## 2012 KEMRI PUBLICATIONS

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<td>1.</td>
<td>Odhiambo FO, Laserson KF, Sewe M, Hamel MJ, Feikin DR, Adazu K, Ogwang S, Obor D, Amek N, Bayoh N, Ombok M, Lindblade K, Desai M, ter Kuile F, Phillips-Howard P, van Eijk AM, Rosen D, Hightower A, Ofware P, Muttai H, Nahlen B, DeCock K, Slutsker L, Breiman RF, Vulule JM. Profile: the KEMRI/CDC Health and Demographic Surveillance System--Western Kenya. Int J Epidemiol. 2012 Aug;41 (4):977-87. <strong>Abstract</strong>&lt;br&gt;The KEMRI/Centers for Disease Control and Prevention (CDC) Health and Demographic Surveillance System (HDSS) is located in Rarieda, Siaya and Gem Districts (Siaya County), lying northeast of Lake Victoria in Nyanza Province, western Kenya. The KEMRI/CDC HDSS, with approximately 220 000 inhabitants, has been the foundation for a variety of studies, including evaluations of insecticide-treated bed nets, burden of diarrhoeal disease and tuberculosis, malaria parasitaemia and anaemia, treatment strategies and immunological correlates of malaria infection, and numerous HIV, tuberculosis, malaria and diarrhoeal disease treatment and vaccine efficacy and effectiveness trials for more than a decade. Current studies include operations research to measure the uptake and effectiveness of the programmatic implementation of integrated malaria control strategies, HIV services, newly introduced vaccines and clinical trials. The HDSS provides general demographic and health information (such as population age structure and density, fertility rates, birth and death rates, in- and out-migrations, patterns of health care access and utilization and the local economics of health care) as well as disease- or intervention-specific information. The HDSS also collects verbal autopsy information on all deaths. Studies take advantage of the sampling frame inherent in the HDSS, whether at individual, household/compound or neighbourhood level. <strong>PubMed link</strong>- <a href="https://pubmed.ncbi.nlm.nih.gov/22933646/">https://pubmed.ncbi.nlm.nih.gov/22933646/</a></td>
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<td>2.</td>
<td>Snow RW, Amratia P, Kabaria CW, Noor AM, Marsh K. The changing limits and incidence of malaria in Africa: 1939-2009. Adv Parasitol. 2012;78:169-262. <strong>Abstract</strong>&lt;br&gt;Understanding the historical, temporal changes of malaria risk following control efforts in Africa provides a unique insight into what has been and might be archived towards a long-term ambition of elimination on the continent. Here, we use archived published and unpublished material combined with biological constraints on transmission</td>
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accompanied by a narrative on malaria control to document the changing incidence of malaria in Africa since earliest reports pre-second World War. One result is a more informed mapped definition of the changing margins of transmission in 1939, 1959, 1979, 1999 and 2009.


Abstract

The Affordable Medicines Facility-malaria (AMFm) has put into place a bold financing plan for artemisinin-combination therapy in a pilot phase in seven countries covering half the population at risk of malaria in Africa. A report of the AMFm independent evaluation, conducted by ICF International and the London School of Hygiene and Tropical Medicine, describes the success of the programme in the pilot sites: Ghana, Kenya, Madagascar, Niger, Nigeria, Tanzania (mainland and Zanzibar) and Uganda, comparing availability and affordability of high-quality artemisinin-combination therapies before and after AMFm launched. Proof of concept was achieved: AMFm increased availability and kept prices low, meeting its initial, ambitious benchmarks in most settings. Despite this overwhelming success, opposition to the programme and dwindling resources for malaria control conspire to cripple or kill AMFm.


Abstract

Although information about the precise world distribution and frequency of the inherited hemoglobin disorders is still limited, there is no doubt that they are going to pose an increasing burden on global health resources in the future. Their high frequency is a reflection of natural selection combined with a high frequency of consanguineous marriages in many countries, together with an epidemiological transition; whereby, as public health measures improve in the poorer countries of the world, more babies with these disorders are surviving to present for treatment.


**Abstract**

**Background:** HIV-1 strains have diversified extensively through mutation and recombination since their initial transmission to human beings many decades ago in Central Africa in the first part of the 20th Century (between 1915 and 1941). The upward trend in global HIV-1 diversity has continued unabated, with newer groups, subtypes, and unique and circulating recombinants increasingly being reported, especially in Africa.

**Objective:** In this review, we focus on the extensive diversity of HIV-1 over a decade (2000-2011), in 51 countries of the three African geographic regions (eastern and southern, western and central, and northern Africa) as per the WHO/UNAIDS 2010 classification.

**Methodology:** References for this review were identified through searches of PubMed, conference abstracts, Google Scholar, and Springer Online Archives Collection. We retrieved 273 citations, of which 200 reported HIV-1 diversity from Africa from January, 2000 to August, 2011. Articles resulting from these searches and relevant references cited in those articles were reviewed. Articles published in English and French were included.

**Findings:** There has been a high diversity of HIV-1 in its epicenter, west-central Africa. A few subtypes, namely, A (A1, A2, A3, A4, A5), C, CRF02_AG, and D accounted for about 85% of new infections. Subtype A and D have been stable in East Africa; C in southern Africa; A, G, CRF02_AG, and CRF06_cpx in western Africa; and subtype B and CRF02_AG in northern Africa. Recently a new putative group, designated P, was reported to be found in two Cameroonian.

**Conclusion:** The regional distributions of individual subtypes and recombinants are broadly stable, although unique/circulating recombinant forms may play an increasing role in the HIV pandemic. Understanding the kinetics and directions of this continuing adaptation and its impact on viral fitness, immunogenicity, and pathogenicity are crucial to the successful design of effective HIV vaccines. There is need for regular monitoring and review updates, such as the one presented here, to assist countries to plan and anticipate complex forms that may be introduced with time.


Abstract

Artemisinin-resistant Plasmodium falciparum malaria has emerged in western Cambodia and has been detected in western Thailand. The situation is ominously reminiscent of the emergence of resistance to chloroquine and to sulfadoxine-pyrimethamine several decades ago. Artemisinin resistance is a major threat to global public health, with the most severe potential effects in sub-Saharan Africa, where the disease burden is highest and systems for monitoring and containment of resistance are inadequate. The mechanisms that underlie artemisinin resistance are not fully understood. The main phenotypic trait associated with resistance is a substantial delay in parasite clearance, so far reported in southeast Asia but not in Africa. One of the pillars of the WHO global plan for artemisinin resistance containment is to increase monitoring and surveillance. In this Personal View, we propose strategies that should be adopted by malaria-endemic countries in Africa: resource mobilisation to reactivate regional surveillance networks, establishment of baseline parasite clearance profiles to serve as benchmarks to track emerging artemisinin resistance, improved data sharing to allow pooled analyses to identify rare events, modelling of risk factors for drug resistance, and development and validation of new approaches to monitor resistance.


Abstract

**Background:** The development of evidence-based clinical practice guidelines has gained wide acceptance in high-income countries and reputable international organizations. Whereas this approach may be a desirable standard, challenges remain in low-income settings with limited capacity and resources for evidence synthesis and guideline development. We present our experience using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach for the recent revision of the Kenyan pediatric clinical guidelines focusing on antibiotic treatment of pneumonia.

**Methods:** A team of health professionals, many with minimal prior experience conducting systematic reviews, carried out evidence synthesis for structured clinical questions. Summaries were compiled and distributed to a panel of clinicians.
academicians and policy-makers to generate recommendations based on best available research evidence and locally-relevant contextual factors.

**Results:** We reviewed six eligible articles on non-severe and 13 on severe/very severe pneumonia. Moderate quality evidence suggesting similar clinical outcomes comparing amoxicillin and cotrimoxazole for non-severe pneumonia received a strong recommendation against adopting amoxicillin. The panel voted strongly against amoxicillin for severe pneumonia over benzyl penicillin despite moderate quality evidence suggesting clinical equivalence between the two and additional factors favoring amoxicillin. Very low quality evidence suggesting ceftriaxone was as effective as the standard benzyl penicillin plus gentamicin for very severe pneumonia received a strong recommendation supporting the standard treatment.

**Conclusions:** Although this exercise may have fallen short of the rigorous requirements recommended by the developers of GRADE, it was arguably an improvement on previous attempts at guideline development in low-income countries and offers valuable lessons for future similar exercises where resources and locally-generated evidence are scarce.


**Abstract**

**Objective:** To explore the evidence translation process during a 1-week national guideline development workshop ("Child Health Evidence Week") in Kenya.

**Study design and setting:** Nonparticipant observational study of the discussions of a multidisciplinary guideline development panel in Kenya. Discussions were aided by GRADE (Grading of Recommendations Assessment, Development, and Evaluation) grid.

**Results:** Three key thematic categories emerged: 1) "referral to other evidence to support or refute the proposed recommendations;" 2) "assessment of the presented research evidence;" and 3) "assessment of the local applicability of evidence." The types of evidence cited included research evidence and anecdotal evidence based on clinician experiences. Assessment of the research evidence revealed important challenges in the translation of evidence into recommendations, including absence of evidence, low quality or inconclusive evidence, inadequate reporting of key features of the management under consideration, and differences in panelists' interpretation of the
research literature. A broad range of factors with potential to affect local applicability of evidence were discussed.

**Conclusion:** The process of the "Child Health Evidence Week" combined with the GRADE grid may aid transparency in the deliberative process of guideline development, and provide a mechanism for comprehensive assessment, documentation, and reporting of multiple factors that influence the quality and applicability of guideline recommendations.


**Abstract**

Public accountability has re-emerged as a top priority for health systems all over the world, and particularly in developing countries where governments have often failed to provide adequate public sector services for their citizens. One approach to strengthening public accountability is through direct involvement of clients, users or the general public in health delivery, here termed 'community accountability'. The potential benefits of community accountability, both as an end in itself and as a means of improving health services, have led to significant resources being invested by governments and non-governmental organizations. Data are now needed on the implementation and impact of these initiatives on the ground. A search of PubMed using a systematic approach, supplemented by a hand search of key websites, identified 21 papers from low- or middle-income countries describing at least one measure to enhance community accountability that was linked with peripheral facilities. Mechanisms covered included committees and groups (n = 19), public report cards (n = 1) and patients' rights charters (n = 1). In this paper we summarize the data presented in these papers, including impact, and factors influencing impact, and conclude by commenting on the methods used, and the issues they raise. We highlight that the international interest in community accountability mechanisms linked to peripheral facilities has not been matched by empirical data, and present a conceptual framework and a set of ideas that might contribute to future studies.


Abstract

**Background:** Specialized drug shops such as pharmacies and drug shops are increasingly becoming important sources of treatment. However, knowledge on their regulatory performance is scarce. We set out to systematically review literature on the characteristics, knowledge and practices of specialized drug shops in Sub-Saharan Africa.

**Methods:** We searched PubMed, EMBASE, WEB of Science, CAB Abstracts, PsycINFO and websites for organizations that support medicine policies and usage. We also conducted open searches using Google Scholar, and searched manually through references of retrieved articles. Our search included studies of all designs that described characteristics, knowledge and practices of specialized drug shops. Information was abstracted on authors, publication year, country and location, study design, sample size, outcomes investigated, and primary findings using a uniform checklist. Finally, we conducted a structured narrative synthesis of the main findings.

**Results:** We obtained 61 studies, mostly from Eastern Africa, majority of which were conducted between 2006 and 2011. Outcome measures were heterogeneous and included knowledge, characteristics, and dispensing and regulatory practices. Shop location and client demand were found to strongly influence dispensing practices. Whereas shops located in urban and affluent areas were more likely to provide correct treatments, those in rural areas provided credit facilities more readily. However, the latter also charged higher prices for medicines. A vast majority of shops simply sold whatever medicines clients requested, with little history taking and counseling. Most shops also stocked popular medicines at the expense of policy recommended treatments. Treatment policies were poorly communicated overall, which partly explained why staff had poor knowledge on key aspects of treatment such as medicine dosage and side effects. Overall, very little is known on the link between regulatory enforcement and practices of specialized drug shops.

**Conclusions:** Evidence suggests that characteristics and practices of specialized drug shops differ across rural and urban locations, and that these providers are highly responsive to client demand. However, there is a dearth in knowledge on how regulatory enforcement influences their characteristics and practices, and what strategies can be employed to strengthen the governance of the retail pharmaceutical sector.


Abstract

To develop a case definition for the Pneumonia Etiology Research for Child Health (PERCH) project, we sought a widely acceptable classification that was linked to existing pneumonia research and focused on very severe cases. We began with the World Health Organization's classification of severe/very severe pneumonia and refined it through literature reviews and a 2-stage process of expert consultation. PERCH will study hospitalized children, aged 1-59 months, with pneumonia who present with cough or difficulty breathing and have either severe pneumonia (lower chest wall indrawing) or very severe pneumonia (central cyanosis, difficulty breastfeeding/drinking, vomiting everything, convulsions, lethargy, unconsciousness, or head nodding). It will exclude patients with recent hospitalization and children with wheeze whose indrawing resolves after bronchodilator therapy. The PERCH investigators agreed upon standard interpretations of the symptoms and signs. These will be maintained by a clinical standardization monitor who conducts repeated instruction at each site and by recurrent local training and testing.


Abstract

Background: Many health systems in Africa are funded primarily through out-of-pocket payments. Out-of-pocket payments prevent people from seeking care, can result to catastrophic health spending and lead to impoverishment. This paper estimates the burden of out-of-pocket payments in Kenya; the incidence and intensity of catastrophic health care expenditure and the effect of health spending on national poverty estimates.

Methods: Data were drawn from a nationally representative health expenditure and utilization survey (n = 8414) conducted in 2007. The survey provided detailed information on out-of-pocket payments and consumption expenditure. Standard data analytical techniques were applied to estimate the incidence and intensity of catastrophic health expenditure. Various thresholds were applied to demonstrate the sensitivity of catastrophic measures.

Results: Each year, Kenyan households spend over a tenth of their budget on health care payments. The burden of out-of-pocket payments is highest among the poor. The poorest households spent a third of their resources on health care payments each year
compared to only 8% spent by the richest households. About 1.48 million Kenyans are pushed below the national poverty line due to health care payments.

**Conclusions:** Kenyans are becoming poorer due to health care payments. The need to protect individuals from health care related impoverishment calls for urgent reforms in the Kenyan health system. An important policy question remains what health system reforms are needed in Kenya to ensure that financial risk protection for all is achieved.


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**Abstract**

Dejan Zurovac and colleagues discuss six areas where text messaging could improve the delivery of health services and health outcomes in malaria in Africa.


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**Abstract**

**Background:** Quinine has anti-epileptic properties in animals. However, in humans this has not been systematically investigated.

**Purpose:** To examine the available research evidence on the effects of quinine on seizures in adults or children.

**Methods:** We searched online databases for published and unpublished studies in any language from January 1966 to March 2011. We considered randomized controlled trials (RCTs) evaluating the use of quinine in comparison to other drugs in humans with malaria or other conditions, and that reported the prevalence of seizures. Random effects meta-analysis was used to pool effect estimates in order to determine the effect of quinine on the prevalence of seizures.

**Results:** We identified six randomized controlled trials on severe malaria. Quinine was compared to the artemisinin derivatives in all trials. A total of 8,244 patients were included. In the meta-analysis, there was no significant effect of quinine on the prevalence of seizures when compared to the artemisinin derivatives (Odds ratio (OR) =0.90, 95% Confidence Interval (95%CI) =0.63-1.30). There was significant
heterogeneity (I(2)=66%, Chi-square=17.44, p=0.008). Subgroup analysis showed that quinine significantly reduced seizures when compared to artemether (OR = 0.66, 95%CI = 0.49-0.88) but when compared to artesunate, prevalence of seizures increased significantly (OR = 1.24, 95%CI = 1.05-1.47).

**Conclusion:** There is no sufficient evidence to conclude that quinine has any antiepileptic properties in humans.


**Abstract**

Reducing childhood mortality in resource-poor regions depends on effective interventions to decrease neonatal mortality from severe infection, which contributes up to a half of all neonatal deaths. There are key differences in resource-poor, compared to resource-rich, countries in terms of diagnosis, supportive care and treatment. In resource-poor settings, diagnosis is based on identifying clinical syndromes from international guidelines; microbiological investigations are restricted to a few research facilities. Low levels of staffing and equipment limit the provision of basic supportive care, and most facilities cannot provide respiratory support. Empiric antibiotic treatment guidelines are based on few aetiological and antimicrobial susceptibility data. Research on improving health care systems to provide effective supportive care, and implementation of simple pragmatic interventions, such as low-cost respiratory support, are essential, together with improved surveillance to monitor emerging drug resistance and treatment failures. Reductions in mortality will also be achieved through prevention of infection; including emerging vaccination and anti-sepsis strategies.


**Abstract**

The aim of this study was to develop and validate a tool to measure perceived stigma among people with epilepsy (PWE) in Kilifi, Kenya. We reviewed existing scales that measured stigma, particularly of epilepsy. We conducted a qualitative study to determine salient concerns related to stigma in Kilifi. Themes were generated, and those related to stigma were used to construct an 18-item stigma scale. A descriptive cross-
sectional survey was then conducted among 673 PWE to assess the reliability and validity of the scale. Internal consistency was calculated using Cronbach's alpha and test-retest reliability with an interclass correlation coefficient. The final scale had 15 items, which had high internal consistency (Cronbach's $\alpha=0.91$) and excellent test-retest reliability ($r=0.92$). Factor analysis indicated that the scale was unidimensional with one factor solution explaining 45.8% of the variance. The Kilifi Stigma Scale for Epilepsy is a culturally appropriate measure of stigma with strong psychometric properties.


**Abstract**

Epilepsy remains misunderstood, particularly in resource poor countries (RPC). We developed and validated a tool to assess beliefs and attitudes about epilepsy among people with epilepsy (PWE) in Kilifi, Kenya. The 50-item scale was developed through a literature review and qualitative study findings, and its reliability and validity were assessed with 673 PWE. A final scale of 34 items had Cronbach's alpha scores for the five subscales: causes of epilepsy ($\alpha=0.71$); biomedical treatment of epilepsy ($\alpha=0.70$); cultural treatment of epilepsy ($\alpha=0.75$); risk and safety concerns about epilepsy ($\alpha=0.56$); and negative attitudes about epilepsy ($\alpha=0.76$) and entire scale ($\alpha=0.70$). Test-retest reliability was acceptable for all the subscales. The Kilifi Epilepsy Beliefs and Attitude Scale is a reliable and valid tool that measures beliefs and attitudes about epilepsy. It may be useful in other RPC or as a tool to assess the effectiveness of interventions to improve knowledge, beliefs, and attitudes about epilepsy.


**Abstract**

Tuberculosis (TB) is a leading cause of death globally. Natural history studies show that young children are at particularly high risk of progression to active TB and severe, disseminated disease following infection. Despite this, high-quality regional and global surveillance data on the burden of childhood TB are lacking. We discuss the unique aspects of TB in children that make diagnosis and therefore surveillance challenging; the limitations of available surveillance data; other data which provide insights into the true burden of childhood TB. Improved surveillance is among the key research priorities
identified for childhood TB, but progress to date has been slow. Recent advances in TB diagnostics, and standardized clinical diagnostic guidelines and case definitions, all provide opportunities for new strategies to improve surveillance. Better-quality data on the burden and trends of childhood TB will inform and improve both public health policy and clinical practice.


Abstract

This study reports pediatric surveillance over 3 years for human rhinovirus (HRV) at the District Hospital of Kilifi, coastal Kenya. Nasopharyngeal samples were collected from children presenting at outpatient clinic with no signs of acute respiratory infection, or with signs of upper respiratory tract infection, and from children admitted to the hospital with lower respiratory tract infection. Samples were screened by real-time reverse transcriptase polymerase chain reaction (real-time RT-PCR) and classified further to species by nucleotide sequencing of the VP4/VP2 junction. Of 441 HRV positives by real-time RT-PCR, 332 were classified to species, with 47% (155) being HRV-A, 5% (18) HRV-B, and 48% (159) HRV-C. There was no clear seasonal pattern of occurrence for any species. The species were present in similar proportions in the inpatient and outpatient sample sets, and no significant association between species distribution and the severity of lower respiratory tract infection in the inpatients could be determined. HRV sequence analysis revealed multiple but separate clusters in circulation particularly for HRV-A and HRV-C. Most HRV-C clusters were distinct from reference sequences downloaded from GenBank. In contrast, most HRV-A and HRV-B sequences clustered with either known serotypes or strains from elsewhere within Africa and other regions of the world. This first molecular epidemiological study of HRV in the region defines species distribution in accord with reports from elsewhere in the world, shows considerable strain diversity and does not identify an association between any species and disease severity.


Abstract

Studies of the fine-scale spatial epidemiology of malaria consistently identify malaria hotspots, comprising clusters of homesteads at high transmission intensity. These hotspots sustain transmission, and may be targeted by malaria-control programmes. Here we describe the spatial relationship between the location of Anopheles larval sites and human malaria infection in a cohort study of 642 children, aged 1-10-years-old. Our data suggest that proximity to larval sites predict human malaria infection, when homesteads are upwind of larval sites, but not when homesteads are downwind of larval sites. We conclude that following oviposition, female Anophelines fly upwind in search for human hosts and, thus, malaria transmission may be disrupted by targeting vector larval sites in close proximity, and downwind to malaria hotspots.


Abstract

Background: Health care utilization is affected by several factors including geographic accessibility. Empirical data on utilization of health facilities is important to understanding geographic accessibility and defining health facility catchments at a national level. Accurately defining catchment population improves the analysis of gaps in access, commodity needs and interpretation of disease incidence. Here, empirical household survey data on treatment seeking for fever were used to model the utilisation of public health facilities and define their catchment areas and populations in northern Namibia.

Method: This study uses data from the Malaria Indicator Survey (MIS) of 2009 on treatment seeking for fever among children under the age of five years to characterize facility utilisation. Probability of attendance of public health facilities for fever treatment was modelled against a theoretical surface of travel times using a three parameter logistic model. The fitted model was then applied to a population surface to predict the number of children likely to use a public health facility during an episode of fever in northern Namibia.

Results: Overall, from the MIS survey, the prevalence of fever among children was 17.6% CI [16.0-19.1] (401 of 2,283 children) while public health facility attendance for fever was 51.1%, [95%CI: 46.2-56.0]. The coefficients of the logistic model of travel time against fever treatment at public health facilities were all significant (p < 0.001).
From this model, probability of facility attendance remained relatively high up to 180 minutes (3 hours) and thereafter decreased steadily. Total public health facility catchment population of children under the age five was estimated to be 162,286 in northern Namibia with an estimated fever burden of 24,830 children. Of the estimated fevers, 8,021 (32.3%) were within 30 minutes of travel time to the nearest health facility while 14,902 (60.0%) were within 1 hour.

**Conclusion:** This study demonstrates the potential of routine household surveys to empirically model health care utilisation for the treatment of childhood fever and define catchment populations enhancing the possibilities of accurate commodity needs assessment and calculation of disease incidence. These methods could be extended to other African countries where detailed mapping of health facilities exists.


**Abstract**

**Background:** The existing case fatality estimates of inpatient childhood pneumonia in developing countries are largely from periods preceding routine use of conjugate vaccines for infant immunization and such primary studies rarely explore hospital variations in mortality. We analysed case fatality rates of children admitted to nine Kenyan hospitals with pneumonia during the era of routine infant immunization with Hib conjugate vaccine to determine if significant variations exist between hospitals.

**Methods:** Pneumonia admissions and outcomes in paediatric wards are described using data collected over two time periods: a one-year period (2007-2008) in nine hospitals, and data from a 9.25-year period (1999-March 2008) in one of the participating hospitals. Hospital case fatality rates for inpatient pneumonia during 2007 to 2008 were modeled using a fixed effect binomial regression model with a logit link. Using an interrupted time series design, data from one hospital were analysed for trends in pneumonia mortality during the period between 1997 and March 2008.

**Results:** Overall, 195 (5.9%) children admitted to all 9 hospitals with pneumonia from March 2007 to March 2008 died in hospital. After adjusting for child's sex, comorbidity, and hospital effect, mortality was significantly associated with child's age (p<0.001) and pneumonia severity (p<0.001). There was evidence of significant variations in mortality between hospitals (LR $\chi^2(2) = 52.19$; p<0.001). Pneumonia mortality remained stable in
the periods before (trend -0.03, 95% CI -0.1 to 0.02) and after Hib introduction (trend 0.04, 95% CI -0.04 to 0.11).

Conclusions: There are important variations in hospital pneumonia case fatality in Kenya and these variations are not attributed to temporal changes. Such variations in mortality are not addressed by existing epidemiological models and need to be considered in allocating resources to improve child health.


Abstract

Objective: To describe out-of-pocket costs of inpatient care for children under 5 years of age in district hospitals in Kenya.

Methods: A total of 256 caretakers of admitted children were interviewed in 2-week surveys conducted in eight hospitals in four provinces in Kenya. Caretakers were asked to report care seeking behaviour and expenditure related to accessing inpatient care. Family socio-economic status was assessed through reported expenditure in the previous month.

Results: Seventy eight percent of caretakers were required to pay user charges to access inpatient care for children. User charges (mean, US$ 8.1; 95% CI, 6.4-9.7) were 59% of total out-of-pocket costs, while transport costs (mean, US$ 4.9; 95% CI, 3.9-6.0) and medicine costs (mean, US$ 0.7; 95% CI, 0.5-1.0) were 36% and 5%, respectively. The mean total out-of-pocket cost per paediatric admission was US$ 14.1 (95% CI, 11.9-16.2). Out-of-pocket expenditures on health were catastrophic for 25.4% (95% CI, 18.4-33.3) of caretakers interviewed. Out-of-pocket expenditures were regressive, with a greater burden being experienced by households with lower socio-economic status.

Conclusion: Despite a policy of user fee exemption for children under 5 years of age in Kenya, our findings show that high unofficial user fees are still charged in district hospitals. Financing mechanisms that will offer financial risk protection to children seeking care need to be developed to remove barriers to child survival.


Abstract

Background: Pneumonia is the leading cause of childhood mortality worldwide. The World Health Organization recommends presumptive treatment based on clinical syndromes. Recent studies raise concerns over the frequency of treatment failure in Africa.

Methods: We applied a definition of treatment failure to data prospectively collected from children who were 2-59 months of age with severe, or very severe, pneumonia admitted to Kilifi District Hospital, Kenya, from May 2007 through May 2008 and treated using World Health Organization guidelines. The primary outcome was treatment failure at 48 hours.

Results: Of 568 children, median age 11 months, 165 (29%) had very severe pneumonia, 30 (5.3%) a positive HIV test and 62 (11%) severe malnutrition. One hundred eleven (20%; 95% confidence interval: 17-23%) children failed treatment at 48 hours and 34 (6.0%) died; 22 (65%) deaths occurred before 48 hours. Of 353 children with severe pneumonia, without HIV or severe malnutrition, 42 (12%) failed to respond at 48 hours, 15 (4.3%) failed at 5 days and 1 child (0.3%) died. Among 215 children with either severe pneumonia complicated by HIV or severe malnutrition, or very severe pneumonia, 69 (32%) failed to treatment at 48 hours, 47 (22%) failed at 5 days and 33 (16%) died. Treatment failure at 48 hours was associated with shock, bacteremia, very severe pneumonia, oxygen saturation in hemoglobin <95%, severe malnutrition, HIV and age <1 year in multivariable models.

Conclusions: In this setting, few children with uncomplicated severe pneumonia fail treatment or die under current guidelines. Deaths mainly occurred early and may be reduced by improving prevention, prehospital care and treatment of sepsis.


Abstract

Background: Pneumococcal meningitis (PM) is a severe and life-threatening disease that is associated with cognitive impairment including learning difficulties, cognitive slowness, short-term memory deficits and poor academic performance. There are
limited data on cognitive outcomes following exposure to PM from Africa mainly due to lack of culturally appropriate tools. We report cognitive processes of exposed children as measured by auditory and visual event-related potentials.

**Methods:** Sixty-five children (32 male, mean 8.4 years, SD 3.0 years) aged between 4-15 years with a history of PM and an age-matched control group of 93 children (46 male; mean 8.4 years, SD 2.7 years) were recruited from a well-demarcated study area in Kilifi. In the present study, both baseline to peak and peak-to-peak amplitude differences are reported.

**Results:** Children with a history of pneumococcal meningitis had significantly longer auditory P1 and P3a latencies and smaller P1 amplitudes compared to unexposed children. In the visual paradigm, children with PM seemingly lacked a novelty P3a component around 350 ms where control children had a maximum, and showed a lack of stimulus differentiation at Nc. Further, children with exposure to PM had smaller peak to peak amplitude (N2-P1) compared to unexposed children.

**Conclusion:** The results suggest that children with a history of PM process novelty differently than do unexposed children, with slower latencies and reduced or absent components. This pattern suggests poorer auditory attention and/or cognitive slowness and poorer visual attention orienting, possibly due to disruption in the functions of the lateral prefrontal and superior temporal cortices. ERPs may be useful for assessment of the development of perceptual-cognitive functions in post brain-injury in African children by providing an alternate way of assessing cognitive development in patient groups for whom more typical standardized neuropsychological assessments are unavailable.


**Abstract**

**Background:** Understanding the relationship between Plasmodium falciparum malaria transmission and health outcomes requires accurate estimates of exposure to infectious mosquitoes. However, measures of exposure such as mosquito density and entomological inoculation rate (EIR) are generally aggregated over large areas and time periods, biasing the outcome-exposure relationship. There are few studies examining the extent and drivers of local variation in malaria exposure in endemic areas.
Methods: We describe the spatio-temporal dynamics of malaria transmission intensity measured by mosquito density and EIR in the KEMRI/CDC health and demographic surveillance system using entomological data collected during 2002-2004. Geostatistical zero inflated binomial and negative binomial models were applied to obtain location specific (house) estimates of sporozoite rates and mosquito densities respectively. Model-based predictions were multiplied to estimate the spatial pattern of annual entomological inoculation rate, a measure of the number of infective bites a person receive per unit of time. The models included environmental and climatic predictors extracted from satellite data, harmonic seasonal trends and parameters describing space-time correlation.

Results: Anopheles gambiae s.l was the main vector species accounting for 86% (n=2309) of the total mosquitoes collected with the remainder being Anopheles funestus. Sixty eight percent (757/1110) of the surveyed houses had no mosquitoes. Distance to water bodies, vegetation and day temperature were strongly associated with mosquito density. Overall annual point estimates of EIR were 6.7, 9.3 and 9.6 infectious bites per annum for 2002, 2003 and 2004 respectively. Monthly mosquito density and EIR varied over the study period peaking in May during the wet season each year. The predicted and observed densities of mosquitoes and EIR showed a strong seasonal and spatial pattern over the study area.

Conclusions: Spatio-temporal maps of malaria transmission intensity obtained in this study are not only useful in understanding variability in malaria epidemiology over small areas but also provide a high resolution exposure surface that can be used to analyse the impact of transmission on malaria related and all-cause morbidity and mortality.


Abstract

The study describes the nature, context and implications of a unique form of transactional sexual relationships in the fishing communities along Lake Victoria in Kisumu County, Kenya. We conducted 12 focus group discussions and 17 key informant interviews among fishermen, fishmongers and fish transporters in Kisumu. Women fishmongers in the fishing communities commonly form relationships with fishermen, which are often sexual, as part of the jaboya system, wherein women who wish to sell fish in the market secure the rights to purchase the fish caught by the fishermen. Due to the nature and context of the sexual intercourse, sex typically occurs
in a hurried manner, often without preparation or protection. Thus, by engaging in a web of these relationships, conducted in contexts that compromise their ability to practice safer sex, men and women in these fishing communities are at increased risk of HIV.


**Abstract**

**Background:** Many people with epilepsy in low-income countries do not receive appropriate biomedical treatment. This epilepsy treatment gap might be caused by patients not seeking biomedical treatment or not adhering to prescribed antiepileptic drugs (AEDs). We measured the prevalence of and investigated risk factors for the epilepsy treatment gap in rural Kenya.

**Methods:** All people with active convulsive epilepsy identified during a cross-sectional survey of 232,176 people in Kilifi were approached. The epilepsy treatment gap was defined as the percentage of people with active epilepsy who had not accessed biomedical services or who were not on treatment or were on inadequate treatment. Information about risk factors was obtained through a questionnaire-based interview of sociodemographic characteristics, socioeconomic status, access to health facilities, seizures, stigma, and beliefs and attitudes about epilepsy. The factors associated with people not seeking biomedical treatment and not adhering to AEDs were investigated separately, adjusted for age.

**Findings:** 673 people with epilepsy were interviewed, of whom 499 (74%) reported seeking treatment from a health facility. Blood samples were taken from 502 (75%) people, of whom 132 (26%) reported taking AEDs, but 189 (38%) had AEDs detectable in the blood. The sensitivity and specificity of self-reported adherence compared with AEDs detected in blood were 38·1% (95% CI 31·1-45·4) and 80·8% (76·0-85·0). The epilepsy treatment gap was 62·4% (58·1-66·6). In multivariable analysis, failure to seek biomedical treatment was associated with a patient holding traditional animistic religious beliefs (adjusted odds ratio 1·85, 95% CI 1·11-2·71), reporting negative attitudes about biomedical treatment (0·86, 0·78-0·95), living more than 30 km from health facilities (3·89, 1·77-8·51), paying for AEDs (2·99, 1·82-4·92), having learning difficulties (2·30, 1·29-4·11), having had epilepsy for longer than 10 years (4·60, 2·07-10·23), and having focal seizures (2·28, 1·50-3·47). Reduced adherence was associated
with negative attitudes about epilepsy (1·10, 1·03-1·18) and taking of AEDs for longer than 5 years (3·78, 1·79-7·98).

**Interpretation:** The sensitivity and specificity of self-reported adherence is poor, but on the basis of AED detection in blood almost two-thirds of patients with epilepsy were not on treatment. Education about epilepsy and making AEDs freely available in health facilities near people with epilepsy should be investigated as potential ways to reduce the epilepsy treatment gap.


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**Abstract**

**Background:** Heterogeneity in malaria exposure complicates survival analyses of vaccine efficacy trials and confounds the association between immune correlates of protection and malaria infection in longitudinal studies. Analysis may be facilitated by taking into account the variability in individual exposure levels, but it is unclear how exposure can be estimated at an individual level.

**Method and findings:** We studied three cohorts (Chonyi, Junju and Ngerenya) in Kilifi District, Kenya to assess measures of malaria exposure. Prospective data were available on malaria episodes, geospatial coordinates, proximity to infected and uninfected individuals and residence in predefined malaria hotspots for 2,425 individuals. Antibody levels to the malaria antigens AMA1 and MSP1(142) were available for 291 children from Junju. We calculated distance-weighted local prevalence of malaria infection within 1 km radius as a marker of individual's malaria exposure. We used multivariable modified Poisson regression model to assess the discriminatory power of these markers for malaria infection (i.e. asymptomatic parasitaemia or clinical malaria). The area under the receiver operating characteristic (ROC) curve was used to assess the discriminatory power of the models. Local malaria prevalence within 1 km radius and AMA1 and MSP1(142) antibodies levels were independently associated with malaria infection. Weighted local malaria prevalence had an area under ROC curve of 0.72 (95%CI: 0.66-0.73), 0.71 (95%CI: 0.69-0.73) and 0.82 (95%CI: 0.80-0.83) among cohorts in Chonyi, Junju and Ngerenya respectively. In a small subset of children from Junju, a model incorporating weighted local malaria prevalence with AMA1 and MSP1(142) antibody levels provided an AUC of 0.83 (95%CI: 0.79-0.88).

**Conclusion:** We have proposed an approach to estimating the intensity of an individual's malaria exposure in the field. The weighted local malaria prevalence can be
used as individual marker of malaria exposure in malaria vaccine trials and longitudinal studies of natural immunity to malaria.


Abstract

**Background:** The 58th World Health Assembly called for all health systems to move towards universal coverage where everyone has access to key promotive, preventive, curative and rehabilitative health interventions at an affordable cost. Universal coverage involves ensuring that health care benefits are distributed on the basis of need for care and not on ability to pay. The distribution of health care benefits is therefore an important policy question, which health systems should address. The aim of this study is to assess the distribution of health care benefits in the Kenyan health system, compare changes over two time periods and demonstrate the extent to which the distribution meets the principles of universal coverage.

**Methods:** Two nationally representative cross-sectional households surveys conducted in 2003 and 2007 were the main sources of data. A comprehensive analysis of the entire health system is conducted including the public sector, private-not-for-profit and private-for-profit sectors. Standard benefit incidence analysis techniques were applied and adopted to allow application to private sector services.

**Results:** The three sectors recorded similar levels of pro-rich distribution in 2003, but in 2007, the private-not-for-profit sector was pro-poor, public sector benefits showed an equal distribution, while the private-for-profit sector remained pro-rich. Larger pro-rich disparities were recorded for inpatient compared to outpatient benefits at the hospital level, but primary health care services were pro-poor. Benefits were distributed on the basis of ability to pay and not on need for care.

**Conclusions:** The principles of universal coverage require that all should benefit from health care according to need. The Kenyan health sector is clearly inequitable and benefits are not distributed on the basis of need. Deliberate efforts should be directed to restructuring the Kenyan health system to address access barriers and ensure that all Kenyans benefit from health care when they need it.


**Abstract**

**Background:** Influenza data gaps in sub-Saharan Africa include incidence, case fatality, seasonal patterns, and associations with prevalent disorders.

**Methods:** Nasopharyngeal samples from children aged <12 years who were admitted to Kilifi District Hospital during 2007-2010 with severe or very severe pneumonia and resided in the local demographic surveillance system were screened for influenza A, B, and C viruses by molecular methods. Outpatient children provided comparative data.

**Results:** Of 2002 admissions, influenza A virus infection was diagnosed in 3.5% (71), influenza B virus infection, in 0.9% (19); and influenza C virus infection, in 0.8% (11 of 1404 tested). Four patients with influenza died. Among outpatients, 13 of 331 (3.9%) with acute respiratory infection and 1 of 196 without acute respiratory infection were influenza positive. The annual incidence of severe or very severe pneumonia, of influenza (any type), and of influenza A, was 1321, 60, and 43 cases per 100,000 <5 years of age, respectively. Peak occurrence was in quarters 3-4 each year, and approximately 50% of cases involved infants: temporal association with bacteremia was absent. Hypoxia was more frequent among pneumonia cases involving influenza (odds ratio, 1.78; 95% confidence interval, 1.04-1.96). Influenza A virus subtypes were seasonal H3N2 (57%), seasonal H1N1 (12%), and 2009 pandemic H1N1 (7%).

**Conclusions:** The burden of influenza was small during 2007-2010 in this pediatric hospital in Kenya. Influenza A virus subtype H3N2 predominated, and 2009 pandemic influenza A virus subtype H1N1 had little impact.


**Abstract**

**Background:** There is general consensus internationally that unfair distribution of the benefits of research is exploitative and should be avoided or reduced. However, what constitutes fair benefits, and the exact nature of the benefits and their mode of provision can be strongly contested. Empirical studies have the potential to contribute viewpoints.
and experiences to debates and guidelines, but few have been conducted. We conducted a study to support the development of guidelines on benefits and payments for studies conducted by the KEMRI-Wellcome Trust programme in Kilifi, Kenya.

**Methods:** Following an initial broad based survey of cash, health services and other items being offered during research by all programme studies (n = 38 studies), interviews were held with research managers (n = 9), and with research staff involved in 8 purposively selected case studies (n = 30 interviewees). Interviews explored how these 'benefits' were selected and communicated, experiences with their administration, and recommendations for future guidelines. Data fed into a consultative workshop attended by 48 research staff and health managers, which was facilitated by an external ethicist.

**Findings:** The most commonly provided benefits were medical care (for example free care, and strengthened quality of care), and lunch or snacks. Most cash given to participants was reimbursement of transport costs (for example to meet appointments or facilitate use of services when unexpectedly sick), but these payments were often described by research participants as benefits. Challenges included: tensions within households and communities resulting from lack of clarity and agreement on who is eligible for benefits; suspicion regarding motivation for their provision; and confusion caused by differences between studies in types and levels of benefits.

**Conclusions:** Research staff differed in their views on how benefits should be approached. Echoing elements of international benefit sharing and ancillary care debates, some research staff saw research as based on goodwill and partnership, and aimed to avoid costs to participants and a commercial relationship; while others sought to maximise participant benefits given the relative wealth of the institution and the multiple community needs. An emerging middle position was to strengthen collateral or indirect medical benefits to communities through collaborations with the Ministry of Health to support sustainability.


**Abstract**

**Objective:** To investigate risk factors, including reported net use, for Plasmodium infection and anaemia among school children and to explore variations in effects across different malaria ecologies occurring in Kenya.
**Methods:** This study analysed data for 49 975 school children in 480 schools surveyed during a national school malaria survey, 2008-2010. Mixed effects logistic regression was used to investigate factors associated with Plasmodium infection and anaemia within different malaria transmission zones.

**Results:** Insecticide-treated net (ITN) use was associated with reduction in the odds of Plasmodium infection in coastal and western highlands epidemic zones and among boys in the lakeside high transmission zone. Other risk factors for Plasmodium infection and for anaemia also varied by zone. Plasmodium infection was negatively associated with increasing socio-economic status in all transmission settings, except in the semi-arid north-east zone. Plasmodium infection was a risk factor for anaemia in lakeside high transmission, western highlands epidemic and central low-risk zones, whereas ITN use was only associated with lower levels of anaemia in coastal and central zones and among boys in the lakeside high transmission zone.

**Conclusions:** The risk factors for Plasmodium infection and anaemia, including the protective associations with ITN use, vary according to malaria transmission settings in Kenya, and future efforts to control malaria and anaemia should take into account such heterogeneities among school children.


**Abstract**

Humans respond to foreign antigen by generating plasma Abs and memory B cells (MBCs). The Ab response then declines, sometimes to below the limit of detection. In contrast, MBCs are generally thought to be long-lived. We tested and compared Plasmodium falciparum (Pf)-specific Ab and MBC responses in two populations of children: (i) previously exposed children who had documented Pf infections several years ago, but minimal exposure since then; and (ii) persistently exposed children living in a separate but nearby endemic area. We found that although Pf-specific plasma Abs were lower in previously exposed children compared with persistently exposed children, their cognate MBCs were maintained at similar frequencies. We conclude that serological analysis by itself would greatly underestimate the true memory of Pf-specific Ab responses in previously exposed children living in areas where Pf transmission has been reduced or eliminated.

Abstract

Mosquitoes (Diptera: Culicidae) are important vectors of human disease-causing pathogens. Mosquitoes are found both in rural and urban areas. Deteriorating infrastructure, poor access to health, water and sanitation services, increasing population density, and widespread poverty contribute to conditions that modify the environment, which directly influences the risk of disease within the urban and peri-urban ecosystem. The objective of this study was to evaluate the mosquito vector abundance and diversity in urban, peri-urban, and rural strata in Malindi along the Kenya coast. The study was conducted in the coastal district of Malindi between January and December 2005. Three strata were selected which were described as urban, peri-urban, and rural. Sampling was done during the wet and dry seasons. Sampling in the wet season was done in the months of April and June to cover the long rainy season and in November and December to cover the short rainy season, while the dry season was between January and March and September and October. Adult mosquito collection was done using Pyrethrum Spray Collection (PSC) and Centers for Disease Control and Prevention (CDC) light traps inside houses and specimens were identified morphologically. In the three strata (urban, peri-urban, and rural), 78.5% of the total mosquito (n = 7,775) were collected using PSC while 18.1% (n = 1,795) were collected using the CDC light traps. Using oviposition traps, mosquito eggs were collected and reared in the insectary which yielded 329 adults of which 83.8% (n = 276) were Aedes aegypti and 16.2% (n = 53) were Culex quinquefasciatus. The mosquito distribution in the three sites varied significantly in each collection site. Anopheles gambiae, Anopheles funestus and Anopheles coustani were predominant in the rural stratum while C. quinquefasciatus was mostly found in urban and peri-urban strata. However, using PSC and CDC light trap collection techniques, A. aegypti was only found in urban strata. In the three strata, mosquitoes were mainly found in high numbers during the wet season. Further, A. gambiae, C. quinquefasciatus, and A. aegypti mosquitoes were found occurring together inside the houses. This in turn exposes the inhabitants to an array of mosquito-borne diseases including malaria, bancroftian filariasis, and arboviruses (dengue fever, Yellow fever, Rift Valley fever, Chikungunya fever, and West Nile Virus). In conclusion, our findings provide useful information for the design of integrated mosquito and disease control programs in East African environments.

Abstract

Chloroquine (CQ) drug was withdrawn in 1998 as a first-line treatment of uncomplicated malaria in Kenya. This was in response to resistance to the drug in Plasmodium falciparum malaria parasite. Investigations were conducted to determine prevalence of CQ resistance genotypes in the parasites in Tiwi, a malaria endemic town in Kenya, before and about a decade after the withdrawal of the drug. Blood samples were collected and spotted on filter papers in 1999 and 2008 from 75 and 77 out-patients respectively with uncomplicated malaria. The sampling was conducted using finger pricking technique. DNA was extracted from individual spots in the papers and screened for the presence of P. falciparum chloroquine resistance transporter (Pfcrt) and multi drug resistance (Pfmdr-1) markers using nested PCR. Nature of mutations (haplotypes) in the Pfcrt and Pfmdr-1 markers in the samples were confirmed using dot blot hybridization technique. Changes in pattern of CQ resistance in the parasite samples in 1999 and 2008 were assessed by Chi Square test. There was a significant (P<0.05) reduction in CQ resistant genotypes of the parasite between 1999 and 2008. Pfmdr and Pfcrt CQ resistant genotypes in 2008 reduced to 54.10 and 63.64% respectively, from 75.39 and 88.0% respectively in 1999. This reduction was accompanied by emergence of Pfcrt specific CQ sensitive (IEK) and intermediate/partially CQ resistant (MET) haplotypes. Results suggest significant reversal of the phenotype of the parasite from chloroquine resistant to wild/sensitive type. The novel haplotypes indicates transitional phase of the parasite to the wild type. Current prevalence of chloroquine resistant genotype is definitely above the threshold for efficacious re-introduction of chloroquine for treatment of malaria in Tiwi.


Abstract

Objective: To assess the inter-observer variability and accuracy of Mid Upper Arm Circumference (MUAC) and weight-for-length Z score (WFLz) among infants aged <6 months performed by community health workers (CHWs) in Kilifi District, Kenya.
Methods: A cross-sectional repeatability study estimated inter-observer variation and accuracy of measurements initially undertaken by an expert anthropometrist, nurses and public health technicians. Then, after training, 18 CHWs (three at each of six sites) repeatedly measured MUAC, weight and length of infants aged <6 months. Intra-class correlations (ICCs) and the Pitman's statistic were calculated.

Results: Among CHWs, ICCs pooled across the six sites (924 infants) were 0.96 (95% CI 0.95-0.96) for MUAC and 0.71 (95% CI 0.68-0.74) for WFLz. MUAC measures by CHWs differed little from their trainers: the mean difference in MUAC was 0.65 mm (95% CI 0.023-1.07), with no significant difference in variance (P = 0.075).

Conclusion: Mid Upper Arm Circumference is more reliably measured by CHWs than WFLz among infants aged <6 months. Further work is needed to define cut-off values based on MUAC’s ability to predict mortality among younger infants.


Abstract

The Plasmodium falciparum erythrocyte membrane protein 1 (PfEMP1) is a variant surface antigen expressed on mature forms of infected erythrocytes. It is considered an important target of naturally acquired immunity. Despite its extreme sequence heterogeneity, variants of PfEMP1 can be stratified into distinct groups. Group A PfEMP1 have been independently associated with low host immunity and severe disease in several studies and are now of potential interest as vaccine candidates. Although antigen-specific antibodies are considered the main effector mechanism in immunity to malaria, the induction of efficient and long-lasting antibody responses requires CD4+ T-cell help. To date, very little is known about CD4+ T-cell responses to PfEMP1 expressed on clinical isolates. The DBLα-tag is a small region from the DBLα-domain of PfEMP1 that can be amplified with universal primers and is accessible in clinical parasite isolates. We identified the dominant expressed PfEMP1 in 41 individual clinical parasite isolates and expressed the corresponding DBLα-tag as recombinant antigen. Individual DBLα-tags were then used to activate CD4+ T-cells from acute and convalescent blood samples in children who were infected with the respective clinical parasite isolate. Here we show that CD4+ T-cell responses to the homologous DBLα-tag were induced in almost all children during acute malaria and maintained in some for 4 months. Children infected with parasites that dominantly expressed group A-like PfEMP1 were more likely to maintain antigen-specific IFNγ-
producing CD4+ T-cells than children infected with parasites dominantly expressing other PfEMP1. These results suggest that group A-like PfEMP1 may induce long-lasting effector memory T-cells that might be able to provide rapid help to variant-specific B cells. Furthermore, a number of children induced CD4+ T-cell responses to heterologous DBLα-tags, suggesting that CD4+ T-cells may recognise shared epitopes between several DBLα-tags.


Abstract

We have analyzed the in vitro activities of pyronaridine and methylene blue against 59 Plasmodium falciparum isolates from Kenya in association with polymorphisms in Pfcrt (codon 76), Pfmdr1 (codon 86), and Pfnhe (full sequence). The median inhibitory concentrations that kill 50% of parasites were 13.5 and 3.3 nM for pyronaridine and methylene blue, respectively. Their activities were not associated with polymorphisms in these genes. The drugs' high in vitro activities indicate that they would be efficacious against Kenyan isolates in vivo.


Abstract

Background: Health facility stock-outs of artemether-lumefantrine (AL), the common first-line therapy for uncomplicated malaria across Africa, adversely affect effective malaria case-management. They have been previously reported on various scales in time and space, however the magnitude of the problem and trends over time are less clear. Here, 2010-2011 data are reported from public facilities in Kenya where alarming stock-outs were revealed in 2008.

Methods: Data were collected between January 2010 and June 2011 as part of 18 monthly cross-sectional surveys undertaken at nationally representative samples of public health facilities. The primary monitoring indicator was total stock-out of all four weight-specific AL packs. The secondary indicators were stock-outs of at least one AL
pack and individual stock-outs for each AL pack. Monthly proportions and summary means of the proportions over the monitoring period were measured for each indicator. Stock-out trends were assessed using linear regression.

**Results:** The number of surveyed facilities across 18 time points ranged between 162 and 176 facilities. The stock-out means of the proportion of health facilities were 11.6% for total AL stock-out, 40.6% for stock-out of at least one AL pack, and between 20.5% and 27.4% for stock-outs of individual AL packs. Monthly decrease of the total AL stock-out was 0.005% (95% CI: -0.5 to +0.5; p = 0.983). Monthly decrease in the stock-out of at least one AL pack was 0.7% (95% CI: -1.5 to +0.3; p = 0.058) while stock-outs of individual AL packs decreased monthly between 0.2% for AL 24-pack and 0.7% for AL six-pack without statistical significance for any of the weight-specific packs.

**Conclusions:** Despite lower levels of AL stock-outs compared to the reports in 2008, the stock-outs at Kenyan facilities during 2010-2011 are still substantial and of particular worry for the most detrimental: simultaneous absence of any AL pack. Only minor decrease was observed in the stock-outs of individual AL packs. Recently launched interventions to eliminate AL stock-outs in Kenya are fully justified.


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**Abstract**

**Background:** The main strategy adopted for Lymphatic Filariasis (LF) elimination globally is annual mass drug administration (MDA) for 4 to 6 rounds. At least 65% of the population at risk should be treated in each round for LF elimination to occur. In Kenya, MDA using diethylcarbamazine citrate (DEC) and albendazole data shows declining compliance (proportion of eligible populations who receive and swallow the drugs) levels (85%-62.8%). The present study's aim was to determine the role of personal opinions and experiences in compliance with MDA.

**Methods/findings:** This was a retrospective cross-sectional study conducted between January and September 2009 in two districts based on December 2008 MDA round. In each district, one location with high and one with low compliance was selected. Through systematic sampling, nine villages were selected and interviewer-based questionnaires administered to 965 household heads or adult representatives also systematically sampled. The qualitative data were generated from opinion leaders, LF patients with clinical signs and community drug distributors (CDDs) all purposively selected and interviewed. Sixteen focus group discussions (FGDs) were also conducted.
with single-sex adult and youth male and female groups. Chi square test was used to assess the statistical significance of differences in compliance with treatment based on the records reviewed. The house-to-house method of drug distribution influenced compliance. Over one-quarter (27%) in low compared to 15% in high compliance villages disliked this method. Problems related to size, number and taste of the drugs were more common in low (16.4%) than in high (14.4%) compliance villages. Reasons for failure to take the drugs were associated with compliance (p<0.001). The reasons given included: feeling that the drugs were not necessary, CDD not visiting to issue the drugs, being absent and thinking that the drugs were meant for only the patients with LF clinical signs. A dislike for modern medicine prevailed more in low (6.7%) than in high (1.2%) compliance villages. Experience of side effects influenced compliance (P<0.001). The common side effects experienced included giddiness, fever, headache and vomiting. Social support, alcohol and substance use were not associated with compliance in both types of villages (p>0.05).

**Conclusions/significance:** Community sensitization on treatment, drugs used, their regimen and distribution method involving all leaders should be strengthened by the Programme Implementers. The communities need to be made aware of the potential side effects of the drugs and that health personnel are on standby for the management of side effects in order to build confidence and increase the compliance levels.


**Abstract**

**Background:** There is little information that describe the burden of respiratory syncytial virus (RSV) associated disease in the tropical African outpatient setting.

**Methods:** We studied a systematic sample of children aged <5 years presenting to a rural district hospital in Kenya with acute respiratory infection (ARI) between May 2002 and April 2004. We collected clinical data and screened nasal wash samples for RSV antigen by immunofluorescence. We used a linked demographic surveillance system to estimate disease incidence.

**Results:** Among 2143 children tested, 166 (8%) were RSV positive (6% among children with upper respiratory tract infection and 12% among children with lower respiratory tract infection (LRTI). RSV was more likely in LRTI than URTI (p<0.001). 51% of RSV cases were aged 1 year or over. RSV cases represented 3.4% of hospital outpatient presentations. Relative to RSV negative cases, RSV positive cases were more
likely to have crackles (RR = 1.63; 95% CI 1.34-1.97), nasal flaring (RR = 2.66; 95% CI 1.40-5.04), in-drawing (RR = 2.24; 95% CI 1.47-3.40), fast breathing for age (RR = 1.34; 95% CI 1.03-1.75) and fever (RR = 1.54; 95% CI 1.33-1.80). The estimated incidence of RSV-ARI and RSV-LRTI, per 100,000 child years, among those aged <5 years was 767 and 283, respectively.

Conclusion: The burden of childhood RSV-associated URTI and LRTI presenting to outpatients in this setting is considerable. The clinical features of cases associated with an RSV infection were more severe than cases without an RSV diagnosis.


Abstract

Background: The intermittent screening and treatment (IST) of school children for malaria is one possible intervention strategy that could help reduce the burden of malaria among school children. Future implementation of IST will not only depend on its efficacy and cost-effectiveness but also on its acceptability to parents of the children who receive IST, as well as those responsible for its delivery. This study was conducted alongside a cluster-randomized trial to investigate local perceptions of school-based IST among parents and other stakeholders on the Kenyan south coast.

Methods: Six out of the 51 schools receiving the IST intervention were purposively sampled, based on the prevalence of Plasmodium infection, to participate in the qualitative study. Twenty-two focus group discussions and 17 in-depth interviews were conducted with parents and other key stakeholders involved in the implementation of school health programmes in the district. Data analysis was guided by the framework analysis method.

Results: High knowledge of the burden of clinical malaria on school children, the perceived benefits of preventing clinical disease through IST and previous positive experiences and interactions with other school health programmes facilitated the acceptability of IST. However, lack of understanding of the consequences of asymptomatic parasitaemia for apparently healthy school children could potentially contribute to non-adherence to treatment, and use of alternative anti-malarial drugs with simpler regimens was generally preferred. The general consensus of stakeholders was that health workers were best placed to undertake the screening and provide treatment, and although teachers' involvement in the programme is critical, most participants were
opposed to teachers taking finger-prick blood samples from children. There was also a strong demand for the distribution of mosquito nets to augment IST.

**Conclusion:** School-based malaria control through IST was acceptable to most parents and other stakeholders, but careful consideration of the various roles of teachers, community health workers, and health workers, and the use of anti-malarial drugs with simpler regimens are critical to its future implementation.


**Abstract**

**Background:** To improve care for children in district hospitals in Kenya, a multifaceted approach employing guidelines, training, supervision, feedback, and facilitation was developed, for brevity called the Emergency Triage and Treatment Plus (ETAT+) strategy. We assessed the cost effectiveness of the ETAT+ strategy, in Kenyan hospitals. Further, we estimate the costs of scaling up the intervention to Kenya nationally and potential cost effectiveness at scale.

**Methods and findings:** Our cost-effectiveness analysis from the provider's perspective used data from a previously reported cluster randomized trial comparing the full ETAT+ strategy (n = 4 hospitals) with a partial intervention (n = 4 hospitals). Effectiveness was measured using 14 process measures that capture improvements in quality of care; their average was used as a summary measure of quality. Economic costs of the development and implementation of the intervention were determined (2009 US$). Incremental cost-effectiveness ratios were defined as the incremental cost per percentage improvement in (average) quality of care. Probabilistic sensitivity analysis was used to assess uncertainty. The cost per child admission was US$50.74 (95% CI 49.26-67.06) in intervention hospitals compared to US$31.1 (95% CI 30.67-47.18) in control hospitals. Each percentage improvement in average quality of care cost an additional US$0.79 (95% CI 0.19-2.31) per admitted child. The estimated annual cost of nationally scaling up the full intervention was US$3.6 million, approximately 0.6% of the annual child health budget in Kenya. A "what-if" analysis assuming conservative reductions in mortality suggests the incremental cost per disability adjusted life year (DALY) averted by scaling up would vary between US$39.8 and US$398.3.

**Conclusion:** Improving quality of care at scale nationally with the full ETAT+ strategy may be affordable for low income countries such as Kenya. Resultant plausible reductions in hospital mortality suggest the intervention could be cost-effective when
compared to incremental cost-effectiveness ratios of other priority child health interventions.


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<td><strong>Abstract</strong></td>
<td><strong>Ethnopharmacological relevance:</strong> Diabetes mellitus is a growing problem in many developing countries and the financial burden associated with it is enormous. In traditional African communities, majority of people relies on traditional medicines and Traditional Health Practitioners as the primary source of health care. Hence, this study was undertaken in the Lower Eastern province of Kenya to document the medicinal plants used by the traditional practitioners to treat diabetes and to assess the existing knowledge in management of this condition.</td>
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<td><strong>Materials and methods:</strong> Data was collected using structured open- and close-ended questionnaires.</td>
<td><strong>Results:</strong> Thirty-nine species belonging to 33 genera and 26 families were encountered and the most frequently cited species were from Caesalpiniaceae, Ebenaceae, Solanaceae and Labiatae families. Twenty-eight percent of the plant species are reported to have hypoglycaemic activity.</td>
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<td><strong>Conclusions:</strong> Currently there is no data on medicinal plants used to treat diabetes in Kenya. Therefore, these findings are important in the management of diabetes and future research on traditional medicine in drug development.</td>
<td><strong>PubMed link-</strong> <a href="https://pubmed.ncbi.nlm.nih.gov/22020309/">https://pubmed.ncbi.nlm.nih.gov/22020309/</a></td>
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<td><strong>Abstract</strong></td>
<td><strong>Background:</strong> Respiratory syncytial virus (RSV) reinfacts individuals repeatedly. The extent to which this is a consequence of RSV antigenic diversity is unclear.</td>
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Methods: Six-hundred thirty-five children from rural Kenya were closely monitored for RSV infection from birth through 3 consecutive RSV epidemics. RSV infections were identified by immunofluorescence testing of nasal washing samples collected during acute respiratory illnesses, typed into group A and B, and sequenced in the attachment (G) protein. A positive sample separated from a previous positive by ≥14 days was defined as a reinfection a priori.

Results: Phylogenetic analysis was undertaken for 325 (80%) of 409 identified infections, including 53 (64%) of 83 reinfections. Heterologous group reinfections were observed in 28 episodes, and homologous group reinfections were observed in 25 episodes; 10 involved homologous genotypes, 5 showed no amino acid changes, and 3 were separated by 21-24 days and were potentially persistent infections. The temporal distribution of genotypes among reinfections did not differ from that of single infections.

Conclusions: The vast majority of infection and reinfection pairs differed by group, genotype, or G amino acid sequence (ie, comprised distinct viruses). The extent to which this is a consequence of immune memory of infection history or prevalent diversity remains unclear.


Abstract

The aims of this study were to record behavioral problems in children with epilepsy (CWE), compare the prevalence with that reported among healthy children without epilepsy, and investigate the risk factors. A child behavioral questionnaire for parents comprising 15 items was administered to the main caregiver of 108 CWE and 108 controls matched for age in Kilifi, Kenya. CWE had a higher mean score for reported behavioral problems than controls (6.9 vs 4.9, t=4.7, P<0.001). CWE with active epilepsy also recorded more behavioral problems than those with inactive epilepsy (8.2 vs 6.2, t=-2.9, P=0.005). A significantly greater proportion of CWE (49% vs 26% of controls) were reported to have behavioral problems. Active epilepsy, cognitive impairment, and focal seizures were the most significant independent covariates of behavioral problems. Behavioral problems in African CWE are common and need to be taken into consideration in planning comprehensive clinical services in this region.


**Abstract**

The candidate malaria vaccine RTS,S/AS01(E) provides significant but partial protection from clinical malaria. On in vitro circumsporozoite protein (CSP) peptide stimulation and intra-cellular cytokine staining of whole blood taken from 407 5-17 month-old children in a phase IIb trial of RTS,S/AS01(E), we identified significantly increased frequencies of two CSP-specific CD4+ T cells phenotypes among RTS,S/AS01(E) vaccinees (IFNγ-IL2+TNF- and IFNγ-IL2+TNF+ CD4+ T cells), and increased frequency of IFNγ-IL2-TNF+ CD4+ T cells after natural exposure. All these T cells phenotypes were individually associated with reductions in the risk of clinical malaria, but IFNγ-IL2-TNF+ CD4+ T cells independently predicted reduced risk of clinical malaria on multi-variable analysis (HR = 0.29, 95% confidence intervals 0.15-0.54, p<0.0005). Furthermore, there was a strongly significant synergistic interaction between CSP-specific IFNγ-IL2-TNF+ CD4+ T cells and anti-CSP antibodies in determining protection against clinical malaria (p = 0.002). Vaccination strategies that combine potent cellular and antibody responses may enhance protection against malaria.


**Abstract**

**Objective:** To determine the rate and predictors of early loss to follow-up (LTFU) for recently diagnosed HIV-infected, antiretroviral therapy (ART)-ineligible adults in rural Kenya.

**Methods:** Prospective cohort study. Clients registering for HIV care between July 2008 and August 2009 were followed up for 6 months. Baseline data were used to assess predictors of pre-ART LTFU (not returning for care within 2 months of a scheduled appointment), LTFU before the second visit and LTFU after the second visit. Logistic regression was used to determine factors associated with LTFU before the second visit, while Cox regression was used to assess predictors of time to LTFU and LTFU after the second visit.
**Results:** Of 530 eligible clients, 178 (33.6%) were LTFU from pre-ART care (11.1/100 person-months). Of these, 96 (53.9%) were LTFU before the second visit. Distance (>5 km vs. <1 km: adjusted hazard ratio 2.6 [1.9-3.7], P < 0.01) and marital status (married vs. single: 0.5 [0.3-0.6], P < 0.01) independently predicted pre-ART LTFU. Distance and marital status were independently associated with LTFU before the second visit, while distance, education status and seasonality showed weak evidence of predicting LTFU after the second visit. HIV disease severity did not predict pre-ART LTFU.

**Conclusions:** A third of recently diagnosed HIV-infected, ART-ineligible clients were LTFU within 6 months of registration. Predictors of LTFU among ART-ineligible clients are different from those among clients on ART. These findings warrant consideration of an enhanced pre-ART care package aimed at improving retention and timely ART initiation.


**Abstract**

This paper presents the results of a qualitative study to investigate the perceptions and experiences of health workers involved in a cluster-randomized controlled trial of a novel intervention to improve health worker malaria case-management in 107 government health facilities in Kenya. The intervention involved sending text-messages about paediatric outpatient malaria case-management accompanied by "motivating" quotes to health workers' mobile phones. Ten malaria messages were developed reflecting recommendations from the Kenyan national guidelines. Two messages were delivered per day for 5 working days and the process was repeated for 26 weeks (May to October 2009). The accompanying quotes were unique to each message. The intervention was delivered to 119 health workers and there were significant improvements in correct artemether-lumefantrine (AL) management both immediately after the intervention (November 2009) and 6 months later (May 2010). In-depth interviews with 24 health workers were undertaken to investigate the possible drivers of this change. The results suggest high acceptance of all components of the intervention, with the active delivery of information in an on the job setting, the ready availability of new and stored text messages and the perception of being kept 'up to date' as important factors influencing practice. Applying the construct of stages of change we infer that in this intervention the SMS messages were operating primarily at the action and maintenance stages of behaviour change achieving their effect by creating an enabling environment and providing a prompt to action for the implementation of case
management practices that had already been accepted as the clinical norm by the health workers. Future trials testing the effectiveness of SMS reminders in creating an enabling environment for the establishment of new norms in clinical practice as well as in providing a prompt to action for the implementation of the new case-management guidelines are justified.


Abstract

Background: Simple interventions for improving health workers' adherence to malaria case-management guidelines are urgently required across Africa. A recent trial in Kenya showed that text-message reminders sent to health workers' mobile phones improved management of pediatric outpatients by 25 percentage points. In this paper we examine costs and cost-effectiveness of this intervention.

Methods/findings: We evaluate costs and cost-effectiveness in 2010 USD under three implementation scenarios: (1) as implemented under study conditions in study areas; (2) if the intervention was routinely implemented by the Ministry of Health (MoH) in the same areas; and (3) if the intervention was scaled up nationally. Under study conditions, intervention costs were 19,342 USD, of which 45% were for developing and pretesting text-messages, 12% for developing text-message distribution system, 29% for collecting health workers' phone numbers, and 13% were costs of sending text-messages and monitoring of the system. If the intervention was implemented in the same areas by the MoH, the costs would be 28% lower (13,920 USD) due to lower costs of collecting health workers' numbers. The cost of national scale-up would be 97,350 USD, and the majority of these costs (66%) would be for sending text-messages. The cost per additional child correctly managed was 0.50 USD under study conditions, 0.36 USD if implemented by the MoH in the same area, and estimated at only 0.03 USD if implemented nationally. Even if the effect size was only 5% or the cost on the national scale was 400% higher than estimated, the cost per additional child correctly managed would be only 0.16 USD.

Conclusions: A simple text-messaging intervention improving health worker adherence to malaria guidelines is effective and inexpensive. Further research is justified to optimize delivery of the intervention and expand targets beyond children and malaria disease.


Abstract

To identify novel biomarkers for HIV-1 resistance, including pathways that may be critical in anti-HIV-1 vaccine design, we carried out a gene expression analysis on blood samples obtained from HIV-1 highly exposed seronegatives (HESN) from a commercial sex worker cohort in Nairobi and compared their profiles to HIV-1 negative controls. Whole blood samples were collected from 43 HIV-1 resistant sex workers and a similar number of controls. Total RNA was extracted and hybridized to the Affymetrix HUG 133 Plus 2.0 micro arrays (Affymetrix, Santa Clara CA). Output data was analysed through ArrayAssist software (Agilent, San Jose CA). More than 2,274 probe sets were differentially expressed in the HESN as compared to the control group (fold change ≥1.3; p value ≤0.0001, FDR <0.05). Unsupervised hierarchical clustering of the differentially expressed genes readily distinguished HESNs from controls. Pathway analysis through the KEGG signaling database revealed a majority of the impacted pathways (13 of 15, 87%) had genes that were significantly down regulated. The most down expressed pathways were glycolysis/gluconeogenesis, pentose phosphate, phosphatidyl inositol, natural killer cell cytotoxicity and T-cell receptor signaling. Ribosomal protein synthesis and tight junction genes were up regulated. We infer that the hallmark of HIV-1 resistance is down regulation of genes in key signaling pathways that HIV-1 depends on for infection.


Abstract

Background: Increase in global health research undertaken in resource poor settings in the last decade though a positive development has raised ethical concerns relating to potential for exploitation. Some of the suggested strategies to address these concerns include calls for providing universal standards of care, reasonable availability of proven interventions and more recently, promoting the overall social value of research especially in clinical research. Promoting the social value of research has been closely associated with providing fair benefits to various stakeholders involved in research. The
debate over what constitutes fair benefits; whether those that addresses micro level issues of justice or those focusing on the key determinants of health at the macro level has continued. This debate has however not benefited from empirical work on what stakeholders consider fair benefits. This study explores practical experiences of stakeholders involved in global health research in Kenya, over what benefits are fair within a developing world context.

**Methods and results:** We conducted in-depth interviews with key informants drawn from within the broader health research system in Kenya including researchers from the mainstream health research institutions, networks and universities, teaching hospitals, policy makers, institutional review boards, civil society organisations and community representative groups. The range of benefits articulated by stakeholders addresses both micro and macro level concerns for justice by for instance, seeking to engage with interests of those facilitating research, and the broader systemic issues that make resource poor settings vulnerable to exploitation. We interpret these views to suggest a need for global health research to engage with current crises that face people in these settings as well as the broader systemic issues that produce them.

**Conclusion:** Global health research should provide benefits that address both the micro and macro level issues of justice in order to forestall exploitation. Embracing the two is however challenging in terms of how the various competing interests/needs should be balanced ethically, especially in the absence of structures to guide the process. This challenge should point to the need for greater dialogue to facilitate value clarification among stakeholders.


**Abstract**

Development of protective immunity against Plasmodium falciparum is partially mediated through binding of malaria-specific IgG to Fc gamma (γ) receptors. Variations in human FcγRIIA-H/R-131 and FcγRIIIB-NA1/NA2 affect differential binding of IgG sub-classes. Since variability in FcγR may play an important role in severe malarial anemia (SMA) pathogenesis by mediating phagocytosis of red blood cells and triggering cytokine production, the relationship between FcγRIIA-H/R131 and FcγRIIIB-NA1/NA2 haplotypes and susceptibility to SMA (Hb < 6.0 g/dL) was investigated in Kenyan children (n = 528) with acute malaria residing in a holoendemic
P. falciparum transmission region. In addition, the association between carriage of the haplotypes and repeated episodes of SMA and all-cause mortality were investigated over a 3-year follow-up period. Since variability in FcγR can alter interferon (IFN)-γ production, a mediator of innate and adaptive immune responses, functional associations between the haplotypes and IFN-γ were also explored. During acute malaria, children with SMA had elevated peripheral IFN-γ levels (P = 0.006). Although multivariate logistic regression analyses (controlling for covariates) revealed no associations between the FcγR haplotypes and susceptibility to SMA during acute infection, the FcγRIIA-131H/FcγRIIIB-NA1 haplotype was associated with decreased peripheral IFN-γ (P = 0.046). Longitudinal analyses showed that carriage of the FcγRIIA-131H/FcγRIIIB-NA1 haplotype was associated with reduced risk of SMA (RR 0.65, 95% CI 0.46-0.90; P = 0.012) and all-cause mortality (P = 0.002). In contrast, carriers of the FcγRIIA-131H/FcγRIIIB-NA2 haplotype had increased susceptibility to SMA (RR 1.47, 95% CI 1.06-2.04; P = 0.020). Results here demonstrate that variation in the FcγR gene alters susceptibility to repeated episodes of SMA and mortality, as well as functional changes in IFN-γ production.


Abstract

in English, French, Spanish, Arabic, Chinese, Russian

Objective: To determine the predictive value for death before 12 months of age of mid-upper arm circumference (MUAC) and weight-for-length Z score (WFLz).

Methods: A retrospective cohort analysis of infants living in Keneba, in rural Gambia, was conducted. Anthropometric measures were obtained from demographic surveillance system records for infants registered between February 1974 and July 2008 who had had MUAC and WFLz recorded at 6-14 weeks of age and vital status recorded at least once more. Hazard ratios (HRs), population attributable fractions and areas under receiver operating characteristic (ROC) curves were estimated to assess the predictive value for death in infancy of MUAC and WFLz.

Findings: Of 2876 infants included in the analysis, 40 died before the age of 12 months. The HR for death in this group versus in well-nourished infants was 5.8 (95% confidence interval, CI: 1.6-21) for a WFLz < -3. HRs for MUACs below the thresholds of 115 mm, 110 mm and 105 mm were 4.5 (95% CI: 1.4-15), 9.5 (95% CI: 2.6-35) and
23 (95% CI: 4.2-122), respectively. The attributable fractions for a MUAC < 130 mm and a WFLz < 0 were 51% and 13%, respectively. The areas under the ROC curve for death in infancy were 0.55 (95% CI: 0.46 to 0.64) for WFLz and 0.64 (95% CI: 0.55 to 0.73) for MUAC.

**Conclusion:** Among infants aged 6 to 14 weeks, unadjusted MUAC showed good performance in identifying infants at increased risk of death.


**Abstract**

Community sensitisation, as a component of community engagement, plays an important role in strengthening the ethics of community-based trials in developing countries and is fundamental to trial success. However, few researchers have shared their community sensitisation strategies and experiences. We report on our perspective as researchers on the sensitisation activities undertaken for a phase II malaria vaccine trial in Kilifi District (Kenya) and Korogwe District (Tanzania), with the aim of informing and guiding the operational planning of future trials. We report wide variability in recruitment rates within both sites; a variability that occurred against a backdrop of similarity in overall approaches to sensitisation across the two sites but significant differences in community exposure to biomedical research. We present a range of potential factors contributing to these differences in recruitment rates, which we believe are worth considering in future community sensitisation plans. We conclude by arguing for carefully designed social science research around the implementation and impact of community sensitisation activities.


**Abstract**
Background: There are few studies on the epidemiology of epilepsy in large populations in Low and Middle Income Countries (LMIC). Most studies in these regions use two-stage population-based screening surveys, which are time-consuming and costly to implement in large populations required to generate accurate estimates. We examined the sensitivity and specificity of a three-stage cross-sectional screening methodology in detecting active convulsive epilepsy (ACE), which can be embedded within on-going census of demographic surveillance systems. We validated a three-stage cross-sectional screening methodology on a randomly selected sample of participants of a three-stage prevalence survey of epilepsy. Diagnosis of ACE by an experienced clinician was used as 'gold standard'. We further compared the expenditure of this method with the standard two-stage methodology.

Results: We screened 4442 subjects in the validation and identified 35 cases of ACE. Of these, 18 were identified as false negatives, most of whom (15/18) were missed in the first stage and a few (3/18) in the second stage of the three-stage screening. Overall, this methodology had a sensitivity of 48.6% and a specificity of 100%. It was 37% cheaper than a two-stage survey.

Conclusion: This was the first study to evaluate the performance of a multi-stage screening methodology used to detect epilepsy in demographic surveillance sites. This method had poor sensitivity attributed mainly to stigma-related non-response in the first stage. This method needs to take into consideration the poor sensitivity and the savings in expenditure and time as well as validation in target populations. Our findings suggest the need for continued efforts to develop and improve case-ascertainment methods in population-based epidemiological studies of epilepsy in LMIC.


Abstract

Background: The use of amodiaquine in prophylaxis is associated with serious toxicity, resulting from its metabolic conversion into a reactive quinone-imine metabolite by the hepatic cytochrome P450. To circumvent this toxicity, several amodiaquine analogues that lack the potential to form a quinone-imine derivative, while retaining antimalarial activity, have been designed. Isoquine is one of these promising molecules that has already reached Phase I clinical trials in humans.
Methods: We analysed the in vitro activity of isoquine against 62 Plasmodium falciparum isolates collected in Kenya and the association of this activity with polymorphisms in pfcr and pfmdr1 genes.

Results: The median concentration of isoquine that inhibited 50% of parasite growth (IC50) was 9 nM, compared with 56 nM chloroquine, 8 nM amodiaquine, 10 nM desethylamodiaquine, 69 nM lumefantrine and 1 nM dihydroartemisinin. Isoquine activity was correlated with polymorphisms in pfcr at codon 76, but not in pfmdr1 at codon 86.

Conclusions: The high activity of isoquine against field isolates, including chloroquine-resistant isolates, with IC50 <10 nM, warrants its further development as an antimalarial.


Abstract

Background: In Kenya, the availability of a cheap diagnostic service for HIV-exposed infants has helped scale-up access to treatment, and provided a means by which programs that support Prevention of Mother to Child Transmission of HIV can be evaluated. As expected for any large testing program, discrepant and indeterminate results present a significant challenge.

Methods: Dried Blood Spots were collected from health centers countrywide and couriered to four laboratories for tests. Results were dispatched either by email, telephone, GSM SMS printer or courier. Between 2006 and 2009, tests were conducted with the Manual Roche v. 1.5 Assay. In 2010 the labs switched fully to the Cobas® AmpliPrep/ Cobas® TaqMan® HIV-1 Qual automated Roche Test.

Results: Between 2006 and 2010, the KEMRI CVR EID Lab conducted 64 591 HIV tests in on children <18 months of age. HIV tests (38 834) used the manual assay, while 17 133 tests used the automated assay. Overall, 10.7% (6915) of the samples tested positive, while 86.6% (55 967) tested negative. A total of 1.6% (1041) tested indeterminate and required a re-bleed of the infant. Two hundred positive tests by the manual assay were retrieved randomly and retested using the automated assay. Among them, 192 (96%) remained positive, 5 (2.5%) were negative while 3 (1.5%) failed. A
total of 160 negative samples by the manual assay were retrieved and retested with the automated assay. Among them, 154 (96.24%) remained negative, 3 (1.88%) tested positive while 3 (1.88%) failed. A total of 215 samples that gave indeterminate results by the manual assay were retested using the automated system. Among them, 62 (28.8%) gave positive results, 144 (66.97%) negative and 6 (2.8%) samples still gave discrepant results. Three (1.4%) did not amplify successfully. A few infants who were apparently positive appeared to test HIV negative with age.

**Conclusions:** Indeterminate results are a significant challenge for HIV diagnostic services, as seen in the Kenyan EID Program. In our experience, they are more often negative than they are positive. False positive and false negative results can arise from clerical error, contamination and limitations of the technologies available. To forestall the consequences of such outcomes, the sensitivity and specificity of available assays must be further improved. All HIV positive samples should be retested for confirmation, and if confirmed, a new sample must be drawn and tested for DNA at the time the infant receives their initial results or starts antiretroviral therapy. Viral clearance is a phenomenon that requires further studies.

**PubMed link:** [https://pubmed.ncbi.nlm.nih.gov/22052701/]