to infection with *Leishmania* parasites whereas IL-4 secreted by Th2 cells, is associated with down-modulation of IFN- $\gamma$ -mediated macrophage activation [21].

In a previous study, 67 tannins were tested for antileishmanial and immunomodulatory potencies and shown to augment and prolong the activation of host defense mechanisms indicating that parasitized macrophages were "primed" to react to activating molecules such as phenol [24]. Further studies demonstrated the effects of IFN- $\gamma$ , lipopolysaccharide (LPS), and some polyphenols as individual stimuli, as well as in various combinations on NO production in non-infected and infected macrophage-like RAW 264.7 with emphasis on the NO/parasite kill relationship. In non-infected and in *Leishmania* parasitized cells, gallic acid significantly inhibited the IFN- $\gamma$  and LPS-induced NO detected in the supernatants [25]. This effect was less prominent in IFN- $\gamma$  - than in LPS-stimulated cells.

Elsewhere, it has been shown that the ethyl acetate portion of *Geranium pyrenaicum* induced significant production of IFN- $\gamma$  and TN [26]. The cytokine-inducing potential of the flavonoids glycosides decreased with increasing polarity [26]. The results provide evidence that flavonoids glycosides possess the capability to stimulate defense mechanisms in *leishmania*-infected RAW 264.7 cells, albeit with moderate potential. This is similar to the observation in the current study where the hexane extract (with low polarity) stimulated production of higher levels of IFN- $\gamma$  compared to the ethyl acetate extract (higher polarity).

In experimental CL, it has been suggested that the healing of lesions depends on the early presence of macrophages, the activation of these cells by type 1 interferon and, later, by low amounts of IFN- $\gamma$  probably produced by NK cells, consequently, the Th1 cells amplify the killing of the parasite when they release more IFN- $\gamma$  [27]. Interferon-gamma is known to be a strong inducer of the macrophage enzyme inducible nitric oxide synthase (iNOS) [28], which mediates the production of nitric oxide that directly kills *L. major* [29].

Previous studies have demonstrated that CL is associated with the expansion of CD4+ T cells that contain high levels of IL-4 mRNA in the draining lymph nodes and spleen [30] and with elevated levels of immunoglobulin E, an IL-4-dependent immunoglobulin isotype [30]. Early production of IL-4 in mice correlates with the dominance of an IL-4-driven Th2 response that causes disease [21]. In the current study the parasite burdens for the SLA, hexane extract plus SLA and ethyl acetate plus SLA groups were comparable to those of the unvaccinated control group four weeks post infection. Indeed by the end of week eight, the lesion sizes of the mice in these groups were similar in size to those of the unvaccinated group indicating exacerbation of disease.

It is postulated that production of high levels of IL-4 interferes with the production or activity of IFN- $\gamma$ . A number of mechanisms by which IL-4 may interfere with the production or activity of IFN- $\gamma$  has been identified, including the direct inhibition of macrophage activation to kill intracellular amastigotes [31]. The ability of IL-4 to block the activation of macrophages has been most consistently demonstrated following prior treatment with IL-4. Indeed, administration of IL-4 after IFN- $\gamma$  may activate macrophage anti-*L. major* activity [32].

These mice were partially protected from cutaneous leishmaniasis as shown by the slow development of lesions. Similar results were reported in immunized BALB/c mice with KM+lectin of *Artocarpus integrifolia* associated, or not with SLA, and partial protection of the animals was observed after challenge with *L. amazonensis* [22].

Mice vaccinated with SLA, ethyl acetate extract, dichloromethane extract and the ethyl acetate plus SLA developed lesions and had higher parasitaemia comparable to the unvaccinated control group. This is in agreement with previous studies where immunization with SLA alone resulted in lesions almost as evident in the controls immunized with PBS [33,34].

## Conclusion

These results suggested that extracts from *W. ugandensis* subsp *ugandensis* contained chemical compounds that possess positive and/or negative modulator effects on the immune system. *Warburgia ugandensis* subsp. *ugandensis* has been used by traditional healers in Kenya for many years. The immunostimulatory effects of the plant can be used to explain the efficacy of this plant in addition to its direct effects on *Leishmania* parasites. Further studies on the mechanisms have potential of unveiling the possibility of targeting this plant for drug development that can be used for the treatment of leishmaniasis.

## Competing interests

The authors declare no competing interests.

## Authors' contributions

Peter Ngunjiri: Principal investigator, proposal development, experimental design, laboratory experiments, data analyses, and manuscript development. Zipporah Ng'ang'a: Experimental design, data analyses, and manuscript review. Albert Kimutai: Proposal development, experimental design, and data analyses. Stella Kepha: Experimental design, laboratory experiments, and data analyses. Samuel Mong'are: Data analyses and manuscript development. Willy Tonui: Proposal development, experimental design, data analyses and manuscript review.

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## Research

# HIV/AIDS communication in four Nigerian mainstream newspapers

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**Introduction:** One consensus in discussions on HIV/AIDS communication in low and middle income countries (LMICs) is the need for communication models to focus on activity rather than cognitive indicators in order to achieve desired improvements in health behaviors and outcomes. Past failures of HIV/AIDS communication efforts in LMICs have been attributed to emphasis on cognitive indicators. This study analyses HIV/AIDS communication models in Nigerian newspapers

**Methods:** Data were obtained through analysis of manifest content of four Nigerian papers issued between 2002 and 2004. Frequency, prominence and space dedicated to HIV/AIDS-related topics were measured. Descriptive statistics were used to highlight the frequency and percentage of cognitive- and activity-oriented information on HIV/AIDS.

**Results:** A total of 464 HIV/AIDS-related articles were identified. Fifty-nine percent (274) of articles were activity-oriented. Over half of articles were news stories. No news story made front and back pages lead. There were only nine editorials on HIV/AIDS.

**Conclusion:** This study shows that the activity model of HIV/AIDS communication dominates the four Nigerian mainstream newspapers studied. However, it is worth noting the limited number of editorials and feature articles, which have the capacity to stimulate debate and foster a social environment in which AIDS is addressed in a spirit of openness. For a country that has the third largest number of people living with HIV/AIDS globally, one would expect the mass media to deliberately play an instrumental and a more active role in the battle against the disease by engaging in in-depth contextual discourse on HIV/AIDS.

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## Introduction

Current thought in HIV/AIDS communication in low and middle income countries foregrounds the need to move beyond the cognitive approach to the activity approach [1]. Cognitive models of behaviour change communication like the Health Belief Model, the Theory of Reasoned Action, Social Learning Theory, and the AIDs Risk Reduction Model (ARRM), which dominated the first decade of social science research on HIV/AIDS, assume that individual reason provides the impetus for human action [2]. The models seek to interpret and analyze health behaviours at the individual level. HIV/AIDS cognitive information refers to information about HIV/AIDS that focuses on individual self-efficacy and emphasizes the simple, linear relationship between individual knowledge and action [3]. The activity model of behaviour change communication derives from the activity theory. This model views behavioral outcome as a product of the individual's context and argues that human activity is complex and socially-bound and driven and not simply the sum of individual actions [4]. HIV/AIDS activity information was defined as information about HIV/

AIDS that extends the framing of HIV/AIDS from primarily an individual function to one that is linked to more macro socio-economic, cultural and political contexts [5].

Although, cognitive models have been effective in western contexts [6], some scholars and practitioners argue that these models are inadequate for HIV/AIDS communication in low and middle income countries [6]. Following this realization, calls have been made for a shift from the cognitive to the activity model of HIV/AIDS communication [6]. The importance of a nationally-driven agenda in lowering incidence and mitigating the impact of HIV/AIDS in low and middle income countries was not lost on Nigeria which, in 2001, launched a multi-sectoral and community-based response to the epidemic, exemplified in the HIV/AIDS Emergency Action Plan (HEAP; 2001-2004) and the National Strategic Framework (NSF; 2005-2009).

However, a dominant view in the literature is that the mass media in low and middle income countries are yet to transition from cognitive models to the activity model of HIV communication [6]. Presently, there is little

literature systematically addressing the response of the mass media to HIV/AIDS in low and middle income countries. The severity of the HIV epidemic in low and middle income countries and the immense potential that the media have to contribute to its prevention and control both justify the need for an examination of their media content in order to ascertain the level of response. Such an examination may yield information that can help strengthen policies and advance effective strategic partnerships in HIV/AIDS prevention efforts.

## Methods

Using data from a recent comparative study on HIV/AIDS cognitive and activity-oriented information content in four mainstream Nigerian newspapers, this paper examines; (a) the number of HIV/AIDS cognitive and activity information carried by Nigerian newspapers (b) amount of space devoted to HIV/AIDS cognitive and activity information by Nigerian newspapers, and (c) the location of HIV/AIDS cognitive and activity information in Nigerian newspapers. In other words, three variables (frequency, space and prominence) were measured in this study which covered a three-year period (2002–2004).

Although HIV was first reported in Nigeria in 1986, the study period coincided with the implementation of the first phase of Nigeria's multi-sectoral and community-based national response to the epidemic. The four newspapers surveyed in the present study are the Guardian, Punch, New Nigerian and Daily Trust. The Guardian and Punch are published in southern Nigeria while New Nigerian and Daily Trust are published in the North. These papers represent an important outlet for health information. They have been in the forefront of the crusade against HIV/AIDS [7]. In addition, newspapers are widely cited sources of information on HIV/AIDS issues in Nigeria [8].

**Coding:** Coders, working in pairs, coded newspaper items independently of one another. Each pair of coders coded all issues of the same newspaper during the study period according to the coding scheme. Coding focused on manifest content. Data extraction and recording were performed manually. All coders were final-year undergraduate students of Mass Communication enrolled in print journalism in three Nigerian tertiary institutions (the University of Lagos, Lagos State University and Kaduna Polytechnic). The coders were carefully recruited and trained to code. The training of coders included one 2-hour session a day for two weeks. The categories for coding HIV/AIDS-related content of the newspapers were based on those developed by Journalists Against AIDS (JAAIDS), Nigeria in 2003 on the coverage of HIV/AIDS in eleven Nigerian newspapers. The JAAIDS categories are similar to those Pratt et al [9] used in their study of HIV/AIDS information in African popular magazines and medical journals. According to Stempel [10], "there are real advantages to using a category system that has been used in other studies" because validity and reliability are largely addressed.

**Intercoder Reliability:** Intercoder reliability was measured using Krippendorff's alpha [11]. Krippendorff's alpha score for the Newspapers ranged from 0.891 to 0.944 (The Guardian, 0.891; The Punch, 0.918; New Nigerian, 0.936; Trust, 0.944). Considering these results, the coding sheet and the coders were deemed fit for the study.

## Analysis

The units of analysis were all newspaper items (news stories, feature articles, editorials, opinions, letters to the editor, photos, cartoons, advertisements etc.). Each unit of analysis was coded as cognitive- or activity-focused based on the following categories: (1) Awareness/Prevention, (2) Treatment/Care, (3) Advocacy and campaign, (4) Cure claims, (5) Policy pronouncements, (6) Litigation, (7) Statistics/Trends, and (8) Research. As such, the frequency of either HIV/AIDS cognitive or activity information was measured by the number of items about HIV/AIDS in Nigerian newspapers. In terms of space, the items were measured in column centimeters (col. cms). The study quantified how much space is given to HIV/AIDS cognitive and activity information by multiplying the number of published HIV/AIDS items' columns in the selected newspapers by their length in centimeters. The centimeters were measured by placing vertically a centimeter ruler alongside columns of published HIV/AIDS items.

A modification of Budd's [12] attention scores technique, a device for measuring news play and usually applied in print media content analysis, was employed in measuring newspaper items prominence. Rather than its limited application to HIV/AIDS news stories which the researcher defined as news stories with an HIV/AIDS theme, the technique was applied to HIV/AIDS information. HIV/AIDS information was defined as all newspaper items (news stories, features, editorials, advertisements etc.) about or relating to HIV/AIDS. Consequently, (1) when an information item in any of the content categories constituted a front page lead, six points (attention scores) were allotted to that item's content category; (2) When an information item constituted a back page lead, five points (attention scores) were allotted to that item's content category; (3) When an information item appeared on the front page, four points (attention scores) were allotted to that item's content category; (4) When an information item appeared on the back page, three points (attention scores) were allotted to that content category; (5) When an information item appeared on page two, two points (attention scores) were allotted to that item's content category; and (6) When an information item appeared on other inside pages, 1 point (attention score) was allotted to that item content category.

It is assumed that the most important items are published on the front page with the lead outstanding, while the degree of priority on information items decreases into the inside pages. The back page is also considered critical and strategic because of its external position. For the study therefore, information items which were not published on front and back pages of the newspapers were considered of least attention or priority. Items that continued from the two pages (front and back) to inside pages have been classified as front and back (page).

## Results

Coders identified a total of 464 pieces of HIV/AIDS-related information in the four newspapers corresponding to a total attention score of 571 and 22293.8 column centimeters of information space. The data were analyzed to ascertain the attention paid to HIV/AIDS cognitive-oriented information and HIV/AIDS activity-oriented information in terms of information frequency, prominence and space. One hundred and forty five (31%) pieces of HIV/AIDS-related information were in The Punch; 116 (25%) in the New Nigerian; 111 (24%) in The Guardian, and 92 (20%) in the Daily Trust. In terms of prominence, The Punch had the highest attention scores, 176 (31%). Daily Trust had 150 (26%); New Nigerian, 131 (23%) and The Guardian, 114 (20%). New Nigerian recorded the highest column centimeters with regards to HIV/AIDS information space, 6771.9 (30%); The Punch, 6023.6 (27%); Daily Trust, 5263.5 (24%) and The Guardian, 4234.8 (19%). The total number of HIV/AIDS activity-oriented information published by the four Nigerian newspapers was more than the total number of HIV/AIDS cognitive-oriented information during the period studied. Two hundred and seventy four (59%) pieces of HIV/AIDS-related information were activity-oriented. Apart from the Daily Trust which published an equal number of activity and cognitive information, all the other newspapers published more activity than cognitive information. The proportions of activity-oriented pieces of HIV/AIDS-related information were 64.7% in the New Nigerian; 61.4% in The Punch; 57.7% in The Guardian and 50% in the Daily Trust.

Altogether, the four newspapers devoted a total of 276 news stories to HIV/AIDS (64.9% activity-oriented). The proportions of activity-oriented HIV/AIDS news stories in the Daily Trust was 59.3%; The Guardian 61.7%; New Nigerian, 67.7%, and The Punch 67.1%. Out of the 279 attention scores allotted to all the news stories in the content categories, activity-oriented news stories had more points than cognitive-oriented news stories; 70.6% (197). No news story on HIV/AIDS made front and back pages lead. There were equal numbers of HIV/AIDS activity and cognitive front page news stories. However, among the news stories which constituted the back page, page 2 and other inside pages, activity-oriented news stories had more attention scores than cognitive-oriented news stories. Overall, HIV/AIDS news stories occupied 11637.8 column centimeters. While HIV/AIDS activity-oriented news stories accounted for 59.7% (6951.9 col.cms), HIV/AIDS cognitive-oriented news stories accounted for 40.3% (or 4685.9 col.cms).

Two of the four newspapers (Daily Trust and New Nigerian) did not publish HIV/AIDS editorials at all during the period studied. There were

nine editorials on HIV/AIDS. Eight of these appeared in The Guardian. Of the eight editorials in The Guardian, five were activity-oriented. The only editorial featured in The Punch was cognitive-oriented.

There were more HIV/AIDS activity-oriented feature articles (60.7%) than HIV/AIDS cognitive-oriented feature articles. Seventy-one percent of feature articles in the Daily Trust were activity oriented as were 56.4% in The Guardian, 60.0% in the New Nigerian, and 63.6% in the Punch. The ratio of space in col.cms occupied by HIV/AIDS activity-oriented feature articles to HIV/AIDS cognitive-oriented feature articles in all the newspapers put together indicates that HIV/AIDS activity-oriented feature articles occupied more space than HIV/AIDS cognitive feature articles. During the period studied, the four Nigerian newspapers devoted a space of 5341.1 col.cms (or 50.6%) to activity-oriented feature articles and a space of 5221 col.cms (or 49.4%) to cognitive-oriented feature articles. In the New Nigerian and the Punch however, HIV/AIDS cognitive-oriented feature articles occupied more space than HIV/AIDS activity-oriented feature articles. In New Nigerian 44.4% (240col.cms) of space was dedicated to activity-oriented feature articles while 48.6% (2040 col. cms) was dedicated to activity-oriented feature stories. The Guardian and the Daily Trust devoted more space to HIV/AIDS activity oriented feature articles (56.4% (2640.5 col.cms) and 70% (420.6 col.cms) respectively.

There were thirty-five HIV/AIDS-related advertisements in the four newspapers. Overall, there were more cognitive-oriented advertisements (60.0%). However, a greater proportion of advertisement messages in The Guardian and New Nigerian had three and two HIV/AIDS-related advertisements respectively, all of which were activity-oriented. The Daily Trust had 21 advertisements of which 16 (76.2%) were cognitive-oriented. There were nine HIV/AIDS-related advertisements in The Punch of which five were cognitive-oriented.

## Discussion

To understand the response of the media in Nigeria to the call for transition from cognitive to activity-oriented models of HIV/AIDS communication, a comparative analysis of HIV/AIDS information in four Nigerian mainstream newspapers was conducted. The predominance in coverage of HIV/AIDS activity-oriented information as identified in the four newspapers suggests that HIV/AIDS contextual issues receive considerable attention. The dominance of activity-oriented HIV/AIDS content information contradicts the view of some scholars [1, 5, 13-16] that insufficient attention has been paid by the mass media in developing countries to the activity model of HIV/AIDS communication. It also suggests that Nigerian newspapers might have been responding to global reviews of HIV/AIDS communication, such as, for example, the new UNAIDS (1999) communication framework. The UNAIDS framework calls for a shift from individual-level theories and models of preventive health behaviours (health belief models, theory of reasoned action, stages of change, AIDS Risk Reduction Model and others) to multilevel models that take into account cultural and contextual factors.

The dominance of activity information further shows that Nigerian newspapers in their expanded roles may be capable of providing national and international models of strategic responses to diseases. The dominance of HIV/AIDS activity-oriented editorials as well as feature articles is critical because these items, more than news stories, have the capacity to lay bare the ways in which HIV/AIDS exacerbates social prejudices, economic inequalities, discriminatory practices and political injustices. Although, editorials and feature articles have the capacity to stimulate debate and foster a social environment in which AIDS is addressed in a spirit of openness, news stories dominated the HIV/AIDS information items studied. The relative lack of editorials and feature articles may suggest ambivalence occasioned by lack of skill and acknowledge on the part of editorial and feature writers.

None of the papers sampled used an HIV/AIDS story as front or back page lead. Furthermore, both HIV/AIDS activity and cognitive stories have very low attention scores on the front and back pages. A number of reasons could be adduced for it. It could be that the urge to sell had conditioned the perception of the newspapers towards considering HIV/AIDS stories less sensational than other news items. It could also be a manifestation of the natural inclination of the papers to follow occurrences that had "greater" social impact. Indeed, the Nigerian mass

media within the period covered by this study focused more on intriguing and sensational social, political and economic issues in Nigeria.

A striking feature of the four Nigerian newspapers coverage of HIV/AIDS information was the dominance of HIV/AIDS cognitive-oriented advertisement messages. This is not surprising, as advertisers and advertisement copy writers in Nigeria as elsewhere determine the content and space of advertisement messages.

Study findings should be interpreted in light of several limitations. First, the sample was not randomized and is based on a small sample of newspapers. Results cannot therefore be generalized to the entire Nigerian newspapers and other mass media. Second, tracing the evolution of newspaper reporting on HIV in Nigeria over a longer period of time would have offered a broader comparative analysis of the transition from cognitive to activity model of communication. These are areas for further research.

## Conclusion

This study shows that the activity model of HIV/AIDS communication dominates the four Nigerian mainstream newspapers studied. It is possible that this trend is common to other Nigerian mass media outlets. Perhaps, the considerable global review of HIV/AIDS communication practices that have taken place and the relative positive national response have provided broader basis for contextual redirection for the mass media in some developing countries. However, it is worth noting the limited number of editorials and feature articles, which have the capacity to stimulate debate and foster a social environment in which AIDS is addressed in a spirit of openness. For a country that has the third largest number of people living with HIV/AIDS, globally, one would expect the mass media to deliberately play an instrumental and a more active role in the battle against the disease by engaging in more in-depth contextual discourse.

## Competing interests

The authors declare no competing interests.

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