### 2015 KEMRI PUBLICATIONS

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**Abstract**

Malaria is among the leading causes of mortality in the younger under-five group of children zero to four years of age. This study aims at describing the relationship between rainfall and temperature on under-five malaria or anaemia mortality in Kenya Medical Research Institute and United States Centers for Disease Control (KEMRI/CDC) Health and Demographic Surveillance System (HDSS). This study was conducted through the ongoing KEMRI and CDC collaboration. A general additive model with a Poisson link function was fit to model the weekly association of lagged cumulative rainfall and average temperature on malaria/anemia mortality in KEMRI/CDC HDSS for the period 2003 to 2008. A trend function was included in the model to control for time trends and seasonality not explained by weather fluctuations. 95% confidence intervals was presented with estimates. Malaria or anemia mortality was found to be associated with changes in temperature and rainfall in the KEMRI HDSS, with a delay up to 16 weeks. The empirical estimates of associations describe established biological relationships well. This information, and particularly, the strength of the relationships over longer lead times can highlight the possibility of developing a predictive forecast with lead times up to 16 weeks in order to enhance preparedness to high transmission episodes.


**Abstract**

Infections are among the leading causes of neonatal mortality, and about 75% of the burden occurs in developing countries. Diagnosis of neonatal sepsis in these countries is dependent on the recognition of a set of nonspecific clinical signs that maximize sensitivity because staff making initial assessments may not have specialist pediatric training. Accurate diagnosis is usually limited by the unavailability of reliable microbiological investigation. The World Health Organization recommends ampicillin (or penicillin; cloxacillin if staphylococcal infection is suspected) plus gentamicin for
empiric treatment of neonates with suspected clinical sepsis or meningitis. However, there is a lack of comprehensive data on the causes of infection and antimicrobial susceptibility in developing countries to support these recommendations, especially in rural settings. Bacterial pathogens (predominantly Gram negative) with reduced susceptibility to empiric medication have been reported, with variations both between and within regions. Nosocomial infections with resistant organisms and high case fatality challenge the first-line use of cephalosporins. Improving local surveillance data using standardized antimicrobial susceptibility testing methods and validation of diagnostic algorithms against microbial findings are essential. Standardized reporting of treatment outcomes is required to evaluate practice, provide guidance on second-line regimes and for studies of new approaches, such as simplified community-based regimens, and to determine the appropriate duration of empiric treatment for apparently low-risk neonates with early resolution of clinical signs, or where available, negative blood cultures. Thus, a multifaceted approach, with attention to microbiological quality assurance, is needed to better guide antimicrobial use and reduce mortality and long-term impairments.


Abstract

Background: The diagnosis of lymphatic filariasis (LF) is based typically on either microfilaraemia as assessed by microscopy or filarial antigenaemia using an immunochromatographic test. While it is known that estimates of antigenaemia are generally higher than estimates of microfilaraemia, the extent of the difference is not known.

Methods: This paper presents the results of an extensive literature search for surveys that estimated both microfilaraemia and antigenaemia in order to better understand the disparity between the two measures.

Results and conclusions: In some settings there was a very large disparity, up to 40-70%, between estimates of microfilaraemia and antigenaemia. Regression analysis was unable to identify any predictable relationship between the two measures. The implications of findings for risk mapping and surveillance of LF are discussed.


Abstract

Continuous monitoring in health and demographic surveillance sites (HDSS) allows for collection of longitudinal demographic data, health related, and socio-economic indicators of the site population. We sought to use household survey data collected between 2002 and 2006 in the Kenya Medical Research Institute in collaboration with Centers for Disease Control and prevention (KEMRI/CDC) HDSS site in Asembo and Gem Western Kenya to estimate socio-economic status (SES) and assess changes of SES over time and space. Data on household assets and characteristics, mainly source of drinking water, cooking fuel, and occupation of household head was annually collected from 44,313 unique households during the study period. An SES index was calculated as a weighted average of assets using weights generated via Principal Component Analysis (PCA), Polychoric PCA, and Multiple Correspondence Analysis (MCA) methods applied to the pooled data. The index from the best method was used to rank households into SES quintiles and assess their transition over time across SES categories. Kriging was employed to produce SES maps at the start and the end of the study period. First component of PCA, Polychoric PCA, and MCA accounted for 13.7%, 31.8%, and 47.3%, respectively of the total variance of all variables. The gap between the poorest and the least poor increased from 1% at the start to 6% at the end of the study period. Spatial analysis revealed that the increase in least poor households was centered in the lower part of study area (Asembo) over time. No significant changes were observed in Gem. The HDSS sites can provide a platform to assess spatial-temporal changes in the SES status of the population. Evidence on how SES varied over time and space within the same geographical area may provide a useful tool to design interventions in health and other areas that have a close bearing to the SES of the population.


Abstract

Sharing individual-level data from clinical and public health research is increasingly being seen as a core requirement for effective and efficient biomedical research. This article discusses the results of a systematic review and multisite qualitative study of key stakeholders' perspectives on best practices in ethical data sharing in low- and middle-income settings. Our research suggests that for data sharing to be effective and sustainable, multiple social and ethical requirements need to be met. An effective model of data sharing will be one in which considered judgments will need to be made about how best to achieve scientific progress, minimize risks of harm, promote fairness and reciprocity, and build and sustain trust.


Abstract

Priority setting research has focused on the macro (national) and micro (bedside) level, leaving the meso (institutional, hospital) level relatively neglected. This is surprising given the key role that hospitals play in the delivery of healthcare services and the large proportion of health systems resources that they absorb. To explore the factors that impact upon priority setting at the hospital level, we conducted a thematic review of empirical studies. A systematic search of PubMed, EBSCOHOST, Econlit databases and Google scholar was supplemented by a search of key websites and a manual search of relevant papers' reference lists. A total of 24 papers were identified from developed and developing countries. We applied a policy analysis framework to examine and synthesize the findings of the selected papers. Findings suggest that priority setting practice in hospitals was influenced by (1) contextual factors such as decision space, resource availability, financing arrangements, availability and use of information, organizational culture and leadership, (2) priority setting processes that depend on the type of priority setting activity, (3) content factors such as priority setting criteria and (4) actors, their interests and power relations. We observe that there is need for studies to examine these issues and the interplay between them in greater depth and propose a conceptual framework that might be useful in examining priority setting practices in hospitals.

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<td><strong>Abstract</strong></td>
<td>Preterm newborns are highly susceptible to bacterial infections. This susceptibility is regarded as being due to immaturity of multiple pathways of the immune system. However, it is unclear whether a mechanism that unifies these different, suppressed pathways exists. Here, we argue that the immune vulnerability of the preterm neonate is critically related to arginine depletion. Arginine, a &quot;conditionally essential&quot; amino acid, is depleted in acute catabolic states, including sepsis. Its metabolism is highly compartmentalized and regulated, including by arginase-mediated hydrolysis. Recent data suggest that arginase II-mediated arginine depletion is essential for the innate immune suppression that occurs in newborn models of bacterial challenge, impairing pathways critical for the immune response. Evidence that arginine depletion mediates protection from immune activation during first gut colonization suggests a regulatory role in controlling gut-derived pathogens. Clinical studies show that plasma arginine is depleted during sepsis. In keeping with animal studies, small clinical trials of L-arginine supplementation have shown benefit in reducing necrotizing enterocolitis in premature neonates. We propose a novel, broader hypothesis that arginine depletion during bacterial challenge is a key factor limiting the neonate's ability to mount an adequate immune response, contributing to the increased susceptibility to infections, particularly with respect to gut-derived sepsis.</td>
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<td><strong>Abstract</strong></td>
<td>Sickle cell disease (SCD) is a single gene disorder causing a debilitating systemic syndrome characterised by chronic anaemia, acute painful episodes, organ infarction and chronic organ damage and by a significant reduction in life expectancy. The origin of SCD lies in the malarial regions of the tropics where carriers are protected against death from malaria and hence enjoy an evolutionary advantage. More recently, population migration has meant that SCD now has a worldwide distribution and that a substantial number of children are born with the condition in higher-income areas,</td>
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including large parts of Europe and North and South America. Newborn screening, systematic clinical follow-up and prevention of sepsis and organ damage have led to an increased life expectancy among people with SCD in many such countries; however, in resource-limited settings where the majority continue to be born, most affected children continue to die in early childhood, usually undiagnosed, due to the lack of effective programmes for its early detection and treatment. As new therapies emerge, potentially leading to disease amelioration or cure, it is of paramount importance that the significant burden of SCD in resource-poor countries is properly recognised.


**Abstract**

Tuberculosis (TB) in pregnancy poses a substantial risk of morbidity to both the pregnant woman and the fetus if not diagnosed and treated in a timely manner. Assessing the risk of having Mycobacterium tuberculosis infection is essential to determining when further evaluation should occur. Obstetrician-gynecologists are in a unique position to identify individuals with infection and facilitate further evaluation and follow up as needed. A TB evaluation consists of a TB risk assessment, medical history, physical examination, and a symptom screen; a TB test should be performed if indicated by the TB evaluation. If a pregnant woman has signs or symptoms of TB or if the test result for TB infection is positive, active TB disease must be ruled out before delivery, with a chest radiograph and other diagnostics as indicated. If active TB disease is diagnosed, it should be treated; providers must decide when treatment of latent TB infection is most beneficial. Most women will not require latent TB infection treatment while pregnant, but all require close follow up and monitoring. Treatment should be coordinated with the TB control program within the respective jurisdiction and initiated based on the woman's risk factors including social history, comorbidities (particularly human immunodeficiency virus [HIV] infection), and concomitant medications.


Abstract

**Background:** Priority setting in healthcare is a key determinant of health system performance. However, there is no widely accepted priority setting evaluation framework. We reviewed literature with the aim of developing and proposing a framework for the evaluation of macro and meso level healthcare priority setting practices.

**Methods:** We systematically searched Econlit, PubMed, CINAHL, and EBSCOhost databases and supplemented this with searches in Google Scholar, relevant websites and reference lists of relevant papers. A total of 31 papers on evaluation of priority setting were identified. These were supplemented by broader theoretical literature related to evaluation of priority setting. A conceptual review of selected papers was undertaken.

**Results:** Based on a synthesis of the selected literature, we propose an evaluative framework that requires that priority setting practices at the macro and meso levels of the health system meet the following conditions: (1) Priority setting decisions should incorporate both efficiency and equity considerations as well as the following outcomes; (a) Stakeholder satisfaction, (b) Stakeholder understanding, (c) Shifted priorities (reallocation of resources), and (d) Implementation of decisions. (2) Priority setting processes should also meet the procedural conditions of (a) Stakeholder engagement, (b) Stakeholder empowerment, (c) Transparency, (d) Use of evidence, (e) Revisions, (f) Enforcement, and (g) Being grounded on community values.

**Conclusion:** Available frameworks for the evaluation of priority setting are mostly grounded on procedural requirements, while few have included outcome requirements. There is, however, increasing recognition of the need to incorporate both consequential and procedural considerations in priority setting practices. In this review, we adapt an integrative approach to develop and propose a framework for the evaluation of priority setting practices at the macro and meso levels that draws from these complementary schools of thought.


Abstract

The last ten years have witnessed a significant scale-up and access to antiretroviral therapy in Africa, which has improved patient quality of life and survival. One major challenge associated with increased access to antiretroviral therapy is the development of antiretroviral resistance due to inconsistent drug supply and/or poor patient adherence. We review the current state of both acquired and transmitted drug resistance in Africa over the past ten years (2001-2011) to identify drug resistance associated with the different drug regimens used on the continent and to help guide affordable strategies for drug resistance surveillance. A total of 161 references (153 articles, six reports and two conference abstracts) were reviewed. Antiretroviral resistance data was available for 40 of 53 African countries. A total of 5,541 adult patients from 99 studies in Africa were included in this analysis. The pooled prevalence of drug resistance mutations in Africa was 10.6%, and Central Africa had the highest prevalence of 54.9%. The highest prevalence of nucleoside reverse transcriptase inhibitor mutations was in the west (55.3%) and central (54.8%) areas; nonnucleoside reverse transcriptase inhibitor mutations were highest in East Africa (57.0%) and protease inhibitors mutations highest in Southern Africa (16.3%). The major nucleoside reverse transcriptase inhibitor mutation in all four African regions was M184V. Major nonnucleoside reverse transcriptase inhibitor as well as protease inhibitor mutations varied by region. The prevalence of drug resistance has remained low in several African countries although the emergence of drug resistance mutations varied across countries. Continued surveillance of antiretroviral therapy resistance remains crucial in gauging the effectiveness of country antiretroviral therapy programs and strategizing on effective and affordable strategies for successful treatment.


Abstract

Background: The importance of early initiation of antiretroviral therapy (ART) for tuberculosis (TB) and HIV-coinfected patients is controversial. We conducted a systematic review and meta-analysis to assess the effect of early initiation of ART (within 2-4 weeks of TB treatment) on several treatment outcomes among TB/HIV-coinfected patients.
**Method:** A systematic search of clinical trials was performed in PubMed, Embase, Google Scholar, Science Direct, Medscape, and the Cochrane library. Clinical trials which were published in any language before the last date of search (March 31, 2015) were included. The qualities of the studies were assessed using criteria from the Cochrane Library. Heterogeneity test was conducted to assess the variations among study outcomes. For each study outcome, the risk ratio (RR) with 95% confidence interval (CI) was calculated as a measure of intervention effect. The Mantel-Haenszel method was used to estimate the RR using a fixed-effects model.

**Findings:** A total of 2272 study participants from 6 trials were included in the meta-analysis. Early ART initiation during TB treatment was associated with reduced all-cause mortality (RR = 0.78; 95% CI = 0.63-0.98) and increased rate of TB-associated immune reconstitution inflammatory syndrome (TB-IRIS; RR = 2.19; 95% CI = 1.77-2.70) and death related to TB-IRIS (RR = 6.94; 95% CI = 1.26-38.22). However, the time of ART initiation has no association with TB cure rate (RR = 0.99; 95% CI = 0.81-1.07), rate of drug toxicity (RR = 1.00; 95% CI = 0.93-1.08), death associated with drug toxicity (RR = 0.40; 95% CI = 0.14-1.16), rate of low viral load (less than 400 copies/mL; RR = 1.00; 95% CI = 0.96-1.04), and rate of new AIDS-defining illness (RR = 0.84; 95% CI = 0.60-1.18). Immunological response in early ART arms of study participant in different trials showed a greater or equal response compared with late ART arms.

**Conclusion:** This systematic review presents conclusive evidence on the reduction of all-cause mortality as a result of early initiation of ART. However, this study also confirms the high rate of TB-IRIS and death associated with it. Operational and implementation research are required to maintain the benefit of early ART initiation and proper management of TB-IRIS. Studies on the timing of ART in extrapulmonary and multidrug-resistant TB are recommended.


**Abstract**

**Background:** Tuberculosis (TB) requires at least six months of treatment. If treatment is incomplete, patients may not be cured and drug resistance may develop. Directly Observed Therapy (DOT) is a specific strategy, endorsed by the World Health Organization, to improve adherence by requiring health workers, community volunteers or family members to observe and record patients taking each dose.
**Objectives:** To evaluate DOT compared to self-administered therapy in people on treatment for active TB or on prophylaxis to prevent active disease. We also compared the effects of different forms of DOT.

**Search methods:** We searched the following databases up to 13 January 2015: the Cochrane Infectious Diseases Group Specialized Register; the Cochrane Central Register of Controlled Trials (CENTRAL), published in the Cochrane Library; MEDLINE; EMBASE; LILACS and mRCT. We also checked article reference lists and contacted relevant researchers and organizations.

**Selection criteria:** Randomized controlled trials (RCTs) and quasi-RCTs comparing DOT with routine self-administration of treatment or prophylaxis at home.

**Data collection and analysis:** Two review authors independently assessed risk of bias of each included trial and extracted data. We compared interventions using risk ratios (RR) with 95% confidence intervals (CI). We used a random-effects model if meta-analysis was appropriate but heterogeneity present (I(2) statistic > 50%). We assessed the quality of the evidence using the GRADE approach.

**Main results:** Eleven trials including 5662 participants met the inclusion criteria. DOT was performed by a range of people (nurses, community health workers, family members or former TB patients) in a variety of settings (clinic, the patient's home or the home of a community volunteer). DOT versus self-administered Six trials from South Africa, Thailand, Taiwan, Pakistan and Australia compared DOT with self-administered therapy for treatment. Trials included DOT at home by family members, community health workers (who were usually supervised); DOT at home by health staff; and DOT at health facilities. TB cure was low with self-administration across all studies (range 41% to 67%), and direct observation did not substantially improve this (RR 1.08, 95% CI 0.91 to 1.27; five trials, 1645 participants, moderate quality evidence). In a subgroup analysis stratified by the frequency of contact between health services in the self-treatment arm, daily DOT may improve TB cure when compared to self-administered treatment where patients in the self-administered group only visited the clinic every month (RR 1.15, 95% CI 1.06 to 1.25; two trials, 900 participants); but with contact in the control becoming more frequent, this small effect was not apparent (every two weeks: RR 0.96, 95% CI 0.83 to 1.12; one trial, 497 participants; every week: RR 0.90, 95% CI 0.68 to 1.21; two trials, 248 participants). Treatment completion showed a similar pattern, ranging from 59% to 78% in the self-treatment groups, and direct observation did not improve this (RR 1.07, 95% CI 0.96 to 1.19; six trials, 1839 participants, moderate quality evidence). DOT at home versus DOT at health facility In four trials that compared DOT at home by family members, or community health workers, with DOT by health workers at a health facility there was little or no difference in cure or treatment completion (cure: RR 1.02, 95% CI 0.88 to
1.18, four trials, 1556 participants, moderate quality evidence; treatment completion: RR 1.04, 95% CI 0.91 to 1.17, three trials, 1029 participants, moderate quality evidence). DOT by family member versus DOT by community health worker Two trials compared DOT at home by family members with DOT at home by community health workers. There was also little or no difference in cure or treatment completion (cure: RR 1.02, 95% CI 0.86 to 1.21; two trials, 1493 participants, moderate quality evidence; completion: RR 1.05, 95% CI 0.90 to 1.22; two trials, 1493 participants, low quality evidence). Specific patient categories A trial of 300 intravenous drug users in the USA evaluated direct observation with no observation in TB prophylaxis to prevent active disease and showed little difference in treatment completion (RR 1.00, 95% CI 0.88 to 1.13; one trial, 300 participants, low quality evidence).

**Authors' conclusions:** From the existing trials, DOT did not provide a solution to poor adherence in TB treatment. Given the large resource and cost implications of DOT, policy makers might want to reconsider strategies that depend on direct observation. Other options might take into account financial and logistical barriers to care; approaches that motivate patients and staff; and defaulter follow-up.


14. Behrens RH, Neave PE, Jones CO. Imported malaria among people who travel to visit friends and relatives: is current UK policy effective or does it need a strategic change? Malar J. 2015 Apr 9;14:149.

**Abstract**

**Background:** The proportion of all imported malaria reported in travellers visiting friends and relatives (VFRs) in the UK has increased over the past decade and the proportion of Plasmodium falciparum malaria affecting this group has remained above 80% during that period. The epidemiological data suggest that the strategies employed in the UK to prevent imported malaria have been ineffective for VFRs. This paper attempts to identify possible reasons for the failure of the malaria prevention strategy among VFRs and suggest potential alternatives.

**Methods:** A review of the current UK malaria prevention guidelines was undertaken and their approach was compared to the few data that are available on malaria perceptions and practices among VFRs.

**Results:** The current UK malaria prevention guidelines focus on educating travellers and health professionals using messages based on the personal threat of malaria and promoting the benefits of avoiding disease through the use of chemoprophylaxis.
While malaria morbidity disproportionately affects VFRs, the mortality rates from malaria in VFRs is eight times, and severe disease eight times lower than in tourist and business travellers. Recent research into VFR malaria perceptions and practices has highlighted the complex socio-ecological context within which VFRs make their decisions about malaria. These data suggest that alternative strategies that move beyond a knowledge-deficit approach are required to address the burden of malaria in VFRs.

**Discussion:** Potential alternative strategies include the use of standby emergency-treatment (SBET) for the management of fevers with an anti-malarial provided pre-travel, the provision of rapid diagnostic testing and treatment regimen based in general-practitioner surgeries, and urgent and walk-in care centres and local accident and emergency (A&E) departments to provide immediate diagnosis and accessible ambulatory treatment for malaria patients. This latter approach would potentially address some of the practical barriers to reducing the burden of malaria in VFRs by moving the process nearer to the community.


**Abstract**

**Background:** An important prelude to developing strategies to control infectious diseases is a detailed epidemiological evidence platform to target cost-effective interventions and define resource needs.

**Methods:** A review of published and un-published reports of malaria vector control and parasite prevention in Uganda was conducted for the period 1900-2013. The objective was to provide a perspective as to how epidemiological intelligence was used to design malaria control before and during the global malaria eradication programme (GMEP) and to contrast this with the evidence generated in support of the Roll Back Malaria (RBM) initiative from 1998 to date.

**Results:** During the GMEP era, comprehensive investigations were undertaken on the effectiveness of vector and parasite control such as indoor residual house-spraying (IRS) and mass drug administration (MDA) at different sites in Uganda. Nationwide malariometric surveys were undertaken between 1964 and 1967 to provide a profile of risk, epidemiology and seasonality leading to an evidence-based national cartography
of risk to characterize the diversity of malaria transmission in Uganda. At the launch of the RBM initiative in the late 1990s, an equivalent level of evidence was lacking. There was no contemporary national evidence-base for the likely impact of insecticide-treated nets (ITN), no new malariometric data, no new national cartography of malaria risk or any evidence of tailored intervention delivery based on variations in the ecology of malaria risk in Uganda.

Discussion: Despite millions of dollars of overseas development assistance over the last ten years in ITN, and more recently the resurrection of the use of IRS, the epidemiological impact of vector control remains uncertain due to an absence of nationwide basic parasite and vector-based field studies.

Conclusion: Readily available epidemiological data should become the future business model to maximize malaria funding from 2015. Over the next five to ten years, accountability, impact analysis, financial business cases supported by a culture of data use should become the new paradigm by which malaria programmes, governments and their development partners operate.


Abstract

The agglutination assay is used to determine the ability of antibodies to recognize parasite variant antigens on the surface of Plasmodium falciparum-infected erythrocytes. In this technique, infected erythrocytes are selectively labelled with a DNA-binding fluorescent dye and mixed with antibodies of interest to allow antibody-surface antigen binding. Recognition of surface antigens by the antibodies can result in the formation of agglutinates containing multiple parasite-infected erythrocytes. These can be viewed and quantified using a fluorescence microscope.


Abstract
**Background:** A variety of in-service emergency care training courses are currently being promoted as a strategy to improve the quality of care provided to seriously ill newborns and children in low-income countries. Most courses have been developed in high-income countries. However, whether these courses improve the ability of health professionals to provide appropriate care in low-income countries remains unclear. This is the first update of the original review.

**Objectives:** To assess the effects of in-service emergency care training on health professionals' treatment of seriously ill newborns and children in low-income countries.

**Search methods:** For this update, we searched the Cochrane Database of Systematic Reviews, part of The Cochrane Library (www.cochranelibrary.com); MEDLINE, Ovid SP; EMBASE, Ovid SP; the Cochrane Central Register of Controlled Trials (CENTRAL), part of The Cochrane Library (www.cochranelibrary.com) (including the Cochrane Effective Practice and Organisation of Care (EPOC) Group Specialised Register); Science Citation Index and Social Sciences Citation Index, Institute for Scientific Information (ISI) Web of Knowledge/Science and eight other databases. We performed database searches in February 2015. We also searched clinical trial registries, websites of relevant organisations and reference lists of related reviews. We applied no date, language or publication status restrictions when conducting the searches.

**Selection criteria:** Randomised trials, non-randomised trials, controlled before and after studies and interrupted-time-series studies that compared the effects of in-service emergency care training versus usual care were eligible for inclusion. We included only hospital-based studies and excluded community-based studies. Two review authors independently screened and selected studies for inclusion.

**Data collection and analysis:** Two review authors independently extracted data and assessed study risk of bias and confidence in effect estimates (certainty of evidence) for each outcome using GRADE (Grades of Recommendation, Assessment, Development and Evaluation). We described results and presented them in GRADE tables.

**Main results:** We identified no new studies in this update. Two randomised trials (which were included in the original review) met the review eligibility criteria. In the first trial, newborn resuscitation training compared with usual care improved provider performance of appropriate resuscitation (trained 66% vs usual care 27%, risk ratio 2.45, 95% confidence interval (CI) 1.75 to 3.42; moderate certainty evidence) and reduced inappropriate resuscitation (trained mean 0.53 vs usual care 0.92, mean difference 0.40, 95% CI 0.13 to 0.66; moderate certainty evidence). Effect on neonatal mortality was inconclusive (trained 28% vs usual care 25%, risk ratio 0.77, 95% CI...
Findings from the second trial suggest that essential newborn care training compared with usual care probably slightly improves delivery room newborn care practices (assessment of breathing, preparedness for resuscitation) (moderate certainty evidence).

**Authors' conclusions:** In-service neonatal emergency care courses probably improve health professionals' treatment of seriously ill babies in the short term. Further multi-centre randomised trials evaluating the effects of in-service emergency care training on long-term outcomes (health professional practice and patient outcomes) are needed.


**Abstract**

Sub-Saharan Africa is a highly diverse geo-political region. Any brief discussion of the progress made over the last 15 years towards the Millennium Development Goals (MDGs) will therefore not do justice to the true complexity of context and events. Our focus will be MDG4—to reduce child mortality by 66% from 1990 levels. We will touch briefly on MDG1, to eradicate extreme poverty and hunger, MDG2, to achieve universal primary education, and MDG5, to improve maternal health, which are inextricably linked with child well-being. We will also draw on an eclectic mix of additional global indicators. Acknowledging the limitations of this approach, we first offer a summary of expected progress and then point to debates on future goals.


**Abstract**

Tuberculosis (TB) today remains a global emergency affecting 9.0 million people globally. The African Region bears the highest global TB/HIV burden and over 50% of TB cases in SSA are co-infected with HIV. An estimated 1.5 million died from the TB globally in 2013. A large majority of the 360,000 HIV-positive TB cases who died
were from sub-Saharan Africa. Research and development is an important pillar of the WHO post-2015 global TB strategy. Advances in development of diagnostics, drugs, host-directed therapies, and vaccines will require evaluation under field conditions through multi-centre clinical trials at different geographical locations. Thus it is critically important that these evaluations are fully supported by all African governments and the capacity, trained staff and infrastructure required to perform the research and evaluations is built and made available. This viewpoint article reviews the opportunities provided by recently launched second programme (2015-2024) of the European & Developing Countries Clinical Trials Partnership (EDCTP2) for tackling the TB epidemic in Africa through its magnanimous portfolio. The unique opportunities provided by EDCTP2 for leadership of scientific research in TB and other diseases fully devolving to Africa are also covered.


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<td><strong>Abstract</strong></td>
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<td>Mutations in the Plasmodium falciparum K13-propeller domain have recently been shown to be important determinants of artemisinin resistance in Southeast Asia. This study investigated the prevalence of K13-propeller polymorphisms across sub-Saharan Africa. A total of 1212 P. falciparum samples collected from 12 countries were sequenced. None of the K13-propeller mutations previously reported in Southeast Asia were found, but 22 unique mutations were detected, of which 7 were nonsynonymous. Allele frequencies ranged between 1% and 3%. Three mutations were observed in &gt;1 country, and the A578S was present in parasites from 5 countries. This study provides the baseline prevalence of K13-propeller mutations in sub-Saharan Africa.</td>
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Abstract

Although global efforts in the past decade have halved the number of deaths due to malaria, there are still an estimated 219 million cases of malaria a year, causing more than half a million deaths. In this forum article, we asked experts working in malaria research and control to discuss the ways in which malaria might eventually be eradicated. Their collective views highlight the challenges and opportunities, and explain how multi-factorial and integrated processes could eventually make malaria eradication a reality.


Abstract

Background: Enteric fever due to Salmonella Typhi (typhoid fever) occurs in urban areas with poor sanitation. While direct fecal-oral transmission is thought to be the predominant mode of transmission, recent evidence suggests that indirect environmental transmission may also contribute to disease spread.

Methods: Data from a population-based infectious disease surveillance system (28,000 individuals followed biweekly) were used to map the spatial pattern of typhoid fever in Kibera, an urban informal settlement in Nairobi Kenya, between 2010-2011. Spatial modeling was used to test whether variations in topography and accumulation of surface water explain the geographic patterns of risk.

Results: Among children less than ten years of age, risk of typhoid fever was geographically heterogeneous across the study area (p = 0.016) and was positively associated with lower elevation, OR = 1.87, 95% CI (1.36-2.57), p <0.001. In contrast, the risk of typhoid fever did not vary geographically or with elevation among individuals more than ten years of age [corrected].

Conclusions: Our results provide evidence of indirect, environmental transmission of typhoid fever among children, a group with high exposure to fecal pathogens in the environment. Spatially targeting sanitation interventions may decrease enteric fever transmission.

Abstract

The global agenda for malaria has, once again, embraced the possibility of eradication. As history has shown, there will be no single magic bullet that can be applied to every epidemiological setting. Africa has a diverse malaria ecology, lending itself to some of the highest disease burden areas of the world and a wide range of clinical epidemiological patterns making control with our current tools challenging. This commentary highlights why the epidemiology of Plasmodium falciparum malaria in Africa should not be forgotten when planning an eradication strategy, and why forgetting Africa will, once again, be the single largest threat to any hope for global eradication.


Abstract

Shigellae cause significant diarrheal disease and mortality in humans, as there are approximately 163 million episodes of shigellosis and 1.1 million deaths annually. While significant strides have been made in the understanding of the pathogenesis, few studies on the genomic content of the Shigella species have been completed. The goal of this study was to characterize the genomic diversity of Shigella species through sequencing of 55 isolates representing members of each of the four Shigella species: S. flexneri, S. sonnei, S. boydii, and S. dysenteriae. Phylogeny inferred from 336 available Shigella and Escherichia coli genomes defined exclusive clades of Shigella; conserved genomic markers that can identify each clade were then identified. PCR assays were developed for each clade-specific marker, which was combined with an amplicon for the conserved Shigella invasion antigen, IpaH3, into a multiplex PCR assay. This assay demonstrated high specificity, correctly identifying 218 of 221 presumptive Shigella isolates, and sensitivity, by not identifying any of 151 diverse E. coli isolates incorrectly as Shigella. This new phylogenomics-based PCR assay represents a valuable tool for rapid typing of uncharacterized Shigella isolates and
provides a framework that can be utilized for the identification of novel genomic markers from genomic data.


Abstract

Background: Soil-transmitted helminths (STHs) infect over a billion individuals worldwide. In India, 241 million children are estimated to need deworming to avert the negative consequences STH infections can have on child health and development. In February-April 2011, 17 million children in Bihar State were dewormed during a government-led school-based deworming campaign. Prior to programme implementation, a study was conducted to assess STH prevalence in the school-age population to direct the programme. The study also investigated risk factors for STH infections, including caste, literacy, and defecation and hygiene practices, in order to inform the development of complementary interventions.

Methods: A cross-sectional survey was conducted among children in 20 schools in Bihar. In addition to providing stool samples for identification of STH infections, children completed a short questionnaire detailing their usual defecation and hygiene practices. Risk factors for STH infections were explored.

Results: In January-February 2011, 1279 school children aged four to seventeen provided stool samples and 1157 children also completed the questionnaire. Overall, 68% of children (10-86% across schools) were infected with one or more soil-transmitted helminth species. The prevalence of ascariasis, hookworm and trichuriasis was 52%, 42% and 5% respectively. The majority of children (95%) practiced open defecation and reported most frequently cleansing hands with soil (61%). Increasing age, lack of maternal literacy and certain castes were independently associated with hookworm infection. Absence of a hand-washing station at the schools was also independently associated with A. lumbricoides infection.

Conclusions: STH prevalence in Bihar is high, and justifies mass deworming in school-aged children. Open defecation is common-place and hands are often cleansed using soil. The findings reported here can be used to help direct messaging appropriate to mothers with low levels of literacy and emphasise the importance of water and sanitation in the control of helminths and other diseases.

Abstract

We implemented a quality management system (QMS) and documented our improvements in a tuberculosis (TB) laboratory in Kisumu, Kenya. After implementation of the QMS, a sustained reduction in culture contamination rates for solid (from 15.4% to 5.3%) and liquid media (from 15.2% to 9.3%) was observed, and waste from product expiry was reduced significantly. External quality assurance (EQA) results were satisfactory before and after QMS implementation, and a client survey after implementation revealed 98% satisfaction. The laboratory attained ISO 15189 accreditation in October 2013. The implementation of QMS facilitated the attainment of target quality indicators, reduced waste due to expiry and led to high client satisfaction.


Abstract

Ready-to-use therapeutic foods (RUTFs) are a key component of a life-saving treatment for young children who present with uncomplicated severe acute malnutrition in resource limited settings. Increasing recognition of the role of balanced dietary omega-6 and omega-3 polyunsaturated fatty acids (PUFA) in neurocognitive and immune development led two independent groups to evaluate RUTFs. Jones et al. (BMC Med 13:93, 2015), in a study in BMC Medicine, and Hsieh et al. (J Pediatr Gastroenterol Nutr 2015), in a study in the Journal of Pediatric Gastroenterology and Nutrition, reformulated RUTFs with altered PUFA content and looked at the effects on circulating omega-3 docosahexaenoic acid (DHA) status as a measure of overall omega-3 status. Supplemental oral administration of omega-3 DHA or reduction of RUTF omega-6 linoleic acid using high oleic peanuts improved DHA status, whereas increasing omega-3 alpha-linolenic acid in RUTF did not. The results of these two small studies are consistent with well-established effects in animal studies and
highlight the need for basic and operational research to improve fat composition in support of omega-3-specific development in young children as RUTF use expands.


Abstract

A cross-sectional survey was conducted in neonatal and maternity units of five Kenyan district public hospitals. Data for 1 year were obtained: 3999 maternal and 1836 neonatal records plus tallies of maternal deaths, deliveries and stillbirths. There were 40 maternal deaths [maternal mortality ratio: 276 per 100 000 live births, 95% confidence interval (CI): 197-376]. Fresh stillbirths ranged from 11 to 43 per 1000 births. A fifth (19%, 263 of 1384, 95% CI: 11-30%) of the admitted neonates died. Compared with normal birth weight, odds of death were significantly higher in all of the low birth weight (LBW, <2500 g) categories, with the highest odds for the extremely LBW (<1000 g) category (odds ratio: 59, 95% CI: 21-158, p < 0.01). The observed maternal mortality, stillbirths and neonatal mortality call for implementation of the continuum of care approach to intervention delivery with particular emphasis on LBW babies.


Abstract

Bacterial vaginosis (BV) is a common vaginal syndrome associated with altered microflora that increases the risk of preterm delivery and acquisition of sexually transmitted diseases. The cause of BV is unknown although toll-like receptors (TLRs), that are central to innate immune responses, may be important. We evaluated associations between TLR SNPs and BV among HIV-1 infected and uninfected African women. Logistic regression was used to assess associations between SNPs (N=99) in TLRs 2-4, 7-9 and BV (as classified by Nugent's criteria). Among HIV-1
uninfected women, TLR7 rs5743737 and TLR7 rs1634323 were associated with a decreased risk of BV, whereas TLR7 rs179012 was associated with an increased risk. TLR2 SNP rs3804099 was associated with a decreased risk of BV among HIV-1 infected women. Our findings indicate that there may be differences in TLRassociation with BV among HIV-1 infected and HIV-1 uninfected women.


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<thead>
<tr>
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<tbody>
<tr>
<td><strong>Abstract</strong></td>
<td><strong>Objective:</strong> The aim of this study was to determine the prevalence of tuberculosis (TB) in adolescents in western Kenya.</td>
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<tr>
<td><strong>Methods:</strong></td>
<td>A cohort study of 5004 adolescents aged 12-18 years was conducted. Adolescents were screened for prevalent TB using clinical criteria, history of TB contact, and a Mantoux test. Cases of suspected TB were investigated through two sputum examinations (microscopy and liquid culture) and chest radiography.</td>
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<td><strong>Results:</strong></td>
<td>Out of 5004 adolescents enrolled, 1960 (39.2%) were identified with suspected TB, including 1544 with a positive Mantoux (prevalence 1544/4808, 32.1%), 515 with symptoms suggestive of TB (10.3%), and 144 (2.9%) with household TB contact. Sixteen culture-confirmed (definite) and 18 probable pulmonary TB (PTB) cases were identified, reflecting a prevalence estimate of 3.2/1000 (definite) and 6.8/1000 all PTB, respectively. Only one smear-positive case was detected. The case notification rate among 12-18-year-old adolescents for all TB was 101/100000,</td>
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yielding a patient diagnostic rate of 0.13 (95% confidence interval 0.03-3.7) cases detected per person-year for all TB.

**Conclusion:** The prevalence of PTB among adolescents is high, with the majority of cases not detected routinely. Innovative active case finding including the wider use of Xpert MTB/RIF is needed to detect smear-negative TB among adolescents.


|---|---|
**Abstract**

**Objective:** An audit of neonatal care services provided by clinical training centres was undertaken to identify areas requiring improvement as part of wider efforts to improve newborn survival in Kenya.

**Design:** Cross-sectional study using indicators based on prior work in Kenya. Statistical analyses were descriptive with adjustment for clustering of data.

**Setting:** Neonatal units of 22 public hospitals.

**Patients:** Neonates aged <7 days.

**Main outcome measures:** Quality of care was assessed in terms of availability of basic resources (principally equipment and drugs) and audit of case records for documentation of patient assessment and treatment at admission.

**Results:** All hospitals had oxygen, 19/22 had resuscitation and phototherapy equipment, but some key resources were missing—for example kangaroo care was available in 14/22. Out of 1249 records, 56.9% (95% CI 36.2% to 77.6%) had a standard neonatal admission form. A median score of 0 out of 3 for symptoms of severe illness (IQR 0-3) and a median score of 6 out of 8 for signs of severe illness (IQR 4-7) were documented. Maternal HIV status was documented in 674/1249 (54%, 95% CI 41.9% to 66.1%) cases. Drug doses exceeded recommendations by >20% in...
prescriptions for penicillin (11.6%, 95% CI 3.4% to 32.8%) and gentamicin (18.5%, 95% CI 13.4% to 25%), respectively.

**Conclusions:** Basic resources are generally available, but there are deficiencies in key areas. Poor documentation limits the use of routine data for quality improvement. Significant opportunities exist for improvement in service delivery and adherence to guidelines in hospitals providing professional training.


| --- | --- |

**Abstract**

The increasing adoption of Electronic Health Records (EHR) by developing countries comes with the need to develop common terminology standards to assure semantic interoperability. In Kenya, where the Ministry of Health has rolled out an EHR at 646 sites, several challenges have emerged including variable dictionaries across implementations, inability to easily share data across systems, lack of expertise in dictionary management, lack of central coordination and custody of a terminology service, inadequately defined policies and processes, insufficient infrastructure, among others. A Concept Working Group was constituted to address these challenges. The country settled on a common Kenya data dictionary, initially derived as a subset of the Columbia International eHealth Laboratory (CIEL)/Millennium Villages Project (MVP) dictionary. The initial dictionary scope largely focuses on clinical needs. Processes and policies around dictionary management are being guided by the framework developed by Bakhshi-Raiez et al. Technical and infrastructure-based approaches are also underway to streamline workflow for dictionary management and distribution across implementations. Kenya's approach on comprehensive common dictionary can serve as a model for other countries in similar settings.


| --- | --- |
Abstract

In children, Mycobacterium tuberculosis (M. tuberculosis) frequently disseminates systemically, presenting with nonspecific signs including fever. We determined prevalence of M. tuberculosis bacteremia among febrile children presenting to hospitals in Nyanza, Kenya (a region with high human immunodeficiency virus (HIV) and M. tuberculosis prevalence). Between March 2013 and February 2014, we enrolled children aged 6 months to 5 years presenting with fever (axillary temperature ≥ 37.5°C) and no recent antibiotic use. Blood samples were collected for bacterial and mycobacterial culture using standard methods. Among 148 children enrolled, median age was 3.1 years (interquartile range: 1.8-4.1 years); 10.3% of children were living with a household member diagnosed with M. tuberculosis in the last year. Seventeen percent of children were stunted (height-for-age z-score < -2), 18.6% wasted (weight-for-height z-score < -2), 2.7% were HIV-infected, and 14.2% were HIV-exposed uninfected. Seventeen children (11.5%) had one or more signs of tuberculosis (TB). All children had a Bacille Calmette-Guerin vaccination scar. Among 134 viable blood cultures, none (95% confidence interval: 0-2.7%) had Mycobacterium isolated. Despite exposure to household TB contacts, HIV exposure, and malnutrition, M. tuberculosis bacteremia was not detected in this pediatric febrile cohort, a finding consistent with other pediatric studies.


Abstract

HIV epidemiology informs prevention trial design and program planning. Nine clinical research centers (CRC) in sub-Saharan Africa conducted HIV observational epidemiology studies in populations at risk for HIV infection as part of an HIV prevention and vaccine trial network. Annual HIV incidence ranged from below 2% to above 10% and varied by CRC and risk group, with rates above 5% observed in Zambian men in an HIV-discordant relationship, Ugandan men from Lake Victoria fishing communities, men who have sex with men, and several cohorts of women. HIV incidence tended to fall after the first three months in the study and over calendar time. Among suspected transmission pairs, 28% of HIV infections were not from the
reported partner. Volunteers with high incidence were successfully identified and enrolled into large scale cohort studies. Over a quarter of new cases in couples acquired infection from persons other than the suspected transmitting partner.


**Abstract**

**Background:** Lack of effective vaccines and therapeutics for important arboviral diseases such as Rift Valley fever (RVF) and dengue, necessitates continuous monitoring of vector populations for infections in them. Plant-based lures as surveillance tools has the potential of targeting mosquitoes of both sexes and females of varied physiological states; yet such lures are lacking for vectors of these diseases. Here, we present evidence of the effectiveness of linalool oxide (LO), a single plant-based lure previously developed for malaria vectors in trapping RVF vectors, Aedes mcintoshi and Aedes ochraceus, and dengue vector, Aedes aegypti.

**Methods:** For RVF vectors, we used CDC traps to evaluate the performance of LO against three vertebrate-based lures: CO2 (dry ice), BioGent (BG) lure, and HONAD (a blend of aldehydes) in 2 experiments with Completely Randomized design: 1) using unlit CDC traps baited separately with LO, HONAD and BG-lure, and unlit CDC trap + CO2 and lit CDC trap as controls, 2) similar treatments but with inclusion of CO2 to all the traps. For dengue vectors, LO was evaluated against BG lure using BG sentinel traps, in a 3 × 6 Latin Square design, first as single lures and then combined with CO2 and traps baited with CO2 included as controls. Trap captures were compared between the treatments using Chi square and GLM.

**Results:** Low captures of RVF vectors were recorded for all lures in the absence of CO2 with no significant difference between them. When combined with CO2, LO performance in trapping these vectors was comparable to BG-lure and HONAD but it was less effective than the lit CDC trap. In the absence of CO2, LO performed comparably with the BG-lure in trapping female Ae. aegypti, but with significantly higher males recorded in traps baited with the plant-based lure. When CO2 was added, LO was significantly better than the BG-lure with a 2.8- fold increase in captures of male Ae. aegypti.
Conclusions: These results highlight the potential of LO as a generalist plant-based lure for mosquito disease vectors, pending further assessment of possible specificity in their response profile to the different stereoisomers of this compound.


Abstract

Retinopathy provides a window into the underlying pathology of life-threatening malarial coma ("cerebral malaria"), allowing differentiation between 1) coma caused by sequestration of Plasmodium falciparum-infected erythrocytes in the brain and 2) coma with other underlying causes. Parasite sequestration in the brain is mediated by PfEMP1; a diverse parasite antigen that is inserted into the surface of infected erythrocytes and adheres to various host receptors. PfEMP1 sub-groups called "DC8" and "DC13" have been proposed to cause brain pathology through interactions with endothelial protein C receptor. To test this we profiled PfEMP1 gene expression in parasites from children with clinically defined cerebral malaria, who either had or did not have accompanying retinopathy. We found no evidence for an elevation of DC8 or DC13 PfEMP1 expression in children with retinopathy. However, the proportional expression of a broad subgroup of PfEMP1 called "group A" was elevated in retinopathy patients suggesting that these variants may play a role in the pathology of cerebral malaria. Interventions targeting group A PfEMP1 may be effective at reducing brain pathology.


Abstract

Chikungunya virus (CHIKV) from a human sample collected during the 2005 Chikungunya outbreak in the Comoros Island, showed distinct and reproducible large (L2) and small (S7) plaques which were characterized in this study. The parent strain and plaque variants were analysed by in vitro growth kinetics in different cell lines and their genetic similarity assessed by whole genome sequencing, comparative sequence
alignment and phylogenetic analysis. In vitro growth kinetic assays showed similar growth patterns of both plaque variants in Vero cells but higher viral titres of S7 compared to L2 in C6/36 cells. Amino acids (AA) alignments of the CHIKV plaque variants and S27 African prototype strain, showed 30 AA changes in the non-structural proteins (nsP) and 22 AA changes in the structural proteins. Between L2 and S7, only two AAs differences were observed. A missense substitution (C642Y) of L2 in the nsP2, involving a conservative AA substitution and a nonsense substitution (R524X) of S7 in the nsP3, which has been shown to enhance O'nyong-nyong virus infectivity and dissemination in Anopheles mosquitoes. The phenotypic difference observed in plaque size could be attributed to one of these AA substitutions. Phylogenetic analysis showed that the parent strain and its variants clustered closely together with each other and with Indian Ocean CHIKV strains indicating circulation of isolates with close evolutionary relatedness in the same outbreak. These observations pave way for important functional studies to understand the significance of the identified genetic changes in virulence and viral transmission in mosquito and mammalian hosts.


**Abstract**

Influenza-associated disease burden among children in tropical sub-Saharan Africa is not well established, particularly outside of the 2009 pandemic period. We estimated the burden of influenza in children aged 0-4 years through population-based surveillance for influenza-like illness (ILI) and acute lower respiratory tract illness (ALRI). Household members meeting ILI or ALRI case definitions were referred to health facilities for evaluation and collection of nasopharyngeal and oropharyngeal swabs for influenza testing by real-time reverse transcription polymerase chain reaction. Estimates were adjusted for health-seeking behavior and those with ILI and ALRI who were not tested. During 2008-2012, there were 9,652 person-years of surveillance among children aged 0-4 years. The average adjusted rate of influenza-associated hospitalization was 4.3 (95% CI 3.0-6.0) per 1,000 person-years in children aged 0-4 years. Hospitalization rates were highest in the 0-5 month and 6-23 month age groups, at 7.6 (95% CI 3.2-18.2) and 8.4 (95% CI 5.4-13.0) per 1,000 person-years, respectively. The average adjusted rate of influenza-associated medically attended (inpatient or outpatient) ALRI in children aged 0-4 years was 17.4 (95% CI 14.2-19.7) per 1,000 person-years. Few children who had severe laboratory-confirmed influenza were clinically diagnosed with influenza by the treating clinician in the inpatient (0/33,
0%) or outpatient (1/109, 0.9%) settings. Influenza-associated hospitalization rates from 2008-2012 were 5-10 times higher than contemporaneous U.S. estimates. Many children with danger signs were not hospitalized; thus, influenza-associated severe disease rates in Kenyan children are likely higher than hospital-based estimates suggest.


Abstract

**Ethnopharmacological relevance:** The plant Neoboutonia macrocalyx has been reported in traditional medicine to be used in the treatment of malaria.

**Aim of the study:** To study the in vitro antiplasmodial activity of compounds from the stem bark of Neoboutonia macrocalyx.

**Materials and methods:** Compounds were extracted and purified from stem bark of Neoboutonia macrocalyx and their structure identified and confirmed by spectroscopic methods. The crude ethyl acetate extract, aqueous extract and the isolated compounds were evaluated for antiplasmodial activity against the chloroquine sensitive Sierra Leone I (D6) and chloroquine-resistant Indochina I (W2) strains of Plasmodium falciparum.

**Results:** Chemical investigation of the ethyl acetate extract of Neoboutonia macrocalyx bark resulted in the identification of one new diterpenoid; neoboutomacroin (1) in addition to the four known compounds which included, a phenanthrene; 3,6-dihydroxy-1,7-dimethyl-9-methoxyphenanthrene (2), a sterol; 3-O-Acetyloleuritolic acid (3) and two diterpenoids; simplexin (4) and montanin (5). Compounds 1 and 5 displayed good antiplasmodial activity of IC50 values less than 10 μg/mL against both strains. However, all the compounds tested displayed high cytotoxic activity against MRC5 cell line with IC50 less than 10 μM.

**Conclusions:** Despite an indirect in vitro antiplasmodial activity of some compounds isolated from the stem bark of Neoboutonia macrocalyx, the identification of these bioactive compounds indicates that they may play a role in the pharmacological properties of this plant.

Kipyab PC, Khaemba BM, Mwangangi JM, Mbogo CM. The physicochemical and environmental factors affecting the distribution of Anopheles merus along the Kenyan coast. Parasit Vectors. 2015 Apr 11;8:221.

Abstract

Background: Members of the Anopheles gambiae complex are the main transmitters of malaria. Anopheles merus is a member of the complex found along the Kenyan coast because it breeds in saline waters. An entomological study was conducted inGarithe Malindi District, to investigate the physicochemical and environmental factors affecting the distribution of An. merus.

Methods: Field and laboratory studies were used to investigate the breeding habitats of the subspecies. Mosquito larvae were sampled using standard dipping technique from small pockets of pools, ponds, hoof prints, road drain, wells and mangrove swamps found in Garithe. All 3(rd) and 4(th) instars of Anopheles larvae sampled were identified microscopically into species. A representative of Anopheles gambiae complex was then identified to specific sibling species using r-DNA PCR technique. The habitats were characterized based on temperature, conductivity, salinity, dissolved oxygen, total dissolved solids, pH, size, distance to nearest house, canopy coverage, surface debris, presence of algae, emergent plants, turbidity and habitat types.

Results: A total of 159 morphologically identified late stage instar Anopheles gambiae s.l larvae were selected for r-DNA analysis by PCR. Out of these, 60.4% (n = 96) were Anopheles merus, 8.8% (n = 14) were Anopheles arabiensis, 18.2% (n = 29) were Anopheles gambiae s.s and 12.6% (n = 20) were unknown. Using paired t-test (t (121) = -3.331, P = 0.001) a significantly high proportion of An. merus was observed in all habitats compared to An. arabiensis, and An. gambiae s. s. In habitat characterization, Pearson's correlation analysis test showed different parameters being associated with the occurrence of An. merus larvae in the different habitats sampled. Six out of the 55 correlation coefficients (10.9%) were statistically significant, suggesting non-random association between some pairs of variables. Those that had a significantly high positive correlation with An. merus included temperature, salinity, conductivity, total dissolved solids and algae.

Conclusions: Different physicochemical parameters and environmental parameters affect the occurrence of An. merus. In this study, higher temperatures accelerate the growth of the larvae and aids in growth of micro-organisms and algae which are food sources for the larvae. Saline waters favour the growth and development of An. merus larvae; they are also able to develop in a range of saline waters. Conductivity, total dissolved solids and canopy coverage are among the important factors influencing the
development and abundance of An. merus larvae in their habitats. Habitat type also influences the abundance of An. merus larvae. They mainly prefer to breed in pools and ponds, but not swamps, hoof prints and wells.


Abstract

Background: Studies have sought to define information needs of health workers within very specific settings or projects. Lacking in the literature is how hospitals in low-income settings are able to meet the information needs of their staff and the use of information communication technologies (ICT) in day-to-day information searching.

Objective: The study aimed to explore where professionals in Kenyan hospitals turn to for work-related information in their day-to-day work. Additionally, it examined what existing solutions are provided by hospitals with regard to provision of best practice care. Lastly, the study explored the use of ICT in information searching.

Design: Data for this study were collected in July 2012. Self-administered questionnaires (SAQs) were distributed across 22 study hospitals with an aim to get a response from 34 health workers per hospital.

Results: SAQs were collected from 657 health workers. The most popular sources of information to guide work were fellow health workers and printed guidelines while the least popular were scientific journals. Of value to health workers were: national treatment policies, new research findings, regular reports from surveillance data, information on costs of services and information on their performance of routine clinical tasks; however, hospitals only partially met these needs. Barriers to accessing information sources included: 'not available/difficult to get' and 'difficult to understand'. ICT use for information seeking was reported and with demographic specific differences noted from the multivariate logistic regression model; nurses compared to medical doctors and older workers were less likely to use ICT for health information searching. Barriers to accessing Internet were identified as: high costs and the lack of the service at home or at work.
Conclusions: Hospitals need to provide appropriate information by improving information dissemination efforts and providing an enabling environment that allows health workers find the information they need for best practice.


Abstract

Background: Acute seizures are a common cause of paediatric admissions to hospitals in Africa, and malaria is an important cause of seizures in endemic areas. Malaria has declined in the past decade whilst neonatal admissions have increased, both which may affect the incidence and phenotypes of acute seizures in African children.

Methods: We examined the effect of recent decline in malaria and the increasing burden of neonatal admissions on the incidence, causes and phenotypes of acute seizures admitted to hospital from 2009-2013. We used logistic regression to measure associations and Poisson regression to calculate the incidence and rate ratios.

Results: The overall incidence of acute seizures over the 5-year period was 312 per 100,000/year (95% CI, 295-329): 116 per 100,000/year (95% CI, 106-127) for complex seizures and 443 per 100,000 live births (95% CI, 383-512) for neonatal seizures. Over the period, there was an increase in incidence of seizures-attributable to malaria (SAM) (incidence rate ratio (IRR) = 1.25; p < 0.001), but neither non-SAM (IRR = 1.03; p = 0.569) nor neonatal seizures (IRR = 0.99; p = 0.905). Important causes of acute seizures were malaria (33%) and respiratory tract infections (19%); and for neonatal seizures were neonatal sepsis (51%), hypoglycemia (41%) and hypoxic-ischemic encephalopathy (21%). Mortality occurred in 6% of all acute seizures, being more common in complex seizures (8%) and neonatal seizures (10 %) than other seizures (p < 0.001 for both comparisons).

Conclusions: Acute seizures remain common in children despite a decline in the incidence of malaria; suggesting that causes for these seizures need to be prevented in the community.


44. Zurovac D, Quintran JO, Donald W, Naket E, Malinga J, Taleo G. Health systems readiness and management of febrile outpatients under low malaria

Abstract

**Background:** Vanuatu, an archipelago country in Western Pacific harbouring low Plasmodium falciparum and Plasmodium vivax malaria transmission, has been implementing a malaria case management policy, recommending parasitological testing of patients with fever and anti-malarial treatment for test-positive only patients. A health facility survey to evaluate the health systems readiness to implement the policy and the quality of outpatient management for patients with fever was undertaken.

**Methods:** A cross-sectional, cluster sample survey, using a range of quality-of-care methods, included all health centres and hospitals in Vanuatu. The main outcome measures were coverage of health facilities and health workers with commodities and support interventions, adherence to test and treatment recommendations, and factors influencing malaria testing.

**Results:** The survey was undertaken in 2014 during the low malaria season and included 41 health facilities, 67 health workers and 226 outpatient consultations for patients with fever. All facilities had capacity for parasitological diagnosis, 95.1 % stocked artemether-lumefantrine and 63.6 % primaquine. The coverage of health workers with support interventions ranged from 50 to 70 %. Health workers' knowledge was high only regarding treatment policy for uncomplicated P. falciparum malaria (83.4 %). History taking and clinical examination practices were sub-optimal. Some 35.0 % (95 % CI 23.4-48.6) of patients with fever were tested for malaria, of which all results were negative and only one patient received anti-malarial treatment. Testing was significantly higher for patients age 5 years and older (OR = 2.33; 95 % CI 1.48-5.02), seen by less qualified health workers (OR = 2.73; 95 % CI 1.48-5.02), health workers who received malaria case management training (OR = 2.39; 95 % CI 1.28-4.47) and patients with increased temperature (OR = 2.56; 95 % CI 1.17-5.57), main complaint of fever (OR = 5.82; 95 % CI 1.26-26.87) and without runny nose (OR = 3.75; 95 % CI 1.36-10.34). Antibiotic use was very high (77.4 %) with sub-optimal dispensing and counselling practices.

**Conclusions:** Health facility and health worker readiness to implement policy is higher for falciparum than vivax malaria. Clinical and malaria testing practices are sub-optimal, however adherence to test negative results is nearly universal. Use of antibiotics is irrational. Quantitative and qualitative improvements of ongoing interventions are needed to re-inforce clinical practices in this area characterized by difficult access, human resource shortages but aspiring towards malaria elimination.
|---------------|---------------------------------------------|
| **Abstract** | **Background:** Controlled human malaria infection (CHMI) studies, in which healthy volunteers are infected with Plasmodium falciparum to assess the efficacy of novel malaria vaccines and drugs, have become a vital tool to accelerate vaccine and drug development. CHMI studies provide a cost-effective and expeditious way to circumvent the use of large-scale field efficacy studies to deselect intervention candidates. However, to date few modern CHMI studies have been performed in malaria-endemic countries.  

**Methods:** An open-label, randomized pilot CHMI study was conducted using aseptic, purified, cryopreserved, infectious P. falciparum sporozoites (SPZ) (Sanaria® PfSPZ Challenge) administered intramuscularly (IM) to healthy Kenyan adults (n = 28) with varying degrees of prior exposure to P. falciparum. The purpose of the study was to establish the PfSPZ Challenge CHMI model in a Kenyan setting with the aim of increasing the international capacity for efficacy testing of malaria vaccines and drugs, and allowing earlier assessment of efficacy in a population for which interventions are being developed. This was part of the EDCTP-funded capacity development of the CHMI platform in Africa.  

**Discussion:** This paper discusses in detail lessons learnt from conducting the first CHMI study in Kenya. Issues pertinent to the African setting, including community sensitization, consent and recruitment are considered. Detailed reasoning regarding the study design (for example, dose and route of administration of PfSPZ Challenge, criteria for grouping volunteers according to prior exposure to malaria and duration of follow-up post CHMI) are given and changes other centres may want to consider for future studies are suggested.  

**Conclusions:** Performing CHMI studies in an African setting presents unique but surmountable challenges and offers great opportunity for acceleration of malaria vaccine and drug development. The reflections in this paper aim to aid other centres and partners intending to use the CHMI model in Africa. |

Abstract

Introduction: Epilepsy is common in sub-Saharan Africa, but there is little data in West Africa, to develop public health measures for epilepsy in this region.

Methods: We conducted a three-stage cross-sectional survey to determine the prevalence and risk factors for active convulsive epilepsy (ACE), and estimated the treatment gap in Kintampo situated in the middle of Ghana.

Results: 249 people with ACE were identified in a study population of 113,796 individuals. After adjusting for attrition and the sensitivity of the screening method, the prevalence of ACE was 10.1/1000 (95% Confidence Interval (95% CI) 9.5-10.7). In children aged <18 years, risk factors for ACE were: family history of seizures (OR=3.31; 95% CI: 1.83-5.96), abnormal delivery (OR=2.99; 95% CI: 1.07-8.34), problems after birth (OR=3.51; 95% CI: 1.02-12.06), and exposure to Onchocerca volvulus (OR=2.32; 95% CI: 1.12-4.78). In adults, a family history of seizures (OR=1.83; 95% CI: 1.05-3.20), never attended school (OR=11.68; 95% CI: 4.80-28.40), cassava consumption (OR=3.92; 95% CI: 1.14-13.54), pork consumption (OR=1.68; 95% CI: 1.09-2.58), history of snoring at least 3 nights per week (OR=3.40; 95% CI: 1.56-7.41), exposure to Toxoplasma gondii (OR=1.99; 95% CI: 1.15-3.45) and Onchocerca volvulus (OR=2.09; 95% CI: 1.29-3.40) were significant risk factors for the development of ACE. The self-reported treatment gap was 86.9% (95% CI: 83.5%-90.3%).

Conclusion: ACE is common within the middle belt of Ghana and could be reduced with improved obstetric care and prevention of parasite infestations such as Onchocerca volvulus and Toxoplasma gondii.


Abstract
**Background:** Five outbreaks of ebola occurred in Uganda between 2000-2012. The outbreaks were quickly contained in rural areas. However, the Gulu outbreak in 2000 was the largest and complex due to insurgency. It invaded Gulu municipality and the slum-like camps of the internally displaced persons (IDPs). The Bundigugyo district outbreak followed but was detected late as a new virus. The subsequent outbreaks in the districts of Luwero district (2011, 2012) and Kibaale (2012) were limited to rural areas.

**Methods:** Detailed records of the outbreak presentation, cases, and outcomes were reviewed and analyzed. Each outbreak was described and the outcomes examined for the different scenarios.

**Results:** Early detection and action provided the best outcomes and results. The ideal scenario occurred in the Luwero outbreak during which only a single case was observed. Rural outbreaks were easier to contain. The community imposed quarantine prevented the spread of ebola following introduction into Masindi district. The outbreak was confined to the extended family of the index case and only one case developed in the general population. However, the outbreak invasion of the town slum areas escalated the spread of infection in Gulu municipality. Community mobilization and leadership was vital in supporting early case detection and isolations well as contact tracing and public education.

**Conclusion:** Palliative care improved survival. Focusing on treatment and not just quarantine should be emphasized as it also enhanced public trust and health seeking behavior. Early detection and action provided the best scenario for outbreak containment. Community mobilization and leadership was vital in supporting outbreak control. International collaboration was essential in supporting and augmenting the national efforts.


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**Abstract**

**Background:** Regular assessment of quality of care allows monitoring of progress towards system goals and identifies gaps that need to be addressed to promote better
outcomes. We report efforts to initiate routine assessments in a low-income country in partnership with government.

**Methods:** A cross-sectional survey undertaken in 22 'internship training' hospitals across Kenya that examined availability of essential resources and process of care based on review of 60 case-records per site focusing on the common childhood illnesses (pneumonia, malaria, diarrhea/dehydration, malnutrition and meningitis).

**Results:** Availability of essential resources was 75% (45/61 items) or more in 8/22 hospitals. A total of 1298 (range 54-61) case records were reviewed. HIV testing remained suboptimal at 12% (95% CI 7-19). A routinely introduced structured pediatric admission record form improved documentation of core admission symptoms and signs (median score for signs 22/22 and 8/22 when form used and not used respectively). Correctness of penicillin and gentamicin dosing was above 85% but correctness of prescribed intravenous fluid or oral feed volumes for severe dehydration and malnutrition were 54% and 25% respectively. Introduction of Zinc for diarrhea has been relatively successful (66% cases) but use of artesunate for malaria remained rare. Exploratory analysis suggests considerable variability of the quality of care across hospitals.

**Conclusion:** Quality of pediatric care in Kenya has improved but can improve further. The approach to monitoring described in this survey seems feasible and provides an opportunity for routine assessments across a large number of hospitals as part of national efforts to sustain improvement. Understanding variability across hospitals may help target improvement efforts.


**Abstract**

**Background:** Mortality in paediatric emergency care units in Africa often occurs within the first 24 h of admission and remains high. Alongside effective triage systems, a practical clinical bedside risk score to identify those at greatest risk could contribute to reducing mortality.

**Methods:** Data collected during the Fluid As Expansive Supportive Therapy (FEAST) trial, a multi-centre trial involving 3,170 severely ill African children, were analysed to
identify clinical and laboratory prognostic factors for mortality. Multivariable Cox regression was used to build a model in this derivation dataset based on clinical parameters that could be quickly and easily assessed at the bedside. A score developed from the model coefficients was externally validated in two admissions datasets from Kilifi District Hospital, Kenya, and compared to published risk scores using Area Under the Receiver Operating Curve (AUROC) and Hosmer-Lemeshow tests. The Net Reclassification Index (NRI) was used to identify additional laboratory prognostic factors.

**Results:** A risk score using 8 clinical variables (temperature, heart rate, capillary refill time, conscious level, severe pallor, respiratory distress, lung crepitations, and weak pulse volume) was developed. The score ranged from 0-10 and had an AUROC of 0.82 (95 % CI, 0.77-0.87) in the FEAST trial derivation set. In the independent validation datasets, the score had an AUROC of 0.77 (95 % CI, 0.72-0.82) amongst admissions to a paediatric high dependency ward and 0.86 (95 % CI, 0.82-0.89) amongst general paediatric admissions. This discriminative ability was similar to, or better than other risk scores in the validation datasets. NRI identified lactate, blood urea nitrogen, and pH to be important prognostic laboratory variables that could add information to the clinical score.

**Conclusions:** Eight clinical prognostic factors that could be rapidly assessed by healthcare staff for triage were combined to create the FEAST Paediatric Emergency Triage (PET) score and externally validated. The score discriminated those at highest risk of fatal outcome at the point of hospital admission and compared well to other published risk scores. Further laboratory tests were also identified as prognostic factors which could be added if resources were available or as indices of severity for comparison between centres in future research studies.


**Abstract**

**Background:** Clinical trials conducted in Africa often require substantial investments to support trial centres and public health facilities. Trial resources could potentially generate benefits for routine health service delivery but may have unintended consequences. Strengthening ethical practice requires understanding the potential effects of trial inputs on the perceptions and practices of routine health care providers.
This study explores the influence of malaria vaccine trials on health service delivery in Ghana, Kenya and Burkina Faso.

**Methods:** We conducted: audits of trial inputs in 10 trial facilities and among 144 health workers; individual interviews with frontline providers (n=99) and health managers (n=14); and group discussions with fieldworkers (n=9 discussions). Descriptive summaries were generated from audit data. Qualitative data were analysed using a framework approach.

**Results:** Facilities involved in trials benefited from infrastructure and equipment upgrades, support with essential drugs, access to trial vehicles, and placement of additional qualified trial staff. Qualified trial staff in facilities were often seen as role models by their colleagues; assisting with supportive supervision and reducing facility workload. Some facility staff in place before the trial also received formal training and salary top-ups from the trials. However, differential access to support caused dissatisfaction, and some interviewees expressed concerns about what would happen at the end of the trial once financial and supervisory support was removed.

**Conclusion:** Clinical trials function as short-term complex health service delivery interventions in the facilities in which they are based. They have the potential to both benefit facilities, staff and communities through providing the supportive environment required for improvements in routine care, but they can also generate dissatisfaction, relationship challenges and demoralisation among staff. Minimising trial related harm and maximising benefits requires careful planning and engagement of key actors at the outset of trials, throughout the trial and on its' completion.


### Abstract

**Background:** The draft Global Technical Strategy for malaria aims to eliminate malaria from at least 10 countries by 2020. Yemen and Saudi Arabia remain the last two countries on the Arabian Peninsula yet to achieve elimination. Over the last 50 years, systematic efforts to control malaria in the Kingdom of Saudi Arabia has successfully reduced malaria cases to a point where malaria is now constrained largely...
to Jazan Province, the most south-western area along the Red Sea. The progress toward elimination in this province is reviewed between 2000 and 2014.

**Methods:** Data were obtained from the Ministry of Health case-reporting systems, activity reports, unpublished consultants reports, and relevant scientific published papers. Sub-provincial population data were obtained the national household censuses undertaken in 2004 and 2010. Rainfall data were obtained from the Meteorological Department in Jazan.

**Results:** Between 2000 and 2014 there were 5522 locally acquired cases of malaria and 9936 cases of imported malaria. A significant reduction in locally acquired malaria cases was observed from 2000 to 2014, resulting in an average annual incidence (2010-2014) of 0.3 cases per 10,000 population. Conversely imported cases, since 2000, remain consistent and higher than locally acquired cases, averaging between 250 and 830 cases per year. The incidence of locally acquired cases is heterogeneous across the Province, with only a few health districts contributing the majority of the cases. The overall decline in malaria case incidence can be attributed to coincidental expansion of control efforts and periods of exceptionally low rainfall.

**Conclusions:** Jazan province is poised to achieve malaria elimination. There is a need to change from a policy of passive case detection to reactively and proactively detecting infectious reservoirs that require new approaches to surveillance. These should be combined with advanced epidemiological tools to improve the definitions of epidemiological receptive and hotspot malaria risk mapping. The single largest threat currently remains the risks posed by imported infections from Yemen.


**Abstract**

As part of a knowledge, attitudes, practices and empowerment (KAPE) project implemented by the United Nations University Institute for Water, Environment and Health (UNU-INWEH) in the Lake Victoria Basin, this paper reports findings from a photovoice study with women in Usoma, a lakeshore community in Western Kenya. Drawing on ecosocial and political ecology theory, findings reveal that access to water, perceptions and practices were shaped by ecological and broader structural factors.
Further, collective actions to improve access were constrained by institutional and economic structures, thus (re)enforcing inequalities.


Abstract

Background: Neonatal Tetanus (NT) is a preventable cause of mortality and neurological sequelae that occurs at higher incidence in resource-poor countries, presumably because of low maternal immunisation rates and unhygienic cord care practices. We aimed to determine changes in the incidence of NT, characterize and investigate the associated risk factors and mortality in a prospective cohort study including all admissions over a 15-year period at a County hospital on the Kenyan coast, a region with relatively high historical NT rates within Kenya.

Methods: We assessed all neonatal admissions to Kilifi County Hospital in Kenya (1999-2013) and identified cases of NT (standard clinical case definition) admitted during this time. Poisson regression was used to examine change in incidence of NT using accurate denominator data from an area of active demographic surveillance. Logistic regression was used to investigate the risk factors for NT and factors associated with mortality in NT amongst neonatal admissions. A subset of sera from mothers (n = 61) and neonates (n = 47) were tested for anti-tetanus antibodies.

Results: There were 191 NT admissions, of whom 187 (98%) were home deliveries. Incidence of NT declined significantly (Incidence Rate Ratio: 0.85 (95% Confidence interval 0.81-0.89), P<0.001) but the case fatality (62%) did not change over the study period (P = 0.536). Younger infant age at admission (P = 0.001) was the only independent predictor of mortality. Compared to neonatal hospital admittee controls, the proportion of home births was higher among the cases. Sera tested for antitetanus antibodies showed most mothers (50/61, 82%) had undetectable levels of antitetanus antibodies, and most (8/9, 89%) mothers with detectable antibodies had a neonate without protective levels.

Conclusions: Incidence of NT in Kilifi County has significantly reduced, with reductions following immunisation campaigns. Our results suggest immunisation efforts are effective if sustained and efforts should continue to expand coverage.

**Abstract**

**Background:** To assess the availability, price and market share of quality-assured artemisinin-based combination therapy (QAACT) in remote areas (RAs) compared with non-remote areas (nRAs) in Kenya and Ghana at end-line of the Affordable Medicines Facility-malaria (AMFm) intervention.

**Methods:** Areas were classified by remoteness using a composite index computed from estimated travel times to three levels of service centres. The index was used to five categories of remoteness, which were then grouped into two categories of remote and non-remote areas. The number of public or private outlets with the potential to sell or distribute anti-malarial medicines, screened in nRAs and RAs, respectively, was 501 and 194 in Ghana and 9980 and 2353 in Kenya. The analysis compares RAs with nRAs in terms of availability, price and market share of QAACT in each country.

**Results:** QAACT were similarly available in RAs as nRAs in Ghana and Kenya. In both countries, there was no statistical difference in availability of QAACT with AMFm logo between RAs and nRAs in public health facilities (PHFs), while private-for-profit (PFP) outlets had lower availability in RA than in nRAs (Ghana: 66.0 vs 82.2 %, p < 0.0001; Kenya: 44.9 vs 63.5 %, p = <0.0001. The median price of QAACT with AMFm logo for PFP outlets in RAs (USD1.25 in Ghana and USD0.69 in Kenya) was above the recommended retail price in Ghana (US$0.95) and Kenya (US$0.46), and much higher than in nRAs for both countries. QAACT with AMFm logo represented the majority of QAACT in RAs and nRAs in Kenya and Ghana. In the PFP sector in Ghana, the market share for QAACT with AMFm logo was significantly higher in RAs than in nRAs (75.6 vs 51.4 %, p < 0.0001). In contrast, in similar outlets in Kenya, the market share of QAACT with AMFm logo was significantly lower in RAs than in nRAs (39.4 vs 65.1 %, p < 0.0001).

**Conclusion:** The findings indicate the AMFm programme contributed to making QAACT more available in RAs in these two countries. Therefore, the AMFm approach can inform other health interventions aiming at reaching hard-to-reach populations, particularly in the context of universal access to health interventions. However, further examination of the factors accounting for the deep penetration of the AMFm
programme into RAs is needed to inform actions to improve the healthcare delivery system, particularly in RAs.


Abstract

Both iron deficiency (ID) and malaria are common among African children. Studies show that the iron-regulatory hormone hepcidin is induced by malaria, but few studies have investigated this relationship longitudinally. We measured hepcidin concentrations, markers of iron status, and antibodies to malaria antigens during two cross-sectional surveys within a cohort of 324 Kenyan children ≤ 8 years old who were under intensive surveillance for malaria and other febrile illnesses. Hepcidin concentrations were the highest in the youngest, and female infants, declined rapidly in infancy and more gradually thereafter. Asymptomatic malaria and malaria antibody titres were positively associated with hepcidin concentrations. Recent episodes of febrile malaria were associated with high hepcidin concentrations that fell over time. Hepcidin concentrations were not associated with the subsequent risk of either malaria or other febrile illnesses. Given that iron absorption is impaired by hepcidin, our data suggest that asymptomatic and febrile malaria contribute to the high burden of ID seen in African children. Further, the effectiveness of iron supplementation may be sub-optimal in the presence of asymptomatic malaria. Thus, strategies to prevent and eliminate malaria may have the added benefit of addressing an important cause of ID for African children.


Abstract

Human respiratory syncytial virus (RSV) is associated with severe childhood respiratory infections. A clear description of local RSV molecular epidemiology, evolution, and transmission requires detailed sequence data and can inform new strategies for virus control and vaccine development. We have generated 27 complete
or nearly complete genomes of RSV from hospitalized children attending a rural coastal district hospital in Kilifi, Kenya, over a 10-year period using a novel full-genome deep-sequencing process. Phylogenetic analysis of the new genomes demonstrated the existence and cocirculation of multiple genotypes in both RSV A and B groups in Kilifi. Comparison of local versus global strains demonstrated that most RSV A variants observed locally in Kilifi were also seen in other parts of the world, while the Kilifi RSV B genomes encoded a high degree of variation that was not observed in other parts of the world. The nucleotide substitution rates for the individual open reading frames (ORFs) were highest in the regions encoding the attachment (G) glycoprotein and the NS2 protein. The analysis of RSV full genomes, compared to subgenomic regions, provided more precise estimates of the RSV sequence changes and revealed important patterns of RSV genomic variation and global movement. The novel sequencing method and the new RSV genomic sequences reported here expand our knowledge base for large-scale RSV epidemiological and transmission studies.

**Importance:** The new RSV genomic sequences and the novel sequencing method reported here provide important data for understanding RSV transmission and vaccine development. Given the complex interplay between RSV A and RSV B infections, the existence of local RSV B evolution is an important factor in vaccine deployment.


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**Background:** Epilepsy is one of the most common neurological conditions globally, estimated to constitute 0.75% of the global burden of disease, with the majority of this burden found in low- and middle-income countries (LMICs). Few studies from LMICs, including much of sub-Saharan Africa, have described the incidence, remission or mortality rates due to epilepsy, which are needed to quantify the burden and inform policy. This study investigates the epidemiological parameters of...
convulsive epilepsy within a context of high HIV prevalence and an emerging burden of cardiovascular disease.

**Methods:** A cross-sectional population survey of 82,818 individuals, in the Agincourt Health and Socio-demographic Surveillance Site (HDSS) in rural northeast South Africa was conducted in 2008, from which 296 people were identified with active convulsive epilepsy. A follow-up survey was conducted in 2012. Incidence and mortality rates were estimated, with duration and remission rates calculated using the DISMOD II software package.

**Results:** The crude incidence for convulsive epilepsy was 17.4/100,000 per year (95%CI: 13.1-23.0). Remission was 4.6% and 3.9% per year for males and females, respectively. The standardized mortality ratio was 2.6 (95%CI: 1.7-3.5), with 33.3% of deaths directly related to epilepsy. Mortality was higher in men than women (adjusted rate ratio (aRR) 2.6 (95%CI: 1.2-5.4)), and was significantly associated with older ages (50+ years versus those 0-5 years old (RR 4.8 (95%CI: 0.6-36.4)).

**Conclusions:** The crude incidence was lower whilst mortality rates were similar to other African studies; however, this study found higher mortality amongst older males. Efforts aimed at further understanding what causes epilepsy in older people and developing interventions to reduce prolonged seizures are likely to reduce the overall burden of ACE in rural South Africa.


**Abstract**

**Background:** Patients with acute HIV-1 infection (AHI) have elevated infectivity, but cannot be diagnosed using antibody-based testing. Approaches to screen patients for AHI are urgently needed to enable counselling and treatment to reduce onward transmission.

**Methods:** We pooled data from four African studies of high-risk adults that evaluated symptoms and signs compatible with acute retroviral syndrome and tested for HIV-1 at each visit. AHI was defined as detectable plasma viral load or p24 antigen in an HIV-1-antibody-negative patient who subsequently seroconverted. Using generalized estimating equation, we identified symptoms, signs, and demographic factors.
predictive of AHI, adjusting for study site. We assigned a predictor score to each statistically significant predictor based on its beta coefficient, summing predictor scores to calculate a risk score for each participant. We evaluated the performance of this algorithm overall and at each site.

**Results:** We compared 122 AHI visits with 45,961 visits by uninfected patients. Younger age (18-29 years), fever, fatigue, body pains, diarrhoea, sore throat, and genital ulcer disease were independent predictors of AHI. The overall area under the receiver operating characteristics curve (AUC) for the algorithm was 0.78, with site-specific AUCs ranging from 0.61 to 0.89. A risk score of at least 2 would indicate AHI testing for 5-50% of participants, substantially decreasing the number needing testing.

**Conclusion:** Our targeted risk score algorithm based on seven characteristics reduced the number of patients needing AHI testing and had good performance overall. We recommend this risk score algorithm for use by HIV programs in sub-Saharan Africa with capacity to test high-risk patients for AHI.


**Abstract**

**Background:** Malaria is a great public health burden and Africa suffers the largest share of malaria-attributed deaths. Despite control efforts targeting indoor malaria transmission, such as insecticide-treated bed nets (ITNs) and deployment of indoor residual spraying, transmission of the parasite in western Kenya is still maintained. This study was carried out to determine the impact of ITNs on indoor vector densities and biting behaviour in western Kenya.

**Methods:** Indoor collection of adult mosquitoes was done monthly in six study sites in western Kenya using pyrethrum spray collections from 2012 to 2014. The rotator trap collections were done in July-August in 2013 and May-June in 2014. Mosquitoes were collected every 2 h between 18.00 and 08.00 h. Human behaviour study was conducted via questionnaire surveys. Species within Anopheles gambiae complex was differentiated by PCR and sporozoite infectivity was determined by ELISA. Species distribution was determined and bed net coverage in the study sites was recorded.

**Results:** During the study a total of 5,469 mosquito vectors were collected from both PSC and Rotator traps comprising 3,181 (58.2%) Anopheles gambiae and 2,288...
Anopheles funestus. Compared to all the study sites, Rae had the highest density of An. gambiae with a mean of 1.2 (P<0.001) while Kombewa had the highest density of An. funestus with a mean of 1.08 (P<0.001). Marani had the lowest density of vectors with 0.06 An. gambiae and 0.17 An. funestus (P<0.001). Among the 700 PCR confirmed An. gambiae s.l. individuals, An. gambiae s.s. accounted for 49% and An. arabiensis 51%. Over 50% of the study population stayed outdoors between 18.00 and 20.00 and 06.00 and 08.00 which was the time when highest densities of blood fed vectors were collected. Anopheles gambie s.s. was the main malaria parasite vector in the highland sites and An. arabiensis in the lowland sites. Bed net ownership in 2012 averaged 87% across the study sites.

Conclusions: This study suggests that mass distribution of ITNs has had a significant impact on vector densities, species distribution and sporozoite rate. However, shift of biting time poses significant threats to the current malaria vector control strategies which heavily rely on indoor controls.


Abstract

The Ebola Virus Disease (EVD) in West Africa has stimulated investments in EVD research. While these research efforts are most welcome, we are concerned about the potential to ignore effective community ethics engagement programmes and critical government regulatory agencies in light of the urgency to conduct clinical trials for EVD therapies and vaccines. We discuss the reasons why community engagement with various research stakeholders is essential, how community engagement should be conducted, and the potential consequences of failing to engage both communities and regulatory agencies by drawing on past experiences in the field of HIV research. We highlight the importance of a) capacity building to enable local researchers design and implement EVD research for future epidemics, b) the need to support community research literacy, and c) the need to build the competency of research regulatory agencies on the continent to address EVD therapy and vaccine research.


Abstract

Background: Haemoglobin variants, Sickle (HbS) and foetal (HbF) have been associated with malaria protection. This study explores epistatic interactions between HbS and HbF on malaria infection.

Methods: The study was conducted between March 2004 and December 2013 within the sickle cell disease (SCD) programme at Muhimbili National Hospital, Tanzania. SCD status was categorized into HbAA, HbAS and HbSS using hemoglobin electrophoresis and High Performance Liquid Chromatography (HPLC). HbF levels were determined by HPLC. Malaria was diagnosed using rapid diagnostic test and/or blood film. Logistic regression and generalized estimating equations models were used to evaluate associations between SCD status, HbF and malaria.

Findings: 2,049 individuals with age range 0-70 years, HbAA 311(15.2%), HbAS 241(11.8%) and HbSS 1,497(73.1%) were analysed. At enrolment, malaria prevalence was significantly higher in HbAA 13.2% compared to HbAS 1.24% and HbSS 1.34% (p<0.001). Mean HbF was lower in those with malaria compared to those without malaria in HbAA (0.43% vs 0.82%) but was the reverse in HbSS (8.10% vs 5.59%). An increase in HbF was associated with a decrease in risk of malaria OR=0.50 (95%CI: 0.28, 0.90; p=0.021) in HbAA, whereas for HbSS the risk of malaria increased OR=2.94 (1.44, 5.98; p=0.003). A similar pattern was seen during multiple visits; HbAA OR=0.52 (0.34, 0.80; p=0.003) vs HbSS OR=2.01 (1.27, 3.23; p=0.003).

Conclusion: Higher prevalence of malaria in HbAA compared to HbAS and HbSS confirmed the protective effect of HbS. Lower prevalence of malaria in HbAA with high HbF supports a protective effect of HbF. However, in HbSS, the higher prevalence of malaria with high levels of HbF suggests loss of malaria protection. This is the first epidemiological study to suggest a negative epistasis between HbF and HbS on malaria.


Abstract
Background: Many Low-and-Middle-Income countries are considering reviewing their health financing systems to meet the principles of Universal Health Coverage (UHC). One financing mechanism, which has dominated UHC reforms, is the development of health insurance schemes. We trace the historical development of the National Health Insurance (NHI) policy, illuminate stakeholders' perceptions on the design to inform future development of health financing policies in Kenya.

Methods: We conducted a retrospective policy analysis of the development of a NHI policy in Kenya using data from document reviews and seven in depth interviews with key stakeholders involved in the NHI design. Analysis was conducted using a thematic framework.

Results: The design of a NHI scheme was marked by complex interaction of the actor's understanding of the design, proposed implementation strategies and the covert opposition of the reform due to several reasons. First, actor's perception of the cost of the NHI design and its implication to the economy generated opposition. This was due to inadequate communication strategies to articulate the policy, leading to a vacuum of factual information flow to various players. Secondly, perceived fear of implications of the changes among private sector players threatened support and success gained. Thirdly, underlying mistrust associated with perceived lack of government's commitment towards transparency and good governance affected active engagement of all key players dampening the spirit of collective bargain breeding opposition. Finally, some international actors perceived a clash of their role and that of international programs based on vertical approaches that were inherent in the health system.

Conclusion: The thrust towards UHC using NHI schemes should not only focus on the design of a viable NHI package but should also involve stakeholder engagements, devise ways of improving the health care system, enhance transparency and develop adequate governance structures to institutions mandated to provide leadership in the reform process to overcome covert opposition.


Abstract
By engaging expert opinion, Marko Kerac and colleagues set research priorities for the management of acute malnutrition in infants.


Abstract

**Background**: Severe anaemia in children is a leading cause of hospital admission and a major cause of mortality in sub-Saharan Africa, yet there are limited published data on blood transfusion in this vulnerable group.

**Methods**: We present data from a large controlled trial of fluid resuscitation (Fluid Expansion As Supportive Therapy (FEAST) trial) on the prevalence, clinical features, and transfusion management of anaemia in children presenting to hospitals in three East African countries with serious febrile illness (predominantly malaria and/or sepsis) and impaired peripheral perfusion.

**Results**: Of 3,170 children in the FEAST trial, 3,082 (97%) had baseline haemoglobin (Hb) measurement, 2,346/3,082 (76%) were anaemic (Hb <10 g/dL), and 33% severely anaemic (Hb <5 g/dL). Prevalence of severe anaemia varied from 12% in Kenya to 41% in eastern Uganda. 1,387/3,082 (45%) children were transfused (81% within 8 hours). Adherence to WHO transfusion guidelines was poor. Among severely anaemic children who were not transfused, 52% (54/103) died within 8 hours, and 90% of these deaths occurred within 2.5 hours of randomisation. By 24 hours, 128/1,002 (13%) severely anaemic children had died, compared to 36/501 (7%) and 71/843 (8%) of those with moderate and mild anaemia, respectively. Among children without severe hypotension who were randomised to receive fluid boluses of 0.9% saline or albumin, mortality was increased (10.6% and 10.5%, respectively) compared to controls (7.2%), regardless of admission Hb level. Repeat transfusion varied from ≤2% in Kenya/Tanzania to 6 to 13% at the four Ugandan centres. Adverse reactions to blood were rare (0.4%).

**Conclusions**: Severe anaemia complicates one third of childhood admissions with serious febrile illness to hospitals in East Africa, and is associated with increased mortality. A high proportion of deaths occurred within 2.5 hours of admission, emphasizing the need for rapid recognition and prompt blood transfusion. Adherence to current WHO transfusion guidelines was poor. The high rates of re-transfusion...
suggest that 20 mL/kg whole blood or 10 mL/kg packed cells may undertreat a significant proportion of anaemic children. Future evaluation of the impact of a larger volume of transfused blood and optimum transfusion management of children with Hb of <6 g/dL is warranted.


| **Abstract** |
| The assessment of naturally-acquired and vaccine-induced immunity to blood-stage Plasmodium falciparum malaria is of long-standing interest. However, the field has suffered from a paucity of in vitro assays that reproducibly measure the anti-parasitic activity induced by antibodies in conjunction with immune cells. Here we optimize the antibody-dependent respiratory burst (ADRB) assay, which assesses the ability of antibodies to activate the release of reactive oxygen species from human neutrophils in response to P. falciparum blood-stage parasites. We focus particularly on assay parameters affecting serum preparation and concentration, and importantly assess reproducibility. Our standardized protocol involves testing each serum sample in singlicate with three independent neutrophil donors, and indexing responses against a standard positive control of pooled hyper-immune Kenyan sera. The protocol can be used to quickly screen large cohorts of samples from individuals enrolled in immuno-epidemiological studies or clinical vaccine trials, and requires only 6 μL of serum per sample. Using a cohort of 86 samples, we show that malaria-exposed individuals induce higher ADRB activity than malaria-naïve individuals. The development of the ADRB assay complements the use of cell-independent assays in blood-stage malaria, such as the assay of growth inhibitory activity, and provides an important standardized cell-based assay in the field. |

| **Abstract** |
Objective: People with epilepsy (PWE) develop complications and comorbidities often requiring admission to hospital, which adds to the burden on the health system, particularly in low-income countries. We determined the incidence, disability-adjusted life years (DALYs), risk factors, and causes of admissions in PWE. We also examined the predictors of prolonged hospital stay and death using data from linked clinical and demographic surveillance system.

Methods: We studied children and adults admitted to a Kenyan rural hospital, between January 2003 and December 2011, with a diagnosis of epilepsy. Poisson regression was used to compute incidence and rate ratios, logistic regression to determine associated factors, and the DALY package of the R-statistical software to calculate years lived with disability (YLD) and years of life lost (YLL).

Results: The overall incidence of admissions was 45.6/100,000 person-years of observation (PYO) (95% confidence interval [95% CI] 43.0-48.7) and decreased with age (p < 0.001). The overall DALYs were 3.1/1,000 (95% CI, 1.8-4.7) PYO and comprised 55% of YLD. Factors associated with hospitalization were use of antiepileptic drugs (AEDs) (odds ratio [OR] 5.36, 95% CI 2.64-10.90), previous admission (OR 11.65, 95% CI 2.65-51.17), acute encephalopathy (OR 2.12, 95% CI 1.07-4.22), and adverse perinatal events (OR 2.87, 95% CI 1.06-7.74). Important causes of admission were epilepsy-related complications: convulsive status epilepticus (CSE) (38%), and postictal coma (12%). Age was independently associated with prolonged hospital stay (OR 1.02, 95% CI 1.00-1.04) and mortality (OR, 1.07, 95% CI 1.04-1.10).

Significance: Epilepsy is associated with significant number of admissions to hospital, considerable duration of admission, and mortality. Improved supply of AEDs in the community, early initiation of treatment, and adherence would reduce hospitalization of PWE and thus the burden of epilepsy on the health system.


Abstract

Background: Podoconiosis is one of the forgotten types of leg swelling (elephantiasis) in the tropics. Unlike the other, better-known types of leg swelling, podoconiosis is not caused by any parasite, virus or bacterium, but by an abnormal reaction to minerals
found in the clay soils of some tropical highland areas. Non-governmental Organizations (NGOs) have been responsible for the development of simple treatment methods without systematic evaluation of its effectiveness. It is essential that a large scale, fully controlled, pragmatic trial of the intervention is conducted. We aim to test the hypothesis that community-based treatment of podoconiosis lymphoedema reduces the frequency of acute dermatolymphangioadenitis episodes ('acute attacks') and improves other clinical, social and economic outcomes.

**Methods/design:** This is a pragmatic, individually randomised controlled trial. We plan to randomly allocate 680 podoconiosis patients from the East Gojjam Zone in northern Ethiopia to one of two groups: 'Standard Treatment' or 'Delayed Treatment'. Those randomised to standard treatment will receive the hygiene and foot-care intervention from May 2015 for one year, whereas those in the control arm will be followed through 2015 and be offered the intervention in 2016. The trial will be preceded by an economic context survey and a Rapid Ethical Assessment to identify optimal methods of conveying information about the trial and the approaches to obtaining informed consent preferred by the community. The primary outcome will be measured by recording patient recall and using a simple, patient-held diary that will be developed to record episodes of acute attacks. Adherence to treatment, clinical stage of disease, quality of life, disability and stigma will be considered secondary outcome measures. Other outcomes will include adverse events and economic productivity. Assessments will be made at baseline and at 3, 6, 9 and 12 months thereafter.

**Discussion:** The evidence is highly likely to inform implementation of the new master plan for integrated control of Neglected Tropical Diseases (NTDs), in which podoconiosis is identified as one of eight NTDs prioritised for control. Potentially, an estimated 3 million patients in Ethiopia will therefore benefit from the results of this trial.


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**Abstract**

**Introduction:** The voltage gated sodium channel mutation Vgsc-1014S (kdr-east) was first reported in Kenya in 2000 and has since been observed to occur at high frequencies in the local Anopheles gambiae s.s.
**Population:** The mutation Vgsc-1014F has never been reported from An. gambiae Complex complex mosquitoes in Kenya.

**Findings:** Molecularly confirmed An. gambiae s.s. (hereafter An. gambiae) and An. arabiensis collected from 4 different parts of western Kenya were genotyped for kdr from 2011 to 2013. Vgsc-1014F was observed to have emerged, apparently, simultaneously in both An. gambiae and An. arabiensis in 2012. A portion of the samples were submitted for sequencing in order to confirm the Vgsc-1014F genotyping results. The resulting sequence data were deposited in GenBank (Accession numbers: KR867642-KR867651, KT758295-KT758303). A single Vgsc-1014F haplotype was observed suggesting, a common origin in both species.

**Conclusion:** This is the first report of Vgsc-1014F in Kenya. Based on our samples, the mutation is present in low frequencies in both An. gambiae and An. arabiensis. It is important that we start monitoring relative frequencies of the two kdr genes so that we can determine their relative importance in an area of high insecticide treated net ownership.


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**Abstract**

The need for a suitable tool for assessing postpartum depression in Kenya led to the process of translation of the 10 items Edinburgh Postnatal Scale into Kiswahili. The idea was to seek semantic, conceptual as well as normative equivalence in this translation. The paper discusses issues and the process of translation and provides in depth discussions around translation from the point of view of cross-cultural mental health research and practice. The English version of the EPDS screening tool was finally successfully translated into Kiswahili and the translated version is attached with this paper.


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Abstract

Background: In western Kenya, maternal mortality is a major public health problem estimated at 730/100,000 live births, higher than the Kenyan national average of 488/100,000 women. Many women do not attend antenatal care (ANC) in the first trimester, half do not receive 4 ANC visits. A high proportion use traditional birth attendants (TBA) for delivery and 1 in five deliver unassisted. The present study was carried out to ascertain why women do not fully utilise health facility ANC and delivery services.

Methods: A qualitative study using 8 focus group discussions each consisting of 8-10 women, aged 15-49 years. Thematic analysis identified the main barriers and facilitators to health facility based ANC and delivery.

Results: Attending health facility for ANC was viewed positively. Three elements of care were important; testing for disease including HIV, checking the position of the foetus, and receiving injections and/or medications. Receiving a bed net and obtaining a registration card were also valuable. Four barriers to attending a health facility for ANC were evident; attitudes of clinic staff, long clinic waiting times, HIV testing and cost, although not all women felt the cost was prohibitive being worth it for the health of the child. Most women preferred to deliver in a health facility due to better management of complications. However cost was a barrier, and a reason to visit a TBA because of flexible payment. Other barriers were unpredictable labour and transport, staff attitudes and husbands' preference.

Conclusions: Our findings suggest that women in western Kenya are amenable to ANC and would be willing and even prefer to deliver in a healthcare facility, if it were affordable and accessible to them. However for this to happen there needs to be investment in health promotion, and transport, as well as reducing or removing all fees associated with antenatal and delivery care. Yet creating demand for service will need to go alongside investment in antenatal services at organisational, staffing and facility level in order to meet both current and future increase in demand.


**Background:** The characteristics, determinants, and potential contribution to transmission of asymptomatic cases of respiratory syncytial virus (RSV) infection have not been well described.

**Methods:** A cohort of 47 households (493 individuals) in coastal Kenya was recruited and followed for a 26-week period spanning a complete RSV season. Nasopharyngeal swab specimens were requested weekly, during the first 4 weeks, and twice weekly thereafter from all household members, regardless of illness status. The samples were screened for a range of respiratory viruses by multiplex real-time polymerase chain reaction.

**Results:** Tests on 16,928 samples yielded 205 RSV infection episodes in 179 individuals (37.1%) from 40 different households. Eighty-six episodes (42.0%) were asymptomatic. Factors independently associated with an increased risk of asymptomatic RSV infection episodes were higher age, shorter duration of infection, bigger household size, lower peak viral load, absence of concurrent RSV infections within the household, infection by RSV group B, and no prior human rhinovirus infections. The propensity of RSV spread in households was dependent on symptom status and amount (duration and load) of virus shed.

**Conclusions:** While asymptomatic RSV was less likely to spread, the high frequency of symptomless RSV infection episodes highlights a potentially important role of asymptomatic infections in the community transmission of RSV.


**Abstract**

**Background:** Non-typhoidal Salmonella (NTS) causes invasive and frequently fatal disease in African children. Existing strategies to prevent, diagnose, and treat NTS disease are inadequate. An improved understanding of the biology of invasive Salmonella infection will facilitate the development of novel NTS control measures. Despite evidence in mice and man showing a clear role for host genetics in NTS susceptibility, there are no published studies investigating host genetic susceptibility to NTS in African populations.
Methods: We conducted a genome-wide association study (SNP Array 6.0, Affymetrix, CA, USA) of NTS bacteraemia in Kenyan children, with replication in Malawian children. We assessed the function of NTS-associated variants in an expression quantitative trait locus (eQTL) dataset of interferon γ (IFNγ) and lipopolysaccharide-stimulated monocytes from 432 healthy European adults. Serum IFNγ (Bio-Plex immunoassay, Bio-Rad Laboratories, CA, USA) in Malawian NTS cases (n=106) during acute disease was correlated with genotype by linear regression.

Findings: After whole-genome imputation and quality control, 180 Kenyan cases and 2677 controls were included in an association analysis at 7 951 614 (additive model) and 4 669 537 (genotypic model) loci. After quality control, 143 Malawian cases and 336 controls were included in the replication analysis. An intronic variant in STAT4 was associated (recessive model) with NTS in both Kenyan and Malawian children (Kenya p=5·6 × 10(-9), Malawi p=0·02, combined p=1·4 × 10(-9); odds ratio 7·2, 95% CI 3·8-13·5). The NTS-associated variant was an eQTL for STAT4 expression in IFNγ-stimulated monocytes (p=9·59 × 10(-6)), the NTS risk allele being associated with lower STAT4 expression. In Malawian children with NTS bacteraemia, the same NTS risk allele was associated with lower serum concentrations of IFNγ (p=0·02) at presentation.

Interpretation: STAT4 is highly plausible as a susceptibility locus for invasive NTS disease. STAT4 mediates IFNγ release in T cells and natural killer cells in response to interleukin 12 (IL12). Individuals with rare mutations elsewhere in the IL12-IFNγ axis are at risk of disseminated NTS infection. We provide the first evidence, to our knowledge, of a host genetic determinant of NTS disease in African children, and of a STAT4 variant conferring susceptibility to an infectious disease in man.

Latent TB infection was diagnosed by tuberculin skin testing. HIV status of participants was assessed. Using a logistic regression model, we determined the adjusted odds of latent TB infection among healthcare workers compared to school workers; and among healthcare workers only, we assessed work-related risk factors for latent TB infection.

**Results:** We enrolled 1005 healthcare workers and 411 school workers. Approximately 60% of both groups were female. A total of 22% of 958 healthcare workers and 12% of 392 school workers tested HIV positive. Prevalence of self-reported history of TB disease was 7.4% among healthcare workers and 3.6% among school workers. Prevalence of latent TB infection was 60% among healthcare workers and 48% among school workers. Adjusted odds of latent TB infection were 1.5 times higher among healthcare workers than school workers (95% confidence interval 1.2–2.0). Healthcare workers at all three facility types had similar prevalence of latent TB infection (P = 0.72), but increasing years of employment was associated with increased odds of LTBI (P < 0.01).

**Conclusion:** Healthcare workers at facilities in western Kenya which offer TB and HIV services are at increased risk of latent TB infection, and the risk is similar across facility types. Implementation of WHO-recommended TB infection control measures are urgently needed in health facilities to protect healthcare workers.


**Abstract**

**Background:** Epidemiological studies indicate that some children experience many more episodes of clinical malaria than their age mates in a given location. Whether this is as a result of the micro-heterogeneity of malaria transmission with some children effectively getting more exposure to infectious mosquitoes than others, or reflects a failure in the acquisition of immunity needs to be elucidated. Here, we investigated the determinants of increased susceptibility to clinical malaria by comparing the intensity of exposure to Plasmodium falciparum and the acquisition of immunity in children at the extreme ends of the over-dispersed distribution of the incidence of clinical malaria.

**Methods:** The study was nested within a larger cohort in an area where the intensity of malaria transmission was low. We identified children who over a five-year period
experienced 5 to 16 clinical malaria episodes (children at the tail-end of the over-dispersed distribution, n = 35), remained malaria-free (n = 12) or had a single episode (n = 26). We quantified antibodies against seven Plasmodium falciparum merozoite antigens in plasma obtained at six cross-sectional surveys spanning these five years. We analyzed the antibody responses to identify temporal dynamics that associate with disease susceptibility.

**Results:** Children experiencing multiple episodes of malaria were more likely to be parasite positive by microscopy at cross-sectional surveys (X^2 test for trend 14.72 P = 0.001) and had a significantly higher malaria exposure index, than those in the malaria-free or single episode groups (Kruskal-Wallis test P = 0.009). In contrast, the five-year temporal dynamics of anti-merozoite antibodies were similar in the three groups. Importantly in all groups, antibody levels were below the threshold concentrations previously observed to be correlated with protective immunity.

**Conclusions:** We conclude that in the context of a low malaria transmission setting, susceptibility to clinical malaria is not accounted for by anti-merozoite antibodies but appears to be a consequence of increased parasite exposure. We hypothesize that intensive exposure is a prerequisite for protective antibody concentrations, while little to modest exposure may manifest as multiple clinical infections with low levels of antibodies. These findings have implications for interventions that effectively lower malaria transmission intensity.


### 75.

**Abstract**

**Background:** Severe respiratory syncytial virus (RSV) disease occurs predominantly in children under 6 months of age. There is no licensed RSV vaccine. Protection of young infants could be achieved by a maternal vaccine to boost titres of passively transferred protective antibodies. Data on the level and kinetics of functional RSV-specific antibody at birth and over the early infant period would inform vaccine product design.

**Methods:** From a birth cohort study (2002-2007) in Kilifi, Kenya, 100 participants were randomly selected for whom cord blood and 2 subsequent 3-monthly blood samples within the first year of life, were available. RSV antibodies against the A2
strain of RSV were assayed and recorded as the logarithm (base 2) plaque reduction neutralisation test (PRNT) titre. Analysis by linear regression accounted for within-person clustering.

**Results:** The geometric mean neutralisation antibody titre was 10.6 (SD: 1.13) at birth with a log-linear decay over the first 6 months of life. The estimated rate of decay was -0.58 (SD: 0.20) log2PRNT titre per month and a half-life of 36 days. There was no significant interaction between cord titre and rate of decay with age. Mean cord titres rose and fell in a pattern temporally tracking community virus transmission.

**Conclusions:** In this study population, RSV neutralising antibody titres decay approximately two-fold every one month. The rate of decay varies widely by individual but is not related to titre at birth. RSV specific cord titres vary seasonally, presumably due to maternal boosting.


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**Abstract**

**Background:** With ambitious targets to eliminate lymphatic filariasis over the coming years, there is a need to identify optimal strategies to achieve them in areas with different baseline prevalence and stages of control. Modelling can assist in identifying what data should be collected and what strategies are best for which scenarios.

**Methods:** We develop a new individual-based, stochastic mathematical model of the transmission of lymphatic filariasis. We validate the model by fitting to a first time point and predicting future timepoints from surveillance data in Kenya and Sri Lanka, which have different vectors and different stages of the control programme. We then simulate different treatment scenarios in low, medium and high transmission settings, comparing once yearly mass drug administration (MDA) with more frequent MDA and higher coverage. We investigate the potential impact that vector control, systematic non-compliance and different levels of aggregation have on the dynamics of transmission and control.

**Results:** In all settings, increasing coverage from 65 to 80 % has a similar impact on control to treating twice a year at 65 % coverage, for fewer drug treatments being distributed. Vector control has a large impact, even at moderate levels. The extent of
aggregation of parasite loads amongst a small portion of the population, which has been estimated to be highly variable in different settings, can undermine the success of a programme, particularly if high risk sub-communities are not accessing interventions.

**Conclusion:** Even moderate levels of vector control have a large impact both on the reduction in prevalence and the maintenance of gains made during MDA, even when parasite loads are highly aggregated, and use of vector control is at moderate levels. For the same prevalence, differences in aggregation and adherence can result in very different dynamics. The novel analysis of a small amount of surveillance data and resulting simulations highlight the need for more individual level data to be analysed to effectively tailor programmes in the drive for elimination.


**Abstract**

**Background:** Under trial conditions insecticide-treated nets have been shown to provide significant clinical and mortality protection under a range of malaria transmission intensity conditions. There are, however, few operational impact data, notably in very intense transmission conditions. This study, reports on malaria infection among Kenyan schoolchildren living in areas of intense malaria transmission and their reported use of insecticide-treated bed nets.

**Methods:** 5188 children in 54 schools were randomly sampled from seven counties surrounding Lake Victoria between May and June 2014. A questionnaire was administered to schoolchildren in classes 2-6 on the use of a long-lasting, insecticide-treated net (LLIN) the night before the survey and provided a single blood sample for a rapid diagnostic test for malaria infection. Analysis of the impact of insecticide-treated net use on malaria prevalence was undertaken using a multivariable, mixed effects, logistic regression at 95% confidence interval (CI), taking into account hierarchical nature of the data and results adjusted for school clusters.

**Results:** The overall prevalence of malaria infection was 48.7%, two-thirds (67.9%) of the children reported using LLIN, 91.3% of the children reported that their households own at least one LLIN and the household LLIN coverage was 2.5 persons per one LLIN. The prevalence of infection showed variation across the counties, with
prevalence being highest in Busia (66.9%) and Homabay (51.8%) counties, and lowest in Migori County (29.6%). Generally, malaria parasite prevalence differed between age groups and gender with the highest prevalence occurring in children below 7 years (50.6%) and males (52.2%). Adjusting for county and school, there was a significant reduction in odds of malaria infection among the schoolchildren who reported LLIN use the previous night by 14 % (aOR 0.86, 95% CI 0.74-0.98, P < 0.027).

**Conclusion:** Malaria transmission continues to be high around Lake Victoria. Despite evidence of increasing pyrethroid resistance and the likely overall efficacy of LLIN distributed several years prior to the survey, LLIN continue to provide protection against infection among school-aged children.


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<td><strong>Abstract</strong></td>
<td>The prevalence of a genetic polymorphism(s) at codon 268 in the cytochrome b gene, which is associated with failure of atovaquone-proguanil treatment, was analyzed in 227 Plasmodium falciparum parasites from western Kenya. The prevalence of the wild-type allele was 63%, and that of the Y268S (denoting a Y-to-S change at position 268) mutant allele was 2%. There were no pure Y268C or Y268N mutant alleles, only mixtures of a mutant allele(s) with the wild type. There was a correlation between parasite 50% inhibitory concentration (IC50) and parasite genetic polymorphism; mutant alleles had higher IC50s than the wild type.</td>
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<td><strong>Abstract</strong></td>
<td><strong>Background:</strong> By 28 June 2015, there were a total of 11,234 deaths from the Ebola virus disease (EVD) in five West African countries (Guinea, Liberia, Mali, Nigeria and Sierra Leone). The objective of this study was to estimate the future productivity losses</td>
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associated with EVD deaths in these West African countries, in order to encourage increased investments in national health systems.

**Methods:** A cost-of-illness method was employed to calculate future non-health (NH) gross domestic product (GDP) (NHGDP) losses associated with EVD deaths. The future non-health GDP loss (NHGDPLoss) was discounted at 3 %. Separate analyses were done for three different age groups (< =14 years, 15-44 years and = >45 years) for the five countries (Guinea, Liberia, Mali, Nigeria, and Sierra Leone) affected by EVD. We also conducted a one-way sensitivity analysis at 5 and 10 % discount rates to gauge their impacts on expected NHGDPLoss.

**Results:** The discounted value of future NHGDPLoss due to the 11,234 deaths associated with EVD was estimated to be Int$ (international dollars) 155,663,244. About 27.86 % of the loss would be borne by Guinea, 34.84 % by Liberia, 0.10 % by Mali, 0.24 % by Nigeria and 36.96 % by Sierra Leone. About 27.27 % of the loss is attributed to those aged under 14 years, 66.27 % to those aged 15-44 years and 6.46 % to those aged over 45 years. The average NHGDPLoss per EVD death was estimated to be Int$ 17,473 for Guinea, Int$ 11,283 for Liberia, Int$ 25,126 for Mali, Int$ 47,364 for Nigeria and Int$ 14,633 for Sierra Leone.

**Conclusion:** In spite of alluded limitations, the estimates of human and economic losses reported in this paper, in addition to those projected by the World Bank, show that EVD imposes a significant economic burden on the affected West African countries. That heavy burden, coupled with human rights and global security concerns, underscores the urgent need for increased domestic and external investments to enable Guinea, Liberia and Sierra Leone (and other vulnerable African countries) to develop resilient health systems, including core capacities to detect, assess, notify, verify and report events, and to respond to public health risks and emergencies.


**Abstract**

**Background:** The evolution of drug-resistant parasites is a major hindrance to malaria control, and thus understanding the behaviour of drug-resistant mutants is of clinical relevance. The study aimed to investigate how resistance against lumefantrine (LU) and piperaquine (PQ), anti-malarials used as partner drugs in artemisinin-based
combination therapy (ACT), impacts parasite fitness. This is important since resistance to ACT, the first-line anti-malarial regimen is increasingly being reported.

**Methods:** The stability of Plasmodium berghei ANKA strain that was previously selected for LU and PQ resistance was evaluated using the 4-day assay and established infection test in mice. Fitness cost of resistance was determined by comparing parasites proliferation rates in absence of drug pressure for the drug-exposed parasites between day 4 and 7 post-infection (pi), relative to the wild-type. Statistical analysis of data to compare mean parasitaemia and growth rates of respective parasite lines was carried out using student’s t-test and one-way analysis of variance, with significance level set at p<0.05.

**Results:** During serial passaging in the absence of the drug, the PQ-resistant parasite maintained low growth rates at day 7 pi (mean parasitaemia, 5.6% ± 2.3) relative to the wild-type (28.4% ± 6.6), translating into a fitness cost of resistance of 80.3%. Whilst resistance phenotype for PQ was stable, that of LU was transient since after several serial passages in the absence of drug, the LU-exposed line assumed the growth patterns of the wild-type.

**Conclusions:** The contrasting behaviour of PQ- and LU-resistance phenotypes support similar findings which indicate that even for drugs within the same chemical class, resistance-conferrred traits may vary on how they influence parasite fitness and virulence. Resistance-mediating polymorphisms have been associated with less fit malaria parasites. In the absence of drug pressure in the field, it is therefore likely that the wild-type parasite will out-compete the mutant form. This implies the possibility of reintroducing a drug previously lost to resistance, after a period of suspended use. Considering the recent reports of high failure rates associated with ACT, high fitness cost of resistance to PQ is therefore of clinical relevance as the drug is a partner in ACT.


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**Abstract**

Infectious diseases in poultry can spread quickly and lead to huge economic losses. In the past decade, on multiple continents, the accelerated spread of highly pathogenic avian Influenza A (H5N1) virus, often through informal trade networks, has led to the death and culling of hundreds of millions of poultry. Endemic poultry diseases like
Newcastle disease and fowl typhoid can also be devastating in many parts of the world. Understanding trade networks in unregulated systems can inform policy decisions concerning disease prevention and containment. From June to December 2008 we conducted a cross-sectional survey of backyard farmers, market traders, and middlemen in 5/8 provinces in Kenya. We administered a standardized questionnaire to each type of actor using convenience, random, snowball, and systematic sampling. Questionnaires addressed frequency, volume, and geography of trade, as well as biosecurity practices. We created a network diagram identifying the most important locations for trade. Of 380 respondents, 51% were backyard farmers, 24% were middlemen and 25% were market traders. Half (50%) of backyard farmers said they raised poultry both for household consumption and for sale. Compared to market traders, middlemen bought their poultry from a greater number of villages (median 4.2 villages for middlemen vs. 1.9 for market traders). Traders were most likely to purchase poultry from backyard farmers. Of the backyard farmers who sold poultry, 51% [CI 40-63] reported selling poultry to market traders, and 54% [CI 44-63] sold to middlemen. Middlemen moved the largest volume of poultry on a weekly basis (median purchases: 187 birds/week [IQR 206]; median sales: 188 birds/week [IQR 412.5]). The highest numbers of birds were traded in Nairobi - Kenya's capital city. Nairobi was the most prominent trading node in the network (61 degrees of centrality). Many smaller sub-networks existed as a result of clustered local trade. Market traders were also integral to the network. The informal poultry trade in Kenya is dependent on the sale of backyard poultry to middlemen and market traders. These two actors play a critical role in poultry movement in Kenya; during any type of disease outbreak middlemen should be targeted for control- and containment-related interventions.


Abstract

Yellow fever (YF), which is caused by a mosquito-borne virus, is an important viral hemorrhagic fever endemic in equatorial Africa and South America. Yellow fever virus (YFV) is the prototype of the family Flaviviridae and genus Flavivirus. The aim of this study was to determine the seroprevalence of YFV in selected health facilities in Western Kenya during the period 2010-2012. A total of 469 serum samples from febrile patients were tested for YFV antibodies using in-house IgM-capture ELISA, in-house indirect IgG ELISA, and 50% focus reduction neutralization test (FRNT50). The present study did not identify any IgM ELISA-positive cases, indicating absence of
recent YFV infection in the area. Twenty-eight samples (6%) tested positive for YFV IgG, because of either YFV vaccination or past exposure to various flaviviruses including YFV. Five cases were confirmed by FRNT50; of these, 4 were either vaccination or natural infection during the YF outbreak in 1992-1993 or another period and 1 case was confirmed as a West Nile virus infection. Domestication and routine performance of arboviral differential diagnosis will help to address the phenomenon of pyrexia of unknown origin, contribute to arboviral research in developing countries, and enhance regular surveillance.


Abstract

This study aimed to assess the prevalence of probable post-traumatic stress disorder (PTSD), and its associated risk factors in a general household population in Kenya. Data were drawn from a cross-sectional household survey of mental disorders and their associated risk factors. The participants received a structured epidemiological assessment of common mental disorders, and symptoms of PTSD, accompanied by additional sections on socio-demographic data, life events, social networks, social supports, disability/activities of daily living, quality of life, use of health services, and service use. The study found that 48% had experienced a severe trauma, and an overall prevalence rate of 10.6% of probable PTSD, defined as a score of six or more on the trauma screening questionnaire (TSQ). The conditional probability of PTSD was 0.26. Risk factors include being female, single, self-employed, having experienced recent life events, having a common mental disorder (CMD) and living in an institution before age 16. The study indicates that probable PTSD is prevalent in this rural area of Kenya. The findings are relevant for the training of front line health workers, their support and supervision, for health management information systems, and for mental health promotion in state boarding schools.


Abstract

Background: There has been no previous household population study of suicidal ideation and attempts in Kenya. Therefore this study aimed to establish the prevalence of suicidal ideation and attempts in a rural population in Kenya, and to assess risk factors.

Methods: An epidemiological survey of a household population, using standardised structured interviews. We examined the prevalence of suicidal ideation and suicide attempts and the predictors of suicidal thoughts and attempts, using STATA to calculate unadjusted and adjusted odds ratios.

Results: A quarter of the sample (24.1 %) had thought that life was not worth living (tedium vitae) at some point in their lives, while a fifth had experienced death wishes at some stage. About 7.9 % reported suicidal thoughts and 1.9 % had made actual suicide attempts at some point in their lives. It can be seen that the prevalence of suicidal thoughts was 0.7 %, 4.2 %, 3.7 % and 7.9 % for last week, last year, at some other time, and lifetime respectively, while the prevalence of suicidal attempts was 0.5 %, 1.2 %, 0.7 and 1.9 % respectively. In the adjusted analysis of factors associated with suicidal thoughts, being female (OR 1.8, p = 0.017), having CMD (OR 2.7, p = 0.001), having a number of recent life events (OR 2.3, p = 0.001 for 2-3 life events and OR 2.6, p = 0.004 for 4 or more life events), and having a large social group size (OR 7.7, p = 0.006 for social group size of 4-8 and OR 9.1, p = 0.003 for social group size of 9 or more) were all associated with increased rates of life time suicidal thoughts, but psychotic symptoms were no longer significant after adjustment for the other variables. In the adjusted analysis of suicide attempts, having any psychotic symptoms (OR 5.1, p = 0.001) was the only factor associated with suicide attempts after adjustment for other factors significant at the bivariate level.

Conclusion: Suicidal ideation and attempts pose a significant public health burden in this poor rural area of Kenya. The findings are relevant for mental health promotion and prevention programmes, public education and professional training programmes in relevant sectors, especially in front line health workers and social workers.


Abstract

**Background:** Respiratory syncytial virus (RSV) is globally ubiquitous, and infection during the first six months of life is a major risk for severe disease and hospital admission; consequently RSV is the most important viral cause of respiratory morbidity and mortality in young children. Development of vaccines for young infants is complicated by the presence of maternal antibodies and immunological immaturity, but vaccines targeted at older children avoid these problems. Vaccine development for young infants has been unsuccessful, but this is not the case for older children (> 6 m). Would vaccinating older children have a significant public health impact? We developed a mathematical model to explore the benefits of a vaccine against RSV.

**Methods and findings:** We have used a deterministic age structured model capturing the key epidemiological characteristics of RSV and performed a statistical maximum-likelihood fit to age-specific hospitalization data from a developing country setting. To explore the effects of vaccination under different mixing assumptions, we included two versions of contact matrices: one from a social contact diary study, and the second a synthesised construction based on demographic data. Vaccination is assumed to elicit an immune response equivalent to primary infection. Our results show that immunisation of young children (5-10 m) is likely to be a highly effective method of protection of infants (<6 m) against hospitalisation. The majority benefit is derived from indirect protection (herd immunity). A full sensitivity and uncertainty analysis using Latin Hypercube Sampling of the parameter space shows that our results are robust to model structure and model parameters.

**Conclusions:** This result suggests that vaccinating older infants and children against RSV can have a major public health benefit.

**PubMed link:** https://pubmed.ncbi.nlm.nih.gov/26390032/


Abstract

**Background:** Intermittent preventive treatment in pregnancy (IPTp) with sulfadoxine-pyrimethamine (SP) is recommended in HIV-negative women to avert malaria, while this relies on cotrimoxazole prophylaxis (CTXp) in HIV-positive women. Alternative
antimalarials are required in areas where parasite resistance to antifolate drugs is high. The cost-effectiveness of IPTp with alternative drugs is needed to inform policy.

**Methods:** The cost-effectiveness of 2-dose IPTp-mefloquine (MQ) was compared with IPTp-SP in HIV-negative women (Benin, Gabon, Mozambique and Tanzania). In HIV-positive women the cost-effectiveness of 3-dose IPTp-MQ added to CTXp was compared with CTXp alone (Kenya, Mozambique and Tanzania). The outcomes used were maternal clinical malaria, anaemia at delivery and non-obstetric hospital admissions. The poor tolerability to MQ was included as the value of women's loss of working days. Incremental cost-effectiveness ratios (ICERs) were calculated and threshold analysis undertaken.

**Results:** For HIV-negative women, the ICER for IPTp-MQ versus IPTp-SP was 136.30 US$ (2012 US$) (95%CI 131.41; 141.18) per disability-adjusted life-year (DALY) averted, or 237.78 US$ (95%CI 230.99; 244.57), depending on whether estimates from Gabon were included or not. For HIV-positive women, the ICER per DALY averted for IPTp-MQ added to CTXp, versus CTXp alone was 6.96 US$ (95%CI 4.22; 9.70). In HIV-negative women, moderate shifts of variables such as malaria incidence, drug cost, and IPTp efficacy increased the ICERs above the cost-effectiveness threshold. In HIV-positive women the intervention remained cost-effective for a substantial (up to 21 times) increase in cost per tablet.

**Conclusions:** Addition of IPTp with an effective antimalarial to CTXp was very cost-effective in HIV-negative women. IPTp with an efficacious antimalarial was more cost-effective than IPTp-SP in HIV-negative women. However, the poor tolerability of MQ does not favour its use as IPTp. Regardless of HIV status, prevention of malaria in pregnancy with a highly efficacious, well tolerated antimalarial would be cost-effective despite its high price.


**Abstract**

**Background:** Progress toward reducing the malaria burden in Africa has been measured, or modeled, using datasets with relatively short time-windows. These restricted temporal analyses may miss the wider context of longer-term cycles of
malaria risk and hence may lead to incorrect inferences regarding the impact of intervention.

**Methods:** 1147 age-corrected Plasmodium falciparum parasite prevalence (PfPR2-10) surveys among rural communities along the Kenyan coast were assembled from 1974 to 2014. A Bayesian conditional autoregressive generalized linear mixed model was used to interpolate to 279 small areas for each of the 41 years since 1974. Best-fit polynomial splined curves of changing PfPR2-10 were compared to a sequence of plausible explanatory variables related to rainfall, drug resistance and insecticide-treated bed net (ITN) use.

**Results:** P. falciparum parasite prevalence initially rose from 1974 to 1987, dipped in 1991-92 but remained high until 1998. From 1998 onwards prevalence began to decline until 2011, then began to rise through to 2014. This major decline occurred before ITNs were widely distributed and variation in rainfall coincided with some, but not all, short-term transmission cycles. Emerging resistance to chloroquine and introduction of sulfadoxine/pyrimethamine provided plausible explanations for the rise and fall of malaria transmission along the Kenyan coast.

**Conclusions:** Progress towards elimination might not be as predictable as we would like, where natural and extrinsic cycles of transmission confound evaluations of the effect of interventions. Deciding where a country lies on an elimination pathway requires careful empiric observation of the long-term epidemiology of malaria transmission.


**Abstract**

**Background:** Recent evidence indicates that pre-school children (PSC) living in S. mansoni highly endemic areas are at similar risk of schistosomiasis infection and morbidity as their school aged siblings. Recognizing this fact, the World Health Organization (WHO) is considering including this age group in highly endemic areas in control programmes using mass drug administration (MDA). However, detailed epidemiological information on S. mansoni infection among PSC is lacking for many endemic areas, specifically in Tanzania. This study was conducted to determine the
prevalence of S. mansoni infection and its associated risk factors among PSC in Ukerewe Island, North-Western Tanzania.

**Methods:** This was a cross-sectional study, which studied 400 PSC aged 1-6 years. The Kato-Katz (K-K) technique and the point of care circulating cathodic antigen (CCA) immunodiagnostic test were used to diagnose S. mansoni infection in stool and urine samples respectively. A pre-tested questionnaire was used to collect demographic data and water contact behaviour of the children from their parents/guardians.

**Results:** Based on the K-K technique, 44.4% (95% CI: 39.4-49.4) pre-school children were infected with S. mansoni and the overall geometric mean eggs per gram of faeces (GM-epg) was 110.6 epg with 38.2 and 14.7% having moderate and heavy intensity infections respectively. Based on the CCA, 80.1%, (95% CI: 76.0-84.0) were infected if a trace was considered positive, and 45.9%, (95% CI: 40.9-50.9), were infected if a trace was considered negative. Reported history of lake visits (AOR = 2.31, 95% CI: 1.06-5.01, P < 0.03) and the proximity to the lake shore (<500 m) (AOR = 2.09, 95% CI: 1.05-4.14, P < 0.03) were significantly associated with S. mansoni infection. Reported lake visit frequency (4-7 days/week) was associated with heavy intensities of S. mansoni infection (P < 0.00).

**Conclusion:** The prevalence of S. mansoni infection in the study population using K-K and CCA-trace-negative was moderate. The frequency of lake visits and the proximity to the lake shore were associated with the infection of S. mansoni and its intensity. These findings call for the need to include the PSC in MDA programmes, public health education and provision of safe water for bathing.


**Abstract**

Plasmodium falciparum parasites that are resistant to artemisinins have been detected in Southeast Asia. Resistance is associated with several polymorphisms in the parasite's K13-propeller gene. The molecular epidemiology of these artemisinin resistance genotypes in African parasite populations is unknown. We developed an assay to
quantify rare polymorphisms in parasite populations that uses a pooled deep-sequencing approach to score allele frequencies, validated it by evaluating mixtures of laboratory parasite strains, and then used it to screen P. falciparum parasites from >1100 African infections collected since 2002 from 14 sites across sub-Saharan Africa. We found no mutations in African parasite populations that are associated with artemisinin resistance in Southeast Asian parasites. However, we observed 15 coding mutations, including 12 novel mutations, and limited allele sharing between parasite populations, consistent with a large reservoir of naturally occurring K13-propeller variation. Although polymorphisms associated with artemisinin resistance in P. falciparum in Southeast Asia are not prevalent in sub-Saharan Africa, numerous K13-propeller coding polymorphisms circulate in Africa. Although their distributions do not support a widespread selective sweep for an artemisinin-resistant phenotype, the impact of these mutations on artemisinin susceptibility is unknown and will require further characterization. Rapid, scalable molecular surveillance offers a useful adjunct in tracking and containing artemisinin resistance.


Abstract

Introduction: Ninety-two percent of Low Birth Weight (LBW) infants are born in developing countries, 70% in Asia and 22% in Africa. WHO and UNICEF estimate LBW in Kenya as 11% and 6% by 2009 Kenya Demographic Health Survey. The same survey estimated LBW to be 5.5% in Central Province, Kenya. Data in Olkalou hospital indicated that prevalence of LBW was high. However, factors giving rise to the problem remained unknown.

Methods: A cross-sectional analytic study was therefore conducted to estimate prevalence and distribution and determine the factors associated with LBW in the hospital. LBW was defined as birth of a live infant less than 2500 g. We collected data using a semi-structured questionnaire and review of health records. A total 327 women were randomly selected from 500 mothers. Data was managed using Epi Info 3.3.2.

Results: The prevalence of LBW was 12.3% (n = 40). The mean age of mothers was 25.6 ± 6.2 years. Mean birth weight was 2928 ± 533 grams. There were 51.1% (n = 165) male neonates and 48.9% (n = 158) females. The following factors were significantly associated with LBW: LBW delivery in a previous birth (OR = 4.7, 95% C.I. = 1.53-14.24), premature rapture of membranes (OR = 2.95, 95% C.I. = 1.14-
7.62), premature births (OR=3.65, 95% C.I. = 1.31-10.38), and female newborn (OR = 2.32, 95% C.I. = 1.15-4.70). On logistic regression only delivery of LBW baby in a previous birth (OR = 5.07, 95% C.I. = 1.59-16.21) and female infant (OR = 3.37, 95% C.I. = 1.14-10.00) were independently associated with LBW.

**Conclusion:** Prevalence of LBW in the hospital was higher than national estimates. Female infant and LBW baby in a previous birth are independent factors. Local prevention efforts are necessary to mitigate the problem. Population-based study is necessary to provide accurate estimates in the area.


| **Abstract** |
| **Objectives:** Food insecurity and HIV/AIDS outcomes are inextricably linked in sub-Saharan Africa. We report on health and nutritional outcomes of a multisectoral agricultural intervention trial among HIV-infected adults in rural Kenya. |
| **Design:** This is a pilot cluster randomized controlled trial. |
| **Methods:** The intervention included a human-powered water pump, a microfinance loan to purchase farm commodities, and education in sustainable farming practices and financial management. Two health facilities in Nyanza Region, Kenya were randomly assigned as intervention or control. HIV-infected adults 18 to 49 years old who were on antiretroviral therapy and had access to surface water and land were enrolled beginning in April 2012 and followed quarterly for 1 year. Data were collected on nutritional parameters, CD4 T-lymphocyte counts, and HIV RNA. Differences in fixed-effects regression models were used to test whether patterns in health outcomes differed over time from baseline between the intervention and control arms. |
| **Results:** We enrolled 72 and 68 participants in the intervention and control groups, respectively. At 12 months follow-up, we found a statistically significant increase in CD4 cell counts (165 cells/μl, P < 0.001) and proportion virologically suppressed in the intervention arm compared with the control arm (comparative improvement in proportion of 0.33 suppressed, odds ratio 7.6, 95% confidence interval: 2.2-26.8). Intervention participants experienced significant improvements in food security (3.6 |
scale points higher, \( P < 0.001 \)) and frequency of food consumption (9.4 times per week greater frequency, \( P = 0.013 \)) compared to controls.

**Conclusion:** Livelihood interventions may be a promising approach to tackle the intersecting problems of food insecurity, poverty and HIV/AIDS morbidity.


| --- | --- |

**Abstract**

**Background:** The prevalence of malaria parasites in adults in Africa is less well researched than in children. Therefore, a demographic surveillance site was used to conduct a household survey of adults in the malaria endemic area of Maseno division in Kisumu County near Lake Victoria.

**Methods:** A random survey of 1,190 adults living in a demographic health surveillance site in a malaria endemic area of 70,805 population size was conducted, measuring presence of malaria parasites by slide microscopy. Data were analysed using STATA to calculate the prevalence of malaria and associated risk factors.

**Results:** The adult prevalence of presence of malaria parasites in Maseno was 28\% (95% CI: 25.4-31.0\%). Gender was a significant sociodemographic risk factor in both univariate (OR 1.5, \( p = 0.005 \)) and multivariate (OR 1.4, \( p = 0.019 \)) analyses. Females were 50\% more likely to have malaria than men.

**Conclusions:** Presence of malaria parasites is common in the adult population of this endemic area, and the rate is greatly increased in women. The presence of such an adult pool of malaria parasites represents a key reservoir factor in transmission of parasites to children, and is relevant for plans to


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<th>93.</th>
<th>Seale AC, Barsosio HC, Koech AC, Berkley JA; KIPMAT group. Embedding surveillance into clinical care to detect serious adverse events in pregnancy. Vaccine. 2015 Nov 25;33(47):6466-8</th>
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**Abstract**
Severe maternal complications in pregnancy in sub-Saharan Africa contribute to high maternal mortality and morbidity. Incidence data on severe maternal complications, life-threatening conditions, maternal deaths and birth outcomes are essential for clinical audit and to inform trial design of the types and frequency of expected severe adverse events (SAEs). However, such data are very limited, especially in sub-Saharan Africa. We set up standardized, systematic clinical surveillance embedded into routine clinical care in a rural county hospital in Kenya. Pregnant women and newborns are systematically assessed and investigated. Data are reported using a standardized Maternal Admission Record that forms both the hospital's clinical record and the data collection tool. Integrating clinical surveillance with routine clinical care is feasible and should be expanded in sub-Saharan Africa, both for improving clinical practice and as a basis for intervention studies to reduce maternal and newborn mortality and morbidity where rates are highest.


**Abstract**

**Background:** Nontyphoidal Salmonellae (NTS) cause a large burden of invasive and gastrointestinal disease among young children in sub-Saharan Africa. No vaccine is currently available. Previous reports indicate the importance of the O-antigen of Salmonella lipopolysaccharide for virulence and resistance to antibody-mediated killing. We hypothesised that isolates with more O-antigen have increased resistance to antibody-mediated killing and are more likely to be invasive than gastrointestinal.

**Methodology/principal findings:** We studied 192 NTS isolates (114 Typhimurium, 78 Enteritidis) from blood and stools, mostly from paediatric admissions in Kenya 2000-2011. Isolates were tested for susceptibility to antibody-mediated killing, using whole adult serum. O-antigen structural characteristics, including O-acetylation and glucosylation, were investigated. Overall, isolates were susceptible to antibody-mediated killing, but S. Enteritidis were less susceptible and expressed more O-antigen than Typhimurium (p<0.0001 for both comparisons). For S. Typhimurium, but not Enteritidis, O-antigen expression correlated with reduced sensitivity to killing ($r = 0.29$, 95% CI = 0.10-0.45, $p = 0.002$). Both serovars expressed O-antigen populations ranging 21-33 kDa average molecular weight. O-antigen from most Typhimurium were O-acetylated on rhamnose and abequose residues, while Enteritidis O-antigen had low
or no O-acetylation. Both Typhimurium and Enteritidis O-antigen were approximately 20%-50% glucosylated. Amount of S. Typhimurium O-antigen and O-antigen glucosylation level were inversely related. There was no clear association between clinical presentation and antibody susceptibility, O-antigen level or other O-antigen features.

**Conclusion/significance:** Kenyan S. Typhimurium and Enteritidis clinical isolates are susceptible to antibody-mediated killing, with degree of susceptibility varying with level of O-antigen for S. Typhimurium. This supports the development of an antibody-inducing vaccine against NTS for Africa. No clear differences were found in the phenotype of isolates from blood and stool, suggesting that the same isolates can cause invasive disease and gastroenteritis. Genome studies are required to understand whether invasive and gastrointestinal isolates differ at the genotypic level.


**Abstract**

**Background:** Effective surveillance and estimation of the biting fraction of Aedes aegypti is critical for accurate determination of the extent of virus transmission during outbreaks and inter-epidemic periods of dengue and chikungunya fever. Here, we describe the development and use of synthetic human odor baits for improved sampling of adult Ae. aegypti, in two dengue and chikungunya fevers endemic areas in Kenya; Kilifi and Busia counties.

**Methods:** We collected volatiles from the feet and trunks of two female and two male volunteers aged between 25 and 45 years. We used coupled gas chromatography-electroantennographic detection (GC/EAD) analysis to screen for antennally-active components from the volatiles and coupled GC-mass spectrometry (GC/MS) to identify the EAD-active components. Using randomized replicated designs, we compared the efficacies of Biogents (BG) sentinel traps baited with carbon dioxide plus either single or blends of the identified compounds against the BG sentinel trap baited with carbon dioxide plus the BG commercial lure in trapping Ae. aegypti. The daily mosquito counts in the different traps were subjected to negative binomial regression following the generalized linear models procedures.

**Results:** A total of ten major EAD-active components identified by GC/MS as mainly aldehydes and carboxylic acids, were consistently isolated from the human feet and
trunk volatiles from at least two volunteers. Field assays with synthetic chemicals of the shared EAD-active components identified from the feet and trunk gave varying results. Ae. aegypti were more attracted to carbon dioxide baited BG sentinel traps combined with blends of aldehydes than to similar traps combined with blends of carboxylic acids. When we assessed the efficacy of hexanoic acid detected in odors of the BG commercial lure and volunteers plus carbon dioxide, trap captures of Ae. aegypti doubled over the trap baited with the commercial BG lure. However, dispensing aldehydes and carboxylic acids together in blends, reduced trap captures of Ae. aegypti by ~45%-50%.

Conclusions: Our results provide evidence for roles of carboxylic acids and aldehydes in Ae. aegypti host attraction and also show that of the carboxylic acids, hexanoic acid is a more effective lure for the vector than the BG commercial lure.


Abstract

Most neglected tropical diseases (NTDs) have complex life cycles and are challenging to control. The "2020 goals" of control and elimination as a public health programme for a number of NTDs are the subject of significant international efforts and investments. Beyond 2020 there will be a drive to maintain these gains and to push for true local elimination of transmission. However, these diseases are affected by variations in vectors, human demography, access to water and sanitation, access to interventions and local health systems. We therefore argue that there will be a need to develop local quantitative expertise to support elimination efforts. If available now, quantitative analyses would provide updated estimates of the burden of disease, assist in the design of locally appropriate control programmes, estimate the effectiveness of current interventions and support 'real-time' updates to local operations. Such quantitative tools are increasingly available at an international scale for NTDs, but are rarely tailored to local scenarios. Localised expertise not only provides an opportunity for more relevant analyses, but also has a greater chance of developing positive feedback between data collection and analysis by demonstrating the value of data. This is essential as rational program design relies on good quality data collection. It is also likely that if such infrastructure is provided for NTDs there will be an additional impact on the health system more broadly. Locally tailored quantitative analyses can
help achieve sustainable and effective control of NTDs, but also underpin the development of local health care systems.


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<td><strong>Abstract</strong></td>
<td>Serum was analyzed from 146 healthy adult volunteers in eastern Africa to evaluate measles virus (MV) and canine distemper virus (CDV) neutralizing antibody (nAb) prevalence and potency. MV plaque reduction neutralization test (PRNT) results indicated that all sera were positive for MV nAbs. Furthermore, the 50% neutralizing dose (ND50) for the majority of sera corresponded to antibody titers induced by MV vaccination. CDV nAbs titers were low and generally were detected in sera with high MV nAb titers. A mutant CDV was generated that was less sensitive to neutralization by human serum. The mutant virus genome had 10 nucleotide substitutions, which coded for single amino acid substitutions in the fusion (F) and hemagglutinin (H) glycoproteins and two substitutions in the large polymerase (L) protein. The H substitution occurred in a conserved region involved in receptor interactions among morbilliviruses, implying that this region is a target for cross-reactive neutralizing antibodies.</td>
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<td><strong>Abstract</strong></td>
<td>The mechanisms of drug resistance development in the Plasmodium falciparum parasite to lumefantrine (LUM), commonly used in combination with artemisinin, are still unclear. We assessed the polymorphisms of Pfmspdbl2 for associations with LUM activity in a Kenyan population. MSPDBL2 codon 591S was associated with reduced susceptibility to LUM (P = 0.04). The high frequency of Pfmspdbl2 codon 591S in</td>
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Kenya may be driven by the widespread use of lumefantrine in artemisinin combination therapy (Coartem).


**Abstract**

**Background:** Alcohol use and hazardous drinking have been studied in school children and in urban areas of Kenya, but there has been no adult survey of these issues in a rural household population.

**Methods:** This study reports the prevalence of alcohol consumption and hazardous drinking in a household survey of a demographic surveillance site in rural Kenya. Information collected included demographic characteristics, socio-economic factors, recent life events and perceived social support. Alcohol consumption was assessed by questions about quantity and frequency. The Alcohol Use Disorders Identification Test (AUDIT) measured hazardous alcohol use. The Clinical Interview Schedule-Revised assessed common mental disorder, and the Psychosis Screening Questionnaire indicated the presence of psychotic symptoms.

**Results:** The study found that lifetime and current alcohol consumption were 10.8% and 9.2% respectively. Current alcohol consumption was significantly higher in men (OR 0.4, p < 0.001 for women) and in the self-employed (OR 1.8, p = 0.013), after adjustment for factors significant at the bivariate level. Hazardous drinking was significantly higher in men (OR 0.3, p < 0.001 for women), people living in larger households (OR 1.8, p = 0.021), people who were single (OR 1.7, p = 0.093), and in those who are self-employed (OR 1.8, p = 0.036), after adjustment for factors significant at the bivariate level.

**Conclusion:** This study suggests that alcohol consumption and hazardous drinking in the general population in a poor rural area in Nyanza Province is still relatively low. This represents an important public health educational opportunity to keep such rates low before increasing income and employment opportunities enable higher access to alcohol and other substances, and before the higher consumption found by studies on urban youth, especially neighbouring Kisumu town, spreads to the rural areas.

Abstract

Background: In sub-Saharan Africa, failure to initiate and sustain HIV treatment contributes to significant health, psychosocial, and economic impacts that burden not only infected individuals but diverse members of their social networks. Yet, due to intense stigma, the responsibility for managing lifelong HIV treatment rests solely, and often secretly, with infected individuals. We introduce the concept of "HIV risk induction" to suggest that social networks of infected individuals share a vested interest in improving long-term engagement with HIV care, and may represent an underutilized resource for improving HIV/AIDS outcomes within high prevalence populations.

Methods: In 2012, we implemented a 'microclinic' intervention to promote social network engagement in HIV/AIDS care and treatment. A microclinic is a therapy management collective comprised of a small group of neighbors, relatives, and friends who are trained as a team to provide psychosocial and adherence support for HIV-infected members. Our study population included 369 patients on ART and members of their social networks on Mfangano Island, Kenya, where HIV prevalence approaches 30%. Here we report qualitative data from 18 focus group discussions conducted with microclinic participants (n = 82), community health workers (n = 40), and local program staff (n = 39).

Results: Participants reported widespread acceptability and enthusiasm for the microclinic intervention. Responses highlight four overlapping community transformations regarding HIV care and treatment, namely (1) enhanced HIV treatment literacy (2) reduction in HIV stigma, (3) improved atmosphere for HIV status disclosure and (4) improved material and psychosocial support for HIV-infected patients. Despite challenges, participants describe an emerging sense of "collective responsibility" for treatment among HIV-infected and HIV-uninfected members of social networks.

Discussion: The lived experiences and community transformations highlighted by participants enrolled in this social network intervention in Western Kenya suggest opportunities to reframe the continuum of HIV care from a secretive individual journey into a network-oriented cycle of engagement.

Abstract

Background: There are concerns that the evidence from studies showing noninferiority of oral amoxicillin to benzyl penicillin for severe pneumonia may not be generalizable to high-mortality settings.

Methods: An open-label, multicenter, randomized controlled noninferiority trial was conducted at 6 Kenyan hospitals. Eligible children aged 2-59 months were randomized to receive amoxicillin or benzyl penicillin and followed up for the primary outcome of treatment failure at 48 hours. A noninferiority margin of risk difference between amoxicillin and benzyl penicillin groups was prespecified at 7%.

Results: We recruited 527 children, including 302 (57.3%) with comorbidity. Treatment failure was observed in 20 of 260 (7.7%) and 21 of 261 (8.0%) of patients in the amoxicillin and benzyl penicillin arms, respectively (risk difference, -0.3% [95% confidence interval, -5.0% to 4.3%]) in per-protocol analyses. These findings were supported by the results of intention-to-treat analyses. Treatment failure by day 5 postenrollment was 11.4% and 11.0% and rising to 13.5% and 16.8% by day 14 in the amoxicillin vs benzyl penicillin groups, respectively. The most frequent cause of cumulative treatment failure at day 14 was clinical deterioration within 48 hours of enrollment (33/59 [55.9%]). Four patients died (overall mortality 0.8%) during the study, 3 of whom were allocated to the benzyl penicillin group. The presence of wheeze was independently associated with less frequent treatment failure.

Conclusions: Our findings confirm noninferiority of amoxicillin to benzyl penicillin, provide estimates of risk of treatment failure in Kenya, and offer important additional evidence for policy making in sub-Saharan Africa.

Abstract

**Background:** Vaccines against human papillomavirus (HPV) infection have the potential to reduce the burden of cervical cancer. School-based delivery of HPV vaccines is cost-effective and successful uptake depends on school teachers' knowledge and acceptability of the vaccine. The aim of this study is to assess primary school teachers' knowledge and acceptability of HPV vaccine and to explore facilitators and barriers of an ongoing Gavi Alliance-supported vaccination program in Kitui County, Kenya.

**Methods:** This was a cross-sectional, mixed methods study in Central Division of Kitui County where the Ministry of Health is offering the quadrivalent HPV vaccine to grade four girls. Data on primary school teachers' awareness, knowledge and acceptability of HPV vaccine as well as facilitators and barriers to the project was collected through self-administered questionnaires and two focus group discussions.

**Results:** 339 teachers (60% female) completed the survey (62% response rate) and 13 participated in 2 focus group discussions. Vaccine awareness among teachers was high (90%), the level of knowledge about HPV and cervical cancer among teachers was moderate (48%, SD = 10.9) and females scored higher than males (50% vs. 46%, p = 0.002). Most teachers (89%) would recommend the vaccine to their daughter or close relatives. Those who would recommend the vaccine had more knowledge than those who would not (p = <0.001). The main barriers were insufficient information about the vaccine, poor accessibility of schools, absenteeism of girls on vaccine days, and fear of side effects.

**Conclusions:** Despite low to moderate levels of knowledge about HPV vaccine among school teachers, vaccine acceptability is high. Teachers with little knowledge on HPV vaccine are less likely to accept the vaccine than those who know more; this may affect uptake if not addressed. Empowering teachers to be vaccine champions in their community may be a feasible way of disseminating information about HPV vaccine and cervical cancer.


103. Munywoki PK, Koech DC, Agoti CN, Kibirige N, Kipkoech J, Cane PA, Medley GF, Nokes DJ. Influence of age, severity of infection, and co-infection on the duration of respiratory syncytial virus (RSV) shedding. Epidemiol Infect. 2015 Mar;143(4):804-12
Abstract

RSV is the most important viral cause of pneumonia and bronchiolitis in children worldwide and has been associated with significant disease burden. With the renewed interest in RSV vaccines, we provide realistic estimates on duration, and influencing factors on RSV shedding which are required to better understand the impact of vaccination on the virus transmission dynamics. The data arise from a prospective study of 47 households (493 individuals) in rural Kenya, followed through a 6-month period of an RSV seasonal outbreak. Deep nasopharyngeal swabs were collected twice each week from all household members, irrespective of symptoms, and tested for RSV by multiplex PCR. The RSV G gene was sequenced. A total of 205 RSV infection episodes were detected in 179 individuals from 40 different households. The infection data were interval censored and assuming a random event time between observations, the average duration of virus shedding was 11.2 (95% confidence interval 10.1-12.3) days. The shedding durations were longer than previous estimates (3.9-7.4 days) based on immunofluorescence antigen detection or viral culture, and were shown to be strongly associated with age, severity of infection, and revealed potential interaction with other respiratory viruses. These findings are key to our understanding of the spread of this important virus and are relevant in the design of control programmes.


Abstract

In this commentary, we discuss a photography competition, launched during the summer of 2014, to explore the everyday stories of how gender plays out within health systems around the world. While no submission fees were charged nor financial awards involved, the winning entries were exhibited at the Global Symposium on Health Systems Research in Cape Town, South Africa, in October 2014, with credits to the photographers involved. Anyone who had an experience of, or interest in, gender and health systems was invited to participate. Underlying the aims of the photo competition was a recognition of the importance of participation of community members, health workers and other non-academics in our research engagement and in venues where their perspectives are often missing. The competition elicited participation from a range of stakeholders engaged in health systems: professional photographers, project managers, donors, researchers, activists and community members. In total, 54 photos were submitted by 29 participants from 15 different nationalities and country locations.
We unpack what the photos suggest about gender and health systems and the pivotal role of community-level systems that support health, including that of close-to-community health providers. Three themes emerged: women active on the frontlines of service delivery and as primary unpaid carers, the visibility of men in gender and health systems and the inter-sectoral nature and intra-household dynamics of community health that embed close-to-community health providers. The question of who has the right to take and display images, under what contexts and for what purpose also permeated the photo competition. We reflect on how photos can be valuable representations of the worlds that we, health workers and health systems are embedded in. Photographs broaden our horizons by capturing and connecting us to subjects from afar in seemingly unmediated ways but also reflect the politics, values and subjectivities of the photographer. They represent stereotypes, but also showcase alternate realities of people and health systems, and thereby can engender further reflection and change. We conclude with thoughts about the place of photography in health systems research and practice in highlighting and potentially transforming how we look at and address close-to-community providers.


Abstract

Background: Worldwide, a total of 6.282 million deaths occurred among children aged less than 5 years in 2013. About 47.4% of those were borne by the 47 Member States of the World Health Organization (WHO) African Region. Sadly, even as we approach the end date for the 2015 Millennium Development Goals (MDGs), only eight African countries are on track to achieve the MDG 4 target 4A of reducing under-five mortality by two thirds between 1990 and 2015. The post-2015 Sustainable Development Goal (SDG) 3 target is "by 2030, end preventable deaths of new-borns and children under 5 years of age". There is urgent need for increased advocacy among governments, the private sector and development partners to provide the resources needed to build resilient national health systems to deliver an integrated package of people-centred interventions to end preventable child morbidity and mortality and other structures to address all the basic needs for a healthy population. The specific objective of this study was to estimate expected/future productivity losses from child deaths in the WHO African Region in 2013 for use in advocacy for increased investments in child health services and other basic services that address children's welfare.
Methods: A cost-of-illness method was used to estimate future non-health GDP losses related to child deaths. Future non-health GDP losses were discounted at 3%. The analysis was undertaken with the countries categorized under three income groups: Group 1 consisted of nine high and upper middle income countries, Group 2 of 13 lower middle income countries, and Group 3 of 25 low income countries. One-way sensitivity analysis at 5% and 10% discount rates assessed the impact of the expected non-health GDP loss.

Results: The discounted value of future non-health GDP loss due to the deaths of children under 5 years old in 2013 will be in the order of Int$ 150.3 billion. Approximately 27.3% of the loss will be borne by Group 1 countries, 47.1% by Group 2 and 25.7% by Group 3. The average non-health GDP lost per child death will be Int$ 174 310 for Group 1, Int$ 57 584 for Group 2 and Int$ 25 508 for Group 3.

Conclusions: It is estimated that the African Region will incur a loss of approximately 6% of its non-health GDP from the future years of life lost among the 2 976 000 child deaths that occurred in 2013. Therefore, countries and development partners should in solidarity sustainably provide the resources essential to build resilient national health systems and systems to address the determinants of health and meet the other basic needs such as for clothing, education, food, shelter, sanitation and clean water to end preventable child morbidity and mortality.


Abstract

in English, French, Spanish

Objective: To evaluate services in hospitals providing internship training to graduate doctors in Kenya.

Methods: A survey of 22 internship training hospitals was conducted. Availability of key resources spanning infrastructure, personnel, equipment and drugs was assessed by observation. Outcomes and process of care for pre-specified priority conditions (head injury, chest injury, fractures, burns and acute abdomen) were evaluated by auditing case records.
Results: Each hospital had at least one consultant surgeon. Scheduled surgical outpatient clinics, major ward rounds and elective (half day) theatre lists were provided once per week in 91%, 55% and 9%, respectively. In all other hospitals, these were conducted twice weekly. Basic drugs were not always available (e.g. gentamicin, morphine and pethidine in 50%, injectable antistaphylococcal penicillins in 5% hospitals). Fewer than half of hospitals had all resources needed to provide oxygen. One hundred and forty-five of 956 cases evaluated underwent operations under general or spinal anaesthesia. We found operation notes for 99% and anaesthetic records for 72%. Pre-operatively measured vital signs were recorded in 80% of cases, and evidence of consent to operation was found in 78%. Blood loss was documented in only one case and sponge and instrument counts in 7%.

Conclusions: Evaluation of surgical services would be improved by development and dissemination of clear standards of care. This survey suggests that internship hospitals may be poorly equipped and documented care suggests inadequacies in quality and training.

Aragon framework of organisation capacity we discuss the multiple accountabilities, daily routines, challenges and coping strategies among PHC facility managers.

**Results:** PHC in-charges perform complex and diverse roles in a difficult environment with relatively little formal preparation. Their key concerns are lack of job clarity and preparedness, the difficulty of balancing multidirectional accountability responsibilities amidst significant resource shortages, and remuneration anxieties. We show that day-to-day management in an environment of resource constraints and uncertainty requires PHC in-charges who are resilient, reflective, and continuously able to learn and adapt. We highlight the importance of leadership development including the building of critical soft skills such as relationship building.


**Abstract**

Education is an effective way to improve girls' self-worth, health, and productivity; however there remains a gender gap between girls' and boys' completion of school. The literature around factors influencing girls' decision to stay in school is limited. Seven focus group discussions took place among 79 girls in forms 2 to 4 at secondary schools in rural western Kenya, to examine their views on why girls absent themselves or dropout from school. Data were analysed thematically. Lack of resources, sexual relationships with boyfriends, and menstrual care problems were reported to lead directly to dropout or school absence. These were tied to girls increased vulnerability to pregnancy, poor performance in school, and punishments, which further increase school absence and risk of dropout. Poverty, unmet essential needs, coercive sexual relationships, and an inequitable school environment collude to counter girls' resolve to complete their schooling. Lack of resources drive girls to have sex with boyfriends or men who provide them with essentials their family cannot afford, such as sanitary pads and transport to school. While these improve quality of their school life, this dynamic increases their exposure to sexual risk, pregnancy, punishment, and dropout. Evaluation of interventions to ameliorate these challenges is warranted, including provision of pocket money to address their needs.


Abstract

**Background:** Plasmodium falciparum resistance to chloroquine (CQ) denied healthcare providers access to a cheap and effective anti-malarial drug. Resistance has been proven to be due to point mutations on the parasite's pfcr gene, particularly on codon 76, resulting in an amino acid change from lysine to threonine. This study sought to determine the prevalence of the pfcr K76T mutation 13 years after CQ cessation in Msambweni, Kenya.

**Methods:** Finger-prick whole blood was collected on 3MM Whatman® filter paper from 99 falciparum malaria patients. Parasite DNA was extracted via the Chelex method from individual blood spots and used as template in nested PCR amplification of pfcr. Apol restriction enzyme was used to digest the amplified DNA to identify the samples as wild type or sensitive at codon 76. Prevalence figures of the mutant pfcr 76T gene were calculated by dividing the number of samples bearing the mutant gene with the total number of samples multiplied by 100 %. Chi square tests were used to test the significance of the findings against previous prevalence figures.

**Results:** Out of 99 clinical samples collected in 2013, prevalence of the mutant pfcr 76T gene stood at 41 %.

**Conclusion:** The results indicate a significant [χ(2) test, P ≤ 0.05 (2006 vs 2013)] reversal to sensitivity by the P. falciparum population in the study site compared to the situation reported in 2006 at the same study site. This could primarily be driven by diminished use of CQ in the study area in line with the official policy. Studies to establish prevalence of the pfcr 76T gene could be expanded countrywide to establish the CQ sensitivity status and predict a date when CQ may be re-introduced as part of malaria chemotherapy.


Abstract

**Background:** Many school children living in Africa are infected with plasmodia and helminth species and are consequently at risk of coinfection. However, the epidemiology of such coinfection and the implications of coinfection for children’s health remain poorly understood. This study describes the epidemiology of Ascaris lumbricoides-Plasmodium and hookworm-Plasmodium coinfection among school children living in western Kenya and investigates the associated risk factors.

**Methods:** As part of a randomized trial, a baseline cross-sectional survey was conducted among school children aged 5-18 years in 23 schools in Bumula District. Single stool samples were collected to screen for helminth infections using the Kato-Katz technique and malaria parasitaemia was determined from a finger prick blood sample. Demographic and anthropometric data were also collected.

**Results:** Overall, 46.4% of the children were infected with Plasmodium falciparum while 27.6% of the children were infected with at least one soil transmitted helminth (STH) species, with hookworm being the most common (16.8%) followed by A. lumbricoides (15.3%). Overall 14.3% of the children had STH-Plasmodium coinfection, with hookworm-Plasmodium (9.0%) coinfection being the most common. Geographical variation in the prevalence of coinfection occurred between schools. In multivariable logistic regression analysis, hookworm was positively associated with P. falciparum infection. In stratified analysis, hookworm infection was associated with increased odds of P. falciparum infection among both boys (P < 0.001) and girls (P = 0.01), whereas there was no association between A. lumbricoides and P. falciparum.

**Conclusion:** These findings demonstrate STH infections are still prevalent, despite the ongoing national deworming programme in Kenya, and that malaria parasitaemia is widespread, such that coinfection occurs among a proportion of children. A subsequent trial will allow us to investigate the implications of coinfection for the risk of clinical malaria.

Abstract

Childhood epilepsy is common in Africa. However, there are little data on the developmental and behavioral problems experienced by children living with epilepsy, especially qualitative data that capture community perceptions of the challenges faced by these children. Identifying these perceptions using qualitative approaches is important not only to help design appropriate interventions but also to help adapt behavioral tools that are culturally appropriate. We documented the description of these problems as perceived by parents and teachers of children with or without epilepsy. The study involved 70 participants. Data were collected using in-depth interviews and focus group discussions and were analyzed using NVIVO to identify major themes. Our analysis identified four major areas that are perceived to be adversely affected among children with epilepsy. These included internalizing and externalizing problems such as aggression, temper tantrums, and excessive crying. Additionally, developmental delay, especially cognitive deficits and academic underachievement, was also identified as a major problematic area. There is a need to supplement these findings with quantitative estimates and to develop psychosocial and educational interventions to rehabilitate children with epilepsy who have these difficulties.


Abstract

Increased global sharing of public health research data has potential to advance scientific progress but may present challenges to the interests of research stakeholders, particularly in low-to-middle income countries. Policies for data sharing should be responsive to public views, but there is little evidence of the systematic study of these from low-income countries. This qualitative study explored views on fair data-sharing processes among 60 stakeholders in Kenya with varying research experience, using a deliberative approach. Stakeholders’ attitudes were informed by perceptions of benefit and concerns for research data sharing, including risks of stigmatization, loss of privacy, and undermining scientific careers and validity, reported in detail elsewhere. In this article, we discuss institutional trust-building processes seen as central to perceptions of fairness in sharing research data in this setting, including forms of
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<td><strong>Abstract</strong></td>
<td>Large datasets are often not amenable to analysis using traditional single-step approaches. Here, our general objective was to apply imputation techniques, principal component analysis (PCA), elastic net and generalized linear models to a large dataset in a systematic approach to extract the most meaningful predictors for a health outcome. We extracted predictors for Plasmodium falciparum infection, from a large covariate dataset while facing limited numbers of observations, using data from the People, Animals, and their Zoonoses (PAZ) project to demonstrate these techniques: data collected from 415 homesteads in western Kenya, contained over 1500 variables that describe the health, environment, and social factors of the humans, livestock, and the homesteads in which they reside. The wide, sparse dataset was simplified to 42 predictors of P. falciparum malaria infection and wealth rankings were produced for all homesteads. The 42 predictors make biological sense and are supported by previous studies. This systematic data-mining approach we used would make many large datasets more manageable and informative for decision-making processes and health policy prioritization.</td>
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<td><strong>Abstract</strong></td>
<td><strong>Background:</strong> Scale up of antiretroviral therapy (ART) has led to substantial declines in HIV related morbidity and mortality. However, attrition from ART care remains a major public health concern and has been identified as one of the key reportable</td>
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indicators in assessing the success of ART programs. This study describes the incidence and predictors of attrition among adults initiating ART in a rural HIV clinic in Coastal Kenya.

**Methods:** A retrospective cohort study design was used. Adults (≥ 15 years) initiated ART between January 2008 and December 2010 were followed up for two years. Attrition was defined as individuals who were either reported dead or lost to follow up (LFU, ≥ 180 days late since the last clinic visit). Kaplan Meier survival probabilities and Weibull baseline hazard regression analyses were used to model the incidence and predictors of time to attrition.

**Results:** Of the 928 eligible participants, 308 (33.2% [95% CI, 30.2 - 36.3]) underwent attrition at an incident rate of 23.1 (95% CI, 20.6 - 25.8)/100 pyo. Attrition at 6 and 12 months was 18.4% (95% CI, 16.0 - 21.1) and 23.2% (95% CI, 19.9 - 25.3) respectively. Gender (male vs. female, adjusted hazard ratio [95% CI], p-value: 1.5 [1.1 - 2.0], p = 0.014), age (15 - 24 vs. ≥ 45 years, 2.2 [1.3 - 3.7], p = 0.034) and baseline CD4 T-cell count (100 - 350 cells/uL vs. < 100 cells/uL, 0.5 [0.3 - 0.7], p = 0.002) were independent predictors of time to attrition.

**Conclusions:** A third of individuals initiating ART were either reported dead or LFU during two years of care, with more than a half of these occurring within six months of treatment initiation. Practical and sustainable biomedical interventions and psychosocial support systems are warranted to improve ART retention in this setting.


**Abstract**

**Background:** Antenatal care early in pregnancy enables service providers to identify and manage risks to mother and fetus. In the global north, ultrasound scans are routinely offered in pregnancy to provide an accurate estimate of gestational age and identify potential problems. In sub-Saharan Africa, such services are rarely available and women often delay initiating antenatal care. This study describes the uptake and provision of antenatal care in a rural Kenyan hospital and explores how pregnant
women and healthcare providers perceived the provision of ultrasound scanning, following its introduction in an international foetal growth study.

**Methods:** A descriptive study, using qualitative and quantitative methods, was conducted in Kilifi District Hospital, Kenya, between June 2011 and April 2012. In-depth interviews were conducted with 10 nurses working in the antenatal clinic (ANC) and 59 pregnant women attending ANC. Structured observations of 357 ANC consultations and 30 ultrasound scans were made.

**Results:** Women sought antenatal care for information about the health of their baby and the protection provided by the ANC services. Uncertainty about pregnancy status contributed to delay in ANC attendance; more than 78% of women were over 20 weeks' gestation at their first visit. Healthcare workers found it difficult to detect pregnancies below 16 weeks gestation and, accurate assessment of gestational age below 20 weeks' gestation could be problematic. Provision of services depended on the pregnancy being detected and gestational age assessed. The "seeing", made possible through ultrasound scanning was perceived by pregnant women and healthcare workers to be beneficial: confirming the pregnancy, and providing reassurance about the fetus' condition. Few participants raised concerns about ultrasound scanning.

**Conclusions:** Uncertainty about pregnancy status and gestational age for women and healthcare providers is a key factor influencing timing of ANC attendance, contributing to delays and restricting early provision of ANC services. Ultrasound scanning was perceived to enhance antenatal care through confirmation of pregnancy status and enabling more accurate estimation of gestational age and the health status of the fetus. There is a need to make available more affordable means of pregnancy testing as a strategy towards encouraging early attendance, and delivery of antenatal care.


**Abstract**

**Background:** Variability in processes of care and outcomes has been reported widely in high-income settings (at geographic, hospital, physician group and individual physician levels); however, such variability and the factors driving it are rarely examined in low-income settings.
Methods: Using data from a cross-sectional survey undertaken in 22 hospitals (60 case records from each hospital) across Kenya that aimed at evaluating the quality of routine hospital services, we sought to explore variability in four binary inpatient paediatric process indicators. These included three prescribing tasks and use of one diagnostic. To examine for sources of variability, we examined intra-class correlation coefficients (ICC) and their changes using multi-level mixed models with random intercepts for hospital and clinician levels and adjusting for patient and clinician level covariates.

Results: Levels of performance varied substantially across indicators and hospitals. The absolute values for ICCs also varied markedly ranging from a maximum of 0.48 to a minimum of 0.09 across the models for HIV testing and prescription of zinc, respectively. More variation was attributable at the hospital level than clinician level after allowing for nesting of clinicians within hospitals for prescription of quinine loading dose for malaria (ICC = 0.30), prescription of zinc for diarrhoea patients (ICC = 0.11) and HIV testing for all children (ICC = 0.43). However, for prescription of correct dose of crystalline penicillin, more of the variability was explained by the clinician level (ICC = 0.21). Adjusting for clinician and patient level covariates only altered, marginally, the ICCs observed in models for the zinc prescription indicator.

Conclusions: Performance varied greatly across place and indicator. The variability that could be explained suggests interventions to improve performance might be best targeted at hospital level factors for three indicators and clinician factors for one. Our data suggest that better understanding of performance and sources of variation might help tailor improvement interventions although further data across a larger set of indicators and sites would help substantiate these findings.


Abstract

There is a theoretical risk of adverse events following immunization with a preservative-free, 2-dose vial formulation of 10-valent-pneumococcal conjugate vaccine (PCV10). We set out to measure this risk. Four population-based surveillance sites in Kenya (total annual birth cohort of 11,500 infants) were used to conduct a 2-year post-introduction vaccine safety study of PCV10. Injection-site abscesses
occurring within 7 days following vaccine administration were clinically diagnosed in all study sites (passive facility-based surveillance) and, also, detected by caregiver-reported symptoms of swelling plus discharge in two sites (active household-based surveillance). Abscess risk was expressed as the number of abscesses per 100,000 injections and was compared for the second vs first vial dose of PCV10 and for PCV10 vs pentavalent vaccine (comparator). A total of 58,288 PCV10 injections were recorded, including 24,054 and 19,702 identified as first and second vial doses, respectively (14,532 unknown vial dose). The risk ratio for abscess following injection with the second (41 per 100,000) vs first (33 per 100,000) vial dose of PCV10 was 1.22 (95% confidence interval [CI] 0.37–4.06). The comparator vaccine was changed from a 2-dose to 10-dose presentation midway through the study. The matched odds ratios for abscess following PCV10 were 1.00 (95% CI 0.12–8.56) and 0.27 (95% CI 0.14–0.54) when compared to the 2-dose and 10-dose pentavalent vaccine presentations, respectively. In Kenya immunization with PCV10 was not associated with an increased risk of injection site abscess, providing confidence that the vaccine may be safely used in Africa. The relatively higher risk of abscess following the 10-dose presentation of pentavalent vaccine merits further study.


Abstract

Background: Success in prevention of mother-to-child transmission (PMTCT) raises the prospect of eliminating pediatric HIV infection. To achieve global elimination, however, strategies are needed to strengthen PMTCT interventions. This study aimed to determine PMTCT outcomes and identify challenges facing its successful implementation in a rural setting in Kenya.

Methods: A retrospective cohort design was used. Routine demographic and clinical data for infants and mothers enrolling for PMTCT care at a rural hospital in Kenya were analysed. Cox and logistic regression were used to determine factors associated with retention and vertical transmission respectively.

Results: Between 2006 and 2012, 1338 infants were enrolled and followed up for PMTCT care with earlier age of enrollment and improved retention observed over time. Mother to child transmission of HIV declined from 19.4% in 2006 to 8.9% in 2012 (non-parametric test for trend p = 0.024). From 2009 to 2012, enrolling for care
after 6 months of age, adjusted Odds Ratio [aOR]: 23.3 [95 % confidence interval (CI): 8.3-65.4], presence of malnutrition ([aOR]: 2.3 [95 % CI: 1.1-5.2]) and lack of maternal use of highly active antiretroviral therapy (HAART) (aOR: 6.5 [95 % CI: 1.4-29.4]) was associated with increased risk of HIV infection. Infant's older age at enrollment, malnutrition and maternal HAART status, were also associated with drop out from care. Infants who were not actively followed up were more likely to drop out from care (adjusted Hazard Ratio: 6.6 [95 % CI: 2.9-14.6]).

**Discussion:** We report a temporal increase in the proportion of infants enrolling for PMTCT care before 3 months of age, improved retention in PMTCT and a significant reduction in the proportion of infants enrolled who became HIV-infected, emphasizing the benefits of PMTCT.

**Conclusion:** A simple set of risk factors at enrollment can identify mother-infant pairs most at risk of infection or drop out for targeted intervention.


**Abstract**

**Background:** The distribution of Plasmodium falciparum clinical malaria episodes is over-dispersed among children in endemic areas, with more children experiencing multiple clinical episodes than would be expected based on a Poisson distribution. There is consistent evidence for micro-epidemiological variation in exposure to P. falciparum. The aim of the current study was to identify children with excess malaria episodes after controlling for malaria exposure.

**Methods:** We selected the model that best fit the data out of the models examined and included the following covariates: age, a weighted local prevalence of infection as an index of exposure, and calendar time to predict episodes of malaria on active surveillance malaria data from 2,463 children of under 15 years of age followed for between 5 and 15 years each. Using parameters from the zero-inflated negative binomial model which best fitted our data, we ran 100 simulations of the model based on our population to determine the variation that might be seen due to chance.
**Results:** We identified 212 out of 2,463 children who had a number of clinical episodes above the 95(th) percentile of the simulations run from the model, hereafter referred to as "excess malaria (EM)". We then identified exposure-matched controls with "average numbers of malaria" episodes, and found that the EM group had higher parasite densities when asymptomatically infected or during clinical malaria, and were less likely to be of haemoglobin AS genotype.

**Conclusions:** Of the models tested, the negative zero-inflated negative binomial distribution with exposure, calendar year, and age acting as independent predictors, fitted the distribution of clinical malaria the best. Despite accounting for these factors, a group of children suffer excess malaria episodes beyond those predicted by the model. An epidemiological framework for identifying these children will allow us to study factors that may explain excess malaria episodes.


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**Abstract**

Attention deficit hyperactivity disorder (ADHD) is a childhood-onset neurodevelopmental disorder with a prevalence of 1·4-3·0%. It is more common in boys than girls. Comorbidity with childhood-onset neurodevelopmental disorders and psychiatric disorders is substantial. ADHD is highly heritable and multifactorial; multiple genes and non-inherited factors contribute to the disorder. Prenatal and perinatal factors have been implicated as risks, but definite causes remain unknown. Most guidelines recommend a stepwise approach to treatment, beginning with non-drug interventions and then moving to pharmacological treatment in those most severely affected. Randomised controlled trials show short-term benefits of stimulant medication and atomoxetine. Meta-analyses of blinded trials of non-drug treatments have not yet proven the efficacy of such interventions. Longitudinal studies of ADHD show heightened risk of multiple mental health and social difficulties as well as premature mortality in adult life.


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Bacteraemia is a leading cause of morbidity in sickle cell anaemia (SCA), but information from studies in Africa is limited. We evaluated 890 admissions from 648 SCA patients at a tertiary hospital in Tanzania. Bacteraemia was present in 43 admissions (4.8%); isolates included Staphylococcus aureus (12/43; 28%), non-Typhi Salmonella (9/43; 21%), Streptococcus pneumoniae (3/43; 7%) and Salmonella Typhi (2/43; 5%). Compared to SCA patients without bacteraemia, SCA patients with bacteraemia had significantly lower haemoglobin [71 g/l vs. 62 g/l, odds ratio 0.72 (95% confidence interval 0.56 - 0.91), P < 0.01]. Further exploration is needed of the relationship between anaemia and bacterial infections in SCA in Africa.


Abstract

Background: Patients' low adherence to artemisinin-based combination therapy has been reported in areas of Kenya bordering the Lake Victoria region, where the burden of malaria remains high. A randomized controlled trial is underway to determine the efficacy of short message service (SMS) text reminders on adherence to artemether-lumefantrine and post-treatment review of children under the age of five. This paper reports on the iterative process of intervention and delivery system development.

Methods: An intervention development workshop involving the research team and other stakeholders was held to determine the content of the text messages. Three focus group discussions were conducted to test caregivers' understanding of the messages developed during the workshop. The tested messages were refined and incorporated into an automated SMS distribution system and piloted with 20 caregivers drawn from facilities neighbouring the study sites. The automated SMS distribution system was repeatedly refined following the pilot and implemented at the start of the trial.

Results: The content of SMS messages underwent major revisions following the focus group discussions. Technical terms and abbreviations were replaced with simplified general terms. Message sign-off was modified to reflect the name of health facility,
removing references to health workers. Day 3 post-treatment review visit reminder was modified to state the purpose of the visit while wording ‘day 28’ was added to the last post-treatment review visit reminder to help the caregiver recall the appointment date. The unscheduled visit prompt was modified to reflect flexibility and practicality of taking the child back to the facility if unwell. Reception of SMS reminders during the pilot was low with only 169/240 (70%) of scheduled messages delivered to the caregivers. The automated distribution system underwent major refinement and repeated testing following the pilot until effective delivery of all scheduled messages was achieved and sustained over a period of 3 months.

Conclusions: Text message interventions should be carefully developed, tested and refined before implementation to ensure they are written in the most appropriate way for their target population. SMS distribution systems should be rigorously tested to ensure efficient delivery of the messages before they are deployed.


Abstract

Background: Schistosomiasis is a major public health problem in Kenya as well as in many other tropical countries and is considered one of the most prevalent diseases in the rural population. Between 2004 and 2009, primary school children in Mwea irrigation scheme were treated for Schistosoma mansoni. In the four year control programme, there was occurrence of light re-infection with S. mansoni. Therefore, the aim of this study was to assess the current prevalence of S. mansoni, infection two years after the withdrawal of mass drug administration (MDA) programme.

Methods: We carried out a cross-sectional study on a population of 387 children attending 3 primary schools located in Mwea irrigation scheme. Children, aged 8-16 years were interviewed and screened for S. mansoni using duplicate Kato-Katz thick smears. Comparisons of prevalence by age group and gender were tested for significance on the basis of the Wald test. Best prediction factors for infection with S. mansoni were selected using forward - stepwise variable selection method.

Results: The overall prevalence of S. mansoni was 53.7 %, (95%CI: 49.0-59.0, p-value = 0.000). Male children had higher prevalence of infection, 66.1 % (95%CI: 59.8-73.2,
p-value = 0.000) compared to females. The gender (sex) of a child was the only factor reported to be significantly associated with S. mansoni infection, (OR = 1.9, p-value = 0.015, 95%CI: 1.13-3.21).

**Conclusions:** There was high prevalence of S. mansoni infections in the study area, two years after the withdrawal of MDA programme. We suggest that treatment should be continued in the school children at regular intervals, monitoring and surveillance intensified to ensure interruption of transmission areas.


**Abstract**

**Background:** In sub-Saharan Africa, children are frequently admitted with severe anaemia needing an urgent blood transfusion, but blood is often unavailable. When conventional blood supplies are inadequate, allogeneic umbilical cord blood could be a feasible alternative. The aim of this study was to assess the safety and efficacy of cord blood transfusion in children with severe anaemia.

**Methods:** Between June 26, 2007, and May 20, 2008, 413 children needing an urgent blood transfusion were admitted to Kilifi District Hospital in Kenya. Of these, 87 children were eligible for our study--ie, younger than 12 years, no signs of critical illness, and haemoglobin 100 g/L or lower (if aged 3 months or younger) or 40 g/L or lower (if older than 3 months). Cord blood was donated at Coast Provincial General Hospital, Mombasa, and screened for transfusion-transmitted infections and bacterial contamination. Red blood cells were stored vertically at 2-6°C to enable sedimentation. After transfusion, children were monitored closely for adverse events and followed up for 28 days. The primary outcome measure was the frequency and nature of adverse reactions associated with the transfusion. Secondary outcomes were the changes in haemoglobin concentrations 24 h and 28 days after transfusion, compared with pretransfusion levels. This trial is registered on ISRCTN.com, number ISRCTN66687527.

**Findings:** Of the 87 children eligible for the study, cord blood was unavailable for 24, six caregivers declined consent, and two children were withdrawn before transfusion. Therefore, 55 children received umbilical cord red blood cells from 74 donations. Ten (18%) children had ten serious adverse events and 43 (78%) had 94 adverse events; the
most frequent adverse events were anaemia (n=14), weight loss (n=12), and vomiting (n=10). An independent expert panel judged none of these adverse events to be probably or certainly caused by the cord blood transfusion (one-sided 97·5% CI 0-6·5).

Haemoglobin increased by a median of 26 g/L (IQR 21-31) 24 h after transfusion and by 50 g/L (10-68) a median of 29 days (28-35) after transfusion.

**Interpretation:** These preliminary data suggest that cord blood could be an important supplementary source of blood for transfusion in children in sub-Saharan Africa. Further studies are needed to compare the safety and efficacy of cord blood with conventional adult-donated blood for transfusions. Challenges associated with cost, infrastructure, and scale up also need investigating.


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Mugambi RM, Agola EL, Mwangi IN, Kinyua J, Shiraho EA, Mkoji GM. Development and evaluation of a Loop Mediated Isothermal Amplification (LAMP) technique for the detection of hookworm (Necator americanus) infection in faecal samples. Parasit Vectors. 2015 Nov 6;8:574.

**Abstract**

**Background:** Hookworm infection is a major concern in sub-Saharan Africa, particularly in children and pregnant women. Necator americanus and Ancylostoma duodenale are responsible for this condition. Hookworm disease is one of the Neglected tropical diseases (NTDs) that are targeted for elimination through global mass chemotherapy. To support this there is a need for reliable diagnostic tools. The conventional diagnostic test, Kato-Katz that is based on microscopic detection of parasite ova in faecal samples, is not effective due to its low sensitivity that is brought about mainly by non-random distribution of eggs in stool and day to day variation in egg output. It is tedious, cumbersome to perform and requires experience for correct diagnosis. LAMP-based tests are simple, relatively cheap, offer greater sensitivity, specificity than existing tests, have high throughput capability, and are ideal for use at the point of care.

**Methods:** We have developed a LAMP diagnostic test for detection of hookworm infection in faecal samples. LAMP relies on auto cycling strand displacement DNA synthesis performed at isothermal temperature by Bst polymerase and a set of 4 specific primers. The primers used in the LAMP assay were based on the second Internal Transcribed Spacer (ITS-2) region and designed using Primer Explorer version 4 Software. The ITS-2 region of the ribosomal gene (rDNA) was identified as a suitable target due to its low mutation rates and substantial differences between
species. DNA was extracted directly from human faecal samples, followed by LAMP amplification at isothermal temperature of 63 °C for 1 h. Amplicons were visualized using gel electrophoresis and SYBR green dye. Both specificity and sensitivity of the assay were determined.

**Results:** The LAMP based technique developed was able to detect *N. americanus* DNA in faecal samples. The assay showed 100 % specificity and no cross-reaction was observed with other helminth parasites (*S. mansoni, A. lumbricoides or T. trichiura*). The developed LAMP assay was 97 % sensitive and DNA at concentrations as low as 0.4 fg were amplified.

**Conclusion:** The LAMP assay developed is an appropriate diagnostic method for the detection of *N. americanus* DNA in human stool samples because of its simplicity, low cost, sensitivity, and specificity. It holds great promise as a useful diagnostic tool for use in disease control where infection intensities have been significantly reduced.


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**Abstract**

**Background:** Ready-to-use therapeutic foods (RUTF) are lipid-based pastes widely used in the treatment of acute malnutrition. Current specifications for RUTF permit a high n-6 polyunsaturated fatty acid (PUFA) content and low n-3 PUFA, with no stipulated requirements for preformed long-chain n-3 PUFA. The objective of this study was to develop an RUTF with elevated short-chain n-3 PUFA and measure its impact, with and without fish oil supplementation, on children's PUFA status during treatment of severe acute malnutrition.

**Methods:** This randomized controlled trial in children with severe acute malnutrition in rural Kenya included 60 children aged 6 to 50 months who were randomized to receive i) RUTF with standard composition; ii) RUTF with elevated short chain n-3 PUFA; or iii) RUTF with elevated short chain n-3 PUFA plus fish oil capsules. Participants were followed-up for 3 months. The primary outcome was erythrocyte PUFA composition.
Results: Erythrocyte docosahexaenoic acid (DHA) content declined from baseline in the two arms not receiving fish oil. Erythrocyte long-chain n-3 PUFA content following treatment was significantly higher for participants in the arm receiving fish oil than for those in the arms receiving RUTF with elevated short chain n-3 PUFA or standard RUTF alone: 3 months after enrollment, DHA content was 6.3% (interquartile range 6.0-7.3), 4.5% (3.9-4.9), and 3.9% (2.4-5.7) of total erythrocyte fatty acids (P <0.001), respectively, while eicosapentaenoic acid (EPA) content was 2.0% (1.5-2.6), 0.7% (0.6-0.8), and 0.4% (0.3-0.5) (P <0.001). RUTF with elevated short chain n-3 PUFA and fish oil capsules were acceptable to participants and carers, and there were no significant differences in safety outcomes.

Conclusions: PUFA requirements of children with SAM are not met by current formulations of RUTF, or by an RUTF with elevated short-chain n-3 PUFA without additional preformed long-chain n-3 PUFA. Clinical and growth implications of revised formulations need to be addressed in large clinical trials.


Abstract

Background: In sub-Saharan Africa, where infectious diseases and nutritional deficiencies are common, severe anaemia is a common cause of paediatric hospital admission, yet the evidence to support current treatment recommendations is limited. To avert overuse of blood products, the World Health Organisation advocates a conservative transfusion policy and recommends iron, folate and anti-helminthics at discharge. Outcomes are unsatisfactory with high rates of in-hospital mortality (9-10%), 6-month mortality and relapse (6%). A definitive trial to establish best transfusion and treatment strategies to prevent both early and delayed mortality and relapse is warranted.

Methods/design: TRACT is a multicentre randomised controlled trial of 3954 children aged 2 months to 12 years admitted to hospital with severe anaemia (haemoglobin < 6 g/dl). Children will be enrolled over 2 years in 4 centres in Uganda and Malawi and followed for 6 months. The trial will simultaneously evaluate (in a factorial trial with a 3 x 2 x 2 design) 3 ways to reduce short-term and longer-term mortality and morbidity.
following admission to hospital with severe anaemia in African children. The trial will compare: (i) R1: liberal transfusion (30 ml/kg whole blood) versus conservative transfusion (20 ml/kg) versus no transfusion (control). The control is only for children with uncomplicated severe anaemia (haemoglobin 4-6 g/dl); (ii) R2: post-discharge multi-vitamin multi-mineral supplementation (including folate and iron) versus routine care (folate and iron) for 3 months; (iii) R3: post-discharge cotrimoxazole prophylaxis for 3 months versus no prophylaxis. All randomisations are open. Enrolment to the trial started September 2014 and is currently ongoing. Primary outcome is cumulative mortality to 4 weeks for the transfusion strategy comparisons, and to 6 months for the nutritional support/antibiotic prophylaxis comparisons. Secondary outcomes include mortality, morbidity (haematological correction, nutritional and infectious), safety and cost-effectiveness.

Discussion: If confirmed by the trial, a cheap and widely available 'bundle' of effective interventions, directed at immediate and downstream consequences of severe anaemia, could lead to substantial reductions in mortality in a substantial number of African children hospitalised with severe anaemia every year, if widely implemented.


Abstract

Background: Bone and joint infection in adults arises most commonly as a complication of joint replacement surgery, fracture fixation and diabetic foot infection. The associated morbidity can be devastating to patients and costs the National Health Service an estimated £20,000 to £40,000 per patient. Current standard of care in most UK centres includes a prolonged course (4-6 weeks) of intravenous antibiotics supported, if available, by an outpatient parenteral antibiotic therapy service. Intravenous therapy carries with it substantial risks and inconvenience to patients, and the antibiotic-related costs are approximately ten times that of oral therapy. Despite this, there is no evidence to suggest that oral therapy results in inferior outcomes. We hypothesise that, by selecting oral agents with high bioavailability, good tissue penetration and activity against the known or likely pathogens, key outcomes in patients managed primarily with oral therapy are non-inferior to those in patients treated by intravenous therapy.
Methods: The OVIVA trial is a parallel group, randomised (1:1), un-blinded, non-inferiority trial conducted in thirty hospitals across the UK. Eligible participants are adults (>18 years) with a clinical syndrome consistent with a bone, joint or metalware-associated infection who have received ≤7 days of intravenous antibiotic therapy from the date of definitive surgery (or the start of planned curative therapy in patients treated without surgical intervention). Participants are randomised to receive either oral or intravenous antibiotics, selected by a specialist infection physician, for the first 6 weeks of therapy. The primary outcome measure is definite treatment failure within one year of randomisation, as assessed by a blinded endpoint committee, according to pre-defined microbiological, histological and clinical criteria. Enrolling 1,050 subjects will provide 90% power to demonstrate non-inferiority, defined as less than 7.5% absolute increase in treatment failure rate in patients randomised to oral therapy as compared to intravenous therapy (one-sided alpha of 0.05).

Discussion: If our results demonstrate non-inferiority of orally administered antibiotic therapy, this trial is likely to facilitate a dramatically improved patient experience and alleviate a substantial financial burden on healthcare services.


Abstract

Background: Soil-transmitted helminths, a class of parasitic intestinal worms, are pervasive in many low-income settings. Infection among children can lead to poor nutritional outcomes, anaemia, and reduced cognition. Mass treatment, typically administered through schools, with yearly or biannual drugs is inexpensive and can reduce worm burden, but reinfection can occur rapidly. Access to and use of sanitation facilities and proper hygiene can reduce infection, but rigorous data are scarce. Among school-age children, infection can occur at home or at school, but little is known about the relative importance of WASH in transmission in these two settings.

Methods: We explored the relationships between school and household water, sanitation, and hygiene conditions and behaviours during the baseline of a large-scale mass drug administration programme in Kenya. We assessed several WASH measures
to quantify the exposure of school children, and developed theory and empirically-based parsimonious models.

**Results:** Results suggest mixed impacts of household and school WASH on prevalence and intensity of infection. WASH risk factors differed across individual worm species, which is expected given the different mechanisms of infection.


**Abstract**

We determined the prevalence of four sexually transmitted infections and the demographic and behavioural correlates associated with having one or more sexually transmitted infections among participants in an HIV incidence cohort study in Kisumu, western Kenya. Participants were enrolled from a convenience sample and underwent aetiologic sexually transmitted infection investigation. Demographic and behavioural information were collected and basic clinical evaluation performed. Multiple regression analysis was done to determine variables associated with having one or more sexually transmitted infections. We screened 846, 18- to 34-year-olds. One-third had at least one sexually transmitted infection with specific prevalence being: syphilis, 1.6%; gonorrhoea, 2.4%; herpes simplex virus type-2, 29.1%; chlamydia, 2.8%; and HIV, 14.8%. Odds of having any sexually transmitted infection were higher among participants who were women, were aged 20-24 or 30-34 years compared to 18-19 years, had secondary or lower education compared to tertiary education, were divorced, widowed or separated compared to singles, reported having unprotected sex compared to those who did not, reported previous sexually transmitted infection treatment, and tested HIV-positive. Multiple strategies are needed to address the overall high prevalence of sexually transmitted infections as well as the gender disparity found in this Kenyan population. Structural interventions may be beneficial in addressing educational and socio-economic barriers, and increasing the uptake of health-promoting practices.


Abstract

Objective: Cervical cancer screening uptake may be influenced by inadequate knowledge in resource-limited settings. This randomized trial evaluated a health talk’s impact on cervical cancer knowledge, attitudes, and screening rates in rural Kenya.

Methods: 419 women attending government clinics were randomized to an intervention (N=207) or control (N=212) group. The intervention was a brief health talk on cervical cancer. Participants completed surveys at enrollment (all), immediately after the talk (intervention arm), and at three-months follow-up (all). The primary outcomes were the change in knowledge scores and the final screening rates at three-months follow-up. Secondary outcomes were changes in awareness about cervical cancer screening, perception of personal cervical cancer risk, cervical cancer and HIV stigma, and screening acceptability.

Results: Mean Knowledge Scores increased by 26.4% (8.7 points increased to 11.0 points) in the intervention arm compared to only 17.6% (8.5 points increased to 10.0 points) in the control arm (p<0.01). Screening uptake was moderate in both the intervention (58.9%; N=122) and control (60.9%; N=129) arms, with no difference between the groups (p=0.60).

Conclusion: A brief health talk increased cervical cancer knowledge, although it did not increase screening over simply informing women about free screening.

Practical implications: Screening programs can increase patient understanding with just a brief educational intervention.


Abstract

Memory B cells are long-lived and could contribute to persistence of humoral immunity by maintaining the plasma-cell pool or making recall responses upon re-exposure to an antigen. We determined the ability of a pneumococcal conjugate vaccine to induce anti-pneumococcal memory B cells. Frequencies of memory B cells
against pneumococcal capsular polysaccharides from serotypes 1, 6B, 14, 19F and 23F were determined by cultured B cell enzyme-linked immunospot (ELISPOT) in 35 children aged 12-23 months who received pneumococcal non-typeable Haemophilus influenzae protein-D conjugate vaccine (PHiD-CV). The relationships between plasma antibodies and memory B cell frequencies were also assessed. After two doses of PHiD-CV, the proportion of subjects with detectable memory B cells against pneumococcal capsular polysaccharides increased significantly for serotypes 1 (3-45%; P < 0·01), 19F (21-66%; P < 0·01) and 23F (13-36%; P = 0·02), but not serotypes 6B (24-42%; P = 0·24) and 14 (21-40%; P = 0·06). Correlations between antibodies and memory B cells were weak. Carriage of serotype 19F at enrolment was associated with poor memory B cell responses against this serotype at subsequent time-points (day 30: non-carriers, 82% versus carriers, 0%, P < 0·01; day 210: non-carriers, 72% versus carriers, 33%, P = 0·07). PHiD-CV is capable of inducing memory B cells against some of the component pneumococcal capsular polysaccharides.


Abstract

A qualitative assessment of Kenyan men who have sex with men taking daily and intermittent oral HIV pre-exposure prophylaxis (PrEP) found stigma, sex work, mobility, and alcohol impacted adherence. We analyzed quantitative data from the same cohort to explore different definitions of intermittent adherence. Volunteers were randomized to daily emtricitabine/tenofovir or placebo, or intermittent (prescription: Mondays/Fridays/after sex, maximum 1 dose/day) emtricitabine/tenofovir or placebo (2:1:2:1), and followed for 4 months. By electronic monitoring, median adherence for daily dosing was 80 %. Median adherence for intermittent dosing was 71 % per a "relaxed" definition (accounting for off-prescription dosing) and 40 % per a "strict" definition (limited to the prescription). Factors associated with lower adherence included travel, transactional sex, and longer follow-up; higher adherence was associated with daily dosing and an income. The definition of intermittent dosing strongly affects interpretation of adherence. These findings suggest interventions should address challenges of mobility, sex work, and long-term PrEP.


**Abstract**

Each year, at least 280,000 children are born with sickle cell disease (SCD) in resource-limited settings. For cost, logistic and political reasons, the availability of SCD testing is limited in such settings and consequently 50-90% of affected children die undiagnosed before their fifth birthday. The recent development of a point of care method for the diagnosis of SCD - the Sickle SCAN™ device - could afford such children the prompt access to appropriate services that has transformed the outlook for affected children in resource-rich areas. In research published in BMC Medicine, Kanter and colleagues describe a small but carefully conducted study involving 208 children and adults, in which they found that by using Sickle SCAN™ it was possible to diagnose the common forms of SCD with 99% sensitivity and 99% specificity, in under 5 minutes. If repeatable both in newborn babies and under real-life conditions, and if marketed at an affordable price, Sickle SCAN™ could revolutionize the survival prospects for children born with SCD in resource-limited areas. Please see related article: http://dx.doi.org/10.1186/s12916-015-0473-6.


**Abstract**

Genetic analysis of molecular markers is critical in tracking the emergence and/or spread of artemisinin resistant parasites. Clinical isolates collected in western Kenya pre- and post- introduction of artemisinin combination therapies (ACTs) were genotyped at SNP positions in regions of strong selection signatures on chromosome 13 and 14, as described in Southeast Asia (SEA). Twenty five SNPs were genotyped using Sequenom MassArray and pfmdr1 gene copy number by real-time PCR. Parasite clearance half-life and in vitro drug sensitivity testing were performed using standard methods. One hundred twenty nine isolates were successfully analyzed. Fifteen SNPs were present in pre-ACTs isolates and six in post-ACTs. None of the SNPs showed
association with parasite clearance half-life. Post-ACTs parasites had significantly higher pfmdr1 copy number compared to pre-ACTs. Seven of eight parasites with multiple pfmdr1 were post-ACTs. When in vitro IC50s were compared for parasites with single vs. multiple gene copies, only amodiaquine and piperaquine reached statistical significance. Data showed SNPs on chromosome 13 and 14 had different frequency and trend in western Kenya parasites compared SEA. Increase in pfmdr1 gene copy is consistent with recent studies in African parasites. Data suggests genetic signature of artemisinin resistance in Africa might be different from SEA.


**Abstract**

**Background:** Progress in reducing the malaria disease burden through the substantial scale up of insecticide-based vector control in recent years could be reversed by the widespread emergence of insecticide resistance. The impact of insecticide resistance on the protective effectiveness of insecticide-treated nets (ITN) and indoor residual spraying (IRS) is not known. A multi-country study was undertaken in Sudan, Kenya, India, Cameroon and Benin to quantify the potential loss of epidemiological effectiveness of ITNs and IRS due to decreased susceptibility of malaria vectors to insecticides. The design of the study is described in this paper.

**Methods:** Malaria disease incidence rates by active case detection in cohorts of children, and indicators of insecticide resistance in local vectors were monitored in each of approximately 300 separate locations (clusters) with high coverage of malaria vector control over multiple malaria seasons. Phenotypic and genotypic resistance was assessed annually. In two countries, Sudan and India, clusters were randomly assigned to receive universal coverage of ITNs only, or universal coverage of ITNs combined
with high coverage of IRS. Association between malaria incidence and insecticide resistance, and protective effectiveness of vector control methods and insecticide resistance were estimated, respectively.

**Results:** Cohorts have been set up in all five countries, and phenotypic resistance data have been collected in all clusters. In Sudan, Kenya, Cameroon and Benin data collection is due to be completed in 2015. In India data collection will be completed in 2016.

**Discussion:** The paper discusses challenges faced in the design and execution of the study, the analysis plan, the strengths and weaknesses, and the possible alternatives to the chosen study design.


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**Abstract**

**Background:** The RTS,S/AS01 malaria vaccine targets the circumsporozoite protein, inducing antibodies associated with the prevention of *Plasmodium falciparum* infection. We assessed the association between anti-circumsporozoite antibody titres and the magnitude and duration of vaccine efficacy using data from a phase 3 trial done between 2009 and 2014.

**Methods:** Using data from 8922 African children aged 5-17 months and 6537 African infants aged 6-12 weeks at first vaccination, we analysed the determinants of immunogenicity after RTS,S/AS01 vaccination with or without a booster dose. We assessed the association between the incidence of clinical malaria and anti-circumsporozoite antibody titres using a model of anti-circumsporozoite antibody dynamics and the natural acquisition of protective immunity over time.

**Findings:** RTS,S/AS01-induced anti-circumsporozoite antibody titres were greater in children aged 5-17 months than in those aged 6-12 weeks. Pre-vaccination anti-
circumsporozoite titres were associated with lower immunogenicity in children aged 6-12 weeks and higher immunogenicity in those aged 5-17 months. The immunogenicity of the booster dose was strongly associated with immunogenicity after primary vaccination. Anti-circumsporozoite titres wane according to a biphasic exponential distribution. In participants aged 5-17 months, the half-life of the short-lived component of the antibody response was 45 days (95% credible interval 42-48) and that of the long-lived component was 591 days (557-632). After primary vaccination 12% (11-13) of the response was estimated to be long-lived, rising to 30% (28-32%) after a booster dose. An anti-circumsporozoite antibody titre of 121 EU/mL (98-153) was estimated to prevent 50% of infections. Waning anti-circumsporozoite antibody titres predict the duration of efficacy against clinical malaria across different age categories and transmission intensities, and efficacy wanes more rapidly at higher transmission intensity.

**Interpretation:** Anti-circumsporozoite antibody titres are a surrogate of protection for the magnitude and duration of RTS,S/AS01 efficacy, with or without a booster dose, providing a valuable surrogate of effectiveness for new RTS,S formulations in the age groups considered.


**Abstract**

Malaria disproportionately affects young children. Clinical trials in African children showed that dihydroartemisinin-piperaquine (DP) is an effective antimalarial and has a longer posttreatment prophylactic (PTP) effect against reinfections than other artemisinin-based combination therapies, including artemether-lumefantrine (AL). Using a previously developed Markov model and individual patient data from a multicenter African drug efficacy trial, we assessed the economic value of the PTP effect of DP versus AL in pediatric malaria patients from health-care provider’s perspective in low-to-moderate and moderate-to-high transmission settings under different drug co-payment scenarios. In low-to-moderate transmission settings, first-line treatment with DP was highly cost-effective with an incremental cost-effectiveness ratio of US$5 (95% confidence interval [CI] = -76 to 196) per disability-adjusted life year (DALY) averted. In moderate-to-high transmission settings, DP first-line treatment led to a mean cost saving of US$1.09 (95% CI = -0.88 to 3.85) and averted
0.05 (95% CI = -0.08 to 0.22) DALYs per child per year. Our results suggested that DP might be superior to AL for first-line treatment of uncomplicated childhood malaria across a range of transmission settings in Africa.


Abstract

Consent processes have attracted significant research attention over the last decade, including in the global south. Although relevant studies suggest consent is a complex negotiated process involving multiple actors, most guidelines assume consent is a one-off encounter with a clear 'yes' or 'no' decision. In this paper we explore the concept of 'silent refusals', a situation where it is not clear whether potential participants want to join studies or those in studies want to withdraw from research, as they were not actively saying no. We draw on participant observation, in-depth interviews and group discussions conducted with a range of stakeholders in two large community based studies conducted by the KEMRI Wellcome Trust programme in coastal Kenya. We identified three broad inter-related rationales for silent refusals: 1) a strategy to avoid conflicts and safeguard relations within households, - for young women in particular-to appear to conform to the wishes of elders; 2) an approach to maintain friendly, appreciative and reciprocal relationships with fieldworkers, and the broader research programme; and 3) an effort to retain study benefits, either for individuals, whole households or wider communities. That refusals and underlying rationales were silent posed multiple dilemmas for fieldworkers, who are increasingly recognised to play a key interface role between researchers and communities in many settings. Silent refusals reflect and reinforce complex power relations embedded in decisions about research participation, with important implications for consent processes and broader research ethics practice. Fieldworkers need support to reflect upon and respond to the ethically charged environment they work in.


Abstract

Objective: Pneumococcal conjugate vaccines reduce the prevalence of vaccine serotypes carried in the nasopharynx. Because this could alter carriage of other potential pathogens, we assessed the nasopharyngeal microbiome of children who had been vaccinated with 10-valent pneumococcal non-typeable Haemophilus influenzae protein-D conjugate vaccine (PHiD-CV).

Methods: Profiles of the nasopharyngeal microbiota of 60 children aged 12-59 months, who had been randomized to receive 2 doses of PHiD-CV (n=30) or Hepatitis A vaccine (n=30) 60 days apart, were constructed by 16S rRNA gene pyrosequencing of swab specimens collected before vaccination and 180 days after dose 1.

Results: Prior to vaccination, Moraxella catarrhalis (median of 12.3% of sequences/subject), Streptococcus pneumoniae (4.4%) and Corynebacterium spp. (5.6%) were the most abundant nasopharyngeal bacterial species. Vaccination with PHiD-CV did not significantly alter the species composition, abundance, or prevalence of known pathogens. Distinct microbiomes were identified based on the abundances of Streptococcus, Moraxella, and Haemophilus species. These microbiomes shifted in composition over the study period and were independent of age, sex, school attendance, antibiotic exposure, and vaccination.

Conclusions: Vaccination of children with two doses of PHiD-CV did not significantly alter the nasopharyngeal microbiome. This suggests limited replacement carriage with pathogens other than non-vaccine strains of S. pneumoniae.


Abstract

The bacterium Clostridium difficile is a significant cause of nosocomial infections worldwide. The pathogenic success of this organism can be attributed to its flexible genome which is characterized by the exchange of mobile genetic elements, and by ongoing genome evolution. Despite its pathogenic status, C. difficile can also be
carried asymptomatically, and has been isolated from natural environments such as water and sediments where multiple strain types (ribotypes) are found in close proximity. These include ribotypes which are associated with disease, as well as those that are less commonly isolated from patients. Little is known about the genomic content of strains in such reservoirs in the natural environment. In this study, draft genomes have been generated for 13 C. difficile isolates from estuarine sediments including clinically relevant and environmental associated types. To identify the genetic diversity within this strain collection, whole-genome comparisons were performed using the assemblies. The strains are highly genetically diverse with regards to the C. difficile "mobilome," which includes transposons and prophage elements. We identified a novel transposon-like element in two R078 isolates. Multiple, related and unrelated, prophages were detected in isolates across ribotype groups, including two novel prophage elements and those related to the transducing phage φC2. The susceptibility of these isolates to lytic phage infection was tested using a panel of characterized phages found from the same locality. In conclusion, estuarine sediments are a source of genetically diverse C. difficile strains with a complex network of prophages, which could contribute to the emergence of new strains in clinics.


Abstract

**Background:** Postpartum haemorrhage (PPH) is the leading cause of maternal mortality worldwide. Prophylactic uterotonic drugs can prevent PPH, and are routinely recommended. There are several uterotonic drugs for preventing PPH but it is still debatable which drug is best.

**Objectives:** To identify the most effective uterotonic drug(s) to prevent PPH, and generate a ranking according to their effectiveness and side-effect profile.

**Search methods:** We searched Cochrane Pregnancy and Childbirth's Trials Register (1 June 2015), ClinicalTrials.gov and the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) for unpublished trial reports (30 June 2015) and reference lists of retrieved studies.
Selection criteria: All randomised controlled comparisons or cluster trials of effectiveness or side-effects of uterotonic drugs for preventing PPH. Quasi-randomised trials and cross-over trials are not eligible for inclusion in this review.

Data collection and analysis: At least three review authors independently assessed trials for inclusion and risk of bias, extracted data and checked them for accuracy. We estimated the relative effects and rankings for preventing PPH \( \geq 500 \) mL and PPH \( \geq 1000 \) mL as primary outcomes. We performed pairwise meta-analyses and network meta-analysis to determine the relative effects and rankings of all available drugs. We stratified our primary outcomes according to mode of birth, prior risk of PPH, healthcare setting, dosage, regimen and route of drug administration, to detect subgroup effects. The absolute risks in the oxytocin are based on meta-analyses of proportions from the studies included in this review and the risks in the intervention groups were based on the assumed risk in the oxytocin group and the relative effects of the interventions.

Main results: This network meta-analysis included 140 randomised trials with data from 88,947 women. There are two large ongoing studies. The trials were mostly carried out in hospital settings and recruited women who were predominantly more than 37 weeks of gestation having a vaginal birth. The majority of trials were assessed to have uncertain risk of bias due to poor reporting of study design. This primarily impacted on our confidence in comparisons involving carbetocin trials more than other uterotonics. The three most effective drugs for prevention of PPH \( \geq 500 \) mL were ergometrine plus oxytocin combination, carbetocin, and misoprostol plus oxytocin combination. These three options were more effective at preventing PPH \( \geq 500 \) mL compared with oxytocin, the drug currently recommended by the WHO (ergometrine plus oxytocin risk ratio (RR) 0.69 (95% confidence interval (CI) 0.57 to 0.83), moderate-quality evidence; carbetocin RR 0.72 (95% CI 0.52 to 1.00), very low-quality evidence; misoprostol plus oxytocin RR 0.73 (95% CI 0.60 to 0.90), moderate-quality evidence). Based on these results, about 10.5% women given oxytocin would experience a PPH of \( \geq 500 \) mL compared with 7.2% given ergometrine plus oxytocin combination, 7.6% given carbetocin, and 7.7% given misoprostol plus oxytocin. Oxytocin was ranked fourth with close to 0% cumulative probability of being ranked in the top three for PPH \( \geq 500 \) mL. The outcomes and rankings for the outcome of PPH \( \geq 1000 \) mL were similar to those of PPH \( \geq 500 \) mL, with the evidence for ergometrine plus oxytocin combination being more effective than oxytocin (RR 0.77 (95% CI 0.61 to 0.95), high-quality evidence) being more certain than that for carbetocin (RR 0.70 (95% CI 0.38 to 1.28), low-quality evidence), or misoprostol plus oxytocin combination (RR 0.90 (95% CI 0.72 to 1.14), moderate-quality evidence). There were no meaningful differences between all drugs for maternal deaths or severe morbidity as these outcomes were so rare in the included randomised trials. Two combination regimens had the poorest rankings for side-effects. Specifically, the ergometrine plus
oxytocin combination had the higher risk for vomiting (RR 3.10 (95% CI 2.11 to 4.56), high-quality evidence; 1.9% versus 0.6%) and hypertension [RR 1.77 (95% CI 0.55 to 5.66), low-quality evidence; 1.2% versus 0.7%), while the misoprostol plus oxytocin combination had the higher risk for fever (RR 3.18 (95% CI 2.22 to 4.55), moderate-quality evidence; 11.4% versus 3.6%) when compared with oxytocin. Carbetocin had similar risk for side-effects compared with oxytocin although the quality evidence was very low for vomiting and for fever, and was low for hypertension.

**Authors' conclusions:** Ergometrine plus oxytocin combination, carbetocin, and misoprostol plus oxytocin combination were more effective for preventing PPH ≥ 500 mL than the current standard oxytocin. Ergometrine plus oxytocin combination was more effective for preventing PPH ≥ 1000 mL than oxytocin. Misoprostol plus oxytocin combination evidence is less consistent and may relate to different routes and doses of misoprostol used in the studies. Carbetocin had the most favourable side-effect profile amongst the top three options; however, most carbetocin trials were small and at high risk of bias. Amongst the 11 ongoing studies listed in this review there are two key studies that will inform a future update of this review. The first is a WHO-led multi-centre study comparing the effectiveness of a room temperature stable carbetocin versus oxytocin (administered intramuscularly) for preventing PPH in women having a vaginal birth. The trial includes around 30,000 women from 10 countries. The other is a UK-based trial recruiting more than 6000 women to a three-arm trial comparing carbetocin, oxytocin and ergometrine plus oxytocin combination. Both trials are expected to report in 2018. Consultation with our consumer group demonstrated the need for more research into PPH outcomes identified as priorities for women and their families, such as women's views regarding the drugs used, clinical signs of excessive blood loss, neonatal unit admissions and breastfeeding at discharge. To date, trials have rarely investigated these outcomes. Consumers also considered the side-effects of uterotonic drugs to be important but these were often not reported. A forthcoming set of core outcomes relating to PPH will identify outcomes to prioritise in trial reporting and will inform futures updates of this review. We urge all trialists to consider measuring these outcomes for each drug in all future randomised trials. Lastly, future evidence synthesis research could compare the effects of different dosages and routes of administration for the most effective drugs.


Abstract

**Background:** Violence toward MSM and female sex workers (FSW) is associated with HIV risk, and its prevention is prioritized in international HIV/AIDS policy.

**Methods:** Sociodemographic and behavioural data derived from HIV risk and follow-up cohorts including MSM and FSW in coastal Kenya between 2005 and 2014 was used to estimate the risk of rape, physical assault and verbal abuse, and to assess associations between first occurrence of assault with individual and recent behavioural factors.

**Results:** Incidence of first reported rape was similar for MSM [3.9, confidence interval (CI) 3.1-5.0 per 100 person-years (pyrs)] and FSW (4.8 CI 3.5-6.4 per 100 pyrs), P = 0.22. Incidence of first reported physical and verbal assault was higher for FSW than MSM (21.1 versus 12.9 per 100 pyrs, P = 0.14 and 51.3 versus 30.9 per 100 pyrs, P = 0.03 respectively). Recent alcohol use was associated with reporting of all forms of assault by MSM [adjusted odds ratio (AOR) 1.8, CI 0.9-3.5] and FSW (AOR 4.4, CI 1.41-14.0), as was recent sale of sex for MSM (AOR 2.0, CI 1.1-3.8). Exclusive sex with men, active sex work, and group sex were also specifically associated with reporting rape for MSM. Perpetrators of sexual and verbal assault were usually unknown, whilst perpetrators of physical violence toward FSW were usually regular sexual partners.

**Conclusion:** MSM and FSW experienced a similarly high incidence of sexual assault in coastal Kenya, in addition to physical and verbal assault. Current national policies focus heavily on gender-based violence against women and young girls, but need to be inclusive of MSM and FSW.


**Abstract**

**Background:** Chronic malnutrition or stunting among children under 5 years old is affected by several household environmental factors, such as food insecurity, disease burden, and poverty. However, not all children experience stunting even in food
insecure conditions. To seek a solution at the local level for preventing stunting, a cross-sectional study was conducted in southeastern Kenya, an area with a high level of food insecurity.

Methods: The study was based on a cohort organized to monitor the anthropometric status of children. A structured questionnaire collected information on the following: demographic characteristics, household food security based on the Household Food Insecurity Access Scale (HFIAS), household socioeconomic status (SES), and child health status. The associations between stunting and potential predictors were examined by bivariate and multivariate stepwise logistic regression analyses. Furthermore, analyses stratified by level of food security were conducted to specify factors associated with child stunting in different food insecure groups.

Results: Among 404 children, the prevalence of stunting was 23.3%. The percentage of households with severe food insecurity was 62.5%. In multivariate analysis, there was no statistically significant association with child stunting. However, further analyses conducted separately according to level of food security showed the following significant associations: in the severely food insecure households, feeding tea/porridge with milk (adjusted Odds Ratio [aOR]: 3.22; 95% Confidence Interval [95% CI]: 1.43-7.25); age 2 to 3 years compared with 0 to 5 months old (aOR: 4.04; 95% CI: 1.01-16.14); in households without severe food insecurity, animal rearing (aOR: 3.24; 95% CI: 1.04-10.07); SES with lowest status as reference (aOR range: from 0.13 to 0.22). The number of siblings younger than school age was not significantly associated, but was marginally associated in the latter household group (aOR: 2.81; 95% CI: 0.92-8.58).

Conclusions: Our results suggest that measures against childhood stunting should be optimized according to food security level observed in each community.


Abstract

Recent years have witnessed an increase in the use of community based participatory research (CBPR) tools for understanding environment and health issues and facilitating social action. This paper explores the application and utility of photovoice for understanding water, sanitation, and hygiene (WASH) behaviours and catalysing
community led solutions to change behaviours. Between June and August 2013, photovoice was conducted with eight (8) women in Usoma, a lakeshore community in Western Kenya with a follow-up community meeting (baraza) in May 2014 to discuss findings with the community members and government officials. In the first part of the study, photovoice one-on-one interviews were used to explore local perceptions and practices around water-health linkages and how the ecological and socio-political environment shapes these perceptions and practices. This paper, which is the second component of the study, uses photovoice group discussions to explore participants' experiences with and (re)action to the photographs and the photovoice project. The findings illustrate that photovoice was an effective CBPR methodology for understanding behaviours, creating awareness, facilitating collective action, and engaging with local government and local health officials at the water-health nexus.


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<td><strong>Abstract</strong></td>
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<td>National health systems performance (HSP) assessments and benchmarking are critical to understanding how well the delivery of healthcare meets the needs of citizens. Benchmarking HSP has often been done between countries to inform the global public health space. However, its impact is likely to be far greater when implemented sub-nationally to inform actual decisions on resource allocations and performance improvements, especially in high disease burden, low-income countries, where the resource envelope available for health is inadequate. In their study, Roberts and colleagues assemble, analyse and map a minimum set of health intervention and outcome indicators from 1990-2011 to assess and benchmark HSP across the 11 regions of Uganda. This is the first empirical sub-national HSP benchmarking study in the country and the results have potentially important health system policy implications. Please see related research: <a href="http://www.biomedcentral.com/1741-7015/13/285">http://www.biomedcentral.com/1741-7015/13/285</a>.</td>
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**Abstract**

**Background:** Integrating antenatal care (ANC) and HIV care may improve uptake and retention in services along the prevention of mother-to-child transmission (PMTCT) cascade. This study aimed to determine whether integration of HIV services into ANC settings improves PMTCT service utilization outcomes.

**Methods:** ANC clinics in rural Kenya were randomized to integrated (6 clinics, 569 women) or nonintegrated (6 clinics, 603 women) services. Intervention clinics provided all HIV services, including highly active antiretroviral therapy (HAART), whereas control clinics provided PMTCT services but referred women to HIV care clinics within the same facility. PMTCT utilization outcomes among HIV-infected women (maternal HIV care enrollment, HAART initiation, and 3-month infant HIV testing uptake) were compared using generalized estimating equations and Cox regression.

**Results:** HIV care enrollment was higher in intervention compared with control clinics [69% versus 36%; odds ratio = 3.94, 95% confidence interval (CI): 1.14 to 13.63]. Median time to enrollment was significantly shorter among intervention arm women (0 versus 8 days, hazard ratio = 2.20, 95% CI: 1.62 to 3.01). Eligible women in the intervention arm were more likely to initiate HAART (40% versus 17%; odds ratio = 3.22, 95% CI: 1.81 to 5.72). Infant testing was more common in the intervention arm (25% versus 18%), however, not statistically different. No significant differences were detected in postnatal service uptake or maternal retention.

**Conclusions:** Service integration increased maternal HIV care enrollment and HAART uptake. However, PMTCT utilization outcomes were still suboptimal, and postnatal service utilization remained poor in both study arms. Further improvements in the PMTCT cascade will require additional research and interventions.


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**149.** Onono M, Guzé MA, Grossman D, Steinfeld R, Bukusi EA, Shade S, Cohen CR, Newmann SJ. Integrating family planning and HIV services in western Kenya: the impact on HIV-infected patients' knowledge of family planning and male attitudes
toward family planning. AIDS Care. 2015;27(6):743-52

**Abstract**

Little information exists on the impact of integrating family planning (FP) services into HIV care and treatment on patients' familiarity with and attitudes toward FP. We conducted a cluster-randomized trial in 18 public HIV clinics with 12 randomized to integrated FP and HIV services and 6 to the standard referral-based system where patients are referred to an FP clinic. Serial cross-sectional surveys were done before (n = 488 women, 486 men) and after (n = 479 women, 481 men) the intervention to compare changes in familiarity with FP methods and attitudes toward FP between integrated and nonintegrated (NI) sites. We created an FP familiarity score based on the number of more effective FP methods patients could identify (score range: 0-6). Generalized estimating equations were used to control for clustering within sites. An increase in mean familiarity score between baseline (mean = 5.16) and post-intervention (mean = 5.46) occurred with an overall mean change of 0.26 (95% confidence intervals [CI] = 0.09, 0.45; p = 0.003) across all sites. At end line, there was no difference in increase of mean FP familiarity scores at intervention versus control sites (mean = 5.41 vs. 5.49, p = 0.94). We observed a relative decrease in the proportion of males agreeing that FP was "women's business" at integrated sites (baseline 42% to end line 30%; reduction of 12%) compared to males at NI sites (baseline 35% to end line 42%; increase of 7%; adjusted odds ration [aOR] = 0.43; 95% CI = 0.22, 0.85). Following FP-HIV integration, familiarity with FP methods increased but did not differ by study arm. Integration was associated with a decrease in negative attitudes toward FP among men.


| 152. | Minakawa N, Kongere JO, Dida GO, Ikeda E, Hu J, Minagawa K, Futami K, Kawada H, Njenga SM, Larson PS. Sleeping on the floor decreases insecticide treated bed net use and increases risk of malaria in children under 5 years of |
Abstract

Background: Several novel tuberculosis vaccines are currently in clinical trials, including AERAS-402, an adenovector encoding a fusion protein of Mycobacterium tuberculosis antigens 85A, 85B, and TB10.4. A multicentred trial of AERAS-402 safety and immunogenicity in healthy infants was conducted in three countries in sub-Saharan Africa, using an adaptive design.

Methods: In a double-blind, randomised, placebo-controlled, dose-finding trial, we enrolled BCG-vaccinated, HIV-uninfected infants aged 16-26 weeks. Infants in the safety/dose-finding phase received two doses of AERAS-402 across three dose levels, or placebo, intramuscularly on days 0 and 28. Infants in the expanded safety phase received three doses of the highest dose level, with the 3rd dose at day 280. Follow up for safety and immunogenicity was for up to two years.

Results: We enrolled 206 infants (52 placebo and 154 AERAS-402 recipients) into the dose-finding phase and 281 (141 placebo and 140 AERAS-402 recipients) into the expanded safety phase. Safety data were acceptable across all dose levels. No vaccine-related deaths were recorded. A single serious adverse event of tachypnoea was deemed related to study vaccine. Antibodies directed largely against Ag85A and Ag85B were detected. Low magnitude CD4+ and CD8+ polyfunctional T cell responses were observed at all dose levels. The addition of a third dose of AERAS-402 at the highest dose level did not increase frequency or magnitude of antibody or CD8+ T cell responses.

Conclusions: AERAS-402 has an acceptable safety profile in infants and was well tolerated at all dose levels. Response rate was lower than previously seen in BCG vaccinated adults, and frequency and magnitude of antigen-specific T cells were not increased by a third dose of vaccine.


Abstract

Implementation of successful prevention of mother-to-child transmission of HIV strategies has resulted in an increased population of HIV-exposed uninfected (HEU) infants. HEU infants have higher rates of morbidity and mortality than HIV-unexposed (HU) infants. Numerous factors may contribute to poor health in HEU infants including immunological alterations. The present study assessed T-cell phenotype and function in HEU infants with a focus on memory Th1 responses to vaccination. We compared cross-sectionally selected parameters at 3 and 12 months of age in HIV-exposed (n = 42) and HU (n = 28) Kenyan infants. We measured ex vivo activated and bulk memory CD4 and CD8 T-cells and regulatory T-cells by flow cytometry. In addition, we measured the magnitude, quality and memory phenotype of antigen-specific T-cell responses to Bacillus Calmette-Guerin and Tetanus Toxoid vaccine antigens, and the magnitude and quality of the T cell response following polyclonal stimulation with staphylococcal enterotoxin B. Finally, the influence of maternal disease markers on the immunological parameters measured was assessed in HEU infants. Few perturbations were detected in ex vivo T-cell subsets, though amongst HEU infants maternal HIV viral load positively correlated with CD8 T cell immune activation at 12 months. Conversely, we observed age-dependent differences in the magnitude and polyfunctionality of IL-2 and TNF-α responses to vaccine antigens particularly in Th1 cells. These changes mirrored those seen following polyclonal stimulation, where at 3 months, cytokine responses were higher in HEU infants compared to HU infants, and at 12 months, HEU infant cytokine responses were consistently lower than those seen in HU infants. Finally, reduced effector memory Th1 responses to vaccine antigens were observed in HEU infants at 3 and 12 months and higher central memory Th1 responses to M. tuberculosis antigens were observed at 3 months only. Long-term monitoring of vaccine efficacy and T-cell immunity in this vulnerable population is warranted.


Abstract

HIV affects the function of all lymphocyte populations, including B cells. Phenotypic and functional defects of B cells in HIV-infected adults have been well characterized, but defects in children have not been studied to the same extent. We determined the proportion of B cell subsets and frequencies of Ag-specific memory B cells in peripheral blood from HIV-infected children and healthy controls, using flow cytometry and B cell ELISPOT, respectively. In addition, we measured the quantities and avidities of plasma Abs against various Ags by ELISA. We also determined plasma levels of BAFF and expression of BAFF receptors on B cells. Children with high HIV viremia had increased proportions of activated mature B cells, tissue-like memory B cells and plasmablasts, and low proportions of naive B cells when compared with community controls and children with low HIV viremia, similar to adults infected with HIV. HIV-infected groups had lower proportions of resting memory B cells than did community controls. Notably, high HIV viremia prevented the age-dependent accumulation of class-switched resting memory B cells. HIV-infected children, regardless of the level of viremia, showed lower quantities and avidities of IgG and lower frequencies of memory B cells against Expanded Program on Immunization vaccines. The HIV-infected children had an altered BAFF profile that could have affected their B cell compartment. Therefore, B cell defects in HIV-infected children are similar to those seen in HIV-infected adults. However, control of HIV viremia is associated with normalization of activated B cell subsets and allows age-dependent accumulation of resting memory B cells.


Abstract

Background: Many HIV-infected pregnant women identified during antenatal care (ANC) do not enroll in long-term HIV care, resulting in deterioration of maternal health and continued risk of HIV transmission to infants.

Methods: We performed a cluster randomized trial to evaluate the effect of integrating HIV care into ANC clinics in rural Kenya. Twelve facilities were randomized to
provide either integrated services (ANC, prevention of mother-to-child transmission, and HIV care delivered in the ANC clinic; n = 6 intervention facilities) or standard ANC services (including prevention of mother-to-child transmission and referral to a separate clinic for HIV care; n = 6 control facilities).

**Results:** There were high patient attrition rates over the course of this study. Among study participants who enrolled in HIV care, there was 12-month follow-up data for 256 of 611 (41.8%) women and postpartum data for only 325 of 1172 (28%) women. By 9 months of age, 382 of 568 (67.3%) infants at intervention sites and 338 of 594 (57.0%) at control sites had tested for HIV [odds ratio (OR) 1.45, 95% confidence interval (CI): 0.71 to 2.82]; 7.3% of infants tested HIV positive at intervention sites compared with 8.0% of infants at control sites (OR 0.89, 95% CI: 0.56 to 1.43). The composite clinical/immunologic progression into AIDS was similar in both arms (4.9% vs. 5.1%, OR 0.83, 95% CI: 0.41 to 1.68).

**Conclusions:** Despite the provision of integrated services, patient attrition was substantial in both arms, suggesting barriers beyond lack of service integration. Integration of HIV services into the ANC clinic was not associated with a reduced risk of HIV transmission to infants and did not appear to affect short-term maternal health outcomes.


**Abstract**

**Background:** The disability adjusted life year (DALY) is a composite measure of disease burden that includes both morbidity and mortality, and is relevant to conditions such as epilepsy that can limit productive functioning. The 2010 Global Burden of Disease (GBD) study introduced a number of new methods and definitions, including a prevalence-based approach and revised disability weights to calculate morbidity and new standard life expectancies to calculate premature mortality. We used these approaches, and local, population-based data, to estimate the burden of convulsive epilepsy in rural South Africa.

**Methods & findings:** Comprehensive prevalence, incidence and mortality data on convulsive epilepsy were collected within the Agincourt sub-district in rural northeastern South Africa between 2008 and 2012. We estimated DALYs using both
prevalence- and incidence-based approaches for calculating years of life lived with disability. Additionally, we explored how changing the disease model by varying the disability weights influenced DALY estimates. Using the prevalence-based approach, convulsive epilepsy in Agincourt resulted in 332 DALYs (95% uncertainty interval (UI): 216-455) and 4.1 DALYs per 1,000 individuals (95%UI: 2.7-5.7) annually. Of this, 26% was due to morbidity while 74% was due to premature mortality. DALYs increased by 10% when using the incidence-based method. Varying the disability weight from 0.072 (treated epilepsy, seizure free) to 0.657 (severe epilepsy) caused years lived with disability to increase from 18 (95%UI: 16-19) to 161 (95%UI: 143-170).

**Conclusions:** DALY estimates are influenced by both the methods applied and population parameters used in the calculation. Irrespective of method, a significant burden of epilepsy is due to premature mortality in rural South Africa, with a lower burden than rural Kenya. Researchers and national policymakers should carefully interrogate the methods and data used to calculate DALYs as this will influence policy priorities and resource allocation.


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Participants of an International Workshop in Kenya on the Role of Frontline Staff in Biomedical Research, July 2014, Kombe F. Enhancing quality and integrity in biomedical research in Africa: an international call for greater focus, investment and standardisation in capacity strengthening for frontline staff. BMC Med Ethics. 2015 Nov 13;16(1):77

**Abstract**

The integrity of biomedical research depends heavily on the quality of research data collected. In turn, data quality depends on processes of data collection, a task undertaken by frontline research staff in many research programmes in Africa and elsewhere. These frontline research staff often have additional responsibilities including translating and communicating research in local languages, seeking informed consent for study participation and maintaining supportive relationships between research institutions and study participants and wider communities. The level of skills that fieldworkers need to undertake these responsibilities clearly affects the quality of data collected, the ethics of research 'on the ground' and the short and long term acceptability of research. We organised an international workshop in Kenya in July 2014 to discuss the role of frontline staff in scientific research. A total of 25 field managers from 9 African countries and the UK met for 2.5 days to discuss the relationship between data quality and institutional performance management systems.
and how they affect career progression and supportive supervision policies of research frontline staff. From this workshop, and supporting an expanding literature on the role of fieldworkers in international health research, participants agreed that fieldworkers' roles present them with practical and ethical challenges that their routine training does not adequately prepare them for. We argue that the common and complex challenges facing fieldworkers should in part be addressed through increased investment and collaborative agreements across types of research institutions in Africa. We call for standardization of core elements of training for this critically important cadre of research staff who perform similar roles and encounter similar challenges in many African settings. Although many valuable training elements are offered in institutions, there is a need to develop broader, more grounded and innovative strategies to address complex realities for fieldworkers, and support the integrity and ethics of health research in these settings.


Abstract

Background: Lymphatic filariasis (LF) is one of the neglected tropical diseases targeted for global elimination. The ability to interrupt transmission is, partly, influenced by the underlying intensity of transmission and its geographical variation. This information can also help guide the design of targeted surveillance activities. The present study uses a combination of geostatistical and mathematical modelling to predict the prevalence and transmission intensity of LF prior to the implementation of large-scale control in sub-Saharan Africa.

Methods: A systematic search of the literature was undertaken to identify surveys on the prevalence of Wuchereria bancrofti microfilaraemia (mf), based on blood smears, and on the prevalence of antigenaemia, based on the use of an immuno-chromatographic card test (ICT). Using a suite of environmental and demographic data, spatiotemporal multivariate models were fitted separately for mf prevalence and ICT-based prevalence within a Bayesian framework and used to make predictions for non-sampled areas. Maps of the dominant vector species of LF were also developed. The maps of predicted prevalence and vector distribution were linked to mathematical
models of the transmission dynamics of LF to infer the intensity of transmission, quantified by the basic reproductive number (R0).

**Results:** The literature search identified 1267 surveys that provide suitable data on the prevalence of mf and 2817 surveys that report the prevalence of antigenaemia. Distinct spatial predictions arose from the models for mf prevalence and ICT-based prevalence, with a wider geographical distribution when using ICT-based data. The vector distribution maps demonstrated the spatial variation of LF vector species. Mathematical modelling showed that the reproduction number (R0) estimates vary from 2.7 to 30, with large variations between and within regions.

**Conclusions:** LF transmission is highly heterogeneous, and the developed maps can help guide intervention, monitoring and surveillance strategies as countries progress towards LF elimination.


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**Abstract**

**Introduction:** Although men who have sex with men (MSM) in sub-Saharan Africa are at high risk for HIV acquisition, access to and quality of health and HIV services within this population are negatively affected by stigma and capacity within the health sector. A recently developed online MSM training programme (www.marps-africa.org) was shown to contribute to reductions in MSM prejudice among healthcare providers (HCPs) in coastal Kenya. In this study, we used qualitative methods to explore the provision of MSM healthcare services two years post-training in coastal Kenya.

**Methods:** From February to July 2014, we held 10 focus group discussions (FGD) with 63 participants, including HCP from 25 facilities, county AIDS coordinators and MSM from local support groups. Participants discussed availability, acceptability and accessibility of HIV healthcare for MSM. HCP also discussed changes in their health service practices after completing the training. FGD were recorded, transcribed verbatim and analyzed using Ritchie and Spencer's "framework approach" for qualitative data.
Results: HCPs described continued improvements in their ability to provide service in a non-stigmatizing way to MSM patients since completing the training programme and expressed comfort engaging MSM patients in care. Four additional recommendations for improving MSM healthcare services were identified: 1) expanding the reach of MSM sensitivity training across the medical education continuum; 2) establishing guidelines to manage sexually transmitted anal infections; 3) promoting legal and policy reforms to support integration of MSM-appropriate services into healthcare; and 4) including MSM information in national reporting tools for HIV services.

Conclusions: Positive impacts of this sensitivity and skills training programme were reflected in HCP attitudes two years post-intervention. Scaling-up of efforts will rely on continued policies to include MSM in healthcare programmes to reduce stigma in health settings and guidelines for MSM STI service delivery.


Abstract

Introduction: As efforts are made to reach universal access to ART in Kenya, the problem of congestion at HIV care clinics is likely to worsen. We evaluated the feasibility and the economic benefits of a designated time appointment system as a solution to decongest HIV care clinics.

Methods: This was an explanatory two-arm open-label randomized controlled trial that enrolled 354 consenting participants during their normal clinic days and followed-up at subsequent clinic appointments for up to nine months. Intervention arm participants were given specific dates and times to arrive at the clinic for their next appointment while those in the control arm were only given the date and had the discretion to decide on the time to arrive as is the standard practice. At follow-up visits, we recorded arrival and departure times and asked the monetary value of work participants engaged in before and after clinic. We conducted multiple imputation to replace missing data in our primary outcome variables to allow for intention-to-treat analysis; and analyzed the data using Mann-Whitney U test.

Results: Overall, 72.1% of the intervention participants arrived on time, 13.3% arrived ahead of time and 14.6% arrived past scheduled time. Intervention arm participants spent a median of 65 [interquartile range (IQR), 52-87] minutes at the clinic compared
to 197 (IQR, 173-225) minutes for control participants (p<0.01). Furthermore, intervention arm participants were more productively engaged on their clinic days valuing their cumulative work at a median of USD 10.5 (IQR, 60.0-16.8) compared to participants enrolled in the control arm who valued their work at USD 8.3 (IQR, 5.5-12.9; p=0.02).

**Conclusions:** A designated time appointment system is feasible and provides substantial time savings associated with greater economic productivity for HIV patients attending a busy HIV care clinic.


**Abstract**

**Background:** The World Health Organization recommends Bacillus Calmette-Guérin (BCG) vaccination against tuberculosis be given at birth. However, in many developing countries, pre-term and low birth weight infants get vaccinated only after they gain the desired weight. In Kenya, the ministry of health recommends pre-term and low birth weight infants to be immunized at the time of discharge from hospital irrespective of their weight. This paper seeks to understand the effects of birth weight on timing of BCG vaccine.

**Methods:** The study was conducted in two Nairobi urban informal settlements, Korogocho and Viwandani which hosts the Nairobi Urban Health and Demographic Surveillance system. All infants born in the study area since September 2006 were included in the study. Data on immunization history and birth weight of the infant were recorded from child's clinic card. Follow up visits were done every four months to update immunization status of the child. A total of 3,602 infants were included in this analysis. Log normal accelerated failure time parametric model was used to assess the association between low birth weight infants and time to BCG immunization.

**Results:** In total, 229 (6.4%) infants were low birth weight. About 16.6% of the low birth weight infants weighed less than 2000 grams and 83.4% weighed between 2000 and 2490 grams. Results showed that, 60% of the low birth weight infants received BCG vaccine after more than five weeks of life. Private health facilities were less likely to administer a BCG vaccine on time compared to public health facilities. The effects of low birth weight on females was 0.60 and 0.97-times that of males for infants weighing 2000-2499 grams and for infants weighing <2000 grams respectively. The
effect of low birth weight among infants born in public health facilities was 1.52 and 3.94-times that of infants delivered in private health facilities for infants weighing 2000-2499 grams and those weighing < 2000 grams respectively.

**Conclusion:** Low birth weight infants received BCG immunization late compared to normal birth weight infants. Low birth weight infants delivered in public health facilities were more likely to be immunized much later compared to private health facilities.


**Abstract**

Respiratory syncytial virus (RSV) is a global respiratory pathogen of humans, with infection occurring characteristically as recurrent seasonal epidemics. Unlike influenza viruses, little attention has been paid to the mechanism underlying worldwide spread and persistence of RSV and how this may be discerned through an improved understanding of the introduction and persistence of RSV in local communities. We analyzed 651 attachment (G) glycoprotein nucleotide sequences of RSV B collected over 11 epidemics (2002 to 2012) in Kilifi, Kenya, and contemporaneous data collected elsewhere in Kenya and 18 other countries worldwide (2002 to 2012). Based on phylogeny, genetic distance and clustering patterns, we set out pragmatic criteria to classify local viruses into distinct genotypes and variants, identifying those newly introduced and those locally persisting. Three genotypes were identified in the Kilifi data set: BA (n = 500), SAB1 (n = 148), and SAB4 (n = 3). Recurrent RSV epidemics in the local population were composed of numerous genetic variants, most of which have been newly introduced rather than persisting in the location from season to season. Global comparison revealed that (i) most Kilifi variants do not cluster closely with strains from outside Kenya, (ii) some Kilifi variants were closely related to those observed outside Kenya (mostly Western Europe), and (iii) many variants were circulating elsewhere but were never detected in Kilifi. These results are consistent with the hypothesis that year-to-year presence of RSV at the local level (i.e., Kilifi) is achieved primarily, but not exclusively, through introductions from a pool of variants that are geographically restricted (i.e., to Kenya or to the region) rather than global.

**Importance:** The mechanism by which RSV persists and reinvades local populations is poorly understood. We investigated this by studying the temporal patterns of RSV
variants in a rural setting in tropical Africa and comparing these variants with contemporaneous variants circulating in other countries. We found that periodic seasonal RSV transmission at the local level appears to require regular new introductions of variants. However, importantly, the evidence suggests that the source of new variants is mostly geographically restricted, and we hypothesize that year-to-year RSV persistence is at the country level rather than the global level. This has implications for control.


Abstract

Background: Despite advances to targeted leishmanicidal chemotherapy, defies around severe toxicity, recent emergence of resistant variants and absence of rational vaccine still persist. This necessitates search and/or progressive validation of accessible medicinal remedies including plant based. The study examined both in vivo and in vitro response of L. major infection to combined therapy of Ricinus communis and Azadirachta indica extracts in BALB/c mice as the mouse model. A comparative study design was applied.

Results: BALB/c mice, treated with combination therapy resulted in significantly (p < 0.05) larger reduction of lesion than those treated with monotherapies. The spleno-somatic index was found to be significantly low with combination therapy than monotherapies. Antiparasitic effect of A. indica and R. communis on amastigote with a 50 % inhibitory concentration (IC50) was of 11.5 and 16.5 µg mL(-1) respectively while combination therapy gave 9.0 µg mL(-1) compared to the standard drugs, Pentostam and amphotericin B which had an IC50 of 6.5 and 4.5 µg ml(-1) respectively. Optimal efficacy of A. indica and R. communis was 72 and 59.5 % respectively, combination therapy gave 88 %, while Pentostam and amphotericin B had 98 and 92 % respectively against amastigotes. Against promastigotes A. indica and R. Communis gave an IC50 of 10.1, 25.5 µg mL(-1) respectively, while combination, 12.2 µg mL(-1) against 4.1 and 5.0 µg ml(-1) for Pentostam and amphotericin B respectively. The optimal efficacy of the compounds against promastigotes was 78.0, 61.5 and 91.2 % (A. indica, R. communis and A. indica + R. communis respectively) against 96.5 and 98 % for Pentostam and amphotericin B respectively. The concentrations at optimal efficacy were significantly different (p < 0.05) among the test
An evaluation of the IC50 values of the combination therapies clearly reveals synergistic effects.

**Conclusion:** Combination therapy of *A. indica* and *R. communis* had best antileishmanial activity than the monotherapies. The active ingredients of both *R. communis* and *A. indica* need to be fractionated, and studied further for activity against Leishmania parasites.


**Abstract**

**Background:** Coverage of civil registration and vital statistics varies globally, with most deaths in Africa and Asia remaining either unregistered or registered without cause of death. One important constraint has been a lack of fit-for-purpose tools for registering deaths and assigning causes in situations where no doctor is involved. Verbal autopsy (interviewing care-givers and witnesses to deaths and interpreting their information into causes of death) is the only available solution. Automated interpretation of verbal autopsy data into cause of death information is essential for rapid, consistent and affordable processing.

**Methods:** Verbal autopsy archives covering 54 182 deaths from five African and Asian countries were sourced on the basis of their geographical, epidemiological and methodological diversity, with existing physician-coded causes of death attributed. These data were unified into the WHO 2012 verbal autopsy standard format, and processed using the InterVA-4 model. Cause-specific mortality fractions from InterVA-4 and physician codes were calculated for each of 60 WHO 2012 cause categories, by age group, sex and source. Results from the two approaches were assessed for concordance and ratios of fractions by cause category. As an alternative metric, the Wilcoxon matched-pairs signed ranks test with two one-sided tests for stochastic equivalence was used.

**Findings:** The overall concordance correlation coefficient between InterVA-4 and physician codes was 0.83 (95% CI 0.75 to 0.91) and this increased to 0.97 (95% CI 0.96 to 0.99) when HIV/AIDS and pulmonary TB deaths were combined into a single category. Over half (53%) of the cause category ratios between InterVA-4 and
physician codes by source were not significantly different from unity at the 99% level, increasing to 62% by age group. Wilcoxon tests for stochastic equivalence also demonstrated equivalence.

**Conclusions:** These findings show strong concordance between InterVA-4 and physician-coded findings over this large and diverse data set. Although these analyses cannot prove that either approach constitutes absolute truth, there was high public health equivalence between the findings. Given the urgent need for adequate cause of death data from settings where deaths currently pass unregistered, and since the WHO 2012 verbal autopsy standard and InterVA-4 tools represent relatively simple, cheap and available methods for determining cause of death on a large scale, they should be used as current tools of choice to fill gaps in cause of death data.


**Abstract**

**Background:** The global prevalence of X-linked glucose-6-phosphate dehydrogenase (G6PD) deficiency is thought to be a result of selection by malaria, but epidemiological studies have yielded confusing results. We investigated the relationships between G6PD deficiency and both malaria and non-malarial illnesses among children in Kenya.

**Methods:** We did this study in Kilifi County, Kenya, where the G6PD c.202T allele is the only significant cause of G6PD deficiency. We tested the associations between G6PD deficiency and severe and complicated Plasmodium falciparum malaria through a case-control study of 2220 case and 3940 control children. Cases were children aged younger than 14 years, who visited the high dependency ward of Kilifi County Hospital with severe malaria between March 1, 1998, and Feb 28, 2010. Controls were children aged between 3-12 months who were born within the same study area between August 2006, and September 2010. We assessed the association between G6PD deficiency and both uncomplicated malaria and other common diseases of childhood in a cohort study of 752 children aged younger than 10 years. Participants of this study were recruited from a representative sample of households within the Ngerenya and Chonyi areas of Kilifi County between Aug 1, 1998, and July 31, 2001. The primary outcome measure for the case-control study was the odds ratio for hospital admission.
Findings: 2863 (73%) children in the control group versus 1643 (74%) in the case group had the G6PD normal genotype, 639 (16%) versus 306 (14%) were girls heterozygous for G6PD c.202T, and 438 (11%) versus 271 (12%) children were either homozygous girls or hemizygous boys. Compared with boys and girls without G6PD deficiency, we found significant protection from severe malaria (odds ratio [OR] 0.82, 95% CI 0.70–0.97; p=0.020) among G6PD c.202T heterozygous girls but no evidence for protection among G6PD c.202T hemizygous boys and homozygous girls (OR 1.18, 0.99–1.40; p=0.056). Median follow-up for the mild disease cohort study was 2.24 years (IQR 2.22–2.85). G6PD c.202T had no effect on other common diseases of childhood in heterozygous girls (incidence rate ratio 0.98, 95% CI 0.86–1.11; p=0.82) or homozygous girls or hemizygous boys (0.93, 0.82–1.04; p=0.25), with the sole exception of a marginally significant increase in the incidence of helminth infections among heterozygous girls.

Interpretation: Heterozygous girls might be the driving force for the positive selection of G6PD deficiency alleles. Further studies are needed to definitively establish the mechanisms by which G6PD deficiency confers an advantage against malaria in heterozygous individuals. Such studies could lead to the development of new treatments.

collected mosquitoes alternatively from 18:00 to 21:00h and 21:00 to 06:00h every week. All collected mosquitoes were morphologically identified. Female Anopheles mosquitoes were classified according to their physiological status as unfed, fed, partially gravid and gravid, sorted and counted. Members of the A. gambiae complex were identified using a Polymerase chain reaction (PCR) method. Enzyme-linked-immunosorbent assay (ELISA) was used to determine blood meal sources and Plasmodium infection rates in A. gambiae s.l. mosquitoes. Blood meal tests were conducted on DNA extracted from gut contents of blood fed A. gambiae s.l. The head and thorax section of dried samples of A. gambiae s.l. were used in testing for the presence of Plasmodium falciparum (Pf) sporozoites. Overall, 735 adult female Anopheles comprising 708 [96.3%] A. gambiae s.l. and 27 [3.7%] Anopheles funestus mosquitoes were collected. A. gambiae s.l. population collected comprised, 615 [86.9%] unfed and 38 [5.4%] fed adult mosquitoes. The rest were either partially or fully gravid. The proportion of A. gambiae s.l. biting indoors within 18:00-21:00h was 15.8% (103/653) at a rate of 3.2 bites per person per hour compared to 84.2% biting from 21:00-06:00h at a rate of 3.8 bites/ per/h. An estimated 97.7% A. gambiae ss and 2.3% A. arabiensis constituted the indoor biting A. gambiae s.l. The population of An. gambiae s.l. biting from 18:00 to 21:00h had a Plasmodium faciparum (pf) sporozoite rate of 3.8% compared to 3.5% observed in populations biting within 21:00-06:00h. Human blood constituted 89% of An. gambiae s.l. blood meal sources. The risk of malaria transmission from 21:00 to 06:00h was approximately 5 fold the risk within 18:00-21:00h. Majority of the infective female A. gambiae s.l. adults were biting deep into the night than in the early hours of the night. Humans remain the preferred source of blood meal for A. gambiae s.s. the dominant malaria vector in the highlands. ITNs remain a fundamental control intervention against malaria transmission since female blood seekers were more during bed time than pre-bed time. Advocacy on enhanced net availability, integrity and usage in Kenyan highlands can reduce Pf transmission. Additional complementary interventions are required to control the biting and parasite transmission encountered before bed-time.


Abstract
Background: Artemisinin-based combination therapies (ACTs) are the recommended first-line treatment for uncomplicated Plasmodium falciparum malaria. Ferroquine is a new combination partner for fast-acting ACTs such as artesunate. We aimed to assess different doses of ferroquine in combination with artesunate against uncomplicated P falciparum malaria in a heterogeneous population in Africa.

Methods: We did a phase 2, multicentre, parallel-group, double-blind, randomised, dose-ranging non-inferiority trial at eight African hospitals (two in Gabon, three in Burkina Faso, one in Benin, and two in Kenya). We recruited patients presenting with acute P falciparum monoinfection (1000-200,000 parasites per μL), and a central body temperature of at least 37.5°C or history of fever in the past 24 h. We assessed patients in two sequential cohorts: cohort 1 contained adults (bodyweight >50 kg) and adolescents (aged ≥14 years, >30 kg), and cohort 2 contained children (aged 2-13 years, 15-30 kg). We randomly assigned patients (1:1:1:1) to receive artesunate 4 mg/kg per day plus ferroquine 2 mg/kg, 4 mg/kg, or 6 mg/kg, given double-blind once per day for 3 days, or ferroquine monotherapy 4 mg/kg per day given single-blind (ie, allocation was only masked from the patient) once per day for 3 days. We did 14 patient visits (screening, 3 treatment days and 48 h post-treatment surveillance, a visit on day 7, then one follow-up visit per week until day 63). The primary endpoint was non-inferiority of treatment in terms of PCR-corrected cure rate against a reference value of 90%, with a 10% non-inferiority margin, assessed in patients treated without major protocol deviations for parasitologically confirmed malaria. We assessed safety in all treated patients. This study is registered with ClinicalTrials.gov, number NCT00988507, and is closed.

Findings: Between Oct 16, 2009, and Sept 22, 2010, we randomly assigned 326 eligible patients to treatment groups, with last follow-up visit on Dec 1, 2010. 284 patients (87%) were available for per-protocol analyses. At day 28, PCR-confirmed cure was noted in 68 (97%, 95% CI 90-100) of 70 patients treated with ferroquine 2 mg/kg plus artesunate, 73 (99%, 93-100) of 74 with ferroquine 4 mg/kg plus artesunate, 71 (99%, 93-100) of 72 with ferroquine 6 mg/kg plus artesunate, and 54 (79%, 68-88) of 68 with ferroquine 4 mg/kg monotherapy. The three dose groups of ferroquine plus artesunate met the non-inferiority hypothesis. The most common adverse events were headache in cohort 1 (30 [19%] of 162 patients) and worsening malaria in cohort 2 (23 [14%] of 164 patients); occurrences were similar between treatment groups.

Interpretation: Ferroquine combined with artesunate was associated with high cure rates and was safe at all doses tested, and could be a promising new drug combination for the treatment of P falciparum malaria. Ferroquine could also partner other drugs to
establish a new generation of antimalarial combinations, especially in regions that have developed resistance to ACTs.


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<td><strong>Abstract</strong></td>
<td>There have been no repeat surveys of psychotic symptoms in Kenya or indeed subSaharan Africa. A mental health epidemiological survey was therefore conducted in a demographic surveillance site of a Kenyan household population in 2013 to test the hypothesis that the prevalence of psychotic symptoms would be similar to that found in an earlier sample drawn from the same sample frame in 2004, using the same overall methodology and instruments. This 2013 study found that the prevalence of one or more psychotic symptoms was 13.9% with one or more symptoms and 3.8% with two or more symptoms, while the 2004 study had found that the prevalence of single psychotic symptoms in rural Kenya was 8% of the adult population, but only 0.6% had two symptoms and none had three or more psychotic symptoms. This change was accounted for by a striking increase in psychotic symptoms in women (17.8% in 2013 compared with 6.9% in 2004, p &lt; 0.001), whereas there was no significant change in men (10.6% in 2013 compared with 9.4% in 2004, p = 0.582). Potential reasons for this increase in rate of psychotic symptoms in women are explored.</td>
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<td><strong>Abstract</strong></td>
<td><strong>Introduction:</strong> In spite of the critical role of Emergency Obstetric Care in treating complications arising from pregnancy and childbirth, very few facilities are equipped in Kenya to offer this service. In Malindi, availability of EmOC services does not meet the UN recommended levels of at least one comprehensive and four basic EmOC facilities per 500,000 populations. This study was conducted to assess priority setting</td>
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process and its implication on availability, access and use of EmOC services at the district level.

**Methods:** A qualitative study was conducted both at health facility and community levels. Triangulation of data sources and methods was employed, where document reviews, in-depth interviews and focus group discussions were conducted with health personnel, facility committee members, stakeholders who offer and/ or support maternal health services and programmes; and the community members as end users. Data was thematically analysed.

**Results:** Limitations in the extent to which priorities in regard to maternal health services can be set at the district level were observed. The priority setting process was greatly restricted by guidelines and limited resources from the national level. Relevant stakeholders including community members are not involved in the priority setting process, thereby denying them the opportunity to contribute in the process.

**Conclusion:** The findings illuminate that consideration of all local plans in national planning and budgeting as well as the involvement of all relevant stakeholders in the priority setting exercise is essential in order to achieve a consensus on the provision of emergency obstetric care services among other health service priorities.


**Abstract**

**Background:** Absolute neutrophil counts (ANCs) are lower in East African adults. To assess the impact of lower ANC, we reviewed data from HIV-infected Kenyan women receiving antiretroviral therapy antepartum and postpartum.

**Methods:** The Kisumu Breastfeeding Study (KiBS) participants received an antiretroviral regimen from 34 weeks' gestation through 6 months postpartum. Measured ANC and subsequent illnesses were reviewed. Adverse events (AEs) potentially attributable to neutropenia were identified, and ANC was graded using the 2004 Division of AIDS table for Grading the Severity of AEs.
**Results:** Among 478 women with ≥1 postpartum ANC measured, 298 (62.1%) women met criteria for an AE (<1.3 × 10^9 cells/L). Of those, 38 (12.5%) women experienced a nonlife-threatening illness potentially attributable to neutropenia.

**Conclusion:** More than half of KiBS women met criteria for neutropenia. The mild clinical experience of most participants with low ANCs supports that these values might be typical for this population and may not result in adverse clinical sequelae.