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**Abstract**

The main forms of childhood malnutrition occur predominantly in children <5 years of age living in low-income and middle-income countries and include stunting, wasting and kwashiorkor, of which severe wasting and kwashiorkor are commonly referred to as severe acute malnutrition. Here, we use the term 'severe malnutrition' to describe these conditions to better reflect the contributions of chronic poverty, poor living conditions with pervasive deficits in sanitation and hygiene, a high prevalence of infectious diseases and environmental insults, food insecurity, poor maternal and fetal nutritional status and suboptimal nutritional intake in infancy and early childhood. Children with severe malnutrition have an increased risk of serious illness and death, primarily from acute infectious diseases. International growth standards are used for the diagnosis of severe malnutrition and provide therapeutic end points. The early detection of severe wasting and kwashiorkor and outpatient therapy for these conditions using ready-to-use therapeutic foods form the cornerstone of modern therapy, and only a small percentage of children require inpatient care. However, the normalization of physiological and metabolic functions in children with malnutrition is challenging, and children remain at high risk of relapse and death. Further research is urgently needed to improve our understanding of the pathophysiology of severe malnutrition, especially the mechanisms causing kwashiorkor, and to develop new interventions for prevention and treatment.


**Abstract**

A strong scientific rationale exists for conducting clinical pharmacology studies in target populations because local factors such as genetics, environment, comorbidities, and diet can affect variability in drug responses. However, clinical pharmacology studies are not widely conducted in sub-Saharan Africa, in part due to limitations in technical expertise...
and infrastructure. Since 2012, a novel public-private partnership model involving research institutions and a pharmaceutical company has been applied to developing increased capability for clinical pharmacology research in multiple African countries.


Abstract

Although the burden of Plasmodium falciparum malaria is gradually declining in many parts of Africa, it is characterized by spatial and temporal variability that presents new and evolving challenges for malaria control programs. Reductions in the malaria burden need to be sustained in the face of changing epidemiology whilst simultaneously tackling significant pockets of sustained or increasing transmission. Large-scale, robust surveillance mechanisms that measure rather than estimate the actual burden of malaria over time from large areas of the continent where such data are lacking need to be prioritized. We review these fascinating developments, caution against complacency, and make the case that improving the extent and quality of malaria surveillance is vital for Africa as she marches on towards elimination.


Abstract

The CH₂Cl₂/MeOH (1:1) extract of the aerial parts of Tephrosia subtriflora afforded a new flavanonol, named subtriflavanonol (1), along with the known flavanone spinoflavanone B, and the known flavanonols MS-II (2) and mundulinol. The structures were elucidated by the use of NMR spectroscopy and mass spectrometry. The absolute configuration of the flavanonols was determined based on quantum chemical ECD calculations. In the antiplasmodial assay, compound 2 showed the highest activity against chloroquine-sensitive Plasmodium falciparum reference clones (D6 and 3D7), artemisinin-sensitive isolate (F32-TEM) as well as field isolate (KSM 009) with
IC$_{50}$ values 1.4-4.6 μM without significant cytotoxicity against Vero and HEp2 cell lines (IC$_{50}$ > 100 μM). The new compound (1) showed weak antiplasmodial activity, IC$_{50}$ 12.5-24.2 μM, but also showed selective anticancer activity against HEp2 cell line (CC$_{50}$ 16.9 μM).


Abstract

Although epidemiological observations, IgG passive transfer studies and experimental infections in humans all support the feasibility of developing highly effective malaria vaccines, the precise antigens that induce protective immunity remain uncertain. Here, we review the methodologies applied to vaccine candidate discovery for Plasmodium falciparum malaria from the pre- to post-genomic era. Probing of genomic and cDNA libraries with antibodies of defined specificities or functional activity predominated the former, whereas reverse vaccinology encompassing high throughput in silico analyses of genomic, transcriptomic or proteomic parasite data sets is the mainstay of the latter. Antibody-guided vaccine design spanned both eras but currently benefits from technological advances facilitating high-throughput screening and downstream applications. We make the case that although we have exponentially increased our ability to identify numerous potential vaccine candidates in a relatively short space of time, a significant bottleneck remains in their validation and prioritization for evaluation in clinical trials. Longitudinal cohort studies provide supportive evidence but results are often conflicting between studies. Demonstration of antigen-specific antibody function is valuable but the relative importance of one mechanism over another with regards to protection remains undetermined. Animal models offer useful insights but may not accurately reflect human disease. Challenge studies in humans are preferable but prohibitively expensive. In the absence of reliable correlates of protection, suitable animal models or a better understanding of the mechanisms underlying protective immunity in humans, vaccine candidate discovery per se may not be sufficient to provide the paradigm shift necessary to develop the next generation of highly effective subunit malaria vaccines.


**Abstract**

Achieving a malaria-free world presents exciting scientific challenges as well as overwhelming health, equity, and economic benefits. WHO and countries are setting ambitious goals for reducing the burden and eliminating malaria through the "Global Technical Strategy" and 21 countries are aiming to eliminate malaria by 2020. The commitment to achieve these targets should be celebrated. However, the need for innovation to achieve these goals, sustain elimination, and free the world of malaria is greater than ever. Over 180 experts across multiple disciplines are engaged in the Malaria Eradication Research Agenda (malERA) Refresh process to address problems that need to be solved. The result is a research and development agenda to accelerate malaria elimination and, in the longer term, transform the malaria community's ability to eradicate it globally.


**Abstract**

Pneumonia accounted for 15% of the 6.3 million deaths among children younger than five years in 2013, a total of approximately 935,000 deaths worldwide. Routine vaccination against common childhood illnesses has been identified as one of the most cost-effective strategies to prevent death from pneumonia. Vaccine-preventable or potentially preventable diseases commonly linked with respiratory tract infections include Streptococcus pneumoniae, Haemophilus influenza type-b (Hib), pertussis, influenza, measles, and tuberculosis. Although here have been great strides in the development and administration of effective vaccines, the countries that carry the largest disease burdens still struggle to vaccinate their children and newer conjugated vaccines remain out of reach for many. The Global Vaccine Action Plan (GVAP) has identified priority areas for innovation in research in all aspects of immunisation development and delivery to ensure equitable access to vaccines for all.

Abstract

Recent efforts in malaria control have led to marked reductions in malaria incidence. However, new strategies are needed to sustain malaria elimination and eradication and achieve the World Health Organization goal of a malaria-free world. The development of highly effective vaccines would contribute to this goal and would be facilitated by a comprehensive understanding of humoral immune responses targeting Plasmodium falciparum and Plasmodium vivax malaria. New tools are required to facilitate the identification of vaccine candidates and the development of vaccines that induce functional and protective immunity. Here we discuss recent published findings, and unpublished work presented at the 2016 Molecular Approaches to Malaria conference, that highlight advancements in understanding humoral immune responses in the context of vaccine development. Highlights include the increased application of 'omics' and 'Big data' platforms to identify vaccine candidates, and the identification of novel functions of antibody responses that mediate protection. The application of these strategies and a global approach will increase the likelihood of rapid development of highly efficacious vaccines.


Abstract

Background: Maternal rectovaginal colonization with group B Streptococcus (GBS) is the most common pathway for GBS disease in mother, fetus, and newborn. This article, the second in a series estimating the burden of GBS, aims to determine the prevalence and serotype distribution of GBS colonizing pregnant women worldwide.
### Methods:
We conducted systematic literature reviews (PubMed/Medline, Embase, Latin American and Caribbean Health Sciences Literature [LILACS], World Health Organization Library Information System [WHOLIS], and Scopus), organized Chinese language searches, and sought unpublished data from investigator groups. We applied broad inclusion criteria to maximize data inputs, particularly from low- and middle-income contexts, and then applied new meta-analyses to adjust for studies with less-sensitive sampling and laboratory techniques. We undertook meta-analyses to derive pooled estimates of maternal GBS colonization prevalence at national and regional levels.

### Results:
The dataset regarding colonization included 390 articles, 85 countries, and a total of 299924 pregnant women. Our adjusted estimate for maternal GBS colonization worldwide was 18% (95% confidence interval [CI], 17%-19%), with regional variation (11%-35%), and lower prevalence in Southern Asia (12.5% [95% CI, 10%-15%]) and Eastern Asia (11% [95% CI, 10%-12%]). Bacterial serotypes I-V account for 98% of identified colonizing GBS isolates worldwide. Serotype III, associated with invasive disease, accounts for 25% (95% CI, 23%-28%), but is less frequent in some South American and Asian countries. Serotypes VI-IX are more common in Asia.

### Conclusions:
GBS colonizes pregnant women worldwide, but prevalence and serotype distribution vary, even after adjusting for laboratory methods. Lower GBS maternal colonization prevalence, with less serotype III, may help to explain lower GBS disease incidence in regions such as Asia. High prevalence worldwide, and more serotype data, are relevant to prevention efforts.


**Abstract**

Substantial evidence indicates that parents of autistic individuals often display milder forms of autistic traits referred to as the broader autism phenotype (BAP). To determine if discrete endophenotypes of autism can be identified, we reviewed the literature to assess the evidence of behavioral, cognitive, and psychiatric profiles of the BAP. A systematic review was conducted using EMBASE, MEDLINE, PsycINFO, PsycEXTRA, and Global Health. Sixty papers met our inclusion criteria and results are discussed according to the proportion of studies that yield significant deficits per domain. The
behavioral, cognitive, and psychiatric endophenotypes in parents of autistic probands are still not clarified; however, evidence suggests mild social/communication deficits, rigid/aloof personality traits, and pragmatic language difficulties as the most useful sociobehavioral candidate endophenotype traits. The existence of deficits in the cognitive domain does suggest familial vulnerability for autism. Furthermore, increased depressed mood and anxiety can also be useful markers; however, findings should be interpreted with caution because of the small number of studies in such heterogeneously broad domains and several methodological limitations.


Abstract

Antimicrobial resistance is an important threat to international health. Therapeutic guidelines for empirical treatment of common life-threatening infections depend on available information regarding microbial aetiology and antimicrobial susceptibility, but sub-Saharan Africa lacks diagnostic capacity and antimicrobial resistance surveillance. We systematically reviewed studies of antimicrobial resistance among children in sub-Saharan Africa since 2005. 18 of 1075 articles reviewed met inclusion criteria, providing data from 67 451 invasive bacterial isolates from inconsistently defined populations in predominantly urban tertiary settings. Among neonates, Gram-negative organisms were the predominant cause of early-onset neonatal sepsis, with a high prevalence of extended-spectrum β-lactamase-producing organisms. Gram-positive bacteria were responsible for a high proportion of infections among children beyond the neonatal period, with high reported prevalence of non-susceptibility to treatment advocated by the WHO therapeutic guidelines. There are few up-to-date or representative studies given the magnitude of the problem of antimicrobial resistance, especially regarding community-acquired infections. Research should focus on differentiating resistance in community-acquired versus hospital-acquired infections, implementation of standardised reporting systems, and pragmatic clinical trials to assess the efficacy of alternative treatment regimens.

Abstract

Background: The growth of Information and Communication Technology in Kenya has facilitated implementation of a large number of eHealth projects in a bid to cost-effectively address health and health system challenges. This systematic review aims to provide a situational analysis of eHealth initiatives being implemented in Kenya, including an assessment of the areas of focus and geographic distribution of the health projects. The search strategy involved peer and non-peer reviewed sources of relevant information relating to projects under implementation in Kenya. The projects were examined based on strategic area of implementation, health purpose and focus, geographic location, evaluation status and thematic area.

Results: A total of 114 citations comprising 69 eHealth projects fulfilled the inclusion criteria. The eHealth projects included 47 mHealth projects, 9 health information system projects, 8 eLearning projects and 5 telemedicine projects. In terms of projects geographical distribution, 24 were executed in Nairobi whilst 15 were designed to have a national coverage but only 3 were scaled up. In terms of health focus, 19 projects were mainly on primary care, 17 on HIV/AIDS and 11 on maternal and child health (MNCH). Only 8 projects were rigorously evaluated under randomized control trials.

Conclusion: This review discovered that there is a myriad of eHealth projects being implemented in Kenya, mainly in the mHealth strategic area and focusing mostly on primary care and HIV/AIDs. Based on our analysis, most of the projects were rarely evaluated. In addition, few projects are implemented in marginalised areas and least urbanized counties with more health care needs, notwithstanding the fact that adoption of information and communication technology should aim to improve health equity (i.e. improve access to health care particularly in remote parts of the country in order to reduce geographical inequities) and contribute to overall health systems strengthening.

Abstract

Background: Audit and feedback is a common intervention for supporting clinical behaviour change. Increasingly, health data are available in electronic format. Yet, little is known regarding if and how electronic audit and feedback (e-A&F) improves quality of care in practice.

Objective: The study aimed to assess the effectiveness of e-A&F interventions in a primary care and hospital context and to identify theoretical mechanisms of behaviour change underlying these interventions.

Methods: In August 2016, we searched five electronic databases, including MEDLINE and EMBASE via Ovid, and the Cochrane Central Register of Controlled Trials for published randomised controlled trials. We included studies that evaluated e-A&F interventions, defined as a summary of clinical performance delivered through an interactive computer interface to healthcare providers. Data on feedback characteristics, underlying theoretical domains, effect size and risk of bias were extracted by two independent review authors, who determined the domains within the Theoretical Domains Framework (TDF). We performed a meta-analysis of e-A&F effectiveness, and a narrative analysis of the nature and patterns of TDF domains and potential links with the intervention effect.

Results: We included seven studies comprising of 81,700 patients being cared for by 329 healthcare professionals/primary care facilities. Given the extremely high heterogeneity of the e-A&F interventions and five studies having a medium or high risk of bias, the average effect was deemed unreliable. Only two studies explicitly used theory to guide intervention design. The most frequent theoretical domains targeted by the e-A&F interventions included 'knowledge', 'social influences', 'goals' and 'behaviour regulation', with each intervention targeting a combination of at least three. None of the interventions addressed the domains 'social/professional role and identity' or 'emotion'. Analyses identified the number of different domains coded in control arm to have the biggest role in heterogeneity in e-A&F effect size.

Conclusions: Given the high heterogeneity of identified studies, the effects of e-A&F were found to be highly variable. Additionally, e-A&F interventions tend to implicitly target only a fraction of known theoretical domains, even after omitting domains presumed not to be linked to e-A&F. Also, little evaluation of comparative effectiveness across trial arms was conducted. Future research should seek to further unpack the theoretical domains essential for effective e-A&F in order to better support strategic individual and team goals.

**Abstract**

Seizures with fever includes both febrile seizures (due to nonneurological febrile infections) and acute symptomatic seizures (due to neurological febrile infections). The cumulative incidence (lifetime prevalence) of febrile seizures in children aged ≤6 years is 2-5% in American and European studies, but there are no community-based data on acute symptomatic seizures in Africa. The incidence of acute symptomatic seizures in sub-Saharan Africa is more than twice that in high-income countries. However, most studies of acute symptomatic seizures from Africa are based on hospital samples or do not conduct surveys in demographic surveillance systems, which underestimates the burden. It is difficult to differentiate between febrile seizures and acute symptomatic seizures in Africa, especially in malaria-endemic areas where malaria parasites can sequester in the brain microvasculature; but this challenge can be addressed by robust identification of underlying causes. The proportion of complex acute symptomatic seizures (i.e., seizures that are focal, repetitive, or prolonged) in Africa are twice that reported in other parts of the world (>60% vs. ~30%), which is often attributed to falciparum malaria. These complex phenotypes of acute symptomatic seizures can be associated with behavioral and emotional problems in high-income countries, and outcomes may be even worse in Africa. One Kenyan study reported behavioral and emotional problems in approximately 10% of children admitted with acute symptomatic seizures, but it is not clear whether the behavioral and emotional problems were due to the seizures, shared genetic susceptibility, etiology, or underlying neurological damage. The underlying neurological damage in acute symptomatic seizures can lead not only to behavioral and emotional problems but also to neurocognitive impairment and epilepsy. Electroencephalography may have a prognostic role in African children with acute symptomatic seizures. There are significant knowledge gaps regarding acute symptomatic seizures in Africa, which results in lack of reliable estimates for planning interventions. Future epidemiological studies of acute symptomatic seizures should be set up in Africa.


Abstract

This editorial discusses a collection of papers examining gender across a range of health policy and systems contexts, from access to services, governance, health financing, and human resources for health. The papers interrogate differing health issues and core health systems functions using a gender lens. Together they produce new knowledge on the multiple impacts of gender on health experiences and demonstrate the importance of gender analyses and gender sensitive interventions for promoting well-being and health systems strengthening. The findings from these papers collectively show how gender intersects with other axes of inequity within specific contexts to shape experiences of health and health seeking within households, communities and health systems; illustrate how gender power relations affect access to important resources; and demonstrate that gender norms, poverty and patriarchy interplay to limit women's choices and chances both within household interactions and within the health sector. Health systems researchers have a responsibility to promote the incorporation of gender analyses into their studies in order to inform more strategic, effective and equitable health systems interventions, programmes, and policies. Responding to gender inequitable systems, institutions, and services in this sector requires an 'all hands-on deck' approach. We cannot claim to take a 'people-centred approach' to health systems if the status quo continues.


Abstract

Autism spectrum disorders (ASD) are thought to be associated with abnormal neural connectivity. Presently, neural connectivity is a theoretical construct that cannot be easily measured. Research in network science and time series analysis suggests that neural network structure, a marker of neural activity, can be measured with electroencephalography (EEG). EEG can be quantified by different methods of analysis to potentially detect brain abnormalities. The aim of this review is to examine evidence for the utility of three methods of EEG signal analysis in the ASD diagnosis and subtype
delineation. We conducted a review of literature in which 40 studies were identified and classified according to the principal method of EEG analysis in three categories: functional connectivity analysis, spectral power analysis, and information dynamics. All studies identified significant differences between ASD patients and non-ASD subjects. However, due to high heterogeneity in the results, generalizations could not be inferred and none of the methods alone are currently useful as a new diagnostic tool. The lack of studies prevented the analysis of these methods as tools for ASD subtypes delineation. These results confirm EEG abnormalities in ASD, but as yet not sufficient to help in the diagnosis. Future research with larger samples and more robust study designs could allow for higher sensitivity and consistency in characterizing ASD, paving the way for developing new means of diagnosis.


Abstract

In this issue of Blood, Dubert et al present the results of a large cohort study conducted across 3 sub-Saharan African countries (Mali, Cameroon, and Ivory Coast) to quantify differences between subphenotypes of sickle cell disease (SCD) based on markers of anemia, hemolysis, and vascular complications.


Abstract

Background: Treatment intensity scores can predict mortality and estimate resource use. They may therefore be of interest for essential neonatal care in low resource settings where neonatal mortality remains high. We sought to systematically review neonatal treatment intensity scores to (1) assess the level of evidence on predictive performance in predicting clinical outcomes and estimating resource utilisation and (2) assess the
applicability of the identified models to decision making for neonatal care in low resource settings.

**Methods:** We conducted a systematic search of PubMed, EMBASE (OVID), CINAHL, Global Health Library (Global index, WHO) and Google Scholar to identify studies published up until 21 December 2016. Included were all articles that used treatments as predictors in neonatal models. Individual studies were appraised using the CHecklist for critical Appraisal and data extraction for systematic Reviews of prediction Modelling Studies (CHARMS). In addition, Grading of Recommendations Assessment, Development, and Evaluation (GRADE) was used as a guiding framework to assess certainty in the evidence for predicting outcomes across studies.

**Results:** Three thousand two hundred forty-nine articles were screened, of which ten articles were included in the review. All of the studies were conducted in neonatal intensive care units with sample sizes ranging from 22 to 9978, with a median of 163. Two articles reported model development, while eight reported external application of existing models to new populations. Meta-analysis was not possible due heterogeneity in the conduct and reporting of the identified studies. Discrimination as assessed by area under receiver operating characteristic curve was reported for in-hospital mortality, median 0.84 (range 0.75-0.96, three studies), early adverse outcome and late adverse outcome (0.78 and 0.59, respectively, one study).

**Conclusion:** Existing neonatal treatment intensity models show promise in predicting mortality and morbidity. There is however low certainty in the evidence on their performance in essential neonatal care in low resource settings as all studies had methodological limitations and were conducted in intensive care. The approach may however be developed further for low resource settings like Kenya because treatment data may be easier to obtain compared to measures of physiological status.


**Abstract**

Universal access to quality newborn health services will be essential to meeting specific Sustainable Development Goals to reduce neonatal and overall child mortality. Data for
decision making are crucial for planning services and monitoring progress in these endeavours. However, gaps in local population-level and facility-based data hinder estimation of health service requirements for effective planning in many low-income and middle-income settings. We worked with local policy makers and experts in Nairobi City County, an area with a population of four million and the highest neonatal mortality rate amongst counties in Kenya, to address this gap, and developed a systematic approach to use available data to support policy and planning. We developed a framework to identify major neonatal conditions likely to require inpatient neonatal care and identified estimates of incidence through literature review and expert consultation, to give an overall estimate for the year 2017 of the need for inpatient neonatal care, taking account of potential comorbidities. Our estimates suggest that almost 1 in 5 newborns (183/1000 live births) in Nairobi City County may need inpatient care, resulting in an estimated 24161 newborns expected to require care in 2017. Our approach has been well received by local experts, who showed a willingness to work together and engage in the use of evidence in healthcare planning. The process highlighted the need for co-ordinated thinking on admission policy and referral care especially in a pluralistic provider environment helping build further appetite for data-informed decision making.


Abstract

Bioinformatics skills have become essential for many research areas; however, the availability of qualified researchers is usually lower than the demand and training to increase the number of able bioinformaticians is an important task for the bioinformatics community. When conducting training or hands-on tutorials, the lack of control over the analysis tools and repositories often results in undesirable situations during training, as unavailable online tools or version conflicts may delay, complicate, or even prevent the successful completion of a training event. The eBioKit is a stand-alone educational platform that hosts numerous tools and databases for bioinformatics research and allows training to take place in a controlled environment. A key advantage of the eBioKit over other existing teaching solutions is that all the required software and databases are locally installed on the system, significantly reducing the dependence on the internet. Furthermore, the architecture of the eBioKit has demonstrated itself to be an excellent balance between portability and performance, not only making the eBioKit an exceptional educational tool but also providing small research groups with a platform to
incorporate bioinformatics analysis in their research. As a result, the eBioKit has formed an integral part of training and research performed by a wide variety of universities and organizations such as the Pan African Bioinformatics Network (H3ABioNet) as part of the initiative Human Heredity and Health in Africa (H3Africa), the Southern Africa Network for Biosciences (SAnBio) initiative, the Biosciences eastern and central Africa (BecA) hub, and the International Glossina Genome Initiative.


Abstract

Aim: Even though systematic reviews have examined how aspects of propensity score methods are used, none has reviewed how the challenge of missing data is addressed with these methods. This review therefore describes how missing data are addressed with propensity score methods in observational comparative effectiveness studies.

Methods: Published articles on observational comparative effectiveness studies were extracted from MEDLINE and EMBASE databases.

Results: Our search yielded 167 eligible articles. Majority of these studies (114; 68%) conducted complete case analysis with only 53 of them stating this in the methods. Only 16 articles reported use of multiple imputation.

Conclusion: Few researchers use correct methods for handling missing data or reported missing data methodology which may lead to reporting biased findings.


Abstract
Rotavirus gastroenteritis is an important cause of childhood morbidity and mortality in Kenya. In July 2014, Kenya introduced the rotavirus vaccine into her national immunization program. Although immunization coverage is crucial in assessing the real-world impact of this vaccine, variability in the vaccine coverage across the country is likely to occur. In view of this, we estimated the extent of coverage for the rotavirus vaccine at two socio-economically different sub-counties using the administrative data. The findings indicate disparities in vaccine coverage and access between the sub-counties and, thus, underscore the need to strengthen immunization systems to facilitate timely, accessible, and equitable vaccine delivery across the country. Both sub-counties recorded high vaccine dropout, suggestive of poor utilization of the vaccine. In this regard, increased social mobilization is needed to encourage vaccine compliance and to enhance tracking of vaccine defaulters. While efforts to improve the accuracy of the administrative coverage estimates are crucial, vaccination coverage surveys will be needed to verify the administrative coverage data and help identify specific factors relating to rotavirus vaccine coverage in the country.


Abstract

Cancer is the third leading cause of death in Kenya. However, there is scarce information on the nutritional status of cancer patients to guide in decision making. The present study sought to assess the risk of malnutrition, and factors associated with malnutrition and cachexia, among cancer out-patients, with the aim of informing nutrition programmes for cancer management in Kenya and beyond. This was a facility-based cross-sectional study performed at Kenyatta National Hospital and Texas Cancer Centre in Nairobi, Kenya. The risk of malnutrition was assessed using the Malnutrition Universal Screening Tool (MUST). Diagnoses of malnutrition and cachexia were done using the European Society of Clinical Nutrition and Metabolism (ESPEN) and Fearon criteria, respectively. A total of 512 participants were assessed. Those at risk of malnutrition were 33·1 % (12·5 % at medium risk, 20·6 % at high risk). Prevalence of malnutrition was 13·4 %. The overall weight loss >5 % over 3 months was 18·2 % and low fat-free mass index was 43·1 %. Prevalence of cachexia was 14·1 % compared with 8·5 % obtained using the local criteria. Only 18·6 % participants had received any form of nutrition services. Age was a predictor of malnutrition and cachexia in addition to site of cancer for malnutrition and cigarette smoking for cachexia. The use of the MUST as a screening tool at the first point
of care should be explored. The predictive value of current nutrition assessment tools, and the local diagnostic criteria for malnutrition and cachexia should be reassessed to inform the development of appropriate clinical guidelines and future capacity-building initiatives that will ensure the correct identification of patients at risk for timely care.


Abstract

**Introduction:** WHO treatment guidelines are widely recommended for guiding treatment for millions of children with pneumonia every year across multiple low-income and middle-income countries. Guidelines are based on synthesis of available evidence that provides moderate certainty in evidence of effects for forms of pneumonia that can result in hospitalisation. However, trials have included fewer children from Africa than other settings, and it is suggested that African children with pneumonia have higher mortality. Thus, despite improving access to recommended treatments and deployment with high coverage of childhood vaccines, pneumonia remains one of the top causes of mortality for children in Kenya. Establishing whether there are benefits of alternative treatment regimens to help reduce mortality would require pragmatic clinical trials. However, these remain relatively expensive and time consuming. This protocol describes an approach to using secondary analysis of a new, large observational dataset as a potentially cheaper and quicker way to examine the comparative effectiveness of penicillin versus penicillin plus gentamicin in treatment of indrawing pneumonia. Addressing this question is important, as although it is now recommended that this form of pneumonia is treated with oral medication as an outpatient, it remains associated with non-trivial mortality that may be higher outside trial populations.

**Methods and analysis:** We will use a large observational dataset that captures data on all admissions to 13 Kenyan county hospitals. These data represent the findings of clinicians in practice and, because the system was developed for large observational research, pose challenges of non-random treatment allocation and missing data. To overcome these challenges, this analysis will use a rigorous approach to study design, propensity score methods and multiple imputation to minimise bias.
Ethics and dissemination: The primary data are held by hospitals participating in the Kenyan Clinical Information Network project with de-identified data shared with the Kenya Medical Research Institute (KEMRI)-Wellcome Trust Research Programme for agreed analyses. The use of data for the analysis described received ethical clearance from the KEMRI scientific and ethical review committee. The findings of this analysis will be published.


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Abstract

Childhood TB diagnosis is challenging. Studies in adults suggest Microscopic Observation Drug Susceptibility (MODS) culture or the Xpert MTB/RIF assay might be used to expand bacteriological diagnosis. However data from children are more limited. We prospectively compared MODS and Xpert MTB/RIF with standard microscopy and culture using the BD MGIT 960 system among 1442 Kenyan children with suspected TB. 97 specimens from 54 children were TB culture-positive: 91 (94%) by MGIT and 74 (76%) by MODS (p = 0.002). 72 (74%) culture-positive and 7 culture-negative specimens were Xpert MTB/RIF positive. Xpert MTB/RIF specificity was 100% (99.7-100%) among 1164 specimens from 892 children in whom TB was excluded, strongly suggesting all Xpert MTB/RIF positives are true positives. The sensitivity of MGIT, MODS and Xpert MTB/RIF was 88%, 71% and 76%, respectively, among all 104 true positive (culture and/or Xpert MTB/RIF positive) specimens. MGIT, MODS and Xpert MTB/RIF on the initial specimen identified 40/51 (78%), 33/51 (65%) and 33/51 (65%) culture-confirmed pulmonary TB cases, respectively; Xpert MTB/RIF detected 5 additional culture-negative cases. The high sensitivity and very high specificity of the Xpert MTB/RIF assay supports its inclusion in the reference standard for bacteriological diagnosis of childhood TB in research and clinical practice.


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Abstract

Background: Rotavirus (RV) is a major agent of gastroenteritis and an important cause of child death worldwide. Immunization (RVI) has been available since 2006, and the Federation of International Societies of Gastroenterology Hepatology and Nutrition (FISPGHAN) identified RVI as a top priority for the control of diarrheal illness. A FISPGHAN working group on acute diarrhea aimed at estimating the current RVI coverage worldwide and identifying barriers to implementation at local level.

Methods: A survey was distributed to national experts in infectious diseases and healthcare authorities (March 2015-April 2016), collecting information on local recommendations, costs and perception of barriers for implementation.

Results: Forty-nine of the 79 contacted countries (62% response rate) provided a complete analyzable data. RVI was recommended in 27/49 countries (55%). Although five countries have recommended RVI since 2006, a large number (16, 33%) included RVI in a National Immunization Schedule between 2012 and 2014. The costs of vaccination are covered by the government (39%), by the GAVI Alliance (10%) or public and private insurance (8%) in some countries. However, in most cases, immunization is paid by families (43%). Elevated cost of vaccine (49%) is the main barrier for implementation of RVI. High costs of vaccination (rs=-0.39, p=0.02) and coverage of expenses by families (rs=0.5, p=0.002) significantly correlate with a lower immunization rate. Limited perception of RV illness severity by the families (47%), public-health authorities (37%) or physicians (24%) and the timing of administration (16%) are further major barriers to large-scale RVI programs.

Conclusions: After 10 years since its introduction, the implementation of RVI is still unacceptably low and should remain a major target for global public health. Barriers to implementation vary according to setting. Nevertheless, public health authorities should promote education for caregivers and health-care providers and interact with local health authorities in order to implement RVI.


Abstract

The malaria parasite *Plasmodium falciparum* invades human red blood cells by a series of interactions between host and parasite surface proteins. By analyzing genome sequence data from human populations, including 1269 individuals from sub-Saharan Africa, we identify a diverse array of large copy-number variants affecting the host invasion receptor genes *GYPA* and *GYPB* We find that a nearby association with severe malaria is explained by a complex structural rearrangement involving the loss of *GYPB* and gain of two *GYPB*-A hybrid genes, which encode a serologically distinct blood group antigen known as Dantu. This variant reduces the risk of severe malaria by 40% and has recently increased in frequency in parts of Kenya, yet it appears to be absent from west Africa. These findings link structural variation of red blood cell invasion receptors with natural resistance to severe malaria.


Abstract

Severe anemia is a leading indication for blood transfusion and a major cause of hospital admission and mortality in African children. Failure to initiate blood transfusion rapidly enough contributes to anemia deaths in sub-Saharan Africa. This article examines delays in accessing blood and outcomes in transfused children in Kenyan hospitals. Children admitted with nonsurgical conditions in 10 Kenyan county hospitals participating in the Clinical Information Network who had blood transfusion ordered from September 2013 to March 2016 were studied. The delay in blood transfusion was calculated from the date when blood transfusion was prescribed to date of actual transfusion. Five percent (2,875/53,174) of admissions had blood transfusion ordered. Approximately half (45%, 1,295/2,875) of children who had blood transfusion ordered at admission had a documented hemoglobin < 5 g/dl and 36% (2,232/6,198) of all children admitted with a diagnosis of anemia were reported to have hemoglobin < 5 g/dL. Of all the ordered
transfusions, 82% were administered and documented in clinical records, and three-quarters of these (75%, 1,760/2,352) were given on the same day as ordered but these proportions varied from 71% to 100% across the 10 hospitals. Children who had a transfusion ordered but did not receive the prescribed transfusion had a mortality of 20%, compared with 12% among those transfused. Malaria-associated anemia remains the leading indication for blood transfusion in acute childhood illness admissions. Delays in transfusion are common and associated with poor outcomes. Variance in delay across hospitals may be a useful indicator of health system performance.


Abstract

**Background:** Recent studies have discovered that α-globin is expressed in blood vessel walls where it plays a role in regulating vascular tone. We tested the hypothesis that blood pressure (BP) might differ between normal individuals and those with α<sup>+</sup>thalassemia, in whom the production of α-globin is reduced.

**Methods and results:** The study was conducted in Nairobi, Kenya, among 938 adolescents aged 11 to 17 years. Twenty-four-hour ambulatory BP monitoring and arterial stiffness measurements were performed using an arteriograph device. We genotyped for α<sup>+</sup>thalassemia by polymerase chain reaction. Complete data for analysis were available for 623 subjects; 223 (36%) were heterozygous (-α/αα) and 47 (8%) were homozygous (-α/-α) for α<sup>+</sup>thalassemia whereas the remaining 353 (55%) were normal (αα/αα). Mean 24-hour systolic BP ±SD was 118±12 mm Hg in αα/αα, 117±11 mm Hg in -α/αα, and 118±11 mm Hg in -α/-α subjects, respectively. Mean 24-hour diastolic BP ±SD in these groups was 64±8, 63±7, and 65±8 mm Hg, respectively. Mean pulse wave velocity (PWV)±SD was 7±0.8, 7±0.8, and 7±0.7 m/s<sup>-1</sup>, respectively. No differences were observed in PWV and any of the 24-hour ambulatory BP monitoring-derived measures between those with and without α<sup>+</sup>thalassemia.

**Conclusions:** These data suggest that the presence of α<sup>+</sup>thalassemia does not affect BP and/or arterial stiffness in Kenyan adolescents.
Abstract

Background: Insecticide resistance has emerged as one of the major challenges facing National Malaria Control Programmes in Africa. A well-coordinated national database on insecticide resistance (IRBase) can facilitate the development of effective strategies for managing insecticide resistance and sustaining the effectiveness of chemical-based vector control measures. The aim of this study was to assemble a database on the current status of insecticide resistance among malaria vectors in Kenya.

Methods: Data was obtained from published literature through PubMed, HINARI and Google Scholar searches and unpublished literature from government reports, research institutions reports and malaria control programme reports. Each data source was assigned a unique identification code and entered into Microsoft Excel 2010 datasheets. Base maps on the distribution of insecticide resistance and resistance mechanisms among malaria vectors in Kenya were generated using ArcGIS Desktop 10.1 (ESRI, Redlands, CA, USA).

Results: Insecticide resistance status among the major malaria vectors in Kenya was reported in all the four classes of insecticides including pyrethroids, carbamates, organochlorines and organophosphates. Resistance to pyrethroids has been detected in Anopheles gambiae (s.s.), An. arabiensis and An. funestus (s.s.) while resistance to carbamates was limited to An. gambiae (s.s.) and An. arabiensis. Resistance to the organochlorine was reported in An. gambiae (s.s.) and An. funestus (s.s.) while resistance to organophosphates was reported in An. gambiae (s.l.) only. The mechanisms of insecticide resistance among malaria vectors reported include the kdr mutations (L1014S and L1014F) and elevated activity in carboxylesterase, glutathione S-transferases (GST) and monooxygenases. The kdr mutations L1014S and L1014F were detected in An. gambiae (s.s.) and An. arabiensis populations. Elevated activity of monooxygenases has been detected in both An. arabiensis and An. gambiae (s.s.) populations while the elevated activity of carboxylesterase and GST has been detected only in An. arabiensis populations.
### Conclusions

The geographical maps show the distribution of insecticide resistance and resistance mechanisms among malaria vectors in Kenya. The database generated will provide a guide to intervention policies and programmes in the fight against malaria.


### Abstract

A monovalent rotavirus vaccine (RV1) was introduced into the National Immunization Program in Kenya in July 2014. We examined the impact of the vaccine on hospitalization for all-cause acute gastroenteritis (AGE) and rotavirus-specific AGE and strain distribution at a large referral hospital which serves a predominantly peri-urban population in Central Kenya. Data on rotavirus AGE and strain distribution were derived from ongoing hospital-based AGE surveillance. Hospital administrative data were used to compare trends in all-cause AGE. Pre-vaccine (July 2009-June 2014) and post-vaccine (July 2014-June 2016) periods were compared for changes in hospitalization for all-cause AGE and rotavirus AGE and strain distribution. Following the vaccine introduction, the proportion of children aged <5 years hospitalized for rotavirus declined by 30% (95% CI: 19-45%) in the first year and 64% (95% CI: 49-77%) in the second year. Reductions in rotavirus positivity were most pronounced among the vaccine-eligible group (<12 months) in the first year post-vaccination at 42% (95% CI: 28-56%). Greater reductions of 67% (95% CI: 51-79%) were seen in the second year in the 12-23 months age group. Similarly, hospitalizations for all-cause AGE among children <5 years of age decreased by 31% (95% CI: 24-40%) in the first year and 58% (95% CI: 49-67%) in the second year of vaccine introduction. Seasonal peaks of rotavirus and all-cause AGE were reduced substantially. There was an increased detection of G2P[4], G3P[6] and G3P[8], which coincided temporally with the timing of the vaccine introduction. Thus, introducing the rotavirus vaccine into the routine immunization program in Kenya has resulted in a notable decline in rotavirus and all-cause AGE hospitalizations in Central Kenya. This provides early evidence for public health policy makers in Kenya to support the sustained use of the rotavirus vaccine in routine immunizations.


**Abstract**

A detailed understanding of the human infectious reservoir is essential for improving malaria transmission-reducing interventions. Here we report a multi-regional assessment of population-wide malaria transmission potential based on 1209 mosquito feeding assays in endemic areas of Burkina Faso and Kenya. Across both sites, we identified 39 infectious individuals. In high endemicity settings, infectious individuals were identifiable by research-grade microscopy (92.6%; 25/27), whilst one of three infectious individuals in the lowest endemicity setting was detected by molecular techniques alone. The percentages of infected mosquitoes in the different surveys ranged from 0.05 (4/7716) to 1.6% (121/7749), and correlate positively with transmission intensity. We also estimated exposure to malaria vectors through genetic matching of blood from 1094 wild-caught bloodfed mosquitoes with that of humans resident in the same houses. Although adults transmitted fewer parasites to mosquitoes than children, they received more mosquito bites, thus balancing


**Abstract**

In two previously described donors, the extracellular domain of LAIR1, a collagen-binding inhibitory receptor encoded on chromosome 19 (ref. 1), was inserted between the V and DJ segments of an antibody. This insertion generated, through somatic mutations, broadly reactive antibodies against RIFINs, a type of variant antigen expressed on the surface of Plasmodium falciparum-infected erythrocytes. To investigate how frequently such antibodies are produced in response to malaria infection, we screened plasma from
two large cohorts of individuals living in malaria-endemic regions. Here we report that 5-10% of malaria-exposed individuals, but none of the European blood donors tested, have high levels of LAIR1-containing antibodies that dominate the response to infected erythrocytes without conferring enhanced protection against febrile malaria. By analysing the antibody-producing B cell clones at the protein, cDNA and gDNA levels, we characterized additional LAIR1 insertions between the V and DJ segments and discovered a second insertion modality whereby the LAIR1 exon encoding the extracellular domain and flanking intronic sequences are inserted into the switch region. By exon shuffling, this mechanism leads to the production of bispecific antibodies in which the LAIR1 domain is precisely positioned at the elbow between the VH and CH1 domains. Additionally, in one donor the genomic DNA encoding the VH and CH1 domains was deleted, leading to the production of a camel-like LAIR1-containing antibody. Sequencing of the switch regions of memory B cells from European blood donors revealed frequent templated inserts originating from transcribed genes that, in rare cases, comprised exons with orientations and frames compatible with expression. These results reveal different modalities of LAIR1 insertion that lead to public and dominant antibodies against infected erythrocytes and suggest that insertion of templated DNA represents an additional mechanism of antibody diversification that can be selected in the immune response against pathogens and exploited for B cell engineering.


Abstract

Paramphistomoids are ubiquitous and widespread digeneans that infect a diverse range of definitive hosts, being particularly speciose in ruminants. We collected adult worms from cattle, goats and sheep from slaughterhouses, and cercariae from freshwater snails from ten localities in Central and West Kenya. We sequenced cox1 (690 bp) and internal transcribed region 2 (ITS2) (385 bp) genes from a small piece of 79 different adult worms and stained and mounted the remaining worm bodies for comparisons with available descriptions. We also sequenced cox1 and ITS2 from 41 cercariae/rediae samples collected from four different genera of planorbid snails. Combining morphological observations, host use information, genetic distance values and phylogenetic methods, we delineated 16 distinct clades of paramphistomoids. For four of the 16 clades, sequences from adult worms and cercariae/rediae matched, providing an independent assessment for their life cycles. Much work is yet to be done to resolve fully
the relationships among paramphistomoids, but some correspondence between sequence- and anatomically based classifications were noted. Paramphistomoids of domestic ruminants provide one of the most abundant sources of parasitic flatworm biomass, and because of the predilection of several species use Bulinus and Biomphalaria snail hosts, have interesting linkages with the biology of animal and human schistosomes to in Africa.


| Abstract |
| There are minimal data to define normal oxygen saturation (SpO₂) levels for infants within the first 24 hours of life and even fewer data generalisable to the 7% of the global population that resides at an altitude of >1500 m. The aim of this study was to establish the reference range for SpO₂ in healthy term and preterm neonates within 24 hours in Nairobi, Kenya, located at 1800 m. A random sample of clinically well infants had SpO₂ measured once in the first 24 hours. A total of 555 infants were enrolled. The 5th-95th percentile range for preductal and postductal SpO₂ was 89%-97% for the term and normal birthweight groups, and 90%-98% for the preterm and low birthweight (LBW) groups. This may suggest that 89% and 97% are reasonable SpO₂ bounds for well term, preterm and LBW infants within 24 hours at an altitude of 1800 m. |

| Abstract |
| Background: Infant feeding in the context of human immunodeficiency virus (HIV) poses unique challenges to mothers and healthcare workers in balancing the perceived |
risks of HIV transmission and nutritional requirements. We aimed to describe the decision-making processes around infant feeding at a rural HIV clinic in Kenya.

**Methods:** We used a qualitative study design. Between March and August 2011, we conducted in-depth interviews \((n=9)\) and focus group discussions \((n=10)\) with purposively selected hospital and community respondents at Kilifi County Hospital, Kenya. These respondents had all experienced of infant feeding in the context of HIV. These interviews were informed by prior structured observations of health care worker interactions with carers during infant feeding counselling sessions.

**Results:** Overall, women living with HIV found it difficult to adhere to the HIV infant feeding guidance. There were three dominant factors that influenced decision making processes: 1) Exclusive breastfeeding was not the cultural norm, therefore practising it raised questions within the family and community about a mother's parenting capabilities and HIV status. 2) Women living with HIV lacked autonomy in decision-making on infant feeding due to socio-cultural factors. 3) Non-disclosure of HIV status to close members due to the stigma.

**Conclusion:** Infant feeding decision-making by women living with HIV in rural Kenya is constrained by a lack of autonomy, stigma and poverty. There is an urgent need to address these challenges through scaling up psycho-social and gender empowerment strategies for women, and introducing initiatives that promote the integration of HIV infant feeding strategies into other child health services.


**Abstract**

At independence in 2011, South Sudan's health sector was almost non-existent. The first national health strategic plan aimed to achieve an integrated health facility network that would mean that 70% of the population were within 5 km of a health service provider. Publically available data on functioning and closed health facilities, population distribution, road networks, land use and elevation were used to compute the fraction of the population within 1 hour walking distance of the nearest public health facility offering curative services. This metric was summarised for each of the 78 counties in South Sudan and compared with simpler metrics of the proportion of the population within 5 km of a health facility. In 2016, it is estimated that there were 1747 public
health facilities, out of which 294 were non-functional in part due to the ongoing civil conflict. Access to a service provider was poor with only 25.7% of the population living within one-hour walking time to a facility and 28.6% of the population within 5 km. These metrics, when applied sub-nationally, identified the same high priority, most vulnerable counties. Simple metrics based upon population distribution and location of facilities might be as valuable as more complex models of health access, where attribute data on travel routes are imperfect or incomplete and sparse. Disparities exist in South Sudan among counties and those with the poorest health access should be targeted for priority expansion of clinical services.


Abstract

Gender equity is imperative to the attainment of healthy lives and wellbeing of all, and promoting gender equity in leadership in the health sector is an important part of this endeavour. This empirical research examines gender and leadership in the health sector, pooling learning from three complementary data sources: literature review, quantitative analysis of gender and leadership positions in global health organisations and qualitative life histories with health workers in Cambodia, Kenya and Zimbabwe. The findings highlight gender biases in leadership in global health, with women underrepresented. Gender roles, relations, norms and expectations shape progression and leadership at multiple levels. Increasing women's leadership within global health is an opportunity to further health system resilience and system responsiveness. We conclude with an agenda and tangible next steps of action for promoting women's leadership in health as a means to promote the global goals of achieving gender equity.


Abstract

**Background:** There is an increasing recognition of malnutrition among infants under 6 mo of age (U6M). Current diagnosis criteria use weight-for-length z scores (WLZs), but the 2006 WHO standards exclude infants shorter than 45 cm. In older children, midupper arm circumference (MUAC) predicts mortality better than does WLZ. Outcomes may also be influenced by exposure to HIV and size or gestational age at birth. Diagnostic thresholds for WLZ, MUAC, and other indexes have not been fully evaluated against mortality risk among U6M infants. **Objective:** The aim was to determine the association of anthropometric indexes with risks of inpatient and postdischarge mortality among U6M infants recruited at the time of hospitalization. **Design:** We analyzed data from a cohort of U6M infants admitted to Kilifi County Hospital (2007-2013), Kenya. The primary outcomes were inpatient death and death during follow-up over 1 y after discharge. We calculated adjusted RR for inpatient mortality and HR for postdischarge mortality for different anthropometric measures and thresholds. Discriminatory value was assessed by using receiver operating characteristic curves. **Results:** A total of 2882 infants were admitted: 140 (4.9%) died in the hospital and 1405 infants were followed up after discharge. Of these, 75 (5.3%) died within 1 y during 1318 child-years of observation. MUAC and weight-for-age z score (WAZ) predicted inpatient and postdischarge mortality better than did WLZ ($P < 0.0001$). A single MUAC threshold of $<11.0$ cm performed similarly to MUAC thresholds that varied with age (all $P > 0.05$) and performed better than WLZ $<-3$ for both inpatient and postdischarge mortality (both $P < 0.001$). Reported small size at birth did not reduce the risk of death associated with anthropometric indexes. **Conclusions:** U6M infants at the highest risk of death are best targeted by using MUAC or WAZ. Further research into the effectiveness of potential interventions is required.


Abstract
**Background:** Four studies previously indicated that the effect of malaria infection during pregnancy on the risk of low birthweight (LBW; <2,500 g) may depend upon maternal nutritional status. We investigated this dependence further using a large, diverse study population.

**Methods and findings:** We evaluated the interaction between maternal malaria infection and maternal anthropometric status on the risk of LBW using pooled data from 14,633 pregnancies from 13 studies (6 cohort studies and 7 randomized controlled trials) conducted in Africa and the Western Pacific from 1996-2015. Studies were identified by the Maternal Malaria and Malnutrition (M3) initiative using a convenience sampling approach and were eligible for pooling given adequate ethical approval and availability of essential variables. Study-specific adjusted effect estimates were calculated using inverse probability of treatment-weighted linear and log-binomial regression models and pooled using a random-effects model. The adjusted risk of delivering a baby with LBW was 8.8% among women with malaria infection at antenatal enrollment compared to 7.7% among uninfected women (adjusted risk ratio [aRR] 1.14 [95% confidence interval (CI): 0.91, 1.42]; N = 13,613), 10.5% among women with malaria infection at delivery compared to 7.9% among uninfected women (aRR 1.32 [95% CI: 1.08, 1.62]; N = 11,826), and 15.3% among women with low mid-upper arm circumference (MUAC <23 cm) at enrollment compared to 9.5% among women with MUAC ≥ 23 cm (aRR 1.60 [95% CI: 1.36, 1.87]; N = 9,008). The risk of delivering a baby with LBW was 17.8% among women with both malaria infection and low MUAC at enrollment compared to 8.4% among uninfected women with MUAC ≥ 23 cm (joint aRR 2.13 [95% CI: 1.21, 3.73]; N = 8,152). There was no evidence of synergism (i.e., excess risk due to interaction) between malaria infection and MUAC on the multiplicative (p = 0.5) or additive scale (p = 0.9). Results were similar using body mass index (BMI) as an anthropometric indicator of nutritional status. Meta-regression results indicated that there may be multiplicative interaction between malaria infection at enrollment and low MUAC within studies conducted in Africa; however, this finding was not consistent on the additive scale, when accounting for multiple comparisons, or when using other definitions of malaria and malnutrition. The major limitations of the study included availability of only 2 cross-sectional measurements of malaria and the limited availability of ultrasound-based pregnancy dating to assess impacts on preterm birth and fetal growth in all studies.

**Conclusions:** Pregnant women with malnutrition and malaria infection are at increased risk of LBW compared to women with only 1 risk factor or none, but malaria and malnutrition do not act synergistically.


Abstract

We sought to determine the genetic and phenotypic antimicrobial resistance (AMR) profiles of commensal Klebsiella spp. circulating in Kenya by testing human stool isolates of 87 K. pneumoniae and three K. oxytoca collected at eight locations. Over one-third of the isolates were resistant to ≥3 categories of antimicrobials and were considered multidrug-resistant (MDR). We then compared the resistance phenotype to the presence/absence of 238 AMR genes determined by a broad-spectrum microarray and PCR. Forty-six genes/gene families were identified conferring resistance to β-lactams (ampC/blaDHA, blaCMY/LAT, blaLEN-1, blaOKP-A/OKP-B1, blaOXA-1-like family, blaOXY-1, blaSHV, blaTEM, blaCTX-M-1 and blaCTX-M-2 families), aminoglycosides (aac(3)-III, aac(6)-Ib, aad(A1/A2), aad(A4), aph(AI), aph3/str(A), aph6/str(B), and rmtB), macrolides (mac(A), mac(B), mph(A)/mph(K)), tetracyclines (tet(A), tet(B), tet(D), tet(G)), ansamycins (arr), phenicols (catA1/cat4, floR, cmlA, cmr), fluoroquinolones (qnrS), quaternary amines (qacEΔ1), streptothricin (sat2), sulfonamides (sul1, sul2, sul3), and diaminopyrimidines (dfrA1, dfrA5, dfrA7, dfrA8, dfrA12, dfrA13/21/22/23 family, dfrA14, dfrA15, dfrA16, dfrA17). This is the first profile of genes conferring resistance to multiple categories of antimicrobial agents in western and central Kenya. The large number and wide variety of resistance genes detected suggest the presence of significant selective pressure. The presence of five or more resistance determinants in almost two-thirds of the isolates points to the need for more effective, targeted public health policies and infection control/prevention measures.


Abstract

Background: In 2013, Kenya transitioned into a devolved system of government with a central government and 47 semi-autonomous county governments. In this paper, we report early experiences of devolution in the Kenyan health sector, with a focus on public
county hospitals. Specifically, we examine changes in hospital autonomy as a result of devolution, and how these have affected hospital functioning.

**Methods:** We used a qualitative case study approach to examine the level of autonomy that hospitals had over key management functions and how this had affected hospital functioning in three county hospitals in coastal Kenya. We collected data by in-depth interviews of county health managers and hospital managers in the case study hospitals (n = 21). We adopted the framework proposed by Chawla et al (1995) to examine the autonomy that hospitals had over five management domains (strategic management, finance, procurement, human resource, and administration), and how these influenced hospital functioning.

**Findings:** Devolution had resulted in a substantial reduction in the autonomy of county hospitals over the five key functions examined. This resulted in weakened hospital management and leadership, reduced community participation in hospital affairs, compromised quality of services, reduced motivation among hospital staff, non-alignment of county and hospital priorities, staff insubordination, and compromised quality of care.

**Conclusion:** Increasing the autonomy of county hospitals in Kenya will improve their functioning. County governments should develop legislation that give hospitals greater control over resources and key management functions.


**Abstract**

**Background:** Although pneumonia is a leading cause of inpatient mortality, deaths may also occur after discharge from hospital. However, prior studies have been small, in selected groups or did not fully evaluate risk factors, particularly malnutrition and HIV. We determined 1-year post-discharge mortality and risk factors among children diagnosed with severe pneumonia.

**Methods:** A cohort study of children aged 1-59 months admitted to Kilifi County Hospital with severe pneumonia (2007-12). The primary outcome was death <1 year
after discharge, determined through Kilifi Health and Demographic Surveillance System (KHDSS) quarterly census rounds.

**Results:** Of 4184 children (median age 9 months) admitted with severe pneumonia, 1041 (25%) had severe acute malnutrition (SAM), 267 (6.4%) had a positive HIV antibody test, and 364 (8.7%) died in hospital. After discharge, 2279 KHDSS-resident children were followed up; 70 (3.1%) died during 2163 child-years: 32 (95% confidence interval (CI) 26, 41) deaths per 1000 child years. Post-discharge mortality was greater after admission for severe pneumonia than for other diagnoses, hazard ratio 2.5 (95% CI 1.2, 5.3). Malnutrition, HIV status, age and prolonged hospitalisation, but not signs of pneumonia severity, were associated with post-discharge mortality. Fifty-two per cent (95% CI 37%, 63%) of post-discharge deaths were attributable to low mid-upper arm circumference and 11% (95% CI 3.3%, 18%) to a positive HIV test.

**Conclusions:** Admission with severe pneumonia is an important marker of vulnerability. Risk stratification and better understanding of the mechanisms underlying post-discharge mortality, especially for undernourished children, are needed to reduce mortality after treatment for pneumonia.


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**Abstract**

**Background:** Malaria control strategies need to respond to geographical hotspots of transmission. Detection of hotspots depends on the sensitivity of the diagnostic tool used.

**Methods:** We conducted cross-sectional surveys in 3 sites within Kilifi County, Kenya, that had variable transmission intensities. Rapid diagnostic test (RDT), microscopy, and polymerase chain reaction (PCR) were used to detect asymptomatic parasitemia, and hotspots were detected using the spatial scan statistic.

**Results:** Eight thousand five hundred eighty-one study participants were surveyed in 3 sites. There were statistically significant malaria hotspots by RDT, microscopy, and PCR for all sites except by microscopy in 1 low transmission site. Pooled data analysis of hotspots by PCR overlapped with hotspots by microscopy at a moderate setting but not at 2 lower transmission settings. However, variations in degree of overlap were noted when
data were analyzed by year. Hotspots by RDT were predictive of PCR/microscopy at the moderate setting, but not at the 2 low transmission settings. We observed long-term stability of hotspots by PCR and microscopy but not RDT.

**Conclusion:** Malaria control programs may consider PCR testing to guide asymptomatic malaria hotspot detection once the prevalence of infection falls.


**Abstract**

**Introduction:** In low-resource settings, empiric case management of febrile illness is routine as a result of limited access to laboratory diagnostics. The use of comprehensive fever syndromic surveillance, with enhanced clinical microbiology, advanced diagnostics and more robust epidemiologic investigation, could enable healthcare providers to offer a differential diagnosis of fever syndrome and more appropriate care and treatment.

**Methods:** We conducted a year-long exploratory study of fever syndrome among patients ≥ 1 year if age, presenting to clinical settings with an axillary temperature of ≥37.5°C and symptomatic onset of ≤5 days. Blood and naso-pharyngeal/oral-pharyngeal (NP/OP) specimens were collected and analyzed, respectively, using AFI and respiratory TaqMan Array Cards (TAC) for multi-pathogen detection of 57 potential causative agents. Furthermore, we examined numerous epidemiologic correlates of febrile illness, and conducted demographic, clinical, and behavioral domain-specific multivariate regression to statistically establish associations with agent detection.

**Results:** From 15 September 2014-13 September 2015, 1007 febrile patients were enrolled, and 997 contributed an epidemiologic survey, including: 14% (n = 139) 1<5yrs, 19% (n = 186) 5-14yrs, and 67% (n = 672) ≥15yrs. AFI TAC and respiratory TAC were performed on 842 whole blood specimens and 385 NP/OP specimens, respectively. Of the 57 agents surveyed, Plasmodium was the most common agent detected. AFI TAC detected nucleic acid for one or more of seven microbial agents in 49% of AFI blood samples, including: Plasmodium (47%), Leptospira (3%), Bartonella (1%), Salmonella enterica (1%), Coxiella burnetii (1%), Rickettsia (1%), and West Nile virus (1%). Respiratory TAC detected nucleic acid for 24 different microbial agents, including 12
viruses and 12 bacteria. The most common agents detected among our surveyed population were: Haemophilus influenzae (67%), Streptococcus pneumoniae (55%), Moraxella catarrhalis (39%), Staphylococcus aureus (37%), Pseudomonas aeruginosa (36%), Human Rhinovirus (25%), influenza A (24%), Klebsiella pneumoniae (14%), Enterovirus (15%) and group A Streptococcus (12%). Our epidemiologic investigation demonstrated both age and symptomatic presentation to be associated with a number of detected agents, including, but not limited to, influenza A and Plasmodium. Linear regression of fully-adjusted mean cycle threshold (Ct) values for Plasmodium also identified statistically significant lower mean Ct values for older children (20.8), patients presenting with severe fever (21.1) and headache (21.5), as well as patients admitted for in-patient care and treatment (22.4).

Conclusions: This study is the first to employ two syndromic TaqMan Array Cards for the simultaneous survey of 57 different organisms to better characterize the type and prevalence of detected agents among febrile patients. Additionally, we provide an analysis of the association between adjusted mean Ct values for Plasmodium and key clinical and demographic variables, which may further inform clinical decision-making based upon intensity of infection, as observed across endemic settings of sub-Saharan Africa.


Abstract

We explain social and organisational processes influencing health professionals in a Kenyan clinical network to implement a form of quality improvement (QI) into clinical practice, using the concept of 'pastoral practices'. Our qualitative empirical case study, conducted in 2015-16, shows the way practices constructing and linking local evidence-based guidelines and data collection processes provided a foundation for QI. Participation in these constructive practices gave network leaders pastoral status to then inscribe use of evidence and data into routine care, through championing, demonstrating, supporting and mentoring, with the support of a constellation of local champions. By arranging network meetings, in which the professional community discussed evidence, data, QI and professionalism, network leaders also facilitated the reconstruction of network members’ collective professional identity. This consequently strengthened top-down and lateral accountability and inspection practices, disciplining evidence and audit-based QI in local hospitals. By explaining pastoral practices in this way and setting, we
contribute to theory about governmentality in health care and extend Foucauldian analysis of QI, clinical networks and governance into low and middle income health care contexts.


Abstract

Background: Malaria transmission intensity is heterogeneous, complicating the implementation of malaria control interventions. We provide a description of the spatial micro-epidemiology of symptomatic malaria and asymptomatic parasitaemia in multiple sites.

Methods: We assembled data from 19 studies conducted between 1996 and 2015 in seven countries of sub-Saharan Africa with homestead-level geospatial data. Data from each site were used to quantify spatial autocorrelation and examine the temporal stability of hotspots. Parameters from these analyses were examined to identify trends over varying transmission intensity.

Results: Significant hotspots of malaria transmission were observed in most years and sites. The risk ratios of malaria within hotspots were highest at low malaria positive fractions (MPFs) and decreased with increasing MPF (p < 0.001). However, statistical significance of hotspots was lowest at extremely low and extremely high MPFs, with a peak in statistical significance at an MPF of ~0.3. In four sites with longitudinal data we noted temporal instability and variable negative correlations between MPF and average age of symptomatic malaria across all sites, suggesting varying degrees of temporal stability.

Conclusions: We observed geographical micro-variation in malaria transmission at sites with a variety of transmission intensities across sub-Saharan Africa. Hotspots are marked at lower transmission intensity, but it becomes difficult to show statistical significance when cases are sparse at very low transmission intensity. Given the predictability with which hotspots occur as transmission intensity falls, malaria control programmes should have a low threshold for responding to apparent clustering of cases.


Abstract

**Background:** An increasing number of countries in sub-Saharan Africa are moving towards malaria-elimination, mostly thanks to successful vector control campaigns. However, elimination has proven challenging, resulting in the persistence of malaria transmission. It is now accepted that in order to eliminate malaria, new complementary vector control approaches must be developed. This study describes the development of a sugar-baited resting place containing a toxic dose of ivermectin for the control of Anopheles arabiensis.

**Results:** Dose response experiments were performed in insectary conditions to determine the LD90 of ivermectin against An. arabiensis. Over 95% of An. arabiensis were knocked down 48 h post-sugar feeding on 10% sucrose solutions containing 0.01% ivermectin. When investigating different juices as attractants, it was observed that An. arabiensis preferred orange, watermelon and commercial guava juice over pawpaw, tomato, mango or banana, but were most likely to feed on simple 10% sugar solution. Using recycled materials, different bait prototypes were tested to determine the best design to maximize sugar feeding. Baits that offered a resting place for the mosquito rather than just a surface to sugar feed were more likely to attract An. arabiensis to sugar feed. The optimized prototype was then placed in different locations within a screenhouse, colour-coded with different food dyes, containing competing vegetation (Ricinus communis) and experimental huts where humans slept under bed nets. Around half of all the released An. arabiensis sugar fed on the sugar baits, and approximately 50% of all sugar fed mosquitoes chose the baits close to outdoor vegetation before entering the huts.

**Conclusions:** Ivermectin is an effective insecticide for use in sugar baits. The design of the sugar bait can influence feeding rates and, therefore, efficacy. Sugar baits that offer a resting surface are more efficient and sugar feeding on the baits is maximized when these are placed close to peri-domestic vegetation. Attractive toxic sugar baited resting places may provide an additional vector control method to complement with existing strategies.

The development of a highly effective vaccine remains a key strategic goal to aid the control and eventual eradication of Plasmodium falciparum malaria. In recent years, the reticulocyte-binding protein homolog 5 (RH5) has emerged as the most promising blood-stage P. falciparum candidate antigen to date, capable of conferring protection against stringent challenge in Aotus monkeys. We report on the first clinical trial to our knowledge to assess the RH5 antigen - a dose-escalation phase Ia study in 24 healthy, malaria-naive adult volunteers. We utilized established viral vectors, the replication-deficient chimpanzee adenovirus serotype 63 (ChAd63), and the attenuated orthopoxvirus modified vaccinia virus Ankara (MVA), encoding RH5 from the 3D7 clone of P. falciparum. Vaccines were administered i.m. in a heterologous prime-boost regimen using an 8-week interval and were well tolerated. Vaccine-induced anti-RH5 serum antibodies exhibited cross-strain functional growth inhibition activity (GIA) in vitro, targeted linear and conformational epitopes within RH5, and inhibited key interactions within the RH5 invasion complex. This is the first time to our knowledge that substantial RH5-specific responses have been induced by immunization in humans, with levels greatly exceeding the serum antibody responses observed in African adults following years of natural malaria exposure. These data support the progression of RH5-based vaccines to human efficacy testing.


**Abstract**

The development and spread of resistance among local vectors to the major classes of insecticides used in Long-Lasting Insecticidal Nets (LLINs) and Indoor
Residual Spraying (IRS) poses a major challenge to malaria vector control programs worldwide. The main methods of evaluating insecticide resistance in malaria vectors are the WHO tube bioassay and CDC bottle assays, with their weakness being determination of resistance at a fixed dose for variable populations. The CDC bottle assay using different insecticide dosages has proved applicable in ascertaining the intensity of resistance.

**Methods:** We determined the status and intensity of permethrin resistance and investigated the efficacy of commonly used LLINs (PermaNet® 2.0, PermaNet® 3.0 and Olyset®) against 3-5 day-old adult female Anopheles mosquitoes from four sub-counties; Teso, Bondo, Rachuonyo and Nyando in western Kenya. Knockdown was assessed to 4 doses of permethrin; 1× (21.5 μg/ml), 2× (43 μg/ml), 5× (107.5 μg/ml) and 10× (215 μg/ml) using CDC bottle assays.

**Results:** Mortality for 0.75% permethrin ranged from 23.5% to 96.1% in the WHO tube assay. Intensity of permethrin resistance was highest in Barkanyango Bondo, with 84% knockdown at the 30 min diagnostic time when exposed to the 10× dose. When exposed to the LLINs, mortality ranged between 0-39% for Olyset®, 12-88% for PermaNet® 2.0 and 26-89% for PermaNet® 3.0. The efficacy of nets was reduced in Bondo and Teso. Results from this study show that there was confirmed resistance in all the sites; however, intensity assays were able to differentiate Bondo and Teso as the sites with the highest levels of resistance, which coincidentally were the two sub-counties with reduced net efficacy.

**Conclusions:** There was a reduced efficacy of nets in areas with high resistance portraying that at certain intensities of resistance, vector control using LLINs may be compromised. It is necessary to incorporate intensity assays in order to determine the extent of threat that resistance poses to malaria control.


**Abstract**

**Background:** HIV-1 sequence variation is a major obstacle to developing molecular based assays for multiple subtypes. This study sought to independently assess
performance characteristics of the ViroSeq™ HIV-1 Integrase RUO Genotyping Kit (Celera, US) for samples of multiple different HIV-1 subtypes.

Methods: 264 samples were tested in the validation, 106 from integrase inhibitor naïve patients' sent for routine HIV-1 drug resistance testing after failing a 1st- or 2nd-line regimen, and 158 samples from an external virology quality assurance program (VQA). For the latter, 53 unique VQA samples were tested in two to five different laboratories to assess assay reproducibility. For all assays, viral RNA was extracted using the ViroSeq extraction module, reverse transcribed, and amplified in a one-step reaction. Four sequencing primers were used to span codons 1-288 of integrase. The Rega subtyping tool was used for subtype assignment. Integrase polymorphisms and mutations were determined as differences from the HXB2 sequence and by the Stanford database, respectively. Sequences obtained from the different laboratories were aligned and sequence homology determined.

Results: HIV-1 RNA in the 264 samples ranged from 3.15 to 6.74 \text{log}_{10}\text{copies/ml}. Successful amplification was obtained for 97% of samples (n=256). The 8 samples that failed to amplify were subtype D (n=3), subtype C (n=1), CRF01_AE (n=1), subtype A1 (n=2), and an unassigned subtype (n=1). Of the 256 that successfully amplified samples, 203 (79%) were successfully sequenced with bidirectional coverage. Of the 53 unsuccessful samples, 13 (5%) failed sequencing and 40 (16%) did not have full bidirectional sequence, as a result of failure of sequencing primers: Primer A (n=1); Primer B (n=18); Primer C (n=1); Primer D (n=7) or short sequences (n=16). For the 135 VQA samples (30 unique samples) that were assayed by different laboratories, homology of the sequences obtained ranged from 92.1% to 100%. However, Laboratory 2 detected more mixtures (74%) compared to the other four laboratories, whereas Laboratory 1 detected the least number of mixtures (35%), likely due to differences between the labs in the methods of sequence analysis. Mutations associated with integrase resistance were observed in seven of the 106 (7%) clinical samples [one sample: Q148K; E138K; G140A; two samples: T97A and four samples: L74I]. Of the four samples with L74I, 3 were subtype G.

Conclusion: Of the total 264 samples tested, 243 (92%) of samples were able to be amplified and sequenced to generate an integrase genotype. Sequencing results were similar between the testing laboratories with the exception of mixture detection. Mutations associated with integrase inhibitor resistance were observed in only 7% of integrase inhibitor naive samples, and some of these mutations are likely to be due to subtype-specific polymorphisms rather than selection by an integrase inhibitor.

Pubmed link: https://pubmed.ncbi.nlm.nih.gov/27993614/

Abstract

**Background:** Burkitt lymphoma (BL) is characterized by overexpression of the c-myc oncogene, which in the vast majority of cases is a consequence of an IGH/MYC translocation. While myc is the seminal event, BL is a complex amalgam of genetic and epigenetic changes causing dysregulation of both coding and non-coding transcripts. Emerging evidence suggest that abnormal modulation of mRNA transcription via miRNAs might be a significant factor in lymphomagenesis. However, the alterations in these miRNAs and their correlations to their putative mRNA targets have not been extensively studied relative to normal germinal center (GC) B cells.

**Methods:** Using more sensitive and specific transcriptome deep sequencing, we compared previously published small miRNA and long mRNA of a set of GC B cells and eBL tumors. MiRWalk2.0 was used to identify the validated target genes for the deregulated miRNAs, which would be important for understanding the regulatory networks associated with eBL development.

**Results:** We found 211 differentially expressed (DE) genes (79 upregulated and 132 downregulated) and 49 DE miRNAs (22 up-regulated and 27 down-regulated). Gene Set enrichment analysis identified the enrichment of a set of MYC regulated genes. Network propagation-based method and correlated miRNA-mRNA expression analysis identified dysregulated miRNAs, including miR-17~95 cluster members and their target genes, which have diverse oncogenic properties to be critical to eBL lymphomagenesis. Central to all these findings, we observed the downregulation of ATM and NLK genes, which represent important regulators in response to DNA damage in eBL tumor cells. These tumor suppressors were targeted by multiple upregulated miRNAs (miR-19b-3p, miR-26a-5p, miR-30b-5p, miR-92a-5p and miR-27b-3p) which could account for their aberrant expression in eBL.

**Conclusion:** Combined loss of p53 induction and function due to miRNA-mediated regulation of ATM and NLK, together with the upregulation of TFAP4, may be a central role for human miRNAs in eBL oncogenesis. This facilitates survival of eBL tumor cells with the IGH/MYC chromosomal translocation and promotes MYC-induced cell cycle progression, initiating eBL lymphomagenesis. This characterization of miRNA-mRNA interactions in eBL relative to GC B cells provides new insights on miRNA-mediated
transcript regulation in eBL, which are potentially useful for new improved therapeutic strategies.

**Pubmed link**: https://pubmed.ncbi.nlm.nih.gov/29132323/

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**Abstract**

**Objective**: To examine the levels, inequalities and factors associated with health insurance coverage in Kenya.

**Methods**: We analysed secondary data from the Kenya Demographic and Health Survey (KDHS) conducted in 2009 and 2014. We examined the level of health insurance coverage overall, and by type, using an asset index to categorise households into five socio-economic quintiles with quintile 5 (Q5) being the richest and quintile 1 (Q1) being the poorest. The high-low ratio (Q5/Q1 ratio), concentration curve and concentration index (CIX) were employed to assess inequalities in health insurance coverage, and logistic regression to examine correlates of health insurance coverage.

**Results**: Overall health insurance coverage increased from 8.17% to 19.59% between 2009 and 2014. There was high inequality in overall health insurance coverage, even though this inequality decreased between 2009 (Q5/Q1 ratio of 31.21, CIX = 0.61, 95% CI 0.52-0.71) and 2014 (Q5/Q1 ratio 12.34, CIX = 0.49, 95% CI 0.45-0.52). Individuals that were older, employed in the formal sector; married, exposed to media; and male, belonged to a small household, had a chronic disease and belonged to rich households, had increased odds of health insurance coverage.

**Conclusion**: Health insurance coverage in Kenya remains low and is characterised by significant inequality. In a context where over 80% of the population is in the informal sector, and close to 50% live below the national poverty line, achieving high and equitable coverage levels with contributory and voluntary health insurance mechanism is problematic. Kenya should consider a universal, tax-funded mechanism that ensures revenues are equitably and efficiently collected, and everyone (including the poor and those in the informal sector) is covered.

**Pubmed link**: https://pubmed.ncbi.nlm.nih.gov/28627085/
Abstract

**Objective:** To investigate the prevalence, risk factors, clinical features, and neurobehavioral comorbidities of epilepsy and acute symptomatic seizures in school-aged children in Kilifi, Kenya.

**Methods:** Randomly selected children (N = 11,223) were screened for epilepsy and other neurodevelopmental disorders. Those who screened positive were invited for further clinical, electroencephalographic (EEG), and neuropsychological evaluations. Prevalence was measured by dividing cases by screened population, providing Agresti-Coull confidence intervals (CIs). Prevalence ratios were computed using log binomial regression, and odds ratios (ORs) were computed using logistic regression; both were implemented with generalized linear models. Attention-deficit hyperactivity disorder (ADHD), autism spectrum disorder (ASD), and other neurodevelopmental impairments were assessed in cases and controls.

**Results:** Prevalence of lifetime epilepsy was 20.9 per 1,000 (95% CI = 18.4-23.7), and that of active epilepsy was 11.5 per 1,000 (95% CI = 9.7-13.6). Prevalence of acute symptomatic seizures was 68.8 per 1,000 (95% CI = 64.2-73.6). Acute symptomatic seizures preceded a diagnosis of epilepsy in 8% of children. Of 98 children diagnosed with epilepsy, focal seizures were seen in 79%, abnormal EEG was seen in 39%, and 83% were not receiving antiepileptic drugs. Childhood absence epilepsy and Lennox-Gastaut epilepsy were the most easily identifiable epilepsy syndromes. Perinatal complications, previous hospitalization, geophagia, and snoring were risk factors for epilepsy. Family history of seizures, abnormal pregnancy, previous hospitalization, and snoring were risk factors for acute symptomatic seizures. Neurobehavioral comorbidities were present in 54% of subjects with lifetime epilepsy and in 3% of controls, with associations for individual comorbidities being statistically significant: ADHD (OR = 14.55, 95% CI = 7.54-28.06), ASD (OR = 36.83, 95% CI = 7.97-170.14), and cognitive impairments (OR = 14.55, 95% CI = 3.52-60.14).

**Significance:** The burden of seizure disorders in this area is higher than in locations in high-income countries, and can be reduced by preventing risk factors. A comprehensive management plan for neurobehavioral comorbidities of epilepsy should be incorporated into standard epilepsy care.
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<td><strong>Abstract</strong></td>
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<td>To be effective, HIV programmes should be responsive to the unique needs of diverse groups of infected adolescents. We highlight a range of adolescent perspectives on HIV services, including those who acquired HIV perinatally or sexually and those who were either in care, had dropped out of care, or had never enrolled in care. We conducted semi-structured interviews with 29 adolescents (aged 15-19) and 14 caregivers in western Kenya. Data were analysed using a descriptive analytical approach. Adolescents who were successfully linked had a supportive adult present during diagnosis; tested during hospitalisation or treatment for a recurrent or severe illness; and initiated treatment soon after diagnosis. Barriers to retention included side effects from HIV drugs, pill burden, and limited access to clean water and nutritious food. Support in family, school, and health facility environments was key for diagnosis, linkage, and retention. We make recommendations that may improve adolescent engagement in HIV services.</td>
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<td><strong>Background:</strong> We investigated the poorly understood impact of declining malaria transmission on maintenance of antibodies to Plasmodium falciparum merozoite antigens and infected erythrocytes (IEs), including functional immunity.</td>
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Methods: In a 3-year longitudinal cohort of 300 Kenyan children, antibodies to different AMA1 and MSP2 alleles of merozoites, IE surface antigens, and antibody functional activities were quantified.

Results: Over a period in which malaria transmission declined markedly, AMA1 and MSP2 antibodies decreased substantially; estimated half-lives of antibody duration were 0.8 year and 1.3 years, respectively. However, 69%-74% of children maintained their seropositivity to AMA1 alleles and 42%-52% to MSP2 alleles. Levels and prevalence of antimerozoite antibodies were consistently associated with increasing age and concurrent parasitemia. Antibodies promoting opsonic phagocytosis of merozoites declined rapidly (half-life, 0.15 years). In contrast, complement-fixing antibodies to merozoites did not decline and antibodies to IE surface antigens expressing virulent phenotypes were much better maintained (half-life, 4-10 years).

Conclusions: A decline in malaria transmission is associated with reduction in naturally acquired immunity. However, loss of immunity is not universal; some key functional responses and antibodies to IEs were better maintained and these may continue to provide some protection. Findings have implications for malaria surveillance and control measures and informing vaccine development.


Abstract

Historically, community engagement (CE) in research has been implemented in the fields of public health, education and agricultural development. In recent years, international discussions on the ethical and practical goals of CE have been extended to human genomic research and biobanking, particularly in the African context. While there is some consensus on the goals and value of CE generally, questions remain about the effectiveness of CE practices and how to evaluate this. Under the auspices of the Human Heredity and Health in Africa Initiative (H3Africa), the H3Africa CE working group organized a workshop in Stellenbosch, South Africa in March 2016 to explore the extent to which communities should be involved in genomic research and biobanking and to examine various methods of evaluating the effectiveness of CE. In this paper, we present the key themes that emerged from the workshop and make a case for the development of
a rigorous application, evaluation and learning around approaches for CE that promote a more systematic process of engaging relevant communities. We highlight the key ways in which CE should be embedded into genomic research and biobanking projects.


Abstract

Background: Three-quarters of the burden of mental health problems occurs in low-and-middle-income countries, but few epidemiological studies of these problems in preschool children from sub-Saharan Africa have been published. Behavioural and emotional problems often start in early childhood, and this might be particularly important in Africa, where the incidence of perinatal and early risk factors is high. We therefore aimed to estimate the prevalence and risk factors of behavioural and emotional problems in young children in a rural area on the Kenyan coast.

Methods: We did a population-based epidemiological study to assess the burden of behavioural and emotional problems in preschool children and comorbidities in the Kilifi Health and Demographic Surveillance System (KHDSS, a database formed of the population under routine surveillance linked to admissions to Kilifi County Hospital). We used the Child Behaviour Checklist (CBCL) to assess behavioural and emotional problems. We then determined risk factors and medical comorbidities associated with behavioural and emotional problems. The strength of associations between the risk factors and the behavioural and emotional problems was estimated using generalised linear models, with appropriate distribution and link functions.

Findings: 3539 families were randomly selected from the KHDSS. Of these, 3273 children were assessed with CBCL. The prevalence of total behavioural and emotional problems was 13% (95% CI 12-14), for externalising problems was 10% (9-11), and for internalising problems was 22% (21-24). The most common CBCL syndrome was somatic problems (21%, 20-23), whereas the most common DSM-IV-oriented scale was anxiety problems (13%, 12-14). Factors associated with total problems included consumption of cassava (risk ratio 5.68, 95% CI 3.22-10.03), perinatal complications (4.34, 3.21-5.81), seizure disorders (2.90, 2.24-3.77), and house status (0.11, 0.08-0.14). Seizure disorders, burn marks, and respiratory problems were important comorbidities of behavioural and emotional problems.
Interpretation: Behavioural and emotional problems are common in preschool children in this Kenyan rural area and are associated with preventable risk factors. Behavioural and emotional problems and associated comorbidities should be identified and addressed in young children.


Abstract

Background: Pneumonia is a leading cause of morbidity and mortality among adults worldwide; however, the risk factors for community-acquired pneumonia in Africa are not well characterized.

Methods: The authors recruited 281 cases of community-acquired pneumonia and 1202 hospital controls among patients aged ≥15 years who attended Kilifi District Hospital/Coast Provincial General Hospital in Kenya between 1994 and 6. Cases were admissions with an acute illness with ≥2 respiratory signs and evidence of consolidation on a chest radiograph. Controls were patients without signs of pneumonia, frequency matched by age, sex and hospital. Risk factors related to socio-demographic factors, drug use, clinical history, contact patterns and exposures to indoor air pollution were investigated by questionnaire, anthropometric measurements and laboratory assays. Associations were evaluated using a hierarchical logistic regression model.

Results: Pneumonia was associated with human immunodeficiency virus (HIV) infection (Odds Ratio [OR] 2.06, 95% CI 1.44-3.08), anemia (OR 1.91, 1.31-2.74), splenomegaly (OR 2.04, 95% CI 1.14-3.41), recent history of pneumonia (OR 4.65, 95% CI 1.66-12.5), history of pneumonia >2 years previously (OR 17.13, 95% CI 5.01-60.26), coryza in the 2 weeks preceding hospitalization (OR 2.09, 95% CI 1.44-3.03), current smoking (2.19, 95% CI 1.39-3.70), use of khat (OR 3.44, 95% CI 1.72-7.15), use of snuff (OR 2.67, 95% CI 1.35-5.49) and contact with several animal species. Presence of a Bacillus Calmette-Guerin (BCG) scar was associated with protection (OR 0.51, 95% CI 0.32-0.82). The risk factors varied significantly by sex.

Conclusion: Pneumonia in Kenyan adults was associated with global risk factors, such as HIV and smoking, but also with specific local factors like drug use and contact with
animals. Intervention strategies should account for sex-specific differences in risk factors.


Abstract

Background. Few hospitals in high malaria endemic countries in Africa have the diagnostic capacity for clinically distinguishing acute bacterial meningitis (ABM) from cerebral malaria (CM). As a result, empirical use of antibiotics is necessary. A biochemical marker of ABM would facilitate precise clinical diagnosis and management of these infections and enable rational use of antibiotics. Methods. We used label-free protein quantification by mass spectrometry to identify cerebrospinal fluid (CSF) markers that distinguish ABM (n=37) from CM (n=22) in Kenyan children. Fold change (FC) and false discovery rates (FDR) were used to identify differentially expressed proteins. Subsequently, potential biomarkers were assessed for their ability to discriminate between ABM and CM using receiver operating characteristic (ROC) curves. Results. The host CSF proteome response to ABM (Haemophilus influenzae and Streptococcus pneumoniae) is significantly different to CM. Fifty two proteins were differentially expressed (FDR<0.01, Log FC≥2), of which 83% (43/52) were upregulated in ABM compared to CM. Myeloperoxidase and lactotransferrin were present in 37 (100%) and 36 (97%) of ABM cases, respectively, but absent in CM (n=22). Area under the ROC curve (AUC), sensitivity, and specificity were assessed for myeloperoxidase (1, 1, and 1; 95% CI, 1-1) and lactotransferrin (0.98, 0.97, and 1; 95% CI, 0.96-1). Conclusion. Myeloperoxidase and lactotransferrin have a high potential to distinguish ABM from CM and thereby improve clinical management. Their validation requires a larger cohort of samples that includes other bacterial aetiologies of ABM.


Abstract

Children with acute and chronic malnutrition are at increased risk of morbidity and mortality following a diarrheal episode. To compare diarrheal disease severity and pathogen prevalence among children with and without acute and chronic malnutrition, we conducted a cross-sectional study of human immunodeficiency virus-uninfected Kenyan children aged 6-59 months, who presented with acute diarrhea. Children underwent clinical and anthropometric assessments and provided stool for bacterial and protozoal pathogen detection. Clinical and microbiological features were compared using log binomial regression among children with and without wasting (mid-upper arm circumference ≤ 125 mm) or stunting (height-for-age z score ≤ -2). Among 1,363 children, 7.0% were wasted and 16.9% were stunted. After adjustment for potential confounders, children with wasting were more likely than nonwasted children to present with at least one Integrated Management of Childhood Illness danger sign (adjusted prevalence ratio [aPR]: 1.3, 95% confidence interval [CI]: 1.0 to 1.5, $P = 0.05$), severe dehydration (aPR: 2.4, 95% CI: 1.5 to 3.8, $P < 0.01$), and enteroaggregative *Escherichia coli* recovered from their stool (aPR: 1.8, 1.1-2.8, $P = 0.02$). There were no differences in the prevalence of other pathogens by wasting status after confounder adjustment. Stunting was not associated with clinical severity or the presence of specific pathogens. Wasted children with diarrhea presented with more severe disease than children without malnutrition which may be explained by a delay in care-seeking or diminished immune response to infection. Combating social determinants and host risk factors associated with severe disease, rather than specific pathogens, may reduce the disparities in poor diarrhea-associated outcomes experienced by malnourished children.


Abstract

**Background:** Africa accounts for 14% of world's population, and the economies of most African countries are considered to be growing, but this is not reflected in the amount of research published by Africans. This study aimed at identifying the challenges that young African scientists face in their career development.
Methods: This was a qualitative exploratory study involving young researchers who attended the Teaching and Research in Natural Sciences for Development (TReND) in Africa scientific writing and communication workshop, which was held in Malawi in September 2015. A semi-structured questionnaire was sent to all workshop participants who consented to taking part in the survey. In total, 28 questionnaires were sent via email and 15 were returned, representing a response rate of 53.6%. Data were analysed using thematic analysis.

Results: Young Africans develop their research interests various ways. The most common career-promoting factors identified by the study participants included formal classroom learning, aspirations to attain academic qualifications, work satisfaction, and the desire to fulfill parents' dreams. Challenges cited by survey respondents included a lack of mentorship, funds, and research and writing skills. Lack of interest in research by policymakers, lack of motivation by peers, and heavy workload (leaving little time for research) were also reported as challenges. Respondents suggested that grants specifically targeting young scientists would be beneficial. Participants also urged for the establishment of mentorship programmes, increasing motivation for research, and more frequent training opportunities.

Conclusions: There is need for improved funding for institutional and research network strengthening in Africa, with particular attention given to expanding opportunities for young researchers.


Abstract

Background: Africa has the lowest childhood vaccination coverage worldwide. If the full benefits of childhood vaccination programmes are to be enjoyed in sub-Saharan Africa, all countries need to improve on vaccine delivery to achieve and sustain high coverage. In this paper, we review trends in vaccination coverage, dropouts between vaccine doses and explored the country-specific predictors of complete vaccination in West Africa. Methods: We utilized datasets from the Demographic and Health Surveys Program, available for Benin, Burkina Faso, The Gambia, Ghana, Guinea, Cote d'Ivoire, Liberia, Mali, Niger, Nigeria, Senegal, Sierra Leone and Togo, to obtain coverage for Bacillus Calmette-Guerin, polio, measles, and diphtheria, pertussis and tetanus (DPT) vaccines in children aged 12 - 23 months. We also calculated the DPT1-to-DPT3 and
DPT1-to-measles dropouts, and proportions of the fully immunised child (FIC). Factors predictive of FIC were explored using Chi-squared tests and multivariable logistic regression. **Results:** Overall, there was a trend of increasing vaccination coverage. The proportion of FIC varied significantly by country (range 24.1-81.4%, mean 49%). DPT1-to-DPT3 dropout was high (range 5.1% -33.9%, mean 16.3%). Similarly, DPT1-measles dropout exceeded 10% in all but four countries. Although no single risk factor was consistently associated with FIC across these countries, maternal education, delivery in a health facility, possessing a vaccine card and a recent post delivery visit to a health facility were the key predictors of complete vaccination. **Conclusions:** The low numbers of fully immunised children and high dropout between vaccine doses highlights weaknesses and the need to strengthen the healthcare and routine immunization delivery systems in this region. Country-specific correlates of complete vaccination should be explored further to identify interventions required to increase vaccination coverage. Despite the promise of an increasing trend in vaccination coverage in West African countries, more effort is required to attain and maintain global vaccination coverage targets.


**Abstract**

**Background:** In Kenya, the National School-Based Deworming Programme (NSBDP) for soil-transmitted helminthes and schistosomiasis in prioritized areas has been going on since the year 2012. By the year 2013 over 6 million School Age Children (SAC) had been treated. A community sensitization supplement containing key messages and answers to frequently asked questions was developed as a guiding tool. Awareness creation methods used include county sensitization meetings, stakeholder forums, town criers and posters. To assess the local stakeholders’ perceptions of community sensitization for programme implementation, a qualitative cross-sectional survey was conducted in four-sub-counties of coastal region.

**Methods:** In-depth interviews (IDIs) were administered to 40 purposively selected opinion leaders so as to explore their perceptions of awareness creation sources, adequacy of information given, length of period of awareness creation and period between which information is given and drugs are administered. Separate IDIs were administered to pre-school teachers (41), community health extension workers (34) and
primary school teachers (38). To elicit more information, 20 focus group discussions (FGDs) categorized by gender and age were conducted among parents of school-age children. Data was audio recorded, transcribed, coded and analyzed manually by study themes.

**Results:** The most commonly reported source of information was school pupils. Due to low literacy levels, use of posters was regarded as ineffective and religious institutions, town criers and vernacular radio stations considered more effective. The information given during programme implementation was considered inadequate and use of complementary methods to reach all targeted children including the non-enrolled, and relay adequate information reported as important. Use of school and chief’s meetings with health personnel being present was mentioned as a useful method that would allow for interaction with participants indicating that they did not understand why adults were not being treated. Repeated awareness creation before deworming day to serve as a reminder and to reach those missing initial messages was also mentioned as important. Furthermore, the awareness creation period needed to be extended as 85% of the participants indicated that they learnt of deworming a day before it took place or after their children had received the drugs.

**Conclusion:** Awareness creation is a key factor in the success of NSBDP implementation. For programme sustainability, preferences of local stakeholders need to be considered as control of worms can only be achieved through an integrated approach of deworming, health education and use of safe water and sanitation facilities which require collaboration with local stakeholders.


**Abstract**

**Background:** Neonatal mortality remains high in sub-Saharan Africa, and a third of deaths are estimated to result from infection. While coagulase-negative staphylococci (CoNS) are leading neonatal pathogens in resource-rich settings, their role, and the need for early anti-Staphylococcal treatment in empiric antibiotic guidelines, is unknown in sub-Saharan Africa.
Methods: We examined systematic clinical and microbiologic surveillance data from all neonatal admissions to Kilifi County Hospital (1998-2013) to determine associated case fatality and/or prolonged duration of admission associated with CoNS in neonates treated according to standard World Health Organization guidelines.

Results: CoNS was isolated from blood culture in 995 of 9552 (10%) neonates. Case fatality among neonates with CoNS isolated from blood did not differ from other neonatal admissions (P = 0.2), and duration of admission was not prolonged [odds ratio (OR) = 0.9 (0.7-1.0), P = 0.040]. Neonates with CoNS were more likely to have convulsions [OR = 1.4 (1.0-1.8), P = 0.031] but less likely to have impaired consciousness or severe indrawing [OR = 0.8 (0.7-0.9), P = 0.025; OR = 0.9 (0.7-1.0), P = 0.065].

Conclusions: CoNS isolation in blood cultures at admission was not associated with adverse clinical outcomes in neonates treated according to standard World Health Organization guidelines for hospital care in this setting. There is no evidence that first-line antimicrobial treatment guidelines should be altered to increase cover for CoNS infections in neonates in this setting.


Abstract

Background: Resistance and tolerance to Plasmodium falciparum can determine the progression of malaria disease. However, quantitative evidence of tolerance is still limited. We investigated variations in the adverse impact of P. falciparum infections among African pregnant women under different intensities of malaria transmission.

Methods: P. falciparum at delivery was assessed by microscopy, quantitative PCR (qPCR) and placental histology in 946 HIV-uninfected and 768 HIV-infected pregnant women from Benin, Gabon, Kenya and Mozambique. Resistance was defined by the proportion of submicroscopic infections and the levels of anti-parasite antibodies
Results: P. falciparum prevalence by qPCR in peripheral and/or placental blood of HIV-uninfected Mozambican, Gabonese and Beninese women at delivery was 6% (21/340), 11% (28/257) and 41% (143/349), respectively. The proportion of peripheral submicroscopic infections was higher in Benin (83%) than in Mozambique (60%) and Gabon (55%; P = 0.033). Past or chronic placental P. falciparum infection was associated with an increased risk of preterm birth in Mozambican newborns (OR = 7.05, 95% CI 1.79 to 27.82). Microscopic infections were associated with reductions in haemoglobin levels at delivery among Mozambican women (-1.17 g/dL, 95% CI -2.09 to -0.24) as well as with larger drops in haemoglobin levels from recruitment to delivery in Mozambican (-1.66 g/dL, 95% CI -2.68 to -0.64) and Gabonese (-0.91 g/dL, 95% CI -1.79 to -0.02) women. Doubling qPCR-peripheral parasite densities in Mozambican women were associated with decreases in haemoglobin levels at delivery (-0.16 g/dL, 95% CI -0.29 to -0.02) and increases in the drop of haemoglobin levels (-0.29 g/dL, 95% CI -0.44 to -0.14). Beninese women had higher anti-parasite IgGs than Mozambican women (P < 0.001). No difference was found in the proportion of submicroscopic infections nor in the adverse impact of P. falciparum infections in HIV-infected women from Kenya (P. falciparum prevalence by qPCR: 9%, 32/351) and Mozambique (4%, 15/417).

Conclusions: The lowest levels of resistance and tolerance in pregnant women from areas of low malaria transmission were accompanied by the largest adverse impact of P. falciparum infections. Exposure-dependent mechanisms developed by pregnant women to resist the infection and minimise pathology can reduce malaria-related adverse outcomes. Distinguishing both types of defences is important to understand how reductions in transmission can affect malaria disease.

POC devices when operated by lay-counselors in the era of task-shifting is unknown. We examined the accuracy of Alere's Pima™ POC device on both capillary and venous blood when performed by lay-counselors and laboratory technicians.

**Methods:** In Phase I, we compared the performance of POC against FACSCalibur™ for 280 venous specimens by laboratory technicians. In Phase II we compared POC performance by lay-counselors versus laboratory technicians using 147 paired capillary and venous specimens, and compared these to FACSCalibur™. Statistical analyses included Bland-Altman analyses, concordance correlation coefficient, sensitivity, and specificity at treatment eligibility thresholds of 200, 350, and 500cells/μl.

**Results:** Phase I: POC sensitivity and specificity were 93.0% and 84.1% at 500cells/μl, respectively. Phase II: Good agreement was observed for venous POC results from both lay-counselors (concordance correlation coefficient (CCC)=0.873, bias -86.4cells/μl) and laboratory technicians (CCC=0.920, bias -65.7cells/μl). Capillary POC had good correlation: lay-counselors (CCC=0.902, bias -71.2cells/μl), laboratory technicians (CCC=0.918, bias -63.0cells/μl). Misclassification at the 500 cells/μl threshold for venous blood was 13.6% and 10.2% for lay-counselors and laboratory technicians and 12.2% for capillary blood in both groups. POC tended to under-classify the CD4 values with increasingly negative bias at higher CD4 values.

**Conclusions:** Pima™ results were comparable to FACSCalibur™ for both venous and capillary specimens when operated by lay-counselors. POC CD4 testing has the potential to improve linkage to HIV care without burdening laboratory technicians in resource-limited settings.


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**Abstract**

Between July 2009 and June 2014, a total of 1,546 fecal specimens were collected from children <5 years of age with acute gastroenteritis admitted to Kiambu County Hospital, Central Kenya. The specimens were screened for group A rotavirus (RVA) using ELISA, and RVA-positive specimens were subjected to semi-nested RT-PCR to determine the G and P genotypes. RVA was detected in 429/1,546 (27.5%) fecal specimens. RVA infections occurred in all age groups <59 months, with an early peak at 6-17 months. The infections persisted year-round with distinct seasonal peaks depending on the year.
G1P[8] (28%) was the most predominant genotype, followed by G9P[8] (12%), G8P[4] (7%), G1P[4] (5%), G9P[4] (4%), and G12P[6] (3%). In the yearly change of G and P genotypes, a major shift from G9P[8] to G1P[8] was found in 2012. Phylogenetic analysis of the nucleotide sequences of the VP7 and VP4 genes of seven strains with unusual G8 or P[6] showed that the VP7 nucleotide sequences of G8 were clustered in lineage 6 in which African strains are included, and that there are at least two distinct VP4 nucleotide sequences of P[6] strains. These results represent basic data on RVA strains circulating in this region before vaccine introduction. J. Med. Virol. 89:809-817, 2017. © 2016 Wiley Periodicals, Inc.


Abstract

Pulmonary non-tuberculous mycobacterial (NTM) disease epidemiology in sub-Saharan Africa is not as well described as for pulmonary tuberculosis. Earlier reviews of global NTM epidemiology only included subject-level data from one sub-Saharan Africa country. We systematically reviewed the literature and searched PubMed, Embase, Popline, OVID and Africa Wide Information for articles on prevalence and clinical relevance of NTM detection in pulmonary samples in sub-Saharan Africa. We applied the American Thoracic Society/Infectious Disease Society of America criteria to differentiate between colonisation and disease. Only 37 articles from 373 citations met our inclusion criteria. The prevalence of pulmonary NTM colonization was 7.5% (95% CI: 7.2%-7.8%), and 75.0% (2325 of 3096) occurred in males, 16.5% (512 of 3096) in those previously treated for tuberculosis and Mycobacterium avium complex predominated (27.7% [95% CI: 27.2-28.9%]). In seven eligible studies, 27.9% (266 of 952) of participants had pulmonary NTM disease and M. kansasii with a prevalence of 69.2% [95% CI: 63.2-74.7%] was the most common cause of pulmonary NTM disease. NTM species were unidentifiable in 29.2% [2,623 of 8,980] of isolates. In conclusion, pulmonary NTM disease is a neglected and emerging public health disease and enhanced surveillance is required.


Abstract

In this study, ticks from pastoral communities in Kenya were tested for Rickettsia spp. infections in geographical regions where the presence of tick-borne arboviruses had previously been reported. Rickettsial and arbovirus infections have similar clinical features which makes differential diagnosis challenging when both diseases occur. The tick samples were tested for Rickettsia spp. by conventional PCR using three primer sets targeting the gltA, ompA, and ompB genes followed by amplicon sequencing. Of the tick pools screened, 25% (95/380) were positive for Rickettsia spp. DNA using the gltA primer set. Of the tick-positive pools, 60% were ticks collected from camels. Rickettsia aeschlimannii and R. africae were the main Rickettsia spp. detected in the tick pools sequenced. The findings of this study indicate that multiple Rickettsia species are circulating in ticks from pastoral communities in Kenya and could contribute to the etiology of febrile illness in these areas. Diagnosis and treatment of rickettsial infections should be a public health priority in these regions.


Abstract

Background: Antimalarial drugs affect the central nervous system, but it is difficult to differentiate the effect of these drugs from that of the malaria illness. We conducted a systematic review to determine the association between anti-malarial drugs and mental and neurological impairment in humans. Methods: We systematically searched online databases, including Medline/PubMed, PsychoInfo, and Embase, for articles published up to 14th July 2016. Pooled prevalence, heterogeneity and factors associated with prevalence of mental and neurological manifestations were determined using meta-analytic techniques. Results: Of the 2,349 records identified in the initial search, 51 human studies met the eligibility criteria. The median pooled prevalence range of mental and neurological manifestations associated with antimalarial drugs ranged from 0.7% (dapsone) to 48.3% (minocycline) across all studies, while it ranged from 0.6% (pyrimethamine) to 42.7% (amodiaquine) during treatment of acute malaria, and 0.7% (primaquine/dapsone) to 55.0% (sulfadoxine) during prophylaxis. Pooled prevalence of mental and neurological manifestations across all studies was associated with an increased number of antimalarial drugs (prevalence ratio= 5.51 (95%CI, 1.05-29.04); P=0.045) in a meta-regression analysis. Headaches (15%) and dizziness (14%) were the
most common mental and neurological manifestations across all studies. Of individual antimalarial drugs still on the market, mental and neurological manifestations were most common with the use of sulphadoxine (55%) for prophylaxis studies and amodiaquine (42.7%) for acute malaria studies. Mefloquine affected more domains of mental and neurological manifestations than any other antimalarial drug. **Conclusions:** Antimalarial drugs, particularly those used for prophylaxis, may be associated with mental and neurological manifestations, and the number of antimalarial drugs taken determines the association. Mental and neurological manifestations should be assessed following the use of antimalarial drugs.


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**Abstract**

**Background:** Childhood mortality from infectious diseases has declined steadily in many low and middle-income (LAMIC) countries, with increased recognition of non-communicable diseases such as neurodevelopmental disorders (NDD). There is lack of data on the burden of NDD in LAMIC. Current global burden of these disorders are largely extrapolated from high-income countries. The main objective of the study was therefore to estimate the burden of NDD in LAMIC using meta-analytic techniques. **Methods:** We systematically searched online databases including Medline/PubMed, PsychoInfo, and Embase for studies that reported prevalence or incidence of NDD. Pooled prevalence, heterogeneity and risk factors for prevalence were determined using meta-analytic techniques. **Results:** We identified 4,802 records, but only 51 studies met the eligibility criteria. Most studies were from Asia (52.2%) and most were on neurological disorders (63.1%). The median pooled prevalence per 1,000 for all NDD was 7.6 (95%CI 7.5-7.7), being 11.3 (11.7-12.0) for neurological disorders and 3.2 (95%CI 3.1-3.3) for mental conditions such as attention-deficit hyperactivity disorder (ADHD). The type of NDD was significantly associated with the greatest prevalence ratio in the multivariable model (PR=2.6(95%CI 0.6-11.6) (P>0.05). Incidence was only reported for epilepsy (mean of 447.7 (95%CI 415.3-481.9) per 100,000). Perinatal complications were the commonest risk factor for NDD. **Conclusion:** The burden of NDD in LAMIC is considerable. Epidemiological surveys on NDD should screen all types of NDD to provide reliable estimates.

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<td><strong>Abstract</strong></td>
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<td><strong>Background:</strong> Rehydration strategies in children with severe acute malnutrition (SAM) and severe dehydration are extremely cautious. The World Health Organization (WHO) SAM guidelines advise strongly against intravenous fluids unless the child is shocked or severely dehydrated and unable to tolerate oral fluids. Otherwise, guidelines recommend oral or nasogastric rehydration using low sodium oral rehydration solutions. There is limited evidence to support these recommendations. <strong>Methods:</strong> We conducted a systematic review of randomised controlled trials (RCTs) and observational studies on June 15th, 2017 comparing different strategies of rehydration therapy in children with acute gastroenteritis and severe dehydration, specifically relating to intravenous rehydration, using standard search terms. Two authors assessed papers for inclusion. The primary endpoint was evidence of fluid overload. <strong>Results:</strong> Four studies were identified, all published in English, including 883 children, all of which were conducted in low resource settings. Two were randomised controlled trials and two observational cohort studies, one incorporated assessment of myocardial and haemodynamic function. There was no evidence of fluid overload or other fluid-related adverse events, including children managed on more liberal rehydration protocols. Mortality was high overall, and particularly in children with shock managed on WHO recommendations (day-28 mortality 82%). There was no difference in safety outcomes when different rates of intravenous rehydration were compared. <strong>Conclusions:</strong> The current 'strong recommendations' for conservative rehydration of children with SAM are not based on emerging evidence. We found no clinical trials providing a direct assessment of the current WHO guidelines, and those that were available suggested that these children have a high mortality and remain fluid depleted on current therapy. Recent studies have reported no evidence of fluid overload or heart failure with more liberal rehydration regimens. Clinical trials are urgently required to inform guidelines on routes and rates of intravenous rehydration therapy for dehydration in children with SAM.</td>
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Abstract

**Background:** Diarrhoea complicates over half of admissions to hospital with severe acute malnutrition (SAM). World Health Organization (WHO) guidelines for the management of dehydration recommend the use of oral rehydration with ReSoMal (an oral rehydration solution (ORS) for SAM), which has lower sodium (45mmols/l) and higher potassium (40mmols/l) content than old WHO ORS. The composition of ReSoMal was designed specifically to address theoretical risks of sodium overload and potential under-treatment of severe hypokalaemia with rehydration using standard ORS. In African children, severe hyponatraemia at admission is a major risk factor for poor outcome in children with SAM complicated by diarrhoea. We therefore reviewed the evidence for oral rehydration therapy in children with SAM. **Methods:** We conducted a systematic review of randomised controlled trials (RCTs) on 18th July 2017 comparing different oral rehydration solutions in severely malnourished children with diarrhoea and dehydration, using standard search terms. The author assessed papers for inclusion. The primary endpoint was frequency of hyponatraemia during rehydration. **Results:** Six RCTs were identified, all published in English and conducted in low resource settings in Asia. A range of ORS were evaluated in these studies, including old WHO ORS, standard hypo-osmolar WHO ORS and ReSoMal. Hyponatraemia was observed in two trials evaluating ReSoMal, three children developed severe hyponatraemia with one experiencing convulsions. Hypo-osmolar ORS was found to have benefits in time to rehydration, reduction of stool output and duration of diarrhoea. No trials reported overhydration or fatalities. **Conclusions:** Current WHO guidelines strongly recommend the use of ReSoMal based on low quality of evidence. Studies indicate a significant risk of hyponatraemia on ReSoMal in Asian children, none have been conducted in Africa, where SAM mortality remains high. Further research should be conducted in Africa to evaluate optimal ORS for children with SAM and to generate evidence based, practical guidelines.


| Abstract |
**Objective:** To clarify the pathways between household livestock and child growth by assessing the relationships between consumption of animal-source foods (ASF) and child growth and evaluating the household livestock correlates of child consumption of ASF.

**Design:** We conducted a longitudinal cohort study of anthropometry and 3 d feeding recalls among children <5 years old between June 2014 and May 2015. In addition, we collected data on wealth, livestock ownership and livestock diseases in the same households. We used linear and negative binomial mixed models to evaluate the relationships between household livestock characteristics, reported consumption of ASF and child growth.

**Setting:** An 1800-household surveillance catchment area in Western Kenya within the structure of human and animal health surveillance systems.

**Subjects:** Children (n 874) <5 years old.

**Results:** Among children >6 months old, reported frequency of egg and milk consumption was associated with increased monthly height gain (for each additional report of consumption over 3 d: adjusted β (95 % CI)=0·010 (0·002, 0·019) cm/month and 0·008 (0·004, 0·013) cm/month, respectively). Poultry ownership was associated with higher reported frequency of egg, milk and chicken consumption (adjusted incidence rate ratio (95 % CI)=1·3 (1·2, 1·4), 1·4 (1·1, 1·6) and 1·3 (1·1, 1·4), respectively). Some livestock diseases were associated with lower reported frequency of ASF intake (livestock digestive diseases-adjusted incidence rate ratio (95 % CI)=0·89 (0·78, 1·00)).

**Conclusions:** Child height gain was associated with milk and egg consumption in this cohort. ASF consumption was related to both household livestock ownership and animal health.


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**Abstract**

**Background:** The transmission patterns of dengue (DENV) and yellow fever (YFV) viruses, especially in urban settings, are influenced by Aedes (Stegomyia) mosquito abundance and behavior. Despite recurrent dengue outbreaks on the Kenyan coast, these
parameters remain poorly defined in this and other areas of contrasting dengue endemicity in Kenya. In assessing the transmission risk of DENV/YFV in three Kenyan cities, we determined adult abundance and resting habits of potential Aedes (Stegomyia) vectors in Kilifi (dengue-outbreak prone), and Nairobi and Kisumu (no dengue outbreaks reported). In addition, mosquito diversity, an important consideration for changing mosquito-borne disease dynamics, was compared.

**Methods:** Between October 2014 and June 2016, host-seeking adult mosquitoes were sampled using CO2-baited BG-Sentinel traps (12 traps daily) placed in vegetation around homesteads, across study sites in the three major cities. Also, indoor and outdoor resting mosquitoes were sampled using Prokopack aspirators. Three samplings, each of five consecutive days, were conducted during the long-rains, short-rains and dry season for each city. Inter-city and seasonal variation in mosquito abundance and diversity was evaluated using general linear models while mosquito-resting preference (indoors vs outdoors) was compared using Chi-square test.

**Results:** Aedes aegypti, which comprised 60% (n = 7772) of the total 12,937 host-seeking mosquitoes collected, had comparable numbers in Kisumu (45.2%, n = 3513) and Kilifi (37.7%, n = 2932), both being significantly higher than Nairobi (17.1%, n = 1327). Aedes aegypti abundance was significantly lower in the short-rains and dry season relative to the long-rains (P < 0.0001). Aedes bromelae, which occurred in low numbers, did not differ significantly between seasons or cities. Mosquito diversity was highest during the long-rains and in Nairobi. Only 10% (n = 43) of the 450 houses aspirated were found positive for resting Ae. aegypti, with overall low captures in all areas. Aedes aegypti densities were comparable indoors/outdoors in Kilifi; but with higher densities outdoors than indoors in Kisumu and Nairobi.

**Conclusions:** The presence and abundance of Ae. aegypti near human habitations and dwellings, especially in Kilifi/Kisumu, is suggestive of increased DENV transmission risk due to higher prospects of human vector contact. Despite low abundance of Ae. bromelae suggestive of low YFV transmission risk, its proximity to human habituation as well as the observed diversity of potential YFV vectors should be of public health concern and monitored closely for targeted control. The largely outdoor resting behavior for Ae. aegypti provides insights for targeted adult vector control especially during emergency outbreak situations.


Abstract

Background: Childhood pneumonia is the leading infectious cause of mortality in children younger than 5 years old. Recent updates to World Health Organization pneumonia guidelines recommend outpatient care for a population of children previously classified as high risk. This revision has been challenged by policymakers in Africa, where mortality related to pneumonia is higher than in other regions and often complicated by comorbidities. This study aimed to identify factors that best discriminate inpatient mortality risk in non-severe pneumonia and explore whether these factors offer any added benefit over the current criteria used to identify children with pneumonia requiring inpatient care.

Methods: We undertook a retrospective cohort study of children aged 2-59 months admitted with a clinical diagnosis of pneumonia at 14 public hospitals in Kenya between February 2014 and February 2016. Using machine learning techniques, we analysed whether clinical characteristics and common comorbidities increased the risk of inpatient mortality for non-severe pneumonia. The topmost risk factors were subjected to decision curve analysis to explore if using them as admission criteria had any net benefit above the current criteria.

Results: Out of 16,162 children admitted with pneumonia during the study period, 10,687 were eligible for subsequent analysis. Inpatient mortality within this non-severe group was 252/10,687 (2.36%). Models demonstrated moderately good performance; the partial least squares discriminant analysis model had higher sensitivity for predicting mortality in comparison to logistic regression. Elevated respiratory rate (≥70 bpm), age 2-11 months and weight-for-age Z-score (WAZ) < -3SD were highly discriminative of mortality. These factors ranked consistently across the different models. For a risk threshold probability of 7-14%, there is a net benefit to admitting the patient sub-populations with these features as additional criteria alongside those currently used to classify severe pneumonia. Of the population studied, 70.54% met at least one of these criteria. Sensitivity analyses indicated that the overall results were not significantly affected by variations in pneumonia severity classification criteria.

Conclusions: Children with non-severe pneumonia aged 2-11 months or with respiratory rate ≥ 70 bpm or very low WAZ experience risks of inpatient mortality comparable to severe pneumonia. Inpatient care is warranted in these high-risk groups of children.

Abstract

**Background:** The first models of malaria transmission assumed a completely mixed and homogeneous population of parasites. Recent models include spatial heterogeneity and variably mixed populations. However, there are few empiric estimates of parasite mixing with which to parametrize such models. **Methods:** Here we genotype 276 single nucleotide polymorphisms (SNPs) in 5199 *P. falciparum* isolates from two Kenyan sites (Kilifi county and Rachuonyo South district) and one Gambian site (Kombo coastal districts) to determine the spatio-temporal extent of parasite mixing, and use Principal Component Analysis (PCA) and linear regression to examine the relationship between genetic relatedness and distance in space and time for parasite pairs. **Results:** Using 107, 177 and 82 SNPs that were successfully genotyped in 133, 1602, and 1034 parasite isolates from The Gambia, Kilifi and Rachuonyo South district, respectively, we show that there are no discrete geographically restricted parasite sub-populations, but instead we see a diffuse spatio-temporal structure to parasite genotypes. Genetic relatedness of sample pairs is predicted by relatedness in space and time. **Conclusions:** Our findings suggest that targeted malaria control will benefit the surrounding community, but unfortunately also that emerging drug resistance will spread rapidly through the population.


Abstract

**Background:** Soil-transmitted helminthes (STHs) are common human parasitic diseases in most of the developing world particularly in Kenya. The ongoing National School-Based Deworming Programme (NSBDP) was launched in 2012 and is currently targeting 28 of the 47 endemic Counties. In an effort to improve treatment intervention strategies among Pre-School Age Children (PSAC) attending Early Childhood Development
Centres (ECDC), we sought to assess parents’ knowledge, perceptions and practices on worm infection.

Methodology: We conducted a qualitative cross-sectional study in four endemic sub-counties of two counties of coastal region of Kenya. A total of 20 focus group discussions (FGDs) categorized by gender were conducted among parents of pre-school age children. Participants were purposively selected based on homogenous characteristics with the saturation model determining the number of focus group discussions conducted. The data collected was analyzed manually by study themes.

Findings: The majority of the parents had knowledge on worms and modes of transmission of the parasitic infections among the pre-school children. Also, most of the participants knew the causes of worm infection and the pre-disposing factors mentioned included poor hygiene and sanitation practices. Due to poor knowledge of signs and symptoms, misconceptions about the drugs administered during the NSBDP were common with a large majority of the parents indicating that the drugs were ineffective in worm control. The findings also indicated that most of the participants sought medical care on the onset of the signs and symptoms of worm infestation and preferred services provided at public health facilities as opposed to private health facilities or buying drugs from the local market citing mistrust of such services. Cultural beliefs, high cost of building and availability of vast pieces of land for human waste disposal were factors that contributed to low or lack of latrine ownership and usage by a large majority of the respondents.

Conclusions: Our results show that to a large extent the parents of the pre-school age children have information on worm infections. However, some cultural beliefs and practices on the pathology and mode of transmission mentioned could be a hindrance to prevention and control efforts. There is need to implement health promotion campaigns to strengthen the impact of control strategies and reduce infection.


Abstract

There is a growing literature documenting the complex realities of consent processes in the field, and the negotiations and ethical dilemmas involved. Much has also been
written about how gender and power shape household decision-making processes. However, these bodies of literature have rarely been brought together to inform research theory and practice in low-income settings. In this paper, qualitative research (observation, focus group discussions and interviews) were used alongside large clinical community-based studies conducted on the Kenyan Coast to explore how gender and power relations within households and communities and between fieldworkers and communities shape consent processes and interactions. This exploration is embedded in relevant literature and the implications for community-based health research policy and practice are considered. Across diverse forms of households, we observed significant consultation on whether or not to participate in research. Although men are typically described as household decision-makers, in practice, decision-making processes are often far more nuanced, with many women using their agency to control, sometimes subtly, the decisions made. Where decisions are made without adequately consulting women, many find strategies to exercise their choice, in ways that safeguard important relationships within households in the longer term. We also found that the gender of field staff who typically conduct research activities in the field, including consent processes, can influence household dynamics and decision-making processes with important implications for the science and ethics of research. It is essential that frontline field staff and their supervisors are aware of the complex and gendered realities of consent processes at household level, and their implications, and that they develop appropriate context-informed approaches that support ethical practice.


Abstract

Multidrug resistant (MDR) Klebsiella pneumoniae is a common cause of nosocomial infections worldwide. Recent years have seen an explosion of resistance to extended-spectrum β-lactamases (ESBLs) and emergence of carbapenem resistance. Here, we examine 198 invasive K. pneumoniae isolates collected from over a decade in Kilifi County Hospital (KCH) in Kenya. We observe a significant increase in MDR K. pneumoniae isolates, particularly to third generation cephalosporins conferred by ESBLs. Using whole-genome sequences, we describe the population structure and the distribution of antimicrobial resistance genes within it. More than half of the isolates examined in this study were ESBL-positive, encoding CTX-M-15, SHV-2, SHV-12 and SHV-27, and 79% were MDR conferring resistance to at least three antimicrobial
classes. Although no isolates in our dataset were found to be resistant to carbapenems we did find a plasmid with the genetic architecture of a known New Delhi metallo-β-lactamase-1 (NDM)-carrying plasmid in 25 isolates. In the absence of carbapenem use in KCH and because of the instability of the NDM-1 gene in the plasmid, the NDM-1 gene has been lost in these isolates. Our data suggests that isolates that encode NDM-1 could be present in the population; should carbapenems be introduced as treatment in public hospitals in Kenya, resistance is likely to ensue rapidly.


Abstract

Background: Direct immuno-fluorescence test (IFAT) and multiplex real-time RT-PCR have been central to RSV diagnosis in Kilifi, Kenya. Recently, these two methods showed discrepancies with an increasing number of PCR undetectable RSV-B viruses.

Objectives: Establish if mismatches in the primer and probe binding sites could have reduced real-time RT-PCR sensitivity.

Study design: Nucleoprotein (N) and glycoprotein (G) genes were sequenced for real-time RT-PCR positive and negative samples. Primer and probe binding regions in N gene were checked for mismatches and phylogenetic analyses done to determine molecular epidemiology of these viruses. New primers and probe were designed and tested on the previously real-time RT-PCR negative samples.

Results: N gene sequences revealed 3 different mismatches in the probe target site of PCR negative, IFAT positive viruses. The primers target sites had no mismatches. Phylogenetic analysis of N and G genes showed that real-time RT-PCR positive and negative samples fell into distinct clades. Newly designed primers-probe pair improved detection and recovered previous PCR undetectable viruses.

Conclusions: An emerging RSV-B variant is undetectable by a quite widely used real-time RT-PCR assay due to polymorphisms that influence probe hybridization affecting PCR accuracy.


Abstract

**Background:** Plasmodium falciparum prevalence (PfPR) is a widely used metric for assessing malaria transmission intensity. This study was carried out concurrently with the RTS,S/AS01 candidate malaria vaccine Phase III trial and estimated PfPR over ≤ 4 standardized cross-sectional surveys.

**Methods:** This epidemiology study ([NCT01190202](https://ClinicalTrials.gov/show/NCT01190202)) was conducted in 8 sites from 6 countries (Burkina Faso, Gabon, Ghana, Kenya, Malawi, and Tanzania), between March 2011 and December 2013. Participants were enrolled in a 2:1:1 ratio according to age category: 6 months-4 years, 5-19 years, and ≥ 20 years, respectively, per year and per centre. All sites carried out surveys 1-3 while survey 4 was conducted only in 3 sites. Surveys were usually performed during the peak malaria parasite transmission season, in one home visit, when medical history and malaria risk factors/prevention measures were collected, and a blood sample taken for rapid diagnostic test, microscopy, and haemoglobin measurement. PfPR was estimated by site and age category.

**Results:** Overall, 6401 (survey 1), 6411 (survey 2), 6400 (survey 3), and 2399 (survey 4) individuals were included in the analyses. In the 6 months-4 years age group, the lowest prevalence (assessed using microscopy) was observed in 2 Tanzanian centres (4.6% for Korogwe and 9.95% for Bagamoyo) and Lambaréné, Gabon (6.0%), while the highest PfPR was recorded for Nanoro, Burkina Faso (52.5%). PfPR significantly decreased over the 3 years in Agogo (Ghana), Kombewa (Kenya), Lilongwe (Malawi), and Bagamoyo (Tanzania), and a trend for increased PfPR was observed over the 4 surveys for Kintampo, Ghana. Over the 4 surveys, for all sites, PfPR was predominantly higher in the 5-19 years group than in the other age categories. Occurrence of fever and anaemia was associated with high P. falciparum parasitaemia. Univariate analyses showed a significant association of anti-malarial treatment in 4 surveys (odds ratios [ORs]: 0.52,
0.52, 0.68, 0.41) and bed net use in 2 surveys (ORs: 0.63, 0.68, 1.03, 1.78) with lower risk of malaria infection.

**Conclusion:** Local PfPR differed substantially between sites and age groups. In children 6 months-4 years old, a significant decrease in prevalence over the 3 years was observed in 4 out of the 8 study sites. Trial registration Clinical Trials.gov identifier: NCT01190202; NCT. GSK Study ID numbers: 114001.


**Abstract**

Mass administration of endectocides, drugs that kill blood-feeding arthropods, has been proposed as a complementary strategy to reduce malaria transmission. Ivermectin is one of the leading candidates given its excellent safety profile. Here we provide proof that the effect of ivermectin can be boosted at two different levels by drugs inhibiting the cytochrome or ABC transporter in the mammal host and the target mosquitoes. Using a mini-pig model, we show that drug-mediated cytochrome P450/ABC transporter inhibition results in a 3-fold increase in the time ivermectin remains above mosquito-killing concentrations. In contrast, P450/ABC transporter induction with rifampicin markedly impaired ivermectin absorption. The same ketoconazole-mediated cytochrome/ABC transporter inhibition also occurs outside the mammal host and enhances the mortality of Anopheles gambiae. This was proven by using the samples from the mini-pig experiments to conduct an ex-vivo synergistic bioassay by membrane-feeding Anopheles mosquitoes. Inhibiting the same cytochrome/xenobiotic pump complex in two different organisms to simultaneously boost the pharmacokinetic and pharmacodynamic activity of a drug is a novel concept that could be applied to other systems. Although the lack of a dose-response effect in the synergistic bioassay warrants further exploration, our study may have broad implications for the control of parasitic and vector-borne diseases.


Abstract

Objective: To examine trends in prescription of cough medicines over the period 2002-2015 in children aged 1 month to 12 years admitted to Kenyan hospitals with cough, difficulty breathing or diagnosed with a respiratory tract infection.

Methods: We reviewed hospitalisation records of children included in four studies providing cross-sectional prevalence estimates from government hospitals for six time periods between 2002 and 2015. Children with an atopic illness were excluded. Amongst eligible children, we determined the proportion prescribed any adjuvant medication for cough. Active ingredients in these medicines were often multiple and were classified into five categories: antihistamines, antitussives, mucolytics/expectorants, decongestants and bronchodilators. From late 2006, guidelines discouraging cough medicine use have been widely disseminated and in 2009 national directives to decrease cough medicine use were issued.

Results: Across the studies, 17 963 children were eligible. Their median age and length of hospital stay were comparable. The proportion of children who received cough medicines shrank across the surveys: approximately 6% [95% CI: 5.4, 6.6] of children had a prescription in 2015 vs. 40% [95% CI: 35.5, 45.6] in 2002. The most common active ingredients were antihistamines and bronchodilators. The relative proportion that included antihistamines has increased over time.

Conclusions: There has been an overall decline in the use of cough medicines among hospitalised children over time. This decline has been associated with educational, policy and mass media interventions.

Young infants are less susceptible to severe episodes of malaria but the targets and mechanisms of protection are not clear. Cord blood antibodies may play an important role in mediating protection but many studies have examined their association with the outcome of infection or non-severe malaria. Here, we investigated whether cord blood IgG to Plasmodium falciparum merozoite antigens and antibody-mediated effector functions were associated with reduced odds of developing severe malaria at different time points during the first year of life. We conducted a case-control study of well-defined severe falciparum malaria nested within a longitudinal birth cohort of Kenyan children. We measured cord blood total IgG levels against five recombinant merozoite antigens and antibody function in the growth inhibition activity and neutrophil antibody-dependent respiratory burst assays. We also assessed the decay of maternal antibodies during the first 6 months of life. The mean antibody half-life range was 2.51 months (95% confidence interval (CI): 2.19-2.92) to 4.91 months (95% CI: 4.47-6.07). The rate of decline of maternal antibodies was inversely proportional to the starting concentration. The functional assay of antibody-dependent respiratory burst activity predicted significantly reduced odds of developing severe malaria during the first 6 months of life (Odds ratio (OR) 0.07, 95% CI: 0.007-0.74, P=0.007). Identification of the targets of antibodies mediating antibody-dependent respiratory burst activity could contribute to the development of malaria vaccines that protect against severe episodes of malaria in early infancy.


Abstract

Background: Reducing tuberculosis (TB) deaths among children requires a better understanding of the gaps in the care cascade from TB diagnosis to treatment
completion. We sought to assess the child TB care cascade in 32 rural communities in Uganda and Kenya using programmatic data.

Methods: This is a retrospective cohort study of 160,851 children (ages <15 years) living in 12 rural communities in Kenya and 22 in Uganda. We reviewed national TB registries from health centers in and adjacent to the 32 communities, and we included all child TB cases recorded from January 1, 2013 to June 30, 2016. To calculate the first step of the child TB care cascade, the number of children with active TB, we divided the number of reported child TB diagnoses by the 2015 World Health Organization (WHO) child TB case detection ratio for Africa of 27%. The remaining components of the Child TB Care Cascade were ascertained directly from the TB registries and included: diagnosed with TB, started on TB treatment, and completed TB treatment.

Results: In two and a half years, a total of 42 TB cases were reported among children living in 32 rural communities in Uganda and Kenya. 40% of the children were co-infected with HIV. Using the WHO child TB case detection ratio, we calculated that 155 children in this cohort had TB during the study period. Of those 155 children, 42 were diagnosed and linked to TB care, 42 were started on treatment, and 31 completed treatment. Among the 42 children who started TB treatment, reasons for treatment non-completion were loss to follow up (7%), death (5%), and un-recorded reasons (5%). Overall, 20% (31/155) of children completed the child TB care cascade.

Conclusion: In 32 rural communities in Uganda and Kenya, we estimate that 80% of children with TB fell off the care cascade. Reducing morbidity and mortality from child TB requires strengthening of the child TB care cascade from diagnosis through treatment completion.


Abstract

Recent health system shocks such as the Ebola disease outbreak have focused global health attention on the notion of resilient health systems. In this commentary, we reflect on the current framing of the concept of resilience in health systems discourse and propose a reframing. Specifically, we propose that: (1) in addition to sudden shocks, health systems face the ongoing strain of multiple factors. Health systems need the capacity to continue to deliver services of good quality and respond effectively to wider
health challenges. We call this capacity everyday resilience; (2) health system resilience entails more than bouncing back from shock. In complex adaptive systems (CAS), resilience emerges from a combination of absorptive, adaptive and transformative strategies; (3) nurturing the resilience of health systems requires understanding health systems as comprising not only hardware elements (such as finances and infrastructure), but also software elements (such as leadership capacity, power relations, values and appropriate organizational culture). We also reflect on current criticisms of the concept of resilient health systems, such as that it assumes systems are apolitical, ignoring actor agency, promoting inaction, and requiring that we accept and embrace vulnerability, rather than strive for stronger and more responsive systems. We observe that these criticisms are warranted to the extent that they refer to notions of resilience that are mismatched with the reality of health systems as CAS. We argue that the observed weaknesses of resilience thinking can be addressed by reframing and applying a resilience lens that is better suited to the attributes of health systems as CAS.


Abstract

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is believed to confer protection against *Plasmodium falciparum* malaria, but the precise nature of the protective effects has proved difficult to define as G6PD deficiency has multiple allelic variants with different effects in males and females, and it has heterogeneous effects on the clinical outcome of *P. falciparum* infection. Here we report an analysis of multiple allelic forms of G6PD deficiency in a large multi-centre case-control study of severe malaria, using the WHO classification of G6PD mutations to estimate each individual's level of enzyme activity from their genotype. Aggregated across all genotypes, we find that increasing levels of
G6PD deficiency are associated with decreasing risk of cerebral malaria, but with increased risk of severe malarial anaemia. Models of balancing selection based on these findings indicate that an evolutionary trade-off between different clinical outcomes of *P. falciparum* infection could have been a major cause of the high levels of G6PD polymorphism seen in human populations.


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**Abstract**

A broad diversity of arthropod-borne viruses (arboviruses) of global health concern are endemic to East Africa, yet most surveillance efforts are limited to just a few key viral pathogens. Additionally, estimates of arbovirus diversity in the tropics are likely to be underestimated as their discovery has lagged significantly over past decades due to limitations in fast and sensitive arbovirus identification methods. Here, we developed a nearly pan-arbovirus detection assay that uses high-resolution melting (HRM) analysis of RT-PCR products from highly multiplexed assays to differentiate broad diversities of arboviruses. We differentiated 15 viral culture controls and seven additional synthetic viral DNA sequence controls, within Flavivirus, Alphavirus, Nairovirus, Phlebovirus, Orthobunyavirus and Thogotovirus genera. Among Bunyamwera, sindbis, dengue and Thogoto virus serial dilutions, detection by multiplex RT-PCR-HRM was comparable to the gold standard Vero cell plaque assays. We applied our low-cost method for enhanced broad-range pathogen surveillance from mosquito samples collected in Kenya and identified diverse insect-specific viruses, including a new clade in anopheline mosquitoes, and Wesselsbron virus, an arbovirus that can cause viral haemorrhagic fever in humans and has not previously been isolated in Kenya, in Culex spp. and Anopheles coustani mosquitoes. Our findings demonstrate how multiplex RT-PCR-HRM can identify novel viral diversities and potential disease threats that may not be included in pathogen detection panels of routine surveillance efforts. This approach can be adapted to other pathogens to enhance disease surveillance and pathogen discovery efforts, as well as the study of pathogen diversity and viral evolutionary ecology.


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Abstract

Background: In sub-Saharan Africa, among patients with advanced human immunodeficiency virus (HIV) infection, the rate of death from infection (including tuberculosis and cryptococcus) shortly after the initiation of antiretroviral therapy (ART) is approximately 10%.

Methods: In this factorial open-label trial conducted in Uganda, Zimbabwe, Malawi, and Kenya, we enrolled HIV-infected adults and children 5 years of age or older who had not received previous ART and were starting ART with a CD4+ count of fewer than 100 cells per cubic millimeter. They underwent simultaneous randomization to receive enhanced antimicrobial prophylaxis or standard prophylaxis, adjunctive raltegravir or no raltegravir, and supplementary food or no supplementary food. Here, we report on the effects of enhanced antimicrobial prophylaxis, which consisted of continuous trimethoprim-sulfamethoxazole plus at least 12 weeks of isoniazid-pyridoxine (coformulated with trimethoprim-sulfamethoxazole in a single fixed-dose combination tablet), 12 weeks of fluconazole, 5 days of azithromycin, and a single dose of albendazole, as compared with standard prophylaxis (trimethoprim-sulfamethoxazole alone). The primary end point was 24-week mortality.

Results: A total of 1805 patients (1733 adults and 72 children or adolescents) underwent randomization to receive either enhanced prophylaxis (906 patients) or standard prophylaxis (899 patients) and were followed for 48 weeks (loss to follow-up, 3.1%). The median baseline CD4+ count was 37 cells per cubic millimeter, but 854 patients (47.3%) were asymptomatic or mildly symptomatic. In the Kaplan-Meier analysis at 24 weeks, the rate of death with enhanced prophylaxis was lower than that with standard prophylaxis (80 patients [8.9% vs. 108 [12.2%]; hazard ratio, 0.73; 95% confidence interval [CI], 0.55 to 0.98; P=0.03); 98 patients (11.0%) and 127 (14.4%), respectively, had died by 48 weeks (hazard ratio, 0.76; 95% CI, 0.58 to 0.99; P=0.04). Patients in the enhanced-prophylaxis group had significantly lower rates of tuberculosis (P=0.02), cryptococcal infection (P=0.01), oral or esophageal candidiasis (P=0.02), death of unknown cause (P=0.03), and new hospitalization (P=0.03). However, there was no significant between-group difference in the rate of severe bacterial infection (P=0.32). There were nonsignificantly lower rates of serious adverse events and grade 4 adverse
events in the enhanced-prophylaxis group (P=0.08 and P=0.09, respectively). Rates of HIV viral suppression and adherence to ART were similar in the two groups.

**Conclusions:** Among HIV-infected patients with advanced immunosuppression, enhanced antimicrobial prophylaxis combined with ART resulted in reduced rates of death at both 24 weeks and 48 weeks without compromising viral suppression or increasing toxic effects. (Funded by the Medical Research Council and others; REALITY Current Controlled Trials number, ISRCTN43622374.).


**Abstract**

For people living with HIV, exposure to sexual violence (SV) is associated with decreased adherence to antiretroviral medication, a primary predictor of their survival. Identification of risk factors for SV is a pressing issue in sub-Saharan Africa, where the global majority of HIV-positive women live and the prevalence of SV against women is high. We used qualitative data to examine SV against HIV-positive women enrolled in HIV care in Kenya. Respondents identified husbands as perpetrators of SV in the context of women's efforts to use condoms as directed by HIV care providers.


**Abstract**

**Background:** The protozoan parasite Trichomonas vaginalis is the most common non-viral, sexually transmitted pathogen. Although T. vaginalis is highly prevalent among women in Kenya, there is lack of data regarding genetic diversity of isolates currently in circulation in Kenya.

**Methods:** Typing was performed on 22 clinical isolates of T. vaginalis collected from women attending the antenatal care clinic at Kilifi County Hospital, Kenya, in 2015.
Genotyping followed a previously proposed restriction fragment length polymorphism (RFLP) scheme, which involved in silico cleavage of the amplified actin gene by HindII, MseI and Rsal restriction enzymes. Phylogenetic analysis of all the sequences was performed to confirm the results obtained by RFLP-analysis and to assess the diversity within the RFLP genotypes. Additionally, we determined carriage of the four different types of Trichomonas vaginalis virus (TVVs) by polymerase chain reaction.

**Results:** In silico RFLP-analysis revealed five actin genotypes; 50.0% of the isolates were of actin genotype E, 27.3% of actin genotype N, 13.6% of actin genotype G and 4.5% of actin genotypes I and P. Phylogenetic analysis was in agreement with the RFLP-analysis, with the different actin genotypes clustering together. Prevalence of TVVs was 43.5% (95% confidence interval, CI: 23.2-65.5). TVV1 was the most prevalent, present in 39.1% of the strains and 90% of the T. vaginalis isolates which harbored TVVs had more than one type of TVV. None of the isolates of actin genotype E harbored any TVV.

**Conclusion:** The presence of five actin genotypes in our study suggests notable diversity among T. vaginalis isolates occurring among pregnant women in Kilifi, Kenya. Isolates of the most prevalent actin genotype E lacked TVVs. We found no association between T. vaginalis genotype, carriage of TVVs and symptoms. Further studies with higher number of strains should be conducted in order to corroborate these results.


94. Nyikuri MM, Tsofa B, Okoth P, Barasa EW, Molyneux S. "We are toothless and hanging, but optimistic": sub county managers' experiences of rapid devolution in coastal Kenya. Int J Equity Health. 2017 Sep 15;16(1):113

**Abstract**

**Background:** In March 2013, Kenya transitioned from a centralized to a devolved system of governance. Within the health sector, this entailed the transfer of service provision functions to 47 newly formed semi-autonomous counties, while policy and regulatory functions were retained at the national level. The devolution process was rapid rather than progressive.

**Methods:** We conducted qualitative research within one county to examine the early experiences of devolution in the health sector. We specifically focused on the experience of change from the perspective of sub-county managers, who form the link between county level managers and health facility managers. We collected data by observing a diverse range of management meetings, support supervision visits and outreach activities involving sub-county managers between May 2013 and June 2015, conducting informal
interviews wherever we could. Informal observations and interviews were supplemented by fifteen tape recorded in depth interviews with purposively selected sub-county managers from three sub-counties.

Results: We found that sub county managers as with many other health system actors were anxious about and ill-prepared for the unexpectedly rapid devolution of health functions to the newly created county government. They experienced loss of autonomy and resources in addition to confused lines of accountability within the health system. However, they harnessed individual, team and stakeholder resources to maintain their jobs, and continued to play a central role in supporting peripheral facility managers to cope with change.

Conclusions: Our study illustrates the importance in accelerated devolution contexts for: 1) mid-level managers to adopt new ways of working and engagement with higher and lower levels in the system; 2) clear lines of communication during reforms to these actors and 3) anticipating and managing the effect of change on intangible software issues such as trust and motivation. More broadly, we show the value of examining organisational change from the perspective of key actors within the system, and highlight the importance in times of rapid change of drawing upon and working with those already in the system. These actors have valuable tacit knowledge, but tapping into and building on this knowledge to enable positive response in times of health system shocks requires greater attention to sustained software capacity building within the health system.


Abstract

Middle East respiratory syndrome coronavirus (MERS-CoV) is a novel zoonotic virus that causes severe respiratory disease in humans with a case fatality rate close to 40%, but for which no vaccines are available. Here, we evaluated the utility of ChAdOx1, a promising replication-deficient simian adenovirus vaccine vector platform with an established safety profile in humans and dromedary camels, for MERS-CoV vaccine development. Using a transgenic lethal BALB/c MERS-CoV mouse model we showed that single dose intranasal or intramuscular immunisation with ChAdOx1 MERS, encoding full-length MERS-CoV Spike glycoprotein, is highly immunogenic and confers protection against lethal viral challenge. Immunogenicity and efficacy were comparable
between immunisation routes. Together these data provide support for further evaluation of ChAdOx1 MERS vaccine in humans and dromedary camels, the animal reservoir of infection.


Abstract

**Background:** Large-scale schistosomiasis control programs are implemented in regions with diverse social and economic environments. A key epidemiological feature of schistosomiasis is its small-scale heterogeneity. Locally profiling disease dynamics including risk factors associated with its transmission is essential for designing appropriate control programs. To determine spatial distribution of schistosomiasis and its drivers, we examined schoolchildren in Kwale, Kenya.

**Methodology/principal findings:** We conducted a cross-sectional study of 368 schoolchildren from six primary schools. Soil-transmitted helminths and Schistosoma mansoni eggs in stool were evaluated by the Kato-Katz method. We measured the intensity of Schistosoma haematobium infection by urine filtration. The geometrical mean intensity of S. haematobium was 3.1 eggs/10 ml urine (school range, 1.4-9.2). The hookworm geometric mean intensity was 3.2 eggs/g feces (school range, 0-17.4). Heterogeneity in the intensity of S. haematobium and hookworm infections was evident in the study area. To identify factors associated with the intensity of helminth infections, we utilized negative binomial generalized linear mixed models. The intensity of S. haematobium infection was associated with religion and socioeconomic status (SES), while that of hookworm infection was related to SES, sex, distance to river and history of anthelmintic treatment.

**Conclusions/significance:** Both S. haematobium and hookworm infections showed micro-geographical heterogeneities in this Kwale community. To confirm and explain our observation of high S. haematobium risk among Muslims, further extensive investigations are necessary. The observed small scale clustering of the S. haematobium
and hookworm infections might imply less uniform strategies even at finer scale for efficient utilization of limited resources


Abstract

Detailed information on the source, spread and evolution of respiratory syncytial virus (RSV) during seasonal community outbreaks remains sparse. Molecular analyses of attachment (G) gene sequences from hospitalized cases suggest that multiple genotypes and variants co-circulate during epidemics and that RSV persistence over successive seasons is characterized by replacement and multiple new introductions of variants. No studies have defined the patterns of introduction, spread and evolution of RSV at the local community and household level. We present a whole genome sequence analysis of 131 RSV group A viruses collected during 6-month household-based RSV infection surveillance in Coastal Kenya, 2010 within an area of 12 km$^2$. RSV infections were identified by regular symptom-independent screening of all household members twice weekly. Phylogenetic analysis revealed that the RSV A viruses in nine households were closely related to genotype GA2 and fell within a single branch of the global phylogeny. Genomic analysis allowed the detection of household-specific variation in seven households. For comparison, using only G gene analysis, household-specific variation was found only in one of the nine households. Nucleotide changes were observed both intra-host (viruses identified from same individual in follow-up sampling) and inter-host (viruses identified from different household members) and these coupled with sampling dates enabled a partial reconstruction of the within household transmission chains. The genomic evolutionary rate for the household dataset was estimated as $2.307 \times 10^{-3}$ (95% highest posterior density: 0.935-4.165 $\times 10^{-3}$) substitutions/site/year. We conclude that (i) at the household level, most RSV infections arise from the introduction of a single virus variant followed by accumulation of household specific variation and (ii) analysis of complete virus genomes is crucial to better understand viral transmission in the community. A key question arising is whether prevention of RSV introduction or spread within the household by vaccinating key transmitting household members would lead to a reduced onward community-wide transmission.


Abstract

**Introduction:** Male partner involvement in elimination of mother-to-child transmission (eMTCT) of HIV activities remains low in Western Kenya, despite its importance in reducing rates of child HIV transmission. We sought to identify factors associated with male partner involvement in eMTCT in Kisumu East sub-County, Western Kenya.

**Methods:** We conducted a cross-sectional study among women aged ≥ 18 years who had children aged ≤ 12 months and were attending a child health clinic for immunization services in one of four Western Kenya health centers between February and April, 2015. We assessed male involvement using an "involvement index" of five factors of equal weight: partner antenatal care (ANC) attendance, partner HIV testing, partner financial support to the woman during ANC, partner awareness of ANC services and partner participation in decision making on contraception including condom use. Male involvement was classified as high or low based on their index score. We calculated odds ratios (OR) and 95% confidence intervals (CI) to identify factors associated with high male partner involvement.

**Results:** We recruited 216 female participants. Mean age was 26.1 years (± 5.5 years), 189 (87.5%) were married. The majority (94.4%) had attended ANC in public health facilities. Nineteen percent of women had high male involvement. Having > 8 years of formal education (AOR 3.9, CI = 1.51-10.08), having male partner who was employed, history of previous couple testing (AOR = 3.2, CI = 1.42-7.22) and reports of partner having read the mother-child booklet during ANC (AOR = 2.9, CI = 1.30-6.49), were associated with high male involvement.

**Conclusion:** Based on our findings, we recommend targeted strategies to actively sensitize men and encourage their involvement in eMTCT, particularly among partners of women with fewer years of education and among partners who are not employed.


Abstract

Background: While HIV testing and counselling is a key entry point for treatment as prevention, over half of HIV-infected adults in Kenya are unaware they are infected. Offering HIV self-testing (HST) at community pharmacies may enhance detection of undiagnosed infections. We assessed the feasibility of pharmacy-based HST in Coastal Kenya.

Methods: Staff at five pharmacies, supported by on-site research assistants, recruited adult clients (≥18 years) seeking services indicative of HIV risk. Participants were offered oral HST kits (OraQuick®) at US$1 per test. Within one week of buying a test, participants were contacted for post-test data collection and counselling. The primary outcome was test uptake, defined as the proportion of invited clients who bought tests. Views of participating pharmacy staff were solicited in feedback sessions during and after the study.

Results: Between November 2015 and April 2016, 463 clients were invited to participate; 174 (38%) were enrolled; and 161 (35% [95% Confidence Interval (CI) 31-39%]) bought a test. Uptake was higher among clients seeking HIV testing compared to those seeking other services (84% vs. 11%, adjusted risk ratio 6.9 [95% CI 4.9-9.8]). Only 4% of non-testers (11/302) stated inability to pay as the reason they did not take up the test. All but one tester reported the process was easy (29%) or very easy (70%). Demand for HST kits persisted after the study and participating service providers expressed interest in continuing to offer the service.

Conclusions: Pharmacy HST is feasible in Kenya and may be in high demand. The uptake pattern observed suggests that a client-initiated approach is more feasible compared to pharmacy-initiated testing. Price is unlikely to be a barrier if set at about US$1 per test. Further implementation research is required to assess uptake, yield, and linkage to care on a larger scale.

### Abstract

**Background.** Malaria control, and finally malaria elimination, requires the identification and targeting of residual foci or hotspots of transmission. However, the level of parasite mixing within and between geographical locations is likely to impact the effectiveness and durability of control interventions and thus should be taken into consideration when developing control programs. **Methods.** In order to determine the geographic-genetic patterns of *Plasmodium falciparum* parasite populations at a sub-national level in Kenya, we used the Sequenom platform to genotype 111 genome-wide distributed single nucleotide polymorphic (SNP) positions in 2486 isolates collected from children in 95 primary schools in western Kenya. We analysed these parasite genotypes for genetic structure using principal component analysis and assessed local and global clustering using statistical measures of spatial autocorrelation. We further examined the region for spatial barriers to parasite movement as well as directionality in the patterns of parasite movement. **Results.** We found no evidence of population structure and little evidence of spatial autocorrelation of parasite genotypes (correlation coefficients <0.03 among parasite pairs in distance classes of 1km, 2km and 5km; p value<0.01). An analysis of the geographical distribution of allele frequencies showed weak evidence of variation in distribution of alleles, with clusters representing a higher than expected number of samples with the major allele being identified for 5 SNPs. Furthermore, we found no evidence of the existence of spatial barriers to parasite movement within the region, but observed directional movement of parasites among schools in two separate sections of the region studied. **Conclusions.** Our findings illustrate a pattern of high parasite mixing within the study region. If this mixing is due to rapid gene flow, then "one-off" targeted interventions may not be currently effective at the sub-national scale in Western Kenya, due to the high parasite movement that is likely to lead to re-introduction of infection from surrounding regions. However repeated targeted interventions may reduce transmission in the surrounding regions.


### Abstract

Malaria causes about half a million deaths annually, with *Plasmodium falciparum* being responsible for 90% of all the cases. Recent reports on artemisinin resistance in
Southeast Asia warrant urgent discovery of novel drugs for the treatment of malaria. However, most bioactive compounds fail to progress to treatments due to safety concerns. Drug repositioning offers an alternative strategy where drugs that have already been approved as safe for other diseases could be used to treat malaria. This study screened approved drugs for antimalarial activity using an in silico chemogenomics approach prior to in vitro verification. All the P. falciparum proteins sequences available in NCBI RefSeq were mined and used to perform a similarity search against DrugBank, TTD and STITCH databases to identify similar putative drug targets. Druggability indices of the potential P. falciparum drug targets were obtained from TDR targets database. Functional amino acid residues of the drug targets were determined using ConSurf server which was used to fine tune the similarity search. This study predicted 133 approved drugs that could target 34 P. falciparum proteins. A literature search done at PubMed and Google Scholar showed 105 out of the 133 drugs to have been previously tested against malaria, with most showing activity. For further validation, drug susceptibility assays using SYBR Green I method were done on a representative group of 10 predicted drugs, eight of which did show activity against P. falciparum 3D7 clone. Seven had IC50 values ranging from 1 μM to 50 μM. This study also suggests drug-target association and hence possible mechanisms of action of drugs that did show antiplasmodial activity. The study results validate the use of proteome-wide target similarity approach in identifying approved drugs with activity against P. falciparum and could be adapted for other pathogens.


**Abstract**

**Introduction:** Early diagnosis of HIV-1 infection and the prompt initiation of antiretroviral therapy are critical to achieving a reduction in the morbidity and mortality of infected infants. The Simple AMplification-Based Assay (SAMBA) HIV-1 Qual Whole Blood Test was developed specifically for early infant diagnosis and prevention of mother-to-child transmission programs implemented at the point-of-care in resource-limited settings.
Methods: We have evaluated the performance of this test run on the SAMBA I semiautomated platform with fresh whole blood specimens collected from 202 adults and 745 infants in Kenya, Uganda, and Zimbabwe. Results were compared with those obtained with the Roche COBAS AmpliPrep/COBAS TaqMan (CAP/CTM) HIV-1 assay as performed with fresh whole blood or dried blood spots of the same subjects, and discrepancies were resolved with alternative assays.

Results: The performance of the SAMBA and CAP/CTM assays evaluated at 5 laboratories in the 3 countries was similar for both adult and infant samples. The clinical sensitivity, specificity, positive predictive value, and negative predictive value for the SAMBA test were 100%, 99.2%, 98.7%, and 100%, respectively, with adult samples, and 98.5%, 99.8%, 99.7%, and 98.8%, respectively, with infant samples.

Discussion: Our data suggest that the SAMBA HIV-1 Qual Whole Blood Test would be effective for early diagnosis of HIV-1 infection in infants at point-of-care settings in sub-Saharan Africa.


Abstract

Background: The national pneumonia treatment guidelines in Kenya changed in February 2016 but such guideline changes are often characterized by prolonged delays in affecting practice. We designed an enhanced feedback intervention, delivered within an ongoing clinical network that provides a general form of feedback, aimed at improving and sustaining uptake of the revised pneumonia treatment policy. The objective was to determine whether an enhanced feedback intervention will improve correctness of classification and treatment of childhood pneumonia, compared to an existing approach to feedback, after nationwide treatment policy change and within an existing hospital network.

Methods/design: A pragmatic, cluster randomized trial conducted within a clinical network of 12 Kenyan county referral hospitals providing inpatient pediatric care to children (aged 2-59 months) with acute medical conditions between March and November 2016. The intervention comprised enhanced feedback (monthly written feedback incorporating goal setting, and action planning delivered by a senior clinical
coordinator for selected pneumonia indicators) and this was compared to standard feedback (2-monthly written feedback on multiple quality of pediatric care indicators) both delivered within a clinical network promoting clinical leadership linked to mentorship and peer-to-peer support, and improved use of health information on service delivery. The 12 hospitals were randomized to receive either enhanced feedback (n = 6) or standard feedback (n = 6) delivered over a 9-month period following nationwide pneumonia treatment policy change. The primary outcome is the proportion of all admitted patients with pneumonia (fulfilling criteria for treatment with orally administered amoxicillin) who are correctly classified and treated in the first 24 h. The secondary outcome will be measured over the course of the admission as any change in treatment for pneumonia after the first 24 h.

**Discussion:** This trial protocol employs a pragmatic trial design during a period of nationwide change in treatment guidelines to address two high-priority areas within implementation research: promoting adoption of health policies and optimizing effectiveness of feedback.


**Abstract**

**Background:** The PfEMP1 family of Plasmodium falciparum antigens play a key role in pathogenesis of severe malaria through their insertion into the surface of parasite infected erythrocytes, and adhesion to host cells. Previous studies have suggested that parasites expressing PfEMP1 subclasses group A and DC8, associated with severe malaria, may have a growth advantage in immunologically naïve individuals. However, this idea has not been tested in longitudinal studies.

**Methods:** Here we assessed expression of the var genes encoding PfEMP1, in parasites sampled from volunteers with varying prior exposure to malaria, following experimental infection by sporozoites (PfSPZ). Using qPCR, we tested for associations between the expression of various var subgroups in surviving parasite populations from each
volunteer and 1) the levels of participants’ antibodies to infected erythrocytes before challenge infection and 2) the apparent in vivo parasite multiplication rate.

**Results:** We show that 1) expression of var genes encoding for group A and DC8-like PfEMP1 were associated with low levels of antibodies to infected erythrocytes (αIE) before challenge, and 2) expression of a DC8-like CIDRα1.1 domain was associated with higher apparent parasite multiplication rate in a manner that was independent of levels of prior antibodies to infected erythrocytes.

**Conclusions:** This study provides insight into the role of antibodies to infected erythrocytes surface antigens in the development of naturally acquired immunity and may help explain why specific PfEMP1 variants may be associated with severe malaria.


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**Abstract**

**Background:** Respiratory syncytial virus (RSV) is the major viral cause of infant and childhood lower respiratory tract disease worldwide. Defining the optimal target product profile (TPP) is complicated due to a wide range of possible vaccine properties, modalities and an incomplete understanding of the mechanism of natural immunity. We report consensus population level impact projections based on two mathematical models applied to a low income setting.

**Method:** Two structurally distinct age-specific deterministic compartmental models reflecting uncertainty associated with the natural history of infection and the mechanism by which immunity is acquired and lost were constructed. A wide range of vaccine TPPs were explored including dosing regime and uptake, and effects in the vaccinated individual on infectiousness, susceptibility, duration of protection, disease severity and interaction with maternal antibodies and natural induced immunity. These were combined with a range of vaccine implementation strategies, targeting the highest priority age group and calibrated using hospitalization data from Kilifi County Hospital, Kenya.
**Findings:** Both models were able to reproduce the data. The impact predicted by the two models was qualitatively similar across the range of TPPs, although one model consistently predicted higher impact than the other. For a proposed realistic range of scenarios of TPP combinations, the models predicted up to 70% reduction in hospitalizations in children under five years old. Vaccine designs which reduced the duration and infectiousness of infection were predicted to have higher impacts. The models were sensitive to the coverage and rate of loss of vaccine protection but not to the interaction between vaccine and maternal/naturally acquired immunity.

**Conclusion:** The results suggest that vaccine properties leading to reduced virus circulation by lessening the duration and infectiousness of infection upon challenge are of major importance in population RSV disease control. These features should be a focus for vaccine development.


**Abstract**

**Background:** The creation of a clinical network was proposed as a means to promote implementation of a set of recommended clinical practices targeting inpatient paediatric care in Kenya. The rationale for selecting a network as a strategy has been previously described. Here, we aim to describe network activities actually conducted over its first 2.5 years, deconstruct its implementation into specific components and provide our 'insider' interpretation of how the network is functioning as an intervention.

**Methods:** We articulate key activities that together have constituted network processes over 2.5 years and then utilise a recently published typology of implementation components to give greater granularity to this description from the perspective of those delivering the intervention. Using the Behaviour Change Wheel we then suggest how the network may operate to achieve change and offer examples of change before making an effort to synthesise our understanding in the form of a realist context-mechanism-outcome configuration.

**Results:** We suggest our network is likely to comprise 22 from a total of 73 identifiable intervention components, of which 12 and 10 we consider major and minor components, respectively. At the policy level, we employed clinical guidelines, marketing and communication strategies with intervention characteristics operating through
incentivisation, persuasion, education, enablement, modelling and environmental restructuring. These might influence behaviours by enhancing psychological capability, creating social opportunity and increasing motivation largely through a reflective pathway.

**Conclusions:** We previously proposed a clinical network as a solution to challenges implementing recommended practices in Kenyan hospitals based on our understanding of theory and context. Here, we report how we have enacted what was proposed and use a recent typology to deconstruct the intervention into its elements and articulate how we think the network may produce change. We offer a more generalised statement of our theory of change in a context-mechanism-outcome configuration. We hope this will complement a planned independent evaluation of 'how things work', will help others interpret results of change reported more formally in the future and encourage others to consider further examination of networks as means to scale up improvement practices in health in lower income countries.


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**Abstract**

**Objectives:** Stigma remains pervasive for people living with HIV (PLHIV) in sub-Saharan Africa, undermining care engagement. Using *everyday, biographical* and *epochal* temporalities, we explored the manifestation of stigma at different stages of the HIV care continuum in seven health and demographic surveillance sites in Eastern and Southern Africa.

**Methods:** Between 2015 and 2016, we conducted qualitative in-depth interviews with 264 PLHIV, 54 health providers and 48 family members of people who had died from HIV. Topic guides explored experiences of HIV testing, care and treatment services. Data were analysed thematically, aided by NVivo 10.

**Results:** In *everyday* time across these communities, stigma was evident in the presence of gossiping and the relative absence of supportive interpersonal discourse, which fuelled judicious disclosure. This was especially disruptive at testing, counselling and early antiretroviral therapy adherence stages of care. *Biographical* time framed
everyday stigma events, highlighting the dilemma of disclosure in relation to sexual relationship norms, as well as the interfacing of age and healthcare continuum points. Epochal patriarchal relations gave a structural context to everyday and biographical stigma dynamics. Historical shifts to social acceptance of PLHIV within these communities, while positive, were complicated by stigma in everyday life and in respect of biographical goals like having a family. Moreover, low community-level resistance to HIV-related stigma jeopardised stigma reduction strategies.

**Conclusions:** Despite improvements to HIV care services, stigma remains pervasive across the HIV care continuum in these sites. Context-specific interventions are needed to address stigma and discrimination of PLHIV within the community and in health services, and greater reflection is required to ensure policies aiming to expand HIV treatment do not exacerbate stigma and result in negative HIV outcomes.


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**Abstract**

The prevalence of iron-deficiency anemia (IDA) is high in infants in Sub-Saharan Africa. Exclusive breastfeeding of infants to 6 months of age is recommended by the World Health Organization, but breast milk is low in iron. Some studies suggest exclusive breastfeeding, although beneficial for the infant, may increase risk for IDA in resource-limited settings. The objective of this study was to determine if duration of exclusive breastfeeding is associated with anemia and iron deficiency in rural Kenyan infants. This was a cross-sectional study of 6- to 10-month-old infants (n = 134) in southern coastal Kenya. Anthropometrics, hemoglobin (Hb), plasma ferritin (PF), soluble transferrin receptor (sTfR), and C-reactive protein were measured. Body iron stores were calculated from the sTfR/PF ratio. Socioeconomic factors, duration of exclusive breastfeeding, nature of complementary diet, and demographic characteristics were determined using a questionnaire. Mean ± SD age of the infants was 7.7 ± 0.8 months. Prevalence of anemia, ID, and IDA were 74.6%, 82.1%, and 64.9%, respectively. Months of exclusive breastfeeding correlated positively with Hb (r = 0.187; p < .05) and negatively with sTfR (r = -0.246; p < .05). sTfR concentrations were lower in infants exclusively breastfed at least 6 months compared with those exclusively breastfed for less than 6 months (7.6 (6.3, 9) vs. 8.9 (6.7, 13.4); p < .05). Controlling for gender, birth weight, and inflammation, months spent exclusively breastfeeding was a significant negative
predictor of sTfR and a positive predictor of Hb (p < .05). The IDA prevalence in rural Kenyan infants is high, and greater duration of exclusive breastfeeding predicts better iron status and higher Hb in this age group.


**Abstract**

Controlled human infection model (CHIM) studies have pivotal importance in vaccine development, being useful for proof of concept, pathogenesis, down-selection and immunogenicity studies. To date, however, they have seldom been carried out in low and middle income countries (LMIC), which is where the greatest burden of vaccine preventable illness is found. This workshop discussed the benefits and barriers to CHIM studies in Malawi. Benefits include improved vaccine effectiveness and host country capacity development in clinical, laboratory and governance domains. Barriers include acceptability, safety and regulatory issues. The report suggests a framework by which ethical, laboratory, scientific and governance issues may be addressed by investigators considering or planning CHIM in LMIC.


**Abstract**

**Background:** The emergence of multidrug-resistant strains of Plasmodium falciparum poses a great threat of increased fatalities in cases of cerebral and other forms of severe malaria infections in which parenteral artesunate monotherapy is the current drug of choice. The study aimed to investigate in a mouse model of human cerebral malaria whether a trioxaquine chemically synthesized by covalent linking of a 4,7-dichloroquinoline pharmacophore to artesunate through a recent drug development
approach termed 'covalent bitherapy' could improve the curative outcomes in cerebral malaria infections.

**Methods:** Human cerebral malaria rodent model, the C57BL/6 male mice were infected intraperitoneally (ip) with Plasmodium berghei ANKA and intravenously (iv) treated with the trioxaquine from day 8 post-infection (pi) at 12.5 and 25 mg/kg, respectively, twice a day for 3 days. Treatments with the trioxaquine precursors (artesunate and 4,7-dichloroqu), and quinine were also included as controls. In vivo safety evaluation for the trioxaquine was done according to Organization for Economic Co-operation and Development (OECD) guidelines 423, where female Swiss albino mice were orally administered with either 300 or 2000 mg/kg of the trioxaquine and monitored for signs of severity, and or mortality for 14 days post-treatment.

**Results:** The trioxaquine showed a potent and a rapid antiplasmodial activity with 80% parasite clearance in the first 24 h for the two dosages used. Long-term parasitaemia monitoring showed a total parasite clearance as the treated mice survived beyond 60 days post-treatment, with no recrudescence observed. Artesunate treated mice showed recrudescence 8 days post-treatment, with all mice in this group succumbing to the infection. Also, 4,7-dichloroquinoline and quinine did not show any significant parasitaemia suppression in the first 24 h post-treatment, with the animals succumbing to the infection.

**Conclusion:** Covalent bitherapy proves to be a viable source of urgently needed new anti-malarials for management of cerebral malaria, and this polypharmacology approach could be a potential strategy to protect artesunate from parasite resistance and in potentially improving clinical outcomes in severe forms of malaria infections.


### Abstract

Although access to antiretroviral therapy for HIV infection is increasing in resource-poor countries, viral load testing for monitoring of treatment efficacy remains limited, expensive, and confined to centralized laboratories. The SAMBA HIV-1 Semi-Q Test is a nucleic acid-based amplification assay developed for viral load monitoring performed on either the semi-automated SAMBA I system for laboratory use or the fully automated
SAMBA II system for point-of-care use. We have assessed the performance characteristics of the SAMBA HIV-1 Semi-Q Test on SAMBA I and SAMBA II systems according to the Common Technical Specifications of the European Community's 98/79 In Vitro Diagnostic Medical Devices Directive. The sensitivity, specificity, reproducibility, and viral subtype coverage of the test were similar on the SAMBA I and SAMBA II platforms. The clinical performance on the SAMBA I system was compared with the Roche CAP/CTM assay and evaluated in-house with 130 patient specimens from London as well as in the field with 390 specimens in Kenya and Zimbabwe. The overall concordance between the SAMBA and CAP/CTM assays was 98.1%. The clinical performance of the test on the SAMBA II platform in comparison with the Abbott HIV-1 RealTime Assay was evaluated in-house with 150 specimens from Ukraine, yielding a concordance of 98.0%. The results thus show that the SAMBA HIV-1 Semi-Q Test performs equivalently on SAMBA I and SAMBA II, and they suggest that the test is suitable for implementation at the point-of-care in resource-poor regions where viral load testing is desperately needed but often unavailable.


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**Abstract**

**Background:** Sub-Saharan Africa accounts for approximately 66% of global maternal deaths. Poor person-centered maternity care, which emphasizes the quality of patient experience, contributes both directly and indirectly to these poor outcomes. Yet, few studies in low resource settings have examined what is important to women during childbirth from their perspective. The aim of this study is to examine women's facility-based childbirth experiences in a rural county in Kenya, to identify aspects of care that contribute to a positive or negative birth experience.

**Methods:** Data are from eight focus group discussions conducted in a rural county in western Kenya in October and November 2016, with 58 mothers aged 15 to 49 years who gave birth in the preceding nine weeks. We recorded and transcribed the discussions and used a thematic approach for data analysis.

**Results:** The findings suggest four factors influence women's perceptions of quality of care: responsiveness, supportive care, dignified care, and effective communication. Women had a positive experience when they were received well at the health facility, treated with kindness and respect, and given sufficient information about their care. The
reverse led to a negative experience. These experiences were influenced by the behavior of both clinical and support staff and the facility environment.

**Conclusions:** This study extends the literature on person-centered maternity care in low resource settings. To improve person-centered maternity care, interventions need to address the responsiveness of health facilities, ensure women receive supportive and dignified care, and promote effective patient-provider communication.


**Abstract**

Recent global crises have brought into sharp relief the absolute necessity of resilient health systems that can recognise and react to societal crises. While such crises focus the global mind, the real work lies, however, in being resilient in the face of routine, multiple challenges. But what are these challenges and what is the work of nurturing everyday resilience in health systems? This paper considers these questions, drawing on long-term, primarily qualitative research conducted in three different district health system settings in Kenya and South Africa, and adopting principles from case study research methodology and meta-synthesis in its analytic approach. The paper presents evidence of the instability and daily disruptions managed at the front lines of the district health system. These include patient complaints, unpredictable staff, compliance demands, organisational instability linked to decentralisation processes and frequently changing, and sometimes unclear, policy imperatives. The paper also identifies managerial responses to these challenges and assesses whether or not they indicate everyday resilience, using two conceptual lenses. From this analysis, we suggest that such resilience seems to arise from the leadership offered by multiple managers, through a combination of strategies that become embedded in relationships and managerial routines, drawing on wider organisational capacities and resources. While stable governance structures and adequate resources do influence everyday resilience, they are not enough to sustain it. Instead, it appears important to nurture the power of leaders across every system to reframe challenges, strengthen their routine practices in ways that encourage mindful staff engagement, and develop social networks within and outside organisations. Further research can build on these insights to deepen understanding.


**Abstract**

**Background:** Many pathogens secrete effector molecules to subvert host immune responses, to acquire nutrients, and/or to prepare host cells for invasion. One of the ways that effector molecules are secreted is through extracellular vesicles (EVs) such as exosomes. Recently, the malaria parasite *P. falciparum* has been shown to produce EVs that can mediate transfer of genetic material between parasites and induce sexual commitment. Characterizing the content of these vesicles may improve our understanding of *P. falciparum* pathogenesis and virulence.

**Methods:** Previous studies of *P. falciparum* EVs have been limited to long-term adapted laboratory isolates. In this study, we isolated EVs from a Kenyan *P. falciparum* clinical isolate adapted to *in vitro* culture for a short period and characterized their protein content by mass spectrometry (data are available via ProteomeXchange, with identifier PXD006925).

**Results:** We show that *P. falciparum* extracellular vesicles (*PfEVs*) are enriched in proteins found within the exomembrane compartments of infected erythrocytes such as Maurer's clefts (MCs), as well as the secretory endomembrane compartments in the apical end of the merozoites, suggesting that these proteins play a role in parasite-host interactions. Comparison of this novel clinically relevant dataset with previously published datasets helps to define a core secretome present in *Plasmodium* EVs.

**Conclusions:** *P. falciparum* extracellular vesicles contain virulence-associated parasite proteins. Therefore, analysis of *PfEVs* contents from a range of clinical isolates, and their functional validation may improve our understanding of the virulence mechanisms of the parasite, and potentially identify targets for interventions or diagnostics.

Abstract

**Background:** Respiratory syncytial virus (RSV) is an important cause of lower respiratory tract disease in early life and a target for vaccine prevention. Data on the age-prevalence of RSV specific antibodies will inform on optimizing vaccine delivery.

**Methods:** Archived plasma samples were randomly selected within age strata from 960 children less than 145 months of age admitted to Kilifi County Hospital pediatric wards between 2007 and 2010. Samples were tested for antibodies to RSV using crude virus IgG ELISA. Seroprevalence (and 95% confidence intervals) was estimated as the proportion of children with specific antibodies above a defined cut-off level. Nested catalytic models were used to explore different assumptions on antibody dynamics and estimate the rates of decay of RSV specific maternal antibody and acquisition of infection with age, and the average age of infection.

**Results:** RSV specific antibody prevalence was 100% at age 0-<1 month, declining rapidly over the first 6 months of life, followed by an increase in the second half of the first year of life and beyond. Seroprevalence was lowest throughout the age range 5-11 months; all children were seropositive beyond 3 years of age. The best fit model to the data yielded estimates for the rate of infection of 0.78/person/year (95% CI 0.65-0.97) and 1.69/person/year (95% CI 1.27-2.04) for ages 0-<1 year and 1-<12 years, respectively. The rate of loss of maternal antibodies was estimated as 2.54/year (95% CI 2.30-2.90), i.e. mean duration 4.7 months. The mean age at primary infection was estimated at 15 months (95% CI 13-18).

**Conclusions:** The rate of decay of maternal antibody prevalence and subsequent age-acquisition of infection are rapid, and the average age at primary infection early. The vaccination window is narrow, and suggests optimal targeting of vaccine to infants 5 months and above to achieve high seroconversion.


Abstract
**Background:** Poliomyelitis is an acute viral infection caused by poliovirus and transmitted via the fecal-oral route. The causative agent is one of the three serotypes of poliovirus (serotypes 1, 2, 3) that differ slightly in capsid protein. Prolonged vaccine-related poliovirus shedding in human immunodeficiency virus (HIV) positive individuals has been linked to possible reservoir for reintroduction of polioviruses after eradication. The study therefore aimed at estimating the duration for vaccine-related poliovirus shedding among potentially and HIV-infected persons.

**Methods:** Poliovirus excretion was studied following vaccination of children aged ≤ 59 month per human immunodeficiency virus status after national immunization days. Their medical records were reviewed to identify the child's HIV status, demographic and immunization data. Sequential stool samples were collected at site 2nd, 4th and 8th week after trivalent oral poliovirus vaccine (tOPV) was administered. To isolate suspected polioviruses and non-polio enteroviruses, characterize poliovirus subtypes by intratypic differentiation and Sabin vaccine derived poliovirus, real time polymerase chain reaction was applied. Shedding for ≥ 24 weeks was defined as long-term persistence.

**Results:** The mean age of the study population was 28.6 months, while the median age was 24 months. Of the children recruited, majority were in the 25-48 months (n = 12; 46.2%) age category. All the HIV-positive children (n = 10) had mild symptomatic HIV status and did shed vaccine-related polioviruses between weeks 2 and 4 respectively. No participant shed polioviruses for ≥ 6 weeks.

**Conclusions:** It was evident mildly symptomatic HIV+ children sustain the capacity to clear vaccine-related poliovirus. The oral poliovirus vaccine-2 (Sabin like) that was detected in one HIV-infected child's stool 6 weeks after the national immunization days was predominantly non revertant. There was no evident prolonged poliovirus shedding among the participants enlisted in the present study. High powered studies are desired to further corroborate these findings.


**Abstract**

**Background:** Bloodstream infection is a common cause of morbidity in children aged <5 years in developing countries. In studies reporting bacteremia in Africa, coagulase-
negative Staphylococci (CoNS) are commonly isolated. However, it is currently unclear whether children who are highly susceptible to infection because of severe acute malnutrition (SAM) or HIV should be treated with antimicrobials specifically to cover CoNS. We aimed to determine the clinical significance of CoNS amongst children admitted to a rural hospital in Kenya in relation to nutritional and HIV status.

**Methods:** Systematically collected clinical and microbiological surveillance data from children aged 6-59 months admitted to Kilifi County Hospital (2007-2013) were analysed. Multivariable regression was used to test associations between CoNS isolation from blood cultures and SAM (MUAC <11.5cm or nutritional oedema (kwashiorkor)), and HIV serostatus; and among children with SAM or HIV, associations between CoNS isolation and mortality, duration of hospitalization and clinical features.

**Results:** CoNS were isolated from blood culture in 906/13,315 (6.8%) children, of whom 135/906 (14.9%) had SAM and 54/906 (6.0%) were HIV antibody positive. CoNS isolation was not associated with SAM (MUAC<11.5cm (aOR 1.11, 95% CI 0.88-1.40) or kwashiorkor (aOR 0.84, 95% CI 0.48-1.49)), or a positive HIV antibody test (aOR 1.25, 95% CI 0.92-1.71). Among children with SAM or a positive HIV antibody test, CoNS isolation was not associated with mortality or prolonged hospitalization.

**Conclusion:** In a large, systematic study, there was no evidence that antimicrobial therapy should specifically target CoNS amongst children with SAM or HIV-infection or exposure.


**Abstract**

**Background:** Prior studies have demonstrated hyporesponsiveness to pneumococcal conjugate vaccines (PCVs) when administered in the presence of homologous carriage. This may be substantially more important in Africa where carriage prevalence is high. Deriving a correlate of protection (CoP) for carriage is important in guiding the future use of extended PCVs as population control of pneumococcal disease by vaccination is now focused principally on its indirect effect. We therefore explored the complex
relationship between existing carriage and vaccine responsiveness, and between serum IgG levels and risk of acquisition.

Methods: We undertook secondary analyses of data from two previously published clinical trials of the safety and immunogenicity of PCV in Kenya. We compared responses to vaccination between serotype-specific carriers and non-carriers at vaccination. We assessed the risk of carriage acquisition in relation to PCV-induced serum IgG levels using either a step- or continuous-risk function.

Results: For newborns, the immune response among carriers was 51-82% lower than that among non-carriers, depending on serotype. Among toddlers, for serotypes 6B, 14 and 19F the post-vaccination response among carriers was lower by between 29 and 70%. The estimated CoP against acquisition ranged from 0.26 to 1.93μg/mL across serotypes, however, these thresholds could not be distinguished statistically from a model with constant probability of carriage independent of assay value.

Conclusion: We have confirmed hyporesponsiveness in an equatorial African setting in both infants and toddlers. Population responses to vaccination are likely to improve with time as carriage prevalence of vaccine serotypes is reduced. We have not found clear correlates of protection against carriage acquisition among toddlers in this population. Assessing the potential of new vaccines through the use of CoP against carriage is still difficult as there are no clear-cut serotype specific correlates.


Abstract

Despite the availability of efficacious prevention of mother-to-child transmission (PMTCT) interventions and improved access to preventive services in many developing countries, vertical HIV transmission persists. A matched case-control study of HIV-exposed infants between January and June 2012 was conducted at 20 clinics in Kenya. Cases were HIV-infected infants and controls were exposed, uninfected infants. Conditional logistic regression analysis was conducted to determine characteristics associated with HIV infection. Forty-five cases and 45 controls were compared. Characteristics associated with HIV-infection included poor PMTCT service uptake such as late infant enrollment (odds ratio [OR]: 7.1, 95% confidence interval [CI]: 2.6-16.7)
and poor adherence to infant prophylaxis (OR: 8.3, 95%CI: 3.2-21.4). Maternal characteristics associated with MTCT included lack of awareness of HIV status (OR: 5.6, 95%CI: 2.2-14.5), failure to access antiretroviral prophylaxis (OR: 22.2, 95%CI: 5.8-84.6), and poor adherence (OR: 8.1, 95%CI: 3.7-17.8). Lack of clinic-based HIV education (OR: 7.7, 95%CI: 2.0-25.0) and counseling (OR: 8.3, 95%CI: 2.2-33.3) were reported by mothers of cases. Poor uptake of PMTCT services and a reported absence of HIV education and counseling at the clinic were associated with MTCT. More emphasis on high-quality, comprehensive PMTCT service provision are urgently needed to minimize HIV transmission to children.


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<td><strong>Abstract</strong></td>
<td>Streptococcus agalactiae (GBS) is the leading cause worldwide of neonatal sepsis. We sought to assess to which extent HIV exposure of neonates is associated with GBS neonatal disease. Furthermore, we assessed to which extent HIV infection in women is associated with maternal rectovaginal GBS carriage, the single most important risk factor for GBS neonatal disease. We searched Pubmed, Embase, and Web of Science for studies assessing the association between neonatal GBS disease and HIV-status of the mother and studies that assessed the association between rectovaginal GBS colonization and HIV status in women. HIV-exposed uninfected neonates were more than twice as likely to have neonatal GBS disease compared to unexposed neonates. HIV-exposed neonates were not at increased risk for early-onset neonatal disease, but were 4.43 times more likely to have late-onset neonatal GBS disease. There was no significant association between HIV infection status and rectovaginal GBS carriage. Public health interventions preventing neonatal GBS disease are urgently needed for the increasing group of HIV-exposed neonates. A framework integrating and explaining our findings highlights opportunities for the clinical practice and global health policy to prevent disease. Well-designed studies should clarify the relation between HIV-status and GBS carriage.</td>
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**Abstract**

**Background:** Hospital mortality data can inform planning for health interventions and may help optimize resource allocation if they are reliable and appropriately interpreted. However such data are often not available in low income countries including Kenya.

**Methods:** Data from the Clinical Information Network covering 12 county hospitals' paediatric admissions aged 2-59 months for the periods September 2013 to March 2015 were used to describe mortality across differing contexts and to explore whether simple clinical characteristics used to classify severity of illness in common treatment guidelines are consistently associated with inpatient mortality. Regression models accounting for hospital identity and malaria prevalence (low or high) were used. Multiple imputation for missing data was based on a missing at random assumption with sensitivity analyses based on pattern mixture missing not at random assumptions.

**Results:** The overall cluster adjusted crude mortality rate across hospitals was 6 · 2% with an almost 5 fold variation across sites (95% CI 4 · 9 to 7 · 8; range 2 · 1% - 11 · 0%). Hospital identity was significantly associated with mortality. Clinical features included in guidelines for common diseases to assess severity of illness were consistently associated with mortality in multivariable analyses (AROC =0 · 86).

**Conclusion:** All-cause mortality is highly variable across hospitals and associated with clinical risk factors identified in disease specific guidelines. A panel of these clinical features may provide a basic common data framework as part of improved health information systems to support evaluations of quality and outcomes of care at scale and inform health system strengthening efforts.


**Abstract**

**Background:** Decentralisation is argued to promote community participation, accountability, technical efficiency, and equity in the management of resources, and has been a recurring theme in health system reforms for several decades. In 2010, Kenya
passed a new constitution that introduced 47 semi-autonomous county governments, with substantial transfer of responsibility for health service delivery from the central government to these counties. Focusing on two key elements of the health system, Human Resources for Health (HRH) and Essential Medicines and Medical Supplies (EMMS) management, we analysed the early implementation experiences of this major governance reform at county level.

**Methods:** We employed a qualitative case study design, focusing on Kilifi County, and adapted the decision space framework developed by Bossert et al., to guide our inquiry and analysis. Data were collected through document reviews, key informant interviews, and participant and non-participant observations between December 2012 and December 2014.

**Results:** As with other county level functions, HRH and EMMS management functions were rapidly transferred to counties before appropriate county-level structures and adequate capacity to undertake these functions were in place. For HRH, this led to major disruptions in staff salary payments, political interference with HRH management functions and confusion over HRH management roles. There was also lack of clarity over specific roles and responsibilities at county and national government, and of key players at each level. Subsequently health worker strikes and mass resignations were witnessed. With EMMS, significant delays in procurement led to long stock-outs of essential drugs in health facilities. However, when the county finally managed to procure drugs, health facilities reported a better order fill-rate compared to the period prior to devolution.

**Conclusion:** The devolved government system in Kenya has significantly increased county level decision-space for HRH and EMMS management functions. However, harnessing the full potential benefits of this increased autonomy requires targeted interventions to clarify the roles and responsibilities of different actors at all levels of the new system, and to build capacity of the counties to undertake certain specific HRH and EMMS management tasks. Capacity considerations should always be central when designing health sector decentralisation policies.


| 123. | Ouma PO, Auto NO, Snow RW, Noor AM. Univariate and multivariate spatial models of health facility utilisation for childhood fevers in an area on the coast of Kenya. Int J Health Geogr. 2017 Sep 18;16(1):34 |

**Abstract**
**Background:** Precise quantification of health service utilisation is important for the estimation of disease burden and allocation of health resources. Current approaches to mapping health facility utilisation rely on spatial accessibility alone as the predictor. However, other spatially varying social, demographic and economic factors may affect the use of health services. The exclusion of these factors can lead to the inaccurate estimation of health facility utilisation. Here, we compare the accuracy of a univariate spatial model, developed only from estimated travel time, to a multivariate model that also includes relevant social, demographic and economic factors.

**Methods:** A theoretical surface of travel time to the nearest public health facility was developed. These were assigned to each child reported to have had fever in the Kenya demographic and health survey of 2014 (KDHS 2014). The relationship of child treatment seeking for fever with travel time, household and individual factors from the KDHS2014 were determined using multilevel mixed modelling. Bayesian information criterion (BIC) and likelihood ratio test (LRT) tests were carried out to measure how selected factors improve parsimony and goodness of fit of the time model. Using the mixed model, a univariate spatial model of health facility utilisation was fitted using travel time as the predictor. The mixed model was also used to compute a multivariate spatial model of utilisation, using travel time and modelled surfaces of selected household and individual factors as predictors. The univariate and multivariate spatial models were then compared using the receiver operating area under the curve (AUC) and a percent correct prediction (PCP) test.

**Results:** The best fitting multivariate model had travel time, household wealth index and number of children in household as the predictors. These factors reduced BIC of the time model from 4008 to 2959, a change which was confirmed by the LRT test. Although there was a high correlation of the two modelled probability surfaces (Adj $R^2 = 88\%$), the multivariate model had better AUC compared to the univariate model; 0.83 versus 0.73 and PCP 0.61 versus 0.45 values.

**Conclusion:** Our study shows that a model that uses travel time, as well as household and individual-level socio-demographic factors, results in a more accurate estimation of use of health facilities for the treatment of childhood fever, compared to one that relies on only travel time.


Abstract

**Purpose:** To systematically review the recent evidence on physical therapy (PT) diagnosis, prognosis, and intervention of congenital muscular torticollis to inform the update to the PT management of congenital muscular torticollis evidence-based clinical practice guideline.

**Methods:** From 2012 to 2017, 7 databases were searched for studies that informed PT diagnosis, prognosis, or intervention of infants and children with congenital muscular torticollis. Studies were appraised for risk of bias and quality.

**Results:** Twenty studies were included. No studies informed PT diagnosis. Fourteen studies informed prognosis, including factors associated with presence of a sternocleidomastoid lesion, extent of symptom resolution, treatment duration, adherence to intervention, cervical spine outcomes, and motor outcome. Six studies informed intervention including stretching frequency, microcurrent, kinesiology tape, group therapy, and postoperative PT.

**Conclusions:** New evidence supports that low birth weight, breech presentation, and motor asymmetry are prognostic factors associated with longer treatment duration. Higher-level evidence is emerging for microcurrent intervention.

**Pubmed link**-https://pubmed.ncbi.nlm.nih.gov/29924060/


Abstract

**Background:** Recent influenza surveillance data from Africa suggest an important burden of influenza-associated morbidity and mortality. In tropical countries where influenza virus transmission may not be confined to a single season alternative strategies for vaccine distribution via antenatal care (ANC) or semiannual campaigns should be considered.

**Methods:** Using data on monthly influenza disease burden in women of child-bearing age and infants aged 0-5 months in Kenya from 2010-2014, we estimated the number of
outcomes (illnesses, medical visits, hospitalizations, and deaths) that occurred and that may have been averted through influenza vaccination of pregnant women using: 1) a year-round immunization strategy through ANC, 2) annual vaccination campaigns, and 3) semiannual vaccination campaigns.

**Results:** During 2010-2014, influenza resulted in an estimated 279,047 illnesses, 36,276 medical visits, 1612 hospitalizations and 243 deaths in pregnant women and 157,053 illnesses, 65,177 medical visits, 4197 hospitalizations, and 755 deaths in infants aged 0-5 months in Kenya. Depending on the mode of distribution and the vaccine coverage achieved, 12.8-31.4% of influenza-associated disease in pregnant women and 11.6-22.1% in infants aged 0-5 months might have been prevented through maternal influenza immunization. In this model, point estimates for influenza-associated disease averted through maternal vaccination delivered year-round in ANC or semiannually in campaigns were higher than vaccination delivered in a single annual campaign, but confidence intervals overlapped.

**Conclusions:** Vaccinating pregnant women against influenza can reduce the burden of influenza-associated illness, hospitalization and death in both pregnant women and their young infants. Alternative immunization strategies may avert more influenza-associated disease in countries where influenza virus transmission occurs throughout the year.

**Pubmed link**-https://pubmed.ncbi.nlm.nih.gov/29283997/


**Abstract**

This longitudinal qualitative study sought to understand how and why a livelihood intervention affected the health and health behaviors of HIV-infected Kenyan adults. The intervention included a microfinance loan, agricultural and financial training, and a human-powered water pump. In-depth interviews were conducted at two time points with intervention and control participants and program staff. We double coded interviews (n = 117) and used thematic content analysis of transcripts following an integrative inductive-deductive approach. Intervention participants described improvements in HIV health, including increased CD4 counts and energy, improved viral suppression, and fewer HIV-related symptoms. Better health was linked to improved clinic attendance and ART adherence through several mechanisms: (1) reductions in food insecurity and abject hunger; (2) improved financial stability; (3) improved productivity which enhanced
social support; (4) better control over work situations; and, (5) renewed desire to prioritize their own health. Livelihood interventions may improve health by influencing upstream determinants of health behavior including food security and poverty.


Abstract

Background: Respiratory diseases cause substantial morbidity and mortality worldwide, with sub-Saharan Africa bearing the greatest burden. Identifying etiologies of respiratory disease is important to inform cost effective treatment, prevention and control strategies. Testing for all of the different pathogens that are potentially associated with respiratory illnesses is challenging. We piloted the use of a multi-pathogen respiratory Taqman Array Cards (TAC) to identify pathogens in respiratory samples collected from non-fatal and fatal cases and their matched asymptomatic controls.

Methods: This is a case control study comparing viral and bacterial pathogens detected among non-fatal and fatal cases to those detected among age and time matched asymptomatic controls. We used McNemar's test to compare proportions of pathogens detected among cases (non-fatal and fatal) to their matched asymptomatic controls. We used Mann-Whitney test to compare the distribution of median Cycle threshold (Ct) values among non-fatal and fatal cases to their corresponding asymptomatic controls.

Results: There were 72 fatal and 72 non-fatal cases matched to 72 controls. We identified at least one pathogen in 109/144 (76%) cases and 59/72 (82%) controls. For most pathogens, the median Ct values were lower among cases (fatal and non-fatal) compared to asymptomatic controls.

Conclusions: Similar rates of pathogen detection among cases and controls make interpretation of results challenging. Ct-values might be helpful in interpreting clinical relevance of detected pathogens using multi-pathogen diagnostic tools.


Abstract

Rift Valley fever (RVF) is a mosquito-borne viral zoonosis that is found in most regions of sub-Saharan Africa, and it affects humans, livestock, and some wild ungulates. Outbreaks are precipitated by an abundance of mosquito vectors associated with heavy persistent rainfall with flooding. We determined the impact of flood-irrigation farming and the effect of environmental parameters on the ecology and densities of primary and secondary vectors of the RVF virus (RVFV) in an RVF-epidemic hotspot in the Tana River Basin, Kenya. Mosquito sampling was conducted in farms and villages (settlements) in an irrigated and a neighboring nonirrigated site (Murukani). Overall, a significantly higher number of mosquitoes were collected in farms in the irrigation scheme compared with villages in the same area (P < 0.001), or farms (P < 0.001), and villages (P = 0.03) in Murukani. In particular, key primary vectors of RVFV, Aedes mcintoshi Marks and Aedes ochraceous Theobald, were more prevalent in the farms compared with villages in the irrigation scheme (P = 0.001) both during the dry and the wet seasons. Similarly, there was a greater abundance of secondary vectors, particularly Culex univittatus Theobald and Culex pipiens (L.) in the irrigation scheme than in the Murukani area. Rainfall and humidity were positively correlated with mosquito densities, particularly the primary vectors. Adult floodwater mosquitoes and Mansonia spp. were collected indoors; immatures of Ae. mcintoshi and secondary vectors were collected in the irrigation drainage canals, whereas those of Ae. ochraceous and Aedes sudanensis Theobald were missing from these water bodies. In conclusion, irrigation in RVF endemic areas provides conducive resting and breeding conditions for vectors of RVFV and other endemic arboviruses.


Abstract

Objectives: The nature of patient-provider interactions and communication is widely documented to significantly impact on patient experiences, treatment adherence and
health outcomes. Yet little is known about the broader contextual factors and dynamics that shape patient-provider interactions in high HIV prevalence and limited-resource settings. Drawing on qualitative research from five sub-Saharan African countries, we seek to unpack local dynamics that serve to hinder or facilitate productive patient-provider interactions.

**Methods:** This qualitative study, conducted in Kisumu (Kenya), Kisesa (Tanzania), Manicaland (Zimbabwe), Karonga (Malawi) and uMkhanyakude (South Africa), draws upon 278 in-depth interviews with purposively sampled people living with HIV with different diagnosis and treatment histories, 29 family members of people who died due to HIV and 38 HIV healthcare workers. Data were collected using topic guides that explored patient testing and antiretroviral therapy treatment journeys. Thematic analysis was conducted, aided by NVivo V.8.0 software.

**Results:** Our analysis revealed an array of inter-related contextual factors and power dynamics shaping patient-provider interactions. These included (1) participants’ perceptions of roles and identities of ‘self’ and ‘other’; (2) conformity or resistance to the ‘rules of HIV service engagement’ and a ‘patient-persona’; (3) the influence of significant others’ views on service provision; and (4) resources in health services. We observed that these four factors/dynamics were located in the wider context of conceptualisations of power, autonomy and structure.

**Conclusion:** Patient-provider interaction is complex, multidimensional and deeply embedded in wider social dynamics. Multiple contextual domains shape patient-provider interactions in the context of HIV in sub-Saharan Africa. Interventions to improve patient experiences and treatment adherence through enhanced interactions need to go beyond the existing focus on patient-provider communication strategies.

**Pubmed link**-https://pubmed.ncbi.nlm.nih.gov/28736392/


**Abstract**

This cross-sectional descriptive study aimed to investigate the incidence of rotavirus and enteric bacterial infections among children up to 5 years old with diarrhea living in suburban and rural areas of Kenya. Between August 2011 and December 2013, a total of
1,060 diarrheal fecal specimens were obtained from 722 children at Kiambu County Hospital (KCH), located in a suburban area, and from 338 children from Mbita District Hospital (MDH), located in a rural part of western Kenya. Of the 1,060 isolates, group A rotavirus was detected in 29.6% (214/722) and 11.2% (38/338) fecal specimens from KCH and MDH, respectively. Diarrheagenic Escherichia coli (DEC) was found to be the most frequently isolated bacterial pathogens in both study areas (32.8% at KCH and 44.1% at MDH). Two different mixed infection patterns (virus/bacteria and bacteria/bacteria) were observed among patients. A significantly higher infection rate of rotavirus (17.6%, p = 0.001) and DEC (10.5%, p = 0.007) were observed during the dry season. Our study found that in both suburban and rural settings in Kenya, rotavirus and DEC are the principal cause of pediatric diarrhea and exhibit higher incidence during the dry season.


Abstract

This paper describes and evaluates the budgeting and planning processes in public hospitals in Kenya. We used a qualitative case study approach to examine these processes in two hospitals in Kenya. We collected data by in-depth interviews of national level policy makers, hospital managers, and frontline practitioners in the case study hospitals (n = 72), a review of documents, and non-participant observations within the hospitals over a 7 month period. We applied an evaluative framework that considers both consequentialist and proceduralist conditions as important to the quality of priority-setting processes. The budgeting and planning process in the case study hospitals was characterized by lack of alignment, inadequate role clarity and the use of informal priority-setting criteria. With regard to consequentialist conditions, the hospitals incorporated economic criteria by considering the affordability of alternatives, but rarely considered the equity of allocative decisions. In the first hospital, stakeholders were aware of - and somewhat satisfied with - the budgeting and planning process, while in the second hospital they were not. Decision making in both hospitals did not result in reallocation of resources. With regard to proceduralist conditions, the budgeting and planning process in the first hospital was more inclusive and transparent, with the stakeholders more empowered compared to the second hospital. In both hospitals, decisions were not based on evidence, implementation of decisions was poor and the community was not included. There were no mechanisms for appeals or to ensure that
the proceduralist conditions were met in both hospitals. Public hospitals in Kenya could improve their budgeting and planning processes by harmonizing these processes, improving role clarity, using explicit priority-setting criteria, and by incorporating both consequentialist (efficiency, equity, stakeholder satisfaction and understanding, shifted priorities, implementation of decisions), and proceduralist (stakeholder engagement and empowerment, transparency, use of evidence, revisions, enforcement, and incorporating community values) conditions.


Abstract

Background: There are a paucity of data on epistaxis as it pertains to sickle cell anaemia. Some case studies suggest epistaxis to be a significant complication in patients with sickle cell anaemia in sub-Saharan Africa; however, no robust studies have sought to establish the epidemiology or pathophysiology of this phenomenon.

Methods: We conducted a case-control study with the aim of investigating the importance of epistaxis among children presenting with sickle cell anaemia at the Mbale Regional Referral Hospital in eastern Uganda. Cases were children aged 2-15 years with an existing diagnosis of laboratory confirmed sickle cell anaemia, while controls were children without sickle cell anaemia who were frequency matched to cases on the basis of age group and gender. The frequency and severity of epistaxis was assessed using a structured questionnaire developed specifically for this study. Odds ratios controlled for age group and gender were calculated using unconditional logistic regression.

Results: A total of 150 children were included, 73 children with sickle cell anaemia and 77 children without sickle cell anaemia. The overall prevalence of epistaxis among children with sickle cell anaemia and children without sickle cell anaemia was 32.9 and 23.4% respectively. The case-control odds ratios for epistaxis, recurrent epistaxis and severe epistaxis were, 1.6 (95%CI 0.8-3.4; \( p = 0.2 \)), 7.4 (1.6-34.5; 0.01), and 8.3 (1.0-69.8; 0.05) respectively.

Conclusions: Our results suggest that in eastern Uganda, children with sickle cell anaemia experience epistaxis more frequently and with greater severity than children
without sickle cell anaemia. Further studies are indicated to confirm this conclusion and investigate aetiology.


Abstract

Background: A common challenge for health sector planning and budgeting has been the misalignment between policies, technical planning and budgetary allocation; and inadequate community involvement in priority setting. Health system decentralisation has often been promoted to address health sector planning and budgeting challenges through promoting community participation, accountability, and technical efficiency in resource management. In 2010, Kenya passed a new constitution that introduced 47 semi-autonomous devolved county governments, and a substantial transfer of responsibility for healthcare from the central government to these counties.

Methods: This study analysed the effects of this major political decentralization on health sector planning, budgeting and overall financial management at county level. We used a qualitative, case study design focusing on Kilifi County, and were guided by a conceptual framework which drew on decentralisation and policy analysis theories. Qualitative data were collected through document reviews, key informant interviews, and participant and non-participant observations conducted over an eighteen months' period.

Results: We found that the implementation of devolution created an opportunity for local level prioritisation and community involvement in health sector planning and budgeting hence increasing opportunities for equity in local level resource allocation. However, this opportunity was not harnessed due to accelerated transfer of functions to counties before county level capacity had been established to undertake the decentralised functions. We also observed some indication of re-centralisation of financial management from health facility to county level.

Conclusion: We conclude by arguing that, to enhance the benefits of decentralised health systems, resource allocation, priority setting and financial management functions between central and decentralised units are guided by considerations around decision space, organisational structure and capacity, and accountability. In acknowledging the political nature of decentralisation polices, we recommend that health sector policy
actors develop a broad understanding of the countries' political context when designing and implementing technical strategies for health sector decentralisation.


**Abstract**

**Background:** In 2011, Kenya introduced the 10-valent pneumococcal conjugate vaccine together with a catch-up campaign for children aged <5 years in Kilifi County. In a post-vaccination surveillance study based in Kilifi, there was a substantial decline in invasive pneumococcal disease (IPD). However, given the continued circulation of the vaccine serotypes it is possible that vaccine-serotype disease may re-emerge once the effects of the catch-up campaign wear off.

**Methods:** We developed a compartmental, age-structured dynamic model of pneumococcal carriage and invasive disease for three serotype groups: the 10-valent vaccine serotypes and two groups of non-vaccine serotypes based on their susceptibility to mutual competition. The model was calibrated to age- and serotype-specific data on carriage and IPD in the pre-vaccination era and used to predict carriage prevalence and IPD up to ten years post-vaccination in Kilifi. The model was validated against the observed carriage prevalence after vaccine introduction.

**Results:** The model predicts a sustained reduction in vaccine-type pneumococcal carriage prevalence from 33% to 8% in infants and from 30% to 8% in 1-5 year olds over the 10-year period following vaccine introduction. The incidence of IPD is predicted to decline across all age groups resulting in an overall reduction of 56% in the population, corresponding to 10.4 cases per 100,000 per year. The vaccine-type IPD incidence is estimated to decline by 83% while non-vaccine-type IPD incidence is predicted to increase by 52%. The model's predictions of carriage prevalence agrees well with the observed data in the first five years post-vaccination.

**Conclusion:** We predict a sustained and substantial decline in IPD through PCV vaccination and that the current regimen is insufficient to fully eliminate vaccine-
serotype circulation in the model. We show that the observed impact is likely to be sustained despite waning effects of the catch-up campaign.


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<td><strong>Abstract</strong></td>
<td>There is a dearth of literature on priority setting and resource allocation (PSRA) practices in hospitals, particularly in low and middle income countries (LMICs). Using a case study approach, we examined PSRA practices in 2 public hospitals in coastal Kenya. We collected data through a combination of in-depth interviews of national level policy makers, hospital managers, and frontline practitioners in the case study hospitals (n = 72), review of documents such as hospital plans and budgets, minutes of meetings and accounting records, and non-participant observations of PSRA practices in case study hospitals over a period of 7 months. In this paper, we apply complex adaptive system (CAS) theory to examine the factors that influence PSRA practices. We found that PSRA practices in the case hospitals were influenced by, 1) inadequate financing level and poorly designed financing arrangements, 2) limited hospital autonomy and decision space, and 3) inadequate management and leadership capacity in the hospital. The case study hospitals exhibited properties of complex adaptive systems (CASs) that exist in a dynamic state with multiple interacting agents. Weaknesses in system 'hardware' (resource scarcity) and 'software' (including PSRA guidelines that reduced hospitals decision space, and poor leadership skills) led to the emergence of undesired properties. The capacity of hospitals to set priorities should be improved across these interacting aspects of the hospital organizational system. Interventions should however recognize that hospitals are CAS. Rather than rectifying isolated aspects of the system, they should endeavor to create conditions for productive emergence.</td>
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Abstract

**Background:** Conventional targeted leishmanicidal chemotherapy has persistently remained prohibitive for most economically deprived communities due to costs, associated time to accessing health services and duration for successful treatment programme. Alternatives are bound to be incorporated in rational management of leishmaniasis by choice or default due to accessibility and cultural beliefs. Therefore, there is need to rigorously investigate and appraise the activity of medicinal compounds that may have anti-leishmanicidal activity especially in the context of products that are already being utilized by the populations for other ailments but have limited information on their therapeutic value and possible cytoxicity. Hence, the study examined both in vivo and in vitro response of L. major infection to Tephrosia vogelii extracts in BALB/c mice as the mouse model.

**Methods:** A comparative study design was applied for the in vivo and in vitro assays of the extract with Pentostam (GlaxoSmithKline, UK) and Amphotericin B [Fungizone™, X-Gen Pharmaceuticals (US)] as standard drugs.

**Results:** In BALB/c mice where the chemotherapeutic extract was administered intraperitoneally, there was significantly (p < 0.05) larger reduction in lesion size and optimal control of parasite burden than those treated orally. However, standard drugs showed better activity. Tephrosia vogelii had 50% inhibitory concentration (IC₅₀) and IC₉₀ of 12 and 68.5 μg/ml respectively, while the standard drugs had IC₅₀ and IC₉₀ of 5.5 and 18 μg/ml for Pentostam and 7.8 and 25.5 μg/ml for Amphotericin B in that order. In the amastigote assay, the infection rates decreased with increase in chemotherapeutic concentration. The multiplication indices for L. major amastigotes in macrophages treated with 200 μg/ml of the standard drugs and extract were significantly different (p < 0.05). 200 μg/ml of T. vogelii extract showed a multiplication index of 20.57, 5.65% for Amphotericin B and 9.56% for Pentostam. There was also significant difference (p < 0.05) in levels of Nitric oxide produced in the macrophages.

**Conclusions:** The findings demonstrated that T. vogelii extract has anti-leishmanial activity and further assays should be done to ascertain the active compounds responsible for anti-leishmanial activity.


Douala, Cameroon. Nutrients. 2017 Jul 3;9(7):693

Abstract

Information on the etiology of anemia is necessary to design effective anemia control programs. Our objective was to measure the prevalence of inherited hemoglobin disorders (IHD) in a representative sample of children in urban Cameroon, and examine the relationships between IHD and anemia. In a cluster survey of children 12-59 months of age (n = 291) in Yaoundé and Douala, we assessed hemoglobin (Hb), malaria infection, and plasma indicators of inflammation and micronutrient status. Hb S was detected by HPLC, and α⁺thalassemia (3.7 kb deletions) by PCR. Anemia (Hb < 110 g/L), inflammation, and malaria were present in 45%, 46%, and 8% of children. A total of 13.7% of children had HbAS, 1.6% had HbSS, and 30.6% and 3.1% had heterozygous and homozygous α⁺thalassemia. The prevalence of anemia was greater among HbAS compared to HbAA children (60.3 vs. 42.0%, p = 0.038), although mean Hb concentrations did not differ, p = 0.38). Hb and anemia prevalence did not differ among children with or without single gene deletion α⁺thalassemia. In multi-variable models, anemia was independently predicted by HbAS, HbSS, malaria, iron deficiency (ID; inflammation-adjusted ferritin <12 µg/L), higher C-reactive protein, lower plasma folate, and younger age. Elevated soluble transferrin receptor concentration (>8.3 mg/L) was associated with younger age, malaria, greater mean reticulocyte counts, inflammation, HbSS genotype, and ID. IHD are prevalent but contribute modestly to anemia among children in urban Cameroon.


Abstract

Alphaviruses, such as chikungunya virus, and flaviviruses, such as dengue virus, are (re)-emerging arboviruses that are endemic in tropical environments. In Africa, arbovirus infections are often undiagnosed and unreported, with febrile illnesses often assumed to be malaria. This cross-sectional study aimed to characterize the seroprevalence of alphaviruses and flaviviruses among children (ages 5-14, n = 250) and adults (ages 15 ≥ 75, n = 250) in western Kenya. Risk factors for seropositivity were explored using Lasso regression. Overall, 67% of participants showed alphavirus seropositivity (CI95 63%-70%), and 1.6% of participants showed flavivirus seropositivity (CI95 0.7%-3%).
Children aged 10-14 were more likely to be seropositive to an alphavirus than adults (p < 0.001), suggesting a recent transmission period. Alphavirus and flavivirus seropositivity was detected in the youngest participants (age 5-9), providing evidence of inter-epidemic transmission. Demographic variables that were significantly different amongst those with previous infection versus those without infection included age, education level, and occupation. Behavioral and environmental variables significantly different amongst those in with previous infection included taking animals for grazing, fishing, and recent village flooding. Experience of recent fever was also found to be a significant indicator of infection (p = 0.027). These results confirm alphavirus and flavivirus exposure in western Kenya, while illustrating significantly higher alphavirus transmission compared to previous studies.

Pubmed link: https://pubmed.ncbi.nlm.nih.gov/29040262/


Abstract

Background: Maternal mortality is noticeably high in sub-Saharan African countries including Ethiopia. Continuous nationwide systematic evaluation and assessment of the problem helps to design appropriate policy and strategy in Ethiopia. This study aimed to investigate the trends and causes of maternal mortality in Ethiopia between 1990 and 2013.

Methods: We used the Global Burden of Diseases and Risk factors (GBD) Study 2013 data that was collected from multiple sources at national and subnational levels. Spatio-temporal Gaussian Process Regression (ST-GPR) was applied to generate best estimates of maternal mortality with 95% Uncertainty Intervals (UI). Causes of death were measured using Cause of Death Ensemble modelling (CODEm). The modified UNAIDS EPP/SPECTRUM suite model was used to estimate HIV related maternal deaths.

Results: In Ethiopia, a total of 16,740 (95% UI: 14,197, 19,271) maternal deaths occurred in 1990 whereas there were 15,234 (95% UI: 11,378, 19,871) maternal deaths occurred in 2013. This finding shows that Maternal Mortality Ratio (MMR) in Ethiopia was still high in the study period. There was a minimal but insignificant change of MMR over the last 23 years. The results revealed Ethiopia is below the target of Millennium Development Goals (MDGs) related to MMR. The top five causes of maternal mortality in 2013 were other direct maternal causes such as complications of anaesthesia,
embolism (air, amniotic fluid, and blood clot), and the condition of peripartum cardiomyopathy (25.7%), complications of abortions (19.6%), maternal haemorrhage (12.2%), hypertensive disorders (10.3%), and maternal sepsis and other maternal infections such as influenza, malaria, tuberculosis, and hepatitis (9.6%). Most of the maternal mortality happened during the postpartum period and majority of the deaths occurred at the age group of 20-29 years. Overall trend showed that there was a decline from 708 per 100,000 live births in 1990 to 497 per 100,000 in 2013. The annual rate of change over these years was -1.6 (95% UI: -2.8 to -0.3).

Conclusion: The findings of the study highlight the need for comprehensive efforts using multisectoral collaborations from stakeholders for reducing maternal mortality in Ethiopia. It is worthwhile for policies to focus on postpartum period.


Abstract

Background: The need to provide quality and equitable health services and protect populations from impoverishing health care costs has pushed universal health coverage (UHC) to the top of global health policy agenda. In many developing countries where the majority of the population works in the informal sector, there are critical debates over the best financing mechanisms to progress towards UHC. In Kenya, government health policy has prioritized contributory financing strategy (social health insurance) as the main financing mechanism for UHC. However, there are currently no studies that have assessed the cost of either social health insurance (SHI) as the contributory approach or an alternative financing mechanism involving non-contributory (general tax funding) approaches to UHC in Kenya. The aim of this study was to critically assess the financial requirements of both contributory and non-contributory mechanisms to financing UHC in Kenya in the context of large informal sector populations.

Methods: SimIns Basic® model, Version 2.1, 2008 (WHO/GTZ), was used to assess the feasibility of UHC in Kenya and provide estimates of financial resource needs for UHC over a 17-year period (2013-2030). Data sources included review of national and international literature on inflation, demography, macro-economy, health insurance, health services unit costs and utilization rates. The data were triangulated across geographic regions for accuracy and integrity of the simulation. SimIns models for 10 years only so data from the final year of the model was used to project for another 7
years. The 17-year period was necessary because the Government of Kenya aims to achieve UHC by 2030.

**Results and conclusions:** The results show that SHI is financially sustainable (Sustainability in this study is used to mean that expenditure does not outstrip revenue.) (revenues and expenditure match) within the first five years of implementation, but it becomes less sustainable with time. Modelling for a non-contributory scenario, on the other hand, showed greater sustainability both in the short- and long-term. The financial resource requirements for universal access to health care through general government revenue are compared with a contributory health insurance scheme approach. Although both funding options would require considerable government subsidies, given the magnitude of the informal sector in Kenya and their limited financial capacity, a tax-funded system would be less costly and more sustainable in the long-term than an insurance scheme approach. However, more innovative financing for health care as well as giving the health sector higher priority in government expenditure will be required to make the non-contributory financing mechanism more sustainable.


**Abstract**

Immuoepidemiological studies typically reveal slow, age-dependent acquisition of immune responses against *Plasmodium falciparum* sporozoites. Naturally acquired immunity against preerythrocytic stages is considered inadequate to confer protection against clinical malaria. To explore previously unrecognized antisporozoite responses, we measured serum levels of naturally acquired antibodies to whole *Plasmodium falciparum* sporozoites (*Pfspz*) and the immunodominant (NANP)₅ repeats of the major sporozoite surface protein, circumsporozoite protein, in a well-characterized Kenyan cohort. Sera were sampled at the start of the malaria transmission season, and all subjects were prospectively monitored for uncomplicated clinical malaria in the ensuing 6 months. We used Kaplan-Meier analysis and multivariable regression to investigate the association of antisporozoite immunity with incidence of clinical malaria. Although naturally acquired humoral responses against *Pfspz* and (NANP)₅ were strongly correlated (*p* < 0.0001), 37% of *Pfspz* responders did not recognize (NANP)₅. The prevalence and magnitude of antisporozoite responses increased with age, although some high *Pfspz* responders were identified among children. Survival analysis revealed a
reduced risk of and increased time to first or only episode of clinical malaria among *Pfsspz* or (NANP)*5* responders carrying microscopically detectable *Plasmodium falciparum* (*Pf*) parasitemia at the start of the transmission season (*p* < 0.03). Our Cox regression interaction models indicated a potentially protective interaction between high anti-*Pfsspz* (*p* = 0.002) or anti-(NANP)*5* (*p* = 0.001) antibody levels and microscopically detectable *Pf* parasitemia on the risk of subsequent clinical malaria. Our findings indicate that robust antisporozoite immune responses can be naturally acquired already at an early age. A potentially protective role of high levels of anti-*Pfsspz* antibodies against clinical episodes of uncomplicated malaria was detected, suggesting that antibody-mediated preerythrocytic immunity might indeed contribute to protection in nature.


Abstract

**Background:** Monitoring and evaluation of entomological, parasitological and clinical data is an important component of malaria control as it is a measure of the success of the interventions. In many studies, clinical data has been used to monitor trends in malaria morbidity and mortality. This study was conducted to demonstrate age dependent prevalence of malaria in the pre- and post-interventions period.

**Methods:** A series of cross-sectional malaria parasitological surveys were conducted in Iguhu, western Kenya. Participants were randomly selected school-aged children between 6 and 13 years. The study was conducted between June 2002-December 2003 and January 2012-February 2015. Sexual and asexual parasite prevalence and densities were determined using microscopy. Age-dependence in parasite infections was compared between 2002-2003 and 2012-2015.

**Results:** *Plasmodium falciparum* had the highest prevalence of 43.5 and 11.5% in the pre- and post-intervention periods. *Plasmodium malariae* had a prevalence of 2.3 and 0.2%, while *Plasmodium ovale* had a prevalence of 0.3 and 0.1% during the pre- and post-intervention period, respectively. There was a 73.7% reduction in prevalence of *P. falciparum* in the post-intervention compared to the pre-intervention period. *Plasmodium falciparum* parasite density increased by 71.2% between pre- and post-intervention period from (geometric mean of) 554.4-949.2 parasites/µl. Geometric mean gametocytaemia in Iguhu was higher in the post-intervention period (106.4 parasites/µl),
when compared to the pre-intervention period (54.1 parasites/µl). Prevalence and density of P. falciparum showed a lower age-dependency during post-intervention period when compared to pre-intervention period.

**Conclusion:** The study provides evidence for reduction of malaria prevalence following the introduction of LLINs and ACT in western Kenya. Fewer people become infected but the few infected may be more infectious as suggested by higher gametocyte densities. The high parasite densities, which were not dependent on age, observed in the post intervention period imply that a more comprehensive integrated malaria management may be required to sustain the current interventions and hence reduce malaria transmission.


**Abstract**

**Background:** Women attending antenatal care (ANC) in resource-limited countries are frequently screened for syphilis and HIV, but rarely for other sexually transmitted infections (STIs). We assessed the prevalence of curable STIs, defined as infection with either Chlamydia trachomatis or Neisseria gonorrhoeae or Trichomonas vaginalis, from July to September 2015.

**Methods:** In a cross-sectional study, women attending ANC at the Kilifi County Hospital, Kenya, had a urine sample tested for C. trachomatis/N. gonorrhoeae by GeneXpert® and a vaginal swab for T. vaginalis by culture. Bacterial vaginosis (BV) was defined as a Nugent score of 7-10 of the Gram stain of a vaginal smear in combination with self-reported vaginal discharge. Genital ulcers were observed during collection of vaginal swabs. All women responded to questions on socio-demographics and sexual health and clinical symptoms of STIs. Predictors for curable STIs were assessed in multivariable logistic regression.

**Results:** A total of 42/202 (20.8%, 95% confidence interval (CI):15.4-27.0) women had a curable STI. The prevalence was 14.9% for C. trachomatis (95% CI:10.2-20.5), 1.0% for N. gonorrhoeae (95% CI: 0.1-3.5), 7.4% for T. vaginalis (95% CI:4.2-12.0), 19.3% for BV (95% CI: 14.1-25.4) and 2.5% for genital ulcers (95% CI: 0.8-5.7). Predictors for infection with curable STIs included women with a genital ulcer (adjusted odds ratio
(AOR) = 35.0, 95% CI: 2.7-461.6) compared to women without a genital ulcer, women who used water for cleaning after visiting the toilet compared to those who used toilet paper or other solid means (AOR = 4.1, 95% CI:1.5-11.3), women who reported having sexual debut ≤ 17 years compared to women having sexual debut ≥ 18 years (AOR = 2.7, 95% CI:1.1-6.6), and BV-positive women (AOR = 2.7, 95% CI:1.1-6.6) compared to BV-negative women.

**Conclusion:** One in five women attending ANC had a curable STI. These infections were associated with genital ulcers, hygiene practices, early sexual debut and bacterial vaginosis.


**Abstract**

**Background:** Use of bednets reduces malaria morbidity and mortality. In Kilifi, Kenya, there was a mass distribution of free nets to children < 5 years in 2006. In 2009, a new policy was implemented to offer bednets to pregnant women and children < 5 years free of charge. Nets were again distributed to children and adults through national mass campaigns in 2012 and 2015. We aimed to evaluate trends in bednet ownership and usage, and the effect of bednets on the incidence of malaria hospitalization in children < 5 years within the Kilifi Health and Demographic Surveillance System (KHDSS).

**Methods:** Bednet ownership and usage were assessed during eight routine enumeration rounds of the KHDSS between 2008 and 2015. Malaria admissions (i.e. admissions to hospital with P. falciparum > 2500 parasitemia per μl) among children < 5 years were captured using a system of continuous vital registration that links admissions at Kilifi County Hospital to the KHDSS population register. Survival analysis was used to assess relative risk of hospitalization with malaria among children that reported using a bednet compared to those who did not.

**Results:** We observed 63% and 62% mean bednet ownership and usage, respectively, over the eight-survey period. Among children < 5 years, reported bednet ownership in October-December 2008 was 69% and in March-August 2009 was 73% (p < 0.001). An increase was also observed following the mass distribution campaigns in 2012 (62% in May-July 2012 vs 90% in May-October 2013, p < 0.001) and 2015 (68% in June-
September 2015 vs 93% in October-November 2015, \( p < 0.001 \). Among children <5 years who reported using a net the night prior to the survey, the incidence of malaria hospitalization per 1000 child-years was 2.91 compared to 4.37 among those who did not (HR = 0.67, 95% CI: 0.52, 0.85 \( [p = 0.001] \)).

**Conclusion:** On longitudinal surveillance, increasing bednet ownership and usage corresponded to mass distribution campaigns; however, this method of delivering bednets did not result in sustained improvements in coverage. Among children < 5 years old bednet use was associated with a 33% decreased incidence of malaria hospitalization.


**Abstract**

Development of antimicrobial resistance (AMR) threatens our ability to treat common and life threatening infections. Identifying the emergence of AMR requires strengthening of surveillance for AMR, particularly in low and middle-income countries (LMICs) where the burden of infection is highest and health systems are least able to respond. This work aimed, through a combination of desk-based investigation, discussion with colleagues worldwide, and visits to three contrasting countries (Ethiopia, Malawi and Vietnam), to map and compare existing models and surveillance systems for AMR, to examine what worked and what did not work. Current capacity for AMR surveillance varies in LMICs, but and systems in development are focussed on laboratory surveillance. This approach limits understanding of AMR and the extent to which laboratory results can inform local, national and international public health policy. An integrated model, combining clinical, laboratory and demographic surveillance in sentinel sites is more informative and costs for clinical and demographic surveillance are proportionally much lower. The speed and extent to which AMR surveillance can be strengthened depends on the functioning of the health system, and the resources available. Where there is existing laboratory capacity, it may be possible to develop 5-20 sentinel sites with a long term view of establishing comprehensive surveillance; but where health systems are weaker and laboratory infrastructure less developed, available expertise and resources may limit this to 1-2 sentinel sites. Prioritising core functions, such as automated blood cultures, reduces investment at each site. Expertise to support AMR surveillance in LMICs may come from a variety of international, or national,
institutions. It is important that these organisations collaborate to support the health systems on which AMR surveillance is built, as well as improving technical capacity specifically relating to AMR surveillance. Strong collaborations, and leadership, drive successful AMR surveillance systems across countries and contexts.


Abstract

PfEMP1 are variant parasite antigens that are inserted on the surface of <i>Plasmodium falciparum</i> infected erythrocytes (IE). Through interactions with various host molecules, PfEMP1 mediate IE sequestration in tissues and play a key role in the pathology of severe malaria. PfEMP1 is encoded by a diverse multi-gene family called var. Previous studies have shown that that expression of specific subsets of var genes are associated with low levels of host immunity and severe malaria. However, in most clinical studies to date, full-length var gene sequences were unavailable and various approaches have been used to make comparisons between var gene expression profiles in different parasite isolates using limited information. Several studies have relied on the classification of a 300 - 500 base-pair "DBLα tag" region in the DBLα domain located at the 5' end of most var genes. We assessed the relationship between various DBLα tag classification methods, and sequence features that are only fully assessable through full-length var gene sequences. We compared these different sequence features in full-length var gene from six fully sequenced laboratory isolates. These comparisons show that despite a long history of recombination, DBLα sequence tag classification can provide functional information on important features of full-length var genes. Notably, a specific subset of DBLα tags previously defined as "group A-like" is associated with CIDRα1 domains proposed to bind to endothelial protein C receptor. This analysis helps to bring together different sources of data that have been used to assess var gene expression in clinical parasite isolates.


Abstract

**Background:** The neglected zoonotic diseases (NZD) are an understudied group that are a major cause of illness throughout the developing world. In general, little is known about the prevalence and burden of NZDs in affected communities, particularly in relation to other infectious diseases with which they are often co-endemic. We describe the design and descriptive epidemiological outputs from an integrated study of human and animal zoonotic and non-zoonotic disease in a rural farming community in western Kenya.

**Methods:** This cross-sectional survey involved 2113 people, their cattle (n = 983) and pigs (n = 91). People and animals were tested for infection or exposure to a wide range of zoonotic and non-zoonotic pathogens. Prevalence estimates, with adjustment for the complex study design, were derived. Evidence for spatial clustering in exposure or infection was identified using the spatial scan statistic.

**Results:** There was a high prevalence of human parasitism in the community, particularly with hookworm (Ancylostoma duodenale or Necator americanus) (36.3% (95% CI 32.8-39.9)), Entamoeba histolytica/dispar (30.1% (95% CI 27.5-32.8)), and Plasmodium falciparum (29.4% (95% CI 26.8-32.0)). Human infection with Taenia spp. was also prevalent (19.7% (95% CI 16.7-22.7)), while exposure to other zoonotic pathogens was comparatively rarer (Brucella spp., 0.6% (95% CI 0.2-0.9); Coxiella burnetii, 2.2% (95% CI 1.5-2.9); Rift Valley fever, 0.5% (95% CI 0.2-0.8)). A low prevalence of exposure to Brucella spp. was observed in cattle (0.26% (95% CI 0-0.56). This was higher for Rift Valley fever virus (1.4% (95% CI 0.5-2.22)) and C. burnetii (10.0% (95% CI 7.7-12.2)). The prevalence of Taenia spp. cysticercosis was 53.5% (95% CI 48.7-58.3) in cattle and 17.2% (95% CI 9.1-25.3) in pigs. Mycobacterium bovis infection was found in 2.2% of cattle (95% CI 1.3-3.2), while the prevalence of infection with Mycobacterium spp. was 8.2% (95% CI 6.8-9.6) in people.

**Conclusion:** Zoonotic infections in people and animals occur in the context of a wide range of co-endemic pathogens in a rural community in western Kenya. The wide diversity of pathogens under study provides a unique opportunity to explore the distribution and determinants of infection in a multi-pathogen, multi-host system.


Abstract

Background: Herpes simplex virus type 2 (HSV-2) infections are associated with increased risk of HIV transmission. We determined HSV-2 prevalence, incidence and associated risk factors, incidence among persons with indeterminate results, and prevalence of HSV-2/HIV co-infection among young adults (18-34 years) and adolescents (16-17 years) enrolled in an HIV incidence cohort study in western Kenya.

Methods: Participants (n = 1106; 846 adults) were screened and those HIV-1 negative were enrolled and followed-up quarterly for one year. HSV-2 was assessed using the Kalon enzyme immunoassay. HSV-2 incidence was calculated separately among HSV-2 seronegative participants and those indeterminate at baseline. Logistic regression was used to estimate the odds of HSV-2 infection and Poisson regression was used to assess HSV-2 incidence and associated factors.

Results: Overall, HSV-2 prevalence was 26.6% [95% confidence interval (CI): 23.9-29.4] and was higher in adults (31.5% [95% CI: 28.3-34.9]) than adolescents (10.7% [95% CI: 7.1-15.3]). Factors associated with prevalent HSV-2 included female gender, increasing age, HIV infection, history of sexually transmitted infection, low level of education, multiple sexual partners, and being married, divorced, separated or widowed. Overall HSV-2 incidence was 4.0 per 100 person-years (/100PY) 95% CI: 2.7-6.1 and was higher in adults (4.5/100PY) and females (5.1/100PY). In multivariable analysis only marital status was associated with HSV-2 incidence. Among 45 participants with indeterminate HSV-2 results at baseline, 22 seroconverted, resulting in an incidence rate of 53.2 /100PY [95% CI: 35.1-80.9]. Inclusion of indeterminate results almost doubled the overall incidence rate to 7.8 /100 PY [95% CI: 5.9-10.5]. Prevalence of HIV/HSV-2 co-infection was higher in female adults than female adolescents (17.1 [95% CI: 13.6-21.0] versus 3.4 [95% CI: 1.1-7.8]).

Conclusion: The high incidence rate among persons with indeterminate results underscores the public health concerns for HSV-2 spread and underreporting of the HSV-2 burden. Careful consideration is needed when interpreting HSV-2 serology results in these settings.

Abstract

Introduction: Malnutrition is an underlying cause of mortality in about half of the cases that occur among children less than five years in developing countries. In Africa including Kenya, this problem may be exacerbated by socio-demographic and socio-economic factors. This study aimed at determining nutritional status and association of demographic characteristics with malnutrition among children aged 1 day to 24 months in Kwale County, Kenya.

Methods: A cross-sectional study was done in Mwaluphamba Location, Kwale County, Kenya. Data was collected using a semi-structured questionnaire and administered to 380 randomly selected mothers who had children under the age of two years. Nutrition status was determined using anthropometric measurements. Data was analyzed using descriptive statistics and associations were determined by univariate logistic regression.

Results: Malnutrition prevalence for children in Kwale was high with 29.2% of the children being stunted and 13.4% being severely stunted. Underweight prevalence was at 20.8% of whom 9.5% were severely underweight. The global acute malnutrition rate was 18.9%. Stunting differed significantly between sex (males 35.1% compared to females 21.7%; p = 0.005). Significant differences were also observed in stunting and underweight due to age (p < 0.005).

Conclusion: The prevalence of stunting, underweight and global acute malnutrition rates was high among the children. Male children were associated with a significantly higher prevalence of stunting than the females. The prevalence of underweight and stunting significantly increased with increasing age.

Pubmed link- [https://pubmed.ncbi.nlm.nih.gov/29881508/]
leaders and health workers. Much of the existing evidence on this topic focuses on women who have already started childbearing. Using primary qualitative data, we explored individual, community and health provider's perceptions about using modern contraceptives to delay the first birth in a high fertility setting.

Methods: A descriptive qualitative study was conducted in Tandahimba district in southern Tanzania between December 2014 and March 2015. We conducted 8 focus group discussions with men and women and 25 in-depth interviews (18 with women, 4 with family planning service providers and 3 with district-level staff). Participants were purposively sampled. Data transcripts were managed and coded using Nvivo 11 software and we employed a thematic framework analysis.

Results: Three main themes emerged about using modern contraceptives to delay first birth: (1) the social and biological status of the woman (2) the type of contraceptive and (3) non-alignment among national policies for adolescents. Use of modern contraceptives to delay first birth was widely acceptable for women who were students, young, unmarried and women in unstable marriage. But long-acting reversible methods such as implants and intrauterine devices were perceived as inappropriate methods for delaying first birth, partly because of fears around delayed return to fecundity, discontinuation once woman's marital status changes and permanently limiting future fertility. The support for use of modern contraceptives to delay a first pregnancy was not unanimous. A small number of participants from both rural and urban areas did not approve the use of contraceptive methods before the birth of a first baby at all, not even for students. There was lack of clarity and consistency on the definition of 'young' and that had direct implications for access, autonomy in decision-making, confidentiality and consent for young people.

Conclusions: Women who wish to delay their first birth face challenges related to restrictions by age and method imposed by stakeholders in accessing and provision of modern contraceptives. There is a need for a clearly communicated policy on minimum age and appropriate method choice for delayers of first birth.


Abstract
Dengue (DEN) and yellow fever (YF) are re-emerging in East Africa, with contributing drivers to this trend being unplanned urbanization and increasingly adaptable anthropophilic Aedes (Stegomyia) vectors. Entomological risk assessment of these diseases remains scarce for much of East Africa and Kenya even in the dengue fever-prone urban coastal areas. Focusing on major cities of Kenya, we compared DEN and YF risk in Kilifi County (DEN-outbreak-prone), and Kisumu and Nairobi Counties (no documented DEN outbreaks). We surveyed water-holding containers for mosquito immature (larvae/pupae) indoors and outdoors from selected houses during the long rains, short rains and dry seasons (100 houses/season) in each County from October 2014-June 2016. House index (HI), Breteau index (BI) and Container index (CI) estimates based on Aedes (Stegomyia) immature infestations were compared by city and season. Aedes aegypti and Aedes bromeliae were the main Stegomyia species with significantly more positive houses outdoors (212) than indoors (88) (n = 900) (χ² = 60.52, P < 0.0001). Overall, Ae. aegypti estimates of HI (17.3 vs 11.3) and BI (81.6 vs 87.7) were higher in Kilifi and Kisumu, respectively, than in Nairobi (HI, 0.3; BI,13). However, CI was highest in Kisumu (33.1), followed by Kilifi (15.1) then Nairobi (5.1). Aedes bromeliae indices were highest in Kilifi, followed by Kisumu, then Nairobi with HI (4.3, 0.3, 0); BI (21.3, 7, 0.7) and CI (3.3, 3.3, 0.3), at the respective sites. HI and BI for both species were highest in the long rains, compared to the short rains and dry seasons. We found strong positive correlations between the BI and CI, and BI and HI for Ae. aegypti, with the most productive container types being jerricans, drums, used/discarded containers and tyres. On the basis of established vector index thresholds, our findings suggest low-to-medium risk levels for urban YF and high DEN risk for Kilifi and Kisumu, whereas for Nairobi YF risk was low while DEN risk levels were low-to-medium. The study provides a baseline for future vector studies needed to further characterise the observed differential risk patterns by vector potential evaluation. Identified productive containers should be made the focus of community-based targeted vector control programs.


Abstract

Background: Fluid therapy in severely malnourished children is hypothesized to be deleterious owing to compromised cardiac function. We evaluated World Health
Organization (WHO) fluid resuscitation guidelines for hypovolaemic shock using myocardial and haemodynamic function and safety endpoints.

Methods: A prospective observational study of two sequential fluid management strategies was conducted at two East African hospitals. Eligible participants were severely malnourished children, aged 6-60 months, with hypovolaemic shock secondary to gastroenteritis. Group 1 received up to two boluses of 15 ml/kg/h of Ringer's lactate (RL) prior to rehydration as per WHO guidelines. Group 2 received rehydration only (10 ml/kg/h of RL) up to a maximum of 5 h. Comprehensive clinical, haemodynamic and echocardiographic data were collected from admission to day 28.

Results: Twenty children were enrolled (11 in group 1 and 9 in group 2), including 15 children (75%) with kwashiorkor, 8 (40%) with elevated brain natriuretic peptide >300 pg/ml, and 9 (45%) with markedly elevated median systemic vascular resistance index (SVRI) >1600 dscm⁻⁵/m² indicative of severe hypovolaemia. Echocardiographic evidence of fluid-responsiveness (FR) was heterogeneous in group 1, with both increased and decreased stroke volume and myocardial fractional shortening. In group 2, these variables were more homogenous and typical of FR. Median SVRI marginally decreased post fluid administration (both groups) but remained high at 24 h. Mortality at 48 h and to day 28, respectively, was 36% (4 deaths) and 81.8% (9 deaths) in group 1 and 44% (4 deaths) and 55.6% (5 deaths) in group 2. We observed no pulmonary oedema or congestive cardiac failure on or during admission; most deaths were unrelated to fluid interventions or echocardiographic findings of response to fluids.

Conclusion: Baseline and cardiac response to fluid resuscitation do not indicate an effect of compromised cardiac function on response to fluid loading or that fluid overload is common in severely malnourished children with hypovolaemic shock. Endocrine response to shock and persistently high SVRI post fluid-therapy resuscitation may indicate a need for further research investigating enhanced fluid volumes to adequately correct volume deficit. The adverse outcomes are concerning, but appear to be unrelated to immediate fluid management.


Abstract
HIV-1 transmitted drug resistance (TDR) is of increasing public health concern in sub-Saharan Africa with the rollout of antiretroviral (ARV) therapy. Such data are, however, limited in Kenya, where HIV-1 drug resistance testing is not routinely performed. From a population-based household survey conducted between September and November 2012 in rural western Kenya, we retrospectively assessed HIV-1 TDR baseline rates, its determinants, and genetic diversity among drug-naïve persons aged 15-59 years with acute HIV-1 infections (AHI) and recent HIV-1 infections (RHI) as determined by nucleic acid amplification test and both Limiting Antigen and BioRad avidity immunoassays, respectively. HIV-1 pol sequences were scored for drug resistance mutations using Stanford HIVdb and WHO 2009 mutation guidelines. HIV-1 subtyping was computed in MEGA6. Eighty seven (93.5%) of the eligible samples were successfully sequenced. Of these, 8 had at least one TDR mutation, resulting in a TDR prevalence of 9.2% (95% CI 4.7-17.1). No TDR was observed among persons with AHI (n = 7). TDR prevalence was 4.6% (95% CI 1.8-11.2) for nucleoside reverse transcriptase inhibitors (NRTIs), 6.9% (95% CI 3.2-14.2) for non- nucleoside reverse transcriptase inhibitors (NNRTIs), and 1.2% (95% CI 0.2-6.2) for protease inhibitors. Three (3.4% 95% CI 0.8-10.1) persons had dual-class NRTI/NNRTI resistance. Predominant TDR mutations in the reverse transcriptase included K103N/S (4.6%) and M184V (2.3%); only M46I/L (1.1%) occurred in the protease. All the eight persons were predicted to have different grades of resistance to the ARV regimens, ranging from potential low-level to high-level resistance. HIV-1 subtype distribution was heterogeneous: A (57.5%), C (6.9%), D (21.8%), G (2.3%), and circulating recombinant forms (11.5%). Only low CD4 count was associated with TDR (p = 0.0145). Our findings warrant the need for enhanced HIV-1 TDR monitoring in order to inform on population-based therapeutic guidelines and public health interventions.


Abstract

Large-scale gridded population datasets are usually produced for the year of input census data using a top-down approach and projected backward and forward in time using national growth rates. Such temporal projections do not include any subnational variation in population distribution trends and ignore changes in geographical covariates such as urban land cover changes. Improved predictions of population distribution changes over...
time require the use of a limited number of covariates that are time-invariant or temporally explicit. Here we make use of recently released multi-temporal high-resolution global settlement layers, historical census data and latest developments in population distribution modelling methods to reconstruct population distribution changes over 30 years across the Kenyan Coast. We explore the methodological challenges associated with the production of gridded population distribution time-series in data-scarce countries and show that trade-offs have to be found between spatial and temporal resolutions when selecting the best modelling approach. Strategies used to fill data gaps may vary according to the local context and the objective of the study. This work will hopefully serve as a benchmark for future developments of population distribution time-series that are increasingly required for population-at-risk estimations and spatial modelling in various fields.


**Abstract**

Intestinal parasitic infections can significantly contribute to the burden of disease, may cause nutritional and energetic stress, and negatively impact the quality of life in low income countries of the world. This cross-sectional study done in Mwea irrigation scheme, in Kirinyaga, central Kenya, assessed the public health significance of soil-transmitted helminthiases (STH), schistosomiasis, and other intestinal parasitic infections, among 361 preschool age children (PSAC) through fecal examination, by measuring anthropometric indices, and through their parents/guardians, by obtaining sociodemographic information. Both intestinal helminth and protozoan infections were detected, and, among the soil-transmitted helminth parasites, there were *Ascaris lumbricoides* (prevalence, 3%), *Ancylostoma duodenale* (<1%), and *Trichuris trichiura* (<1%). Other intestinal helminths were *Hymenolepis nana* (prevalence, 3.6%) and *Enterobius vermicularis* (<1%). *Schistosoma mansoni* occurred at a prevalence of 5.5%. Interestingly, the protozoan, *Giardia lamblia* (prevalence, 14.7%), was the most common among the PSAC. Other protozoans were *Entamoeba coli* (3.9%) and *Entamoeba histolytica* (<1). Anthropometric indices showed evidence of malnutrition. Intestinal parasites were associated with hand washing behavior, family size, water purification, and home location. These findings suggest that *G.*
*lamblia* infection and malnutrition may be significant causes of ill health among the PSAC in Mwea, and, therefore, an intervention plan is needed.


**Abstract**

**Introduction:** African countries are rapidly adopting guidelines to offer antiretroviral therapy (ART) to all HIV-infected individuals, regardless of CD4 count. For this policy of 'treat all' to succeed, millions of new patients must be initiated on ART as efficiently as possible. Studies have documented high losses of treatment-eligible patients from care before they receive their first dose of antiretrovirals (ARVs), due in part to a cumbersome, resource-intensive process for treatment initiation, requiring multiple clinic visits over a several-week period.

**Methods and analysis:** The Simplified Algorithm for Treatment Eligibility (SLATE) study is an individually randomised evaluation of a simplified clinical algorithm for clinicians to reliably determine a patient's eligibility for immediate ART initiation without waiting for laboratory results or additional clinic visits. SLATE will enrol and randomise (1:1) 960 adult, HIV-positive patients who present for HIV testing or care and are not yet on ART in South Africa and Kenya. Patients randomised to the standard arm will receive routine, standard of care ART initiation from clinic staff. Patients randomised to the intervention arm will be administered a symptom report, medical history, brief physical exam and readiness assessment. Patients who have positive (satisfactory) results for all four components of SLATE will be dispensed ARVs immediately, at the same clinic visit. Patients who have any negative results will be referred for further clinical investigation, counselling, tests or other services prior to being dispensed ARVs. After the initial visit, follow-up will be by passive medical record review. The primary outcomes will be ART initiation ≤28 days and retention in care 8 months after study enrolment.

**Ethics and dissemination:** Ethics approval has been provided by the Boston University Institutional Review Board, the University of the Witwatersrand Human Research Ethics Committee (Medical) and the KEMRI Scientific and Ethics Review Unit. Results will be
published in peer-reviewed journals and made widely available through presentations and briefing documents.


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<td><strong>Abstract</strong></td>
<td>The success of women's microbicide use for HIV/AIDS prevention may hinge on health programs' ability to engage men to support it. In this qualitative study in Kenya, most women did not or would not tell their partners prior to initiating use, and/or would use despite their objections. Men generally did not agree with this, yet male partners of trial participants who discovered that their partners were using microbicides without their knowledge did not seem concerned. Findings suggest that efforts to engage men in microbicide use should avoid &quot;awakening&quot; patriarchal gender norms, and support women to use microbicides without involving their partners.</td>
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<td><strong>Abstract</strong></td>
<td>Drug-resistant infections caused by bacteria with increasing antimicrobial resistance (AMR) threaten our ability to treat life-threatening conditions. Tackling AMR requires international collaboration and partnership. An early and leading priority to do this is to strengthen AMR surveillance, particularly in low-income countries where the burden of infectious diseases is highest and where data are most limited. The World Health Organization (WHO) has developed the Global AMR Surveillance System (GLASS) as one of a number of measures designed to tackle the problem of AMR, and WHO member states have been encouraged to produce National Action Plans for AMR by 2017. However, low-income countries are unlikely to have the resources or capacity to implement all the components in the GLASS manual. To facilitate their efforts, we developed a guideline that is aligned to the GLASS procedures, but written specifically for implementation in low-income countries. The guideline allows for flexibility across different systems, but has sufficient standardisation of core protocols to ensure that, if followed, data will be valid and comparable. This will ensure that the surveillance</td>
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programme can provide health intelligence data to inform evidence-based interventions at local, national and international levels.


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**Abstract**

**Background:** Aedes aegypti, the principal vector for dengue and other emerging arboviruses, breeds preferentially in various man-made and natural container habitats. In the absence of vaccine, epidemiological surveillance and vector control remain the best practices for preventing dengue outbreaks. Effective vector control depends on a good understanding of larval and adult vector ecology of which little is known in Kenya. In the current study, we sought to characterize breeding habitats and establish container productivity profiles of Ae. aegypti in rural and urban sites in western and coastal Kenya.

**Methods:** Twenty sentinel houses in each of four study sites (in western and coastal Kenya) were assessed for immature mosquito infestation once a month for a period of 24 months (June 2014 to May 2016). All water-holding containers in and around the households were inspected for Ae. aegypti larvae and pupae.

**Results:** Collections were made from a total of 22,144 container visits: Chulaimbo (7575) and Kisumu (8003) in the west, and from Msambweni (3199) and Ukunda (3367) on the coast. Of these, only 4.5-5.6% were positive for Ae. aegypti immatures. In all four sites, significantly more positive containers were located outdoors than indoors. A total of 17,537 Ae. aegypti immatures were sampled from 10 container types. The most important habitat types were buckets, drums, tires, and pots, which produced over 75%
of all the pupae. Key outdoor containers in the coast were buckets, drums and tires, which accounted for 82% of the pupae, while pots and tires were the only key containers in the western region producing 70% of the pupae. Drums, buckets and pots were the key indoor containers, producing nearly all of the pupae in the coastal sites. No pupae were collected indoors in the western region. The coastal region produced significantly more Ae. aegypti immatures than the western region both inside and outside the sentinel houses.

**Conclusions:** These results indicate that productive Ae. aegypti larval habitats are abundant outdoors and that only a few containers produce a majority of the pupae. Although the numbers were lower, productive habitats were detected within households. Targeting source reduction efforts towards these productive containers both inside and outside homes is likely to be a cost-effective way to reduce arboviral transmission in these regions.


**Abstract**

**Background:** The human malaria parasite *Plasmodium falciparum* has evolved complex drug evasion mechanisms to all available antimalarials. To date, the combination of amodiaquine-artesunate is among the drug of choice for treatment of uncomplicated malaria. In this combination, a short acting, artesunate is partnered with long acting, amodiaquine for which resistance may emerge rapidly especially in high transmission settings. Here, we used a rodent malaria parasite *Plasmodium berghei* ANKA as a surrogate of *P. falciparum* to investigate the mechanisms of amodiaquine resistance. **Methods:** We used serial technique to select amodiaquine resistance by submitting the parasites to continuous amodiaquine pressure. We then employed the 4-Day Suppressive Test to monitor emergence of resistance and determine the cross-resistance profiles. Finally, we genotyped the resistant parasite by PCR amplification, sequencing and relative quantitation of mRNA transcript of targeted genes. **Results:** Submission of *P. berghei* ANKA to amodiaquine pressure yielded resistant parasite within thirty-six passages. The effective dosage that reduced 90% of parasitaemia (ED₉₀) of sensitive line and resistant line were 4.29mg/kg and 19.13mg/kg, respectively. After freezing at -80°C for one month, the resistant parasite remained stable
with an ED$_{90}$ of 18.22mg/kg. Amodiaquine resistant parasites are also resistant to chloroquine (6fold), arteether (10fold), primaquine (5fold), piperazine (2fold) and lumefantrine (3fold). Sequence analysis of *Plasmodium berghei* chloroquine resistant transporter revealed His95Pro mutation. No variation was identified in *Plasmodium berghei* multidrug resistance gene-1 (Pbmdr1), *Plasmodium berghei* deubiquitinating enzyme-1 or *Plasmodium berghei* Kelch13 domain nucleotide sequences. Amodiaquine resistance is also accompanied by high mRNA transcripts of key transporters; Pbmdr1, V-type/H$^+$ pumping pyrophosphatase-2 and sodium hydrogen ion exchanger-1 and Ca$^{2+}$/H$^+$ antiporter. **Conclusions:** Selection of amodiaquine resistance yielded stable "multidrug-resistant" parasites and thus may be used to study common resistance mechanisms associated with other antimalarial drugs. Genome wide studies may elucidate other functionally important genes controlling AQ resistance in *P. berghei*.


**Abstract**

**Background:** School-based deworming is widely implemented in various countries to reduce the burden of soil-transmitted helminths (STHs), however, the frequency of drug administration varies in different settings. In this study, we compared the impact of a single annual treatment and 4-monthly treatment over a follow-up among Kenyan school children, and investigated the factors associated with residual infection.

**Methods:** We performed a secondary analysis of data from a randomized trial investigating whether deworming for STHs alters risk of acquiring malaria. Children received either a single treatment or 4-monthly albendazole treatments were followed longitudinally from February 2014 to October 2014. The relative impact of treatment and factors associated with residual infections were investigated using mixed-effects regression models. Predisposition to infection was assessed based on Spearman's rank and Kendall's Tau correlation coefficients.

**Results:** In the 4-monthly treatment group, the proportion of children infected with hookworm decreased from 59.9 to 5.7%, while Ascaris lumbricoides infections dropped from 55.7 to 6.2%. In the single treatment group, hookworm infections decreased over
the same time period from 58.7 to 18.3% (12.6% absolute difference in reduction, 95% CI: 8.9-16.3%), and A. lumbricoides from 56.7 to 23.3% (17.1% absolute difference in reduction, 95% CI: 13.1-21.1%). There was strong evidence for predisposition to both STH types. Residual hookworm infection among children on 4-monthly treatment were associated with male sex and baseline nutritional status, whereas A. lumbricoides infection was associated with individual and school-level infection at baseline, latrine cleanliness at schools.

Conclusions: This study found that 4-monthly treatment was more effective than single annual treatment. Repeated treatments led to dramatic reductions in the intensities of STHs, but did not completely clear infections among school children in Kenya, a presumed reflection of reinfection in a setting where there is ongoing transmission.

95% CI = 0.37-3.33; p = 0.860). When correct timing in taking each dose was considered a criteria for adherence, 72.3% (209/289) were adherent in the control and 69.2% (189/273) in the intervention group (OR = 0.82; 95% CI = 0.56-1.19; p = 0.302). Sending SMS reminders significantly increased odds of children returning to the facility on day 3 (81.4 vs 74.0%; OR = 1.55; 95% CI = 1.15-2.08; p = 0.004) and on day 28 (63.4 vs 52.5%; OR = 1.58; 95% CI = 1.30-1.92; p < 0.001).

Conclusions: In this efficacy trial, SMS reminders increased post-treatment return to the health facility, but had no effect on AL adherence which was high in both control and intervention groups. Further effectiveness studies under the real world conditions are needed to determine the optimum role of SMS reminders. Trial registration ISRCTN39512726.


Abstract

Background: Audit and feedback (A&F) is widely used in healthcare but there are few examples of how to deploy it at scale in low-income countries. Establishing the Clinical Information Network (CIN) in Kenya provided an opportunity to examine the effect of A&F delivered as part of a wider set of activities to promote paediatric guideline adherence.

Methods: We analysed data collected from medical records on discharge for children aged 2-59 months from 14 Kenyan hospitals in the CIN. Hospitals joined CIN in phases and for each we analysed their initial 25 months of participation that occurred between December 2013 and March 2016. A total of 34 indicators of adherence to recommendations were selected for evaluation each classified by form of feedback (passive, active and none) and type of task (simple or difficult documentation and those requiring cognitive work). Performance change was explored graphically and using generalised linear mixed models with attention given to the effects of time and use of a standardised paediatric admission record (PAR) form.

Results: Data from 60,214 admissions were eligible for analysis. Adherence to recommendations across hospitals significantly improved for 24/34 indicators.
Improvements were not obviously related to nature of feedback, may be related to task type and were related to PAR use in the case of documentation indicators. There was, however, marked variability in adoption and adherence to recommended practices across sites and indicators. Hospital-specific factors, low baseline performance and specific contextual changes appeared to influence the magnitude of change in specific cases.

**Conclusion:** Our observational data suggest some change in multiple indicators of adherence to recommendations (aspects of quality of care) can be achieved in low-resource hospitals using A&F and simple job aides in the context of a wider network approach.


**Abstract**

**Introduction:** In 2010, WHO recommended a new first-line treatment for visceral leishmaniasis (VL) in Eastern Africa. The new treatment, a combination of intravenous (IV) or intramuscular (IM) sodium stibogluconate (SSG) and IM paromomycin (PM) was an improvement over SSG monotherapy, the previous first-line VL treatment in the region. To monitor the new treatment's safety and effectiveness in routine clinical practice a pharmacovigilance (PV) programme was developed.

**Methods:** A prospective PV cohort was developed. Regulatory approval was obtained in Sudan, Kenya, Uganda and Ethiopia. Twelve sentinel sites sponsored by the Ministries of Health, Médecins Sans Frontières (MSF) and Drugs for Neglected Diseases initiative (DNDi) participated. VL patients treated using the new treatment were consented and included in a common registry that collected demographics, baseline clinical characteristics, adverse events, serious adverse events and treatment outcomes. Six-monthly periodic safety update reports (PSUR) were prepared and reviewed by a PV steering committee.

**Results:** Overall 3126 patients were enrolled: 1962 (62.7%) from Sudan, 652 (20.9%) from Kenya, 322 (10.3%) from Ethiopia and 190 (6.1%) from Uganda. Patients were
mostly male children (68.1%, median age 11 years) with primary VL (97.8%). SSG-PM initial cure rate was 95.1%; no geographical differences were noted. HIV/VL co-infected patients and patients older than 50 years had initial cure rates of 56 and 81.4%, respectively, while 1063 (34%) patients had at least one adverse event (AE) during treatment and 1.92% (n = 60) had a serious adverse event (SAE) with a mortality of 1.0% (n = 32). There were no serious unexpected adverse drug reactions.

Conclusions: This first regional PV programme in VL supports SSG-PM combination as first-line treatment for primary VL in Eastern Africa. SSG-PM was effective and safe except in HIV/VL co-infected or older patients. Active PV surveillance of targeted safety, effectiveness and key VL outcomes such as VL relapse, PKDL and HIV/VL co-infection should continue and PV data integrated to national and WHO PV databases.


Abstract

We have developed and validated a novel, sensitive, selective and reproducible reversed-phase high-performance liquid chromatography method coupled with electrospray ionization mass spectrometry (HPLC-ESI-MS/MS) for the simultaneous quantitation of ceftriaxone (CEF), metronidazole (MET) and hydroxymetronidazole (MET-OH) from only 50 µL of human plasma, and unbound CEF from 25 µL plasma ultra-filtrate to evaluate the effect of protein binding. Cefuroxime axetil (CEFU) was used as an internal standard (IS). The analytes were extracted by a protein precipitation procedure with acetonitrile and separated on a reversed-phase Polaris 5 C18-Analytical column using a mobile phase composed of acetonitrile containing 0.1% (v/v) formic acid and 10 mM aqueous ammonium formate pH 2.5, delivered at a flow-rate of 300 µL/min. Multiple reaction monitoring was performed in the positive ion mode using the transitions m/z555.1→m/z396.0 (CEF), m/z172.2→m/z 128.2 (MET), m/z188.0→m/z125.9 (MET-OH) and m/z528.1→m/z 364.0 (CEFU) to quantify the drugs. Calibration curves in spiked plasma and ultra-filtrate were linear (r² ≥ 0.9948) from 0.4-300 µg/mL for CEF, 0.05-50 µg/mL for MET and 0.02 - 30 µg/mL for MET-OH. The intra- and inter-assay precisions were less than 9% and the mean extraction recoveries were 94.0% (CEF), 98.2% (MET), 99.6% (MET-OH) and 104.6% (CEF in ultra-filtrate); the recoveries for the IS were 93.8% (in plasma) and 97.6% (in ultra-filtrate). The validated method was successfully applied to a pharmacokinetic study
of CEF, MET and MET-OH in hospitalized children with complicated severe acute malnutrition following an oral administration of MET and intravenous administration of CEF over the course of 72 hours.


| Obiero CW, Ndiaye AGW, Sciré AS, Kaunyangi BM, Marchetti E, Gone AM, Schütte LD, Riccucci D, Auerbach J, Saul A, Martin LB, Bejon P, Njuguna P, Podda A. A Phase 2a Randomized Study to Evaluate the Safety and Immunogenicity of the 1790GAHB Generalized Modules for Membrane Antigen Vaccine against <i>Shigella sonnei</i> Administered Intramuscularly to Adults from a Shigellosis-Endemic Country. Front Immunol. 2017 Dec 22;8:1884 |

**Abstract**

Shigellosis is a mild-to-severe diarrheal infection, caused by the genus *Shigella*, and is responsible for significant morbidity and mortality worldwide. We evaluated the safety and immunogenicity of an investigational *Shigella sonnei* vaccine (1790GAHB) based on generalized modules for membrane antigens (GMMA) in Kenya, a *Shigella*-endemic country. This phase 2a, observer-blind, controlled randomized study (NCT02676895) enrolled 74 healthy adults aged 18-45 years, of whom 72 were vaccinated. Participants received, in a 1:1:1 ratio, two vaccinations with the 1790GAHB vaccine at doses of either 1.5/25 μg of O antigen (OAg)/protein (group 1.5/25 μg) or 5.9/100 μg (group 5.9/100 μg) at day (D) 1 and D29, or vaccination with a quadrivalent meningococcal vaccine at D1 and tetanus, diphtheria, and acellular pertussis vaccine at D29 (control group). Solicited and unsolicited adverse events (AEs), serious AEs (SAEs), and AEs of special interest (neutropenia and reactive arthritis) were collected. Anti-*S. sonnei* lipopolysaccharide (LPS) serum immunoglobulin G (IgG) geometric mean concentrations (GMC) were evaluated at D1, D29, and D57 and compared to anti-*S. sonnei* LPS antibody levels in convalescent patients naturally exposed to *S. sonnei*. The percentages of participants with seroresponse were also calculated. The most frequently reported solicited local and systemic AEs across all groups were pain and headache, respectively. Only one case of severe systemic reaction was reported (severe headache after first vaccination in group 5.9/100 μg). Seven and three episodes of neutropenia, assessed as probably or possibly related to vaccination respectively, were reported in the investigational and control groups, respectively. No other SAEs were reported. Despite very high baseline anti-*S. sonnei* LPS serum IgG levels, the 1790GAHB vaccine induced robust antibody responses. At D29, GMC increased 2.10- and 4.43-fold from baseline in groups 1.5/25 and 5.9/100 μg, respectively, whereas no increase was observed in the control group. Antibody titers at D57 were not statistically different from those at D29. Seroresponse was 68% at D29 and 90% at D57 in group 1.5/25 μg, and 96% after each
vaccination in group 5.9/100 μg. The 1790GAHB vaccine was well tolerated and highly immunogenic in a population of African adults, regardless of the GMMA OAg/protein content used.


Abstract

Introduction: Home Based Testing and Counselling (HBTC) aims at reaching individuals who have low HIV risk perception and experience barriers which prevent them from seeking HIV testing and counseling (HTC) services. Saturating the community with HTC is needed to achieve the ambitious 90-90-90 targets of knowledge of HIV status, ARV treatment and viral suppression. This paper describes the use of health belief model and community participation principles in HBTC to achieve increased household coverage and HTC uptake.

Methods: This cross sectional survey was done between August 2009 and April 2011 in Kibera slums, Nairobi city. Using three community participation principles; defining and mobilizing the community, involving the community, overcoming barriers and respect to cultural differences and four constructs of the health belief model; risk perception, perceived severity, perceived benefits of changed behavior and perceived barriers; we offered HTC services to the participants. Descriptive statistics were used to describe socio-demographic characteristics, calculate uptake and HIV prevalence.

Results: There were 72,577 individuals enumerated at the start of the program; 75,141 residents were found during service delivery. Of those, 71,925 (95.7%) consented to participate, out of which 71,720 (99.7%) took the HIV test. First time testers were (39%). The HIV prevalence was higher (6.4%) among repeat testers than first time testers (4.0%) with more women (7.4%) testing positive than men (3.6%) and an overall 5.5% slum prevalence.

Conclusion: This methodology demonstrates that the use of community participation principles combined with a psychosocial model achieved high HTC uptake, coverage and diagnosed HIV in individuals who believed they are HIV free. This novel approach provides baseline for measuring HTC coverage in a community.
|---|

**Abstract**

**Background:** Home based HIV testing and counseling (HBTC) increases access to services and is associated with high testing uptake. Alongside testing, individuals are offered HIV prevention messages with an aim of helping them reduce HIV high risk sexual behaviors. This study explored the level of provision and subsequent utilization of HIV prevention messages and associated change in behavior among individuals who had received HBTC previously in an informal settlement.

**Methods:** In a mixed method cross sectional study, we interviewed 1257 individuals and conducted 6 focus group discussions (FGD). Multiple correspondence analysis (MCA) was used to construct provision of prevention messages and behavior change indices using STATA 3.0. Pearson's chi-square statistics was used to test for bivariate association between the outcomes and logistic regression analysis was carried out with the behavior change index as the outcome of interest and the predictors considered significant (p<0.1). Thematic content analysis for qualitative data was done using Atlas 3.0.

**Results:** Out of the 1257 participants, 1078 (85.8%) had ever tested for HIV, with 74.2% having tested in the Kibera HBTC program. Nearly all (97.4%) rated HBTC experience as either excellent (62.4%) or good (37%) and would recommend it to a friend. Provision of prevention messages was high among HBTC clients compared to clients from other testing sites; partner reduction counselling (64% versus 52%) and faithfulness (78.3% versus 67%); p=0.001. Self-reported behavior change after HBTC was generally low with condom use at 10.7% and men more likely to practice safer sex (p = 0.002). Trust of the sexual partners and fear of suspicion were the main reasons given for not using condoms. Clients testing HIV positive after previous negative result were 3.4%. The focus group discussions reported multiple sexual partnerships among both HIV negative and positive residents alike.

**Conclusion:** Although prevention messages delivered during HBTC are accepted and appreciated in this community, their utilization is low in both HIV negative and positive
individuals. Innovative strategies for change of normative beliefs about sexual behavior are urgently needed.


Abstract

The last decade has seen rapid evolution in guidance from the WHO concerning the provision of HIV services along the diagnosis-to-treatment continuum, but the extent to which these recommendations are adopted as national policies in Kenya, and subsequently implemented in health facilities, is not well understood. Identifying gaps in policy coverage and implementation is important for highlighting areas for improving service delivery, leading to better health outcomes. We compared WHO guidance with national policies for HIV testing and counselling, prevention of mother-to-child transmission, HIV treatment and retention in care. We then investigated implementation of these national policies in health facilities in one rural (Kisumu) and one urban (Nairobi) sites in Kenya. Implementation was documented using structured questionnaires that were administered to in-charge staff at 10 health facilities in Nairobi and 34 in Kisumu. Policies were defined as widely implemented if they were reported to occur in > 70% facilities, partially implemented if reported to occur in 30-70% facilities, and having limited implementation if reported to occur in < 30% facilities. Overall, Kenyan national HIV care and treatment policies were well aligned with WHO guidance. Policies promoting access to treatment and retention in care were widely implemented, but there was partial or limited implementation of several policies promoting access to HIV testing, and the more recent policy of Option B+ for HIV-positive pregnant women. Efforts are needed to improve implementation of policies designed to increase rates of diagnosis, thus facilitating entry into HIV care, if morbidity and mortality burdens are to be further reduced in Kenya, and as the country moves towards universal access to antiretroviral therapy.


Abstract

Background: The Schistosomiasis Consortium for Operational Research and Evaluation (SCORE) focus is on randomized trials of different approaches to mass drug administration (MDA) in endemic countries in Africa. Because their studies provided an opportunity to evaluate the effects of mass treatment on Schistosoma-associated morbidity, nested cohort studies were developed within SCORE's intervention trials to monitor changes in a suite of schistosomiasis disease outcomes. This paper describes the process SCORE used to select markers for prospective monitoring and the baseline prevalence of these morbidities in four parallel cohort studies.

Methods: In July 2009, SCORE hosted a discussion of the potential impact of MDA on morbidities due to Schistosoma infection that might be measured in the context of multi-year control. Candidate markers were reviewed and selected for study implementation. Baseline data were then collected from cohorts of children in four country studies: two in high endemic S. mansoni sites (Kenya and Tanzania), and two in high endemic S. haematobium sites (Niger and Mozambique), these cohorts to be followed prospectively over 5 years.

Results: At baseline, 62% of children in the S. mansoni sites had detectable eggs in their stool, and 10% had heavy infections (≥ 400 eggs/g feces). Heavy S. mansoni infections were found to be associated with increased baseline risk of anemia, although children with moderate or heavy intensity infections had lower risk of physical wasting. Prevalence of egg-positive infection in the combined S. haematobium cohorts was 27%, with 5% of individuals having heavy infection (≥50 eggs/10 mL urine). At baseline, light intensity S. haematobium infection was associated with anemia and with lower scores in the social domain of health-related quality-of-life (HRQoL) assessed by Pediatric Quality of Life Inventory.

Conclusions: Our consensus on practical markers of Schistosoma-associated morbidity indicated that height, weight, hemoglobin, exercise tolerance, HRQoL, and ultrasound abnormalities could be used as reference points for gauging treatment impact. Data collected over five years of program implementation will provide guidance for future evaluation of morbidity control in areas endemic for schistosomiasis.
Abstract

Background: Training teachers to diagnose uncomplicated malaria using malaria rapid diagnostic tests and treat with artemisinin-based combination therapy has the potential to improve the access of primary school children (6-14 years) to prompt and efficient treatment for malaria, but little is known about the acceptability of such an intervention. This qualitative study explored experiences and perceptions of users and implementers of a programme of school-based malaria case management via a first-aid kit-the Learner Treatment Kit (LTK)-implemented as part of a cluster-randomized controlled trial in Zomba district, Malawi.

Methods: From 29 primary schools where teachers were trained to test and treat school children for malaria using the LTK, six schools were purposively selected on the basis of relative intervention usage (low, medium or high); school size and geographical location. In total eight focus group discussions were held with school children, parents and guardians, and teachers; and 20 in-depth interviews were conducted with key stakeholders at the school, district and national levels. Interviews were recorded, transcribed, and analysed using a thematic analysis approach.

Results: The LTK was widely perceived by respondents to be a worthwhile intervention, with the opinion that trained teachers were trusted providers of malaria testing and treatment to school children. Benefits of the programme included a perception of improved access to malaria treatment for school children; decreased school absenteeism; and that the programme supported broader national health and education policies. Potential barriers to successful implementation expressed included increased teacher workloads, a feeling of inadequate supervision from health workers, lack of incentives and concerns for the sustainability of the programme regarding the supply of drugs and commodities.

Conclusion: Training teachers to test for and treat uncomplicated malaria in schools was well received by both users and implementers alike, and was perceived by the majority of stakeholders to be a valuable programme. Factors raised as critical to the success of such a programme included ensuring an effective supervisory system, a reliable supply
chain, and the training of greater numbers of teachers per school to manage high consultation numbers, especially during the peak malaria transmission season.


Abstract

**Background:** The World Health Organisation recommends the use of catch-up campaigns as part of the introduction of pneumococcal conjugate vaccines (PCVs) to accelerate herd protection and hence PCV impact. The value of a catch-up campaign is a trade-off between the costs of vaccinating additional age groups and the benefit of additional direct and indirect protection. There is a paucity of observational data, particularly from low- and middle-income countries, to quantify the optimal breadth of such catch-up campaigns.

**Methods:** In Kilifi, Kenya, PCV10 was introduced in 2011 using the three-dose Expanded Programme on Immunisation infant schedule and a catch-up campaign in children <5 years old. We fitted a transmission dynamic model to detailed local data, including nasopharyngeal carriage and invasive pneumococcal disease (IPD), to infer the marginal impact of the PCV catch-up campaign over hypothetical routine cohort vaccination in that setting and to estimate the likely impact of alternative campaigns and their dose efficiency.

**Results:** We estimated that, within 10 years of introduction, the catch-up campaign among children <5 years old prevents an additional 65 (48-84) IPD cases across age groups, compared to PCV cohort introduction alone. Vaccination without any catch-up campaign prevented 155 (121-193) IPD cases and used 1321 (1058-1698) PCV doses per IPD case prevented. In the years after implementation, the PCV programme gradually accrues herd protection, and hence its dose efficiency increases: 10 years after the start of cohort vaccination alone the programme used 910 (732-1184) doses per IPD case averted. We estimated that a two-dose catch-up among children <1 year old uses an additional 910 (732-1184) doses per additional IPD case averted. Furthermore, by extending a single-dose catch-up campaign to children aged 1 to <2 years and subsequently to those aged 2 to <5 years, the campaign uses an additional 412 (296-606)
and 543 (403-763) doses per additional IPD case averted. These results were not sensitive to vaccine coverage, serotype competition, the duration of vaccine protection or the relative protection of infants.

**Conclusions:** We find that catch-up campaigns are a highly dose-efficient way to accelerate population protection against pneumococcal disease.


**Abstract**

**Background:** We report the first-in-human safety and immunogenicity evaluation of PENNVAX-G DNA/modified vaccinia Ankara-Chiang Mai double recombinant (MVA-CMDR) prime-boost human immunodeficiency virus (HIV) vaccine, with intramuscular DNA delivery by either Biojector 2000 needle-free injection system (Biojector) or CELLECTRA electroporation device.

**Methods:** Healthy, HIV-uninfected adults were randomized to receive 4 mg of PENNVAX-G DNA delivered intramuscularly by Biojector or electroporation at baseline and week 4 followed by intramuscular injection of 108 plaque forming units of MVA-CMDR at weeks 12 and 24. The open-label part A was conducted in the United States, followed by a double-blind, placebo-controlled part B in East Africa. Solicited and unsolicited adverse events were recorded, and immune responses were measured.

**Results:** Eighty-eight of 100 enrolled participants completed all study injections, which were generally safe and well tolerated, with more immediate, but transient, pain in the electroporation group. Cellular responses were observed in 57% of vaccine recipients tested and were CD4 predominant. High rates of binding antibody responses to CRF01_AE antigens, including gp70 V1V2 scaffold, were observed. Neutralizing antibodies were detected in a peripheral blood mononuclear cell assay, and moderate antibody-dependent, cell-mediated cytotoxicity activity was demonstrated.
Discussion: The PVG/MVA-CMDR HIV-1 vaccine regimen is safe and immunogenic. Substantial differences in safety or immunogenicity between modes of DNA delivery were not observed.

Pubmed link: https://pubmed.ncbi.nlm.nih.gov/28968759/


Abstract

Background: The World Health Organization (WHO) rehydration management guidelines (Plan C) for children with acute gastroenteritis (AGE) and severe dehydration are widely practiced in resource-poor settings, yet have never been formally evaluated in a clinical trial. A recent audit of outcome of AGE at Kilifi County Hospital, Kenya noted that 10% of children required high dependency care (20% mortality) and a number developed fluid-related complications. The fluid resuscitation trial, FEAST, conducted in African children with severe febrile illness, demonstrated higher mortality with fluid bolus therapy and raised concerns regarding the safety of rapid intravenous rehydration therapy. Those findings warrant a detailed physiological study of children's responses to rehydration therapy incorporating quantification of myocardial performance and haemodynamic changes. Methods: GASTRO is a multi-centre, unblinded Phase II randomised controlled trial of 120 children aged 2 months to 12 years admitted to hospital with severe dehydration secondary to AGE. Children with severe malnutrition, chronic diarrhoea and congenital/rheumatic heart disease are excluded. Children will be enrolled over 18 months in 3 centres in Kenya and Uganda and followed until 7 days post-discharge. The trial will randomise children 1:1 to standard rapid rehydration using Ringers Lactate (WHO plan 'C' - 100mls/kg over 3-6 hours according to age, plus additional 0.9% saline boluses for children presenting in shock) or to a slower rehydration regimen (100mls/kg given over 8 hours and without the addition of fluid boluses). Enrolment started in November 2016 and is on-going. Primary outcome is frequency of adverse events, particularly related to cardiovascular compromise and neurological sequelae. Secondary outcomes focus on clinical, biochemical, and physiological measures related to assessment of severity of dehydration, and response to treatment by intravenous rehydration.
Discussion: Results from this pilot will contribute to generating robust definitions of outcomes (in particular for non-mortality endpoints) for a larger Phase III trial.


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Abstract

Background: Schistosome infection and soil-transmitted helminths (STHs) are major public health problems in many developing countries where they contribute to the suffering of populations living in poor settings. A cross-sectional survey was conducted in four rural villages in central region of Kenya to provide information on the status of schistosome and STH infections. Previous studies conducted in the area among primary school children showed that there were high STH and *Schistosoma mansoni* infections. This paper presents the results of a parasitological investigation and the associated risk factors of infection among adults living in the study villages.

Methods: A total of 495 adults (18-84 years) from systematically selected households were sampled during this cross-sectional survey. They were interviewed and screened for *S. mansoni* and STHs using duplicate Kato-Katz thick smears. Comparison of prevalence by age group and gender was explored by confidence interval plots, and 95% CI were obtained by generalized least squares (GLS) random effects model. Risk factors associated with *S. mansoni* infection were determined using mixed effects logistic regression at 95% CI taking into account household clusters.

Results: The study revealed that the prevalence of *S. mansoni* infection was 33.5% (95% CI 29.6-38.0) among adults in the study villages, while the prevalence of STH infection was 0.2% (95% CI 0-1.4) with hookworm being the only detected STH species. However, the village and education level were the only risk factors which showed significant evidence of association with *S. mansoni* infections.

Conclusions: The current study shows that adult communities in the study area were highly infected with *S. mansoni*. The study suggests that it may be necessary to develop contemporary approaches towards preventive chemotherapy interventions to adults in high endemic areas to complement the ongoing school-based deworming programme.


Abstract

**Background:** Naturally-acquired immunity to Plasmodium falciparum malaria develops after several episodes of infection. Fc gamma receptors (FcγRs) bind to immunoglobulin G (IgG) antibodies and mediate phagocytosis of opsonized microbes, thereby, linking humoral and cellular immunity. FcγR polymorphisms influence binding affinity to IgGs and consequently, can influence clinical malaria outcomes. Specifically, variations in FcγRIIA -131Arg/His, FcγRIIIA-176F/V and FcγRIIB-NA1/NA2 modulate immune responses through altered binding preferences to IgGs and immune complexes. Differential binding, in turn, changes ability of immune cells to respond to infection through production of inflammatory mediators during P. falciparum infection.

**Methods:** We determined the association between haplotypes of FcγRIIA-131Arg/His, FcγRIIIA-176F/V and FcγRIIB-NA1/NA2 variants and severe malarial anemia (SMA; hemoglobin < 6.0 g/dL, any density parasitemia) in children (n = 274; aged 6-36 months) presenting for their first hospital visit with P. falciparum malaria in a holoendemic transmission region of western Kenya. FcγRIIA-131Arg/His and FcγRIIIA-176F/V genotypes were determined using TaqMan® SNP genotyping, while FcγRIIBNA1/NA2 genotypes were determined using restriction fragment length polymorphism. Hematological and parasitological indices were measured in all study participants.

**Results:** Carriage of FcγRIIA-131Arg/FcγRIIIA-176F/FcγRIIBNA2 haplotype was associated with susceptibility to SMA (OR = 1.70; 95% CI; 1.02-2.93; P = 0.036), while the FcγRIIA-131His/ FcγRIIIA-176F/ FcγRIIB NA1 haplotype was marginally associated with enhanced susceptibility to SMA (OR: 1.80, 95% CI; 0.98-3.30, P = 0.057) and higher levels of parasitemia (P = 0.009). Individual genotypes of FcγRIIA-131Arg/His, FcγRIIIA-176F/V and FcγRIIB-NA1/NA2 were not associated with susceptibility to SMA.

**Conclusion:** The study revealed that haplotypes of FcγRs are important in conditioning susceptibility to SMA in immune-naïve children from P. falciparum holoendemic region of western Kenya.


Abstract

Background: Little is known about the state of mental health systems in Kenya. In 2010, Kenya promulgated a new constitution, which devolved national government and the national health system to 47 counties including Kilifi County. There is need to provide evidence from mental health systems research to identify priority areas in Kilifi's mental health system for informing county health sector decision making. We conducted an initial assessment of state of mental health systems in Kilifi County and documented resources, policy and legislation and spectrum of mental, neurological and substance use disorders.

Methods: This was a pilot study that used the brief version of the World Health Organization's Assessment Instrument for Mental Health Systems Version 2.2 to collect data. Data collection was based on the year 2014.

Results: Kilifi county has two public psychiatric outpatient units that are part of general hospitals. There is no standalone mental hospital in Kilifi. There are no inpatients or community based facilities for people with mental health problems. Although the psychiatric facilities in Kilifi have an essential drugs list, supply of drugs is erratic with frequent shortages. There is no psychiatrist or psychologist in Kilifi with only two psychiatric nurses for a population of approximately 1.2 million people. Schizophrenia was the commonest reason for visiting outpatient facilities (47.1%) while suicidal ideation was the least common (0.4%). Kenya's mental health policy, which is being used by Kilifi County, is outdated and does not cater for the current mental health needs of Kilifi. There is no specific legislation to protect the rights of people with mental health problems. No budget exists specifically for mental health care. There have been no efforts to integrate mental health care into primary care in Kilifi, and there is no empirical research work to evaluate its feasibility.

Conclusion: There is an urgent need to increase resources allocated for mental health in particular infrastructure and human resource. Policy and legislations need to be established to protect the rights of people with mental illnesses, and mental health should be integrated with primary care to increase access to services.


Abstract

The study sought to determine clientlevel and facility-level factors that affect perinatal outcomes among women attending comparable public (government owned) and non-public health facilities (non-government owned) in Kisii County-Kenya in the context of free maternity care. A total of 365 pregnant mothers recruited in 4 health facilities during their ANC visit and followed up to 2 weeks post-delivery but only 287 attended all follow-up visits. Study subjects were recruited proportionate to number of deliveries each of the facilities had conducted in the preceding 6 months. The dependent variable was perinatal outcome; independent variables were demographic and clinical factors. Analysis was done using $\chi^2$, logistic regression, paired t and McNemar’s tests. Maternal BMI and a mother's parity were statistically correlated with perinatal outcome ($\chi^2 = 8.900, \text{ d.f}=3, P=0.031$ and $\chi^2 = 13.232, \text{ d.f}=4, P=0.039$) respectively. Mothers with 1 parity were 4.5 times more likely to have normal perinatal outcomes (OR =4.5, 95% CI 2.25-14.29, P=0.012). There was a significant relationship between a mother’s knowledge of pregnancy-related issues and the baby's weight (t=-67.8 d.f. 213 P<0.001). Mothers’ knowledge on pregnancy issues and spousal involvement influences perinatal outcomes. Dietary Diversity Score (DDS) of a mother does not have a direct influence on the outcome of a pregnancy. There is need to focus on maternal factors that affect perinatal outcomes besides free maternity care.


Abstract

Background: Schistosomiasis represents a major public health problem in Tanzania despite ongoing national control efforts. This study examined whether intestinal schistosomiasis is associated with malaria and assessed the contribution of intestinal
schistosomiasis and malaria on anaemia and undernutrition in school children in Mara region, North-western Tanzania.

Methods: Stool samples were collected from each of 928 school children randomly selected from 5 schools and examined for intestinal schistosomiasis using the Kato Katz method. Finger prick blood samples were collected and examined for malaria parasites and haemoglobin concentrations using the Giemsa stain and Haemocue methods, respectively. Nutritional status was assessed by taking anthropometric measurements.

Results: The overall prevalence and infection intensity of S. mansoni was 85.6% (794/928) and 192 (100-278), respectively. The prevalence of malaria was 27.4% (254/928) with significant differences among villages ($\chi^2 = 96.11, p < 0.001$). The prevalence of anaemia was 42.3% (392/928) with significant differences among villages ($\chi^2 = 39.61, p < 0.001$). The prevalence of stunting, thinness and underweight was 21, 6.8 and 1.3%, respectively. Stunting varied significantly by sex ($\chi^2 = 267.8, p < 0.001$), age group ($\chi^2 = 96.4, p < 0.001$) and by village ($\chi^2 = 20.5, p < 0.001$). Out of the 825 infected children, 217 (26.4%) had multiple parasite infections (two to three parasites). The prevalence of co-infections occurred more frequently in boys than in girls ($\chi^2 = 21.65, p = 0.010$). Mean haemoglobin concentrations for co-infected children was significantly lower than that of children not co-infected (115.2 vs 119.6; $t = 0.01, p = 0.002$). Co-infected children were more likely to be stunted than children who were not co-infected ($\chi^2 = 11.6, p = 0.003$). On multivariate analysis, age group, village of residence and severe anaemia were significant predictors of stunting after adjusting for sex and infection status.

Conclusions: Intestinal schistosomiasis and malaria are prevalent in Mara region. Coinfections of these parasites as well as chronic undernutrition were also common. We recommend Mara region to be included in national schistosomiasis control programmes.


Abstract

Globally, about 1.5 billion people are infected with at least one species of soil-transmitted helminth (STH). Soil is a critical environmental reservoir of STH, yet there is no standard method for detecting STH eggs in soil. We developed a field method for
enumerating STH eggs in soil and tested the method in Bangladesh and Kenya. The US Environmental Protection Agency (EPA) method for enumerating Ascaris eggs in biosolids was modified through a series of recovery efficiency experiments; we seeded soil samples with a known number of Ascaris suum eggs and assessed the effect of protocol modifications on egg recovery. We found the use of 1% 7X as a surfactant compared to 0.1% Tween 80 significantly improved recovery efficiency (two-sided t-test, \( t = 5.03, p = 0.007 \)) while other protocol modifications—including different agitation and flotation methods—did not have a significant impact. Soil texture affected the egg recovery efficiency; sandy samples resulted in higher recovery compared to loamy samples processed using the same method (two-sided t-test, \( t = 2.56, p = 0.083 \)). We documented a recovery efficiency of 73% for the final improved method using loamy soil in the lab. To field test the improved method, we processed soil samples from 100 households in Bangladesh and 100 households in Kenya from June to November 2015. The prevalence of any STH (Ascaris, Trichuris or hookworm) egg in soil was 78% in Bangladesh and 37% in Kenya. The median concentration of STH eggs in soil in positive samples was 0.59 eggs/g dry soil in Bangladesh and 0.15 eggs/g dry soil in Kenya. The prevalence of STH eggs in soil was significantly higher in Bangladesh than Kenya (chi-square, \( \chi^2 = 34.39, p < 0.001 \)) as was the concentration (Mann-Whitney, \( z = 7.10, p < 0.001 \)). This new method allows for detecting STH eggs in soil in low-resource settings and could be used for standardizing soil STH detection globally.


Abstract

**Background:** Men who have sex with men (MSM) in South Africa experience discrimination from healthcare workers (HCWs), impeding health service access.

**Objectives:** To evaluate the outcomes of an MSM sensitisation training programme for HCWs implemented in the Western Cape province (South Africa).

**Methods:** A training programme was developed to equip HCWs with the knowledge, awareness and skills required to provide non-discriminatory, non-judgemental and appropriate services to MSM. Overall, 592 HCWs were trained between February 2010 and May 2012. Trainees completed self-administered pre- and post-training
questionnaires assessing changes in knowledge. Two-sample t-tests for proportion were used to assess changes in specific answers and the Wilcoxon rank-sum test for overall knowledge scores. Qualitative data came from anonymous post-training evaluation forms completed by all trainees, in combination with four focus group discussions (n = 28) conducted six months after their training.

**Results:** Fourteen per cent of trainees had received previous training to counsel clients around penile-anal intercourse, and 16% had previously received training around sexual health issues affecting MSM. There was a statistically significant improvement in overall knowledge scores (80% - 87%, p < 0.0001), specifically around penile-anal intercourse, substance use and depression after the training. Reductions in negative attitudes towards MSM and increased ability for HCWs to provide non-discriminatory care were reported as a result of the training.

**Conclusion:** MSM sensitisation training for HCWs is an effective intervention to increase awareness on issues pertaining to MSM and how to engage around them, reduce discriminatory attitudes and enable the provision of non-judgemental and appropriate services by HCWs.


**Abstract**

**Background:** Despite guidelines for cervical cancer prevention in low-resource countries, a very small proportion of women in these settings undergo screening, and even fewer women are successfully treated. Using pilot data from western Kenya and World Health Organization recommendations, we developed a protocol to implement evidence-based cervical cancer screening and linkage to treatment strategies to the rural communities. We describe the protocol for a cluster-randomized trial to compare two implementation strategies for human-papillomavirus (HPV)-based cervical cancer screening program using metrics described in the RE-AIM (reach, efficacy, adaption, implementation and maintenance) framework.

**Methods:** The study is a three-year, two-phase cluster-randomized trial in 18 communities in western Kenya. During Phase 1, six control communities were offered screening in health facilities; and six intervention communities were offered screening in
community health campaigns. Screening was done with human-papillomavirus testing through self-collected specimens. Phase 1 ended and we are working in partnership with communities to further contextualize the implementation strategy for screening, and develop an enhanced linkage to treatment plan. This plan will be tested in an additional six communities in Phase 2 (enhanced intervention). We will compare the reach, efficacy, cost-effectiveness and adaptability of the implementation strategies.

Discussion: Effective low-cost cervical cancer prevention technologies are becoming more widely available in low- and middle-income countries. Despite increasing government support for cervical cancer prevention, there remains a sizeable gap in service availability. We will use implementation science to identify the most effective strategies to fill this gap through development of context-specific evidence-based solutions. This protocol design and results can help guide implementation of cervical cancer screening in similar settings, where women are most underserved and at highest risk for disease.


Abstract

Objectives To construct growth curves for mid-upper-arm circumference (MUAC)-for-age z score for 5-19 year olds that accord with the World Health Organization growth standards, and to evaluate their discriminatory performance for subsequent mortality. Design Growth curve construction and longitudinal cohort study. Setting United States and international growth data, and cohorts in Kenya, Uganda, and Zimbabwe. Participants The Health Examination Survey (HES)/National Health and Nutrition Examination Survey (NHANES) US population datasets (age 5-25 years), which were used to construct the 2007 WHO growth reference for body mass index in this age group, were merged with an imputed dataset matching the distribution of the WHO 2006 growth standards age 2-6 years. Validation data were from 685 HIV infected children aged 5-17 years participating in the Antiretroviral Research for Watoto (ARROW) trial in Uganda and Zimbabwe; and 1741 children aged 5-13 years discharged from a rural Kenyan hospital (3.8% HIV infected). Both cohorts were followed-up for survival during one year. Main outcome measures Concordance with WHO 2006 growth standards at age 60 months and survival during one year according to MUAC-for-age and body mass index-for-age z scores. Results The new growth curves
transitioned smoothly with WHO growth standards at age 5 years. MUAC-for-age z scores of -2 to -3 and less than -3, compared with -2 or more, was associated with hazard ratios for death within one year of 3.63 (95% confidence interval 0.90 to 14.7; P=0.07) and 11.1 (3.40 to 36.0; P<0.001), respectively, among ARROW trial participants; and 2.22 (1.01 to 4.9; P=0.04) and 5.15 (2.49 to 10.7; P<0.001), respectively, among Kenyan children after discharge from hospital. The AUCs for MUAC-for-age and body mass index-for-age z scores for discriminating subsequent mortality were 0.81 (95% confidence interval 0.70 to 0.92) and 0.75 (0.63 to 0.86) in the ARROW trial (absolute difference 0.06, 95% confidence interval -0.032 to 0.16; P=0.2) and 0.73 (0.65 to 0.80) and 0.58 (0.49 to 0.67), respectively, in Kenya (absolute difference in AUC 0.15, 0.07 to 0.23; P=0.0002).

**Conclusions** The MUAC-for-age z score is at least as effective as the body mass index-for-age z score for assessing mortality risks associated with undernutrition among African school aged children and adolescents. MUAC can provide simplified screening and diagnosis within nutrition and HIV programmes, and in research.


**Abstract**

**Background:** Disability-adjusted life years (DALYs) provide a summary measure of health and can be a critical input to guide health systems, investments, and priority-setting in Ethiopia. We aimed to determine the leading causes of premature mortality and disability using DALYs and describe the relative burden of disease and injuries in Ethiopia.

**Methods:** We used results from the Global Burden of Diseases, Injuries, and Risk Factors Study 2015 (GBD 2015) for non-fatal disease burden, cause-specific mortality, and all-cause mortality to derive age-standardized DALYs by sex for Ethiopia for each year. We calculated DALYs by summing years of life lost due to premature mortality (YLLs) and years lived with disability (YLDs) for each age group and sex. Causes of death by age, sex, and year were measured mainly using Causes of Death Ensemble modeling. To estimate YLDs, a Bayesian meta-regression method was used. We reported DALY rates per 100,000 for communicable, maternal, neonatal, and nutritional (CMNN)
disorders, non-communicable diseases, and injuries, with 95% uncertainty intervals (UI) for Ethiopia.

**Results:** Non-communicable diseases caused 23,118.1 (95% UI, 17,124.4-30,579.6), CMNN disorders resulted in 20,200.7 (95% UI, 16,532.2-24,917.9), and injuries caused 3781 (95% UI, 2642.9-5500.6) age-standardized DALYs per 100,000 in Ethiopia in 2015. Lower respiratory infections, diarrheal diseases, and tuberculosis were the top three leading causes of DALYs in 2015, accounting for 2998 (95% UI, 2173.7-4029), 2592.5 (95% UI, 1850.7-3495.1), and 2562.9 (95% UI, 1466.1-4220.7) DALYs per 100,000, respectively. Ischemic heart disease and cerebrovascular disease were the fourth and fifth leading causes of age-standardized DALYs, with rates of 2535.7 (95% UI, 1603.7-3843.2) and 2159.9 (95% UI, 1369.7-3216.3) per 100,000, respectively. The following causes showed a reduction of 60% or more over the last 25 years: lower respiratory infections, diarrheal diseases, tuberculosis, neonatal encephalopathy, preterm birth complications, meningitis, malaria, protein-energy malnutrition, iron-deficiency anemia, measles, war and legal intervention, and maternal hemorrhage.

**Conclusions:** Ethiopia has been successful in reducing age-standardized DALYs related to most communicable, maternal, neonatal, and nutritional deficiency diseases in the last 25 years, causing a major ranking shift to types of non-communicable disease. Lower respiratory infections, diarrheal disease, and tuberculosis continue to be leading causes of premature death, despite major declines in burden. Non-communicable diseases also showed reductions as premature mortality declined; however, disability outcomes for these causes did not show declines. Recently developed non-communicable disease strategies may need to be amended to focus on cardiovascular diseases, cancer, diabetes, and major depressive disorders. Increasing trends of disabilities due to neonatal encephalopathy, preterm birth complications, and neonatal disorders should be emphasized in the national newborn survival strategy. Generating quality data should be a priority through the development of new initiatives such as vital events registration, surveillance programs, and surveys to address gaps in data. Measuring disease burden at subnational regional state levels and identifying variations with urban and rural population health should be conducted to support health policy in Ethiopia.

Abstract

**Background:** Ethiopia lacks a complete vital registration system that would assist in measuring disease burden and risk factors. We used the Global Burden of Diseases, Injuries, and Risk Factors Study 2015 (GBD 2015) estimates to describe the mortality burden from communicable, non-communicable, and other diseases in Ethiopia over the last 25 years.

**Methods:** GBD 2015 mainly used cause of death ensemble modeling to measure causes of death by age, sex, and year for 195 countries. We report numbers of deaths and rates of years of life lost (YLL) for communicable, maternal, neonatal, and nutritional (CMNN) disorders, non-communicable diseases (NCDs), and injuries with 95% uncertainty intervals (UI) for Ethiopia from 1990 to 2015.

**Results:** CMNN causes of death have declined by 65% in the last two-and-a-half decades. Injury-related causes of death have also decreased by 70%. Deaths due to NCDs declined by 37% during the same period. Ethiopia showed a faster decline in the burden of four out of the five leading causes of age-standardized premature mortality rates when compared to the overall sub-Saharan African region and the Eastern sub-Saharan African region: lower respiratory infections, tuberculosis, HIV/AIDS, and diarrheal diseases; however, the same could not be said for ischemic heart disease and other NCDs. Non-communicable diseases, together, were the leading causes of age-standardized mortality rates, whereas CMNN diseases were leading causes of premature mortality in 2015. Although lower respiratory infections, tuberculosis, and diarrheal disease were the leading causes of age-standardized death rates, they showed major declines from 1990 to 2015. Neonatal encephalopathy, iron-deficiency anemia, protein-energy malnutrition, and preterm birth complications also showed more than a 50% reduction in burden. HIV/AIDS-related deaths have also decreased by 70% since 2005. Ischemic heart disease, hemorrhagic stroke, and ischemic stroke were among the top causes of premature mortality and age-standardized death rates in Ethiopia in 2015.

**Conclusions:** Ethiopia has been successful in reducing deaths related to communicable, maternal, neonatal, and nutritional deficiency diseases and injuries by 65%, despite unacceptably high maternal and neonatal mortality rates. However, the country’s performance regarding non-communicable diseases, including cardiovascular disease, diabetes, cancer, and chronic respiratory disease, was minimal, causing these diseases to join the leading causes of premature mortality and death rates in 2015. While the country is progressing toward universal health coverage, prevention and control strategies in Ethiopia should consider the double burden of common infectious diseases and non-communicable diseases: lower respiratory infections, diarrhea, tuberculosis, HIV/AIDS,
cardiovascular disease, cancer, and diabetes. Prevention and control strategies should also pay special attention to the leading causes of premature mortality and death rates caused by non-communicable diseases: cardiovascular disease, cancer, and diabetes. Measuring further progress requires a data revolution in generating, managing, analyzing, and using data for decision-making and the creation of a full vital registration system in the country.


Abstract

**Introduction:** male partner involvement in elimination of mother-to-child transmission (eMTCT) of HIV activities remains low in Western Kenya, despite its importance in reducing rates of child HIV transmission. We sought to identify factors associated with male partner involvement in eMTCT in Kisumu East sub-County, Western Kenya.

**Methods:** we conducted a cross-sectional study among women aged ≥ 18 years who had children aged ≤ 12 months and were attending a child health clinic for immunization services in one of four Western Kenya health centers between February and April, 2015. We assessed male involvement using an "involvement index" of five factors of equal weight: partner antenatal care (ANC) attendance, partner HIV testing, partner financial support to the woman during ANC, partner awareness of ANC services and partner participation in decision making on contraception including condom use. Male involvement was classified as high or low based on their index score. We calculated odds ratios (OR) and 95% confidence intervals (CI) to identify factors associated with high male partner involvement.

**Results:** we recruited 216 female participants. Mean age was 26.1 years (± 5.5 years), 189 (87.5%) were married. The majority (94.4%) had attended ANC in public health facilities. Nineteen percent of women had high male involvement. Having > 8 years of formal education (AOR 3.9, CI = 1.51-10.08), having male partner who was employed, history of previous couple testing (AOR = 3.2, CI = 1.42-7.22) and reports of partner having read the mother-child booklet during ANC (AOR = 2.9, CI = 1.30-6.49), were associated with high male involvement.
**Conclusion**: based on our findings, we recommend targeted strategies to actively sensitize men and encourage their involvement in eMTCT, particularly among partners of women with fewer years of education and among partners who are not employed.