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**Abstract**

**Background:** The candidate malaria vaccine RTS,S/AS01 is being evaluated in order to inform a decision regarding its inclusion in routine vaccination schedules.

**Methods:** We conducted 7 years of follow-up in children who had been randomly assigned, at 5 to 17 months of age, to receive three doses of either the RTS,S/AS01 vaccine or a rabies (control) vaccine. The end point was clinical malaria (temperature of $\geq 37.5^\circ C$ and infection with Plasmodium falciparum of $> 2500$ parasites per cubic millimeter). In an analysis that was not prespecified, the malaria exposure of each child was estimated with the use of information on the prevalence of malaria among residents within a 1-km radius of the child's home. Vaccine efficacy was defined as $1 - \text{hazard ratio}$ or the incidence-rate ratio, multiplied by 100, in the RTS,S/AS01 group versus the control group.

**Results:** Over 7 years of follow-up, we identified 1002 episodes of clinical malaria among 223 children randomly assigned to the RTS,S/AS01 group and 992 episodes among 224 children randomly assigned to the control group. The vaccine efficacy, as assessed by negative binomial regression, was 4.4% (95% confidence interval [CI], -17.0 to 21.9; $P=0.66$) in the intention-to-treat analysis and 7.0% (95% CI, -14.5 to 24.6; $P=0.52$) in the per-protocol analysis. Vaccine efficacy waned over time ($P=0.006$ for the interaction between vaccination and time), including negative efficacy during the fifth year among children with higher-than-average exposure to malaria parasites (intention-to-treat analysis: $-43.5%$; 95% CI, -100.3 to -2.8 [$P=0.03$]; per-protocol analysis: $-56.8%$; 95% CI, -118.7 to -12.3 [$P=0.008$]).

**Conclusions:** A three-dose vaccination with RTS,S/AS01 was initially protective against clinical malaria, but this result was offset by rebound in later years in areas with higher-than-average exposure to malaria parasites. (Funded by the PATH Malaria Vaccine Initiative and others; ClinicalTrials.gov number, NCT00872963.)

**Abstract**

**Rationale:** Several studies have demonstrated links between infectious diseases and cardiovascular conditions. Malaria and hypertension are widespread in many low- and middle-income countries, but the possible link between them has not been considered.

**Objective:** In this article, we outline the basis for a possible link between malaria and hypertension and discuss how the hypothesis could be confirmed or refuted.

**Methods and results:** We reviewed published literature on factors associated with hypertension and checked whether any of these were also associated with malaria. We then considered various study designs that could be used to test the hypothesis. Malaria causes low birth weight, malnutrition, and inflammation, all of which are associated with hypertension in high-income countries. The hypothetical link between malaria and hypertension can be tested through the use of ecological, cohort, or Mendelian randomization studies, each of which poses specific challenges.

**Conclusions:** Confirmation of the existence of a causative link with malaria would be a paradigm shift in efforts to prevent and control hypertension and would stimulate wider research on the links between infectious and noncommunicable disease.


**Abstract**

Malnutrition, which encompasses under- and overnutrition, is responsible for an enormous morbidity and mortality burden globally. Malnutrition results from disordered nutrient assimilation but is also characterized by recurrent infections and chronic inflammation, implying an underlying immune defect. Defects emerge before birth via modifications in the immunoepigenome of malnourished parents, and these may contribute to intergenerational cycles of malnutrition. This review summarizes key recent studies from experimental animals, in vitro models, and human cohorts, and proposes that immune dysfunction is both a cause and
a consequence of malnutrition. Focusing on childhood undernutrition, we highlight gaps in current understanding of immune dysfunction in malnutrition, with a view to therapeutically targeting immune pathways as a novel means to reduce morbidity and mortality.


**Abstract**

Christian Lienhardt and colleagues describe the research efforts needed to end the global tuberculosis epidemic by 2035.


**Abstract**

**Objective:** Do newborns, children and adolescents up to 19 years have lower mortality rates, lower morbidity and shorter length of stay in health facilities where pulse oximeters are used to inform diagnosis and treatment (excluding surgical care) compared with health facilities where pulse oximeters are not used?

**Design:** Studies were obtained for this systematic literature review by systematically searching the Database of Abstracts of Reviews of Effects, Cochrane, Medion, PubMed, Web of Science, Embase, Global Health, CINAHL, WHO Global Health Library, international health organisation and NGO websites, and study references.

**Patients:** Children 0-19 years presenting for the first time to hospitals, emergency departments or primary care facilities.

**Interventions:** Included studies compared outcomes where pulse oximeters were used for diagnosis and/or management, with outcomes where pulse oximeters were not used.
Main outcome measures: mortality, morbidity, length of stay, and treatment and management changes.

Results: The evidence is low quality and hypoxaemia definitions varied across studies, but the evidence suggests pulse oximeter use with children can reduce mortality rates (when combined with improved oxygen administration) and length of emergency department stay, increase admission of children with previously unrecognised hypoxaemia, and change physicians' decisions on illness severity, diagnosis and treatment. Pulse oximeter use generally increased resource utilisation.

Conclusions: As international organisations are investing in programmes to increase pulse oximeter use in low-income settings, more research is needed on the optimal use of pulse oximeters (eg, appropriate oxygen saturation thresholds), and how pulse oximeter use affects referral and admission rates, length of stay, resource utilisation and health outcomes.


Abstract

Similarity between two individuals in the combination of genetic markers along their chromosomes indicates shared ancestry and can be used to identify historical connections between different population groups due to admixture. We use a genome-wide, haplotype-based, analysis to characterise the structure of genetic diversity and gene-flow in a collection of 48 sub-Saharan African groups. We show that coastal populations experienced an influx of Eurasian haplotypes over the last 7000 years, and that Eastern and Southern Niger-Congo speaking groups share ancestry with Central West Africans as a result of recent population expansions. In fact, most sub-Saharan populations share ancestry with groups from outside of their current geographic region as a result of gene-flow within the last 4000 years. Our in-depth analysis provides insight into haplotype sharing across different ethno-linguistic groups and the recent movement of alleles into new environments, both of which are relevant to studies of genetic epidemiology.


Abstract

Prevalence of autism spectrum disorders has increased over recent years, however, little is known about the identification and management of autism spectrum disorder in Africa. This report summarizes a workshop on autism spectrum disorder in Africa under the auspices of the International Child Neurology Association and the African Child Neurology Association through guided presentations and working group reports, focusing on identification, diagnosis, management, and community support. A total of 47 delegates participated from 14 African countries. Although there was a huge variability in services across the countries represented, numbers of specialists assessing and managing autism spectrum disorder was small relative to populations served. Strategies were proposed to improve identification, diagnosis, management and support delivery for individuals with autism spectrum disorder across Africa in these culturally diverse, low-resource settings. Emphasis on raising public awareness through community engagement and improving access to information and training in autism spectrum disorder. Special considerations for the cultural, linguistic, and socioeconomic factors within Africa are discussed.


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<tr>
<td>Abstract</td>
<td>Joint United Nations Programme on HIV/AIDS (UNAIDS) established 90-90-90 HIV treatment targets for 2020 including the following: 90 % of HIV-infected people know their HIV status, 90 % of HIV-infected people who know their status are on treatment, and 90 % of people on HIV treatment have a suppressed viral load. Integration of HIV and other programs into the national health system provides an important pathway to reach those targets. We examine the case for integrating HIV and other health services to ensure sustainability and improve health outcomes within national health systems. In this non-systematic review, we examined recent studies on integrating HIV, tuberculosis (TB), maternal-child health (MCH), and sexually transmitted infection (STI) programs. Existing evidence is limited about the effectiveness of integration of HIV and other services. Most studies found that service integration increased uptake of services, but evidence is mixed about the effect on health</td>
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outcomes or quality of health services. More rigorous studies of different strategies to promote integration over a wider range of services and settings are needed. Research on how best to maximize benefits, including sustainability, of integrated services is necessary to help inform international and national policy. We recommend additional interventions to test how best to integrate HIV and MCH services, HIV and TB services, HIV testing and treatment, and STI testing and treatment.


Abstract

**Background:** Group B streptococcus (GBS) is a leading neonatal sepsis pathogen globally. Investment in GBS disease prevention, such as maternal vaccination, requires evidence of disease burden, particularly in high infant mortality regions like sub-Saharan Africa. We aimed to provide such evidence by conducting a systematic literature review and meta-analysis to estimate maternal colonization proportion, GBS disease incidence and GBS serotype distribution.

**Methods:** MEDLINE, MEDLINE in process and Cochrane Library were searched for studies published during 1990-2014, pertaining to sub-Saharan Africa. Eligible studies were used to estimate the proportion of pregnant women colonized with GBS, early-onset GBS disease incidence, late-onset GBS disease incidence and respective serotype distributions. Random effects meta-analysis was conducted to estimate weighted means and confidence intervals (CIs).

**Results:** We identified 17 studies of colonization, 9 of disease incidence, and 6 of serotype distribution meeting inclusion criteria. 21.8% (95% CI: 18.3, 25.5) of expectant women were colonized with GBS. The incidence of early-onset GBS disease was 1.3 per 1000 births (95% CI: 0.81, 1.9), that of late-onset GBS disease 0.73 per 1000 births (95% CI: 0.48, 1.0). The most common disease-causing serotype was 3, followed by 1a. Serotypes 1b, 2 and 5 were next most common in frequency.

**Conclusion:** Despite methodological factors leading to underestimation, GBS disease incidence appears high in sub-Saharan Africa. A small number of GBS serotypes cause almost
all disease. GBS disease burden in sub-Saharan Africa suggests that safe, effective and affordable GBS disease prevention is needed.


**Abstract**

Ebola virus is categorized as one of the most dangerous pathogens in the world. Although there is no known cure for Ebola virus, there is some evidence that the severity of the disease can be curtailed using plasma from survivors. Although there is a general consensus on the importance of research, methodological and ethical challenges for conducting research in an emergency situation have been identified. Performing clinical trials is important, especially for health conditions that are of public health significance (including rare epidemics) to develop new therapies as well as to test the efficacy and effectiveness of new interventions. However, routine clinical trial procedures can be difficult to apply in emergency public health crises hence require a consideration of alternative approaches on how therapies in these situations are tested and brought to the market. This paper examines some of the ethical issues that arise when conducting clinical trials during a highly dangerous pathogen outbreak, with a special focus on the Ebola virus outbreak in West Africa. The issues presented here come from a review of a protocol that was submitted to the Global Emerging Pathogens Treatment Consortium (GET). In reviewing the proposal, which was about conducting a clinical trial to evaluate the safety and efficacy of using convalescent plasma in the management of Ebola virus disease, the authors deliberated on various issues, which were documented as minutes and later used as a basis for this paper. The experiences and reflections shared by the authors, who came from different regions and disciplines across Africa, present wide-ranging perspectives on the conduct of clinical trials during a dangerous disease outbreak in a resource-poor setting.


**Abstract**
**Aims and objectives:** To review systematically, qualitative literature covering the implementation of task shifting in sub-Saharan Africa to address the growing interest in interventions of this kind. This review aims to distil the key practical findings to both guide a specific project aiming to improve the quality of neonatal care in Kenya and to contribute to the broader literature.

**Background:** Task-shifting programmes aim to improve access to healthcare by delegating specific tasks from higher to lower skilled health workers. Evidence suggests that task-shifting programmes in sub-Saharan Africa may improve patient outcomes, but they have also been criticised for providing fragmented, unsustainable services. This systematic review of qualitative literature summarises factors affecting implementation of task shifting and how such interventions in sub-Saharan Africa may have affected health workers’ feelings about their own positions and their ability to provide care.

**Design:** Following literature search, a modified Critical Appraisal Skills Program (CASP) framework was used to assess quality. Thereafter, analysis adopted a thematic synthesis approach.

**Methods:** A systematic literature search identified qualitative studies examining task-shifting interventions in sub-Saharan Africa. Thematic synthesis was used to identify overarching themes arising from across the studies and infer how task-shifting interventions may impact on the health workers from whom tasks are being shifted.

**Results:** From the 230 studies screened, 13 met the inclusion criteria. Overarching themes identified showed that task shifting has been associated with jurisdictional debates linked to new cadres working beyond their scope of practice, and tension around compensation and career development for those taking on tasks that were being delegated.

**Conclusions:** Based on the qualitative data available, it appears that task shifting may negatively impact the sense of agency and the ability to perform of health workers’ from whom tasks are shifted. The potential implications of task shifting on all health workers should be considered prior to implementing task-shifting solutions.


### Abstract

Mosquitoes, especially Aedes aegypti, are becoming important models for studying invasion biology. We characterized genetic variation at 12 microsatellite loci in 79 populations of Ae. aegypti from 30 countries in six continents, and used them to infer historical and modern patterns of invasion. Our results support the two subspecies Ae. aegypti formosus and Ae. aegypti aegypti as genetically distinct units. Ae. aegypti aegypti populations outside Africa are derived from ancestral African populations and are monophyletic. The two subspecies co-occur in both East Africa (Kenya) and West Africa (Senegal). In rural/forest settings (Rabai District of Kenya), the two subspecies remain genetically distinct, whereas in urban settings, they introgress freely. Populations outside Africa are highly genetically structured likely due to a combination of recent founder effects, discrete discontinuous habitats and low migration rates. Ancestral populations in sub-Saharan Africa are less genetically structured, as are the populations in Asia. Introduction of Ae. aegypti to the New World coinciding with trans-Atlantic shipping in the 16th to 18th centuries was followed by its introduction to Asia in the late 19th century from the New World or from now extinct populations in the Mediterranean Basin. Aedes mascarensis is a genetically distinct sister species to Ae. aegypti s.l. This study provides a reference database of genetic diversity that can be used to determine the likely origin of new introductions that occur regularly for this invasive species. The genetic uniqueness of many populations and regions has important implications for attempts to control Ae. aegypti, especially for the methods using genetic modification of populations.


### Abstract

**Background:** Malaria causes ill health and death in Africa. Treating illness promptly with artemisinin-based combination therapy (ACT) is likely to cure people and avoid the disease progressing to more severe forms and death. In many countries, ACT use remains low. Part of the problem is that most people seek treatment from the retail sector where ACTs are expensive; this expense is a barrier to their use. The Global Fund and other international organisations are subsidising the cost of ACTs for private retail providers to improve access to ACTs. The subsidy was initially organised through a stand-alone initiative, called the Affordable Medicines Facility-malaria (AMFm), but has since been integrated into the Global Fund core grant management and financial processes.
Objectives: To assess the effect of programmes that include ACT price subsidies for private retailers on ACT use, availability, price and market share.

Search methods: We searched the Cochrane Central Register of Controlled Trials (CENTRAL; 2015, Issue 1, The Cochrane Library, including the Cochrane Effective Practice and Organisation of Care (EPOC) Group Specialised Register); MEDLINE (OvidSP), EMBASE (OvidSP), CINAHL (EbscoHost), EconLit (ProQuest), Global Health (OvidSP), Regional Indexes (Global Health Library, WHO), LILACS (Global Health Library, WHO), Science Citation Index and Social Sciences Citation Index (ISI Web of Science) and Health Management (ProQuest). All databases were searched February 2015, except for Health Management which was searched November 2013, without any date, language or publication status restrictions. We also searched the International Clinical Trials Registry Platform (ICTRP; WHO), ClinicalTrials.gov (NIH) and various grey literature sources. We also conducted a cited reference search for all included studies in ISI Web of Knowledge, checked references of identified articles and contacted authors to identify additional studies.

Selection criteria: Randomised trials, non-randomised trials, controlled before-after studies and interrupted-time-series studies that compared the effects of ACT price subsidies for private retailers to no subsidies or alternative ACT financing mechanisms were eligible for inclusion. Two authors independently screened and selected studies for inclusion.

Data collection and analysis: Two review authors independently extracted data, assessed study risk of bias and confidence in effect estimates (certainty of evidence) using Grading of Recommendations, Assessment, Development and Evaluation (GRADE).

Main results: We included four trials (two cluster-randomised trials reported in three articles and two non-randomised cluster trials). Three trials assessed retail sector ACT subsidies combined with supportive interventions (retail outlet provider training, community awareness and mass media campaigns). One trial assessed vouchers provided to households to purchase subsidised ACTs. Price subsidies ranged from 80% to 95%. One trial enrolled children under five years of age; the other three trials studied people of all age groups. The studies were done in rural districts in East Africa (Kenya, Uganda and Tanzania). In this East Africa setting, these ACT subsidy programmes increased the percentage of children under five years of age receiving ACTs on the day, or following day, of fever onset by 25 percentage points (95% confidence interval (CI) 14.1 to 35.9 percentage points; 1 study, high certainty evidence). This suggests that in practice, among febrile children under five years of age with an ACT usage rate of 5% without a subsidy, subsidy programmes would increase usage by between 19% and 41% over a one year period. The ACT subsidy programmes increased the percentage of retail outlets stocking ACTs for children under five years of age by 31.9 percentage points (95% CI 26.3 to 37.5 percentage points; 1 study, high certainty evidence). Effects on ACT stocking for patients of any age is unknown because the certainty of evidence was very low. The ACT
subsidy programmes decreased the median cost of ACTs for children under five years of age by US$ 0.84 (median cost per ACT course without subsidy: US$ 1.08 versus with subsidy: US$ 0.24; 1 study, high certainty evidence). The ACT subsidy programmes increased the market share of ACTs for children under five years of age by between 23.6 and 63.0 percentage points (1 study, high certainty evidence). The ACT subsidy programmes decreased the use of older antimalarial drugs (such as amodiaquine and sulphadoxine-pyrimethamine) among children under five years of age by 10.4 percentage points (95% CI 3.9 to 16.9 percentage points; 1 study, high certainty evidence). None of the three studies of ACT subsidies reported the number of patients treated who had confirmed malaria. Vouchers increased the likelihood that an illness is treated with an ACT by 16 to 23 percentage points; however, vouchers were associated with a high rate of over-treatment of malaria (only 56% of patients taking ACTs from the drug shop tested positive for malaria under the 92% subsidy; 1 study, high certainty evidence).

**Authors' conclusions:** Programmes that include substantive subsidies for private sector retailers combined with training of providers and social marketing improved use and availability of ACTs for children under five years of age with suspected malaria in research studies from three countries in East Africa. These programmes also reduced prices of ACTs, improved market share of ACTs and reduced the use of older antimalarial drugs among febrile children under five years of age. The research evaluates drug delivery but does not assess whether the patients had confirmed (parasite-diagnosed) malaria. None of the included studies assessed patient outcomes; it is therefore not known whether the effects seen in the studies would translate to an impact on health.


**Abstract**

Robert W. Snow discusses the importance of empirical evidence, such as that provided in the trial published this week by Milligan and colleagues, in guiding malaria control in Africa.


Abstract

**Background:** Wasting and stunting are global public health problems that frequently co-exist. However, they are usually separated in terms of policy, guidance, programming and financing. Though both wasting and stunting are manifestations of undernutrition caused by disease and poor diet, there are critical gaps in our understanding of the physiological relationship between them, and how interventions for one may affect the other. The aim of this exercise was to establish research priorities in the relationships between wasting and stunting to guide future research investments.

**Methods and findings:** We used the CHNRI (Child Health and Nutrition Research Initiative) methodology for setting research priorities in health. We utilised a group of experts in nutrition, growth and child health to prioritise 30 research questions against three criteria (answerability, usefulness and impact) using an online survey. Eighteen of 25 (72%) experts took part and prioritised research directly related to programming, particularly at the public health level. The highest-rated questions were: "Can interventions outside of the 1000 days, e.g. pre-school, school age and adolescence, lead to catch-up in height and in other developmental markers?"; "What timely interventions work to mitigate seasonal peaks in both wasting and stunting?"; and "What is the optimal formulation of ready-to-use foods to promote optimal ponderal growth and also support linear growth during and after recovery from severe acute malnutrition?" There was a high level of agreement between experts, particularly for the highest ranking questions.

**Conclusions:** Increased commitment to rigorous evaluations of treatment and prevention interventions at the public health level, addressing questions of the timing of intervention, and the extent to which impacts for both wasting and stunting can be achieved, is needed to inform global efforts to tackle undernutrition and its consequences.


Abstract

**Background:** Giardia duodenalis is an important intestinal protozoan in humans worldwide with high infection rates occurring in densely populated and low resource settings. The parasite
has been recorded to cause diarrhea in children. This study was carried out to identify G. duodenalis assemblages and sub-assemblages in children presenting with diarrhea in Kenya.

**Methods:** A total of 2112 faecal samples were collected from children aged ≤ 5 years and screened for the presence of Giardia cysts using microscopy. A total of 96 (4.5%) samples were identified as Giardia positive samples and were genotyped using glutamate dehydrogenase (gdh), triose phosphate isomerase (tpi) and β-giardin loci.

**Results:** The three markers successfully genotyped 72 isolates and grouped 2 (1.4) isolates as Assemblage A, 64 (88.9) as Assemblage B and 7 (9.7%) consisted of mixed infections with assemblage A and B. A further analysis of 50 isolates using GDH Polymerase Chain Reaction and Restriction Fragment Length Polymorphism (PCR-RFLP) categorized 2 assemblage A isolates as sub-assemblage AII while 6 and 14 assemblage B isolates were categorized into sub-assemblage BIII and BIV respectively. A mixed infection with sub-assemblage BIII and BIV was recorded in 28 isolates. Over half (55.6%) of Giardia infections were recorded among the children between 13 to 48 months old.

**Conclusion:** This paper reports the first data on the assemblages and sub-assemblages of Giardia duodenalis in children representing with diarrhea in Kenya.


**Abstract**

The majority of anti-HIV drug susceptibility tests have been performed on subtype B HIV-1 strains, since these are the most prevalent in countries designing, testing, and manufacturing the current anti-HIV agents. The increasing global spread of HIV subtype highlights the need to determine the activity of anti-HIV drugs against subtypes of HIV other than subtype B. Furthermore an increasing number of individuals infected with many of the non subtype B virus strains now receive antiretroviral therapy because of rollout programs in developing countries as well as increasing migration to the developed world. The phenotypic susceptibility of two laboratory strains HIV-1JFRL and HIV-1IIB (representing subtype B) and two clinical isolates HIV-104RTA and HIV-1025RTA (representing subtypes A and D respectively) was determined. The in vitro drug susceptibility testing of the isolates was carried out in C8166 cell line and in peripheral blood mononuclear cells (PBMCs). The study revealed that the drugs used in the Kenyan national ART program inhibited HIV-1 replication in-vitro as their inhibitory concentrations (IC50) compared well with the standard Inhibitory concentration
values. The results also suggest a biochemical similarity of the reverse transcriptase (RT) and protease enzymes from these subtypes despite the divergence at the genetic level. The findings suggest that similar clinical benefits of antiviral therapy obtain in persons infected with other subtypes of HIV-1 other than subtype B and that the generic drugs used in the national ART program in Kenya are as efficacious as branded drugs in inhibiting HIV replication in vitro despite the limited number of the viruses studied.


**Abstract**

Primer-independent agnostic deep sequencing was used to generate three human rhinovirus (HRV) B genomes and one HRV C genome from samples collected in a household respiratory survey in rural coastal Kenya. The study provides the first rhinovirus genomes from Kenya and will help improve the sensitivity of local molecular diagnostics.


**Abstract**

Group B streptococcus (GBS) capsular serotypes are major determinants of virulence and affect potential vaccine coverage. Here we report a whole-genome-sequencing-based method for GBS serotype assignment. This method shows strong agreement (kappa of 0.92) with conventional methods and increased serotype assignment (100%) to all 10 capsular types.


Abstract

Serology has become an increasingly important tool for the surveillance of a wide range of infectious diseases. It has been particularly useful to monitor malaria transmission in elimination settings where existing metrics such as parasite prevalence and incidence of clinical cases are less sensitive. Seroconversion rates, based on antibody prevalence to Plasmodium falciparum asexual blood-stage antigens, provide estimates of transmission intensity that correlate with entomological inoculation rates but lack precision in settings where seroprevalence is still high. Here we present a new and widely applicable method, based on cross-sectional data on individual antibody levels. We evaluate its use as a sero-surveillance tool in a Tanzanian setting with declining malaria prevalence. We find that the newly developed mathematical models produce more precise estimates of transmission patterns, are robust in high transmission settings and when sample sizes are small, and provide a powerful tool for serological evaluation of malaria transmission intensity.


Abstract

**Introduction:** Research on the challenges of raising a child with autism is mostly conducted in Europe, North America and Australia, and has revealed that parents have to come to terms with living with a lifelong developmental disability. In addition, parents are faced with numerous concerns, such as caring burdens, poor prognosis, and negative public attitudes. Virtually no research has been conducted in Africa on this subject.

**Methods:** Thirty-seven interviews and eight focus group discussions were conducted with parents of children with autism and professionals in regular contact with these parents from rural and urban counties of the Kenyan coast. The study investigated challenges faced by parents and how they cope with those challenges. A purposive-convenience sampling procedure was used in selecting the study participants. A digital recorder was used to record all the interviews and focus group discussions. Transcriptions were done in Swahili, translated into English, and then imported to the NVivo software program for content analysis.

**Results:** The results indicate that parents of children with autism on the Kenyan coast experience common challenges including stigma, lack of appropriate treatment, financial and caring burdens regardless of their religious and cultural backgrounds. Coping strategies applied
by parents comprised problem-focused aspects that involve diet management and respite care, and emotion-focused aspects that consist of beliefs in supernatural powers, prayers and spiritual healing.

**Conclusions:** This qualitative study reveals a range of challenges that could have significant impact when caring for a child with autism. Coping strategies applied by parents target the physical health of the child and the psychological wellbeing of the parent. Consideration of these outcomes is vital as they could impact the initiation of a community-based rehabilitation service delivery in rural settings where parents play an active role.


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<td><strong>Abstract</strong></td>
<td>Cervical cancer is a leading cause of cancer-related death amongst women in sub-Saharan Africa, largely due to the lack of early screening and treatment. In addition to poor access to screening services, inadequate uptake of available services is a barrier to early identification of precancerous lesions. Given that cervical cancer is caused by a sexually transmitted virus and is associated with HIV positivity, stigma is one of the potential barriers to the utilization of cervical cancer programs in sub-Saharan Africa. We conducted a cross-sectional survey of 419 women attending health facilities in rural western Kenya to measure levels of cervical cancer and HIV stigma and to measure the associations between cervical cancer stigma, HIV stigma, and HIV status. Women who qualified for cervical cancer screening were asked to complete an oral questionnaire using a modified 9-point HIV stigma scale. Low cervical cancer stigma was reported in this study, with only 85/419 (20.3%) of respondents answering yes to at least one cervical cancer stigma question. However, cervical cancer stigma was highly correlated with HIV stigma (correlation coefficient 0.72) and was significantly lower in HIV-positive women (p &lt; 0.001). Reducing cervical cancer stigma in the general population is an important part of promoting screening in sub-Saharan Africa.</td>
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Abstract

In this paper, we discuss the role of mobile technology in developing training tools for health workers, with particular reference to low-income countries (LICs). The global and technological context is outlined, followed by a summary of approaches to using and evaluating mobile technology for learning in healthcare. Finally, recommendations are made for those developing and using such tools, based on current literature and the authors' involvement in the field.

Pubmed link: https://pubmed.ncbi.nlm.nih.gov/27658948/


Abstract

Dengue outbreaks were first reported in East Africa in the late 1970s to early 1980s including the 1982 outbreak on the Kenyan coast. In 2011, dengue outbreaks occurred in Mandera in northern Kenya and subsequently in Mombasa city along the Kenyan coast in 2013-2014. Following laboratory confirmation of dengue fever cases, an entomologic investigation was conducted to establish the mosquito species, and densities, causing the outbreak. Affected parts of the city were identified with the help of public health officials. Adult Ae. aegypti mosquitoes were collected using various tools, processed and screened for dengue virus (DENV) by cell culture and RT-PCR. All containers in every accessible house and compound within affected suburbs were inspected for immatures. A total of 2,065 Ae. aegypti adults were collected and 192 houses and 1,676 containers inspected. An overall house index of 22%, container index, 31.0% (indoor = 19; outdoor = 43) and Breteau index, 270.1, were observed, suggesting that the risk of dengue transmission was high. Overall, jerry cans were the most productive containers (18%), followed by drums (17%), buckets (16%), tires (14%) and tanks (10%). However, each site had specific most-productive container-types such as tanks (17%) in Kizingo; Drums in Nyali (30%) and Changamwe (33%), plastic basins (35%) in Nyali-B and plastic buckets (81%) in Ganjoni. We recommend that for effective control of the dengue vector in Mombasa city, all container types would be targeted. Measures would include proper covering of water storage containers and eliminating discarded containers outdoors through a public participatory environmental clean-up exercise. Providing reliable piped water to all households would minimize the need for water storage and reduce aquatic habitats. Isolation of DENV from male Ae. aegypti mosquitoes is a first observation in Kenya and provides further
evidence that transovarial transmission may have a role in DENV circulation and/or maintenance in the environment.


Abstract

Genome-wide searches for loci involved in human resistance to malaria are currently being conducted on a large scale in Africa using case-control studies. Here, we explore the utility of an alternative approach-"environmental correlation analysis, ECA," which tests for clines in allele frequencies across a gradient of an environmental selection pressure to identify genes that have historically protected against death from malaria. We collected genotype data from 12,425 newborns on 57 candidate malaria resistance loci and 9,756 single nucleotide polymorphisms (SNPs) selected at random from across the genome, and examined their allele frequencies for geographic correlations with long-term malaria prevalence data based on 84,042 individuals living under different historical selection pressures from malaria in coastal Kenya. None of the 57 candidate SNPs showed significant (P < 0.05) correlations in allele frequency with local malaria transmission intensity after adjusting for population structure and multiple testing. In contrast, two of the random SNPs that had highly significant correlations (P < 0.01) were in genes previously linked to malaria resistance, namely, CDH13, encoding cadherin 13, and HS3ST3B1, encoding heparan sulfate 3-O-sulfotransferase 3B1. Both proteins play a role in glycoprotein-mediated cell-cell adhesion which has been widely implicated in cerebral malaria, the most life-threatening form of this disease. Other top genes, including CTNND2 which encodes δ-catenin, a molecular partner to cadherin, were significantly enriched in cadherin-mediated pathways affecting inflammation of the brain vascular endothelium. These results demonstrate the utility of ECA in the discovery of novel genes and pathways affecting infectious disease.


Abstract

We report the clinical findings, epidemiology, and risk factors for moderate-to-severe diarrhea (MSD) associated with Aeromonas species in children 0-59 months of age, from the Global Enteric Multicenter Study, conducted at three sites in south Asia and four sites in sub-Saharan Africa. Children with MSD were enrolled along with controls matched for age, gender, and neighborhood. Pooled, age-stratified conditional logistic regression models were applied to evaluate the association of Aeromonas infection controlling for coinfecting pathogens and sociodemographic variables. A pooled, age-stratified, multivariate logistic regression analysis was done to identify risk factors associated with Aeromonas positivity in MSD cases. A total of 12,110 cases and 17,291 matched controls were enrolled over a period of 48 months. Aeromonas was identified as a significant pathogen in 736 cases of MSD in Pakistan and Bangladesh (22.2%). Aeromonas remained a significant pathogen even after adjustment for the presence of other pathogens and sociodemographic factors. Odds ratio (OR) for Aeromonas were higher in the presence of Shigella (matched OR: 6.2, 95% confidence interval [CI]: 1.9-20.2). Cases of Aeromonas were likely to present with dysentery, particularly in the 0-11 months (OR: 1.4, 95% CI 1.0-2.0) and 12-23 months (OR: 1.8, 95% CI: 1.3-2.5) age group. The odds of Aeromonas increased with increasing degree of stunting, being highest for severe stunting (OR: 10.1, 95% CI: 3.6-28.9). Aeromonas is a significant pathogen for MSD in Pakistan and Bangladesh. Presence of dysentery and co-occurrence with other pathogens, notably Shigella spp. are significant features of Aeromonas-associated diarrhea.


Abstract

Gender—the socially constructed roles, behaviours, activities and attributes that a given society considers appropriate for males, females and other genders—affects how people live, work and relate to each other at all levels, including in relation to the health system. Health systems research (HSR) aims to inform more strategic, effective and equitable health systems interventions, programs and policies; and the inclusion of gender analysis into HSR is a core part of that endeavour. We outline what gender analysis is and how gender analysis can be incorporated into HSR content, process and outcomes Starting with HSR content, i.e. the substantive focus of HSR, we recommend exploring whether and how gender power relations affect females and males in health systems through the use of sex disaggregated data, gender
frameworks and questions. Sex disaggregation flags female-male differences or similarities that warrant further analysis; and further analysis is guided by gender frameworks and questions to understand how gender power relations are constituted and negotiated in health systems. Critical aspects of understanding gender power relations include examining who has what (access to resources); who does what (the division of labour and everyday practices); how values are defined (social norms) and who decides (rules and decision-making). Secondly, we examine gender in HSR process by reflecting on how the research process itself is imbued with power relations. We focus on data collection and analysis by reviewing who participates as respondents; when data is collected and where; who is present; who collects data and who analyses data. Thirdly, we consider gender and HSR outcomes by considering who is empowered and disempowered as a result of HSR, including the extent to which HSR outcomes progressively transform gender power relations in health systems, or at least do not further exacerbate them.


Abstract

Human African trypanosomiasis (HAT) is a disease caused by Kinetoplastid infection. Serological tests are useful for epidemiological surveillance. The aim of this study was to develop a multiplex serological assay for HAT to assess the diagnostic value of selected HAT antigens for sero-epidemiological surveillance. We cloned loci encoding eight antigens from Trypanosoma brucei gambiense, expressed the genes in bacterial systems, and purified the resulting proteins. Antigens were subjected to Luminex multiplex assays using sera from HAT and VL patients to assess the antigens' immunodiagnostic potential. Among T. b. gambiense antigens, the 64-kDa and 65-kDa invariant surface glycoproteins (ISGs) and flagellar calcium binding protein (FCaBP) had high sensitivity for sera from T. b. gambiense patients, yielding AUC values of 0.871, 0.737 and 0.858 respectively in receiver operating characteristics (ROC) analysis. The ISG64, ISG65, and FCaBP antigens were partially cross-reactive to sera from Trypanosoma brucei rhodesiense patients. The GM6 antigen was cross-reactive to sera from T. b. rhodesiense patients as well as to sera from VL patients. Furthermore, heterogeneous antibody responses to each individual HAT antigen were observed. Testing for multiple HAT antigens in the same panel allowed specific and sensitive detection. Our results demonstrate the utility of applying multiplex assays for development and evaluation of HAT antigens for use in sero-epidemiological surveillance.


Abstract

Parasite proteins called PfEMP1 that are inserted on the surface of infected erythrocytes, play a key role in the severe pathology associated with infection by the Plasmodium falciparum malaria parasite. These proteins mediate binding of infected cells to the endothelial lining of blood vessels as a strategy to avoid clearance by the spleen and are major targets of naturally acquired immunity. PfEMP1 is encoded by a large multi-gene family called var. Mutually-exclusive transcriptional switching between var genes allows parasites to escape host antibodies. This study examined in detail the patterns of expression of var in a well-characterized sample of parasites from Kenyan Children. Instead of observing clear inverse relationships between the expression of broad sub-classes of PfEMP1, we found that expression of different PfEMP1 groups vary relatively independently. Parasite adaptation to host antibodies also appears to involve a general reduction in detectable var gene expression. We suggest that parasites switch both between different PfEMP1 variants and between high and low expression states. Such a strategy could provide a means of avoiding immunological detection and promoting survival under high levels of host immunity.


Abstract

**Background:** The cell type, cell status and specific localization of Prothymosin α (PTMA) within cells seemingly determine its function. PTMA undergoes 2 types of protease proteolytic modifications that are useful in elucidating its interactions with other molecules; a factor that typifies its roles. Preferably a nuclear protein, PTMA has been shown to function in the cytoplasm and extracellularly with much evidence leaning on pathognomonic status. As such, determination of its cellular distribution under normal physiological context while utilizing varied techniques is key to illuminating prospective validation of its distinct functions in different tissues. Differential distribution insights at normal physiology would also portent better basis for further clarification of its interactions and proteolytic modifications under pathological conditions like numerous cancer, ischemic stroke and immunomodulation. We
therefore raised an antibody against the C terminal of PTMA to use in tandem with available antibody against the N terminal in a murine model to explicate the differences in its distribution in brain cell types and major peripheral organs through western blotting and immunohistochemical approaches.

**Results:** The newly generated antibody was applied against the N-terminal antibody to distinguish truncated versions of PTMA or deduce possible masking of the protein by other interacting molecules. Western blot analysis indicated presence of a truncated form of the protein only in the thymus, while immunohistochemical analysis showed that in brain hippocampus the full-length PTMA was stained prominently in the nucleus whereas in the stomach full-length PTMA staining was not observed in the nucleus but in the cytoplasm.

**Conclusion:** Truncated PTMA could not be detected by western blotting when both antibodies were applied in all tissues examined except the thymus. However, immunohistochemistry revealed differential staining by these antibodies suggesting possible masking of epitopes by interacting molecules. The differential localization patterns observed in the context of nucleic versus cytoplasmic presence as well as punctate versus diffuse pattern in tissues and cell types, warrant further investigations as to the forms of PTMA interacting partners.


**Abstract**

**Background:** Viral hepatitis is a major concern worldwide, with hepatitis A (HAV) and E (HEV) viruses showing sporadic outbreaks while hepatitis B (HBV) and C (HCV) viruses are associated with chronic hepatitis, cirrhosis and hepatocellular carcinoma. The present study determined the proportion, geographic distribution and molecular characterization of hepatitis viruses among patients seeking medical services at hospitals throughout Kenya.

**Methods:** Patients presenting with jaundice at four selected hospitals were recruited (n = 389). Sera were tested for the presence of antibody to hepatitis viruses A through E, and HBV surface antigen (HBsAg). Nucleic acid from anti-HAV IgM antibody and HBsAg positive samples was extracted, amplified and sequenced.

**Results:** Chronic HBV infection was the leading cause of morbidity among patients with symptoms of liver disease seeking medical help. Incident HCV, HEV and HDV infection were
not detected among the patients in this study, while the proportion of acute HAV was low; HAV IgM positivity was observed in 6.3 % of patients and sequencing revealed that all cases belonged to genotype 1B. HCV seropositivity upon initial screening was 3.9 % but none were confirmed positive by a supplementary immunoblot assay. There was no serological evidence of HDV and acute HEV infection (anti-HEV IgM). HBsAg was found in 50.6 % of the patients and 2.3 % were positive for IgM antibody to the core protein, indicating probable acute infection. HBV genotype A was predominant (90.3 %) followed by D (9.7 %) among HBV DNA positive specimens. Full genome analysis showed HBV/D isolates having similarity to both D4 and D6 subgenotypes and D/E recombinant reference sequences. Two recombinant sequences demonstrated > 4 % nucleotide divergence from other previously known D/E recombinants.

Conclusions: HBV is highly prevalent among patients seeking care for symptoms consistent with hepatitis, compared to the general population. Molecular characterization of HBV isolates indicated recombinant strains that may give rise to new circulating variants. There is a need to document the prevalence, clinical manifestation and distribution of the variants observed. HAV genotype 1B, prevalent in Africa, was observed; however, the absence of HCV, HDV and acute HEV in this study does not rule out their presence in Kenya.


Abstract

Background: Population genomic features such as nucleotide diversity and linkage disequilibrium are expected to be strongly shaped by changes in population size, and might therefore be useful for monitoring the success of a control campaign. In the Kilifi district of Kenya, there has been a marked decline in the abundance of the malaria vector Anopheles gambiae subsequent to the rollout of insecticide-treated bed nets.

Methods: To investigate whether this decline left a detectable population genomic signature, simulations were performed to compare the effect of population crashes on nucleotide diversity, Tajima's D, and linkage disequilibrium (as measured by the population recombination parameter ρ). Linkage disequilibrium and ρ were estimated for An. gambiae from Kilifi, and compared them to values for Anopheles arabiensis and Anopheles merus at the same location, and for An. gambiae in a location 200 km from Kilifi.
Results: In the first simulations, \( \rho \) changed more rapidly after a population crash than the other statistics, and therefore is a more sensitive indicator of recent population decline. In the empirical data, linkage disequilibrium extends 100-1000 times further, and \( \rho \) is 100-1000 times smaller, for the Kilifi population of An. gambiae than for any of the other populations. There were also significant runs of homozygosity in many of the individual An. gambiae mosquitoes from Kilifi.

Conclusions: These results support the hypothesis that the recent decline in An. gambiae was driven by the rollout of bed nets. Measuring population genomic parameters in a small sample of individuals before, during and after vector or pest control may be a valuable method of tracking the effectiveness of interventions.


Abstract

There is a widening mental health treatment gap for children and adolescents in sub-Saharan Africa. The region has few economic or human resources dedicated to the mental health of children and young people. The World Health Organization's Mental Health Gap Action Plan and the push for mental health to be included in the Millennium Development Goals have raised the profile of child mental health but comparatively few studies have estimated prevalence rates or assessed needs or tested interventions in African countries. In most countries there is no clear pathway to access treatment, especially in-patient facilities. This article considers these issues from clinical, educational and research perspectives.


Abstract

Background: The impacts of vaccination on the transmission of Rift Valley fever virus (RVFV) have not been evaluated. We have developed a RVFV transmission model comprising two hosts-cattle as a separate host and sheep and goats as one combined host (herein after referred to as sheep)-and two vectors-Aedes species (spp) and Culex spp-and used it to predict
the impacts of: (1) reactive vaccination implemented at various levels of coverage at pre-
determined time points, (2) targeted vaccination involving either of the two host species, and
(3) a periodic vaccination implemented biannually or annually before an outbreak.

**Methodology/principal findings:** The model comprises coupled vector and host modules
where the dynamics of vectors and hosts are described using a system of difference equations.
Vector populations are structured into egg, larva, pupa and adult stages and the latter stage is
further categorized into three infection categories: susceptible, exposed and infectious
mosquitoes. The survival rates of the immature stages (egg, larva and pupa) are dependent on
rainfall densities extracted from the Tropical Rainfall Measuring Mission (TRMM) for a Rift
Valley fever (RVF) endemic site in Kenya over a period of 1827 days. The host populations
are structured into four age classes comprising young, weaners, yearlings and adults and four
infection categories including susceptible, exposed, infectious, and immune categories. The
model reproduces the 2006/2007 RVF outbreak reported in empirical surveys in the target area
and other seasonal transmission events that are perceived to occur during the wet seasons.
Mass reactive vaccination strategies greatly reduce the potential for a major outbreak. The
results also suggest that the effectiveness of vaccination can be enhanced by increasing the
vaccination coverage, targeting vaccination on cattle given that this species plays a major role
in the transmission of the virus, and using both periodic and reactive vaccination strategies.

**Conclusion/significance:** Reactive vaccination can be effective in mitigating the impacts of
RVF outbreaks but practically, it is not always possible to have this measure implemented
satisfactorily due to the rapid onset and evolution of RVF epidemics. This analysis
demonstrates that both periodic and reactive vaccination ought to be used strategically to
effectively control the disease.


**Abstract**

Plasmodium falciparum antigens expressed on the surface of infected erythrocytes are
important targets of naturally acquired immunity against malaria, but their high number and
variability provide the pathogen with a powerful means of escape from host antibodies.
Although broadly reactive antibodies against these antigens could be useful as therapeutics and
in vaccine design, their identification has proven elusive. Here we report the isolation of human monoclonal antibodies that recognize erythrocytes infected by different *P. falciparum* isolates and opsonize these cells by binding to members of the RIFIN family. These antibodies acquired broad reactivity through a novel mechanism of insertion of a large DNA fragment between the V and DJ segments. The insert, which is both necessary and sufficient for binding to RIFINs, encodes the entire 98 amino acid collagen-binding domain of LAIR1, an immunoglobulin superfamily inhibitory receptor encoded on chromosome 19. In each of the two donors studied, the antibodies are produced by a single expanded B-cell clone and carry distinct somatic mutations in the LAIR1 domain that abolish binding to collagen and increase binding to infected erythrocytes. These findings illustrate, with a biologically relevant example, a novel mechanism of antibody diversification by interchromosomal DNA transposition and demonstrate the existence of conserved epitopes that may be suitable candidates for the development of a malaria vaccine.


**Abstract**

Effective use of dihydroartemisinin (DHA) is limited by poor water-solubility, poor pharmacokinetic profile and unsatisfactory clinical outcome especially in monotherapy. To reduce such limitations, we reformulated DHA into solid lipid nanoparticles (SLNs) as a nanomedicine drug delivery system. DHA-SLNs were characterized for physical parameters and evaluated for in vitro and in vivo antimalarial efficacy. DHA-SLNs showed desirable particle characteristics including particle size (240.7 nm), particle surface charge (+17.0 mV), drug loadings (13.9 wt %), encapsulation efficacy (62.3%), polydispersity index (0.16) and a spherical appearance. Storage stability up to 90 days and sustained release of drug over 20 h was achieved. Enhanced in vitro (IC50 0.25 ng/ml) and in vivo (97.24% chemosuppression at 2mg/kg/day) antimalarial activity was observed. Enhancement in efficacy was 24% when compared to free DHA. These encouraging results show potential of using the described formulation for DHA drug delivery for clinical application.

**From the clinical editor:** Malaria still poses a significant problem worldwide. One of the current drugs, artemisinin has been shown to be effective, but has poor water-solubility. The authors here described their formulation of making dihydroartemisinin (DHA) into solid lipid
nanoparticles, with subsequent enhancement in efficacy. These results would have massive potential in the clinical setting.


**Abstract**

**Objectives:** The association between blood levels of hemoglobin (B-hgb) and blood pressure (BP) has been widely investigated in Caucasians and Asians but there is a paucity of data in rural black Africans. The objective was to investigate the association between B-hgb and BP in a rural black African population.

**Methods:** A cross-sectional study was conducted in three districts in Kenya (Bondo, Kitui, and Transmara) with the inclusion of participants aged ≥17 years. Background information, anthropometry, BP, B-hgb, hepatic insulin resistance (HOMA2-IR), standard lipid profile, and oral glucose tolerance test were obtained in each participant.

**Results:** Background characteristics among 1,167 participants showed that anemic and non-anemic participants differed significantly from each other as there were more women, lower body mass index and waist circumference (WC), lower degree of hepatic insulin resistance and plasma cholesterols among the anemic participants. Furthermore, anemic participants had significantly lower systolic and diastolic BP (P < 0.01) but not a significantly different prevalence of hypertension (P = 0.08). Multivariate linear regression models adjusted for-age, sex, plasma total-cholesterol, WC, Log2(HOMA2-IR), ethnicity, and smoking status-revealed that B-hgb (per mmol/l increment) was significantly associated with systolic BP (estimate: 1.18 (0.37-1.98)) and diastolic BP (estimate: 1.06 (0.54-1.57)) (P < 0.01).

**Conclusions:** B-hgb is associated with BP in rural black Africans.


Abstract

Background: Intermittent mass screening and treatment (iMSaT) is currently being evaluated as a possible additional tool for malaria control and prevention in western Kenya. The literature identifying success and/or barriers to drug trial compliance and acceptability on malaria treatment and control interventions is considerable, especially as it relates to specific target groups, such as school-aged children and pregnant women, but there is a lack of such studies for mass screening and treatment and mass drug administration in the general population.

Methods: A qualitative study was conducted to explore community perceptions of the iMSaT intervention, and specifically of testing and treatment in the absence of symptoms, before and after implementation in order to identify aspects of iMSaT that should be improved in future rounds. Two rounds of qualitative data collection were completed in six randomly selected study communities: a total of 36 focus group discussions (FGDs) with men, women, and opinion leaders, and 12 individual or small group interviews with community health workers. All interviews were conducted in the local dialect Dholuo, digitally recorded, and transcribed into English. English transcripts were imported into the qualitative software programme NVivo8 for content analysis.

Results: There were mixed opinions of the intervention. In the pre-implementation round, respondents were generally positive and willing to participate in the upcoming study. However, there were concerns about testing in the absence of symptoms including fear of covert HIV testing and issues around blood sampling. There were fewer concerns about treatment, mostly because of the simpler dosing regimen of the study drug (dihydroartemisinin-piperaquine) compared to the current first-line treatment (artemether-lumefantrine). After the first implementation round, there was a clear shift in perceptions with less common concerns overall, although some of the same issues around testing and general misconceptions about research remained.

Conclusions: Although iMSaT was generally accepted throughout the community, proper sensitization activities-and arguably, a more long-term approach to community engagement-are necessary for dispelling fears, clarifying misconceptions, and educating communities on the consequences of asymptomatic malaria.


Owor BE, Masankwa GN, Mwango LC, Njeru RW, Agoti CN, Nokes DJ. Human metapneumovirus epidemiological and evolutionary patterns in Coastal Kenya,
Abstract

**Background:** Human metapneumovirus (HMPV) is an important global cause of severe acute respiratory infections in young children and the elderly. The epidemiology of HMPV in sub-Saharan Africa is poorly described and factors that allow its recurrent epidemics in communities not understood.

**Methods:** We undertook paediatric inpatient surveillance for HMPV in Kilifi County Hospital (KCH) of Coastal Kenya between 2007 and 2011. Nasopharyngeal samples collected from children aged 1 day-59 months admitted with severe or very severe pneumonia, were tested for HMPV using real-time polymerase chain reaction (RT-PCR). Partial nucleotide sequences of the attachment (G) and fusion (F) surface proteins of positive samples were determined and phylogenetically analyzed.

**Results:** HMPV was detected in 4.8 % (160/3320) of children [73.8 % (118/160) of these less than one year of age], ranging between 2.9 and 8.8 % each year over the 5 years of study. HMPV infections were seasonal in occurrence, with cases predominant in the months of November through April. These months frequently coincided with low rainfall, high temperature and low relative humidity in the location. Phylogenetic analysis of partial F and G sequences revealed three subgroups of HMPV, A2 (74 %, 91/123), B1 (3.2 %, 4/123) and B2 (22.8 %, 28/123) in circulation, with subgroup A2 predominant in majority of the epidemic seasons. Comparison of G sequences (local and global) provided a greater phylogenetic resolution over comparison of F sequences and indicated presence of probable multiple G antigenic variants within the subgroups due to differences in amino acid sequence, encoded protein length and glycosylation patterns.

**Conclusion:** The present study reveals HMPV is an important seasonal contributor to respiratory disease hospitalization in coastal Kenya, with an evolutionary pattern closely relating to that of respiratory syncytial virus.

Abstract

Background: The efficacy of condoms for protection against transmission of herpes simplex virus type 2 (HSV-2) has been examined in a variety of populations with different effect measures. Often the efficacy has been assessed as change in hazard of transmission with consistent vs inconsistent use, independent of the number of acts. Condom efficacy has not previously measured on a per-act basis.

Methods: We examined the per-act HSV-2 transmission rates with and without condom use among 911 African HSV-2 and human immunodeficiency virus type 1 (HIV-1) serodiscordant couples followed for an average of 18 months in an HIV prevention study. Infectivity models were used to associate the log10 probability of HSV-2 transmission over monthly risk periods with reported numbers of protected and unprotected sex acts. Condom efficacy was computed as the proportionate reduction in transmission risk for protected relative to unprotected sex acts.

Results: Transmission of HSV-2 occurred in 68 couples, including 17 with susceptible women and 51 with susceptible men. The highest rate of transmission was from men to women: 28.5 transmissions per 1000 unprotected sex acts. We found that condoms were differentially protective against HSV-2 transmission by sex; condom use reduced per-act risk of transmission from men to women by 96% (P < .001) and marginally from women to men by 65% (P = .060).

Conclusions: Condoms are recommended as an effective preventive method for heterosexual transmission of HSV-2.


Abstract

Antiretroviral therapy-naive HIV-1 infected infants experience poor viral containment and rapid disease progression compared to adults. Viral factors (e.g. transmitted cytotoxic T-lymphocyte (CTL) escape mutations) or infant factors (e.g. reduced CTL functional capacity) may explain this observation. We assessed CTL functionality by analysing selection in CTL-
targeted HIV-1 epitopes following perinatal infection. HIV-1 gag, pol and nef sequences were generated from a historical repository of longitudinal specimens from 19 vertically infected infants. Evolutionary rate and selection were estimated for each gene and in CTL-restricted and non-restricted epitopes. Evolutionary rate was higher in nef and gag vs. pol, and lower in infants with non-severe immunosuppression vs. severe immunosuppression across gag and nef. Selection pressure was stronger in infants with non-severe immunosuppression vs. severe immunosuppression across gag. The analysis also showed that infants with non-severe immunosuppression had stronger selection in CTL-restricted vs. non-restricted epitopes in gag and nef. Evidence of stronger CTL selection was absent in infants with severe immunosuppression. These data indicate that infant CTLs can exert selection pressure on gag and nef epitopes in early infection and that stronger selection across CTL epitopes is associated with favourable clinical outcomes. These results have implications for the development of paediatric HIV-1 vaccines.


Abstract

Background: Animal hosts may vary in their attraction and acceptability as components of the host location process for assessing preference, and biting rates of vectors and risk of exposure to pathogens. However, these parameters remain poorly understood for mosquito vectors of the Rift Valley fever (RVF), an arboviral disease, and for a community of mosquitoes.

Methods: Using three known livestock amplifiers of RVF virus including sheep, goat and cattle as bait in enclosure traps, we investigated the host-feeding patterns for a community of mosquitoes in Naivasha, an endemic area of Rift Valley fever (RVF), in a longitudinal study for six months (June-November 2015). We estimated the incidence rate ratios (IRR) where mosquitoes chose cow over the other livestock hosts by comparing their attraction (total number collected) and engorgement rate (proportion freshly blood-fed) on these hosts.

Results: Overall, significant differences were observed in host preference parameters for attraction (F2,15 = 4.1314, P = 0.037) and engorgement (F2,15 = 6.24, P = 0.01) with cow consistently attracting about 3-fold as many mosquitoes as those engorged on sheep (attraction: IRR = 2.9, 95 % CI 1.24-7.96; engorgement: IRR = 3.2, 95 % CI = 1.38-7.38) or goat (attraction: IRR = 2.7, 95 % CI 1.18-7.16; engorgement: IRR = 3.28, 95 % CI 1.47-7.53).
However, there was no difference between the attraction elicited by sheep and goat (IRR = 1.08; 95 % CI 0.35-3.33 or engorgement rate (IRR = 0.96, 95 % CI 0.36-2.57).

**Conclusion:** Despite the overall attractive pattern to feed preferentially on cows, the engorgement rate was clearly independent of the number attracted for certain mosquito species, notably among the flood water Aedes spp., largely incriminated previously as primary vectors of RVF. Our findings suggest that insecticide treated cattle (ITC) can be exploited in enclosure traps as contact bait in the monitoring and control of disease-causing mosquitoes in RVF endemic areas.


**Abstract**

Severe malaria (SM) is a life-threatening complication of infection with Plasmodium falciparum. Epidemiological observations have long indicated that immunity against SM is acquired relatively rapidly, but prospective studies to investigate its immunological basis are logistically challenging and have rarely been undertaken. We investigated the merozoite targets and antibody-mediated mechanisms associated with protection against SM in Kenyan children aged 0 to 2 years. We designed a unique prospective matched case-control study of well-characterized SM clinical phenotypes nested within a longitudinal birth cohort of children (n= 5,949) monitored over the first 2 years of life. We quantified immunological parameters in sera collected before the SM event in cases and their individually matched controls to evaluate the prospective odds of developing SM in the first 2 years of life. Anti-AMA1 antibodies were associated with a significant reduction in the odds of developing SM (odds ratio [OR] = 0.37; 95% confidence interval [CI] = 0.15 to 0.90; P= 0.029) after adjustment for responses to all other merozoite antigens tested, while those against MSP-2, MSP-3, Plasmodium falciparum Rh2 [PfRh2], MSP-119, and the infected red blood cell surface antigens were not. The combined ability of total IgG to inhibit parasite growth and mediate the release of reactive oxygen species from neutrophils was associated with a marked reduction in the odds of developing SM (OR = 0.07; 95% CI = 0.006 to 0.82;P= 0.03). Assays of these two functional mechanisms were poorly correlated (Spearman rank correlation coefficient [rs] = 0.12;P= 0.07). Our data provide epidemiological evidence that multiple antibody-dependent mechanisms contribute to protective immunity via distinct targets whose identification could accelerate the development of vaccines to protect against SM.

Abstract

Setting: Fifteen human immunodeficiency virus (HIV) clinics in Nyanza Region, Western Kenya.

Objective: To describe routine tuberculosis (TB) screening and diagnostic practices among newly enrolled people living with HIV (PLHIV) prior to the implementation of World Health Organization recommended TB intensified case finding.

Design: Retrospective chart abstraction of PLHIV aged ≥7 years who were newly enrolled in HIV care in July and August 2009, and who had not received antiretroviral treatment in the preceding 2 years or been diagnosed with TB in the previous year. Factors associated with evidence of TB diagnostic evaluation among symptomatic PLHIV were assessed.

Results: Of 1020 patients included in the analysis, 995 (98%) were screened for TB at enrolment and 613 (62%) reported TB symptoms. Ninety-six (16%) patients with symptoms had evidence of referral for TB diagnostic evaluation, including patients at large clinics, those with advanced HIV disease and those reporting multiple TB symptoms. Among the 43 (45%) with documented evaluation results, 26 (60%) were diagnosed with TB.

Conclusion: Although most PLHIV were screened for TB, very few underwent an evaluation, and the proportion diagnosed with TB was very low. Efforts to improve TB screening should focus on standardizing the intensified case finding algorithm and linkage to, and adequate infrastructure for, TB diagnostic evaluation.


Abstract

Background. School age children are at high risk of soil-transmitted helminth (STH) worldwide. In Kenya, STH infections in children remain high despite the periodic
administration of anthelmintic drugs. Our study assessed the prevalence and intensity of STH in primary school-aged children in Kakamega County, western Kenya. Methodology. We carried out a cross-sectional study on a population of 731 children attending 7 primary schools in March 2014. Children aged 4-16 years were examined for STH by the quantitative Kato-Katz technique. Infection intensities were expressed as eggs per gram (epg) of faeces.

Findings. Among 731 school children examined for STH, 44.05% were infected. Highest prevalence of STH was in Shitaho primary school where 107 participants were examined and 62.6% were infected with mean intensity of 11667 epg. Iyenga had the least prevalence where 101 participants were examined and 26.7% were infected with mean intensity of 11772 epg. A. lumbricoides was the most prevalent STH species with 43.5% infected, while hookworm infections were low with 1.8% infected. Conclusion. Prevalence of STHs infections in Kakamega County remains high. We recommend guidelines and other control strategies to be scaled up to break transmission cycles.


Abstract

Background: Children with severe malaria are at increased risk of invasive bacterial disease particularly infection with enteric gram-negative organisms. These organisms are likely to originate from the gut, however, how and why they breach the intestinal interface in the context of malaria infection remains unclear. One explanation is that accumulation of infected red blood cells (iRBCs) in the intestinal microvasculature contributes to tissue damage and subsequent microbial translocation which can be addressed through investigation of the impact of cytoadhesion in patients with malaria and intestinal damage.

Methods: Using a static adhesion assay, cytoadhesion of iRBCs was quantified in 48 children with malaria to recombinant proteins constitutively expressed on endothelial cell surfaces. Cytoadhesive phenotypes between children with and without biochemical evidence of intestinal damage [defined as endotoxemia or elevated plasma intestinal fatty acid binding protein (I-FABP)] was compared.

Results: The majority of parasites demonstrated binding to the endothelial receptors CD36 and to a lesser extent to ICAM-1. Reduced adhesion to CD36 but not adhesion to ICAM-1 or rosetting was associated with malarial anaemia (p = 0.004). Increased adhesion of iRBCs to ICAM-1 in children who had evidence of elevated I-FABP (p = 0.022), a marker of intestinal
ischaemia was observed. There was no correlation between the presence of endotoxemia and increased adhesion to any of the recombinant proteins.

**Conclusion:** Increased parasite adhesion to ICAM-1 in children with evidence of intestinal ischaemia lends further evidence to a link between the cytoadherence of iRBCs in gut microvasculature and intestinal damage.


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**Abstract**

**Background:** The burden of typhoid in sub-Saharan African (SSA) countries has been difficult to estimate, in part, due to suboptimal laboratory diagnostics. However, surveillance blood cultures at two sites in Nigeria have identified typhoid associated with Salmonella enterica serovar Typhi (S. Typhi) as an important cause of bacteremia in children.

**Methods:** A total of 128 S. Typhi isolates from these studies in Nigeria were whole-genome sequenced, and the resulting data was used to place these Nigerian isolates into a worldwide context based on their phylogeny and carriage of molecular determinants of antibiotic resistance.

**Results:** Several distinct S. Typhi genotypes were identified in Nigeria that were related to other clusters of S. Typhi isolates from north, west and central regions of Africa. The rapidly expanding S. Typhi clade 4.3.1 (H58) previously associated with multiple antimicrobial resistances in Asia and in east, central and southern Africa, was not detected in this study. However, antimicrobial resistance was common amongst the Nigerian isolates and was associated with several plasmids, including the IncHI1 plasmid commonly associated with S. Typhi.

**Conclusions:** These data indicate that typhoid in Nigeria was established through multiple independent introductions into the country, with evidence of regional spread. MDR typhoid appears to be evolving independently of the haplotype H58 found in other typhoid endemic
This study highlights an urgent need for routine surveillance to monitor the epidemiology of typhoid and evolution of antimicrobial resistance within the bacterial population as a means to facilitate public health interventions to reduce the substantial morbidity and mortality of typhoid.


**Abstract**

**Objective:** The prevalence of epilepsy is high in Africa, and people with epilepsy often have a history of acute seizures. We determined whether acute seizures are associated with risk for epilepsy in rural Africa, where both conditions are common and may have shared risk factors.

**Methods:** A total of 16,438 children (2,991 with acute seizures and 13,447 without seizures) admitted to Kilifi County Hospital from 2002 to 2008 were followed up with epidemiological surveys conducted in 2003 and 2008 to assess the prevalence of epilepsy and the associated risk factors. Cox proportional hazards regression models were used to identify the risk factors. Prevalence ratios were computed using log binomial regression models.

**Results:** The prevalence of epilepsy was higher in admissions with acute seizures (5.0% [95% confidence interval (CI), 4.3-5.9%]) than in those without seizures (0.7% [95% CI, 0.5-0.8%]), p < 0.0001). Acute seizures were associated with epilepsy after accounting for potential confounders in a Cox regression model (hazard ratio [HR] = 1.53 [95% CI, 1.10-2.14]). Prevalence was greater in complex acute seizures (5.9%; prevalence ratio [PR] = 1.58 [95% CI, 1.13-2.20]) or status epilepticus (7.5%; PR = 1.96 [95% CI, 1.32-2.91]) than in simple acute seizures (3.7%). Factors independently associated with epilepsy following acute seizures in Cox regression models were perinatal complications (HR = 3.60 [95% CI, 1.89-6.87]), cerebral palsy (HR = 1491.51 [95% CI, 144.30-15,416.21]), duration of follow-up (HR = 1.21 [95% CI, 1.09-1.35]), and malnutrition (relative risk [RR] = 0.24 [95% CI, 0.08-0.69]).

**Significance:** Acute seizures in children are associated with subsequent risk for epilepsy that is greater than in the general population. The burden of epilepsy may be reduced by control of causes of acute seizures.

Streptococcus agalactiae (group B streptococcus, GBS) causes neonatal disease and stillbirth, but its burden in sub-Saharan Africa is uncertain. We assessed maternal recto-vaginal GBS colonization (7,967 women), stillbirth and neonatal disease. Whole-genome sequencing was used to determine serotypes, sequence types and phylogeny. We found low maternal GBS colonization prevalence (934/7,967, 12%), but comparatively high incidence of GBS-associated stillbirth and early onset neonatal disease (EOD) in hospital (0.91 (0.25-2.3)/1,000 births and 0.76 (0.25-1.77)/1,000 live births, respectively). However, using a population denominator, EOD incidence was considerably reduced (0.13 (0.07-0.21)/1,000 live births). Treated cases of EOD had very high case fatality (17/36, 47%), especially within 24 h of birth, making under-ascertainment of community-born cases highly likely, both here and in similar facility-based studies. Maternal GBS colonization was less common in women with low socio-economic status, HIV infection and undernutrition, but when GBS-colonized, they were more probably colonized by the most virulent clone, CC17. CC17 accounted for 267/915 (29%) of maternal colonizing (265/267 (99%) serotype III; 2/267 (0.7%) serotype IV) and 51/73 (70%) of neonatal disease cases (all serotype III). Trivalent (Ia/II/III) and pentavalent (Ia/Ib/II/III/V) vaccines would cover 71/73 (97%) and 72/73 (99%) of disease-causing serotypes, respectively. Serotype IV should be considered for inclusion, with evidence of capsular switching in CC17 strains.

studies however showed that their dichloromethane, methanol (1:1) extracts were more active against Plasmodium parasite than the aqueous extracts.

**Aim of the study:** To determine the in vitro and in vivo antiplasmodial activity of dichloromethane, methanol (1:1) extracts of Chromolaena odorata, Tithonia diversifolia and Lawsonia inermis in combination and evaluate their safety using acute limit toxicity test.

**Materials and methods:** Dichloromethane, methanol (1:1) extracts of Chromolaena odorata, Tithonia diversifolia and Lawsonia inermis leaves were combined at ratios 1:1, 1:3, 3:1, 1:5 and 5:1 using in vitro semi-automated microdilution technique against P. falciparum Chloroquine sensitive (D6) and Chloroquine resistant (W2) strains, with chloroquine and artemisinin as controls. The in vivo antiplasmodial activity of the crude extracts was carried out singly, and in combination at the different combination ratios on Plasmodium berghei Anka infected Swiss albino mice using Peters’ 4-day suppressive test. Acute toxicity test was done in mice at 5000mg/kg.

**Results:** The in vitro combination of L. inermis and T. diversifolia (1:1) extracts against P. falciparum showed the highest synergy with IC50 of 0.43±0.02μg/mL and 2.55±0.19μg/mL against D6 and W2 respectively; while the combination of C. odorata with T. diversifolia and L. inermis were antagonistic. A synergy with chemosuppression of 83.6% against P. berghei infected mice was observed in L. inermis and T. diversifolia (1:1) treated animals. In contrast to the in vitro result, combination of C. odorata with T. diversifolia and L. inermis showed some degrees of synergy in vivo. Extracts were not toxic at the concentration tested.

**Conclusion:** These findings rationalized the use of these plants in combination as antimalarials in traditional medicine. However, the combination of Chromolaena odorata with other medicinal plants should be used with caution because of its possible antagonistic effect.


**Abstract**

**Background:** Lymphatic filariasis is a debilitating neglected tropical disease that affects impoverished communities. Rapid diagnostic tests of antigenaemia are a practical alternative to parasitological tests of microfilaraemia for mapping and surveillance. However the
relationship between these two methods of measuring burden has previously been difficult to interpret.

**Methods:** A statistical model of the distribution of worm burden and microfilariae (mf) and resulting antigenaemic and mf prevalence was developed and fitted to surveys of two contrasting sentinel sites undergoing interventions. The fitted model was then used to explore the relationship in various pre- and post-intervention scenarios.

**Results:** The model had good quantitative agreement with the data and provided estimates of the reduction in mf output due to treatment. When extrapolating the results to a range of prevalences there was good qualitative agreement with published data.

**Conclusions:** The observed relationship between antigenamic and mf prevalence is a natural consequence of the relationship between prevalence and intensity of adult worms and mf production. The method described here allows the estimation of key epidemiological parameters and consequently gives insight into the efficacy of an intervention programme.


**Abstract**

**Background:** Malaria remains a major health and development challenge in the sub-Saharan African economies including Kenya, yet it can be prevented. Technologies to prevent malaria are available but are not universally adopted by male- and female-headed households. The study thus, examined the role of gender in malaria prevention, examining adoption behaviour between male- and female-headed households in Kenya.

**Methods:** The study uses a recent baseline cross-section survey data collected from 2718 households in parts of western and eastern Kenya. Two separate models were estimated for male- and female-headed households to determine if the drivers of adoption differ between the two categories of households.

**Results:** The findings from the study show that: access to public health information, residing in villages with higher experience in malaria prevention, knowledge on the cause and transmission of malaria significantly increase the number of practices adopted in both male- and female-headed households. On the other hand, formal education of the household head and
livestock units owned exhibited a positive and significant effect on adoption among male-headed households, but no effect among female-headed households.

**Conclusions:** The findings from this study suggest that universal policy tools can be used to promote uptake of integrated malaria prevention practices, for female- and male-headed households.


**Abstract**

**Background:** The BD FACSPresto™ Near-Patient CD4 Counter was developed to expand HIV/AIDS management in resource-limited settings. It measures absolute CD4 counts (AbsCD4), percent CD4 (%CD4), and hemoglobin (Hb) from a single drop of capillary or venous blood in approximately 23 minutes, with throughput of 10 samples per hour. We assessed the performance of the BD FACSPresto system, evaluating accuracy, stability, linearity, precision, and reference intervals using capillary and venous blood at KEMRI/CDC HIV-research laboratory, Kisumu, Kenya, and precision and linearity at BD Biosciences, California, USA.

**Methods:** For accuracy, venous samples were tested using the BD FACSCalibur™ instrument with BD Tritest™ CD3/CD4/CD45 reagent, BD Trucount™ tubes, and BD Multiset™ software for AbsCD4 and %CD4, and the Sysmex™ KX-21N for Hb. Stability studies evaluated duration of staining (18-120-minute incubation), and effects of venous blood storage <6-24 hours post-draw. A normal cohort was tested for reference intervals. Precision covered multiple days, operators, and instruments. Linearity required mixing two pools of samples, to obtain evenly spaced concentrations for AbsCD4, total lymphocytes, and Hb.

**Results:** AbsCD4 and %CD4 venous/capillary (N = 189/ N = 162) accuracy results gave Deming regression slopes within 0.97-1.03 and R2 ≥0.96. For Hb, Deming regression results were R2 ≥0.94 and slope ≥0.94 for both venous and capillary samples. Stability varied within 10% 2 hours after staining and for venous blood stored less than 24 hours. Reference intervals results showed that gender—but not age-differences were statistically significant (p<0.05). Precision results had <3.5% coefficient of variation for AbsCD4, %CD4, and Hb, except for
low AbsCD4 samples (<6.8%). Linearity was 42-4,897 cells/μL for AbsCD4, 182-11,704 cells/μL for total lymphocytes, and 2-24 g/dL for Hb.

**Conclusions:** The BD FACSPresto system provides accurate, precise clinical results for capillary or venous blood samples and is suitable for near-patient CD4 testing.


### Abstract

Bacteremia (bacterial bloodstream infection) is a major cause of illness and death in sub-Saharan Africa but little is known about the role of human genetics in susceptibility. We conducted a genome-wide association study of bacteremia susceptibility in more than 5,000 Kenyan children as part of the Wellcome Trust Case Control Consortium 2 (WTCCC2). Both the blood-culture-proven bacteremia case subjects and healthy infants as controls were recruited from Kilifi, on the east coast of Kenya. Streptococcus pneumoniae is the most common cause of bacteremia in Kilifi and was thus the focus of this study. We identified an association between polymorphisms in a long intergenic non-coding RNA (lincRNA) gene (AC011288.2) and pneumococcal bacteremia and replicated the results in the same population (p combined = 1.69 × 10(-9); OR = 2.47, 95% CI = 1.84-3.31). The susceptibility allele is African specific, derived rather than ancestral, and occurs at low frequency (2.7% in control subjects and 6.4% in case subjects). Our further studies showed AC011288.2 expression only in neutrophils, a cell type that is known to play a major role in pneumococcal clearance. Identification of this novel association will further focus research on the role of lincRNAs in human infectious disease.


Abstract

Objective: To identify unique characteristics of recent versus established HIV infections and describe sexual transmission networks, we characterized circulating HIV-1 strains from two randomly selected populations of ART-naïve participants in rural western Kenya.

Methods: Recent HIV infections were identified by the HIV-1 subtype B, E and D, immunoglobulin G capture immunoassay (IgG BED-CEIA) and BioRad avidity assays. Genotypic and phylogenetic analyses were performed on the pol gene to identify transmitted drug resistance (TDR) mutations, characterize HIV subtypes and potential transmission clusters. Factors associated with recent infection and clustering were assessed by logistic regression.

Results: Of the 320 specimens, 40 (12.5%) were concordantly identified by the two assays as recent infections. Factors independently associated with being recently infected were age ≤19 years (P = 0.001) and history of sexually transmitted infections (STIs) in the past six months (P = 0.004). HIV subtype distribution differed in recently versus chronically infected participants, with subtype A observed among 53% recent vs. 68% chronic infections (p = 0.04) and subtype D among 26% recent vs. 12% chronic infections (p = 0.012). Overall, the prevalence of primary drug resistance was 1.16%. Of the 258 sequences, 11.2% were in monophyletic clusters of between 2-4 individuals. In multivariate analysis factors associated with clustering included having recent HIV infection P = 0.043 and being from Gem region P = 0.002.

Conclusions: Recent HIV-1 infection was more frequent among 13-19 year olds compared with older age groups, underscoring the ongoing risk and susceptibility of younger persons for acquiring HIV infection. Our findings also provide evidence of sexual networks. The association of recent infections with clustering suggests that early infections may be contributing significant proportions of onward transmission highlighting the need for early diagnosis and treatment as prevention for ongoing prevention. Larger studies are needed to better understand the structure of these networks and subsequently implement and evaluate targeted interventions.


Abstract

Introduction: While relatively rare events, abrupt disruptions in heroin availability have a significant impact on morbidity and mortality risk among those who are heroin dependent. A heroin shortage occurred in Coast Province, Kenya from December 2010 to March 2011. This qualitative analysis describes the shortage events and consequences from the perspective of heroin users, along with implications for health and other public sectors.

Methods: As part of a rapid assessment, 66 key informant interviews and 15 focus groups among heroin users in Coast Province, Kenya were conducted. A qualitative thematic analysis was undertaken in Atlas.ti. to identify salient themes related to the shortage.

Results: Overall, participant accounts were rooted in a theme of desperation and uncertainty, with emphasis on six sub-themes: (1) withdrawal and strategies for alleviating withdrawal, including use of medical intervention and other detoxification attempts; (2) challenges of dealing with unpredictable drug availability, cost, and purity; (3) changes in drug use patterns, and actions taken to procure heroin and other drugs; (4) modifications in drug user relationship dynamics and networks, including introduction of risky group-level injection practices; (5) family and community response; and (6) new challenges with the heroin market resurgence.

Conclusions: The heroin shortage led to a series of consequences for drug users, including increased risk of morbidity, mortality and disenfranchisement at social and structural levels. Availability of evidence-based services for drug users and emergency preparedness plans could have mitigated this impact.


ABSTRACT

The characteristic recurrent epidemics of human respiratory syncytial virus (RSV) within communities may result from the genetic variability of the virus and associated evolutionary
adaptation, reducing the efficiency of preexisting immune responses. We analyzed the molecular evolutionary changes in the attachment (G) glycoprotein of RSV-A viruses collected over 13 epidemic seasons (2000 to 2012) in Kilifi ($n = 649$), Kenya, and contemporaneous sequences ($n = 1,131$) collected elsewhere within Kenya and 28 other countries. Genetic diversity in the G gene in Kilifi was dynamic both within and between epidemics, characterized by frequent new variant introductions and limited variant persistence between consecutive epidemics. Four RSV-A genotypes were detected in Kilifi: ON1 (11.9%), GA2 (75.5%), GA5 (12.3%), and GA3 (0.3%), with predominant genotype replacement of GA5 by GA2 and then GA2 by ON1. Within these genotypes, there was considerable variation in potential N-glycosylation sites, with GA2 and ON1 viruses showing up to 15 different patterns involving eight possible sites. Further, we identified 15 positively selected and 34 genotype-distinguishing codon sites, with six of these sites exhibiting both characteristics. The mean substitution rate of the G ectodomain for the Kilifi data set was estimated at $3.58 \times 10^{-3}$ (95% highest posterior density interval = 3.04 to 4.16) nucleotide substitutions/site/year. Kilifi viruses were interspersed in the global phylogenetic tree, clustering mostly with Kenyan and European sequences. Our findings highlight ongoing genetic evolution and high diversity of circulating RSV-A strains, locally and globally, with potential antigenic differences. Taken together, these provide a possible explanation on the nature of recurrent local RSV epidemics.

**IMPORTANCE** The mechanisms underlying recurrent epidemics of RSV are poorly understood. We observe high genetic diversity in circulating strains within and between epidemics in both local and global settings. On longer time scales (~7 years) there is sequential replacement of genotypes, whereas on shorter time scales (one epidemic to the next or within epidemics) there is a high turnover of variants within genotypes. Further, this genetic diversity is predicted to be associated with variation in antigenic profiles. These observations provide an explanation for recurrent RSV epidemics and have potential implications on the long-term effectiveness of vaccines.


**Abstract**

Youth are particularly vulnerable to acquiring HIV, yet reaching them with HIV prevention interventions and engaging and retaining those infected in care and treatment remains a challenge. We sought to determine the incidence rate of loss to follow-up (LTFU) and explore socio-demographic and clinical characteristics associated with LTFU among HIV-positive youth aged 15-21 years accessing outpatient care and treatment clinics in Kisumu, Kenya. Between July 2007 and September 2010, youth were enrolled into two different HIV care and treatment clinics, one youth specific and the other family oriented. An individual was defined
as LTFU when absent from the HIV treatment clinic for ≥ 4 months regardless of their antiretroviral treatment status. The incidence rate of LTFU was calculated and Cox regression analysis used to identify factors associated with LTFU. A total of 924 youth (79% female) were enrolled, with a median age of 20 years (IQR 18-21). Over half, (529 (57%)), were documented as LTFU, of whom 139 (26%) were LTFU immediately after enrolment. The overall incidence rate of LTFU was 52.9 per 100 person-years (p-y). Factors associated with LTFU were pregnancy during the study period (crude HR 0.68, 95% CI 0.53-0.89); CD4 cell count >350 (adjusted hazard ratios (AHR) 0.59, 95% CI 0.39-0.90); not being on antiretroviral therapy (AHR 4.0, 95% CI 2.70-5.88); and non-disclosure of HIV infection status (AHR 1.43, 95% CI 1.10-1.89). The clinic of enrolment, age, marital status, employment status, WHO clinical disease stage and education level were not associated with LTFU. Interventions to identify and enrol youth into care earlier, support disclosure, and initiate ART earlier may improve retention of youth and need further investigation. Further research is also needed to explore the reasons for LTFU from care among HIV-infected youth and the true outcomes of these patients.


Abstract

The Plasmodium falciparum in vitro culture system is critical for genotypic and phenotypic analyses of the parasites. For genotypic analysis, the genomic DNA can be obtained directly from the patient blood sample or from culture adapted parasites whereas for phenotypic analysis, immediate ex vivo or in vitro culture adapted parasites are used. However, parasite biology studies have not investigated whether culture adaptation process affects genotypic and/or phenotypic characteristics of the parasites in short- or long-term cultures. Here, we set out to study the dynamics and stability of parasite genetic and phenotypic profiles as field isolate parasites were adapted in continuous cultures. Parasites collected from three different patients presenting with uncomplicated malaria were adapted and maintained in drug-free continuous cultures. Aliquots from the continuous cultures were collected every 24-48 hours for analyses. Each aliquot was treated as a separate parasite sample. For genetic analysis, microsatellite (MS) typing and single nucleotide polymorphism (SNP) analyses of 23 drug resistance markers were done. The 50% inhibitory concentrations (IC50) for some of the samples were also established for four antimalarial drugs. Samples from each patient (parasite-line) were compared as they were passed through the continuous culture. Data revealed genotypic and phenotypic profiles for the three parasite-lines fluctuated from one generation to
the next with no specific pattern or periodicity. With few exceptions, multilocus analysis revealed samples from each parasite-line had high genetic diversity with unique haplotypes. Interestingly, changes in MS and SNP profiles occurred simultaneously. The difference in the IC50s of samples in each parasite-line reached statistical significance. However, phenotypic changes did not correspond or correlate to genotypic changes. Our study revealed parasite genetic and phenotypic characteristics fluctuates in short- and long-term cultures, which indicates parasite genetic information obtained even in short cultures is likely to be different from the natural infection parasites.


Abstract

**Background:** New vector control tools are needed to combat insecticide resistance and reduce malaria transmission. The World Health Organization (WHO) endorses larviciding as a supplementary vector control intervention using larvicides recommended by the WHO Pesticides Evaluation Scheme (WHOPES). The decision to scale-up larviciding in Nigeria provided an opportunity to investigate the factors influencing policy adoption and assess the role that actors and evidence play in the policymaking process, in order to draw lessons that help accelerate the uptake of new methods for vector control.

**Methods:** A retrospective policy analysis was carried out using in-depth interviews with national level policy stakeholders to establish normative national vector control policy or strategy decision-making processes and compare these with the process that led to the decision to scale-up larviciding. The interviews were transcribed, then coded and analyzed using NVivo10. Data were coded according to pre-defined themes from an analytical policy framework developed a priori.

**Results:** Stakeholders reported that the larviciding decision-making process deviated from the normative vector control decision-making process. National malaria policy is normally strongly influenced by WHO recommendations, but the potential of larviciding to contribute to national economic development objectives through larvicide production in Nigeria was cited as a key factor shaping the decision. The larviciding decision involved a restricted range of policy actors, and notably excluded actors that usually play advisory, consultative and evidence
generation roles. Powerful actors limited the access of some actors to the policy processes and content. This may have limited the influence of scientific evidence in this policy decision.

**Conclusions:** This study demonstrates that national vector control policy change can be facilitated by linking malaria control objectives to wider socioeconomic considerations and through engaging powerful policy champions to drive policy change and thereby accelerate access to new vector control tools.


**Abstract**

**Background:** Anti-malarial drugs are the major focus in the prevention and treatment of malaria. Artemisinin-based combination therapy (ACT) is the WHO recommended first-line treatment for *Plasmodium falciparum* malaria across the endemic world. Also ACT is increasingly relied upon in treating *Plasmodium vivax* malaria where chloroquine is failing. The emergence of artemisinin drug-resistant parasites is a serious threat faced by global malaria control programmes. Therefore, the success of treatment and intervention strategies is highly pegged on understanding the genetic basis of resistance.

**Methods:** Here, resistance in *P. falciparum* was generated in vitro for artemisinin to produce levels above clinically relevant concentrations in vivo, and the molecular haplotypes investigated. Genomic DNA was extracted using the QIAamp mini DNA kit. DNA sequences of Pfk13, Pfcrt and Pfmdr1 genes were amplified by PCR and the amplicons were successfully sequenced. Single nucleotide polymorphisms were traced by standard bidirectional sequencing and reading the transcripts against wild-type sequences in Codon code Aligner Version 5.1 and NCBI blast.

**Results:** Exposure of parasite strains D6 and W2 to artemisinin resulted in a decrease in parasite susceptibility to artemisinin (W2 and D6) and lumefantrine (D6 only). The parasites exhibited elevated IC50s to multiple artemisinins, with >twofold resistance to artemisinin; however, the resistance index obtained with standard methods was noticeably less than expected for parasite lines recovered from 50 µg/ml 48 h drug pressure. The change in parasite susceptibility was associated with Pfmdr-185K mutation, a mutation never reported before. The Pfcrt-CVMNK genotype (Pfcrt codons 72-76) was retained and notably, the study did not
detect any polymorphisms reported to reduce P. falciparum susceptibility in vivo in the coding sequences of the Pfk13 gene.

Discussion: This data demonstrate that P. falciparum has the capacity to develop resistance to artemisinin derivatives in vitro and that this phenotype is achieved by mutations in Pfmdr1, the genetic changes that are also underpinning lumefantrine resistance. This finding is of practical importance, because artemisinin drugs in Kenya are used in combination with lumefantrine for the treatment of malaria.

Conclusion: Artemisinin resistance phenotype as has been shown in this work, is a decrease in parasites susceptibility to artemisinin derivatives together with the parasite's ability to recover from drug-induced dormancy after exposure to drug dosage above the in vivo clinical concentrations. The study surmises that Pfmdr1 may play a role in the anti-malarial activity of artemisinin.


Abstract

Operational planning is considered an important tool for translating government policies and strategic objectives into day-to-day management activities. However, developing countries suffer from persistent misalignment between policy, planning and budgeting. The Medium Term Expenditure Framework (MTEF) was introduced to address this misalignment. Kenya adopted the MTEF in the early 2000s, and in 2005, the Ministry of Health adopted the Annual Operational Plan process to adapt the MTEF to the health sector. This study assessed the degree to which the health sector Annual Operational Plan process in Kenya has achieved alignment between planning and budgeting at the national level, using document reviews, participant observation and key informant interviews. We found that the Kenyan health sector was far from achieving planning and budgeting alignment. Several factors contributed to this problem including weak Ministry of Health stewardship and institutionalized separation between planning and budgeting processes; a rapidly changing planning and budgeting environment; lack of reliable data to inform target setting and poor participation by key stakeholders in the process including a top-down approach to target setting. We conclude that alignment is unlikely to be achieved without consideration of the specific institutional contexts and the power relationships between stakeholders. In particular, there is a need for institutional integration of the planning and budgeting processes into a common cycle and framework with
common reporting lines and for improved data and local-level input to inform appropriate and realistic target setting. © 2015 The Authors. International Journal of Health Planning and Management published by John Wiley & Sons, Ltd.


**Abstract**

**Background:** Low- and middle-income countries need to sustain efficiency and equity in health financing on their way to universal health care coverage. However, systems meant to generate quality economic information are often deficient in such settings. We assessed the feasibility of streamlining cost accounting systems within the Kenyan health sector to illustrate the pragmatic challenges and opportunities.

**Design:** We reviewed policy documents, and conducted field observations and semi-structured interviews with key informants in the health sector. We used an adapted Human, Organization and Technology fit (HOT-fit) framework to analyze the components and standards of a cost accounting system.

**Results:** Among the opportunities for a viable cost accounting system, we identified a supportive broad policy environment, political will, presence of a national data reporting architecture, good implementation experience with electronic medical records systems, and the availability of patient clinical and resource use data. However, several practical issues need to be considered in the design of the system, including the lack of a framework to guide the costing process, the lack of long-term investment, the lack of appropriate incentives for ground-level staff, and a risk of overburdening the current health management information system.

**Conclusion:** To facilitate the implementation of cost accounting into the health sector, the design of any proposed system needs to remain simple and attuned to the local context.


| 64. | Opanda SM, Wamunyokoli F, Khamadi S, Coldren R, Bulimo WD. Genotyping of enteroviruses isolated in Kenya from pediatric patients using partial VP1 |
Abstract

Enteroviruses (EV) are responsible for a wide range of clinical diseases in humans. Though studied broadly in several regions of the world, the genetic diversity of human enteroviruses (HEV) circulating in the sub-Saharan Africa remains under-documented. In the current study, we molecularly typed 61 HEV strains isolated in Kenya between 2008 and 2011 targeting the 3'-end of the VP1 gene. Viral RNA was extracted from the archived isolates and part of the VP1 gene amplified by RT-PCR, followed by sequence analysis. Twenty-two different EV types were detected. Majority (72.0%) of these belonged to Enterovirus B species followed by Enterovirus D (21.3%) and Enterovirus A (6.5%). The most frequently detected types were Enterovirus-D68 (EV-D68), followed by Coxsackievirus B2 (CV-B2), CV-B1, CV-B4 and CV-B3. Phylogenetic analyses of these viruses revealed that Kenyan CV-B1 isolates were segregated among sequences of global CV-B1 strains. Conversely, the Kenyan CV-B2, CV-B3, CV-B4 and EV-D68 strains generally grouped together with those detected from other countries. Notably, the Kenyan EV-D68 strains largely clustered with sequences of global strains obtained between 2008 and 2010 than those circulating in recent years. Overall, our results indicate that HEV strains belonging to Enterovirus D and Enterovirus B species predominantly circulated and played a significant role in pediatric respiratory infection in Kenya, during the study period. The Kenyan CV-B1 strains were genetically divergent from those circulating in other countries. Phylogenetic clustering of Kenyan EV-D68 strains with sequences of global strains circulating between 2008 and 2010 than those obtained in recent years suggests a high genomic variability associated with the surface protein encoding VP1 gene in these enteroviruses.


Abstract

Genetically determined artemisinin resistance in Plasmodium falciparum has been described in Southeast Asia. The relevance of recently described Kelch 13-propeller mutations for artemisinin resistance in Sub-Saharan Africa parasites is still unknown. Southeast Asia parasites have low genetic diversity compared to Sub-Saharan Africa, where parasites are highly genetically diverse. This study attempted to elucidate whether genetics provides a basis
for discovering molecular markers in response to artemisinin drug treatment in P. falciparum in Kenya. The genetic diversity of parasites collected pre- and post- introduction of artemisinin combination therapy (ACT) in western Kenya was determined. A panel of 12 microsatellites and 91 single nucleotide polymorphisms (SNPs) distributed across the P. falciparum genome were genotyped. Parasite clearance rates were obtained for the post-ACT parasites. The 12 microsatellites were highly polymorphic with post-ACT parasites being significantly more diverse compared to pre-ACT (p < 0.0001). The median clearance half-life was 2.55 hours for the post-ACT parasites. Based on SNP analysis, 15 of 90 post-ACT parasites were single-clone infections. Analysis revealed 3 SNPs that might have some causal association with parasite clearance rates. Further, genetic analysis using Bayesian tree revealed parasites with similar clearance phenotypes were more closely genetically related. With further studies, SNPs described here and genetically determined response to artemisinin treatment might be useful in tracking artemisinin resistance in Kenya.


Abstract

Background: Soil transmitted helminthes (STH) are significant health problems among school-age children. In Kenya's coastal region, the prevalence among pre-school age children (PSAC) ranges from 27.8 to 66.7 %. Whereas some pre-schools are as far as 7 km from the nearest primary schools, the National School-Based Deworming Programme (NSBDP) requires the pre-school teachers to walk with the children to primary schools for deworming by trained primary school teachers. The long distances may contribute in making drug delivery ineffective and unsustainable.

Methods: To assess the pre-school teachers' knowledge, experiences and perceptions of STH and the NSBDP, a cross-sectional study using qualitative methods was conducted in four sub-counties of the Coast Region. Through purposive sampling, 41 pre-schools which are 2 or more kilometers away from a primary school were selected and in-depth interviews administered to the teachers. Separate in-depth interviews were administered to 34 community health extension workers, 40 opinion leaders and 38 primary school teachers all purposively selected to assess their perceptions of the role of pre-school teachers in the NSBDP. Data was audio recorded, transcribed, coded and analyzed manually by study themes.
Results: A third of the pre-school teachers were aware of signs of STHs and a half indicated that poor hygiene and sanitation practices are major causes. A majority of the pre-school teachers reported that health education and environmental sanitation are key control methods. Majority (39) had received information on NSBDP from various sources and all took part in community sensitization and in treating the pre-school children. A large majority of all study participants indicated that treating the children at pre-schools is ideal for increased coverage. Majority of the pre-school teachers perceived the NSBDP as important in improving the health status of the children. All study participants felt that the parents needed to be given adequate information on STHs and training the pre-school teachers to assist in community sensitization and drug administration would be useful.

Conclusion: Pre-school teachers are a potential resource to the NSBDP that should be utilized to instill proper water and sanitation practices to the young children and assist in community sensitization. They should be empowered and allowed to administer treatment for STH control. County Governments, their current employers should find ways of engaging them in worm control efforts.


Abstract

Background: The use of malaria infection prevalence among febrile patients at clinics has a potential to be a valuable epidemiological surveillance tool. However, routine data are incomplete and not all fevers are tested. This study was designed to screen all fevers for malaria infection in Kenya to explore the epidemiology of fever test positivity rates.

Methods: Random sampling was used within five malaria epidemiological zones of Kenya (i.e., high lake endemic, moderate coast endemic, highland epidemic, seasonal low transmission and low risk zones). The selected sample was representative of the number of hospitals, health centres and dispensaries within each zone. Fifty patients with fever presenting to each sampled health facility during the short rainy season were screened for malaria infection using a rapid diagnostic test (RDT). Details of age, pregnancy status and basic demographics were recorded for each patient screened.

Results: 10,557 febrile patients presenting to out-patient clinics at 234 health facilities were screened for malaria infection. 1633 (15.5%) of the patients surveyed were RDT positive for
malaria at 124 (53.0%) facilities. Infection prevalence among non-pregnant patients varied between malaria risk zones, ranging from 0.6% in the low risk zone to 41.6% in the high lake endemic zone. Test positivity rates (TPR) by age group reflected the differences in the intensity of transmission between epidemiological zones. In the lake endemic zone, 6% of all infections were among children aged less than 1 year, compared to 3% in the coast endemic, 1% in the highland epidemic zone, less than 1% in the seasonal low transmission zone and 0% in the low risk zone. Test positivity rate was 31% among febrile pregnant women in the high lake endemic zone compared to 9% in the coast endemic and highland epidemic zones, 3.2% in the seasonal low transmission zone and zero in the low risk zone.

**Conclusion:** Malaria infection rates among febrile patients, with supporting data on age and pregnancy status presenting to clinics in Kenya can provide invaluable epidemiological data on spatial heterogeneity of malaria and serve as replacements to more expensive community-based infection rates to plan and monitor malaria control.


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**Abstract**

Safer conception strategies can prevent HIV transmission between HIV-discordant partners while allowing them to conceive. However, HIV care providers in sub-Saharan Africa report they are not trained in safer conception, and patients are not routinely offered safer conception services. This mixed-methods pilot study evaluated the impact, acceptability, and feasibility of a novel Safer Conception Counseling Toolkit among providers and patients in Kenya. We enrolled 20 HIV-positive women, 10 HIV-discordant couples, and 10 providers from HIV care and treatment clinics. Providers completed questionnaires before/after training, and then counseled HIV-affected patients. Change in patient knowledge was assessed before/after counseling. Qualitative interviews were conducted among providers and patients. The Toolkit was associated with large, significant increases in patient knowledge, and provider confidence, knowledge, and favorable attitudes toward safer conception counseling; 20% felt confident before versus 100% after training (p < 0.01).


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Idris ZM, Chan CW, Kongere J, Gitaka J, Logedi J, Omar A, Obonyo C, Machini

Abstract

Kenya is intensifying its national efforts in malaria control to achieve malaria elimination. Detailed characterization of malaria infection among populations living in the areas where the disease is endemic in Kenya is a crucial priority, especially for planning and evaluating future malaria elimination strategy. This study aimed to investigate the distribution and extent of malaria infection on islands in Lake Victoria of Kenya to aid in designing new interventions for malaria elimination. Five cross-sectional surveys were conducted between January 2012 and August 2014 on four islands (Mfangano, Takawiri, Kibuogi and Ngodhe) in Lake Victoria and a coastal mainland (Ungoye). Malaria prevalence varied significantly among settings: highest in Ungoye, followed by the large island of Mfangano and lowest in the three remaining small islands. Of the 3867 malaria infections detected by PCR, 91.8% were asymptomatic, 50.3% were sub-microscopic, of which 94% were also asymptomatic. We observed geographical differences and age dependency in both proportion of sub-microscopic infections and asymptomatic parasite carriage. Our findings highlighted the local heterogeneity in malaria prevalence on islands and a coastal area in Lake Victoria, and provided support for the inclusion of mass drug administration as a component of the intervention package to eliminate malaria on islands.


Abstract

**Objective:** We investigated the prevalence and pattern of electroencephalographic (EEG) features of epilepsy and the associated factors in Africans with active convulsive epilepsy (ACE).
**Methods:** We characterized electroencephalographic features and determined associated factors in a sample of people with ACE in five African sites. Mixed-effects modified Poisson regression model was used to determine factors associated with abnormal EEGs.

**Results:** Recordings were performed on 1426 people of whom 751 (53%) had abnormal EEGs, being an adjusted prevalence of 2.7 (95% confidence interval (95% CI), 2.5-2.9) per 1000. 52% of the abnormal EEG had focal features (75% with temporal lobe involvement). The frequency and pattern of changes differed with site. Abnormal EEGs were associated with adverse perinatal events (risk ratio (RR)=1.19 (95% CI, 1.07-1.33)), cognitive impairments (RR=1.50 (95% CI, 1.30-1.73)), use of anti-epileptic drugs (RR=1.25 (95% CI, 1.05-1.49)), focal seizures (RR=1.09 (95% CI, 1.00-1.19)) and seizure frequency (RR=1.18 (95% CI, 1.10-1.26) for daily seizures; RR=1.22 (95% CI, 1.10-1.35) for weekly seizures and RR=1.15 (95% CI, 1.03-1.28) for monthly seizures)).

**Conclusions:** EEG abnormalities are common in Africans with epilepsy and are associated with preventable risk factors.

**Significance:** EEG is helpful in identifying focal epilepsy in Africa, where timing of focal aetiologies is problematic and there is a lack of neuroimaging services.


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**Abstract**

Mike English and colleagues argue that as efforts are made towards achieving universal health coverage it is also important to build capacity to develop regionally relevant evidence to improve healthcare.


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Abstract

Close proximity interactions between individuals influence how infections spread. Quantifying close contacts in developing world settings, where such data is sparse yet disease burden is high, can provide insights into the design of intervention strategies such as vaccination. Recent technological advances have enabled collection of time-resolved face-to-face human contact data using radio frequency proximity sensors. The acceptability and practicalities of using proximity devices within the developing country setting have not been investigated. We present and analyse data arising from a prospective study of 5 households in rural Kenya, followed through 3 consecutive days. Pre-study focus group discussions with key community groups were held. All residents of selected households carried wearable proximity sensors to collect data on their close (<1.5 metres) interactions. Data collection for residents of three of the 5 households was contemporaneous. Contact matrices and temporal networks for 75 individuals are defined and mixing patterns by age and time of day in household contacts determined. Our study demonstrates the stability of numbers and durations of contacts across days. The contact durations followed a broad distribution consistent with data from other settings. Contacts within households occur mainly among children and between children and adults, and are characterised by daily regular peaks in the morning, midday and evening. Inter-household contacts are between adults and more sporadic when measured over several days. Community feedback indicated privacy as a major concern especially regarding perceptions of non-participants, and that community acceptability required thorough explanation of study tools and procedures. Our results show for a low resource setting how wearable proximity sensors can be used to objectively collect high-resolution temporal data without direct supervision. The methodology appears acceptable in this population following adequate community engagement on study procedures. A target for future investigation is to determine the difference in contact networks within versus between households. We suggest that the results from this study may be used in the design of future studies using similar electronic devices targeting communities, including households and schools, in the developing world context.


Abstract
Background: Perturbations of blood sodium are the most frequently encountered electrolyte disorder in sick children, and may influence fluid therapy. We examined the frequency of blood sodium perturbations, and factors and outcomes associated with hyponatremia in children admitted to a rural Kenyan hospital and investigated the risk factors associated with deaths in hyponatremic children.

Methods: Plasma sodium levels and other laboratory parameters were measured in children admitted to a rural Kenyan hospital. Clinical measurements were collected using standard forms and entered into a computer database. The proportion of children admitted with hyponatremia was determined. Logistic regression models were used to investigate factors associated with hyponatremia, and death in those with hyponatremia.

Results: Abnormal plasma sodium occurred in 46.6% (95% confidence interval (95%CI) 43.5-49.6%) of 1026 pediatric admissions. Hyponatremia occurred in 44.4% (95%CI 41.4-47.5%) and hypernatremia in 2.1% (95%CI 1.3-3.0%). Malaria (40.8%) was the most common underlying primary diagnosis in hyponatremic children. Malaria, hyperglycemia, wasting, high creatinine levels and preserved consciousness were associated with hyponatremia. Pallor and seizures were associated with increased mortality in hyponatremic children.

Conclusions: Sodium disturbances are common in pediatric admissions to a County hospital in rural Kenya. Seizures and pallor were predictors of mortality in hyponatremic children.


Abstract

Background: Shock may complicate several acute childhood illnesses in hospitals within low-income countries and has a high case fatality. Hypovolemic shock secondary to diarrhoea/dehydration and septic shock are thought to be common, but there are few reliable data on prevalence or treatment that differ for the two major forms of shock. Examining prevalence and treatment practices has become important since reports suggest high risks from liberal use of fluid boluses in African children. The present study aims to estimate the prevalence, fluid management practices and outcomes of shock among hospitalised children.

Methods: We analysed paediatric in-patient data collected using discharge case record review between October 2013 and February 2016 from 14 hospitals in Kenya which are part of a network (referred to as the Clinical Information Network) using similar tools for standardised
clinical records with care directed by the local clinical team leaders. Data are from a period after dissemination of national guidance seeking to limit use of bolus fluids.

**Results:** A total of 74,402 children were admitted between October 2013 and February 2016. Children aged < 30 days or > 5 years, with severe acute malnutrition, surgical/burns, or cases with pre-defined minimum data sets were excluded from analysis. This resulted in 42,937 patients meeting the inclusion criteria. Prevalence of clinically diagnosed shock was 1.5 % (n = 622) and overall bolus use was 0.9 % (n = 366); 41 % (256/622) of children with clinically diagnosed shock did not receive a fluid bolus (but had a fluid plan for management of dehydration). Identified cases appeared mostly to be hypovolaemic shock secondary to dehydration/diarrhoea (94 %, 582/622), with a high case fatality (34 %, 211/622). Overall mortality for all admitted children was 5 % (2115/42,937) and was 7.9 % (798/10,096) in children with dehydration/diarrhoea. The diagnosis of hypovolaemic shock was nearly always accompanied by additional clinical diagnosis (99 %), most often pneumonia or malaria. Where bolus fluids were used, they were prescribed in accordance with guidelines (isotonic fluid at correct volume) in 92 % of cases. Inappropriate use of bolus fluids to treat milder forms of impared circulation appeared very rarely.

**Conclusion:** A diagnosis of shock is uncommon at admission and use of fluid bolus is rare in admissions to Kenyan hospitals. A fluid bolus, when prescribed, is mostly used in children with hypovolemic shock secondary to dehydration and case fatality in these cases is high. We found little evidence of liberal use of fluid bolus that might cause harm in a period following dissemination of national guidelines suggesting very strict criteria for fluid bolus use.


Background: Country-specific studies in Africa have indicated that Plasmodium falciparum is associated with invasive nontyphoidal Salmonella (iNTS) disease. We conducted a multicenter study in 13 sites in Burkina Faso, Ethiopia, Ghana, Guinea-Bissau, Kenya, Madagascar, Senegal, South Africa, Sudan, and Tanzania to investigate the relationship between the occurrence of iNTS disease, other systemic bacterial infections, and malaria.

Methods: Febrile patients received a blood culture and a malaria test. Isolated bacteria underwent antimicrobial susceptibility testing, and the association between iNTS disease and malaria was assessed.

Results: A positive correlation between frequency proportions of malaria and iNTS was observed (P = .01; r = 0.70). Areas with higher burden of malaria exhibited higher odds of iNTS disease compared to other bacterial infections (odds ratio [OR], 4.89; 95% CI, 1.61-14.90; P = .005) than areas with lower malaria burden. Malaria parasite positivity was associated with iNTS disease (OR, 2.44; P = .031) and gram-positive bacteremias, particularly Staphylococcus aureus, exhibited a high proportion of coinfection with Plasmodium malaria. Salmonella Typhimurium and Salmonella Enteritidis were the predominant NTS serovars (53/73; 73%). Both moderate (OR, 6.05; P = .0001) and severe (OR, 14.62; P < .0001) anemia were associated with iNTS disease.

Conclusions: A positive correlation between iNTS disease and malaria endemicity, and the association between Plasmodium parasite positivity and iNTS disease across sub-Saharan Africa, indicates the necessity to consider iNTS as a major cause of febrile illness in malaria-holoendemic areas. Prevention of iNTS disease through iNTS vaccines for areas of high malaria endemicity, targeting high-risk groups for Plasmodium parasitic infection, should be considered.


Abstract

Background: The World Health Organization (WHO) recommended physician to population ratio is 23:10,000. Kenya has a physician to population ratio of 1.8:10,000 and is among 57 countries listed as having a serious shortage of health workers. Approximately 52% of physicians work in urban areas, 6% in rural and 42% in peri-urban locations. This study
explored factors influencing the choice of career specialization and location for practice among final year medical students by gender.

**Methods:** A descriptive cross-sectional study was carried out on final year students in 2013 at the University of Nairobi's, School of Medicine in Kenya. Sample size was calculated at 156 students for simple random sampling. Data collected using a pre-tested self-administered questionnaire included socio-demographic characteristics of the population, first and second choices for specialization. Outcome variables collected were factors affecting choice of specialty and location for practice. Bivariate analysis by gender was carried out between the listed factors and outcome variables with calculation of odds ratios and chi-square statistics at an alpha level of significance of 0.05. Factors included in a binomial logistic regression model were analysed to score the independent categorical variables affecting choice of specialty and location of practice.

**Results:** Internal medicine, Surgery, Obstetrics/Gynaecology and Paediatrics accounted for 58.7% of all choices of specialization. Female students were less likely to select Obs/Gyn (OR 0.41, 95% CI =0.17-0.99) and Surgery (OR 0.33, 95% CI = 0.13-0.86) but eight times more likely to select Paediatrics (OR 8.67, 95% CI = 1.91-39.30). Surgery was primarily selected because of the 'perceived prestige of the specialty' (OR 4.3 95% CI = 1.35-14.1). Paediatrics was selected due to 'Ease of raising a family' (OR 4.08 95% CI = 1.08-15.4). Rural origin increased the odds of practicing in a rural area (OR 2.5, 95% CI = 1.04-6.04). Training abroad was more likely to result in preference for working abroad (OR 9.27 95% CI = 2.1-41.9).

**Conclusions:** The 4 core specialties predominate as career preferences. Females are more likely to select career choices due to 'ease of raising a family'. Rural origin of students was found to be the most important factor for retention of rural health workforce. This data can be used to design prospective cohort studies in an effort to understand the dynamic influence that governments, educational institutions, work environments, family and friends exert on medical students' careers

Background: Diagnosis followed by effective treatment of tuberculosis (TB) reduces transmission and saves lives in persons living with HIV (PLHIV). Sputum smear microscopy is widely used for diagnosis, despite limited sensitivity in PLHIV. Evidence is needed to determine the optimal diagnostic approach for these patients.

Methods: From May 2011 through June 2012, we recruited PLHIV from 15 HIV treatment centers in western Kenya. We collected up to three sputum specimens for Ziehl-Neelsen (ZN) and fluorescence microscopy (FM), GeneXpert MTB/RIF (Xpert), and culture, regardless of symptoms. We calculated the incremental yield of each test, stratifying results by CD4 cell count and specimen type; data were analyzed to account for complex sampling.

Results: From 778 enrolled patients, we identified 88 (11.3%) laboratory-confirmed TB cases. Of the 74 cases who submitted 2 specimens for microscopy and Xpert testing, ZN microscopy identified 25 (33.6%); Xpert identified those plus an additional 18 (incremental yield = 24.4%). Xpert testing of spot specimens identified 48 (57.0%) of 84 cases; whereas Xpert testing of morning specimens identified 50 (66.0%) of 76 cases. Two Xpert tests detected 22/24 (92.0%) TB cases with CD4 counts <100 cells/μL and 30/45 (67.0%) of cases with CD4 counts ≥100 cells/μL.

Conclusions: In PLHIV, Xpert substantially increased diagnostic yield compared to smear microscopy and had the highest yield when used to test morning specimens and specimens from PLHIV with CD4 count <100 cells/μL. TB programs unable to replace smear microscopy with Xpert for all symptomatic PLHIV should consider targeted replacement and using morning specimens.


Abstract

Background: Up to 90% of the global burden of malaria morbidity and mortality occurs in sub-Saharan Africa and children under-five bear a disproportionately high malaria burden. Effective inpatient case management can reduce severe malaria mortality and morbidity, but there are few reports of how successfully international and national recommendations are adopted in management of inpatient childhood malaria.

Methods: A descriptive cross-sectional study of inpatient malaria case management practices was conducted using data collected over 24 months in five hospitals from high malaria risk
areas participating in the Clinical Information Network (CIN) in Kenya. This study describes documented clinical features, laboratory investigations and treatment of malaria in children (2-59 months) and adherence to national guidelines.

**Results:** A total of 13,014 children had a malaria diagnosis on admission to the five hospitals between March, 2014 and February, 2016. Their median age was 24 months (IQR 12-36 months). The proportion with a diagnostic test for malaria requested was 11,981 (92.1 %). Of 10,388 patients with malaria test results documented, 8050 (77.5 %) were positive and anti-malarials were prescribed in 6745 (83.8 %). Malaria treatment was prescribed in 1613/2338 (69.0 %) children with a negative malaria result out of which only 52 (3.2 %) had a repeat malaria test done as recommended in national guidelines. Documentation of clinical features was good across all hospitals, but quinine remained the most prescribed malaria drug (47.2 % of positive cases) although a transition to artesunate (46.1 %) was observed. Although documented clinical features suggested approximately half of positive malaria patients were not severe cases artemether-lumefantrine was prescribed on admission in only 3.7 % cases.

**Conclusions:** Despite improvements in inpatient malaria care, high rates of presumptive treatment for test negative children and likely over-use of injectable anti-malarial drugs were observed. Three years after national policy change, there is a gradual transition to artesunate. Continued efforts to support improved routine inpatient malaria care through dissemination and implementation of guidelines, and access to recommended drugs are needed together with improved capacity of hospitals to investigate other causes of severe illness in children. Efforts to improve clinical information could help track progress.


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**Abstract**

**Background:** School children living in the tropics are often concurrently infected with plasmodium and helminth parasites. It has been hypothesized that immune responses evoked by helminths may modify malaria-specific immune responses and increase the risk of malaria.

**Methods:** We performed a randomized, open-label, equivalence trial among 2436 school children in western Kenya. Eligible children were randomized to receive either 4 repeated doses or a single dose of albendazole and were followed up during 13 months to assess the
incidence of clinical malaria. Secondary outcomes were Plasmodium prevalence and density, assessed by repeat cross-sectional surveys over 15 months. Analysis was conducted on an intention-to-treat basis with a prespecified equivalence range of 20%.

**Results:** During 13 months of follow-up, the incidence rate of malaria was 0.27 episodes/person-year in the repeated treatment group and 0.26 episodes/person-year in the annual treatment group (incidence difference, 0.01; 95% confidence interval, -0.03 to .06). The prevalence and density of malaria parasitemia did not differ by treatment group at any of the cross-sectional surveys.

**Conclusions:** Our findings suggest that repeated deworming does not alter risks of clinical malaria or malaria parasitemia among school children and that school-based deworming in Africa may have no adverse consequences for malaria.


**Abstract**

Integrated approaches provide better understanding of HIV/AIDS epidemics. We optimised a multiassay algorithm (MAA) and assessed HIV incidence, correlates of recent infections, viral diversity, plus transmission clusters among participants screened for Kisumu Incidence Cohort Study (KICoS1) (2007-2009). We performed BED-CEIA, Limiting antigen (LAg) avidity, Biorad avidity, and viral load (VL) tests on HIV-positive samples. Genotypic analyses focused on HIV-1 pol gene. Correlates of testing recent by MAA were assessed using logistic regression model. Overall, 133 (12%, 95% CI: 10.2-14.1) participants were HIV-positive, of whom 11 tested recent by MAA (BED-CEIA OD-n < 0.8 + LAg avidity OD-n < 1.5 + VL > 1000 copies/mL), giving an incidence of 1.46% (95% CI: 0.58-2.35) per year. This MAA-based incidence was similar to longitudinal KICoS1 incidence. Correlates of testing recent included sexually transmitted infection (STI) treatment history (OR = 3.94, 95% CI: 1.03-15.07) and syphilis seropositivity (OR = 10.15, 95% CI: 1.51-68.22). Overall, HIV-1 subtype A (63%), D (15%), C (3%), G (1%) and recombinants (18%), two monophyletic dyads and intrinsic viral mutations (V81I, V81I/V, V108I/V and K101Q) were observed. Viral diversity mirrored known patterns in this region, while resistance mutations reflected likely non-
exposure to antiretroviral drugs. Management of STIs may help address ongoing HIV transmission in this region.


Abstract

Although the severe acute respiratory illness (SARI) case definition is increasingly used for inpatient influenza surveillance, pneumonia is a more familiar term to clinicians and policymakers. We evaluated WHO case definitions for severe acute respiratory illness (SARI) and pneumonia (Integrated Management of Childhood Illnesses (IMCI) for children aged <5 years and Integrated Management of Adolescent and Adult Illnesses (IMAI) for patients aged ≥13 years) for detecting laboratory-confirmed influenza among hospitalized ARI patients. Sensitivities were 84% for SARI and 69% for IMCI pneumonia in children aged <5 years and 60% for SARI and 57% for IMAI pneumonia in patients aged ≥13 years. Clinical pneumonia case definitions may be a useful complement to SARI for inpatient influenza surveillance.


Abstract

Background: Nutrition plays an important role in child survival and development. Treatment action in the management of child health and nutrition is influenced by perceptions of illness, and gender plays an important role. However, little is known about if and how moderate undernutrition is recognised among lay populations, or how local social norms and intra-household dynamics affect decisions to seek biomedical assistance for nutritional concerns. In this paper we describe how childhood nutritional problems are recognised and understood within rural households. We demonstrate how context influences local constructs of ‘normal’,
and suggest the centrality of gender in the management of child health and nutrition in our research context.

**Methods:** This qualitative study was undertaken in Kilifi County on the Kenyan Coast. A set of 15 households whose children were engaged in a community-based nutrition intervention were followed up over a period of twelve months. Over a total of 54 household visits, group and individual in-depth interviews were conducted with a range of respondents, supplemented by non-participant observations. Eight in-depth interviews with community representatives were also conducted.

**Results:** Local taxonomies of childhood undernutrition were found to overlap with, but differ from, biomedical categories. In particular, moderate undernutrition was generally not recognised as a health problem requiring treatment action, but rather as routine and manageable, typically seasonal, weight-loss. Where symptoms were considered more serious and requiring remedial action, household management strategies were typically based on perceived aetiology of the illness. Additionally, gender emerged as a potentially central theme in childhood nutrition problems and related management. Women reported that they have primary responsibility for ensuring children's good health and nutritional status, and that they are often held accountable when their children are of sub-optimal health.

**Conclusion:** Perceptions of child nutrition and illness and gendered roles within households influence treatment action, and engagement with nutrition interventions. Community-based nutrition interventions must recognise these complex realities.


**Abstract**

*Ascaris lumbricoides* is a nematode parasite that causes the common tropical infection ascariasis in humans. It is also considered among the neglected tropical diseases. Diagnosis relies mainly on microscopy-based methods which are laborious, are limited by low sensitivity, and require high expertise. We have developed a loop mediated isothermal amplification (LAMP) for diagnosis of ascariasis in fecal samples, based on the first internal transcribed (ITS-1) spacer region of the ribosomal DNA. We used Primer Explorer V4 software to design primers. *Ascaris* adult and ova were obtained from naturally infected school children, whose
parents/guardians gave consent for their participation in the study. Genomic DNA was extracted using alkaline lysis method and amplified by LAMP at 63°C for 45 minutes. LAMP products were visualized by naked eyes after adding SYBR Green dye and also on agarose gel. LAMP successfully and reliably detected Ascaris DNA from a single egg and in fecal samples. The assay specifically detected Ascaris DNA without amplifying DNA from ova of other parasites which commonly coexist with A. lumbricoides in feces. The developed LAMP assay has great potential for use in ascariasis diagnosis at the point of care and in low infection intensity situation that characterize control and elimination campaigns.


Abstract

The leading circumsporozoite protein (CSP) based malaria vaccine, RTS,S, though promising, has shown limited efficacy in field studies. There is therefore, still a need to identify other malaria vaccine targets. Merozoite antigens are potential vaccine candidates, since naturally acquired antibodies generated against them inhibit erythrocyte invasion and in some cases result in the clinical protection from disease. We thus used in silico tools (BCPreds, NetMHCcons and NetMHCIIpan 3.0) to predict B-cell epitopes (BCEs) and T-cell epitopes (TCEs) in two merozoite invasion proteins, EBA175-RII and Rh5. Initially, we validated these tools using CSP to determine whether the algorithms could predict the epitopes in the RTS,S vaccine. In EBA175-RII, we prioritised three BCEs 15REKRKGMKWDCKKKNDRSNY34, 420SNRKLVGKINTNSNYVHRNKQ440 and 528WISKKKEEYNKQAKQYQEYQ547, a CD8+ epitope 553KMYSEFKSI561 and a CD4+ epitope 440QNDKLFHDEWWKVIKKD456. Three Rh5 epitopes were prioritised, a BCE 344SCYNNNFEXTNGIRYHYDEY363, a CD8+ epitope 198STYGKCIAV206 and a Rh5 CD4+ epitope 180TFLDYYKHLSYNSIYHKSSTY200. All these epitopes are in the region involved in the proteins' interaction with their erythrocyte receptors, thus enabling erythrocyte invasion. Therefore, upon validation of their immunogenicity, by ELISA using serum from a malaria endemic population, antibodies to these epitopes may inhibit erythrocyte invasion. All the epitopes we predicted in EBA175-RII and Rh5 are novel. We also identified polymorphic epitopes that may escape host immunity, as some variants were not predicted as epitopes, suggesting that they may not be immunogenic regions. We present a set of epitopes that following in vitro validation provide a set of molecules to screen as potential vaccine candidates.

Abstract

Background: Trachoma is the leading infectious cause of blindness in the world. It is commonly found in cultural groups with poor hygiene. Trachoma control includes Surgery, Antibiotics, Facial cleanliness and Environmental Improvement (SAFE). Potentially blinding and active trachoma are monitored using trachomatous trichiasis (TT) in adults and trachoma inflammation-follicular (TF) in children aged 1-9 years respectively. A cross-sectional study to assess the knowledge, practices and perceptions of trachoma and its control was conducted in the endemic communities in Narok County.

Methods: Qualitative methods were used for data collection. Using purposive sampling, 12 focus group discussions (FGDs) with single sex adult and young men and women groups of homogenous characteristics, 12 key informant interviews with opinion leaders and 5 in-depth interviews (IDIs) with trichiasis patients and 6 with persons who have undergone trichiasis surgery were conducted. Data was audio recorded, transcribed, coded and analyzed manually by study themes; knowledge, practices and perceptions of trachoma transmission, infection signs, prevention and control.

Results: Majority of the community members had knowledge of trachoma and its transmission. The practices that contributed to transmission of infection included: failure to wash faces and bathe regularly, sharing of water basins and towels for face washing, traditional methods of trachoma treatment and dirty household environment. Due to socio-cultural perceptions, toilets were unacceptable and use of bushes for human waste disposal was common. Poor perceptions on disease susceptibility, flies on children's faces, latrine ownership and usage and separation of human and animal dwellings also played a role in the transmission of trachoma. Fear of loss of sight during surgery was a deterrent to its uptake and a desire to be able to see and take care of domestic animals promoted surgery uptake. Majority of the community members were appreciative of Mass Drug Administration (MDA) though side effect such as vomiting and diarrhoea were reported.

Conclusion: Poor practices and related socio-cultural perceptions are important risk factors in sustaining trachoma infection and transmission. Community members require health education
for behavior change and awareness creation about surgery, MDA and its potential side effects for elimination of trachoma in Narok County, Kenya.


Abstract

Background: Streptococcus pneumoniae is a leading cause of pneumonia, meningitis and sepsis in developing countries, particularly among children and HIV-infected persons. Pneumococcal oropharyngeal (OP) or nasopharyngeal (NP) colonization is a precursor to development of invasive disease. New conjugate vaccines hold promise for reducing colonization and disease.

Methods: Prior to introduction of 10-valent pneumococcal conjugate vaccine (PCV10), we conducted a cross-sectional survey among HIV-infected parents of children <5 years old in rural Kenya. Other parents living with an HIV-infected adult were also enrolled. After broth enrichment, NP and OP swabs were cultured for pneumococcus. Serotypes were identified by Quellung. Antimicrobial susceptibility was performed using broth microdilution.

Results: We enrolled 973 parents; 549 (56.4%) were HIV-infected, 153 (15.7%) were HIV-uninfected and 271 (27.9%) had unknown HIV status. Among HIV-infected parents, the median age was 32 years (range 15-74) and 374/549 (68%) were mothers. Pneumococci were isolated from 237/549 (43.2%) HIV-infected parents and 41/153 (26.8%) HIV-non-infected parents (p = 0.0003). Colonization with PCV10 serotypes was not significantly more frequent in HIV-infected (12.9%) than HIV-uninfected parents (11.8%; p = 0.70). Among HIV-infected parents, cooking site separate from sleeping area and CD4 count >250 were protective (OR = 0.6; 95% CI 0.4, 0.9 and OR = 0.5; 95% CI 0.2, 0.9, respectively); other associations were not identified. Among 309 isolates tested from all parents, 255 (80.4%) were penicillin non-susceptible (MIC ≥0.12 μg/ml).

Conclusions: Prevalence of pneumococcal colonization is high among HIV-infected parents in rural Kenya. If young children are the pneumococcal reservoir for this population, PCV10
introduction may reduce vaccine-type colonization and disease among HIV-infected parents through indirect protection.


Abstract

Transmission intensity, movement of human and vector hosts, biogeographical features, and malaria control measures are some of the important factors that determine Plasmodium falciparum parasite genetic variability and population structure. Kenya has different malaria ecologies which might require different disease intervention methods. Refined parasite population genetic studies are critical for informing malaria control and elimination strategies. This study describes the genetic diversity and population structure of P. falciparum parasites from the different malaria ecological zones in Kenya. Twelve multi-locus microsatellite (MS) loci previously described were genotyped in 225 P. falciparum isolates collected between 2012 and 2013 from five sites; three in lowland endemic regions (Kisumu, Kombewa, and Malindi) and two in highland, epidemic regions (Kisii and Kericho). Parasites from the lowland endemic and highland epidemic regions of western Kenya had high genetic diversity compared to coastal lowland endemic region of Kenya [Malindi]. The Kenyan parasites had a mean genetic differentiation index (FST) of 0.072 (p=0.011). The multi-locus genetic analysis of the 12 MS revealed all the parasites had unique haplotypes. Significant linkage disequilibrium (LD) was observed in all the five parasite populations. Kisumu had the most significant index of association values (0.16; p<0.0001) whereas Kisii had the least significant index of association values (0.03; p<0.0001). Our data suggest high genetic diversity in Kenyan parasite population with the exception of parasite from Malindi where malaria has been on the decline. The presence of significant LD suggests that there is occurrence of inbreeding in the parasite population. Parasite populations from Kisii showed the strongest evidence for epidemic population structure whereas the rest of the regions showed panmixia. Defining the genetic diversity of the parasites in different ecological regions of Kenya after introduction of the artemether-lumefantrine is important in refining the spread of drug resistant strains and malaria transmission for more effective control and eventual elimination of malaria in Kenya.


88. Kinyoki DK, Berkley JA, Moloney GM, Odundo EO, Kandala NB, Noor AM. Space-
Abstract

Objective: To determine the sub-national seasonal prevalence and trends in wasting from 2007 to 2010 among children aged 6-59 months in Somalia using remote sensing and household survey data from nutritional surveys.

Methods: Bayesian hierarchical space-time model was implemented using a stochastic partial differential equation (SPDE) approach in integrated nested Laplace approximations (INLA) to produce risk maps of wasting at 1 × 1 km(2) spatial resolution and predict to seasons in each year of study from 2007 to 2010.

Results: The prevalence of wasting was generally at critical levels throughout the country, with most of the areas remaining in the upper classes of critical and very critical levels. There was minimal variation in wasting from year-to-year, but a well-defined seasonal variation was observed. The mean difference of the prevalence of wasting between the dry and wet season ranges from 0% to 5%. The risks of wasting in the South Central zone were highest in the Gedo (37%) and Bay (32%) regions. In North East zone the risk was highest in Nugaal (25%) and in the North West zone the risk was high in Awdal and Woqooyi Galbeed regions with 23%.

Conclusion: There was a clear seasonal variation in wasting with minimal year-to-year variability from 2007 to 2010 in Somalia. The prevalence was high during the long dry season, which affects the prevalence in the preceding long rainy season. Understanding the seasonal fluctuations of wasting in different locations and at different times is important to inform timely interventions.


Abstract

Background: Stunting among children under five years old is associated with long-term effects on cognitive development, school achievement, economic productivity in adulthood.
and maternal reproductive outcomes. Accurate estimation of stunting and tools to forecast risk are key to planning interventions. We estimated the prevalence and distribution of stunting among children under five years in Somalia from 2007 to 2010 and explored the role of environmental covariates in its forecasting.

Methods: Data from household nutritional surveys in Somalia from 2007 to 2010 with a total of 1,066 clusters covering 73,778 children were included. We developed a Bayesian hierarchical space-time model to forecast stunting by using the relationship between observed stunting and environmental covariates in the preceding years. We then applied the model coefficients to environmental covariates in subsequent years. To determine the accuracy of the forecasting, we compared this model with a model that used data from all the years with the corresponding environmental covariates.

Results: Rainfall (OR = 0.994, 95 % Credible interval (CrI): 0.993, 0.995) and vegetation cover (OR = 0.719, 95 % CrI: 0.603, 0.858) were significant in forecasting stunting. The difference in estimates of stunting using the two approaches was less than 3 % in all the regions for all forecast years.

Conclusion: Stunting in Somalia is spatially and temporally heterogeneous. Rainfall and vegetation are major drivers of these variations. The use of environmental covariates for forecasting of stunting is a potentially useful and affordable tool for planning interventions to reduce the high burden of malnutrition in Somalia.


Abstract

Almost one-quarter of the world's population is infected with soil-transmitted helminths (STH). We conducted a study to determine the prevalence and location of STH-Ascaris, Trichuris, and hookworm spp.-egg contamination in soil within rural household plots in Kenya. Field staff collected soil samples from July to September 2014 from the house entrance and the latrine entrance of households in Kakamega County; additional spatial sampling was conducted at a subset of households (N = 22 samples from 3 households). We analyzed soil samples using a modified version of the US Environmental Protection Agency (EPA) method for enumerating Ascaris in biosolids. We found 26.8% of households had one or more species of STH eggs present in the soil in at least one household location (n = 18 out of 67
households), and Ascaris was the most commonly detected STH (19.4%, n = 13 out of 67 households). Prevalence of STH eggs in soil was equally likely at the house entrance (19.4%, N = 67) as at the latrine entrance (11.3%, N = 62) (p = 0.41). We also detected STH eggs at bathing and food preparation areas in the three houses revisited for additional spatial sampling, indicating STH exposure can occur at multiple sites within a household plot, not just near the latrine. The highest concentration of eggs in one house occurred in the child's play area. Our findings suggest interventions to limit child exposure to household soil could complement other STH control strategies.


Abstract

Background: Undernutrition remains highly prevalent in African children, highlighting the need for accurately assessing dietary intake. In order to do so, the assessment method must be validated in the target population. A triple pass 24 hour dietary recall with volumetric portion size estimation has been described but not previously validated in African children. This study aimed to establish the relative validity of 24-hour dietary recalls of daily food consumption in healthy African children living in Mbale and Soroti, eastern Uganda compared to simultaneous weighed food records.

Methods: Quantitative assessment of daily food consumption by weighed food records followed by two independent assessments using triple pass 24-hour dietary recall on the following day. In conjunction with household measures and standard food sizes, volumes of liquid, dry rice, or play dough were used to aid portion size estimation. Inter-assessor agreement, and agreement with weighed food records was conducted primarily by Bland-Altman analysis and secondly by intraclass correlation coefficients and quartile cross-classification.

Results: 19 healthy children aged 6 months to 12 years were included in the study. Bland-Altman analysis showed 24-hour recall only marginally under-estimated energy (mean difference of 149kJ or 2.8%; limits of agreement -1618 to 1321kJ), protein (2.9g or 9.4%; -12.6 to 6.7g), and iron (0.43mg or 8.3%; -3.1 to 2.3mg). Quartile cross-classification was correct in 79% of cases for energy intake, and 89% for both protein and iron. The intraclass
Correlation coefficient between the separate dietary recalls for energy was 0.801 (95% CI, 0.429-0.933), indicating acceptable inter-observer agreement.

**Conclusions:** Dietary assessment using 24-hour dietary recall with volumetric portion size estimation resulted in similar and acceptable estimates of dietary intake compared with weighed food records and thus is considered a valid method for daily dietary intake assessment of children in communities with similar diets. The method will be utilised in a sub-study of a large randomised controlled trial addressing treatment in severe childhood anaemia.


**Abstract**

An influenza pandemic caused by a novel influenza virus A(H1N1)pdm09 spread worldwide in 2009 and is estimated to have caused between 151,700 and 575,400 deaths globally. While whole genome data on new virus enables a deeper insight in the pathogenesis, epidemiology, and drug sensitivities of the circulating viruses, there are relatively limited complete genetic sequences available for this virus from African countries. We describe herein the full genome analysis of influenza A(H1N1)pdm09 viruses isolated in Kenya between June 2009 and August 2010. A total of 40 influenza A(H1N1)pdm09 viruses isolated during the pandemic were selected. The segments from each isolate were amplified and directly sequenced. The resulting sequences of individual gene segments were concatenated and used for subsequent analysis. These were used to infer phylogenetic relationships and also to reconstruct the time of most recent ancestor, time of introduction into the country, rates of substitution and to estimate a time-resolved phylogeny. The Kenyan complete genome sequences clustered with globally distributed clade 2 and clade 7 sequences but local clade 2 viruses did not circulate beyond the introductory foci while clade 7 viruses disseminated country wide. The time of the most recent common ancestor was estimated between April and June 2009, and distinct clusters circulated during the pandemic. The complete genome had an estimated rate of nucleotide substitution of 4.9x10(-3) substitutions/site/year and greater diversity in surface expressed proteins was observed. We show that two clades of influenza A(H1N1)pdm09 virus were introduced into Kenya from the UK and the pandemic was sustained as a result of importations. Several closely related but distinct clusters co-circulated locally during the peak pandemic phase but only one cluster dominated in the late phase of the pandemic suggesting that it possessed greater adaptability.

**Abstract**  
**Background:** HIV infection has been associated with impaired language development in prenatally exposed children. Although most of the burden of HIV occurs in sub-Saharan Africa, there have not been any comprehensive studies of HIV exposure on multiple aspects of language development using instruments appropriate for the population.  
**Methods:** We compared language development in children exposed to HIV in utero to community controls (N = 262, 8-30 months) in rural Kenya, using locally adapted and validated communicative development inventories.  
**Results:** The mean score of the younger HIV-exposed uninfected infants (8-15 months) was not significantly below that of the controls; however older HIV-exposed uninfected children had significantly poorer language scores, with HIV positive children scoring more poorly than community controls, on several measures.  
**Conclusions:** Our preliminary data indicates that HIV infection is associated with impaired early language development, and that the methodology developed would be responsive to a more detailed investigation of the variability in outcome amongst children exposed to HIV, irrespective of their infection status.  
|---|---|
**Abstract**  
No data exist on hepatitis B virus (HBV) incidence among African men who have sex with men (MSM). We tested plasma samples archived between 2005 and 2014 for HBV core antibody or surface antigen seroconversion in a cohort of 312 initially human immunodeficiency virus (HIV)-1-negative MSM with no evidence of prior HBV infection. |
Hepatitis B virus incidence was 6.0/100 person-years (95% confidence interval [CI], 3.9-9.1). Hepatitis B virus acquisition was associated with being uncircumcised (adjusted incidence rate ratio [aIRR], 5.0; 95% CI, 1.5-16.8), recent HIV-1 acquisition (aIRR, 2.9; 95% CI, 1.1-7.7), rape (aIRR, 5.0; 95% CI, 1.2-20.4), and any tertiary education (aIRR, 3.2; 95% CI, 1.1-9.7). African MSM have a substantial risk of HBV acquisition and require vaccination urgently.


Abstract

Background: The upsurge in the uptake of antiretroviral therapy (ART) has led to a significant increase in the survival of vertically acquired HIV infected children, many of whom are currently living into adolescence and early adulthood. However little if anything is known of the lived experiences and the challenges faced by HIV positive adolescents in the African context. We set out to investigate psychosocial challenges faced by HIV infected adolescents on the Kenyan coast.

Methods: A total of 44 participants (12 HIV-infected adolescents, 7 HIV uninfected adolescents, and 25 key informants) took part in this qualitative study, using individually administered in-depth interviews. A framework approach was used to analyze the data using NVIVO software.

Results: We observed that the challenges faced by adolescents in rural Kenya could be placed into six major themes: poverty, poor mental and physical health, the lack of a school system that is responsive to their needs, challenges in how to disclose to peers and family members, high levels of stigma in its various forms, and challenges of medical adherence leading to the need for close monitoring.

Conclusion: In this African community, vertically acquired HIV-infected adolescents face a complex set of social, economic and medical challenges. Our study points to the urgent need to develop multisectorial intervention support programmes to fully address these challenges.


Abstract

Background: Malaria among school children is increasingly receiving attention, yet the burden of malaria in this age group is poorly defined. This study presents data on malaria morbidity among school children in Bungoma county, western Kenya.

Method: This study investigated the burden and risk factors of Plasmodium falciparum infection, clinical malaria, and anaemia among 2346 school children aged 5-15 years, who were enrolled in an individually randomized trial evaluating the effect of anthelmintic treatment on the risks of malaria. At baseline, children were assessed for anaemia and nutritional status and information on household characteristics was collected. Children were followed-up for 13 months to assess the incidence of clinical malaria by active detection, and P. falciparum infection and density evaluated using repeated cross-sectional surveys over 15 months.

Results: On average prevalence of P. falciparum infection was 42% and ranged between 32 and 48% during the five cross-sectional surveys. Plasmodium falciparum prevalence was significantly higher among boys than girls. The overall incidence of clinical malaria was 0.26 episodes per person year (95% confidence interval, 0.24-0.29) and was significantly higher among girls (0.23 versus 0.31, episodes per person years). Both infection prevalence and clinical disease varied by season. In multivariable analysis, P. falciparum infection was associated with being male, lower socioeconomic status and stunting. The risk of clinical malaria was associated with being female.

Conclusion: These findings show that the burden of P. falciparum parasitaemia, clinical malaria and anaemia among school children is not insignificant, and suggest that malaria control programmes should be expanded to include this age group.

Abstract

Cost-effective HIV prevention programs should target persons at high risk of HIV acquisition. We conducted an observational HIV incidence cohort study in Kisumu, Kenya, where HIV prevalence is triple that of the national rate. We used referral and venue-sampling approaches to enroll HIV-negative persons for a 12-month observational cohort, August 2010 to September 2011, collected data using computer-assisted interviews, and performed HIV testing quarterly. Among 1292 eligible persons, 648 (50%) were excluded for HIV positivity and other reasons. Of the 644 enrollees, 52% were women who were significantly older than men (P<.01). In all, 7 persons seroconverted (incidence rate [IR] per 100 person-years=1.11; 95% confidence interval [CI] 0.45-2.30), 6 were women; 5 (IR=3.14; 95% CI 1.02-7.34) of whom were ≤25 years. Most new infections occurred in young women, an observation consistent with other findings in sub-Saharan Africa that women aged ≤25 years are an important population for HIV intervention trials in Africa.


Abstract

Background: Antiretroviral therapy scale-up in Sub-Saharan Africa has created a growing, aging HIV-positive population at risk for non-communicable diseases such as hypertension. However, the prevalence and risk factors for hypertension in this population remain incompletely understood.

Methods: We measured blood pressure and collected demographic data on over 65,000 adults attending multi-disease community health campaigns in 20 rural Ugandan communities (SEARCH Study: NCT01864603). Our objectives were to determine (i) whether HIV is an independent risk factor for hypertension, and (ii) awareness and control of hypertension in HIV-positive adults and the overall population.

Results: Hypertension prevalence was 14% overall, and 11% among HIV-positive individuals. 79% of patients were previously undiagnosed, 85% were not taking medication, and 50% of patients on medication had uncontrolled blood pressure. Multivariate predictors of
hypertension included older age, male gender, higher BMI, lack of education, alcohol use, and residence in Eastern Uganda. HIV-negative status was independently associated with higher odds of hypertension (OR 1.2, 95% CI: 1.1-1.4). Viral suppression of HIV did not significantly predict hypertension among HIV-positives.

**Significance:** The burden of hypertension is substantial and inadequately controlled, both in HIV-positive persons and overall. Universal HIV screening programs could provide counseling, testing, and treatment for hypertension in Sub-Saharan Africa.


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**Abstract**

**Background:** With more than half of Africa's population expected to live in urban settlements by 2030, the burden of malaria among urban populations in Africa continues to rise with an increasing number of people at risk of infection. However, malaria intervention across Africa remains focused on rural, highly endemic communities with far fewer strategic policy directions for the control of malaria in rapidly growing African urban settlements. The complex and heterogeneous nature of urban malaria requires a better understanding of the spatial and temporal patterns of urban malaria risk in order to design effective urban malaria control programs. In this study, we use remotely sensed variables and other environmental covariates to examine the predictability of intra-urban variations of malaria infection risk across the rapidly growing city of Dar es Salaam, Tanzania between 2006 and 2014.

**Methods:** High resolution SPOT satellite imagery was used to identify urban environmental factors associated malaria prevalence in Dar es Salaam. Supervised classification with a random forest classifier was used to develop high resolution land cover classes that were combined with malaria parasite prevalence data to identify environmental factors that influence localized heterogeneity of malaria transmission and develop a high resolution predictive malaria risk map of Dar es Salaam.

**Results:** Results indicate that the risk of malaria infection varied across the city. The risk of infection increased away from the city centre with lower parasite prevalence predicted in administrative units in the city centre compared to administrative units in the peri-urban suburbs. The variation in malaria risk within Dar es Salaam was shown to be influenced by varying environmental factors. Higher malaria risks were associated with proximity to dense
vegetation, inland water and wet/swampy areas while lower risk of infection was predicted in densely built-up areas.

**Conclusions:** The predictive maps produced can serve as valuable resources for municipal councils aiming to shrink the extents of malaria across cities, target resources for vector control or intensify mosquito and disease surveillance. The semi-automated modelling process developed can be replicated in other urban areas to identify factors that influence heterogeneity in malaria risk patterns and detect vulnerable zones. There is a definite need to expand research into the unique epidemiology of malaria transmission in urban areas for focal elimination and sustained control agendas.


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**Abstract**

**Introduction:** Cancer registration is an important activity for informing cancer control activities. Cancer registries in Sub-Saharan Africa have limited resources to effectively operate because of competing priorities. To date, there has not been an assessment of the resources and funding needed to perform all the activities essential for cancer registration in Kenya. Evidence will help registries to quantify and advocate for the funds needed to sustain, enhance, and expand high quality cancer registration in Kenya.

**Methods:** In this study, we used the Centers for Disease Control and Prevention's (CDC’s) International Registry Costing Tool (IntRegCosting Tool) to evaluate the funding, cost, and labor resources used to perform the cancer registry operations in Nairobi County for two annual periods between July 2012 and June 2014.

**Results:** Funding from grants, research studies, and international organizations provided 70% of the registry operations’ cost. For both time periods, the most-costly registry activities were related to administration, management, and training, along with data acquisition activities such as data abstraction, entry, and validation. Even among these core registry activities, however, substantial variations existed.

**Conclusions:** Stable funding for cancer registry operations is necessary to sustain core registry activities in other to deliver high-quality data, which in turn is necessary to foster evidence-
based policies to improve cancer outcomes. As stakeholders look into expanding the Nairobi Cancer Registry into a national program, the cost data provided in this study will help justify the funding required for sustaining and expanding registry activities.


Abstract

Bacteremia and malaria coinfection is a common and life-threatening condition in children residing in sub-Saharan Africa. We previously showed that coinfection with Gram negative (G[-]) enteric Bacilli and Plasmodium falciparum (Pf[+]) was associated with reduced high-density parasitemia (HDP, >10,000 parasites/μL), enhanced respiratory distress, and severe anemia. Since inflammatory mediators are largely unexplored in such coinfections, circulating cytokines were determined in four groups of children (n = 206, aged <3 yrs): healthy; Pf[+] alone; G[-] coinfected; and G[+] coinfected. Staphylococcus aureus and non-Typhi Salmonella were the most frequently isolated G[+] and G[-] organisms, respectively. Coinfected children, particularly those with G[-] pathogens, had lower parasite burden (peripheral and geometric mean parasitemia and HDP). In addition, both coinfected groups had increased IL-4, IL-5, IL-7, IL-12, IL-15, IL-17, IFN-γ, and IFN-α and decreased TNF-α relative to malaria alone. Children with G[-] coinfection had higher IL-1β and IL-1Ra and lower IL-10 than the Pf[+] group and higher IFN-γ than the G[+] group. To determine how the immune response to malaria regulates parasitemia, cytokine production was investigated with a multiple mediation model. Cytokines with the greatest mediational impact on parasitemia were IL-4, IL-10, IL-12, and IFN-γ. Results here suggest that enhanced immune activation, especially in G[-] coinfected children, acts to reduce malaria parasite burden.


Abstract

Background: Pragmatic randomized trials aim to examine the effects of interventions in the full spectrum of patients seen by clinicians who receive routine care. Such trials should be employed in parallel with efforts to implement many interventions which appear promising but where evidence of effectiveness is limited. We illustrate this need taking the case of essential interventions to reduce inpatient neonatal mortality in low and middle income countries (LMIC) but suggest the arguments are applicable in most clinical areas.

Discussion: A set of basic interventions have been defined, based on available evidence, that could substantially reduce early neonatal deaths if successfully implemented at scale within district and sub-district hospitals in LMIC. However, we illustrate that there remain many gaps in the evidence available to guide delivery of many inpatient neonatal interventions, that existing evidence is often from high income settings and that it frequently indicates uncertainty in the magnitude or even direction of estimates of effect. Furthermore generalizing results to LMIC where conditions include very high patient staff ratios, absence of even basic technologies, and a reliance on largely empiric management is problematic. Where there is such uncertainty over the effectiveness of interventions in different contexts or in the broad populations who might receive the intervention in routine care settings pragmatic trials that preserve internal validity while promoting external validity should be increasingly employed. Many interventions are introduced without adequate evidence of their effectiveness in the routine settings to which they are introduced. Global efforts are needed to support pragmatic research to establish the effectiveness in routine care of many interventions intended to reduce mortality or morbidity in LMIC. Such research should be seen as complementary to efforts to optimize implementation.


Abstract

Background: Behavioural/emotional problems may be common in preschool children living in resource-poor settings, but assessment of these problems in preschool children from poor areas is challenging owing to lack of appropriate behavioural screening tools. The child behaviour checklist (CBCL) is widely known for its reliability in identifying
behavioural/emotional problems in preschool children, but it has not been validated for use in sub-Saharan Africa.

**Methods:** With permission from developers of CBCL, we translated this tool into Ki-Swahili and adapted the items to make them culturally appropriate and contextually relevant and examined the psychometric properties of the CBCL, particularly reliability, validity and factorial structure in a Kenyan community preschool sample of 301 children. It was also re-administered after 2 weeks to 38 randomly selected respondents, for the purpose of evaluating retest reliability. To evaluate inter-informant reliability, the CBCL was administered to 46 respondents (17 alternative caretakers and 29 fathers) alongside the child's mother. Generalised linear model was used to measure associations with behavioural/emotional scores. We used structural equation modelling to perform a confirmatory factor analysis to examine the seven-syndrome CBCL structure.

**Results:** During the first phase we found that most of the items could be adequately translated and easily understood by the participants. The inter-informant agreement for CBCL scores was excellent between the mothers and other caretakers [Pearson's correlation coefficient (r) = 0.89, p < 0.001] and fathers (r = 0.81; p < 0.001). The test-retest reliability was acceptable (r = 0.76; p < 0.001). The scale internal consistency coefficients were excellent for total problems [Cronbach's alpha (α) = 0.95] and between good and excellent for most CBCL sub-scales (α = 0.65-0.86). Behavioural/emotional scores were associated with pregnancy complications [adjusted beta coefficient (β) = 0.44 (95 % CI, 0.07-0.81)] and adverse perinatal events [β = 0.61 (95 % CI, 0.09-1.13)] suggesting discriminant validity of the CBCL. Most fit indices for the seven-syndrome CBCL structure were within acceptable range, being <0.09 for root mean squared error of approximation and >0.90 for Tucker-Lewis Index and Comparative Fit Index.

**Conclusion:** The CBCL has good psychometric properties and the seven-syndrome structure fits well with the Kenyan preschool children suggesting it can be used to assess behavioural/emotional problems in this rural area.

**Pubmed link:** https://pubmed.ncbi.nlm.nih.gov/26793272/

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**Abstract**

**Background:** Fever is common among patients seeking care in sub-Saharan Africa (sSA), but causes other than malaria are rarely diagnosed. We assessed dengue and chikungunya virus
infections among young febrile adults evaluated for acute HIV infection (AHI) and malaria in coastal Kenya.

Methods: We tested plasma samples obtained in a cross-sectional study from febrile adult patients aged 18-35 years evaluated for AHI and malaria at urgent care seeking at seven health facilities in coastal Kenya in 2014-2015. Dengue virus (DENV) and chikungunya virus (CHIKV) were amplified using quantitative real-time reverse-transcription polymerase chain reaction. We conducted logistic regression analyses to determine independent predictors of dengue virus infection.

Results: 489 samples that were negative for both AHI and malaria were tested, of which 43 (8.8%, 95% confidence interval [CI]: 6.4-11.7) were positive for DENV infection. No participant was positive for CHIKV infection. DENV infections were associated with clinic visits in the rainy season (adjusted odds ratio (AOR) = 3.0, 95% CI: 1.3-6.5) and evaluation at a private health facility (AOR 5.2, 95% CI: 2.0-13.1) or research health facility (AOR = 25.6, 95% CI: 8.9-73.2) instead of a public health facility.

Conclusion: A high prevalence of DENV infections was found in febrile young adult patients evaluated for AHI. Our data suggests that DENV, along with AHI and malaria, should be considered in the differential diagnosis of the adult patient seeking care for fever in coastal Kenya.


Abstract

HIV is still a major health problem in developing countries. Even though high HIV-risk-taking behaviors have been reported in African fishing villages, local distribution patterns of HIV infection in the communities surrounding these villages have not been thoroughly analyzed. The objective of this study was to investigate the geographical distribution patterns of HIV infection in communities surrounding African fishing villages. In 2011, we applied age- and sex-stratified random sampling to collect 1,957 blood samples from 42,617 individuals registered in the Health and Demographic Surveillance System in Mbita, which is located on the shore of Lake Victoria in western Kenya. We used these samples to evaluate existing antibody detection assays for several infectious diseases, including HIV antibody titers. Based
on the results of the assays, we evaluated the prevalence of HIV infection according to sex, age, and altitude of participating households. We also used Kulldorff's spatial scan statistic to test for HIV clustering in the study area. The prevalence of HIV at our study site was 25.3%. Compared with the younger age group (15-19 years), adults aged 30-34 years were 6.71 times more likely to be HIV-positive, and the estimated HIV-positive population among women was 1.43 times larger than among men. Kulldorff's spatial scan statistic detected one marginally significant ($P = 0.055$) HIV-positive and one significant HIV-negative cluster ($P = 0.047$) in the study area. These results suggest a homogeneous HIV distribution in the communities surrounding fishing villages. In addition to individual behavior, more complex and diverse factors related to the social and cultural environment can contribute to a homogeneous distribution pattern of HIV infection outside of African fishing villages. To reduce rates of transmission in HIV-endemic areas, HIV prevention and control programs optimized for the local environment need to be developed.


**Abstract**

**Objective:** To share approaches and innovations adopted to deliver a relatively inexpensive clinical data management (CDM) framework within a low-income setting that aims to deliver quality pediatric data useful for supporting research, strengthening the information culture and informing improvement efforts in local clinical practice.

**Materials and methods:** The authors implemented a CDM framework to support a Clinical Information Network (CIN) using Research Electronic Data Capture (REDCap), a noncommercial software solution designed for rapid development and deployment of electronic data capture tools. It was used for collection of standardized data from case records of multiple hospitals' pediatric wards. R, an open-source statistical language, was used for data quality enhancement, analysis, and report generation for the hospitals.

**Results:** In the first year of CIN, the authors have developed innovative solutions to support the implementation of a secure, rapid pediatric data collection system spanning 14 hospital sites with stringent data quality checks. Data have been collated on over 37 000 admission episodes, with considerable improvement in clinical documentation of admissions observed. Using meta-programming techniques in R, coupled with branching logic, randomization, data
lookup, and Application Programming Interface (API) features offered by REDCap, CDM tasks were configured and automated to ensure quality data was delivered for clinical improvement and research use.

**Conclusion:** A low-cost clinically focused but geographically dispersed quality CDM (Clinical Data Management) in a long-term, multi-site, and real world context can be achieved and sustained and challenges can be overcome through thoughtful design and implementation of open-source tools for handling data and supporting research.


**Abstract**

**Background:** In 2012, the Kenyan Ministries of Health and of Education began a programme to deworm all school-age children living in areas at high risk of soil-transmitted helminths (STH) and schistosome infections. The impact of this school-based mass drug administration (MDA) programme in Kenya is monitored by the Kenya Medical Research Institute (KEMRI) as part of a five-year (2012-2017) study. This article focuses on the impact of MDA on STH infections and presents the overall achieved reductions from baseline to mid-term, as well as yearly patterns of reductions and subsequent re-infections per school community.

**Methods:** The study involved a series of pre- and post-intervention, repeat cross-sectional surveys in a representative, stratified, two-stage sample of schools across Kenya. The programme contained two tiers of monitoring: a national baseline and mid-term survey including 200 schools, and surveys conducted among 60 schools pre- and post-intervention. Stool samples were collected from randomly selected school children and tested for helminth infections using Kato-Katz technique. The prevalence and mean intensity of each helminth species were calculated at the school and county levels and 95% confidence intervals (CIs) were obtained by binomial and negative binomial regression, respectively, taking into account clustering by schools.

**Results:** The overall prevalence of STH infection at baseline was 32.3% (hookworms: 15.4%; Ascaris lumbricoides: 18.1%; and Trichuris trichiura: 6.7%). After two rounds of MDA,
the overall prevalence of STH had reduced to 16.4% (hookworms: 2.3%; A. lumbricoides: 11.9%; and T. trichiura: 4.5%). The relative reductions of moderate to heavy intensity of infections were 33.7% (STH combined), 77.3% (hookworms) and 33.9% (A. lumbricoides). For T. trichiura, however, moderate to heavy intensity of infections increased non-significantly by 18.0% from baseline to mid-term survey.

**Conclusion:** The school-based deworming programme has substantially reduced STH infections, but because of ongoing transmission additional strategies may be required to achieve a sustained interruption of transmission.


**Abstract**

**Background:** Sickle cell anemia (SCA) is an inherited hematological disorder that causes a large but neglected global health burden, particularly in Africa. Hydroxyurea represents the only available disease-modifying therapy for SCA, and has proven safety and efficacy in high-resource countries. In sub-Saharan Africa, there is minimal use of hydroxyurea, due to lack of data, absence of evidence-based guidelines, and inexperience among healthcare providers.

**Procedure:** A partnership was established between investigators in North America and sub-Saharan Africa, to develop a prospective multicenter research protocol designed to provide data on the safety, feasibility, and benefits of hydroxyurea for children with SCA.

**Results:** The Realizing Effectiveness Across Continents with Hydroxyurea (REACH, ClinicalTrials.gov NCT01966731) trial is a prospective, phase I/II open-label dose escalation study of hydroxyurea that will treat a total of 600 children age 1-10 years with SCA: 150 at each of four different clinical sites within sub-Saharan Africa (Angola, Democratic Republic of Congo, Kenya, and Uganda). The primary study endpoint will be severe hematological toxicities that occur during the fixed-dose treatment phase. REACH has an adaptive statistical design that allows for careful assessment of toxicities to accurately identify a safe hydroxyurea dose.

**Conclusions:** REACH will provide data that address critical gaps in knowledge for the treatment of SCA in sub-Saharan Africa. By developing local expertise with the use of
hydroxyurea and helping to establish treatment guidelines, the REACH trial results will have the potential to transform care for children with SCA in Africa.


Abstract

In many African countries, user fees have failed to achieve intended access and quality of care improvements. Subsequent user fee reduction or elimination policies have often been poorly planned, without alternative sources of income for facilities. We describe early implementation of an innovative national health financing intervention in Kenya: the health sector services fund (HSSF). In HSSF, central funds are credited directly into a facility's bank account quarterly, and facility funds are managed by health facility management committees (HFMCs) including community representatives. HSSF is therefore a finance mechanism with potential to increase access to funds for peripheral facilities, support user fee reduction and improve equity in access. We conducted a process evaluation of HSSF implementation based on a theory of change underpinning the intervention. Methods included interviews at national, district and facility levels, facility record reviews, a structured exit survey and a document review. We found impressive achievements: HSSF funds were reaching facilities; funds were being overseen and used in a way that strengthened transparency and community involvement; and health workers' motivation and patient satisfaction improved. Challenges or unintended outcomes included: complex and centralized accounting requirements undermining efficiency; interactions between HSSF and user fees leading to difficulties in accessing crucial user fee funds; and some relationship problems between key players. Although user fees charged had not increased, national reduction policies were still not being adhered to. Finance mechanisms can have a strong positive impact on peripheral facilities, and HFMCs can play a valuable role in managing facilities. Although fiduciary oversight is essential, mechanisms should allow for local decision-making and ensure that unmanageable paperwork is avoided. There are also limits to what can be achieved with relatively small funds in contexts of enormous need. Process evaluations tracking (un)intended consequences of interventions can contribute to regional financing and decentralization debates.


Abstract

Objectives: Emotional/behavioral disorders are often comorbid with childhood epilepsy, but both may be predicted by social disadvantage and fetal risk indicators (FRIs). We used data from a British birth cohort, to assess the association of epilepsy, single unprovoked seizures, and febrile seizures with the later development of emotional/behavioral problems.

Methods: A total of 17,416 children in the 1958 British birth cohort were followed up until age 16 years. Logistic and modified Poisson regression models were used to determine a) the association of social disadvantage at birth and FRI with epilepsy, single unprovoked seizures, and febrile seizures at 7 years, and emotional/behavioral disorders in later childhood, and (ii) the association of childhood seizures by age 7 years with emotional/behavioral disorders in later childhood, after accounting for social disadvantage and FRI.

Results: Higher scores on FRI and social disadvantage were associated with emotional/behavioral problems at 7, 11, and 16 years, but not with seizure disorders at age 7 years. Epilepsy was associated with emotional/behavioral problems at 7 years (odds ratio [OR] = 2.50, 95% confidence interval [CI] = 1.29-4.84), 11 years (OR = 2.00, 95% CI = 1.04-3.81), and 16 years (OR = 5.47, 95% CI = 1.65-18.08), whereas single unprovoked seizures were associated with emotional/behavioral problems at 16 years (OR = 1.44, 95% CI = 1.02-2.01), after adjustment for FRI and social disadvantage. Febrile convulsions were not associated with increased risk for emotional/behavioral problems.

Conclusions: Emotional/behavioral problems in children are related to an earlier diagnosis of epilepsy and single unprovoked seizures after accounting for social disadvantage and FRI, whereas febrile convulsions are not associated with emotional/behavioral problems.


Abstract
**Background:** Naturally acquired immunity to malaria may be lost with lack of exposure. Recent heterogeneous reductions in transmission in parts of Africa mean that large populations of previously protected people may lose their immunity while remaining at risk of infection.

**Methods:** Using two ethnically similar long-term cohorts of children with historically similar levels of exposure to Plasmodium falciparum who now experience very different levels of exposure, we assessed the effect of decreased parasite exposure on antimalarial immunity. Peripheral blood mononuclear cells (PBMCs) from children in each cohort were stimulated with P. falciparum and their P. falciparum-specific proliferative and cytokine responses were compared.

**Results:** We demonstrate that, while P. falciparum-specific CD4+ T cells are maintained in the absence of exposure, the proliferative capacity of these cells is altered considerably. P. falciparum-specific CD4+ T cells isolated from children previously exposed, but now living in an area of minimal exposure ("historically exposed") proliferate significantly more upon stimulation than cells isolated from children continually exposed to the parasite. Similarly, PBMCs from historically exposed children expressed higher levels of pro-inflammatory cytokines and lower levels of anti-inflammatory cytokines after stimulation with P. falciparum. Notably, we found a significant positive association between duration since last febrile episode and P. falciparum-specific CD4+ T cell proliferation, with more recent febrile episodes associated with lower proliferation.

**Conclusion:** Considered in the context of existing knowledge, these data suggest a model explaining how immunity is lost in absence of continuing exposure to P. falciparum.


**Abstract**

Inadequate protection of water sources, and poor household hygienic and handling practices have exacerbated fecal water contamination in Kenya. This study evaluated the rate and correlates of thermotolerant coliform (TTC) household water contamination in Kericho District, Western Kenya. Culture and multiplex polymerase chain reaction (PCR) techniques were used to characterize TTCs. The disk diffusion method was used for antibiotic susceptibility profiling of pathogenic Escherichia coli. Out of the 103 households surveyed, 48 (46.6%) had TTC contaminated drinking water (TTC levels of >10 cfu/100 mL). Five of these...
households were contaminated with pathogenic E. coli, including 40% enteroaggregative E. coli, 40% enterotoxigenic E. coli, and 20% enteropathogenic E. coli. All these pathogenic E. coli strains were multidrug resistant to sulfamethoxazole/trimethoprim, ampicillin, tetracycline and ampicillin/sulbactam. Rural household locality, drinking water hand contact, water storage container cleaning practice, hand washing before water withdrawal, water source total coliforms <10 cfu/100 mL, temperature, and free chlorine levels were associated with TTC contamination of household drinking water. Significant proportions of household drinking water in Kericho District are contaminated with TTCs including with pathogenic multidrug-resistant E. coli. Source and household hygiene and practices contribute significantly to drinking water contamination.


Abstract

Background: Although prompt, effective treatment is a cornerstone of malaria control, information on provider adherence to malaria in pregnancy (MIP) treatment guidelines is limited. Incorrect or sub-optimal treatment can adversely affect the mother and fetus. This study assessed provider knowledge of and adherence to national case management guidelines for uncomplicated MIP.

Methods: We conducted a cross-sectional study from September to November 2013, in 51 health facilities (HF) and a randomly-selected sample of 39 drug outlets (DO) in the KEMRI/CDC Health and Demographic Surveillance System area in western Kenya. Provider knowledge of national treatment guidelines was assessed with standardized questionnaires. Correct practice required adequate diagnosis, pregnancy assessment, and treatment with correct drug and dosage. In HF, we conducted exit interviews in all women of childbearing age assessed for fever. In DO, simulated clients posing as first trimester pregnant women or as relatives of third trimester pregnant women collected standardized information.

Results: Correct MIP case management knowledge and practice were observed in 45% and 31% of HF and 0% and 3% of DO encounters, respectively. The correct drug and dosage for pregnancy trimester was prescribed in 62% of HF and 42% of DO encounters; correct prescription occurred less often in first than in second/ third trimesters (HF: 24% vs. 65%, p<0.01; DO: 0% vs. 40%, p<0.01). Sulfadoxine-pyrimethamine, which is not recommended for malaria treatment, was prescribed in 3% of HF and 18% of DO encounters. Exposure to artemether-lumefantrine in first trimester, which is contraindicated, occurred in 29% and 49% of HF and DO encounters, respectively.

Conclusion: This study highlights knowledge inadequacies and incorrect prescribing practices in the treatment of MIP. Particularly concerning is the prescription of contraindicated medications in the first trimester. These issues should be addressed through comprehensive trainings and increased supportive supervision. Additional innovative means to improve care should be explored.


Abstract

Background: Young infants have reduced susceptibility to febrile malaria compared with older children, but the mechanism for this remains unclear. There are conflicting data on the role of passively acquired antibodies. Here, we examine antibody titres to merozoite surface antigens in the protection of children in their first two years of life in two settings with differing malaria transmission intensity and compare these titres to previously established protective thresholds.

Methods: Two cohorts of children aged four to six weeks were recruited in Banfora, Burkina and Keur Soce, Senegal and followed up for two years. Malaria infections were detected by light microscopic examination of blood smears collected at active and passive case detection visits. The titres of antibodies to the Plasmodium falciparum recombinant merozoite proteins (AMA1-3D7, MSP1-19, MSP2-Dd2, and MSP3-3D7) were measured by enzyme-linked immunosorbent assay at 1-6, 9, 12, 15 and 18 months of age and compared with the protective thresholds established in Kenyan children.

Results: Antibody titres were below the protective thresholds throughout the study period and we did not find any association with protection against febrile malaria. Antibodies to AMA1 and MSP1-19 appeared to be markers of exposure in the univariate analysis (and so associated with increasing risk) and adjusting for exposure reduced the strength and significance of this association.

Conclusion: The antibody levels we measured are unlikely to be responsible for the apparent protection against febrile malaria seen in young infants. Further work to identify protective antibody responses might include functional assays and a wider range of antigens.

**Background:** Mental disorders are the leading global cause of years lived with disability; the majority of this burden exists in low and middle income countries (LMICs). Over half of mental illness is attributable to depression and anxiety disorders, both of which have known treatments. While the scarcity of mental health care providers is recognized as a major contributor to the magnitude of untreated disorders in LMICs, studies in LMICs find that evidence-based treatments for depression and anxiety disorders, such as brief, structured psychotherapies, are feasible, acceptable and have strong efficacy when delivered by local non-specialist personnel. However, most mental health treatment studies using non-specialist providers in LMICs deploy traditional efficacy designs (T1) without the benefit of integrated mental health treatment models shown to succeed over vertical interventions or methods derived from new implementation science to speed policy change. Here, we describe an effectiveness-implementation hybrid study that evaluates non-specialist delivery of mental health treatment within an HIV clinic for HIV-positive (HIV+) women affected by gender-based violence (GBV) (HIV+ GBV+) in the Nyanza region of Kenya.

**Methods/design:** In this effectiveness-implementation hybrid type I design, 200 HIV+ women with major depressive disorder (MDD) and posttraumatic stress disorder (PTSD) who are receiving care at a Family AIDS Care Education and Services (FACES)-supported clinic in Kisumu, Kenya will be randomized to: (1) interpersonal psychotherapy (IPT) + treatment as usual (TAU) or (2) TAU, both delivered within the HIV clinic. IPT will consist of 12 weekly 60-minute individual IPT sessions, delivered by non-specialists trained to provide IPT. Primary effectiveness outcomes will include MDD and PTSD diagnosis on the Mini International Diagnostic Interview (MINI). Primary implementation outcomes will include treatment cost-benefit, acceptability, appropriateness, feasibility and fidelity of the IPT delivery within an HIV clinic.

**Discussion:** This trial leverages newly defined effectiveness-implementation hybrid designs to gather data on mental health treatment implementation within an HIV care clinic, while testing the effectiveness of an evidence-based treatment for use with a large underserved population (HIV+ GBV+ women) in Kenya.


Abstract

Objectives: Reproductive tract infections (RTIs), including sexually acquired, among adolescent girls is a public health concern, but few studies have measured prevalence in low-middle-income countries. The objective of this study was to examine prevalence in rural schoolgirls in Kenya against their reported symptoms.

Methods: In 2013, a survey was conducted in 542 adolescent schoolgirls aged 14-17 years who were enrolled in a menstrual feasibility study. Vaginal self-swabbing was conducted after girls were interviewed face-to-face by trained nurses on symptoms. The prevalence of girls with symptoms and laboratory-confirmed infections, and the sensitivity, specificity, positive and negative predictive values of symptoms compared with laboratory results, were calculated.

Results: Of 515 girls agreeing to self-swab, 510 answered symptom questions. A quarter (24%) reported one or more symptoms; most commonly vaginal discharge (11%), pain (9%) or itching (4%). Laboratory tests confirmed 28% of girls had one or more RTI. Prevalence rose with age; among girls aged 16-17 years, 33% had infections. Bacterial vaginosis was the most common (18%), followed by Candida albicans (9%), Chlamydia trachomatis (3%), Trichomonas vaginalis (3%) and Neisseria gonorrhoeae (1%). Reported symptoms had a low sensitivity and positive predictive value. Three-quarters of girls with bacterial vaginosis and C. albicans, and 50% with T. vaginalis were asymptomatic.

Conclusions: There is a high prevalence of adolescent schoolgirls with RTI in rural Kenya. Public efforts are required to identify and treat infections among girls to reduce longer-term sequelae but poor reliability of symptom reporting minimises utility of symptom-based diagnosis in this population.


Abstract

Background: The clinical and epidemiological implications of using ambulatory blood pressure monitoring (ABPM) for the diagnosis of hypertension have not been studied at a
population level in sub-Saharan Africa. We examined the impact of ABPM use among Kenyan adults.

**Methods and results:** We performed a nested case-control study of diagnostic accuracy. We selected an age-stratified random sample of 1248 adults from the list of residents of the Kilifi Health and Demographic Surveillance System in Kenya. All participants underwent a screening blood pressure (BP) measurement. All those with screening BP ≥ 140/90 mm Hg and a random subset of those with screening BP < 140/90 mm Hg were invited to undergo ABPM. Based on the 2 tests, participants were categorized as sustained hypertensive, masked hypertensive, "white coat" hypertensive, or normotensive. Analyses were weighted by the probability of undergoing ABPM. Screening BP ≥ 140/90 mm Hg was present in 359 of 986 participants, translating to a crude population prevalence of 23.1% (95% CI 16.5-31.5%). Age-standardized prevalence of screening BP ≥ 140/90 mm Hg was 26.5% (95% CI 19.3-35.6%). On ABPM, 186 of 415 participants were confirmed to be hypertensive, with crude prevalence of 15.6% (95% CI 9.4-23.1%) and age-standardized prevalence of 17.1% (95% CI 11.0-24.4%). Age-standardized prevalence of masked and white coat hypertension were 7.6% (95% CI 2.8-13.7%) and 3.8% (95% CI 1.7-6.1%), respectively. The sensitivity and specificity of screening BP measurements were 80% (95% CI 73-86%) and 84% (95% CI 79-88%), respectively. BP indices and validity measures showed strong age-related trends.

**Conclusions:** Screening BP measurement significantly overestimated hypertension prevalence while failing to identify ≈50% of true hypertension diagnosed by ABPM. Our findings suggest significant clinical and epidemiological benefits of ABPM use for diagnosing hypertension in Kenyan adults.

was higher than the other members' scores by 11%. No significant differences in scores were obtained in relation to duration of REC membership (p = .72), interval since last research ethics training (p = .94), and gender (p = .27). The MERETI tool is thus consistent irrespective of who performs the assessment.


Abstract

Reproduction is important to many HIV-affected individuals and couples and healthcare providers (HCPs) are responsible for providing resources to help them safely conceive while minimizing the risk of sexual and perinatal HIV transmission. In order to fulfill their reproductive goals, HIV-affected individuals and their partners need access to information regarding safer methods of conception. The objective of this qualitative study was to develop a Safer Conception Counseling Toolkit that can be used to train HCPs and counsel HIV-affected individuals and couples in HIV care and treatment clinics in Kenya. We conducted a two-phased qualitative study among HCPs and HIV-affected individuals and couples from eight HIV care and treatment sites in Kisumu, Kenya. We conducted in-depth interviews (IDIs) and focus group discussions (FGDs) to assess the perspectives of HCPs and HIV-affected individuals and couples in order to develop and refine the content of the Toolkit. Subsequently, IDIs were conducted among HCPs who were trained using the Toolkit and FGDs among HIV-affected individuals and couples who were counseled with the Toolkit. HIV-related stigma, fears, and recommendations for delivery of safer conception counseling were assessed during the discussions. One hundred and six individuals participated in FGDs and IDIs; 29 HCPs, 49 HIV-affected women and men, and 14 HIV-serodiscordant couples. Participants indicated that a safer conception counseling and training program for HCPs is needed and that routine provision of safer conception counseling may promote maternal and child health by enhancing reproductive autonomy among HIV-affected couples. They also reported that the Toolkit may help dispel the stigma and fears associated with reproduction in HIV-affected couples, while supporting them in achieving their reproductive goals. Additional research is needed to evaluate the Safer Conception Toolkit in order to support its implementation and use in HIV care and treatment programs in Kenya and other HIV endemic regions of sub-Saharan Africa.


Abstract

Objectives: Conduct a feasibility study on the effect of menstrual hygiene on schoolgirls' school and health (reproductive/sexual) outcomes.

Design: 3-arm single-site open cluster randomised controlled pilot study.

Setting: 30 primary schools in rural western Kenya, within a Health and Demographic Surveillance System.

Participants: Primary schoolgirls 14-16 years, experienced 3 menses, no precluding disability, and resident in the study area.

Interventions: 1 insertable menstrual cup, or monthly sanitary pads, against 'usual practice' control. All participants received puberty education preintervention, and hand wash soap during intervention. Schools received hand wash soap.

Primary and secondary outcome measures: Primary: school attrition (drop-out, absence); secondary: sexually transmitted infection (STI) (Trichomonas vaginalis, Chlamydia trachomatis, Neisseria gonorrhoea), reproductive tract infection (RTI) (bacterial vaginosis, Candida albicans); safety: toxic shock syndrome, vaginal Staphylococcus aureus.

Results: Of 751 girls enrolled 644 were followed-up for a median of 10.9 months. Cups or pads did not reduce school dropout risk (control=8.0%, cups=11.2%, pads=10.2%). Self-reported absence was rarely reported and not assessable. Prevalence of STIs in the end-of-study survey among controls was 7.7% versus 4.2% in the cups arm (adjusted prevalence ratio (aPR) 0.48, 0.24 to 0.96, p=0.039), 4.5% with pads (aPR=0.62; 0.37 to 1.03, p=0.063), and 4.3% with cups and pads pooled (aPR=0.54, 0.34 to 0.87, p=0.012). RTI prevalence was 21.5%, 28.5% and 26.9% among cup, pad and control arms, 71% of which were bacterial vaginosis, with a prevalence of 14.6%, 19.8% and 20.5%, per arm, respectively. Bacterial vaginosis was less prevalent in the cups (12.9%) compared with pads (20.3%, aPR=0.65, 0.44 to 0.97, p=0.034) and control (19.2%, aPR=0.67, 0.43 to 1.04, p=0.075) arm girls enrolled for 9 months or longer. No adverse events were identified.
Conclusions: Provision of menstrual cups and sanitary pads for ~1 school-year was associated with a lower STI risk, and cups with a lower bacterial vaginosis risk, but there was no association with school dropout. A large-scale trial on menstrual cups is warranted.


Abstract

Background: Although anti-malarial medicines are free in Kenyan public health facilities, patients often seek treatment from private sector retail drug outlets. In mid-2010, the Affordable Medicines Facility-malaria (AMFm) was introduced to make quality-assured artemisinin-based combination therapy (ACT) accessible and affordable in private and public sectors.

Methods: Private sector retail drug outlets stocking anti-malarial medications within a surveillance area of approximately 220,000 people in a malaria perennial high-transmission area in rural western Kenya were identified via a census in September 2013. A cross-sectional study was conducted in September–October 2013 to determine availability and price of anti-malarial medicines and malaria rapid diagnostic tests (RDTs) in drug outlets. A standardized questionnaire was administered to collect drug outlet and personnel characteristics and availability and price of anti-malarials and RDTs.

Results: Of 181 drug outlets identified, 179 (99 %) participated in the survey. Thirteen percent were registered pharmacies, 25 % informal drug shops, 46 % general shops, 13 % homesteads and 2 % other. One hundred sixty-five (92 %) had at least one ACT type: 162 (91 %) had recommended first-line artemether-lumefantrine (AL), 22 (12 %) had recommended second-line dihydroartemisinin-piperaquine (DHA-PPQ), 85 (48 %) had sulfadoxine-pyrimethamine (SP), 60 (34 %) had any quinine (QN) formulation, and 14 (8 %) had amodiaquine (AQ) monotherapy. The mean price (range) of an adult treatment course for AL was $1.01 ($0.35-4.71); DHA-PPQ was $4.39 ($0.71-7.06); QN tablets were $2.24 ($0.12-4.71); SP was $0.62 ($0.24-2.35); AQ monotherapy was $0.42 ($0.24-1.06). The mean AL price with or without the AMFm logo did not differ significantly ($1.01 and 1.07, respectively; p = 0.45). Only 17 (10 %) drug outlets had RDTs; 149 (84 %) never stocked RDTs. The mean RDT price was $0.92 ($0.24-2.35).
**Conclusions:** Most outlets never stocked RDTs; therefore, testing prior to treatment was unlikely for customers seeking treatment in the private retail sector. The recommended first-line treatment, AL, was widely available. Although SP and AQ monotherapy are not recommended for treatment, both were less expensive than AL, which might have caused preferential use by customers. Interventions that create community demand for malaria diagnostic testing prior to treatment and that increase RDT availability should be encouraged.


**Abstract**

Improved HIV care has led to an increase in the number of HIV-exposed uninfected (HEU) infants born to HIV-infected women. Although they are uninfected, these infants experience increased morbidity and mortality. One explanation may be that their developing immune system is altered by HIV exposure, predisposing them to increased postnatal infections. We explored the impact of HIV exposure on the B-cell compartment by determining the B-cell subset distribution, the frequency of common vaccine antigen-specific memory B cells (MBCs), and the levels of antibodies to the respective antigens in HEU and HIV-unexposed uninfected (HUU) infants born to uninfected mothers, using flow cytometry, a B-cell enzyme-linked immunosorbent spot assay, and an enzyme-linked immunosorbent assay, respectively, during the first 2 years of life. For the majority of the B-cell subsets, there were no differences between HEU and HUU infants. However, HIV exposure was associated with a lower proportion of B cells in general and MBCs in particular, largely due to a lower proportion of unswitched memory B cells. This reduction was maintained even after correcting for age. These phenotypic differences in the MBC compartment did not affect the ability of HEU infants to generate recall responses to previously encountered antigens or reduce the antigen-specific antibody levels at 18 months of life. Although HIV exposure was associated with a transient reduction in the proportion of MBCs, we found that the ability of HEU infants to mount robust MBC and serological responses was unaffected.


124. Lu L, Zhang SM, Mutuku MW, Mkoji GM, Loker ES. Relative compatibility of
Schistosoma mansoni with Biomphalaria sudanica and B. pfeifferi from Kenya as assessed by PCR amplification of the S. mansoni ND5 gene in conjunction with traditional methods. Parasit Vectors. 2016 Mar 21;9:166

Abstract

Background: Schistosoma mansoni is hosted by several species of Biomphalaria spp. snails in Africa. We were interested in determining if there were differences in compatibility of S. mansoni with Biomphalaria sudanica from Lake Victoria, or with B. pfeifferi from streams and smaller water bodies in Kenya. Does this parasite develop with equal efficiency in both snail species, and does this have implications for transmission in different habitat types?

Methods: Primers for PCR amplification of the S. mansoni ND5 gene were designed and tested for sensitivity and specificity. We exposed laboratory-reared B. sudanica and field-derived B. pfeifferi to single miracidium infections and at 1, 2, 4, 8, 16 and 24 days post-exposure (dpe), snails were extracted for the PCR assay. Snails were also shed for cercariae and/or dissected prior to extraction. Additionally, B. sudanica and B. pfeifferi were collected from field locations and tested with the PCR assay.

Results: The ND5 PCR assay was sensitive (>0.1 fg S. mansoni genomic DNA) and allowed S. mansoni to be differentiated from other relevant schistosome species or snails. The number of PCR positive snails at 1-4 dpe was higher for B. pfeifferi than for B. sudanica, but not significantly so (P = 0.052). From 8-24 dpe, more B. pfeifferi harbored successfully developing parasites (positive by both dissection and PCR) than did B. sudanica (P = 0.008). At 40 dpe, more B. pfeifferi than B. sudanica shed cercariae or harbored dissection positive/PCR positive infections (P < 0.001). Both immature and failed (dissection negative but PCR positive) S. mansoni infections could also be detected in naturally infected snails of both species.

Conclusions: The PCR assay detected S. mansoni infections in snails exposed to one miracidium for one day. Both B. sudanica and B. pfeifferi supported full development of S. mansoni, but B. pfeifferi was more compatible, with significantly more dissection positive/PCR positive or shedding infections, and significantly fewer failed infections (dissection negative/PCR positive). This highlights the relatively lower compatibility of B. sudanica with S. mansoni, and suggests the factors responsible for incompatibility and how they might affect transmission of S. mansoni in habitats like Lake Victoria deserve additional study.


Abstract

**Background:** Although chronic morbidity in humans from soil transmitted helminth (STH) infections can be reduced by anthelmintic treatment, inconsistent diagnostic tools make it difficult to reliably measure the impact of deworming programs and often miss light helminth infections.

**Methods:** Cryopreserved stool samples from 796 people (aged 2-81 years) in four villages in Bungoma County, western Kenya, were assessed using multi-parallel qPCR for 8 parasites and compared to point-of-contact assessments of the same stools by the 2-stool 2-slide Kato-Katz (KK) method. All subjects were treated with albendazole and all Ascaris lumbricoides expelled post-treatment were collected. Three months later, samples from 633 of these people were re-assessed by both qPCR and KK, re-treated with albendazole and the expelled worms collected.

**Results:** Baseline prevalence by qPCR (n = 796) was 17% for A. lumbricoides, 18% for Necator americanus, 41% for Giardia lamblia and 15% for Entamoeba histolytica. The prevalence was <1% for Trichuris trichiura, Ancylostoma duodenale, Strongyloides stercoralis and Cryptosporidium parvum. The sensitivity of qPCR was 98% for A. lumbricoides and N. americanus, whereas KK sensitivity was 70% and 32%, respectively. Furthermore, qPCR detected infections with T. trichiura and S. stercoralis that were missed by KK, and infections with G. lamblia and E. histolytica that cannot be detected by KK. Infection intensities measured by qPCR and by KK were correlated for A. lumbricoides (r = 0.83, p < 0.0001) and N. americanus (r = 0.55, p < 0.0001). The number of A. lumbricoides worms expelled was correlated (p < 0.0001) with both the KK (r = 0.63) and qPCR intensity measurements (r = 0.60).

**Conclusions:** KK may be an inadequate tool for stool-based surveillance in areas where hookworm or Strongyloides are common or where intensity of helminth infection is low after repeated rounds of chemotherapy. Because deworming programs need to distinguish between populations where parasitic infection is controlled and those where further treatment is required, multi-parallel qPCR (or similar high throughput molecular diagnostics) may provide new and important diagnostic information.

Abstract

**Purpose:** The Maternal Malaria and Malnutrition (M3) initiative has pooled together 13 studies with the hope of improving understanding of malaria-nutrition interactions during pregnancy and to foster collaboration between nutritionists and malariologists.

**Participants:** Data were pooled on 14,635 singleton, live birth pregnancies from women who had participated in 1 of 13 pregnancy studies. The 13 studies cover 8 countries in Africa and Papua New Guinea in the Western Pacific conducted from 1996 to 2015.

**Findings to date:** Data are available at the time of antenatal enrolment of women into their respective parent study and at delivery. The data set comprises essential data such as malaria infection status, anthropometric assessments of maternal nutritional status, presence of anaemia and birth weight, as well as additional variables such gestational age at delivery for a subset of women. Participating studies are described in detail with regard to setting and primary outcome measures, and summarised data are available from each contributing cohort.

**Future plans:** This pooled birth cohort is the largest pregnancy data set to date to permit a more definite evaluation of the impact of plausible interactions between poor nutritional status and malaria infection in pregnant women on fetal growth and gestational length. Given the current comparative lack of large pregnancy cohorts in malaria-endemic settings, compilation of suitable pregnancy cohorts is likely to provide adequate statistical power to assess malaria-nutrition interactions, and could point towards settings where such interactions are most relevant. The M3 cohort may thus help to identify pregnant women at high risk of adverse outcomes who may benefit from tailored intensive antenatal care including nutritional supplements and alternative or intensified malaria prevention regimens, and the settings in which these interventions would be most effective.


127. Matoke-Muhia D, Gimnig JE, Kamau L, Shililu J, Bayoh MN, Walker ED. Decline in frequency of the 2La chromosomal inversion in Anopheles gambiae (s.s.) in

Abstract

**Background:** The 2La chromosomal inversion, a genetic polymorphism in An. gambiae (sensu stricto) (s.s.), is associated with adaptation to microclimatic differences in humidity and desiccation resistance and mosquito behaviors. Ownership of insecticide-treated bed nets (ITNs) for malaria control has increased markedly in western Kenya in the last 20 years. An increase in the frequency of ITNs indoors could select against house entering or indoor resting of Anopheles mosquitoes. Thus, the frequency of the 2La inversion is postulated to change in An. gambiae (s.s.) with the increase of ITN ownership over time.

**Methods:** Anopheles gambiae mosquitoes were sampled between 1994 and 2011 using pyrethrum knockdown, bednet traps and human landing catches (HLC) from Asembo and Seme, western Kenya. The 2La inversion was detected by a PCR assay with primers designed for proximal breakpoints of the 2La/a and 2L+(a)/+(a) chromosomal conformation. Mosquitoes were tested for malaria parasite infection by sporozoite ELISA.

**Results:** The frequency of the 2La chromosomal inversion declined from 100 % of all chromosomes in 1994 to 17 % in 2005 and remained low through 2011 (21 %). ITN ownership increased from 0 to > 90 % of houses in the study area during this interval. The decline in the frequency of the 2La chromosomal inversion was significantly, negatively correlated with year \(r = -0.93\) and with increase in ITN ownership \(r = -0.96\). The frequency of the homo- and heterokaryotypes departed significantly from Hardy-Weinberg equilibrium, suggesting that 2La/a karyotype was under selection, earlier in its favor and later, against it. Precipitation and maximum monthly temperature did not vary over time, therefore there was no trend in climate that could account for the decline. There was no significant difference in frequency of the 2La inversion in An. gambiae (s.s.) females sampled indoors or outdoors in HLC in 2011, nor was there an association between the 2La inversion and infection with Plasmodium falciparum sporozoites.

**Conclusions:** The increase in ITN ownership in the study area was negatively correlated with the frequency of 2La inversion. The decline in 2La frequency in western Kenya is postulated to be due to differential impacts of ITNs on mosquitoes with different 2La karyotypes, possibly mediated by differences in behavior associated with the 2La karyotypes. Further research is required to determine if this is a widespread phenomenon, to further determine the association of the 2La karyotypes with mosquito behavior, and to assess whether ITNs are exerting selection mediated by differences in behavior on the different karyotypes.


**Abstract**

The malaria SYBR green assay, which is used to profile in vitro drug susceptibility of *Plasmodium falciparum*, is a reliable drug screening and surveillance tool. Malaria field surveillance efforts provide isolates with various low levels of parasitemia. To be advantageous, malaria drug sensitivity assays should perform reproducibly among various starting parasitemia levels rather than at one fixed initial value. We examined the SYBR green assay standardized procedure developed by the Worldwide Antimalarial Resistance Network (WWARN) for its sensitivity and ability to accurately determine the drug concentration that inhibits parasite growth by 50% (IC50) in samples with a range of initial parasitemia levels. The initial sensitivity determination of the WWARN procedure yielded a detection limit of 0.019% parasitemia. *P. falciparum* laboratory strains and field isolates with various levels of initial parasitemia were then subjected to a range of doses of common antimalarials. The IC50s were comparable for laboratory strains with between 0.0375% and 0.6% parasitemia and for field isolates with between 0.075% and 0.6% parasitemia for all drugs tested. Furthermore, assay quality (Z') analysis indicated that the WWARN procedure displays high robustness, allowing for drug testing of malaria field samples within the derived range of initial parasitemia. The use of the WWARN procedure should allow for the inclusion of more malaria field samples in malaria drug sensitivity screens that would have otherwise been excluded due to low initial parasitemia levels.


**Abstract**

**Background**: Schistosomes and soil-transmitted helminths (STH) (hookworm, *Trichuris trichiura* and *Ascaris lumbricoides*) are widely distributed in developing countries where they
infect over 230 million and 1.5 billion people, respectively. The parasites are frequently co-endemic and many individuals are co-infected with two or more of the species, but information on how the parasites interact in co-infected individuals is scarce. The present study assessed Schistosoma haematobium and STH infection and morbidity patterns among school children in a hyper-endemic focus in the Tana River delta of coastal Kenya.

Methods: Two hundred and sixty-two children aged 5-12 years from two primary schools were enrolled in the study. For each child, urine was examined for S. haematobium eggs and haematuria, stool was examined for STH eggs, peripheral blood was examined for eosinophilia and haemoglobin level, the urinary tract was ultrasound-examined for S. haematobium-related pathology, and the height and weight was measured and used to calculate the body mass index (BMI).

Results: Prevalences of S. haematobium, hookworm, T. trichiura and A. lumbricoides infection were 94, 81, 88 and 46 %, respectively. There was no significant association between S. haematobium and STH infection but intensity of hookworm infection significantly increased with that of T. trichiura. Lower BMI scores were associated with high intensity of S. haematobium (difference =-0.48, p > 0.05) and A. lumbricoides (difference =-0.67, p < 0.05). Haematuria (both macro and micro) was common and associated with S. haematobium infection, while anaemia was associated with high intensity of S. haematobium (OR = 2.08, p < 0.001) and high hookworm infections OR = 4.75; p < 0.001). The majority of children had eosinophilia, which was significantly associated with high intensity of hookworm infection (OR = 5.34, p < 0.05). Overall 38 % of the children had ultrasound-detectable urinary tract morbidity, which was associated with high intensity of S. haematobium infection (OR = 3.13, p < 0.05).

Conclusion: Prevalences of S. haematobium and STH infections among the primary school children were high and the parasites were responsible for significant morbidity. A clear synergistic interaction was observed between hookworm and T. trichiura infections. Increased coverage in administration of praziquantel and albendazole in the area is recommended to control morbidity due to these infections.


Abstract

Background: We assessed the safety and immunogenicity of the RTS,S/AS01 malaria vaccine in a subset of children identified as HIV-infected during a large phase III randomized controlled trial conducted in seven sub-Saharan African countries.

Methods: Infants 6-12 weeks and children 5-17 months old were randomized to receive 4 RTS,S/AS01 doses (R3R group), 3 RTS,S/AS01 doses plus 1 comparator vaccine dose (R3C group), or 4 comparator vaccine doses (C3C group) at study months 0, 1, 2 and 20. Infants and children with WHO stage III/IV HIV disease were excluded but HIV testing was not routinely performed on all participants; our analyses included children identified as HIV-infected based on medical history or clinical suspicion and confirmed by polymerase chain reaction or antibody testing. Serious adverse events (SAEs) and anti-circumsporozoite (CS) antibodies were assessed.

Results: Of 15459 children enrolled in the trial, at least 1953 were tested for HIV and 153 were confirmed as HIV-infected (R3R: 51; R3C: 54; C3C: 48). Among these children, SAEs were reported for 92.2% (95% CI: 81.1-97.8) in the R3R, 85.2% (72.9-93.4) in the R3C and 87.5% (74.8-95.3) in the C3C group over a median follow-up of 39.3, 39.4 and 38.3 months, respectively. Fifteen HIV-infected participants in each group (R3R: 29.4%, R3C: 27.8%, C3C: 31.3%) died during the study. No deaths were considered vaccination-related. In a matched case-control analysis, 1 month post dose 3 anti-CS geometric mean antibody concentrations were 193.3 EU/mL in RTS,S/AS01-vaccinated HIV-infected children and 491.5 EU/mL in RTS,S/AS01-vaccinated immunogenicity controls with unknown or negative HIV status (p = 0.0001).

Conclusions: The safety profile of RTS,S/AS01 in HIV-infected children was comparable to that of the comparator (meningococcal or rabies) vaccines. RTS,S/AS01 was immunogenic in HIV-infected children but antibody concentrations were lower than in children with an unknown or negative HIV status.


Abstract

**Objective:** To assess the performance of symptom-based screening for tuberculosis (TB), alone and with chest radiography among people living with HIV (PLHIV), including pregnant women, in Western Kenya.

**Design:** Prospective cohort study.

**Methods:** PLHIV from 15 randomly-selected HIV clinics were screened with three clinical algorithms [World Health Organization (WHO), Ministry of Health (MOH), and "Improving Diagnosis of TB in HIV-infected persons" (ID-TB/HIV) study], underwent chest radiography (unless pregnant), and provided two or more sputum specimens for smear microscopy, liquid culture, and Xpert MTB/RIF. Performance of clinical screening was compared to laboratory results, controlling for the complex design of the survey.

**Results:** Overall, 738 (85.6%) of 862 PLHIV enrolled were included in the analysis. Estimated TB prevalence was 11.2% (95% CI, 9.9-12.7). Sensitivity of the three screening algorithms was similar [WHO, 74.1% (95% CI, 64.1-82.2); MOH, 77.5% (95% CI, 68.6-84.5); and ID-TB/HIV, 72.5% (95% CI, 60.9-81.7)]. Sensitivity of the WHO algorithm was significantly lower among HIV-infected pregnant women [28.2% (95% CI, 14.9-46.7)] compared to non-pregnant women [78.3% (95% CI, 67.3-86.4)] and men [77.2% (95% CI, 68.3-84.2)]. Chest radiography increased WHO algorithm sensitivity and negative predictive value to 90.9% (95% CI, 86.4-93.9) and 96.1% (95% CI, 94.4-97.3), respectively, among asymptomatic men and non-pregnant women.

**Conclusions:** Clinical screening missed approximately 25% of laboratory-confirmed TB cases among all PLHIV and more than 70% among HIV-infected pregnant women. National HIV programs should evaluate the feasibility of laboratory-based screening for TB, such as a single Xpert MTB/RIF test for all PLHIV, especially pregnant women, at enrollment in HIV services.


Abstract
Background: Plasmodium falciparum merozoite antigens elicit antibody responses in malaria-endemic populations, some of which are clinically protective, which is one of the reasons why merozoite antigens are the focus of malaria vaccine development efforts. Polymorphisms in several merozoite antigen-encoding genes are thought to arise as a result of selection by the human immune system.

Methods: The allele frequency distribution of 15 merozoite antigens over a two-year period, 2007 and 2008, was examined in parasites obtained from children with uncomplicated malaria. In the same population, allele frequency changes pre- and post-anti-malarial treatment were also examined. Any gene which showed a significant shift in allele frequencies was also assessed longitudinally in asymptomatic and complicated malaria infections.

Results: Fluctuating allele frequencies were identified in codons 147 and 148 of reticulocyte-binding homologue (Rh) 5, with a shift from HD to YH haplotypes over the two-year period in uncomplicated malaria infections. However, in both the asymptomatic and complicated malaria infections YH was the dominant and stable haplotype over the two-year and ten-year periods, respectively. A logistic regression analysis of all three malaria infection populations between 2007 and 2009 revealed, that the chance of being infected with the HD haplotype decreased with time from 2007 to 2009 and increased in the uncomplicated and asymptomatic infections.

Conclusion: Rh5 codons 147 and 148 showed heterogeneity at both an individual and population level and may be under some degree of immune selection.


Abstract

Given the high morbidity for mother and fetus associated with malaria in pregnancy, safe and efficacious drugs are needed for treatment. Artemisinin derivatives are the most effective antimalarials, but are associated with teratogenic and embryotoxic effects in animal models when used in early pregnancy. However, several organ systems are still under development later in pregnancy. We conducted a systematic review and meta-analysis of the occurrence of adverse pregnancy outcomes among women treated with artemisinins monotherapy or as artemisinin-based combination therapy during the 2nd or 3rd trimesters relative to pregnant
women who received non-artemisinin antimalarials or none at all. Pooled odds ratio (POR) were calculated using Mantel-Haenszel fixed effects model with a 0.5 continuity correction for zero events. Eligible studies were identified through Medline, Embase, and the Malaria in Pregnancy Consortium Library. Twenty studies (11 cohort studies and 9 randomized controlled trials) contributed to the analysis, with 3,707 women receiving an artemisinin, 1,951 a non-artemisinin antimalarial, and 13,714 no antimalarial. The PORs (95% confidence interval (CI)) for stillbirth, fetal loss, and congenital anomalies when comparing artemisinin versus quinine were 0.49 (95% CI 0.24-0.97, I² = 0%, 3 studies); 0.58 (95% CI 0.31-1.16, I² = 0%, 6 studies); and 1.00 (95% CI 0.27-3.75, I² = 0%, 3 studies), respectively. The PORs comparing artemisinin users to pregnant women who received no antimalarial were 1.13 (95% CI 0.77-1.66, I² = 86.7%, 3 studies); 1.10 (95% CI 0.79-1.54, I² = 0%, 4 studies); and 0.79 (95% CI 0.37-1.67, I² = 0%, 3 studies) for miscarriage, stillbirth and congenital anomalies respectively. Treatment with artemisinin in 2nd and 3rd trimester was not associated with increased risks of congenital malformations or miscarriage and may be was associated with a reduced risk of stillbirths compared to quinine. This study updates the reviews conducted by the WHO in 2002 and 2006 and supports the current WHO malaria treatment guidelines malaria in pregnancy.


Abstract

Background
The epidemiology of enteric pathogens has not been well studied in Kenya because of wide disparities in health status across the country. Therefore, the present study describes the prevalence of enteropathogenic bacteria, their seasonal variation, and antibiotic resistance profiles among hospitalized diarrheic children in a suburban region of central Kenya.

Methods
Fecal samples were collected between July 2009 and December 2013 from a total of 1410 children younger than 5 years, hospitalized with acute diarrhea in Kiambu County Hospital, Kenya. Conventional culture, biochemical, and molecular methods were conducted to identify causative bacterial pathogens and their virulence factors. Antimicrobial susceptibility tests were performed using E-test strips and VITEK-2 advanced expert system (AES) to evaluate the drug-resistance pattern of the isolates.
Results

Of the 1410 isolates, bacterial infections were identified in 474 cases. Diarrheagenic *Escherichia coli* (DEC) was the most frequently isolated pathogen (86.5%). Other pathogens such as *Aeromonas* (5.5%), *Shigella* (4%), *Salmonella* (3.4%), *Providencia* (3.2%), *Vibrio* spp. (1.1%), *Yersinia enterocolitica* (1.1%), and *Plesiomonas shigelloides* (0.2%) were also identified. Mixed bacterial infection was observed among 11.1% of the cases. The highest infection rate was found during the dry season (59.3%, \( p = 0.04 \)). Most of the DEC was found to be multidrug resistant to trimethoprim/sulfamethoxazole 97.6%, amoxicillin 97.6%, erythromycin 96.9%, ampicillin 96.6%, and streptomycin 89%.

Conclusions

This study suggests that DEC is the leading diarrhea-causing bacterial pathogen circulating in central Kenya, and seasonality has a significant effect on its transmission. Proper antibiotic prescription and susceptibility testing is important to guide appropriate antimicrobial therapy.


### Abstract

**Background:** Education, as a key indicator of human capital, is considered one of the major determinants of internal migration, with previous studies suggesting that human capital accumulates in urban areas at the expense of rural areas. However, there is fragmentary evidence concerning the educational correlates of internal migration in sub-Saharan Africa.

**Objectives:** The study questions whether more precise measures of migration in Health and Demographic Surveillance System (HDSS) populations support the hypothesis that migrants are self-selected on human capital and more educated people are more likely to leave rural areas or enter urban areas within a geographical region.

**Methods:** Using unique longitudinal data representing approximately 900,000 people living in eight sub-Saharan African HDSS sites that are members of the INDEPTH Network, the paper uses Event History Analysis techniques to examine the relationship between formal educational attainment and in-and out-migration, over the period 2009 to 2011.
**Results:** Between 7% and 27% of these local populations are moving in or out of the HDSS area over this period. Education is positively associated with both in-and out-migration in the Kenyan HDSS areas; however, the education effect has no clear pattern in the HDSS sites in Burkina Faso, Mozambique, and South Africa.

**Conclusions:** Empirical results presented in this paper confirm a strong age profile of migration consistent with human capital expectation, yet the results point to variability in the association of education and the propensity to migrate. In particular, the hypothesis of a shift of human capital from rural to urban areas is not universally valid.


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**Abstract**

**Introduction:** Globally, pregnancy related complications contribute to more than half of the deaths among women annually. Antenatal care (ANC) is important for the prevention of maternal and fetal mortality and morbidity. This study identifies the socio-demographic and economic characteristics; knowledge and attitude and; health service provision for focused antenatal care (FANC) services.

**Methods:** A cross-sectional comparative study conducted among 385 women of reproductive age who visited 5 public health facilities in Malindi and Magarini Sub Counties. Data collection was conducted between June 2013 and September 2013 through structured questionnaires, Key Informant Interviews (KII) s and Focused Group Discussions (FGDs) and analyzed through descriptive summary statistics and test of associations of the various variables using chi square.

**Results:** About 35% of women sought 1st and 2nd ANC services at the health facilities. These women went ahead to complete the recommended 4 minimum visits as recommended by World Health Organization (WHO). Compared to Catholics, Muslims were less likely to attend a rural health facility (Odds ratio (OR) = 0.25, 95% Confidence Interval (CI) 0.10, 0.62, p=0.003). According to education levels, those with secondary (OR=0.07, 95% CI 0.03, 0.18, p<0.001) or tertiary (OR=0.09, 95% CI 0.03-0.17, p<0.001) levels of education were less likely to seek FANC at rural facility. Women seeking rural ANC services started at 2nd or 3rd trimester (OR=5.40 95% CI 2.97-10.06, p<0.001) while those in urban setup start at 1st trimester. Among the women who were aware of FANC, only 27% utilized its services. Long
waiting hours, unavailability of services, and departmental disharmony were major causes of dissatisfaction to mothers visiting the facilities.

**Conclusion:** Utilization and awareness of FANC services in both rural and urban health facilities among women in Malindi and Magarini Sub Counties continues to be low which is associated by socio-demographic characteristics, and health facility inefficiencies. Thus there is need to standardize services across health facilities and increase awareness on FANC in both rural and urban.


**Abstract**

**Introduction:** Follow-up visits are recommended to all voluntary medical male circumcision clients (VMMC), however, adherence is variable. High lost-to-follow-up cases limit knowledge about clinical status of clients and adverse events. This study sought to establish Motivators and Barriers to the Uptake of VMMC post-operative follow-up services in Siaya County, Kenya.

**Methods:** 277 clients from five VMMC sites in Yala were recruited immediately post-operation to participate in a telephone interview between the 21st and 31st day post-surgery during which a semi-structured questionnaire was administered. Descriptive and inferential statistics was used to analyse quantitative information using SPSS while responses from open ended questions were grouped into themes, sieved out, coded and analyzed.

**Results:** 137(49.5%) of the 277 participants utilized the follow-up services. Health education (31.4%) and emergency reviews/adverse events (24.1%) were the main motivation for returning for follow-up while occupational and other engagements (29.7%) and presumption of healing (24.6%) were the main barriers. Type of facility attended (p=0.0173), satisfaction with the discharge process (p=0.0150) and residency in Yala (p<0.001) were statistically significant to the respondents' return for follow-up. 85(62.0%) of the participants returned on the 7th day, 9(6.6%) returned after 7 days, and 43(31.4%) returned before 7 days.

**Conclusion:** VMMC health education should include and emphasize the benefits of follow-up care to the clients and the providers should address the barriers to accessing follow-up
services. Our results will inform the programme on areas identified to improve care for VMMC clients and reduce subsequent lost-to-follow-up cases.


**Abstract**

**Background:** Epilepsy is a common neurological disorder, with over 80% of cases found in low- and middle-income countries (LMICs). Studies from high-income countries find a significant economic burden associated with epilepsy, yet few studies from LMICs, where out-of-pocket costs for general healthcare can be substantial, have assessed out-of-pocket costs and health care utilization for outpatient epilepsy care.

**Methods:** Within an established health and socio-demographic surveillance system in rural South Africa, a questionnaire to assess self-reported health care utilization and time spent traveling to and waiting to be seen at health facilities was administered to 250 individuals, previously diagnosed with active convulsive epilepsy. Epilepsy patients' out-of-pocket, medical and non-medical costs and frequency of outpatient care visits during the previous 12-months were determined.

**Results:** Within the last year, 132 (53%) individuals reported consulting at a clinic, 162 (65%) at a hospital and 34 (14%) with traditional healers for epilepsy care. Sixty-seven percent of individuals reported previously consulting with both biomedical caregivers and traditional healers. Direct outpatient, median costs per visit varied significantly (p < 0.001) between hospital (2010 International dollar ($) 9.08; IQR: $6.41-$12.83) and clinic consultations ($1.74; IQR: $0-$5.58). Traditional healer fees per visit were found to cost $52.36 (IQR: $34.90-$87.26) per visit. Average annual outpatient, clinic and hospital out-of-pocket costs totaled $58.41. Traveling to and from and waiting to be seen by the caregiver at the hospital took significantly longer than at the clinic.

**Conclusions:** Rural South Africans with epilepsy consult with both biomedical caregivers and traditional healers for both epilepsy and non-epilepsy care. Traditional healers were the most expensive mode of care, though utilized less often. While higher out-of-pocket costs were incurred at hospital visits, more people with ACE visited hospitals than clinics for epilepsy.
Promoting increased use and effective care at clinics and reducing travel and waiting times could substantially reduce the out-of-pocket costs of outpatient epilepsy care.


Abstract

Background: Encouraging progress has been seen with reductions in Plasmodium falciparum malaria transmission in some parts of Africa. Reduced transmission might lead to increasing susceptibility to malaria among older children due to lower acquired immunity, and this has implications for ongoing control strategies.

Methods and findings: We conducted a longitudinal observational study of children admitted to Kilifi County Hospital in Kenya and linked it to data on residence and insecticide-treated net (ITN) use. This included data from 69,104 children aged from 3 mo to 13 y admitted to Kilifi County Hospital between 1 January 1990 and 31 December 2014. The variation in malaria slide positivity among admissions was examined in logistic regression models using the following predictors: location of the residence, calendar time, the child's age, ITN use, and the enhanced vegetation index (a proxy for soil moisture). The proportion of malaria slide-positive admissions declined from 0.56 (95% confidence interval [CI] 0.54-0.58) in 1998 to 0.07 (95% CI 0.06-0.08) in 2009 but then increased again through to 0.24 (95% CI 0.22-0.25) in 2014. Older children accounted for most of the increase after 2009 (0.035 [95% CI 0.030-0.040] among young children compared to 0.22 [95% CI 0.21-0.23] in older children). There was a nonlinear relationship between malaria risk and prevalence of ITN use within a 2 km radius of an admitted child's residence such that the predicted malaria positive fraction varied from ~0.4 to <0.1 as the prevalence of ITN use varied from 20% to 80%. In this observational analysis, we were unable to determine the cause of the decline in malaria between 1998 and 2009, which pre-dated the dramatic scale-up in ITN distribution and use.

Conclusion: Following a period of reduced transmission, a cohort of older children emerged who have increased susceptibility to malaria. Further reductions in malaria transmission are needed to mitigate the increasing burden among older children, and universal ITN coverage is a promising strategy to achieve this goal.
Deribew A, Ojal J, Karia B, Bauni E, Oteinde M. Under-five mortality rate variation between the Health and Demographic Surveillance System (HDSS) and Demographic and Health Survey (DHS) approaches. BMC Public Health. 2016 Oct 24;16(1):1118

Abstract

Background: Several low and middle-income countries (LMIC) use Demographic and Health Surveys (DHS) and/or Health and Demographic Surveillance System (HDSS) to monitor the health of their population. The level and trends of under-five mortality rates could be different in the HDSS sites compared to the DHS reports. In this study, we investigated the change in under-five mortality rates overtime in the HDSS sites and the corresponding DHS reports in eight countries and 13 sites.

Methods: Under-five mortality rates in the HDSS sites were determined using number of under-five deaths (numerator) and live births (denominator). The trends and annualized rate of change (ARC) of under-five mortality rates in the HDSS sites and the DHS reports were compared by fitting exponential function.

Results: Under-five mortality rates declined substantially in most of the sites during the last 10-15 years. Ten out of 13 (77 %) HDSS sites have consistently lower under-five mortality rates than the DHS under-five mortality rates. In the Kilifi HDSS in Kenya, under-five mortality rate declined by 65.6 % between 2003 and 2014 with ARC of 12.2 % (95 % CI: 9.4-15.0). In the same period, the DHS under-five mortality rate in the Coastal region of Kenya declined by 50.8 % with ARC of 6 % (95 % CI: 2.0-9.0). The under-five mortality rate reduction in the Mlomp (78.1 %) and Niakhar (80.8 %) HDSS sites in Senegal during 1993-2012 was significantly higher than the mortality decline observed in the DHS report during the same period. On the other hand, the Kisumu HDSS in Kenya had lower under-five mortality reduction (15.8 %) compared to the mortality reduction observed in the DHS report (27.7 %) during 2003-2008. Under-five mortality rate rose by 27 % in the Agincourt HDSS in South Africa between 1998 to 2003 that was contrary to the 18 % under-five mortality reduction in the DHS report during the same period.

Conclusions: The inconsistency between HDSS and DHS approaches could have global implication on the estimation of child mortality and ethical issues on mortality inequalities. Further studies should be conducted to investigate the reasons of child mortality variation between the HDSS and the DHS approaches.

**Abstract**  
Mobile technology is very prevalent in Kenya-mobile phone penetration is at 88% and mobile data subscriptions form 99% of all internet subscriptions. While there is great potential for such ubiquitous technology to revolutionise access and quality of healthcare in low-resource settings, there have been few successes at scale. Implementations of electronic health (e-Health) and mobile health (m-Health) technologies in countries like Kenya are yet to tackle human resource constraints or the political, ethical and financial considerations of such technologies. We outline recent innovations that could improve access and quality while considering the costs of healthcare. One is an attempt to create a scalable clinical decision support system by engaging a global network of specialist doctors and reversing some of the damaging effects of medical brain drain. The other efficiently extracts digital information from paper-based records using low-cost and locally produced tools such as rubber stamps to improve adherence to clinical practice guidelines. By bringing down the costs of remote consultations and clinical audit, respectively, these projects offer the potential for clinics in resource-limited settings to deliver high-quality care. This paper makes a case for continued and increased investment in social enterprises that bridge academia, public and private sectors to deliver sustainable and scalable e-Health and m-Health solutions.  
**Abstract**  
**Background** A better understanding of respiratory syncytial virus (RSV) epidemiology requires realistic estimates of RSV shedding patterns, quantities shed, and identification of the related underlying factors. **Methods** RSV infection data arise from a cohort study of 47 households with 493 occupants, in coastal Kenya, during the 2009/2010 RSV season. Nasopharyngeal swabs were taken every 3 to 4 days and screened for RSV using a real time polymerase chain reaction (PCR) assay. The amount of virus shed was quantified by calculating the ‘area under the curve’ using the trapezoidal rule applied to rescaled PCR cycle threshold output. Multivariable linear regression was used to identify correlates of amount of virus shed. **Results** The median quantity of virus shed per infection episode was 29.4 (95% CI: |
15.2, 54.2) log_{10} ribonucleic acid (RNA) copies. Young age (<1 year), presence of upper respiratory symptoms, intra-household acquisition of infection, an individual's first infection episode in the RSV season, and having a co-infection of RSV group A and B were associated with increased amount of virus shed. **Conclusions** The findings provide insight into which groups of individuals have higher potential for transmission, information which may be useful in designing RSV prevention strategies.


**Abstract**

in **English, French, Spanish**

**Background:** Evaluating clinician compliance with recommended steps in clinical guidelines provides one measure of quality of process of care but can result in a multiplicity of indicators across illnesses, making it problematic to produce any summative picture of process quality, information that may be most useful to policy-makers and managers.

**Objective:** We set out to develop a clinically logical summative measure of the quality of care provided to children admitted to hospital in Kenya spanning the three diagnoses present in 60% or more of admissions that would provide a patient-level measure of quality of care in the face of comorbidity.

**Methods:** We developed a conceptual model of care based on three domains: assessment, diagnosis and treatment of illnesses. Individual items within domains correspond to recommended processes of care within national clinical practice guidelines. Summative scores were created to reduce redundancy and enable aggregation across illnesses while maintaining a clear link to clinical domains and our conceptual model. The potential application of the score was explored using data from more than 12,000 children from eight hospitals included in a prior intervention study in Kenya.

**Results:** Summative scores obtained from items representing discrete clinical decision points reduced redundancy, aided balance of score contribution across domains and enabled direct comparison of disease-specific scores and the calculation of scores for children with comorbidity.
## Conclusion

This work describes the development of a summative Paediatric Admission Quality of Care score measured at the patient level that spans three common diseases. The score may be an efficient tool for assessing quality with an ability to adjust for case mix or other patient-level factors if needed. The score principles may have applicability to multiple illnesses and settings. Future analysis will be needed to validate the score.


**Abstract**

**Objective**: We set out to adapt the Beck Depression Inventory (BDI)-II in Kenya and examine its factorial structure.

**Methods**: In the first phase we carried out in-depth interviews involving 29 adult members of the community to elicit their understanding of depression and identify aspects of the BDI-II that required adaptation. In the second phase, a modified version of BDI-II was administered to 221 adults randomly selected from the community to allow for the evaluation of its psychometric properties. In the third phase of the study we evaluated the discriminative validity of BDI-II by comparing a randomly chosen community sample (n = 29) with caregivers of adolescents affected by HIV (n = 77).

**Results**: A considerable overlap between the BDI symptoms and those generated in the interviews was observed. Relevant idioms and symptoms such as 'thinking too much' and 'Kuchoka moyo (having a tired heart)' were identified. The administration of the BDI had to be modified to make it suitable for the low literacy levels of our participants. Fit indices for several models (one factorial, two-factor model and a three factor model) were all within acceptable range. Evidence indicated that while multidimensional models could be fitted, the strong correlations between the factors implied that a single factor model may be the best suited solution (alpha [0.89], and a significant correlation with locally identified items [r = 0.51]) confirmed the good psychometric properties of the adapted BDI-II. No evidence was found to support the hypothesis that somatization was more prevalent. Lastly, caregivers of HIV affected adolescents had significantly higher scores compared to adults randomly selected from the community F(1, 121) = 23.31, p < .001 indicating the discriminative validity of the adapted BDI = II.
Conclusions: With an adapted administration procedure, the BDI-II provides an adequate measure of depressive symptoms which can be used alongside other measures for proper diagnosis in a low literacy population.


145. Barasa EW, Cleary S, English M, Molyneux S. The influence of power and actor relations on priority setting and resource allocation practices at the hospital level in Kenya: a case study. BMC Health Serv Res. 2016 Sep 30;16(1):536

Abstract

Background: Priority setting and resource allocation in healthcare organizations often involves the balancing of competing interests and values in the context of hierarchical and politically complex settings with multiple interacting actor relationships. Despite this, few studies have examined the influence of actor and power dynamics on priority setting practices in healthcare organizations. This paper examines the influence of power relations among different actors on the implementation of priority setting and resource allocation processes in public hospitals in Kenya.

Methods: We used a qualitative case study approach to examine priority setting and resource allocation practices in two public hospitals in coastal Kenya. We collected data by a combination of in-depth interviews of national level policy makers, hospital managers, and frontline practitioners in the case study hospitals (n = 72), review of documents such as hospital plans and budgets, minutes of meetings and accounting records, and non-participant observations in case study hospitals over a period of 7 months. We applied a combination of two frameworks, Norman Long's actor interface analysis and VeneKlasen and Miller's expressions of power framework to examine and interpret our findings

RESULTS: The interactions of actors in the case study hospitals resulted in socially constructed interfaces between: 1) senior managers and middle level managers 2) non-clinical managers and clinicians, and 3) hospital managers and the community. Power imbalances resulted in the exclusion of middle level managers (in one of the hospitals) and clinicians and the community (in both hospitals) from decision making processes. This resulted in, amongst others, perceptions of unfairness, and reduced motivation in hospital staff. It also puts to question the legitimacy of priority setting processes in these hospitals.

Conclusions: Designing hospital decision making structures to strengthen participation and inclusion of relevant stakeholders could improve priority setting practices. This should however, be accompanied by measures to empower stakeholders to contribute to decision
making. Strengthening soft leadership skills of hospital managers could also contribute to managing the power dynamics among actors in hospital priority setting processes.


**Abstract**

**Background:** The burden of non-communicable diseases (NCDs) has increased in sub-Saharan countries, including Ethiopia. The contribution of dietary behaviours to the NCD burden in Ethiopia has not been evaluated. This study, therefore, aimed to assess diet-related burden of disease in Ethiopia between 1990 and 2013.

**Method:** We used the 2013 Global Burden of Disease (GBD) data to estimate deaths, years of life lost (YLLs) and disability-adjusted life years (DALYs) related to eight food types, five nutrients and fibre intake. Dietary exposure was estimated using a Bayesian hierarchical meta-regression. The effect size of each diet-disease pair was obtained based on meta-analyses of prospective observational studies and randomized controlled trials. A comparative risk assessment approach was used to quantify the proportion of NCD burden associated with dietary risk factors.

**Results:** In 2013, dietary factors were responsible for 60,402 deaths (95% Uncertainty Interval [UI]: 44,943-74,898) in Ethiopia—almost a quarter (23.0%) of all NCD deaths. Nearly nine in every ten diet-related deaths (88.0%) were from cardiovascular diseases (CVD) and 44.0% of all CVD deaths were related to poor diet. Suboptimal diet accounted for 1,353,407 DALYs (95% UI: 1,010,433-1,672,828) and 1,291,703 YLLs (95% UI: 961,915-1,599,985). Low intake of fruits and vegetables and high intake of sodium were the most important dietary factors. The proportion of NCD deaths associated with low fruit consumption slightly increased (11.3% in 1990 and 11.9% in 2013). In these years, the rate of burden of disease related to poor diet slightly decreased; however, their contribution to NCDs remained stable.

**Conclusions:** Dietary behaviour contributes significantly to the NCD burden in Ethiopia. Intakes of diet low in fruits and vegetables and high in sodium are the leading dietary risks. To
effectively mitigate the oncoming NCD burden in Ethiopia, multisectoral interventions are required; and nutrition policies and dietary guidelines should be developed.


Abstract

Dengue is the major public health burden in Sri Lanka. Kalutara is one of the highly affected districts. Understanding the drivers of dengue is vital in controlling and preventing the disease spread. This study focuses on quantifying the influence of weather variability on dengue incidence over 10 Medical Officer of Health (MOH) divisions of Kalutara district. Weekly weather variables and data on dengue notifications, measured at 10 MOH divisions in Kalutara from 2009 to 2013, were retrieved and analysed. Distributed lag non-linear model and hierarchical-analysis was used to estimate division specific and overall relationships between weather and dengue. We incorporated lag times up to 12 weeks and evaluated models based on the Akaike Information Criterion. Consistent exposure-response patterns between different geographical locations were observed for rainfall, showing increasing relative risk of dengue with increasing rainfall from 50 mm per week. The strongest association with dengue risk centred around 6 to 10 weeks following rainfalls of more than 300 mm per week. With increasing temperature, the overall relative risk of dengue increased steadily starting from a lag of 4 weeks. We found similarly a strong link between the Oceanic Niño Index to weather patterns in the district in Sri Lanka and to dengue at a longer latency time confirming these relationships. Part of the influences of rainfall and temperature can be seen as mediator in the causal pathway of the Ocean Niño Index, which may allow a longer lead time for early warning signals. Our findings describe a strong association between weather, El Niño-Southern Oscillation and dengue in Sri Lanka.


Abstract

**Background:** Ethiopia has made remarkable progress in reducing child mortality over the last two decades. However, the under-5 mortality rate in Ethiopia is still higher than the under-5 mortality rates of several low- and middle-income countries (LMIC). On the other hand, the patterns and causes of child mortality have not been well investigated in Ethiopia. The objective of this study was to investigate the mortality trend, causes of death, and risk factors among children under 5 in Ethiopia during 1990-2013.

**Methods:** We used Global Burden of Disease (GBD) 2013 data. Spatiotemporal Gaussian Process Regression (GPR) was applied to generate best estimates of child mortality with 95% uncertainty intervals (UI). Causes of death by age groups, sex, and year were measured using Cause of Death Ensemble modeling (CODEm). For estimation of HIV/AIDS mortality rate, the modified UNAIDS EPP-SPECTRUM suite model was used.

**Results:** Between 1990 and 2013 the under-5 mortality rate declined from 203.9 deaths/1000 live births to 74.4 deaths/1000 live births with an annual rate of change of 4.6%, yielding a total reduction of 64%. Similarly, child (1-4 years), post-neonatal, and neonatal mortality rates declined by 75%, 64%, and 52%, respectively, between 1990 and 2013. Lower respiratory tract infection (LRI), diarrheal diseases, and neonatal syndromes (preterm birth complications, neonatal encephalopathy, neonatal sepsis, and other neonatal disorders) accounted for 54% of the total under-5 deaths in 2013. Under-5 mortality rates due to measles, diarrhea, malaria, protein-energy malnutrition, and iron-deficiency anemia declined by more than two-thirds between 1990 and 2013. Among the causes of under-5 deaths, neonatal syndromes such as sepsis, preterm birth complications, and birth asphyxia ranked third to fifth in 2013. Of all risk-attributable deaths in 1990, 25% of the total under-5 deaths (112,288/435,962) and 48% (112,288/232,199) of the deaths due to diarrhea, LRI, and other common infections were attributable to childhood wasting. Similarly, 19% (43,759/229,333) of the total under-5 deaths and 45% (43,759/97,963) of the deaths due to diarrhea and LRI were attributable to wasting in 2013. Of the total diarrheal disease- and LRI-related deaths ($n = 97,963$) in 2013, 59% (57,923/97,963) of them were attributable to unsafe water supply, unsafe sanitation, household air pollution, and no handwashing with soap.

**Conclusions:** LRI, diarrheal diseases, and neonatal syndromes remain the major causes of under-5 deaths in Ethiopia. These findings call for better-integrated newborn and child survival interventions focusing on the main risk factors.


Abstract

**Background:** The target group for severe respiratory syncytial virus (RSV) disease prevention is infants under 6 months of age. Vaccine boosting of antibody titres in pregnant mothers could protect these young infants from severe respiratory syncytial virus (RSV) associated disease. Quantifying protective levels of RSV-specific maternal antibody at birth would inform vaccine development.

**Methods:** A case control study nested in a birth cohort (2002-07) was conducted in Kilifi, Kenya; where 30 hospitalised cases of RSV-associated severe disease were matched to 60 controls. Participants had a cord blood and 2 subsequent 3-monthly blood samples assayed for RSV-specific neutralising antibody by the plaque reduction neutralisation test (PRNT). Two sample paired t test and conditional logistic regression were used in analyses of log2PRNT titres.

**Results:** The mean RSV log2PRNT titre at birth for cases and controls were not significantly different (P = 0.4) and remained so on age-stratification. Cord blood PRNT titres showed considerable overlap between cases and controls. The odds of RSV disease decreased with increase in log2PRNT cord blood titre. There was a 30% reduction in RSV disease per unit increase in log2PRNT titre (<3months age group) but not significant (P = 0.3).

**Conclusions:** From this study, there is no strong evidence of protection by maternal RSV specific antibodies from severe RSV disease. Cord antibody levels show wide variation with considerable overlap between cases and controls. It is likely that, there are additional factors to specific PRNT antibody levels which determine susceptibility to severe RSV disease. In addition, higher levels of neutralizing antibody beyond the normal range may be required for protection; which it is hoped can be achieved by a maternal RSV vaccine.


Abstract

**Background:** Aedes aegypti is a competent arthropod vector of chikungunya virus (CHIKV). The rate at which the virus disseminate in the vector is limited by temperature of their environment which can be an important determinant of geographical and seasonal limits to transmission by the arthropods in the tropics. This study investigated the vector competence of Ae. aegypti for CHIKV at ambient temperature of 32 and 26 °C (Coastal and Western Kenya respectively) reared at Extrinsic Incubation Temperature (EIT) of 32 and 26 °C that resembles those in the two regions.

**Methods:** Ae. aegypti eggs were collected from coastal and Western Kenya, hatched in the insectary and reared to F1 generation. Four-day old mosquitoes were exposed to CHIKV through a membrane feeding. They were then incubated in temperatures mimicking the mean annual temperatures for Trans-Nzoia (26 °C) and Lamu (32 °C). After every 7, 10 and 13 days post infection (DPI); one third of exposed mosquitoes were sampled and assayed for virus infection and dissemination.

**Results:** The midgut infection rates (MIR) of Ae. aegypti sampled from Coastal Region was significantly (p < 0.05) higher than those sampled from Western Kenya, with no statistical differences observed for the coastal Ae. aegypti at EIT 26 and at 32 °C. The MIR of Ae. aegypti from the Western Region was significantly (p < 0.05) affected by the EIT, with mosquito reared at EIT 32 °C exhibiting higher MIR than those reared at EIT 26 °C. There was a significant (p < 0.05) interactive effects of the region, EIT and DPI on MIR. The disseminated infection rates for the CHIKV in Ae. aegypti in the legs (DIR-L) was higher in mosquitoes sampled from Coast regardless of the EIT while those from Western Kenya, dissemination rates were significantly higher at higher EIT of 32 °C.

**Conclusions:** Vector competence was higher in mosquito populations reared under high temperatures which weakens the midgut infection barrier. Hence, suggesting Lamu population is more susceptible to CHIKV therefore having a weaker mid gut infection barrier than the Trans Nzoia population. These underscores importance of examining the course of infection at various ambient temperatures and EIT between regions mosquito populations.


Abstract

Background: Diarrheal disease is the second leading cause of disease in children less than 5 y of age. Poor water, sanitation, and hygiene conditions are the primary routes of exposure and infection. Sanitation and hygiene interventions are estimated to generate a 36% and 48% reduction in diarrheal risk in young children, respectively. Little is known about whether the number of households sharing a sanitation facility affects a child's risk of diarrhea. The objective of this study was to describe sanitation and hygiene access across the Global Enteric Multicenter Study (GEMS) sites in Africa and South Asia and to assess sanitation and hygiene exposures, including shared sanitation access, as risk factors for moderate-to-severe diarrhea (MSD) in children less than 5 y of age.

Methods/findings: The GEMS matched case-control study was conducted between December 1, 2007, and March 3, 2011, at seven sites in Basse, The Gambia; Nyanza Province, Kenya; Bamako, Mali; Manhiça, Mozambique; Mirzapur, Bangladesh; Kolkata, India; and Karachi, Pakistan. Data was collected for 8,592 case children aged <5 y old experiencing MSD and for 12,390 asymptomatic age, gender, and neighborhood-matched controls. An MSD case was defined as a child with a diarrheal illness <7 d duration comprising ≥3 loose stools in 24 h and ≥1 of the following: sunken eyes, skin tenting, dysentery, intravenous (IV) rehydration, or hospitalization. Site-specific conditional logistic regression models were used to explore the association between sanitation and hygiene exposures and MSD. Most households at six sites (>93%) had access to a sanitation facility, while 70% of households in rural Kenya had access to a facility. Practicing open defecation was a risk factor for MSD in children <5 y old in Kenya. Sharing sanitation facilities with 1-2 or ≥3 other households was a statistically significant risk factor for MSD in Kenya, Mali, Mozambique, and Pakistan. Among those with a designated handwashing area near the home, soap or ash were more frequently observed at control households and were significantly protective against MSD in Mozambique and India.

Conclusions: This study suggests that sharing a sanitation facility with just one to two other households can increase the risk of MSD in young children, compared to using a private facility. Interventions aimed at increasing access to private household sanitation facilities may reduce the burden of MSD in children. These findings support the current World Health Organization/United Nations Children’s Emergency Fund (UNICEF) system that categorizes shared sanitation as unimproved.


Abstract

Background: Haemophilus influenzae type b (Hib) conjugate vaccine, delivered as a three-dose series without a booster, was introduced into the childhood vaccination programme in Kenya in 2001. The duration of protection and need for a booster dose are unknown. We aimed to assess vaccine effectiveness, the impact of the vaccine on nasopharyngeal carriage, and population immunity after introduction of conjugate Hib vaccine in infancy without a booster dose in Kenya.

Methods: This study took place in the Kilifi Health and Demographic Surveillance System (KHDSS), an area of Kenya that has been monitored for vital events and migration every 4 months since 2000. We analysed sterile site cultures for H influenzae type b from children (aged ≤12 years) admitted to the Kilifi County Hospital (KCH) from Jan 1, 2000, through to Dec 31, 2014. We determined the prevalence of nasopharyngeal carriage by undertaking cross-sectional surveys in random samples of KHDSS residents (of all ages) once every year from 2009 to 2012, and measured Hib antibody concentrations in five cross-sectional samples of children (aged ≤12 years) within the KHDSS (in 1998, 2000, 2004-05, 2007, and 2009). We calculated incidence rate ratios between the prevaccine era (2000-01) and the routine-use era (2004-14) and defined vaccine effectiveness as 1 minus the incidence rate ratio, expressed as a percentage.

Findings: 40,482 children younger than 13 years resident in KHDSS were admitted to KCH between 2000 and 2014, 38,206 (94%) of whom had their blood cultured. The incidence of invasive H influenzae type b disease in children younger than 5 years declined from 62.6 (95% CI 46.0-83.3) per 100,000 in 2000-01 to 4.5 (2.5-7.5) per 100,000 in 2004-14, giving a vaccine effectiveness of 93% (95% CI 87-96). In the final 5 years of observation (2010-14), only one case of invasive H influenzae type b disease was detected in a child younger than 5 years. Nasopharyngeal H influenzae type b carriage was detected in one (0.2%) of 623 children younger than 5 years between 2009 and 2012. In the 2009 serosurvey, 92 (79%; 95% CI 70-86) of 117 children aged 4-35 months had long-term protective antibody concentrations.

Interpretation: In this region of Kenya, use of a three-dose primary series of Hib vaccine without a booster dose has resulted in a significant and sustained reduction in invasive H influenzae type b disease. The prevalence of nasopharyngeal carriage is low and the profile of Hib antibodies suggests that protection wanes only after the age at greatest risk of disease.
Although continued surveillance is important to determine whether effective control persists, these findings suggest that a booster dose is not currently required in Kenya.


Abstract

Background: Innovative approaches are needed to complement existing tools for malaria elimination. Ivermectin is a broad spectrum antiparasitic endectocide clinically used for onchocerciasis and lymphatic filariasis control at single doses of 150 to 200 mcg/kg. It also shortens the lifespan of mosquitoes that feed on individuals recently treated with ivermectin. However, the effect after a 150 to 200 mcg/kg oral dose is short-lived (6 to 11 days). Modeling suggests higher doses, which prolong the mosquitocidal effects, are needed to make a significant contribution to malaria elimination. Ivermectin has a wide therapeutic index and previous studies have shown doses up to 2000 mcg/kg (ie, 10 times the US Food and Drug Administration approved dose) are well tolerated and safe; the highest dose used for onchocerciasis is a single dose of 800 mcg/kg.

Objective: The aim of this study is to determine the safety, tolerability, and efficacy of ivermectin doses of 0, 300, and 600 mcg/kg/day for 3 days, when provided with a standard 3-day course of the antimalarial dihydroartemisinin-piperaquine (DP), on mosquito survival.

Methods: This is a double-blind, randomized, placebo-controlled, parallel-group, 3-arm, dose-finding trial in adults with uncomplicated malaria. Monte Carlo simulations based on pharmacokinetic modeling were performed to determine the optimum dosing regimens to be tested. Modeling showed that a 3-day regimen of 600 mcg/kg/day achieved similar median (5 to 95 percentiles) maximum drug concentrations (Cmax) of ivermectin to a single of dose of 800 mcg/kg, while increasing the median time above the lethal concentration 50% (LC50, 16 ng/mL) from 1.9 days (1.0 to 5.7) to 6.8 (3.8 to 13.4) days. The 300 mcg/kg/day dose was chosen at 50% of the higher dose to allow evaluation of the dose response. Mosquito survival will be assessed daily up to 28 days in laboratory-reared Anopheles gambiae s.s. populations fed on patients' blood taken at days 0, 2 (Cmax), 7 (primary outcome), 10, 14, 21, and 28 after the start of treatment. Safety outcomes include QT-prolongation and mydriasis. The trial will be conducted in 6 health facilities in western Kenya and requires a sample size of 141.
participants (47 per arm). Sub-studies include (1) rich pharmacokinetics and (2) direct skin versus membrane feeding assays.

**Results:** Recruitment started July 20, 2015. Data collection was completed July 2, 2016. Unblinding and analysis will commence once the database has been completed, cleaned, and locked.

**Conclusions:** High-dose ivermectin, if found to be safe and well tolerated, might offer a promising new tool for malaria elimination.


**Abstract**

**Background:** Children with complicated severe acute malnutrition (SAM) have a greatly increased risk of mortality from infections while in hospital and after discharge. In HIV-infected children, mortality and admission to hospital are prevented by daily co-trimoxazole prophylaxis, despite locally reported bacterial resistance to co-trimoxazole. We aimed to assess the efficacy of daily co-trimoxazole prophylaxis on survival in children without HIV being treated for complicated SAM.

**Methods:** We did a multicentre, double-blind, randomised, placebo-controlled study in four hospitals in Kenya (two rural hospitals in Kilifi and Malindi, and two urban hospitals in Mombasa and Nairobi) with children aged 60 days to 59 months without HIV admitted to hospital and diagnosed with SAM. We randomly assigned eligible participants (1:1) to 6 months of either daily oral co-trimoxazole prophylaxis (given as water-dispersible tablets; 120 mg per day for age <6 months, 240 mg per day for age 6 months to 5 years) or matching placebo. Assignment was done with computer-generated randomisation in permuted blocks of 20, stratified by centre and age younger or older than 6 months. Treatment allocation was concealed in opaque, sealed envelopes and patients, their families, and all trial staff were masked to treatment assignment. Children were given recommended medical care and feeding, and followed up for 12 months. The primary endpoint was mortality, assessed each month for the first 6 months, then every 2 months for the second 6 months. Secondary endpoints were nutritional recovery, readmission to hospital, and illness episodes treated as an outpatient.
Analysis was by intention to treat. This trial was registered at ClinicalTrials.gov, number NCT00934492.

**Findings:** Between Nov 20, 2009, and March 14, 2013, we recruited and assigned 1778 eligible children to treatment (887 to co-trimoxazole prophylaxis and 891 to placebo). Median age was 11 months (IQR 7-16 months), 306 (17%) were younger than 6 months, 300 (17%) had oedematous malnutrition (kwashiorkor), and 1221 (69%) were stunted (length-for-age Z score <-2). During 1527 child-years of observation, 122 (14%) of 887 children in the co-trimoxazole group died, compared with 135 (15%) of 891 in the placebo group (unadjusted hazard ratio [HR] 0·90, 95% CI 0·71-1·16, p=0·429; 16·0 vs 17·7 events per 100 child-years observed (CYO); difference -1·7 events per 100 CYO, 95% CI -5·8 to 2·4). In the first 6 months of the study (while participants received study medication), 63 suspected grade 3 or 4 associated adverse events were recorded among 57 (3%) children; 31 (2%) in the co-trimoxazole group and 32 (2%) in the placebo group (incidence rate ratio 0·98, 95% CI 0·58-1·65). The most common adverse events of these grades were urticarial rash (grade 3, equally common in both groups), neutropenia (grade 4, more common in the co-trimoxazole group), and anaemia (both grades equally common in both groups). One child in the placebo group had fatal toxic epidermal necrolysis with concurrent Pseudomonas aeruginosa bacteraemia.

**Interpretation:** Daily co-trimoxazole prophylaxis did not reduce mortality in children with complicated SAM without HIV. Other strategies need to be tested in clinical trials to reduce deaths in this population.


**Abstract**

**Background:** WHO recommends combinations of an artemisinin derivative plus an antimalarial drug of longer half-life as treatment options for uncomplicated Plasmodium falciparum infection. In Africa, artemether-lumefantrine is the most widely used artemisinin-based combination therapy, whereas artesunate-mefloquine is used infrequently because of a perceived poor tolerance to mefloquine. WHO recommends reconsideration of the use of artesunate-mefloquine in Africa. We compared the efficacy and safety of fixed-dose
Artesunate-mefloquine with that of artemether-lumefantrine for treatment of children younger than 5 years with uncomplicated P falciparum malaria.

Methods: We did this multicentre, phase 4, open-label, non-inferiority trial in Burkina Faso, Kenya, and Tanzania. Children aged 6-59 months with uncomplicated malaria were randomly assigned (1:1), via a computer-generated randomisation list, to receive 3 days' treatment with either one or two artesunate-mefloquine tablets (25 mg artesunate and 55 mg mefloquine) once a day or one or two artemether-lumefantrine tablets (20 mg artemether and 120 mg lumefantrine) twice a day. Parasitological assessments were done independently by two microscopists who were blinded to treatment allocation. The primary outcome was the PCR-corrected rate of adequate clinical and parasitological response (ACPR) at day 63 in the per-protocol population. Non-inferiority was shown if the lower limit of the 95% CI for the difference between groups was greater than -5%. Early vomiting was monitored and neuropsychiatric status assessed regularly during follow-up. This study is registered with ISRCTN, number ISRCTN17472707, and the Pan African Clinical Trials Registry, number PACTR201202000278282.

Findings: 945 children were enrolled and randomised, 473 to artesunate-mefloquine and 472 to artemether-lumefantrine. The per-protocol population consisted of 407 children in each group. The PCR-corrected ACPR rate at day 63 was 90.9% (370 patients) in the artesunate-mefloquine group and 89.7% (365 patients) in the artemether-lumefantrine group (treatment difference 1.23%, 95% CI -2.84% to 5.29%). At 72 h after the start of treatment, no child had detectable parasitaemia and less than 6% had fever, with a similar number in each group (21 in the artesunate-mefloquine group vs 24 in the artemether-lumefantrine group). The safety profiles of artesunate-mefloquine and artemether-lumefantrine were similar, with low rates of early vomiting (71 [15.3%] of 463 patients in the artesunate-mefloquine group vs 79 [16.8%] of 471 patients in the artemether-lumefantrine group in any of the three dosing days), few neurological adverse events (ten [2.1%] of 468 vs five [1.1%] of 465), and no detectable psychiatric adverse events.

Interpretation: Artesunate-mefloquine is effective and safe, and an important treatment option, for children younger than 5 years with uncomplicated P falciparum malaria in Africa.