In Search of Better Health

KEMRI PUBLICATIONS (2021)

1.	Uyoga S, Adetifa IMO, Karanja HK, Nyagwange J, Tuju J, Wanjiku P, Aman R, Mwangangi M, Amoth P, Kasera K, Ng'ang'a W, Rombo C, Yegon C, Kithi K, Odhiambo E, Rotich T, Orgut I, Kihara S, Otiende M, Bottomley C, Mupe ZN, Kagucia EW, Gallagher KE, Etyang A, Voller S, Gitonga JN, Mugo D, Agoti CN, Otieno E, Ndwiga L, Lambe T, Wright D, Barasa E, Tsofa B, Bejon P, Ochola-Oyier LI, Agweyu A, Scott JAG, Warimwe GM. Seroprevalence of anti-SARS-CoV-2 IgG antibodies in Kenyan blood donors. Science. 2021 Jan 1;371(6524):79-82. **Abstract** The spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in Africa is poorly described. The first case of SARS-CoV-2 in Kenya was reported on 12 March 2020, and an overwhelming number of cases and deaths were expected, but by 31 July 2020, there were only 20,636 cases and 341 deaths. However, the extent of SARS-CoV-2 exposure in the community remains unknown. We determined the prevalence of anti-SARS-CoV-2 immunoglobulin G among blood donors in Kenya in April-June 2020. Crude seroprevalence was 5.6% (174 of 3098). Population-weighted, test-performance-adjusted national seroprevalence was 4.3% (95% confidence interval, 2.9 to 5.8%) and was highest in urban counties Mombasa (8.0%), Nairobi (7.3%), and Kisumu (5.5%). SARS-CoV-2 exposure is more extensive than indicated by case-based surveillance, and these results will help guide the pandemic response in Kenya and across Africa. **Pubmed link-** https://pubmed.ncbi.nlm.nih.gov/33177105/
2.	Chepkirui C, Ochieng PJ, Sarkar B, Hussain A, Pal C, Yang LJ, Coghi P, Akala HM, Derese S, Ndakala A, Heydenreich M, Wong VKW, Erdélyi M, Yenesew A. Antiplasmodial and antileishmanial flavonoids from Mundulea sericea. Fitoterapia. 2021 Mar; 149:104796. **Abstract** Five known compounds (1-5) were isolated from the extract of Mundulea sericea leaves. Similar investigation of the roots of this plant afforded an additional three known compounds (6-8). The structures were elucidated using NMR spectroscopic and mass spectrometric analyses. The absolute configuration of 1 was established using ECD spectroscopy. In an antiplasmodial activity assay, compound 1 showed good activity with an IC50 of 2.0 μM against chloroquine-resistant W2, and 6.6 μM against the chloroquine-sensitive 3D7 strains of Plasmodium falciparum. Some of the compounds were also tested for antileishmanial activity. Dehydrolupinifolinol (2) and sericetin (5) were active against drug-sensitive Leishmania donovani (MHOM/IN/83/AG83) with IC50 values of 9.0 and 5.0 μM, respectively. In a cytotoxicity assay, lupinifolin (3) showed significant activity on BEAS-2B (IC50 4.9 μM) and HePG2 (IC50 10.8 μM) human cell lines. All the other compounds showed low cytotoxicity (IC50 > 30 μM) against human lung adenocarcinoma cells (A549), human liver cancer cells

	(HepG2), lung/bronchus cells (epithelial virus transformed) (BEAS-2B) and immortal human hepatocytes (LO2). **Pubmed link**- https://pubmed.ncbi.nlm.nih.gov/33271256/
3.	Rose EB, Nyawanda BO, Munywoki PK, Murunga N, Bigogo GM, Otieno NA, Onyango C, Chaves SS, Verani JR, Emukule GO, Widdowson MA, Nokes DJ, Gerber SI, Langley GE. Respiratory syncytial virus seasonality in three epidemiological zones of Kenya. Influenza Other Respir Viruses. 2021 Mar;15(2):195-201. **Abstract** Understanding respiratory syncytial virus (RSV) circulation patterns is necessary to guide the timing of limited-duration interventions such as vaccines. We describe RSV circulation over multiple seasons in three distinct counties of Kenya during 2006-2018. Kilifi and Siaya counties each had consistent but distinct RSV seasonality, lasting on average 18-22 weeks. Based on data from available years, RSV did not have a clear pattern of circulation in Nairobi. This information can help guide the timing of vaccines and immunoprophylaxis products that are under development. **Pubmed link**- https://pubmed.ncbi.nlm.nih.gov/33305543/

4: Abuga KM, Jones-Warner W, Hafalla JCR. Immune responses to malaria pre-

erythrocytic stages: Implications for vaccine development. Parasite Immunol.

2021 Feb;43(2): e12795.

Abstract

Radiation-attenuated sporozoites induce sterilizing immunity and remain the 'gold standard' for malaria vaccine development. Despite practical challenges in translating these whole sporozoite vaccines to large-scale intervention programmes, they have provided an excellent platform to dissect the immune responses to malaria pre-erythrocytic (PE) stages, comprising both sporozoites and exoerythrocytic forms. Investigations in rodent models have provided insights that led to the clinical translation of various vaccine candidates-including RTS,S/AS01, the most advanced

candidate currently in a trial implementation programme in three African countries. With advances in immunology, transcriptomics and proteomics, and application of lessons from past failures, an effective, long-lasting and wide-scale malaria PE vaccine remains feasible. This review underscores the progress in PE vaccine development, focusing on our understanding of host-parasite immunological crosstalk in the tissue environments of the skin and the liver. We highlight possible gaps in the current knowledge of PE immunity that can impact future malaria vaccine development efforts.

Pubmed link-https://pubmed.ncbi.nlm.nih.gov/32981095/

5: Muinga N, Abejirinde IO, Paton C, English M, Zweekhorst M. Designing paper-

based records to improve the quality of nursing documentation in hospitals: A

scoping review. J Clin Nurs. 2021 Jan;30(1-2):56-71.

Abstract

Background: Inpatient nursing documentation facilitates multi-disciplinary team care and tracking of patient progress. In both high- and low- and middle-income settings, it is largely paper-based and may be used as a template for electronic medical records. However, there is limited evidence on how they have been developed.

Objective: To synthesise evidence on how paper-based nursing records have been developed and implemented in inpatient settings to support documentation of nursing care.

Design: A scoping review guided by the Arksey and O'Malley framework and reported using PRISMA-ScR guidelines.

Eligibility criteria: We included studies that described the process of designing paper-based inpatient records and excluded those focussing on electronic records. Included studies were published in English up to October 2019.

Sources of evidence: PubMed, CINAHL, Web of Science and Cochrane supplemented by free-text searches on Google Scholar and snowballing the reference sections of included papers.

Results: 12 studies met the eligibility criteria. We extracted data on study characteristics, the development process and outcomes related to documentation of inpatient care. Studies reviewed followed a process of problem identification, literature review, chart (re)design, piloting, implementation and evaluation but varied in their execution of each step. All studies except one reported a positive change in inpatient documentation or the adoption of charts amid various challenges.

Conclusions: The approaches used seemed to work for each of the studies but could be strengthened by following a systematic process. Human-centred Design provides a clear process that prioritises the healthcare professional's needs and their context to deliver a usable product. Problems with the chart could be addressed during the design phase rather than during implementation, thereby promoting chart ownership and uptake since users are involved throughout the design. This will translate to better documentation of inpatient care thus facilitating better patient tracking, improved team communication and better patient outcomes.

Relevance to clinical practice: Paper-based charts should be designed in a systematic and clear process that considers patient's and healthcare professional's needs contributing to improved uptake of charts and therefore better documentation.

Pubmed link- https://pubmed.ncbi.nlm.nih.gov/33113237/

6: Mwai J, Njenga S, Barasa M. Retraction Note: Knowledge, attitude and

practices in relation to prevention and control of schistosomiasis infection in

Mwea Kirinyaga county, Kenya. BMC Public Health. 2021 Feb 9;21(1):326.

Pubmed link-https://pubmed.ncbi.nlm.nih.gov/33563236/

7: Obiero CW, Mturi N, Mwarumba S, Ngari M, Newton C, Boele van Hensbroek M,

Berkley JA. Clinical features to distinguish meningitis among young infants at a

rural Kenyan hospital. Arch Dis Child. 2021 Feb;106(2):130-136.

Abstract

Background: Detection of meningitis is essential to optimise the duration and choice of antimicrobial agents to limit mortality and sequelae. In low and middle-income countries most health facilities lack laboratory capacity and rely on clinical features to empirically treat meningitis.

Objective: We conducted a diagnostic validation study to investigate the performance of clinical features (fever, convulsions, irritability, bulging fontanel and temperature ≥39°C) and WHO-recommended signs (drowsiness, lethargy, unconsciousness, convulsions, bulging fontanel, irritability or a high-pitched cry) in discriminating meningitis in young infants.

Design: Retrospective cohort study.

Setting: Kilifi County Hospital.

Patients: Infants aged <60 days hospitalised between 2012 and 2016.

Main outcome measure: Definite meningitis defined as positive cerebrospinal fluid (CSF) culture, microscopy or antigen test, or leucocytes ≥0.05 x 10∧9/L.

Results: Of 4809 infants aged <60 days included, 81 (1.7%) had definite meningitis. WHO-recommended signs had sensitivity of 58% (95% CI 47% to 69%) and specificity of 57% (95% CI 56% to 59%) for definite meningitis. Addition of history of fever improved sensitivity to 89% (95% CI 80% to 95%) but reduced specificity to 26% (95% CI 25% to 27%). Presence of ≥1 of 5 previously identified signs had sensitivity of 79% (95% CI 69% to 87%) and specificity of 51% (95% CI 50% to 53%).

Conclusions: Despite a lower prevalence of definite meningitis, the performance of previously identified signs at admission in predicting meningitis was unchanged. Presence of history of fever improves the sensitivity of WHO-recommended signs but loses specificity. Careful evaluation, repeated assessment and capacity for lumbar puncture and CSF microscopy to exclude meningitis in most young infants with potential signs are essential to management in this age group.

8: Zhao Y, Musitia P, Boga M, Gathara D, Nicodemo C, English M. Tools for

measuring medical internship experience: a scoping review. Hum Resour Health.

2021 Jan 14;19(1):10.

Abstract

Background: Appropriate and well-resourced medical internship training is important to ensure psychological health and well-being of doctors in training and also to recruit and retain these doctors. However, most reviews focused on clinical competency of medical interns instead of the non-clinical aspects of training. In this scoping review, we aim to review what tools exist to measure medical internship experience and summarize the major domains assessed.

Method: The authors searched MEDLINE, Embase, PsycINFO, ERIC, and the Cochrane Library for peer-reviewed studies that provided quantitative data on medical intern's (house officer, foundation year doctor, etc.) internship experience and published between 2000 and 2019. Three reviewers screened studies for eligibility with inclusion criteria. Data including tools used, key themes examined, and psychometric properties within the study population were charted, collated, and summarized. Tools that were used in multiple studies, and tools with internal validity or reliability assessed directed in their intern population were reported.

Results: The authors identified 92 studies that were included in the analysis. The majority of studies were conducted in the US (n = 30, 32.6%) and the UK (n = 20, 21.7%), and only 14 studies

(15.2%) were conducted in low- and middle-income countries. Major themes examined for internship experience included well-being, educational environment, and work condition and environment. For measuring well-being, standardized tools like the Maslach Burnout Inventory (for measuring burnout), Patient Health Questionnaire-9 (depression), General Health Questionnaire-12 or 30 (psychological distress) and Perceived Stress Scale (stress) were used multiple times. For educational environment and work condition and environment, there is a lack of widely used tools for interns that have undergone psychometric testing in this population other than the Postgraduate Hospital Educational Environment Measure, which has been used in four different countries.

Conclusions: There are a large number of tools designed for measuring medical internship experience. International comparability of results from future studies would benefit if tools that have been more widely used are employed in studies on medical interns with further testing of their psychometric properties in different contexts.

Pubmed link- https://pubmed.ncbi.nlm.nih.gov/33446218/

9: Kariuki S, Kiiru J. Detection and Characterization of Salmonella enterica

Serotypes by Simple PCR Technologies. Methods Mol Biol. 2021; 2182:161-177.

Abstract

Polymerase chain reaction (PCR) is a molecular-based technology that has revolutionized diagnostics and characterization of pathogens, and thus affecting how we understand disease landscape. This technology has been found amenable to application on various strategies for management and control of infectious diseases. The main advantage with PCR technologies, when applied optimally, is the high sensitivity and short-turn-around time for results, thus rendering the strategy attractive to researchers in infectious diseases and public health. In this chapter, we describe PCR approaches that are innovative and easy to deploy in a laboratory with medium range infrastructure investment.

Pubmed link-https://pubmed.ncbi.nlm.nih.gov/32894495/

10: English M, Ogola M, Aluvaala J, Gicheha E, Irimu G, McKnight J, Vincent CA.

First do no harm: practitioners' ability to 'diagnose' system weaknesses and

improve safety is a critical initial step in improving care quality. Arch Dis

Child. 2021 Apr;106(4):326-332.

Abstract

Healthcare systems across the world and especially those in low-resource settings (LRS) are under pressure and one of the first priorities must be to prevent any harm done while trying to deliver care. Health care workers, especially department leaders, need the diagnostic abilities to identify local safety concerns and design actions that benefit their patients. We draw on concepts from the safety sciences that are less well-known than mainstream quality improvement techniques in LRS. We use these to illustrate how to analyse the complex interactions between resources and tools, the organisation of tasks and the norms that may govern behaviours, together with the strengths and vulnerabilities of systems. All interact to influence care and outcomes. To employ these techniques leaders will need to focus on the best attainable standards of care, build trust and shift away from the blame culture that undermines improvement. Health worker education should include development of the technical and relational skills needed to perform these system diagnostic roles. Some safety challenges need leadership from professional associations to provide important resources, peer support and mentorship to sustain safety work.

Pubmed link- https://pubmed.ncbi.nlm.nih.gov/33361068/

11: Alegana VA, Suiyanka L, Macharia PM, Ikahu-Muchangi G, Snow RW. Malaria

micro-stratification using routine surveillance data in Western Kenya. Malar J.

2021 Jan 7;20(1):22.

Abstract

Background: There is an increasing need for finer spatial resolution data on malaria risk to provide micro-stratification to guide sub-national strategic plans. Here, spatial-statistical techniques are used to exploit routine data to depict sub-national heterogeneities in test positivity rate (TPR) for malaria among patients attending health facilities in Kenya.

Methods: Routine data from health facilities (n = 1804) representing all ages over 24 months (2018-2019) were assembled across 8 counties (62 sub-counties) in Western Kenya. Statistical model-based approaches were used to quantify heterogeneities in TPR and uncertainty at fine spatial resolution adjusting for missingness, population distribution, spatial data structure, month, and type of health facility.

Results: The overall monthly reporting rate was 78.7% (IQR 75.0-100.0) and public-based health facilities were more likely than private facilities to report ≥ 12 months (OR 5.7, 95% CI 4.3-7.5).

There was marked heterogeneity in population-weighted TPR with sub-counties in the north of the lake-endemic region exhibiting the highest rates (exceedance probability > 70% with 90% certainty) where approximately 2.7 million (28.5%) people reside. At micro-level the lowest rates were in 14 sub-counties (exceedance probability < 30% with 90% certainty) where approximately 2.2 million (23.1%) people lived and indoor residual spraying had been conducted since 2017.

Conclusion: The value of routine health data on TPR can be enhanced when adjusting for underlying population and spatial structures of the data, highlighting small-scale heterogeneities in malaria risk often masked in broad national stratifications. Future research should aim at relating these heterogeneities in TPR with traditional community-level prevalence to improve tailoring malaria control activities at sub-national levels.

Pubmed link- https://pubmed.ncbi.nlm.nih.gov/33413385/

12: Karisa J, Muriu S, Omuoyo D, Karia B, Ngari M, Nyamwaya D, Rono M, Warimwe G, Mwangangi J, Mbogo CM. Urban Ecology of Arboviral Mosquito Vectors Along the Kenyan Coast. J Med Entomol. 2021 Jan 12;58(1):428-438.

Abstract

The purpose of this study was to determine the ecology of the common arboviral mosquito vectors in Mombasa, Kilifi and Malindi urban areas of coastal Kenya. Mosquito larvae were collected using standard dippers and pipettes. Egg survivorship in dry soil was evaluated by collecting soil samples from dry potential larval developmental sites, re-hydrating them for hatching and rearing of the eventual larvae to adults. Adult mosquitoes were collected with CDC light traps and BG-Sentinel traps. All blood-fed females were tested for bloodmeal origin. Mosquitoes were screened for arboviruses using RT-qPCR. Overall, the predominant species were Culex quinquefasciatus (Say) 72.4% (n = 2,364) and Aedes aegypti (L.), 25.7%, (n = 838). A total of 415 larval developmental sites were identified indoors (n = 317) and outdoors (n = 98). The most productive larval developmental sites, both indoors and outdoors, were assorted small containers, water tanks, drainages, drums, and jerricans. Overall, 62% (n = 18) of the soil samples collected were positive for larvae which were used as a proxy to measure the presence of eggs. The mosquitoes fed on humans (29.8%) and chickens (3.7%). Of 259 mosquitoes tested for viral infection, 11.6% were positive for Flavivirus only. The most productive larval developmental sites for arboviral vectors indoors were small containers, water tanks, jerricans, and drums whereas small containers, water tanks, drainage channels, buckets, tires, and water troughs were the productive larval developmental sites outdoors.

Pubmed link- https://pubmed.ncbi.nlm.nih.gov/32623459/

13: Maina M, McKnight J, Tosas-Auguet O, Schultsz C, English M. Using treatment guidelines to improve antibiotic use: insights from an antibiotic point prevalence survey in Kenya. BMJ Glob Health. 2021 Jan;6(1): e003836.

Pubmed link- https://pubmed.ncbi.nlm.nih.gov/33419928/

14: Onditi F, Nyadera IN, Obimbo MM, Muchina SK. How urban 'informality' can inform response to COVID-19: a research agenda for the future. Hist Philos Life Sci. 2021 Jan 12;43(1):6.

Abstract

In the era of increasingly defined ontological insecurity and uncertainty driven by the ravages of COVID-19, urban informal settlement has emerged as a source of resilience. Indeed, the effects of a pandemic transcends its epidemiological characteristics to political economy and societal resilience. If resilience is the capacity of a system to adapt successfully to significant challenges that threaten the function or development of the human society, then ontological insecurity is about the lack of such capacity. Drawing on Keith Hartian's understanding of 'informality' of spaces, this policy brief attempts to identify and frame a research agenda for the future. The agenda would assist future researchers and policymakers provide responses that appropriately recognize groups and actors that define the urban informal space.

Pubmed link-https://pubmed.ncbi.nlm.nih.gov/33433753/

15: Warimwe GM, Francis MJ, Bowden TA, Thumbi SM, Charleston B. Using cross-species vaccination approaches to counter emerging infectious diseases. Nat Rev Immunol. 2021 Jun 17.

Abstract

Since the initial use of vaccination in the eighteenth century, our understanding of human and animal immunology has greatly advanced and a wide range of vaccine technologies and delivery systems have been developed. The COVID-19 pandemic response leveraged these innovations to enable rapid development of candidate vaccines within weeks of the viral genetic sequence being made available. The development of vaccines to tackle emerging infectious diseases is a priority

for the World Health Organization and other global entities. More than 70% of emerging infectious diseases are acquired from animals, with some causing illness and death in both humans and the respective animal host. Yet the study of critical host-pathogen interactions and the underlying immune mechanisms to inform the development of vaccines for their control is traditionally done in medical and veterinary immunology 'silos'. In this Perspective, we highlight a 'One Health vaccinology' approach and discuss some key areas of synergy in human and veterinary vaccinology that could be exploited to accelerate the development of effective vaccines against these shared health threats.

Pubmed link- https://pubmed.ncbi.nlm.nih.gov/34140665/

16: Ngari MM, Obiero C, Mwangome MK, Nyaguara A, Mturi N, Murunga S, Otiende M, Iversen PO, Fegan GW, Walson JL, Berkley JA. Mortality during and following hospital admission among school-aged children: a cohort study. Wellcome Open Res. 2021 Jan 4; 5:234.

Abstract

Background: Far less is known about the reasons for hospitalization or mortality during and after hospitalization among school-aged children than among under-fives in low- and middle-income countries. This study aimed to describe common types of illness causing hospitalisation; inpatient mortality and post-discharge mortality among school-age children at Kilifi County Hospital (KCH), Kenya. Methods: A retrospective cohort study of children 5-12 years old admitted at KCH, 2007 to 2016, and resident within the Kilifi Health Demographic Surveillance System (KHDSS). Children discharged alive were followed up for one year by quarterly census. Outcomes were inpatient and one-year post-discharge mortality. Results: We included 3,907 admissions among 3,196 children with a median age of 7 years 8 months (IQR 74-116 months). Severe anaemia (792, 20%), malaria (749, 19%), sickle cell disease (408, 10%), trauma (408, 10%), and severe pneumonia (340, 8.7%) were the commonest reasons for admission. Comorbidities included 623 (16%) with severe wasting, 386 (10%) with severe stunting, 90 (2.3%) with oedematous malnutrition and 194 (5.0%) with HIV infection. 132 (3.4%) children died during hospitalisation. Inpatient death was associated with signs of disease severity, age, bacteraemia, HIV infection and severe stunting. After discharge, 89/2,997 (3.0%) children died within one year during 2,853 child-years observed (31.2 deaths [95%CI, 25.3-38.4] per 1,000 child-years). 63/89 (71%) of post-discharge deaths occurred within three months and 45% of deaths occurred outside hospital. Post-discharge mortality was positively associated with weak pulse, tachypnoea, severe anaemia, HIV

infection and severe wasting and negatively associated with malaria. Conclusions: Reasons for admissions are markedly different from those reported in under-fives. There was significant post-discharge mortality, suggesting hospitalisation is a marker of risk in this population. Our findings inform guideline development to include risk stratification, targeted post-discharge care and facilitate access to healthcare to improve survival in the early months post-discharge in school-aged children.

Pubmed link- https://pubmed.ncbi.nlm.nih.gov/33195820/

17: Khan G, Kagwanja N, Whyle E, Gilson L, Molyneux S, Schaay N, Tsofa B, Barasa E, Olivier J. Health system responsiveness: a systematic evidence mapping review of the global literature. Int J Equity Health. 2021 May 1;20(1):112.

Abstract

Background: The World Health Organisation framed responsiveness, fair financing and equity as intrinsic goals of health systems. However, of the three, responsiveness received significantly less attention. Responsiveness is essential to strengthen systems' functioning; provide equitable and accountable services; and to protect the rights of citizens. There is an urgency to make systems more responsive, but our understanding of responsiveness is limited. We therefore sought to map existing evidence on health system responsiveness.

Methods: A mixed method systemized evidence mapping review was conducted. We searched PubMed, EbscoHost, and Google Scholar. Published and grey literature; conceptual and empirical publications; published between 2000 and 2020 and English language texts were included. We screened titles and abstracts of 1119 publications and 870 full texts.

Results: Six hundred twenty-one publications were included in the review. Evidence mapping shows substantially more publications between 2011 and 2020 (n = 462/621) than earlier periods. Most of the publications were from Europe (n = 139), with more publications relating to High Income Countries (n = 241) than Low-to-Middle Income Countries (n = 217). Most were empirical studies (n = 424/621) utilized quantitative methodologies (n = 232), while qualitative (n = 127) and mixed methods (n = 63) were more rare. Thematic analysis revealed eight primary conceptualizations of 'health system responsiveness', which can be fitted into three dominant categorizations: 1) unidirectional user-service interface; 2) responsiveness as feedback loops between users and the health system; and 3) responsiveness as accountability between public and the system.

Conclusions: This evidence map shows a substantial body of available literature on health system responsiveness, but also reveals evidential gaps requiring further development, including: a clear definition and body of theory of responsiveness; the implementation and effectiveness of feedback loops; the systems responses to this feedback; context-specific mechanism-implementation experiences, particularly, of LMIC and fragile-and conflict affected states; and responsiveness as it relates to health equity, minority and vulnerable populations. Theoretical development is required, we suggest separating ideas of services and systems responsiveness, applying a stronger systems lens in future work. Further agenda-setting and resourcing of bridging work on health system responsiveness is suggested.

Pubmed link- https://pubmed.ncbi.nlm.nih.gov/33933078/

18: Ndwiga L, Kimenyi KM, Wamae K, Osoti V, Akinyi M, Omedo I, Ishengoma DS, Duah-Quashie N, Andagalu B, Ghansah A, Amambua-Ngwa A, Tukwasibwe S, Tessema SK, Karema C, Djimde AA, Dondorp AM, Raman J, Snow RW, Bejon P, Ochola-Oyier LI. A review of the frequencies of Plasmodium falciparum Kelch 13 artemisinin resistance mutations in Africa. Int J Parasitol Drugs Drug Resist. 2021 Jun 10; 16:155-161.

Abstract

Artemisinin resistance (AR) emerged in South East Asia 13 years ago and the identification of the resistance conferring molecular marker, Plasmodium falciparum Kelch 13 (Pfk13), 7 years ago has provided an invaluable tool for monitoring AR in malaria endemic countries. Molecular Pfk13 surveillance revealed the resistance foci in the Greater Mekong Subregion, an independent emergence in Guyana, South America, and a low frequency of mutations in Africa. The recent identification of the R561H Pfk13 AR associated mutation in Tanzania, Uganda and in Rwanda, where it has been associated with delayed parasite clearance, should be a concern for the continent. In this review, we provide a summary of Pfk13 resistance associated propeller domain mutation frequencies across Africa from 2012 to 2020, to examine how many other countries have identified these mutations. Only four African countries reported a recent identification of the M476I, P553L, R561H, P574L, C580Y and A675V Pfk13 mutations at low frequencies and with no reports of clinical treatment failure, except for Rwanda. These mutations present a threat to malaria control across the continent, since the greatest burden of malaria remains in Africa. A rise in the frequency of these mutations and their spread would reverse the gains made in the reduction of malaria over the last 20 years, given the lack of new antimalarial treatments in the event artemisinin-based combination therapies fail. The review highlights the frequency of Pfk13 propeller domain

mutations across Africa, providing an up-to-date perspective of Pfk13 mutations, and appeals for an urgent and concerted effort to monitoring antimalarial resistance markers in Africa and the efficacy of antimalarials by re-establishing sentinel surveillance systems.

Pubmed link-https://pubmed.ncbi.nlm.nih.gov/34146993/

19: Kombe IK, Agoti CN, Munywoki PK, Baguelin M, Nokes DJ, Medley GF.

Integrating epidemiological and genetic data with different sampling intensities

into a dynamic model of respiratory syncytial virus transmission. Sci Rep. 2021

Jan 14;11(1):1463.

Abstract

Respiratory syncytial virus (RSV) is responsible for a significant burden of severe acute lower respiratory tract illness in children under 5 years old; particularly infants. Prior to rolling out any vaccination program, identification of the source of infant infections could further guide vaccination strategies. We extended a dynamic model calibrated at the individual host level initially fit to social-temporal data on shedding patterns to include whole genome sequencing data available at a lower sampling intensity. The study population was 493 individuals (55 aged < 1 year) distributed across 47 households, observed through one RSV season in coastal Kenya. We found that 58/97 (60%) of RSV-A and 65/125 (52%) of RSV-B cases arose from infection probably occurring within the household. Nineteen (45%) infant infections appeared to be the result of infection by other household members, of which 13 (68%) were a result of transmission from a household co-occupant aged between 2 and 13 years. The applicability of genomic data in studies of transmission dynamics is highly context specific; influenced by the question, data collection protocols and pathogen under investigation. The results further highlight the importance of pre-school and school-aged children in RSV transmission, particularly the role they play in directly infecting the household infant. These age groups are a potential RSV vaccination target group.

Pubmed link- https://pubmed.ncbi.nlm.nih.gov/33446831/

20: Muttai H, Guyah B, Musingila P, Achia T, Miruka F, Wanjohi S, Dande C, Musee

P, Lugalia F, Onyango D, Kinywa E, Okomo G, Moth I, Omondi S, Ayieko C, Nganga

L, Joseph RH, Zielinski-Gutierrez E. Development and Validation of a

Sociodemographic and Behavioral Characteristics-Based Risk-Score Algorithm for

Targeting HIV Testing Among Adults in Kenya. AIDS Behav. 2021 Feb;25(2):297-310.

Abstract

To inform targeted HIV testing, we developed and externally validated a risk-score algorithm that incorporated behavioral characteristics. Outpatient data from five health facilities in western Kenya, comprising 19,458 adults ≥ 15 years tested for HIV from September 2017 to May 2018, were included in univariable and multivariable analyses used for algorithm development. Data for 11,330 adults attending one high-volume facility were used for validation. Using the final algorithm, patients were grouped into four risk-score categories: ≤ 9, 10-15, 16-29 and ≥ 30, with increasing HIV prevalence of 0.6% [95% confidence interval (CI) 0.46-0.75], 1.35% (95% CI 0.85-1.84), 2.65% (95% CI 1.8-3.51), and 15.15% (95% CI 9.03-21.27), respectively. The algorithm's discrimination performance was modest, with an area under the receiver-operating-curve of 0.69 (95% CI 0.53-0.84). In settings where universal testing is not feasible, a risk-score algorithm can identify sub-populations with higher HIV-risk to be prioritized for HIV testing.

Pubmed link- https://pubmed.ncbi.nlm.nih.gov/32651762/

21: Muraya K, Ogutu M, Mwadhi M, Mikusa J, Okinyi M, Magawi C, Zakayo S, Njeru R, Haribondhu S, Uddin MF, Marsh V, Walson JL, Berkley J, Molyneux S. Applying a gender lens to understand pathways through care for acutely ill young children in Kenyan urban informal settlements. Int J Equity Health. 2021 Jan 6;20(1):17.

Abstract

Background: In many African settings, gender strongly influences household treatment-seeking and decision-making for childhood illnesses. While mothers are often the primary engagers with health facilities, their independence in illness-related decisions is shaped by various factors. Drawing on a gender lens, we explored treatment-seeking pathways pre- and post-hospital admission for acutely ill young children living in low income settlements in Nairobi, Kenya; and the gendered impact of child illness both at the household and health system level.

Methods: Household members of 22 children admitted to a public hospital were interviewed intheir homes several times post hospital discharge. In-depth interviews covered the child's household situation, health and illness; and the family's treatment-seeking choices and experiences. Children were selected from an observational cohort established by the Childhood Acute Illness and Nutrition (CHAIN) Network.

Results: Treatment-seeking pathways were often long and complex, with mothers playing the key role in caring for their children and in treatment decision-making. Facing many anxieties and

dilemmas, mothers often consulted with significant influencers - primarily women - particularly where illnesses were prolonged or complex. In contrast to observations in rural African contexts, fathers were less prominent as influencers than (often female) neighbours, grandparents and other relatives. Mothers were sometimes blamed for their child's condition at home and at health facilities. Children's illness episode and associated treatment-seeking had significant gendered socio-economic consequences for households, including through mothers having to take substantial time off work, reduce their working hours and income, or even losing their jobs.

Conclusion: Women in urban low-income settings are disproportionately impacted by acute child illness and the related treatment-seeking and recovery process. The range of interventions needed to support mothers as they navigate their way through children's illnesses and recovery include: deliberate engagement of men in child health to counteract the dominant perception of child health and care as a 'female-domain'; targeted economic strategies such as cash transfers to safeguard the most vulnerable women and households, combined with more robust labour policies to protect affected women; as well as implementing strategies at the health system level to improve interactions between health workers and community members.

Pubmed link- https://pubmed.ncbi.nlm.nih.gov/33407524/

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Keaikitse S, Kormos A, Littler K, Lwetoijera D, Vargas de Moraes R, Mumba N,

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Odiwuor Ondiek S, Rivera S, Roberts AJ, Robinson B, Sambakunsi R, Saxena A,

Sykes N, Tarimo BB, Tiffin N, Tountas KH. Proceedings of an expert workshop on

community agreement for gene drive research in Africa - Co-organised by KEMRI,

PAMCA and Target Malaria. Gates Open Res. 2021 Mar 24; 5:19.

Abstract

Gene drive research is progressing towards future field evaluation of modified mosquitoes for malaria control in sub-Saharan Africa. While many literature sources and guidance point to the inadequacy of individual informed consent for any genetically modified mosquito release, including gene drive ones, (outside of epidemiological studies that might require blood samples) and at the need for a community-level decision, researchers often find themselves with no specific guidance on how that decision should be made, expressed and by whom. Target Malaria, the Kenya Medical Research Institute and the Pan African Mosquito Control Association co-organised a workshop with researchers and practitioners on this topic to question the model proposed by Target

Malaria in its research so far that involved the release of genetically modified sterile male mosquitoes and how this could be adapted to future studies involving gene drive mosquito releases for them to offer reflections about potential best practices. This paper shares the outcomes of that workshop and highlights the remaining topics for discussion before a comprehensive model can be designed.

Pubmed link- https://pubmed.ncbi.nlm.nih.gov/33884362/

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Pathways to Depression and Poor Quality of Life Among Adolescents in Western

Kenya: Role of Anticipated HIV Stigma, HIV Risk Perception, and Sexual

Behaviors. AIDS Behav. 2021 May;25(5):1423-1437.

Abstract

Depression is a major cause of disease burden and is linked to poor quality of life (QOL) among adolescents. We examined the roles of sexual behaviors, HIV risk perception, and anticipated HIV stigma on depressive symptomatology and QOL among 4096 adolescents in a rural region of western Kenya with a high burden of HIV. Participants were aged 15-19 years, had not been tested for HIV in the previous 6 months, and had never been diagnosed with HIV. Anticipated stigma and risk perception were directly associated with depressive symptomatology and QOL. There was evidence of small indirect effects-through stigma-of risk perception on depressive symptomatology and QOL. Gender moderated relationships between sexual behavior and risk perception, depressive symptomatology, and QOL. Results suggest that developing effective gender-based interventions to address stigma, sexual behavior, and risk perception may be important for improving adolescent well-being in high HIV prevalence contexts.

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Survival Models for Case-Based Tuberculosis Progression. Front Public Health.

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Abstract

Introduction: Tuberculosis (TB) disease continues to be responsible for a high global burden with an estimated 10 million people falling ill each year and an estimated 1.45 million deaths. Widely carried out analyses to utilize routine data coming from this disease, and well-established in literature, have paid attention to time-to-event with sputum smear results being considered only at

baseline or even ignored. Also, logistic regression models have been used to demonstrate importance of sputum smear results in patient outcomes. A feature presented by this disease, however, is that each individual patient is usually followed over a period of time with sputum smear results being documented at different points of the treatment curve. This provides both repeated measures and survival times, which may require a joint modeling approach. This study aimed to investigate the association between sputum smear results and the risk of experiencing unfavorable outcome among TB patients and dynamically predict survival probabilities. Method: A joint model for longitudinal and time-to-event data was used to analyze longitudinally measured smear test results with time to experiencing unfavorable outcome for TB patients. A generalized linear mixed-effects model was specified for the longitudinal submodel and cox proportional hazards model for the time-to-event submodel with baseline hazard approximated using penalized B-splines. The two submodels were then assumed to be related via the current value association structure. Bayesian approach was used to approximate parameter estimates using Markov Chain Monte Carlo (MCMC) algorithm. The obtained joint model was used to predict the subject's future risk of survival based on sputum smear results trajectories. Data were sourced from routinely collected TB data stored at National TB Program database. Results: The average baseline age was 35 (SD: 15). Female TB patients constituted 36.42%. Patients with previous history of TB treatment constituted 6.38% (event: 15.25%; no event: 5.29%). TB/HIV co-infection was at 31.23% (event: 47.87%; no event: 29.20%). The association parameter 1.03 (CI[1.03,1.04]) was found to be positive and significantly different from zero, interpreted as follows: The estimate of the association parameter $\alpha = 1.033$ denoted the log hazard ratio for a unit increase in the log odds of having smear positive results. HIV status (negative) 0.47 (CI [0.46,49]) and history of TB treatment (previously treated) (2.52 CI [2.41,2.63]), sex (female) (0.82 CI [0.78,0.84]), and body mass index (BMI) categories (severe malnutrition being reference) were shown to be statistically significant. Conclusion: Sputum smear result is important in estimating the risk to unfavorable outcome among TB patients. Men, previously treated, TB/HIV co-infected and severely malnourished TB patients are at higher risk of unfavorable outcomes.

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Abstract

Background: Visceral leishmaniasis (VL) and zoonotic cutaneous leishmaniasis (ZCL) are of public health concern in Merti sub-County, Kenya, but epidemiological data on transmission, vector abundance, distribution, and reservoir hosts remain limited. To better understand the disease and inform control measures to reduce transmission, we investigated the abundance and distribution of sand fly species responsible for Leishmania transmission in the sub-County and their blood-meal hosts.

Methods: We conducted an entomological survey in five villages with reported cases of VL in Merti sub-County, Kenya, using CDC miniature light traps and castor oil sticky papers. Sand flies were dissected and identified to the species level using standard taxonomic keys and PCR analysis of the cytochrome c oxidase subunit 1 (cox1) gene. Leishmania parasites were detected and identified by PCR and sequencing of internal transcribed spacer 1 (ITS1) genes. Blood-meal sources of engorged females were identified by high-resolution melting analysis of vertebrate cytochrome b (cyt-b) gene PCR products.

Results: We sampled 526 sand flies consisting of 8 species, Phlebotomus orientalis (1.52%; n = 8), and 7 Sergentomyia spp. Sergentomyia squamipleuris was the most abundant sand fly species (78.71%; n = 414) followed by Sergentomyia clydei (10.46%; n = 55). Leishmania major, Leishmania donovani, and Trypanosoma DNA were detected in S. squamipleuris specimens. Humans were the main sources of sand fly blood meals. However, we also detected mixed blood meals; one S. squamipleuris specimen had fed on both human and mouse (Mus musculus) blood, while two Ph. orientalis specimens fed on human, hyrax (Procavia capensis), and mouse (Mus musculus) blood.

Conclusions: Our findings implicate the potential involvement of S. squamipleuris in the transmission of Leishmania and question the dogma that human leishmaniases in the Old World are exclusively transmitted by sand flies of the Phlebotomus genus. The presence of Trypanosoma spp. may indicate mechanical transmission, whose efficiency should be investigated. Host preference analysis revealed the possibility of zoonotic transmission of leishmaniasis and other pathogens in the sub-County. Leishmania major and L. donovani are known to cause ZCL and VL, respectively. However, the reservoir status of the parasites is not uniform. Further studies are needed to determine the reservoir hosts of Leishmania spp. in the area.

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TFR, Graham SM, Operario D, Sanders EJ. "I wish to remain HIV negative": Pre-

exposure prophylaxis adherence and persistence in transgender women and men who

have sex with men in coastal Kenya. PLoS One. 2021 Jan 19;16(1): e0244226.

Abstract

Background: Transgender women (TGW) and men who have sex with men (MSM) in sub-Saharan Africa have high HIV acquisition risks and can benefit from daily pre-exposure prophylaxis (PrEP). We assessed PrEP adherence by measuring tenofovir-diphosphate (TFV-DP) levels and explore motives for PrEP persistence in TGW and MSM.

Methods: Participants were enrolled in a one-year PrEP programme and made quarterly visits irrespective of whether they were still using PrEP. At their month 6 visit, participants provided a dried blood spot to test for TFV-DP levels; protective levels were defined as those compatible with ≥4 pills per week (700-1249 fmol/punch). Before TFV-DP levels were available, a sub-set of these participants were invited for an in-depth interview (IDI). Semi-structured IDI topic guides were used to explore motives to uptake, adhere to, and discontinue PrEP. IDI data were analyzed thematically.

Results: Fifty-three participants (42 MSM and 11 TGW) were enrolled. At month 6, 11 (20.7%) participants (8 MSM and 3 TGW) were lost to follow up or stopped taking PrEP. Any TFV-DP was detected in 62.5% (5/8) of TGW vs. 14.7% of MSM (5/34, p = 0.01). Protective levels were detected in 37.5% of TGW (3/8), but not in any MSM. Nineteen IDI were conducted with 7 TGW and 9 MSM on PrEP, and 1 TGW and 2 MSM off PrEP. Unplanned or frequent risky sexual risk behaviour were the main motives for PrEP uptake. Among participants on PrEP, TGW had a more complete understanding of the benefits of PrEP. Inconsistent PrEP use was attributed to situational factors. Motives to discontinue PrEP included negative reactions from partners and stigmatizing healthcare services.

Conclusion: While MSM evinced greater adherence challenges in this PrEP programme, almost 40% of TGW were protected by PrEP. Given high HIV incidences in TGW these findings hold promise for TGW PrEP programming in the region.

Pubmed link- https://pubmed.ncbi.nlm.nih.gov/33465090/

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E, Ongeri L. Interpersonal psychotherapy delivered by nonspecialists for

depression and posttraumatic stress disorder among Kenyan HIV-positive women affected by gender-based violence: Randomized controlled trial. PLoS Med. 2021 Jan 11;18(1): e1003468.

Abstract

Background: HIV-positive women suffer a high burden of mental disorders due in part to gender-based violence (GBV). Comorbid depression and posttraumatic stress disorder (PTSD) are typical psychiatric consequences of GBV. Despite attention to the HIV-GBV syndemic, few HIV clinics offer formal mental healthcare. This problem is acute in sub-Saharan Africa, where the world's majority of HIV-positive women live and prevalence of GBV is high.

Methods and findings: We conducted a randomized controlled trial at an HIV clinic in Kisumu, Kenya. GBV-affected HIV-positive women with both major depressive disorder (MDD) and PTSD were randomized to 12 sessions of interpersonal psychotherapy (IPT) plus treatment as usual (TAU) or Wait List+TAU. Nonspecialists were trained to deliver IPT inside the clinic. After 3 months, participants were reassessed, and those assigned to Wait List+TAU were given IPT. The primary outcomes were diagnosis of MDD and PTSD (Mini International Neuropsychiatric Interview) at 3 months. Secondary outcomes included symptom measures of depression and PTSD, intimate partner violence (IPV), and disability. A total of 256 participants enrolled between May 2015 and July 2016. At baseline, the mean age of the women in this study was 37 years; 61% reported physical IPV in the past week; 91% reported 2 or more lifetime traumatic events and monthly income was 18USD. Multilevel mixed-effects logistic regression showed that participants randomized to IPT+TAU had lower odds of MDD (odds ratio [OR] 0.26, 95% CI [0.11 to 0.60], p = 0.002) and lower odds of PTSD (OR 0.35, [0.14 to 0.86], p = 0.02) than controls. IPT+TAU participants had lower odds of MDD-PTSD comorbidity than controls (OR 0.36, 95% CI [0.15 to 0.90], p = 0.03). Linear mixed models were used to assess secondary outcomes: IPT+TAU participants had reduced disability (-6.9 [-12.2, -1.5], p = 0.01), and nonsignificantly reduced work absenteeism (-3.35 [-6.83, 0.14], p = 0.06); partnered IPT+TAU participants had a reduction of IPV (-2.79 [-5.42, -0.16], p = 0.04). Gains were maintained across 6-month follow-up. Treatment group differences were observed only at month 3, the time point at which the groups differed in IPT status (before cross over). Study limitations included 35% attrition inclusive of follow-up assessments, generalizability to populations not in HIV care, and data not collected on TAU resources accessed.

Conclusions: IPT for MDD and PTSD delivered by nonspecialists in the context of HIV care yielded significant improvements in HIV-positive women's mental health, functioning, and GBV (IPV) exposure, compared to controls.

Pubmed link-https://pubmed.ncbi.nlm.nih.gov/33428625/

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of the quality of conduct and reporting of survival analyses of tuberculosis

outcomes in Africa. BMC Med Res Methodol. 2021 Apr 27;21(1):89.

Abstract

Background: Survival analyses methods (SAMs) are central to analysing time-to-event outcomes. Appropriate application and reporting of such methods are important to ensure correct interpretation of the data. In this study, we systematically review the application and reporting of SAMs in studies of tuberculosis (TB) patients in Africa. It is the first review to assess the application and reporting of SAMs in this context.

Methods: Systematic review of studies involving TB patients from Africa published between January 2010 and April 2020 in English language. Studies were eligible if they reported use of SAMs. Application and reporting of SAMs were evaluated based on seven author-defined criteria.

Results: Seventy-six studies were included with patient numbers ranging from 56 to 182,890. Forty-three (57%) studies involved a statistician/epidemiologist. The number of published papers per year applying SAMs increased from two in 2010 to 18 in 2019 (P = 0.004). Sample size estimation was not reported by 67 (88%) studies. A total of 22 (29%) studies did not report summary follow-up time. The survival function was commonly presented using Kaplan-Meier survival curves (n = 51, (67%) studies) and group comparisons were performed using log-rank tests (n = 44, (58%) studies). Sixty seven (91%), 3 (4.1%) and 4 (5.4%) studies reported Cox proportional hazard, competing risk and parametric survival regression models, respectively. A total of 37 (49%) studies had hierarchical clustering, of which 28 (76%) did not adjust for the clustering in the analysis. Reporting was adequate among 4.0, 1.3 and 6.6% studies for sample size estimation, plotting of survival curves and test of survival regression underlying assumptions, respectively. Forty-five (59%), 52 (68%) and 73 (96%) studies adequately reported comparison of survival curves, follow-up time and measures of effect, respectively.

Conclusion: The quality of reporting survival analyses remains inadequate despite its increasing application. Because similar reporting deficiencies may be common in other diseases in low- and middle-income countries, reporting guidelines, additional training, and more capacity building are needed along with more vigilance by reviewers and journal editors.

Pubmed link- https://pubmed.ncbi.nlm.nih.gov/33906605/

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Examining unit costs for COVID-19 case management in Kenya. BMJ Glob Health.

2021 Apr;6(4): e004159.

Abstract

Introduction: We estimated unit costs for COVID-19 case management for patients with asymptomatic, mild-to-moderate, severe and critical COVID-19 disease in Kenya.

Methods: We estimated per-day unit costs of COVID-19 case management for patients. We used a bottom-up approach to estimate full economic costs and adopted a health system perspective and patient episode of care as our time horizon. We obtained data on inputs and their quantities from data provided by three public COVID-19 treatment hospitals in Kenya and augmented this with guidelines. We obtained input prices from a recent costing survey of 20 hospitals in Kenya and from market prices for Kenya.

Results: Per-day, per-patient unit costs for asymptomatic patients and patients with mild-to-moderate COVID-19 disease under home-based care are 1993.01 Kenyan shilling (KES) (US$18.89) and 1995.17 KES (US$18.991), respectively. When these patients are managed in an isolation centre or hospital, the same unit costs for asymptomatic patients and patients with mild-to-moderate disease are 6717.74 KES (US$63.68) and 6719.90 KES (US$63.70), respectively. Per-day unit costs for patients with severe COVID-19 disease managed in general hospital wards and those with critical COVID-19 disease admitted in intensive care units are 13 137.07 KES (US$124.53) and 63 243.11 KES (US$599.51).

Conclusion: COVID-19 case management costs are substantial, ranging between two and four times the average claims value reported by Kenya's public health insurer. Kenya will need to mobilise substantial resources and explore service delivery adaptations that will reduce unit costs.

Pubmed link- https://pubmed.ncbi.nlm.nih.gov/33853843/

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Berkley JA. Clinical features of bacterial meningitis among hospitalised

children in Kenya. BMC Med. 2021 Jun 4;19(1):122.

Abstract

Background: Diagnosing bacterial meningitis is essential to optimise the type and duration of antimicrobial therapy to limit mortality and sequelae. In sub-Saharan Africa, many public hospitals lack laboratory capacity, relying on clinical features to empirically treat or not treat meningitis.

We investigated whether clinical features of bacterial meningitis identified prior to the introduction of conjugate vaccines still discriminate meningitis in children aged ≥60 days.

Methods: We conducted a retrospective cohort study to validate seven clinical features identified in 2002 (KCH-2002): bulging fontanel, neck stiffness, cyanosis, seizures outside the febrile convulsion age range, focal seizures, impaired consciousness, or fever without malaria parasitaemia and Integrated Management of Childhood Illness (IMCI) signs: neck stiffness, lethargy, impaired consciousness or seizures, and assessed at admission in discriminating bacterial meningitis after the introduction of conjugate vaccines. Children aged ≥60 days hospitalised between 2012 and 2016 at Kilifi County Hospital were included in this analysis. Meningitis was defined as positive cerebrospinal fluid (CSF) culture, organism observed on CSF microscopy, positive CSF antigen test, leukocytes ≥50/μL, or CSF to blood glucose ratio <0.1.

Results: Among 12,837 admissions, 98 (0.8%) had meningitis. The presence of KCH-2002 signs had a sensitivity of 86% (95% CI 77-92) and specificity of 38% (95% CI 37-38). Exclusion of 'fever without malaria parasitaemia' reduced sensitivity to 58% (95% CI 48-68) and increased specificity to 80% (95% CI 79-80). IMCI signs had a sensitivity of 80% (95% CI 70-87) and specificity of 62% (95% CI 61-63).

Conclusions: A lower prevalence of bacterial meningitis and less typical signs than in 2002 meant the lower performance of KCH-2002 signs. Clinicians and policymakers should be aware of the number of lumbar punctures (LPs) or empirical treatments needed for each case of meningitis. Establishing basic capacity for CSF analysis is essential to exclude bacterial meningitis in children with potential signs.

Pubmed Link- https://pubmed.ncbi.nlm.nih.gov/34082778/

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Abstract

Background: HIV-related maternal deaths and HIV infection among infants remain unacceptably high across sub-Saharan Africa despite increased antenatal care attendance and provision of antiretroviral therapy to pregnant women. In the Jamii Bora ("Better Family" in Swahili) Study, we seek to test the efficacy of an interdependence theory-based couple intervention. The

intervention reaches pregnant women and male partners through home visits by male-female pairs of lay health workers. The aim is to increase access to home-based couples' HIV testing and counseling services to improve family health.

Methods: This is a three-arm randomized control trial among 1080 pregnant women 15 years of age or older, living with their male partners, and who have not undergone couples' HIV testing and counseling in Kisumu and Migori Counties in Kenya. Couples will be randomized into three groups: home-based couple visits, HIV self-testing kits for couple use, or standard care (male partner clinic invitation letters). Participants will be followed up to 18 months postpartum. The study has three aims: in aim 1, we will determine the effects of the intervention on our primary outcome of couple HIVtesting, compared to HIV self-testing kits and standard care; in aim 2, we will examine the intervention impact on HIV prevention behaviors, facility delivery, and postnatal healthcare utilization, as well as secondary health outcomes of maternal viral suppression and HIV-free child survival up to 18 months for couples living with HIV; and in aim 3, we will compare the cost-effectiveness of the home-based couple intervention to the less resource-intensive strategies used in the other two study arms. Assessments with couples are conducted at baseline, late pregnancy, and at months 3, 6, 12, and 18 after birth.

Discussion: The results from this study will inform decision-makers about the cost-effective strategies to engage pregnant couples in the prevention of mother-to-child transmission and family health, with important downstream benefits for maternal, paternal, and infant health.

Pubmed link-https://pubmed.ncbi.nlm.nih.gov/33407784/

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Abstract

Background: Most of the deaths among neonates in low-income and middle-income countries (LMICs) can be prevented through universal access to basic high-quality health services including essential facility-based inpatient care. However, poor routine data undermines data-informed efforts to monitor and promote improvements in the quality of newborn care across hospitals.

Methods: Continuously collected routine patients' data from structured paper record forms for all admissions to newborn units (NBUs) from 16 purposively selected Kenyan public hospitals that are part of a clinical information network were analysed together with data from all paediatric

admissions ages 0-13 years from 14 of these hospitals. Data are used to show the proportion of all admissions and deaths in the neonatal age group and examine morbidity and mortality patterns, stratified by birth weight, and their variation across hospitals.

Findings: During the 354 hospital months study period, 90 222 patients were admitted to the 14 hospitals contributing NBU and general paediatric ward data. 46% of all the admissions were neonates (aged 0-28 days), but they accounted for 66% of the deaths in the age group 0-13 years. 41 657 inborn neonates were admitted in the NBUs across the 16 hospitals during the study period. 4266/41 657 died giving a crude mortality rate of 10.2% (95% CI 9.97% to 10.55%), with 60% of these deaths occurring on the first-day of admission. Intrapartum-related complications was the single most common diagnosis among the neonates with birth weight of 2000 g or more who died. A threefold variation in mortality across hospitals was observed for birth weight categories 1000-1499 g and 1500-1999 g.

Interpretation: The high proportion of neonatal deaths in hospitals may reflect changing patterns of childhood mortality. Majority of newborns died of preventable causes (>95%). Despite availability of high-impact low-cost interventions, hospitals have high and very variable mortality proportions after stratification by birth weight.

Pubmed link- https://pubmed.ncbi.nlm.nih.gov/34059493/

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Jit M, Funk S, Smits G, van Gageldonk PGM, van der Klis FRM, Tabu C, Nokes DJ;

LSHTM CMMID COVID-19 Working Group, Scott J, Flasche S, Adetifa I. The

importance of supplementary immunisation activities to prevent measles outbreaks

during the COVID-19 pandemic in Kenya. BMC Med. 2021 Feb 3;19(1):35.

Abstract

Background: The COVID-19 pandemic has disrupted routine measles immunisation and supplementary immunisation activities (SIAs) in most countries including Kenya. We assessed the risk of measles outbreaks during the pandemic in Kenya as a case study for the African Region.

Methods: Combining measles serological data, local contact patterns, and vaccination coverage into a cohort model, we predicted the age-adjusted population immunity in Kenya and estimated the probability of outbreaks when contact-reducing COVID-19 interventions are lifted. We considered various scenarios for reduced measles vaccination coverage from April 2020.

Results: In February 2020, when a scheduled SIA was postponed, population immunity was close to the herd immunity threshold and the probability of a large outbreak was 34% (8-54). As the COVID-19 contact restrictions are nearly fully eased, from December 2020, the probability of a large measles outbreak will increase to 38% (19-54), 46% (30-59), and 54% (43-64) assuming a 15%, 50%, and 100% reduction in measles vaccination coverage. By December 2021, this risk increases further to 43% (25-56), 54% (43-63), and 67% (59-72) for the same coverage scenarios respectively. However, the increased risk of a measles outbreak following the lifting of all restrictions can be overcome by conducting a SIA with ≥ 95% coverage in under-fives.

Conclusion: While contact restrictions sufficient for SAR-CoV-2 control temporarily reduce measles transmissibility and the risk of an outbreak from a measles immunity gap, this risk rises rapidly once these restrictions are lifted. Implementing delayed SIAs will be critical for prevention of measles outbreaks given the roll-back of contact restrictions in Kenya.

Pubmed link- https://pubmed.ncbi.nlm.nih.gov/33531015/

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Laurent Z, Otieno JR, Sang R, Kamau E, Cheruiyot S, Otieno E, Agoti CN, Bejon P,

Thumbi SM, Warimwe GM . Endemic chikungunya fever in Kenyan children: a

prospective cohort study. BMC Infect Dis. 2021 Feb 18;21(1):186.

Abstract

Background: Chikungunya fever (CHIKF) was first described in Tanzania in 1952. Several epidemics including East Africa have occurred, but there are no descriptions of longitudinal surveillance of endemic disease. Here, we estimate the incidence of CHIKF in coastal Kenya and describe the associated viral phylogeny.

Methods: We monitored acute febrile illnesses among 3500 children visiting two primary healthcare facilities in coastal Kenya over a 5-year period (2014-2018). Episodes were linked to a demographic surveillance system and blood samples obtained. Cross-sectional sampling in a community survey of a different group of 435 asymptomatic children in the same study location was done in 2016. Reverse-transcriptase PCR was used for chikungunya virus (CHIKV) screening, and viral genomes sequenced for phylogenetic analyses.

Results: We found CHIKF to be endemic in this setting, associated with 12.7% (95% CI 11.60, 13.80) of all febrile presentations to primary healthcare. The prevalence of CHIKV infections among asymptomatic children in the community survey was 0.7% (95% CI 0.22, 2.12). CHIKF incidence among children < 1 year of age was 1190 cases/100,000-person years and 63

cases/100,000-person years among children aged ≥10 years. Recurrent CHIKF episodes, associated with fever and viraemia, were observed among 19 of 170 children with multiple febrile episodes during the study period. All sequenced viral genomes mapped to the ECSA genotype albeit distinct from CHIKV strains associated with the 2004 East African epidemic.

Conclusions: CHIKF may be a substantial public health burden in primary healthcare on the East African coast outside epidemic years, and recurrent infections are common.

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Abstract

Malaria and iron deficiency (ID) are common and interrelated public health problems in African children. Observational data suggest that interrupting malaria transmission reduces the prevalence of ID1. To test the hypothesis that malaria might cause ID, we used sickle cell trait (HbAS, rs334), a genetic variant that confers specific protection against malaria2, as an instrumental variable in Mendelian randomization analyses. HbAS was associated with a 30% reduction in ID among children living in malaria-endemic countries in Africa (n = 7,453), but not among individuals living in malaria-free areas (n = 3,818). Genetically predicted malaria risk was associated with an odds ratio of 2.65 for ID per unit increase in the log incidence rate of malaria. This suggests that

an intervention that halves the risk of malaria episodes would reduce the prevalence of ID in African children by 49%.

Pubmed link- https://pubmed.ncbi.nlm.nih.gov/33619371/

37: Kariuki SM, Ngugi AK, Kombe MZ, Kazungu M, Chengo E, Odhiambo R, Nyaguara A,

Neville BG, Newton CR. Prevalence and mortality of epilepsies with convulsive

and non-convulsive seizures in Kilifi, Kenya. Seizure. 2021 May 14; 89:51-55.

Abstract

Objectives: The prevalence of all epilepsies (both convulsive and non-convulsive seizures) in Low- and Middle-Income Countries (LMIC), particularly sub-Saharan Africa is unknown. Under estimation of non-convulsive epilepsies in data from these countries may lead to inadequate and sub-optimal allocation of resources to control and prevent epilepsy. We determined the prevalence of all types of epilepsies and compared the mortality between convulsive seizures and non-convulsive seizures in a resource limited rural area in Kenya.

Methods: Trained clinicians identified cases of epilepsy in a randomly selected sample of 4,441 residents in the Kilifi Health and Demographic Surveillance System site using a cross-sectional survey design. Seizure types were classified by epileptologists using the current guidelines of the International League Against Epilepsy (ILAE). We estimated prevalence for epilepsy with convulsive seizures and non-convulsive seizures and for epilepsy with non-convulsive seizures only and compared premature mortality between these groups of seizures.

Results: Of the 4441 people visited, 141 had lifetime epilepsy and 96 active epilepsy, which is a crude prevalence of 31.7/1,000 persons (95% CI: 26.6-36.9) and 21.6/1,000 (95% CI: 17.3-25.9), respectively. Both convulsive and non-convulsive seizures occurred in 7% people with epilepsy (PWE), only convulsive seizures in 52% and only non-convulsive seizures in 35% PWE; there was insufficient information to classify epilepsy in the remainder 6%. The age- and sex-adjusted prevalence of lifetime people was 23.5/1,000 (95% CI: 11.0-36.0), with the adjusted prevalence of epilepsy with non-convulsive seizures only estimated at 8.2/1,000 (95%CI:3.9-12.6). The mortality rate in PWE was 6.3/1,000 (95%CI: 3.4-11.8), compared to 2.8/1,000 (2.3-3.3) in those without epilepsy; hazard ratio (HR) =2.31 (1.22-4.39; p=0.011). The annual mortality rate was 11.2/1,000 (95%CI: 5.3-23.4) in PWE with convulsive and non-convulsive seizures and none died in PWE with non-convulsive seizures alone.

Conclusions: Our study shows that epilepsy with non-convulsive seizures is common and adds to the prevalence of previously reported estimates of active convulsive epilepsy. Both epilepsy with

convulsive seizures and that with non-convulsive seizures should be identified for optimising treatment and for planning resource allocation.

Pubmed link-https://pubmed.ncbi.nlm.nih.gov/34000517/

38: Kamau A, Mtanje G, Mataza C, Bejon P, Snow RW. Spatial-temporal clustering

of malaria using routinely collected health facility data on the Kenyan Coast.

Malar J. 2021 May 20;20(1):227.

Abstract

Background: The over-distributed pattern of malaria transmission has led to attempts to define malaria "hotspots" that could be targeted for purposes of malaria control in Africa. However, few studies have investigated the use of routine health facility data in the more stable, endemic areas of Africa as a low-cost strategy to identify hotspots. Here the objective was to explore the spatial and temporal dynamics of fever positive rapid diagnostic test (RDT) malaria cases routinely collected along the Kenyan Coast.

Methods: Data on fever positive RDT cases between March 2018 and February 2019 were obtained rom patients presenting to six out-patients health-facilities in a rural area of Kilifi County on the Kenyan Coast. To quantify spatial clustering, homestead level geocoded addresses were used as well as aggregated homesteads level data at enumeration zone. Data were sub-divided into quarterly intervals. Kulldorff's spatial scan statistics using Bernoulli probability model was used to detect hotspots of fever positive RDTs across all ages, where cases were febrile individuals with a positive test and controls were individuals with a negative test.

Results: Across 12 months of surveillance, there were nine significant clusters that were identified using the spatial scan statistics among RDT positive fevers. These clusters included 52% of all fever positive RDT cases detected in 29% of the geocoded homesteads in the study area. When the resolution of the data was aggregated at enumeration zone (village) level the hotspots identified were located in the same areas. Only two of the nine hotspots were temporally stable accounting for 2.7% of the homesteads and included 10.8% of all fever positive RDT cases detected.

Conclusion: Taking together the temporal instability of spatial hotspots and the relatively modest fraction of the malaria cases that they account for; it would seem inadvisable to re-design the sub-county control strategies around targeting hotspots.

Pubmed link- https://pubmed.ncbi.nlm.nih.gov/34016100/

39: Nyangi M, Kigondu E, Irungu B, Nganga M, Gachanja A, Murigi M, Nyangacha R, Muniu E, Kamau L, Gathirwa J. Integrity, use and care of long-lasting insecticidal nets in Kirinyaga County, Kenya. BMC Public Health. 2021 May 3;21(1):856.

Abstract

Background: Vector control is an essential component in prevention and control of malaria in malaria endemic areas. Insecticide treated nets is one of the standard tools recommended for malaria vector control. The objective of the study was to determine physical integrity and insecticidal potency of long-lasting insecticidal nets (LLINs) used in control of malaria vector in Kirinyaga County, Kenya.

Method: The study targeted households in an area which had received LLINs during mass net distribution in 2016 from Ministry of Health. A total of 420 households were sampled using systematic sampling method, where the household heads consented to participate in the study. A semi-structured questionnaire was administered to assess care and use while physical examination was used to determine integrity. Chemical concentration was determined by gas chromatography mass spectroscopy (GC-MS). Data analysis was done using Statistical Package for Social Sciences (SPSS) version 19.

Results: After 18 months of use, 96.9% (95% CI: 95.2-98.6%) of the distributed nets were still available. Regarding net utilization, 94.1% of household heads reported sleeping under an LLIN the previous night. After physical examination, 49.9% (95% CI: 43-52.8%) of the bed nets had at least one hole. The median number of holes of any size was 2[interquartile range (IQR) 1-4], and most holes were located on the lower part of the nets, [median 3 (IQR 2-5)]. Only 15% of the nets with holes had been repaired. The median concentration for α-cypermethrin was 7.15 mg/m2 (IQR 4.25-15.31) and 0.00 mg/g (IQR 0.00-1.99) for permethrin. Based on pHI, Chi-square test varied significantly with the manufacturer (X (6, N = 389) = 29.14, p = 0.04). There was no significant difference between nets with different number of washes (X2(2) = 4.55, p = 0.103).

Conclusion: More than three-quarters of the nets supplied had survived and insecticidal potency was adequate in vector control. Standard procedure for field evaluation of surface insecticidal content available to a mosquito after landing on a net to rest is recommended.

Pubmed link- https://pubmed.ncbi.nlm.nih.gov/33941135/

40: Barasa E, Kazungu J, Nguhiu P, Ravishankar N. Examining the level and inequality in health insurance coverage in 36 sub-Saharan African countries. BMJ

Glob Health. 2021 Apr;6(4): e004712.

Abstract

Introduction: Low/middle-income countries (LMICs) in sub-Saharan Africa (SSA) are increasingly turning to public contributory health insurance as a mechanism for removing financial barriers to access and extending financial risk protection to the population. Against this backdrop, we assessed the level and inequality of population coverage of existing health insurance schemes in 36 SSA countries.

Methods: Using secondary data from the most recent Demographic and Health Surveys, we computed mean population coverage for any type of health insurance, and for specific forms of health insurance schemes, by country. We developed concentration curves, computed concentration indices, and rich-poor differences and ratios to examine inequality in health insurance coverage. We decomposed the concentration index using a generalised linear model to examine the contribution of household and individual-level factors to the inequality in health insurance coverage.

Results: Only four countries had coverage levels with any type of health insurance of above 20% (Rwanda-78.7% (95% CI 77.5% to 79.9%), Ghana-58.2% (95% CI 56.2% to 60.1%), Gabon-40.8% (95% CI 38.2% to 43.5%), and Burundi 22.0% (95% CI 20.7% to 23.2%)). Overall, health insurance coverage was low (7.9% (95% CI 7.8% to 7.9%)) and pro-rich; concentration index=0.4 (95% CI 0.3 to 0.4, p<0.001). Exposure to media made the greatest contribution to the pro-rich distribution of health insurance coverage (50.3%), followed by socioeconomic status (44.3%) and the level of education (41.6%).

Conclusion: Coverage of health insurance in SSA is low and pro-rich. The four countries that had health insurance coverage levels greater than 20% were all characterised by substantial funding from tax revenues. The other study countries featured predominantly voluntary mechanisms. In a context of high informality of labour markets, SSA and other LMICs should rethink the role of voluntary contributory health insurance and instead embrace tax funding as a sustainable and feasible mechanism for mobilising resources for the health sector.

Pubmed link-https://pubmed.ncbi.nlm.nih.gov/33903176/

41: Nyongesa MK, Mwangi P, Kinuthia M, Hassan AS, Koot HM, Cuijpers P, Newton CRJC, Abubakar A. Prevalence, risk and protective indicators of common mental disorders among young people living with HIV compared to their uninfected peers from the Kenyan coast: a cross-sectional study. BMC Psychiatry. 2021 Feb

10;21(1):90.

Abstract

Background: In sub-Saharan Africa, common mental disorders (CMDs) like depression and anxiety are under-investigated amongst young people living with HIV (YLWH). To address the gap, in Kenya we: a) determined the prevalence of CMDs among YLWH compared to their uninfected peers; b) investigated HIV status as an independent predictor of CMDs in young people; c) investigated CMDs risk and protective indicators with more focus on YLWH.

Methods: Between November 2018 and September 2019, 819 young people aged 18-24 years (407 HIV-infected) were recruited from two Counties on the Kenyan coast. Locally adapted pre-existing mental health measures, Patient Health Questionnaire (9-item) and Generalized Anxiety Disorder scale (7-item), were administered among other questionnaires via audio computer-assisted self-interview. Logistic regression was used to determine the correlates of CMDs.

Results: Prevalence of CMDs was significantly elevated among YLWH compared to their uninfected peers i.e. 29% vs. 12%; $p < 0.001$ for depressive symptoms, 19% vs. 8%; $p < 0.001$ for anxiety symptoms, and 16% vs. 5%; $p < 0.001$ for comorbid depressive and anxiety symptoms. HIV status independently predicted depressive symptoms and its co-occurrence with anxiety symptoms. Among YLWH, negative life events, higher perceived HIV-related stigma and low adherence to antiretroviral therapy were the risk indicators for elevated CMDs. Among HIV-uninfected youths, death of both parents was a risk indicator for elevated depressive symptoms. Protective indicators against CMDs among youths with and without HIV included higher social support and health-related quality of life.

Conclusion: At the Kenyan coast, YLWH have significantly higher burden of CMDs compared to their uninfected peers. Being HIV-positive as a youth in this setting is predictive of more depressive symptoms and its comorbidity with anxiety symptoms. YLWH at high risk of CMDs in coastal Kenya can benefit from early detection, referral and treatment if routine screening for CMDs is integrated in their care package. The mental wellbeing of bereaving HIV-unaffected youths could be improved through continued support to help them come to terms with their loss. At the community level, programmes strengthening the social capital or improving the overall quality of life of youths with or without HIV may be beneficial to their mental health.

Pubmed link- https://pubmed.ncbi.nlm.nih.gov/33568115/

42: Abuga JA, Kariuki SM, Kinyanjui SM, Boele van Hensbroek M, Newton CR.

Premature Mortality, Risk Factors, and Causes of Death Following Childhood-Onset

Neurological Impairments: A Systematic Review. Front Neurol. 2021 Apr

9; 12:627824.

Abstract

Background: Neurological impairment (NI) and disability are associated with reduced life expectancy, but the risk and magnitude of premature mortality in children vary considerably across study settings. We conducted a systematic review to estimate the magnitude of premature mortality following childhood-onset NI worldwide and to summarize known risk factors and causes of death. Methods: We searched various databases for published studies from their inception up to 31st October 2020. We included all cohort studies that assessed the overall risk of mortality in individuals with childhood-onset epilepsy, intellectual disability (ID), and deficits in hearing, vision and motor functions. Comparative measures of mortality such as the standardized mortality ratio (SMR), risk factors and causes were synthesized quantitatively under each domain of impairment. This review is registered on the PROSPERO database (registration number CRD42019119239). Results: The search identified 2,159 studies, of which 24 studies were included in the final synthesis. Twenty-two (91.7%) studies originated from high-income countries (HICs). The median SMR was higher for epilepsy compared with ID (7.1 [range 3.1-22.4] vs. 2.9 [range 2.0-11.6]). In epilepsy, mortality was highest among younger age groups, comorbid neurological disorders, generalized seizures (at univariable levels), untreatable epilepsy, soon after diagnosis and among cases with structural/metabolic types, but there were no differences by sex. Most deaths (87.5%) were caused by non-epilepsy-related causes. For ID, mortality was highest in younger age groups and girls had a higher risk compared to the general population. Important risk factors for premature mortality were severe-to-profound severity, congenital disorders e.g., Down Syndrome, comorbid neurological disorders and adverse pregnancy and perinatal events. Respiratory infections and comorbid neurological disorders were the leading causes of death in ID. Mortality is infrequently examined in impairments of vision, hearing and motor functions. Summary: The risk of premature mortality is elevated in individuals with childhood-onset NI, particularly in epilepsy and lower in ID, with a need for more studies for vision, hearing, and motor impairments. Survival in NI could be improved through interventions targeting modifiable risk factors and underlying causes.

Pubmed link- https://pubmed.ncbi.nlm.nih.gov/33897590/

43: Omondi BR, Muthui MK, Muasya WI, Orindi B, Mwakubambanya RS, Bousema T,

Drakeley C, Marsh K, Bejon P, Kapulu MC. Antibody Responses to Crude Gametocyte

Extract Predict Plasmodium falciparum Gametocyte Carriage in Kenya. Front

Immunol. 2021 Feb 3; 11:609474.

Abstract

Background: Malaria caused by Plasmodium falciparum remains a serious global public health challenge especially in Africa. Interventions that aim to reduce malaria transmission by targeting the gametocyte reservoir are key to malaria elimination and/or eradication. However, factors that are associated with gametocyte carriage have not been fully explored. Consequently, identifying predictors of the infectious reservoir is fundamental in the elimination campaign.

Methods: We cultured P. falciparum NF54 gametocytes (to stage V) and prepared crude gametocyte extract. Samples from a total of 687 participants (aged 6 months to 67 years) representing two cross-sectional study cohorts in Kilifi, Kenya were used to assess IgG antibody responses by ELISA. We also analyzed IgG antibody responses to the blood-stage antigen AMA1 as a marker of asexual parasite exposure. Gametocytemia and asexual parasitemia data quantified by microscopy and molecular detection (QT-NASBA) were used to determine the relationship with antibody responses, season, age, and transmission setting. Multivariable logistic regression models were used to study the association between antibody responses and gametocyte carriage. The predictive power of the models was tested using the receiver operating characteristic (ROC) curve.

Results: Multivariable logistic regression analysis showed that IgG antibody response to crude gametocyte extract predicted both microscopic (OR=1.81 95% CI: 1.06-3.07, p=0.028) and molecular (OR=1.91, 95% CI: 1.11-3.29, p=0.019) P. falciparum gametocyte carriage. Antibody responses to AMA1 were also associated with both microscopic (OR=1.61 95% CI: 1.08-2.42, p=0.020) and molecular (OR=3.73 95% CI: 2.03-6.74, p<0.001) gametocytemia. ROC analysis showed that molecular (AUC=0.897, 95% CI: 0.868-0.926) and microscopic (AUC=0.812, 95% CI: 0.758-0.865) multivariable models adjusted for gametocyte extract showed very high predictive power. Molecular (AUC=0.917, 95% CI: 0.891-0.943) and microscopic (AUC=0.806, 95% CI: 0.755-0.858) multivariable models adjusted for AMA1 were equally highly predictive.

Conclusion: In our study, it appears that IgG responses to crude gametocyte extract are not an independent predictor of gametocyte carriage after adjusting for AMA1 responses but may predict gametocyte carriage as a proxy marker of exposure to parasites. Serological responses to AMA1 or to gametocyte extract may facilitate identification of individuals within populations who contribute to malaria transmission and support implementation of transmission-blocking interventions.

Pubmed link-https://pubmed.ncbi.nlm.nih.gov/33633729/

44: Omoke S, English M, Aluvaala J, Gathara D, Agweyu A, Akech S; Clinical Information Network. Prevalence and fluid management of dehydration in children without diarrhoea admitted to Kenyan hospitals: a multisite observational study.

BMJ Open. 2021 Jun 18;11(6): e042079.

Abstract

Objectives: To examine the prevalence of dehydration without diarrhoea among admitted children aged 1-59 months and to describe fluid management practices in such cases.

Design: A multisite observational study that used routine in-patient data collected prospectively between October 2013 and December 2018.

Settings: Study conducted in 13 county referral hospitals in Kenya.

Participants: Children aged 1-59 months with admission or discharge diagnosis of dehydration but had no diarrhoea as a symptom or diagnosis. Children aged <28 days and those with severe acute malnutrition were excluded.

Results: The prevalence of dehydration in children without diarrhoea was 3.0% (2019/68 204) and comprised 15.9% (2019/12 702) of all dehydration cases. Only 55.8% (1127/2019) of affected children received either oral or intravenous fluid therapy. Where fluid treatment was given, the volumes, type of fluid, duration of fluid therapy and route of administration were similar to those used in the treatment of dehydration secondary to diarrhoea. Pneumonia (1021/2019, 50.6%) and malaria (715/2019, 35.4%) were the two most common comorbid diagnoses. Overall case fatality in the study population was 12.9% (260/2019).

Conclusion: Sixteen per cent of children hospitalised with dehydration do not have diarrhoea but other common illnesses. Two-fifths do not receive fluid therapy; a regimen similar to that used in diarrhoeal cases is used in cases where fluid is administered. Efforts to promote compliance with guidance in routine clinical settings should recognise special circumstances where guidelines do not apply, and further studies on appropriate management for dehydration in the absence of diarrhoea are required.

Pubmed link-https://pubmed.ncbi.nlm.nih.gov/34145005/

45: Lutomiah J, Mulwa F, Mutisya J, Koskei E, Langat S, Nyunja A, Koka H, Konongoi S, Chepkorir E, Ofula V, Owaka S, Eyase F, Sang R. Probable contribution of Culex quinquefasciatus mosquitoes to the circulation of

chikungunya virus during an outbreak in Mombasa County, Kenya, 2017-2018.

Parasit Vectors. 2021 Mar 5;14(1):138.

Abstract

Background: Chikungunya virus is an alphavirus, primarily transmitted by Aedes aegypti and Ae. albopictus. In late 2017-2018, an outbreak of chikungunya occurred in Mombasa county, Kenya, and investigations were conducted to establish associated entomological risk factors.

Methods: Homes were stratified and water-filled containers inspected for immature Ae. aegypti, and larval indices were calculated. Adult mosquitoes were collected in the same homesteads using BG-Sentinel and CDC light traps and screened for chikungunya virus. Experiments were also conducted to determine the ability of Culex quinquefasciatus to transmit chikungunya virus.

Results: One hundred thirty-one houses and 1637 containers were inspected; 48 and 128 of them, respectively, were positive for immature Ae. aegypti, with the house index (36.60), container index (7.82) and Breteau index (97.71) recorded. Jerry cans (n = 1232; 72.26%) and clay pots (n = 2; 0.12%) were the most and least inspected containers, respectively, while drums, the second most commonly sampled (n = 249; 15.21%), were highly positive (65.63%) and productive (60%). Tires and jerry cans demonstrated the highest and lowest breeding preference ratios, 11.36 and 0.2, respectively. Over 6900 adult mosquitoes were collected and identified into 15 species comprising Cx. quinquefasciatus (n = 4492; 65.04%), Aedes vittatus (n = 1137; 16.46%) and Ae. aegypti (n = 911; 13.19%) and 2 species groups. Simpson's dominance and Shannon-Wiener diversity indices of 0.4388 and 1.1942 were recorded, respectively. Chikungunya virus was isolated from pools of Ae. aegypti (1) and Cx. quinquefasciatus (4), two of which were males. Minimum infection rates of 3.0 and 0.8 were observed for female Ae. aegypti and Cx. quinquefasciatus, respectively. Between 25 and 31.3% of exposed mosquitoes became infected with CHIKV 7, 14 and 21 days post-exposure. For the experimentally infected Cx. quinquefasciatus mosquitoes, between 13 and 40% had the virus disseminated, with 100% transmission being observed among those with disseminated infection.

Conclusions: These results demonstrated high risk of chikungunya transmission for residents in the sampled areas of Mombasa. Transmission data confirmed the probable role played by Cx. quinquefasciatus in the outbreak while the role of Ae. vittatus in the transmission of chikungunya virus remains unknown.

Pubmed link-https://pubmed.ncbi.nlm.nih.gov/33673872/

46: Mugo PM, Agutu CA, Wahome E, Juma M, Nzioka J, Mohamed K, Mumba T, Shally M,

Fauz I, Omar A, Rinke de Wit TF, van der Elst EM, Graham SM, Sanders EJ. Trends

and predictors of HIV positivity and time since last test at voluntary

counselling and testing encounters among adults in Kilifi, Kenya, 2006-2017.

Wellcome Open Res. 2021 Jun 4; 4:127.

Abstract

Background: Little is known about HIV retesting uptake among key populations (KP) and general populations (GP) in Kenya. We assessed trends and predictors of first-time testing (FTT), late retesting (previous test more than one year ago for GP or three months for KP), and test positivity at three voluntary counselling and testing (VCT) centres in coastal Kenya. Methods: Routine VCT data covering 2006-2017 was collected from three VCT centres in Kilifi County. We analysed HIV testing history and test results from encounters among adults 18-39 years, categorized as GP men, GP women, men who have sex with men (MSM), and female sex workers (FSW). Results: Based on 24,728 test encounters (32% FTT), we observed declines in HIV positivity (proportion of encounters where the result was positive) among GP men, GP women, first-time testers and MSM but not among FSW. The proportion of encounters for FTT and late retesting decreased for both GP and KP but remained much higher in KP than GP. HIV positivity was higher at FTT and late retesting encounters; at FSW and MSM encounters; and at encounters with clients reporting lower educational attainment and sexually transmitted infection (STI) symptoms. HIV positivity was lower in GP men, never married clients and those less than 35 years of age. FTT was associated with town, risk group, age 18-24 years, never-married status, low educational attainment, and STI symptoms. Late retesting was less common among encounters with GP individuals who were never married, had Muslim or no religious affiliation, had lower educational attainment, or reported STI symptoms. Conclusions: HIV positive test results were most common at encounters with first-time testers and late re-testers. While the proportion of encounters at which late retesting was reported decreased steadily over the period reviewed, efforts are needed to increase retesting among the most at-risk populations.

Pubmed link- https://pubmed.ncbi.nlm.nih.gov/33884308/

47: Asiimwe BB, Kiiru J, Mshana SE, Neema S, Keenan K, Kesby M, Mwanga JR, Sloan DJ, Mmbaga BT, Smith VA, Gillespie SH, Lynch AG, Sandeman A, Stelling J, Elliott A, Aanensen DM, Kibiki GE, Sabiiti W, Holden MTG; HATUA Consortium. Protocol for an interdisciplinary cross-sectional study investigating the social, biological and community-level drivers of antimicrobial resistance (AMR): Holistic Approach to Unravel Antibacterial Resistance in East Africa (HATUA). BMJ Open. 2021 Mar

8;11(3): e041418.

Abstract

Introduction: Antimicrobial resistance (AMR) is a global health threat that requires urgent research using a multidisciplinary approach. The biological drivers of AMR are well understood, but factors related to treatment seeking and the social contexts of antibiotic (AB) use behaviours are less understood. Here we describe the Holistic Approach to Unravel Antibacterial Resistance in East Africa, a multicentre consortium that investigates the diverse drivers of drug resistance in urinary tract infections (UTIs) in East Africa.

Methods and analysis: This study will take place in Uganda, Kenya and Tanzania. We will conduct geospatial mapping of AB sellers, and conduct mystery client studies and in-depth interviews (IDIs) with drug sellers to investigate AB provision practices. In parallel, we will conduct IDIs with doctors, alongside community focus groups. Clinically diagnosed patients with UTI will be recruited from healthcare centres, provide urine samples and complete a questionnaire capturing retrospective treatment pathways, sociodemographic characteristics, attitudes and knowledge. Bacterial isolates from urine and stool samples will be subject to culture and antibiotic sensitivity testing. Genomic DNA from bacterial isolates will be extracted with a subset being sequenced. A follow-up household interview will be conducted with 1800 UTI-positive patients, where further environmental samples will be collected. A subsample of patients will be interviewed using qualitative tools. Questionnaire data, microbiological analysis and qualitative data will be linked at the individual level. Quantitative data will be analysed using statistical modelling, including Bayesian network analysis, and all forms of qualitative data analysed through iterative thematic content analysis.

Ethics and dissemination: Approvals have been obtained from all national and local ethical review bodies in East Africa and the UK. Results will be disseminated in communities, with local and global policy stakeholders, and in academic circles. They will have great potential to inform policy, improve clinical practice and build regional pathogen surveillance capacity.

Pubmed link- https://pubmed.ncbi.nlm.nih.gov/34006022/

48: Adoke Y, Zoleko-Manego R, Ouoba S, Tiono AB, Kaguthi G, Bonzela JE, Duong

TT, Nahum A, Bouyou-Akotet M, Ogutu B, Ouedraogo A, Macintyre F, Jessel A,

Laurijssens B, Cherkaoui-Rbati MH, Cantalloube C, Marrast AC, Bejuit R, White D,

Wells TNC, Wartha F, Leroy D, Kibuuka A, Mombo-Ngoma G, Ouattara D, Mugenya I,

Phuc BQ, Bohissou F, Mawili-Mboumba DP, Olewe F, Soulama I, Tinto H; FALCI Study

Group. A randomized, double-blind, phase 2b study to investigate the efficacy,

safety, tolerability and pharmacokinetics of a single-dose regimen of ferroquine

with artefenomel in adults and children with uncomplicated Plasmodium falciparum

malaria. Malar J. 2021 May 19;20(1):222.

Abstract

Background: For uncomplicated Plasmodium falciparum malaria, highly efficacious single-dose treatments are expected to increase compliance and improve treatment outcomes, and thereby may slow the development of resistance. The efficacy and safety of a single-dose combination of artefenomel (800 mg) plus ferroquine (400/600/900/1200 mg doses) for the treatment of uncomplicated P. falciparum malaria were evaluated in Africa (focusing on children ≤ 5 years) and Asia.

Methods: The study was a randomized, double-blind, single-dose, multi-arm clinical trial in patients aged > 6 months to < 70 years, from six African countries and Vietnam. Patients were followed up for 63 days to assess treatment efficacy, safety and pharmacokinetics. The primary efficacy endpoint was the polymerase chain reaction (PCR)-adjusted adequate clinical and parasitological response (ACPR) at Day 28 in the Per-Protocol [PP] Set comprising only African patients ≤ 5 years. The exposure-response relationship for PCR-adjusted ACPR at Day 28 and prevalence of kelch-13 mutations were explored.

Results: A total of 373 patients were treated: 289 African patients ≤ 5 years (77.5%), 64 African patients > 5 years and 20 Asian patients. None of the treatment arms met the target efficacy criterion for PCR-adjusted ACPR at Day 28 (lower limit of 95% confidence interval [CI] > 90%). PCR-adjusted ACPR at Day 28 [95% CI] in the PP Set ranged from 78.4% [64.7; 88.7%] to 91.7% [81.6; 97.2%] for the 400 mg to 1200 mg ferroquine dose. Efficacy rates were low in Vietnamese patients, ranging from 20 to 40%. A clear relationship was found between drug exposure (artefenomel and ferroquine concentrations at Day 7) and efficacy (primary endpoint), with higher concentrations of both drugs resulting in higher efficacy. Six distinct kelch-13 mutations were detected in parasite isolates from 10/272 African patients (with 2 mutations known to be associated with artemisinin resistance) and 18/20 Asian patients (all C580Y mutation). Vomiting within 6 h of initial artefenomel administration was common (24.6%) and associated with lower drug exposures.

Conclusion: The efficacy of artefenomel/ferroquine combination was suboptimal in African children aged ≤ 5 years, the population of interest, and vomiting most likely had a negative impact on efficacy.

Pubmed link-https://pubmed.ncbi.nlm.nih.gov/34011358/

49: Njunge JM, Gonzales GB, Ngari MM, Thitiri J, Bandsma RHJ, Berkley JA.

Systemic inflammation is negatively associated with early post discharge growth

following acute illness among severely malnourished children - a pilot study.

Wellcome Open Res. 2021 Mar 16; 5:248.

Abstract

Background: Rapid growth should occur among children with severe malnutrition (SM) with medical and nutritional management. Systemic inflammation (SI) is associated with death among children with SM and is negatively associated with linear growth. However, the relationship between SI and weight gain during therapeutic feeding following acute illness is unknown. We hypothesised that growth post-hospital discharge is associated with SI among children with SM. Methods: We conducted secondary analysis of data from HIV-uninfected children with SM (n=98) who survived and were not readmitted to hospital during one year of follow-up. We examined the relationship between changes in absolute deficits in weight and mid-upper-arm circumference (MUAC) from enrolment at stabilisation to 60 days and one year later, and untargeted plasma proteome, targeted cytokines/chemokines, leptin, and soluble CD14 using multivariate regularized linear regression. Results: The mean change in absolute deficit in weight and MUAC was -0.50kg (standard deviation; SD±0.69) and -1.20cm (SD±0.89), respectively, from enrolment to 60 days later. During the same period, mean weight and MUAC gain was 3.3g/kg/day (SD±2.4) and 0.22mm/day (SD±0.2), respectively. Enrolment interleukins; IL17-alpha and IL-2, and serum amyloid P were negatively associated with weight and MUAC gain during 60 days. Lipopolysaccharide binding protein and complement component 2 were negatively associated with weight gain only. Leptin was positively associated with weight gain. Soluble CD14, beta-2 microglobulin, and macrophage inflammatory protein 1 beta were negatively associated with MUAC gain only. Glutathione peroxidase 3 was positively associated with weight and MUAC gain during one year. Conclusions: Early post-hospital discharge weight and MUAC gain were rapid and comparable to children with uncomplicated SM treated in the community. Higher concentrations of SI markers were associated with less weight and MUAC gain, suggesting inflammation negatively impacts recovery from wasting. This finding warrants further research on reducing inflammation on growth among children with SM.

Pubmed link- https://pubmed.ncbi.nlm.nih.gov/33969227/

50: Macharia PM, Joseph NK, Snow RW, Sartorius B, Okiro EA. The impact of child

health interventions and risk factors on child survival in Kenya, 1993-2014: a

Bayesian spatio-temporal analysis with counterfactual scenarios. BMC Med. 2021

May 4;19(1):102.

Abstract

Background: During the millennium development goals period, reduction in under-five mortality (U5M) and increases in child health intervention coverage were characterised by sub-national disparities and inequities across Kenya. The contribution of changing risk factors and intervention coverage on the sub-national changes in U5M remains poorly defined.

Methods: Sub-national county-level data on U5M and 43 factors known to be associated with U5M spanning 1993 and 2014 were assembled. Using a Bayesian ecological mixed-effects regression model, the relationships between U5M and significant intervention and infection risk ecological factors were quantified across 47 sub-national counties. The coefficients generated were used within a counterfactual framework to estimate U5M and under-five deaths averted (U5-DA) for every county and year (1993-2014) associated with changes in the coverage of interventions and disease infection prevalence relative to 1993.

Results: Nationally, the stagnation and increase in U5M in the 1990s were associated with rising human immunodeficiency virus (HIV) prevalence and reduced maternal autonomy while improvements after 2006 were associated with a decline in the prevalence of HIV and malaria, increase in access to better sanitation, fever treatment-seeking rates and maternal autonomy. Reduced stunting and increased coverage of early breastfeeding and institutional deliveries were associated with a smaller number of U5-DA compared to other factors while a reduction in high parity and fully immunised children were associated with under-five lives lost. Most of the U5-DA occurred after 2006 and varied spatially across counties. The highest number of U5-DA was recorded in western and coastal Kenya while northern Kenya recorded a lower number of U5-DA than western. Central Kenya had the lowest U5-DA. The deaths averted across the different regions were associated with a unique set of factors.

Conclusion: Contributions of interventions and risk factors to changing U5M vary sub-nationally. This has important implications for targeting future interventions within decentralised health systems such as those operated in Kenya. Targeting specific factors where U5M has been high and intervention coverage poor would lead to the highest likelihood of sub-national attainment of sustainable development goal (SDG) 3.2 on U5M in Kenya

Pubmed link- https://pubmed.ncbi.nlm.nih.gov/33941185/

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audience wanting more: An entertaining approach to stimulate engagement with health research among publics in coastal Kenya through 'Magnet Theatre'.

Wellcome Open Res. 2021 Jan 11; 6:2.

Abstract

Background: Magnet Theatre (MT), a form of participatory community theatre, is one of several public engagement approaches used to facilitate engagement between KEMRI-Wellcome Trust Research Programme (KWTRP) researchers and public audiences in Coastal Kenya. We describe how we used MT as an entertaining forum where audiences learn about research, and where researchers learn about how the public views research. Methods: Drama scripts depicting community interaction with different aspects of research were developed iteratively with research staff, a theatre company and community members. Six fortnightly theatre outreaches per site over two months, attracting a total of 1454 audience members were held in Mida, a rural village 30 km north of Kilifi; and in Mtwapa, a peri-urban town 45 km to the south. Audiences were presented with dramatized health research-related dilemmas and subsequently invited to enact their responses. Evaluation comprised, notes and observations from meetings, rehearsals and outreaches, transcripts from a review workshop with repeat audience members (n=21), a reflection meeting with KWTRP engagement staff (n=12), and a group discussion with the theatre company (n=9). Discussions were recorded, transcribed, translated to English and analysed using thematic approach. Results: Despite being costly in terms of time and expense, we argue that MT in public spaces can assist audience members to navigate 'border-crossings' between everyday contexts and scientific/research concepts. This can enable audiences to share their views and concerns and enact their responses to research-related dilemmas. Conclusions: While reporting on MT's successes, drawing from literature on rumours, we acknowledge the limitations of individual engagement activities in providing long-term solutions to address alternative interpretations and rumours about research, in the context of local and global inequities. MT, however, presents an opportunity for researchers to express respect to public audiences through making research more accessible and providing opportunities to listen to public views and concerns.

Pubmed link- https://pubmed.ncbi.nlm.nih.gov/33824910/

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Incorporating oral PrEP into standard prevention services for South African

women: a nested interrupted time-series study. Lancet HIV. 2021 Jun 11: S2352-3018(21)00048-5.

Abstract

Background: As oral pre-exposure prophylaxis (PrEP) becomes the standard of prevention globally, its potential effect on HIV incidence in clinical trials of new prevention interventions is unknown, particularly for trials among women. In a trial measuring HIV incidence in African women, oral PrEP was incorporated into the standard of prevention in the trial's last year. We assessed the effect of on-site access to PrEP on HIV incidence in this natural experiment.

Methods: We did a nested interrupted time-series study using data from the ECHO trial. At 12 sites in four countries (Eswatini, Kenya, South Africa, and Zambia), women (aged 16-35 years) were randomly assigned to receive one of three contraceptives between Dec 14, 2015, and Sept 12, 2017, and followed up quarterly for up to 18 months to determine the effect of contraceptive method on HIV acquisition. Women were eligible if they wanted long-acting contraception, were medically qualified to receive study contraceptives, and had not used any of the study contraceptives in the past 6 months. The present analyses are limited to nine South African sites where on-site access to oral PrEP was implemented between March 13 and June 12, 2018. Using an interrupted time-series design, we compared HIV incidence before versus after PrEP access, limited to quarterly study visits at which on-site PrEP access was available to at least some participants and, in a sensitivity analysis, to the 180 days before and after access. The outcome was incident HIV infection, detected using two rapid HIV tests done in parallel for each participant at every scheduled follow-up visit. This study is registered on ClinicalTrials.gov, NCT02550067.

Findings: 2124 women were followed up after on-site PrEP access began, of whom 543 (26%) reported PrEP use. A total of 12 HIV seroconversions were observed in 556 person-years (incidence 2·16%) after on-site PrEP access, compared with 133 HIV seroconversions in 2860 person-years (4·65%) before PrEP access (adjusted incidence rate ratio [IRR] 0·45, 95% CI 0·25-0·82, p=0·0085). Similar results were also observed when limiting the analysis to 180 days before versus after PrEP access. A total of 46 HIV seroconversions were observed in 919 person-years within 180 days before PrEP access, compared with 11 seroconversions in 481 person-years in the 180 days following PrEP access (incidence 5·00 vs 2·29 per 100 person-years; IRR 0·43, 95% CI 0·22-0·88, p=0·012).

Interpretation: On-site access to PrEP as part of standard of prevention in a clinical trial among women in South Africa was associated with halving HIV incidence, when approximately a quarter of women started PrEP. Providing access to on-site PrEP could decrease incidence in HIV prevention trials. These data are also among the first to show in any setting that access to PrEP is associated with decreased HIV acquisition among South African women.

Pubmed link-https://pubmed.ncbi.nlm.nih.gov/34126052/

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EClinicalMedicine. 2021 Apr 6; 34:100800.

Abstract

Background: There is limited evidence on the impact of the use of progestin-only hormonal contraception (POC) on weight change. We conducted a secondary analysis of prospective weight change among women enrolled in the Evidence for Contraceptive options and HIV Outcomes (ECHO) trial.

Methods: The ECHO trial was conducted at 12 sites in eSwatini, Kenya, South Africa and Zambia between December 2015 and October 2018. HIV negative, women aged 16-35 years, desiring contraception, were randomised (1:1:1) to either 3-monthly intramuscular depot medroxyprogesterone acetate (DMPA-IM), levonorgestrel (LNG) implant or copper intrauterine device (IUD). Follow-up was up to 18 months. Weight (kg) was measured at baseline and study exit. Analysis was performed as intention to treat (ITT) and time on continuous contraceptive use. The primary outcome of this secondary analysis is weight change from study enrolment to the final visit at study month 12-18. The ECHO trial is registered with ClinicalTrials.gov, NCT02550067.

Findings: 7829 women were randomly assigned to DMPA-IM (n = 2609), copper IUD (n = 2607) or LNG implant (n = 2613). The ITT population included 7014 women 2293 DMPA-IM group, 2372 copper IUD group and 2349 LNG group) who were not lost to follow-up, pregnant on study, or missing weight data. The mean weight increased in all groups but was significantly different in magnitude: 3.5 kg (SD = 6.3), 2.4 kg (SD = 5.9) and 1.5 kg (SD = 5.7) in the DMPA-IM, LNG implant and copper IUD groups, respectively. Comparative differences between groups were (2.02 kg (95% CI, 1.68, 2.36, $p < 0.001$) for DMPA-IM versus copper IUD, 0.87 kg (0.53,1.20 $p < 0.001$) for LNG implant compared to copper IUD and 1.16 kg (0.82, 1.50, $p < 0.001$) for DMPA-IM compared with LNG implant. Results for continuous contraceptive use were similar.

Interpretation: We found differences in weight gain between POC users compared to the non-hormonal copper IUD group over 12-18 months of use. Women using POCs should be counselled about this potential side effect when choosing a contraceptive method.

Pubmed link-https://pubmed.ncbi.nlm.nih.gov/33898953/

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Regression Model of Water, Sanitation, and Hygiene; Treatment Coverage; and

Environmental Influences on School-Level Soil-Transmitted Helminths and

Schistosome Prevalence in Kenya: Secondary Analysis of the National Deworming

Program Data. Am J Trop Med Hyg. 2021 Apr 12;104(6):2251–63.

Abstract

According to the Kenya National School-Based Deworming program launched in 2012 and implemented for the first 5 years (2012-2017), the prevalence of soil-transmitted helminths (STH) and schistosomiasis substantially reduced over the mentioned period among the surveyed schools. However, this reduction is heterogeneous. In this study, we aimed to determine the factors associated with the 5-year school-level infection prevalence and relative reduction (RR) in prevalence in Kenya following the implementation of the program. Multiple variables related to treatment, water, sanitation, and hygiene (WASH) and environmental factors were assembled and included in mixed-effects linear regression models to identify key determinants of the school location STH and schistosomiasis prevalence and RR. Reduced prevalence of Ascaris lumbricoides was associated with low (< 1%) baseline prevalence, seven rounds of treatment, high (50-75%) self-reported coverage of household handwashing facility equipped with water and soap, high (20-25°C) land surface temperature, and community population density of 5-10 people per 100 m2. Reduced hookworm prevalence was associated with low (< 1%) baseline prevalence and the presence of a school feeding program. Reduced Trichuris trichiura prevalence was associated with low (< 1%) baseline prevalence. Reduced Schistosoma mansoni prevalence was associated with low (< 1%) baseline prevalence, three treatment rounds, and high (> 75%) reported coverage of a household improved water source. Reduced Schistosoma haematobium was associated with high aridity index. Analysis indicated that a combination of factors, including the number of treatment rounds, multiple related program interventions, community- and school-level WASH, and several environmental factors had a major influence on the school-level infection transmission and reduction.

Pubmed link- https://pubmed.ncbi.nlm.nih.gov/33844645/

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Comparative analysis of spatial-temporal patterns of human metapneumovirus and respiratory syncytial virus in Africa using genetic data, 2011-2014. Virol J. 2021 May 29;18(1):104.

Abstract

Background: Human metapneumovirus (HMPV) and respiratory syncytial virus (RSV) are leading causes of viral severe acute respiratory illnesses in childhood. Both the two viruses belong to the Pneumoviridae family and show overlapping clinical, epidemiological and transmission features. However, it is unknown whether these two viruses have similar geographic spread patterns which may inform designing and evaluating their epidemic control measures.

Methods: We conducted comparative phylogenetic and phylogeographic analyses to explore the spatial-temporal patterns of HMPV and RSV across Africa using 232 HMPV and 842 RSV attachment (G) glycoprotein gene sequences obtained from 5 countries (The Gambia, Zambia, Mali, South Africa, and Kenya) between August 2011 and January 2014.

Results: Phylogeographic analyses found frequently similar patterns of spread of RSV and HMPV. Viral sequences commonly clustered by region, i.e., West Africa (Mali, Gambia), East Africa (Kenya) and Southern Africa (Zambia, South Africa), and similar genotype dominance patterns were observed between neighbouring countries. Both HMPV and RSV country epidemics were characterized by co-circulation of multiple genotypes. Sequences from different African sub-regions (East, West and Southern Africa) fell into separate clusters interspersed with sequences from other countries globally.

Conclusion: The spatial clustering patterns of viral sequences and genotype dominance patterns observed in our analysis suggests strong regional links and predominant local transmission. The geographical clustering further suggests independent introduction of HMPV and RSV variants in Africa from the global pool, and local regional diversification.

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Abstract

Background: The epidemiology of human urinary schistosomiasis caused by Schistosoma haematobium can be complicated by the presence of ruminant schistosomiasis caused, primarily by S. bovis. The two schistosome species may be transmitted by the same Bulinus species, they may occur sympatrically in the same habitat, and their cercariae are very similar in morphology and therefore, difficult to tell them apart. Screening of snails collected from freshwater habitats for schistosome infections is often used to identify transmission sites or to evaluate success or failure of interventions. However, pin-pointing sites involved in S. haematobium transmission can be complicated by the presence of other mammalian schistosomes such as the bovine schistosome, which is a fairly common parasite. A PCR-RFLP method targeting a unique segment of the second internal transcribed spacer (ITS2) region of the ribosomal DNA (rDNA) in the schistosomes was used to identify mammalian schistosome cercariae shed by bulinid snails collected from endemic freshwater habitats located within Machakos county in south-eastern Kenya, with the aim to identify the transmission sites and assess the distribution each of the parasite species in the study area.

Results: A total of 5,034 bulinid snails were collected from 41 different sites and screened for schistosome infections, and out of these, 43 (<1%) were found to be shedding mammalian schistosome cercariae. On analysis using the Polymerase chain reaction- Restriction Fragment Length Polymorphisms (PCR-RFLP) assay, cercariae from 32 snails were identified as S. haematobium while cercariae from 11 snails turned out to be S. bovis. Only two sites out of 40 namely Kisukioni and Katiwa, were active transmission sites. Both sites were active transmission sites for both S. haematobium and S. bovis. The assay reliably identified and distinguished between S. haematobium and S. bovis cercariae, even when only a few cercariae (5-10) were present in the sample, or when the parasite DNA concentrations were as low as five pico grammes (5pg). The FTA® paper offered a more reliable way of collecting, transporting and storing DNA material, and the samples.

Conclusion: The PCR-based assay can potentially be used to support schistosomiasis control efforts, in epidemiological studies of urinary schistosomiasis, or in transmission ecology studies of S. haematobium and S. bovis.

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Otieno V, Raballah E, Anyona S, Ouma C, Chain PSG, Perkins DJ, Mukundan H,

McMahon BH, Doggett NA. Comparative genomic and phenotypic characterization of

invasive non-typhoidal Salmonella isolates from Siaya, Kenya. PLoS Negl Trop

Dis. 2021 Feb 1;15(2): e0008991.

Abstract

Non-typhoidal Salmonella (NTS) is a major global health concern that often causes bloodstream infections in areas of the world affected by malnutrition and comorbidities such as HIV and malaria. Developing a strategy to control the emergence and spread of highly invasive and antimicrobial resistant NTS isolates requires a comprehensive analysis of epidemiological factors and molecular pathogenesis. Here, we characterize 11 NTS isolates that caused bloodstream infections in pediatric patients in Siaya, Kenya from 2003-2010. Nine isolates were identified as S. Typhimurium sequence type 313 while the other two were S. Enteritidis. Comprehensive genotypic and phenotypic analyses were performed to compare these isolates to those previously identified in sub-Saharan Africa. We identified a S. Typhimurium isolate referred to as UGA14 that displayed novel plasmid, pseudogene and resistance features as compared to other isolates reported from Africa. Notably, UGA14 is able to ferment both lactose and sucrose due to the acquisition of insertion elements on the pKST313 plasmid. These findings show for the first time the co-evolution of plasmid-mediated lactose and sucrose metabolism along with cephalosporin resistance in NTS further elucidating the evolutionary mechanisms of invasive NTS phenotypes. These results further support the use of combined genomic and phenotypic approaches to detect and characterize atypical NTS isolates in order to advance biosurveillance efforts that inform countermeasures aimed at controlling invasive and antimicrobial resistant NTS.

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Costs of integrating hypertension care into HIV care in rural East African

clinics. AIDS. 2021 May 1;35(6):911-919.

Abstract

Objective: Sub-Saharan Africa faces twin epidemics of HIV and noncommunicable diseases including hypertension. Integrating hypertension care into chronic HIV care is a global priority,

but cost estimates are lacking. In the SEARCH Study, we performed population-level HIV/hypertension testing, and offered integrated streamlined chronic care. Here, we estimate costs for integrated hypertension/HIV care for HIV-positive individuals, and costs for hypertension care for HIV-negative individuals in the same clinics.

Design: Microcosting analysis of healthcare expenditures within Ugandan HIV clinics.

Methods: SEARCH (NCT: 01864603) conducted community health campaigns for diagnosis and linkage to care for both HIV and hypertension. HIV-positive patients received hypertension/HIV care jointly including blood pressure monitoring and medications; HIV-negative patients received hypertension care at the same clinics. Within 10 Ugandan study communities during 2015-2016, we estimated incremental annual per-patient hypertension care costs using micro-costing techniques, time-and-motion personnel studies, and administrative/clinical records review.

Results: Overall, 70 HIV-positive and 2355 HIV-negative participants received hypertension care. For HIV-positive participants, average incremental cost of hypertension care was $6.29 per person per year, a 2.1% marginal increase over prior estimates for HIV care alone. For HIV-negative participants, hypertension care cost $11.39 per person per year, a 3.8% marginal increase over HIV care costs. Key costs for HIV-positive patients included hypertension medications ($6.19 per patient per year; 98% of total) and laboratory testing ($0.10 per patient per year; 2%). Key costs for HIV-negative patients included medications ($5.09 per patient per year; 45%) and clinic staff salaries ($3.66 per patient per year; 32%).

Conclusion: For only 2-4% estimated additional costs, hypertension care was added to HIV care, and also expanded to all HIV-negative patients in prototypic Ugandan clinics, demonstrating substantial synergy. Our results should encourage accelerated scale-up of hypertension care into existing clinics.

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Chaccour C. Potential metabolic resistance mechanisms to ivermectin in Anopheles

gambiae: a synergist bioassay study. Parasit Vectors. 2021 Mar 20;14(1):172.

Abstract

Background: Despite remarkable success obtained with current malaria vector control strategies in the last 15 years, additional innovative measures will be needed to achieve the ambitious goals for malaria control set for 2030 by the World Health Organization (WHO). New tools will need to address insecticide resistance and residual transmission as key challenges. Endectocides such as

ivermectin are drugs that kill mosquitoes which feed on treated subjects. Mass administration of ivermectin can effectively target outdoor and early biting vectors, complementing the still effective conventional tools. Although this approach has garnered attention, development of ivermectin resistance is a potential pitfall. Herein, we evaluate the potential role of xenobiotic pumps and cytochrome P450 enzymes in protecting mosquitoes against ivermectin by active efflux and metabolic detoxification, respectively.

Methods: We determined the lethal concentration 50 for ivermectin in colonized Anopheles gambiae; then we used chemical inhibitors and inducers of xenobiotic pumps and cytochrome P450 enzymes in combination with ivermectin to probe the mechanism of ivermectin detoxification.

Results: Dual inhibition of xenobiotic pumps and cytochromes was found to have a synergistic effect with ivermectin, greatly increasing mosquito mortality. Inhibition of xenobiotic pumps alone had no effect on ivermectin-induced mortality. Induction of xenobiotic pumps and cytochromes may confer partial protection from ivermectin.

Conclusion: There is a clear pathway for development of ivermectin resistance in malaria vectors. Detoxification mechanisms mediated by cytochrome P450 enzymes are more important than xenobiotic pumps in protecting mosquitoes against ivermectin.

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Alter G, Moore PL. Coordinated Fc-effector and neutralization functions in HIV-

infected children define a window of opportunity for HIV vaccination. AIDS. 2021

Jun 10.

Abstract

Objectives: Antibody function has been extensively studied in HIV-infected adults but is relatively understudied in children. Emerging data suggests enhanced development of broadly neutralizing antibodies (bNAbs) in children but Fc effector functions in this group are less well defined. Here, we profiled overall antibody function in HIV-infected children.

Design: Plasma samples from a cross-sectional study of 50 antiretroviral therapy-naive children (aged 1-11 years) vertically infected with HIV-1 clade A were screened for HIV-specific binding antibody levels and neutralizing and Fc-mediated functions.

Methods: Neutralization breadth was determined against a globally representative panel of 12 viruses. HIV-specific antibody levels were determined using a multiplex assay. Fc-mediated antibody functions measured were antibody-dependent: cellular phagocytosis (ADCP); neutrophil phagocytosis (ADNP); complement deposition (ADCD) and natural killer function (ADNK).

Results: All children had HIV gp120-specific antibodies, largely of the IgG1 subtype. Fifty-four percent of the children exhibited more than 50% neutralization breadth, with older children showing significantly broader neutralization activity. Apart from ADCC, observed only in 16% children, other Fc-mediated functions were common (>58% children). Neutralization breadth correlated with Fc-mediated functions suggesting shared determinants of enhanced antibody function exist.

Conclusions: These results are consistent with previous observations that children may develop high levels of neutralization breadth. Furthermore, the striking association between neutralization breadth and Fc effector function suggests that HIV vaccination in children could yield multifunctional antibodies. Paediatric populations may therefore provide an ideal window of opportunity for HIV vaccination strategies.

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Stronger Innate Immune Response During Hyperacute HIV-1 Infection is associated

with ACUTE retroviral syndrome. Clin Infect Dis. 2021 Feb 15: ciab139.

Abstract

Background: Acute retroviral syndrome (ARS) is associated with human immunodeficiency virus type 1 (HIV-1) subtype and disease progression, but the underlying immunopathological pathways are poorly understood. We aimed to elucidate associations between innate immune responses during hyperacute HIV-1 infection (hAHI) and ARS.

Methods: Plasma samples obtained from volunteers (≥18.0 years) before and during hAHI, defined as HIV-1 antibody negative and RNA or p24 antigen positive, from Kenya, Rwanda, Uganda, Zambia, and Sweden were analyzed. Forty soluble innate immune markers were measured using multiplexed assays. Immune responses were differentiated into volunteers with stronger and

comparatively weaker responses using principal component analysis. Presence or absence of ARS was defined based on 11 symptoms using latent class analysis. Logistic regression was used to determine associations between immune responses and ARS.

Results: Of 55 volunteers, 31 (56%) had ARS. Volunteers with stronger immune responses (n = 36 [65%]) had increased odds of ARS which was independent of HIV-1 subtype, age, and risk group (adjusted odds ratio, 7.1 [95% confidence interval {CI}: 1.7-28.8], P = .003). Interferon gamma-induced protein (IP)-10 was 14-fold higher during hAHI, elevated in 7 of the 11 symptoms and independently associated with ARS. IP-10 threshold >466.0 pg/mL differentiated stronger immune responses with a sensitivity of 84.2% (95% CI: 60.4-96.6) and specificity of 100.0% (95% CI]: 90.3-100.0).

Conclusions: A stronger innate immune response during hAHI was associated with ARS. Plasma IP-10 may be a candidate biomarker of stronger innate immunity. Our findings provide further insights on innate immune responses in regulating ARS and may inform the design of vaccine candidates harnessing innate immunity.

Pubmed link- https://pubmed.ncbi.nlm.nih.gov/33588436/

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estimates of factors associated with under-five mortality in Kenya: a spatio-

temporal analysis, 1993-2014. BMJ Glob Health. 2021 Apr;6(4): e004544.

Abstract

Background: To improve child survival, it is necessary to describe and understand the spatial and temporal variation of factors associated with child survival beyond national aggregates, anchored at decentralised health planning units. Therefore, we aimed to provide subnational estimates of factors associated with child survival while elucidating areas of progress, stagnation and decline in Kenya.

Methods: Twenty household surveys and three population censuses conducted since 1989 were assembled and spatially aligned to 47 subnational Kenyan county boundaries. Bayesian spatio-temporal Gaussian process regression models accounting for inadequate sample size and spatio-temporal relatedness were fitted for 43 factors at county level between 1993 and 2014.

Results: Nationally, the coverage and prevalence were highly variable with 38 factors recording an improvement. The absolute percentage change (1993-2014) was heterogeneous ranging between 1% and 898%. At the county level, the estimates varied across space and over time with a majority showing improvements after 2008 which was preceded by a period of deterioration

(late-1990 to early-2000). Counties in Northern Kenya were consistently observed to have lower coverage of interventions and remained disadvantaged in 2014 while areas around Central Kenya had and historically have had higher coverage across all intervention domains. Most factors in Western and South-East Kenya recorded moderate intervention coverage although having a high infection prevalence of both HIV and malaria.

Conclusion: The heterogeneous estimates necessitates prioritisation of the marginalised counties to achieve health equity and improve child survival uniformly across the country. Efforts are required to narrow the gap between counties across all the drivers of child survival. The generated estimates will facilitate improved benchmarking and establish a baseline for monitoring child development goals at subnational level.

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Dorlo TPC. Geographical Variability in Paromomycin Pharmacokinetics Does Not

Explain Efficacy Differences between Eastern African and Indian Visceral

Leishmaniasis Patients. Clin Pharmacokinet. 2021 Jun 9.

Abstract

Introduction: Intramuscular paromomycin monotherapy to treat visceral leishmaniasis (VL) has been shown to be effective for Indian patients, while a similar regimen resulted in lower efficacy in Eastern Africa, which could be related to differences in paromomycin pharmacokinetics.

Methods: Pharmacokinetic data were available from two randomized controlled trials in VL patients from Eastern Africa and India. African patients received intramuscular paromomycin monotherapy (20 mg/kg for 21 days) or combination therapy (15 mg/kg for 17 days) with sodium stibogluconate. Indian patients received paromomycin monotherapy (15 mg/kg for 21 days). A population pharmacokinetic model was developed for paromomycin in Eastern African and Indian VL patients.

Results: Seventy-four African patients (388 observations) and 528 Indian patients (1321 observations) were included in this pharmacokinetic analysis. A one-compartment model with first-order kinetics of absorption and elimination best described paromomycin in plasma. Bioavailability (relative standard error) was 1.17 (5.18%) times higher in Kenyan and Sudanese

patients, and 2.46 (24.5%) times higher in Ethiopian patients, compared with Indian patients. Ethiopian patients had an approximately fourfold slower absorption rate constant of 0.446 h-1 (18.2%). Area under the plasma concentration-time curve for 24 h at steady-state (AUCτ,SS) for 15 mg/kg/day (median [interquartile range]) was higher in Kenya and Sudan (172.7 μg·h/mL [145.9-214.3]) and Ethiopia (230.1 μg·h/mL [146.3-591.2]) compared with India (97.26 μg·h/mL [80.83-123.4]).

Conclusion: The developed model provides detailed insight into the pharmacokinetic differences among Eastern African countries and India, however the resulting differences in paromomycin exposure do not seem to explain the geographical differences in paromomycin efficacy in the treatment of VL patients.

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Inflammatory Factors Converge in the Pathogenesis of Moderate Acute Malnutrition

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22;104(5):1877–88.

Abstract

Acute malnutrition affects more than 50 million children worldwide. These children are at an increased risk of morbidity and mortality from infectious disease. However, the pathogenesis of acute malnutrition and mechanisms underlying the increased risk and poor outcomes from infection are not well understood. Our objective was to identify differences in inflammation and inflammatory responses between children with moderate acute malnutrition (MAM) and healthy controls (HCs), and search for environmental, pathophysiological, and metabolic factors that may influence this response. Sixteen children with MAM and 16 HCs aged 18-36 months were studied in Nairobi, Kenya. None of the children had symptoms of an infectious disease (fever, diarrhea, or cough) in the 2 weeks before enrollment and sample collection. Demographic and health data were provided by their primary caregivers. Blood samples were collected to measure various biomarkers and the response to an inflammatory stimulus. Children with MAM were more frequently from households with contaminated water, crowding, and unstable income sources. They also had increases in basal inflammation, circulating bacterial lipopolysaccharide (LPS), markers of intestinal damage, and an exaggerated whole blood inflammatory response to LPS. Metabolic changes in children with MAM led to increased plasma levels of long-chain fatty acids, which were found to contribute to the pro-inflammatory state. These exploratory findings suggest

convergence of multiple factors to promote dysregulated inflammatory responses and prompt several mechanistic hypotheses that can be pursued to better understand the pathogenesis of MAM.

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Abstract

Extracts from Securidaca longipedunculata showed antiplasmodial activities against reference clones and clinical isolates using SYBR Green I method. A new benzophenone, 2,3,4,5-tetramethoxybenzophenone (1) was isolated and characterized along with seven known compounds: 4-hydroxy-2,3-dimethoxybenzophenone (2); 3-hydroxy-5-methoxybiphenyl (3), methyl-2-hydroxy-6-methoxybenzoate (4), benzyl-2-hydroxy-6-methoxybenzoate (5), 2-hydroxy-6-methoxybenzoic acid (6), 2,4,5-trimethoxybenzophenone (7) and 2-methoxy-3,4-methylenedioxybenzophenone (8). Compounds 1 and 2 showed ex vivo antiplasmodial activities (IC50 28.8 µM and 18.6 µM, respectively); while 5 and 8 showed in vivo activities (IC50 19.7 µM and 14.5 µM, respectively) against D6 strain. In a cytotoxicity assay, all the extracts (with an exception of the MeOH extract of the leaves) and pure compounds were not toxic to the normal LO2 and BEAS cell-lines, while the methanol roots extract (IC50 66.4 µg/mL against A549, and 77.4 µg/mL against HepG2), compounds 6 (IC50 22.2 µM against A549) and 7 (IC50 45.2 µM against HepG2) were weakly active against cancerous cell-lines.

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Abstract

Background: We tested the hypothesis that patient-centered, streamlined human immunodeficiency virus (HIV) care would achieve lower mortality than the standard treatment model for persons with HIV and CD4 ≤ 350/uL in the setting of population-wide HIV testing.

Methods: In the SEARCH (Sustainable East Africa Research in Community Health) Study (NCT01864603), 32 communities in rural Uganda and Kenya were randomized to country-guided antiretroviral therapy (ART) versus streamlined ART care that included rapid ART start, visit spacing, flexible clinic hours, and welcoming environment. We assessed persons with HIV and CD4 ≤ 350/uL, ART eligible in both arms, and estimated the effect of streamlined care on ART initiation and mortality at 3 years. Comparisons between study arms used a cluster-level analysis with survival estimates from Kaplan-Meier; estimates of ART start among ART-naive persons treated death as a competing risk.

Results: Among 13 266 adults with HIV, 2973 (22.4%) had CD4 ≤ 350/uL. Of these, 33% were new diagnoses, and 10% were diagnosed but ART-naive. Men with HIV were almost twice as likely as women with HIV to have CD4 ≤ 350/uL and be untreated (15% vs 8%, respectively). Streamlined care reduced mortality by 28% versus control (risk ratio [RR] = 0.72; 95% confidence interval [CI]: .56, .93; P = .02). Despite eligibility in both arms, persons with CD4 ≤ 350/uL started ART faster under streamlined care versus control (76% vs 43% by 12 months, respectively; P < .001). Mortality was reduced substantially more among men (RR = 0.61; 95% CI: .43, .86; P = .01) than among women (RR = 0.90; 95% CI: .62, 1.32; P = .58).

Conclusions: After population-based HIV testing, streamlined care reduced population-level mortality among persons with HIV and CD4 ≤ 350/uL, particularly among men. Streamlined HIV care models may play a key role in global efforts to reduce AIDS deaths.

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Chuma J. Examining health sector application and utility of program-based

budgeting: County level experiences in Kenya. Int J Health Plann Manage. 2021

May 6.

Abstract

Introduction: In 2012, Kenya enacted a new Public Finance Management Act to guide the public-sector planning and budgeting process. This new law replaced the previous line item budgeting, with a new program-based budgeting (PBB) process. This study examined the experience of health sector PBB implementation at the county level in Kenya.

Methods: We carried out a review of the literature documenting the health sector application and utility of PBB in low- and middle-income countries. We then collected empirical data to examine the experience of health sector application of PBB at County Level in Kenya.

Results: In the financial year 2017/18, counties utilised the PBB approach for health sector planning. The PBB approach was perceived by key stakeholders; to have improved the alignment of technical priorities with budgetary allocation, and to have increased transparency, accountability and openness of the process. Its challenges included lack of clear tools and guidelines to support implementation, low capacity at county level, political interference and the organisation of the public sector electronic financial management system around line item budgeting system.

Conclusion: PBB is potentially a useful tool for aligning health sector planning and budgeting and ensuring the Annual Work Plan is more result oriented. However, realisation of this goal would be enhanced by the developing clear tools and guidelines to support its implementation, building capacity for county health sector managers to better understand the PBB application, and reforming the public-sector budgetary management system to align it with the PBB approach.

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Safety and Tolerability of Mass Diethylcarbamazine and Albendazole

Administration for the Elimination of Lymphatic Filariasis in Kenya: An Active

Surveillance Study. Pharmaceuticals (Basel). 2021 Mar 15;14(3):264.

Abstract

Preventive chemotherapy with diethylcarbamazine citrate (DEC) and albendazole (ALB) is the core intervention strategy to eliminate lymphatic filariasis (LF). We conducted a large-scale prospective active safety surveillance study to identify the incidence, type, severity, and risk factors for adverse events (AEs) following mass drug administration (MDA) of single-dose DEC and ALB in 10,010 participants from Kilifi County, Kenya. AEs were actively monitored and graded at 24 h, 48 h, and on day 7 Post-MDA. Out of 10,010 enrolled study participants, 1621 participants reported a total of 3102 AEs during a seven-day follow-up. The cumulative incidence of AEs was 16.2% (95% CI, 15.5-16.9%). The proportion of participants who experienced one, two, or ≥three types of AEs was 9.2%, 4.6%, 2.4%, respectively. AEs were mild (87.3%), moderate (12.4%), and severe (0.3%) and resolved within 72 h. The five most common AEs were dizziness (5.9%), headache (5.6%), loss of appetite (3.3%), fever (2.9%), and drowsiness (2.6%). Older age, taking concurrent medications, ≥three tablets of DEC, and type of meal taken before MDA were significant predictors of AEs. One in six participants experienced systemic mild-to-moderate

severity grading and transient AEs. DEC and ALB co-administration for the elimination of LF is generally safe and well-tolerated.

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JF. IV and oral fosfomycin pharmacokinetics in neonates with suspected clinical

sepsis. J Antimicrob Chemother. 2021 Jun 18;76(7):1855-1864.

Abstract

Background: Fosfomycin has the potential to be re-purposed as part of a combination therapy to treat neonatal sepsis where resistance to current standard of care (SOC) is common. Limited data exist on neonatal fosfomycin pharmacokinetics and estimates of bioavailability and CSF/plasma ratio in this vulnerable population are lacking.

Objectives: To generate data informing the appropriate dosing of IV and oral fosfomycin in neonates using a population pharmacokinetic analysis of plasma and CSF data.

Methods: The NeoFosfo study (NCT03453177) was a randomized trial that examined the safety and pharmacokinetics of fosfomycin comparing SOC versus SOC plus fosfomycin. Sixty-one neonates received fosfomycin (100 mg/kg IV q12h for 48 h) and then they converted to oral therapy at the same dose. Two plasma pharmacokinetic samples were taken following the first IV and oral doses, sample times were randomized to cover the whole pharmacokinetic profile and opportunistic CSF pharmacokinetic samples were collected. A population pharmacokinetic model was developed in NONMEM and simulations were performed.

Results: In total, 238 plasma and 15 CSF concentrations were collected. A two-compartment disposition model, with an additional CSF compartment and first-order absorption, best described the data. Bioavailability was estimated as 0.48 (95% CI = 0.347-0.775) and the CSF/plasma ratio as 0.32 (95% CI = 0.272-0.409). Allometric weight and postmenstrual age (PMA) scaling was applied; additional covariates included postnatal age (PNA) on clearance and CSF protein on CSF/plasma ratio.

Conclusions: Through this analysis a population pharmacokinetic model has been developed that can be used alongside currently available pharmacodynamic targets to select a neonatal fosfomycin dose based on an infant's PMA, PNA and weight.

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Pediatr Infect Dis J. 2021 May 4.

Abstract

Background: In resource-limited settings, acute respiratory infections continue to be the leading cause of death in young children. We conducted postmortem investigations in children <5 years hospitalized with a clinical diagnosis of respiratory disease at Kenya's largest referral hospital.

Methods: We collected respiratory and other tissues postmortem to examine pathologic processes using histology, molecular and immunohistochemistry assays. Nasopharyngeal, trachea, bronchi and lung specimens were tested using 21-target respiratory pathogen real-time reverse transcription polymerase chain reaction assays deployed on Taqman Array Cards. Expert panels reviewed all findings to determine causes of death and associated pathogens.

Results: From 2014 to 2015, we investigated 64 pediatric deaths (median age 7 months). Pneumonia was determined as cause of death in 70% (42/52) of cases where death was associated with an infectious disease process. The main etiologies of pneumonia deaths were respiratory syncytial virus (RSV) (n = 7, 19%), Pneumocystis jirovecii (n = 7, 19%), influenza A (n = 5, 14%) and Streptococcus pneumoniae (n = 5, 14%)-10% of cases had multi-pathogen involvement. Among the other 10 deaths associated with a nonpneumonia infectious process, 4 did not have an etiology assigned, the others were associated with miliary tuberculosis (2), cerebral thrombosis due to HIV (1), Enterobacteriaceae (1), rotavirus (1), and 1 case of respiratory infection with severe hypokalemia associated with RSV.

Conclusions: In spite of well-established vaccination programs in Kenya, some deaths were still vaccine preventable. Accelerated development of RSV monoclonal antibodies and vaccines,

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Abstract

Serotype-specific surveillance for invasive pneumococcal disease (IPD) is essential for assessing the impact of 10- and 13-valent pneumococcal conjugate vaccines (PCV10/13). The Pneumococcal Serotype Replacement and Distribution Estimation (PSERENADE) project aimed to evaluate the global evidence to estimate the impact of PCV10/13 by age, product, schedule, and syndrome. Here we systematically characterize and summarize the global landscape of routine serotype-specific IPD surveillance in PCV10/13-using countries and describe the subset that are included in PSERENADE. Of 138 countries using PCV10/13 as of 2018, we identified 109 with

IPD surveillance systems, 76 of which met PSERENADE data collection eligibility criteria. PSERENADE received data from most (n = 63, 82.9%), yielding 240,639 post-PCV10/13 introduction IPD cases. Pediatric and adult surveillance was represented from all geographic regions but was limited from lower income and high-burden countries. In PSERENADE, 18 sites evaluated PCV10, 42 PCV13, and 17 both; 17 sites used a 3 + 0 schedule, 38 used 2 + 1, 13 used 3 + 1, and 9 used mixed schedules. With such a sizeable and generally representative dataset, PSERENADE will be able to conduct robust analyses to estimate PCV impact and inform policy at national and global levels regarding adult immunization, schedule, and product choice, including for higher valency PCVs on the horizon.

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of pretomanid, moxifloxacin and pyrazinamide for pulmonary TB. Int J Tuberc Lung

Dis. 2021 Apr 1;25(4):305-314.

Abstract

BACKGROUND: Treatment for TB is lengthy and toxic, and new regimens are needed.METHODS: Participants with pulmonary drug-susceptible TB (DS-TB) were randomised to receive: 200 mg pretomanid (Pa, PMD) daily, 400 mg moxifloxacin (M) and 1500 mg pyrazinamide (Z) for 6 months (6Pa200MZ) or 4 months (4Pa200MZ); 100 mg pretomanid daily for 4 months in the same combination (4Pa100MZ); or standard DS-TB treatment for 6 months. The primary outcome was treatment failure or relapse at 12 months post-randomisation. The non-inferiority margin for between-group differences was 12.0%. Recruitment was paused following three deaths and not resumed.RESULTS: Respectively 4/47 (8.5%), 11/57 (19.3%), 14/52 (26.9%) and 1/53 (1.9%) DS-TB outcomes were unfavourable in patients on 6Pa200MZ, 4Pa200MZ, 4Pa100MZ and controls. There was a 6.6% (95% CI -2.2% to 15.4%) difference per protocol and 9.9% (95%CI -4.1% to 23.9%) modified intention-to-treat difference in unfavourable responses between the control and 6Pa200MZ arms. Grade 3+ adverse events affected 68/203 (33.5%) receiving experimental regimens, and 19/68 (27.9%) on control. Ten of 203 (4.9%) participants on experimental arms and 2/68 (2.9%) controls died.CONCLUSION: PaMZ regimens did not achieve non-inferiority in this under-powered trial. An ongoing evaluation of PMD remains a priority.

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with growth and neurodevelopment at 2 years of age: INTERBIO-21st Fetal Study.

Nat Med. 2021 Apr;27(4):647-652.

Abstract

Many observational studies and some randomized trials demonstrate how fetal growth can be influenced by environmental insults (for example, maternal infections)1 and preventive interventions (for example, multiple-micronutrient supplementation)2 that can have a long-lasting

effect on health, growth, neurodevelopment and even educational attainment and income in adulthood3. In a cohort of pregnant women (n = 3,598), followed-up between 2012 and 2019 at six sites worldwide4, we studied the associations between ultrasound-derived fetal cranial growth trajectories, measured longitudinally from <14 weeks' gestation, against international standards5,6, and growth and neurodevelopment up to 2 years of age7,8. We identified five trajectories associated with specific neurodevelopmental, behavioral, visual and growth outcomes, independent of fetal abdominal growth, postnatal morbidity and anthropometric measures at birth and age 2. The trajectories, which changed within a 20-25-week gestational age window, were associated with brain development at 2 years of age according to a mirror (positive/negative) pattern, mostly focused on maturation of cognitive, language and visual skills. Further research should explore the potential for preventive interventions in pregnancy to improve infant neurodevelopmental outcomes before the critical window of opportunity that precedes the divergence of growth at 20-25 weeks' gestation.

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Abstract

The diversity of circulating human B cells is unknown. We use single-cell RNA sequencing (RNA-seq) to examine the diversity of both antigen-specific and total B cells in healthy subjects and malaria-exposed individuals. This reveals two B cell lineages: a classical lineage of activated and resting memory B cells and an alternative lineage, which includes previously described atypical B cells. Although atypical B cells have previously been associated with disease states, the alternative lineage is common in healthy controls, as well as malaria-exposed individuals. We further track Plasmodium-specific B cells after malaria vaccination in naive volunteers. We find that alternative lineage cells are primed after the initial immunization and respond to booster doses. However, alternative lineage cells develop an atypical phenotype with repeated boosts. The data highlight

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Abstract

Background: Few studies have assessed the seroprevalence of antibodies against SARS-CoV-2 among Health Care Workers (HCWs) in Africa. We report findings from a survey among HCWs in three counties in Kenya.

Methods: We recruited 684 HCWs from Kilifi (rural), Busia (rural) and Nairobi (urban) counties. The serosurvey was conducted between 30th July 2020 and 4th December 2020. We tested for IgG antibodies to SARS-CoV-2 spike protein using ELISA. Assay sensitivity and specificity were 93% (95% CI 88-96%) and 99% (95% CI 98-99.5%), respectively. We adjusted prevalence estimates using Bayesian modeling to account for assay performance.

Results: Crude overall seroprevalence was 19.7% (135/684). After adjustment for assay performance seroprevalence was 20.8% (95% CrI 17.5-24.4%). Seroprevalence varied significantly (p<0.001) by site: 43.8% (CrI 35.8-52.2%) in Nairobi, 12.6% (CrI 8.8-17.1%) in Busia and 11.5% (CrI 7.2-17.6%) in Kilifi. In a multivariable model controlling for age, sex and site, professional cadre was not associated with differences in seroprevalence.

Conclusion: These initial data demonstrate a high seroprevalence of antibodies to SARS-CoV-2 among HCWs in Kenya. There was significant variation in seroprevalence by region, but not by cadre.

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Abstract

There is an urgent need for reliable region-specific hematological reference values for clinical monitoring. Laboratory reference ranges are important for assessing study participant eligibility, toxicity grading and management of adverse events in clinical trials and clinical diagnosis. Most clinical laboratories in Kenya rely on hematological reference values provided by instrument manufacturers and/or textbooks, which are based on population from Europe or North America. The use of such values in medical practice could result in improper patient management, selection bias in selection of appropriate participants for clinical trials and flawed classification of the clinical adverse events when applied to African populations. The aim of this study was to establish local laboratory hematological reference values in infants aged 1 month to 17 months from

Kombewa Sub-county that could be true representative of the existing rural population. The study participants in the current study were those who had previously been recruited from GSK-sponsored study. This study was a phase III, Double Blind, Randomized, GSK-sponsored, Malaria Vaccine Clinical Trial that was conducted in infants aged 1month to 17months. 1,509 participants were included in the study analysis. Data were partitioned into 3 different age groups (1-6 months[m], 6-12 m and 12-17 m) and differences between gender were compared within each group. Data were analyzed using Graphpad prism V5 to generate 95% reference ranges (2.5th-97.5th percentile). There was evidence of gender differences in hemoglobin values ($p = 0.0189$) and platelet counts ($p = 0.0005$) in the 1 to 6m group. For the 12-17m group, there were differences in MCV ($p<0.0001$) and MCH ($p = 0.0003$). Comparing gender differences for all age groups, differences were noted in percent lymphocytes ($p = 0.0396$), percent monocytes ($p = 0.0479$), percent granulocytes ($p = 0.0044$), hemoglobin ($p = 0.0204$), hematocrit ($p = 0.0448$), MCV ($p = 0.0092$), MCH ($p = 0.0089$), MCHC ($p = 0.0336$) and absolute granulocytes ($p = 0.0237$). In 1 to 6m age group and all age groups assessed, for WBCs, hemoglobin, hematocrit, MCV and lymphocytes absolute counts, both 2.5th and 97.5th percentiles for Kisumu infants were higher than those from Kilifi. Platelet ranges for Kisumu children were narrower compared to Kilifi ranges. Kisumu hematology reference ranges were observed to be higher than the ranges of Tanzanian children for the WBCs, absolute lymphocyte and monocyte counts, hemoglobin, hematocrit and MCV. Higher ranges of WBCs, absolute lymphocyte and monocyte counts were observed compared to the values in US/Europe. Wider ranges were observed in hemoglobin, hematocrit, and MCV. Wider ranges were observed in platelet counts in Kisumu infants compared to the US/Europe ranges. Compared to Harriet Lane Handbook reference values that are used in the area, higher counts were observed in WBC counts, both absolute and percent lymphocyte counts, as well as monocyte counts for current study. Wider ranges were observed in RBC, platelets and RDW, while lower ranges noted in the current study for hemoglobin, hematocrit and granulocyte counts. This study underscores the importance of using locally established hematology reference ranges of different age groups in support of proper patient management and for clinical trials.

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Imwong M, Tarning J, Day NPJ, White NJ, Bejon P, Dondorp AM. Arterolane-

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children: a single-centre, open-label, randomised, non-inferiority trial. Lancet

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Abstract

Background: Triple antimalarial combination therapies combine potent and rapidly cleared artemisinins or related synthetic ozonides, such as arterolane, with two, more slowly eliminated partner drugs to reduce the risk of resistance. We aimed to assess the safety, tolerability, and efficacy of arterolane-piperaquine-mefloquine versus arterolane-piperaquine and artemether-lumefantrine for the treatment of uncomplicated falciparum malaria in Kenyan children.

Methods: In this single-centre, open-label, randomised, non-inferiority trial done in Kilifi County Hospital, Kilifi, coastal Kenya, children with uncomplicated Plasmodium falciparum malaria were recruited. Eligible patients were aged 2-12 years and had an asexual parasitaemia of 5000-250 000 parasites per μL. The exclusion criteria included the presence of an acute illness other than malaria, the inability to tolerate oral medications, treatment with an artemisinin derivative in the previous 7 days, a known hypersensitivity or contraindication to any of the study drugs, and a QT interval corrected for heart rate (QTc interval) longer than 450 ms. Patients were randomly assigned (1:1:1), by use of blocks of six, nine, and 12, and opaque, sealed, and sequentially numbered envelopes, to receive either arterolane-piperaquine, arterolane-piperaquine-mefloquine, or artemether-lumefantrine. Laboratory staff, but not the patients, the patients' parents or caregivers, clinical or medical officers, nurses, or trial statistician, were masked to the intervention groups. For 3 days, oral artemether-lumefantrine was administered twice daily (target dose 5-24 mg/kg of bodyweight of artemether and 29-144 mg/kg of bodyweight of lumefantrine), and oral arterolane-piperaquine (arterolane dose 4 mg/kg of bodyweight; piperaquine dose 20 mg/kg of bodyweight) and oral arterolane-piperaquine-mefloquine (mefloquine dose 8 mg/kg of bodyweight) were administered once daily. All patients received 0·25 mg/kg of bodyweight of oral primaquine at hour 24. All patients were admitted to Kilifi County Hospital for at least 3 consecutive days and followed up at day 7 and, thereafter, weekly for up to 42 days. The primary endpoint was 42-day PCR-corrected efficacy, defined as the absence of treatment failure in the first 42 days post-treatment, of arterolane-piperaquine-mefloquine versus artemether-lumefantrine, and, along with safety, was analysed in the intention-to-treat population, which comprised all patients who received at least one dose of a study drug. The 42-day PCR-corrected efficacy of arterolane-piperaquine-mefloquine versus arterolane-piperaquine was an important secondary endpoint and was also analysed in the intention-to-treat population. The non-inferiority margin for the risk difference between treatments was -7%. The study is registered in ClinicalTrials.gov, NCT03452475, and is completed.

Findings: Between March 7, 2018, and May 2, 2019, 533 children with P falciparum were screened, of whom 217 were randomly assigned to receive either arterolane-piperaquine (n=73), arterolane-piperaquine-mefloquine (n=72), or artemether-lumefantrine (n=72) and comprised the

intention-to-treat population. The 42-day PCR-corrected efficacy after treatment with arterolane-piperaquine-mefloquine (100%, 95% CI 95-100; 72/72) was non-inferior to that after treatment with artemether-lumefantrine (96%, 95% CI 88-99; 69/72; risk difference 4%, 95% CI 0-9; p=0·25). The 42-day PCR-corrected efficacy of arterolane-piperaquine-mefloquine was non-inferior to that of arterolane-piperaquine (100%, 95% CI 95-100; 73/73; risk difference 0%). Vomiting rates in the first hour post-drug administration were significantly higher in patients treated with arterolane-piperaquine (5%, 95% CI 2-9; ten of 203 drug administrations; p=0·0013) or arterolane-piperaquine-mefloquine (5%, 3-9; 11 of 209 drug administrations; p=0·0006) than in patients treated with artemether-lumefantrine (1%, 0-2; three of 415 drug administrations). Upper respiratory tract complaints (n=26 for artemether-lumefantrine; n=19 for arterolane-piperaquine-mefloquine; n=23 for arterolane-piperaquine), headache (n=13; n=4; n=5), and abdominal pain (n=7; n=5; n=5) were the most frequently reported adverse events. There were no deaths.

Interpretation: This study shows that arterolane-piperaquine-mefloquine is an efficacious and safe treatment for uncomplicated falciparum malaria in children and could potentially be used to prevent or delay the emergence of antimalarial resistance.

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