## **International Health Alerts 2019-4 Contents**

#### **Child Health**

1. <u>BMJ 2019;366:15576</u> News Analysis

Vaccination uptake: access is still biggest barrier, experts warn

2. <u>Lancet</u> 2019;394(10210):1724–36

Effect of community-initiated kangaroo mother care on survival of infants with low birthweight: a randomized controlled trial

> 3. <u>bmjgh-2019-001643</u> <u>Practice</u>

Early implementation of guidelines for managing young infants with possible serious bacterial infection in Bangladesh

#### **Communicable Diseases**

4. <u>BMJ 2019;367:15894</u> <u>Research</u>

Transmissibility and potential for disease progression of drug resistant Mycobacterium tuberculosis: prospective cohort study

#### **Gender/Equity**

5. <u>BMJ 2019;367:15825</u> Practice Clinical Update

Caring for long term health needs in women with a history of sexual trauma

## **Health Financing/ Health Policy**

6. <u>Lancet</u> 2019;394(10204):1132

World Report| Cuba's doctors-abroad programme comes under fire

> 7. <u>BMJ 2019;366:15327</u> Feature Essay

How moves towards universal health coverage could encourage poor quality drugs: an essay by Elizabeth Pisani

#### 8. <u>BMJ 2019;366:15664</u> News

Increase investment in primary healthcare by 1% of GDP, says WHO

9. <u>bmjgh-2019-001788</u> Research

Effects of appointment scheduling on waiting time and utilisation of antenatal care in Mozambique

> 10. <u>bmjgh-2019-001809</u> Research

The catastrophic and impoverishing effects of out-of-pocket healthcare payments in Kenya, 2018

11. <u>bmjgh-2019-002151</u> <u>Editorial</u>

Poor-quality medical products: social and ethical issues in accessing 'quality' in global health

#### **HIV/AIDS**

12. <u>TMIH</u> 2019;24(10):1221-8

Safety and efficacy of Option B+ ART in Malawi: few severe maternal toxicity events or infant HIV infections among pregnant women initiating tenofovir/lamiyudine/efavirenz

#### **Infectious diseases**

13. <u>Lancet</u> 2019;394(10205):1217

World Report Polio returns to the Philippines

#### Malaria

14. <u>Am J Trop Med Hyg.</u> 2019 101 (6), 1434-1441 Dec 2019

Spatial Effects of Permethrin-Impregnated Bed Nets on Child Mortality: 26 Years on, a Spatial Reanalysis of a Cluster Randomized Trial.

#### 15. <u>Am J Trop Med Hyg.</u> 2019 101 (6), 1416-1423 <u>Dec 2019</u>

Direct Estimation of Sensitivity of Plasmodium falciparum Rapid Diagnostic Test for Active Case Detection in a High-Transmission Community Setting.

> 16. <u>Am J Trop Med Hyg.</u> 2019 101 (6), 1204-1211 Dec 2019

Origin and Spread of Evolving Artemisinin-Resistant Plasmodium falciparum Malarial Parasites in Southeast Asia.

> 17. <u>Am J Trop Med Hyg.</u> 2019 101 (6), 1405-1415 Dec 2019

The Economic Burden of Malaria: Revisiting the Evidence.

18. Am J Trop Med Hyg. 2019 Nov 4[Online ahead of print]

Estimation of Malaria-Attributable Fever in Malaria Test-Positive Febrile Outpatients in Three Provinces of Mozambique, 2018.

19. <u>Lancet</u>
2019;394(10203):10561112

Malaria eradication within a generation: ambitious, achievable, and necessary

## Non Communicable Diseases

20. Am J Trop Med Hyg. 2019 Nov 25. [Online ahead of print]

Integrated Cross-Sectional Multiplex Serosurveillance of IgG Antibody Responses to Parasitic Diseases and Vaccines in Coastal Kenya.

> 21. <u>TMIH 2019;4(9):1032-</u> 41

Methotrexate exposure and risk of strongyloidiasis

#### **Sexual and Reproductive Health**

22. <u>Lancet</u> 2019;394(10210):1750– 63

How women are treated during facility-based childbirth in four countries: a cross-sectional study with labour observations and community-based surveys

#### Miscellaneous

23. <u>Lancet</u> 2019;394(10203):997-8

World Report Blood transfusion in Kenya faces an uncertain future

## 24. <u>bmjgh-2019-001853</u> <u>Research</u>

Stuck in the middle: a systematic review of authorship in collaborative health research in Africa, 2014–2016

# **International Health Alerts 2019-4 Abstracts**

#### **Child Health**

1. BMJ 2019;366:l5576 News Analysis

Vaccination uptake: access is still biggest barrier, experts warn

Elisabeth Mahase, The BMJ

Lack of access is still the main factor hindering vaccine coverage and must not be overlooked in the fight to increase uptake. This was the message delivered at the first ever global vaccine summit, cohosted by the European Commission and World Health Organization.

Speaking at the conference in Brussels on 12 September, WHO's director general, Tedros Adhanom Ghebreyesus, said that although there was a "serious problem of misinformation" and increasing vaccine hesitancy, especially in rich countries, access to vaccines remained the world's "main problem."

"Even in Europe children are dying from measles," said Tedros in his speech calling for action. "This is a wake-up call. We were fighting it [measles], it was declining, but now it's coming back and it could be with a vengeance."

2. Lancet 2019;394(10210):1724-36

Effect of community-initiated kangaroo mother care on survival of infants with low birthweight: a randomized controlled trial

Mazumder S et al., <nita.bhandari@sas.org.in>

Background. Coverage of kangaroo mother care remains very low despite WHO recommendations for its use for babies with low birthweight in health facilities for over a decade. Initiating kangaroo mother care at the community level is a promising strategy to increase coverage. However, knowledge of the efficacy of community-initiated kangaroo mother care is still lacking. We aimed to assess the effect of community-initiated kangaroo mother care provided to babies weighing 1500–2250 g on neonatal and infant survival.

Methods. In this randomised controlled, superiority trial, undertaken in Haryana, India, we enrolled babies weighing 1500–2250 g at home within 72 h of birth, if not already initiated in kangaroo mother care, irrespective of place of birth (ie, home or health facility) and who were stable and feeding. The first eligible infants in households were randomly assigned (1:1) to the intervention (community-initiated kangaroo mother care) or control group by block randomisation using permuted blocks of variable size. Twins were allocated to the same group. For second eligible infants in the same household as an enrolled infant, if the first infant was assigned to the intervention group

the second infant was also assigned to this group, whereas if the first infant was assigned to the control group the second infant was randomly assigned (1:1) to the intervention or control group. Mothers and infants in the intervention group were visited at home (days 1–3, 5, 7, 10, 14, 21, and 28) to support kangaroo mother care (ie, skin-to-skin contact and exclusive breastfeeding). The control group received routine care. The two primary outcomes were mortality between enrolment and 28 days and between enrolment and 180 days. Analysis was by intention to treat and adjusted for clustering within households. The effect of the intervention on mortality was assessed with person-time in the denominator using Cox proportional hazards model. This study is registered with ClinicalTrials.gov, NCT02653534 and NCT02631343, and is now closed to new participants. Findings. Between July 30, 2015, and Oct 31, 2018, 8402 babies were enrolled, of whom 4480 were assigned to the intervention group and 3922 to the control group. Most births (6837 [81.4%]) occurred at a health facility, 36.2% (n=3045) had initiated breastfeeding within 1 h of birth, and infants were enrolled at an average of about 30 h (SD 17) of age. Vital status was known for 4470 infants in the intervention group and 3914 in the control group at age 28 days, and for 3653 in the intervention group and 3331 in the control group at age 180 days. Between enrolment and 28 days, 73 infants died in 4423 periods of 28 days in the intervention group and 90 deaths in 3859 periods of 28 days in the control group (hazard ratio [HR] 0.70, 95% CI 0.51-0.96; p=0.027). Between enrolment and 180 days, 158 infants died in 3965 periods of 180 days in the intervention group and 184 infants died in 3514 periods of 180 days in the control group (HR 0.75, 0.60-0.93; p=0.010). The risk ratios for death were almost the same as the HRs (28-day mortality 0.71, 95% CI 0.52-0.97; p=0.032; 180day mortality 0.76, 0.60-0.95; p=0.017).

Interpretation. Community-initiated kangaroo mother care substantially improves newborn baby and infant survival. In low-income and middle-income countries, incorporation of kangaroo mother care for all infants with low birthweight, irrespective of place of birth, could substantially reduce neonatal and infant mortality.

## 3. bmjgh-2019-001643 Practice

# Early implementation of guidelines for managing young infants with possible serious bacterial infection in Bangladesh

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#### **Abstract**

Neonatal infections remain a leading cause of newborn deaths globally. In 2015, WHO issued guidelines for managing possible serious bacterial infection (PSBI) in young infants (0-59 days) with simpler antibiotic regimens if hospital referral is not feasible. Bangladesh was one of the first countries to adapt WHO guidance into national guidelines for implementation in primary healthcare facilities. Early implementation was led by the Ministry of Health and Family Welfare (MOHFW) in 10 subdistricts of Bangladesh with support from USAID's MaMoni Health System Strengthening project. This mixed methods implementation research case study explores programme feasibility and acceptability through analysis of service delivery data from 4590 sick young infants over a 15-month period, qualitative interviews with providers and MOHFW managers and documentation by project staff. Multistakeholder collaboration was key to ensuring facility readiness and feasibility of programme delivery. For the 514 (11%) infants classified as PSBI, provider adherence to prereferral treatment and follow-up varied across infection subcategories. Many clinical severe infection cases for whom referral was not feasible received the recommended two doses of injectable gentamicin and follow-up, suggesting delivery of simplified antibiotic treatment is feasible. However, prereferral antibiotic treatment was low for infants whose families accepted hospital referral, which highlights the need for additional focus on managing these cases in training and supervision. Systems for tracking sick infants that accept hospital referral are needed, and follow-up of all PSBI cases requires

strengthening to ensure sick infants receive the recommended treatment, to monitor outcomes and assess the effectiveness of the programme. Only 11.2% (95% CI 10.3 to 12.1) of the expected PSBI cases sought care from the selected service delivery points in the programme period. However, increasing trends in utilisation suggest improved awareness and acceptability of services among families of young infants as the programme matured. Future programme activities should include interviews with caregivers to explore the complexities around referral feasibility and acceptability of simplified antibiotic treatment.

#### **Communicable Diseases**

#### 4. BMJ 2019;367:I5894 Research

# Transmissibility and potential for disease progression of drug resistant Mycobacterium tuberculosis: prospective cohort study

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#### **Abstract**

Objective To measure the association between phenotypic drug resistance and the risk of tuberculosis infection and disease among household contacts of patients with pulmonary tuberculosis.

Setting 106 district health centers in Lima, Peru between September 2009 and September 2012. Design Prospective cohort study.

Participants 10 160 household contacts of 3339 index patients with tuberculosis were classified on the basis of the drug resistance profile of the patient: 6189 were exposed to drug susceptible strains of Mycobacterium tuberculosis, 1659 to strains resistant to isoniazid or rifampicin, and 1541 to strains that were multidrug resistant (resistant to isoniazid and rifampicin).

Main outcome measures Tuberculosis infection (positive tuberculin skin test) and the incidence of active disease (diagnosed by positive sputum smear or chest radiograph) after 12 months of follow-up.

Results Household contacts exposed to patients with multidrug resistant tuberculosis had an 8% (95% confidence interval 4% to 13%) higher risk of infection by the end of follow-up compared with household contacts of patients with drug sensitive tuberculosis. The relative hazard of incident tuberculosis disease did not differ among household contacts exposed to multidrug resistant tuberculosis and those exposed to drug sensitive tuberculosis (adjusted hazard ratio 1.28, 95% confidence interval 0.9 to 1.83).

Conclusion Household contacts of patients with multidrug resistant tuberculosis were at higher risk of tuberculosis infection than contacts exposed to drug sensitive tuberculosis. The risk of developing tuberculosis disease did not differ among contacts in both groups. The evidence invites guideline producers to take action by targeting drug resistant and drug sensitive tuberculosis, such as early detection and effective treatment of infection and disease.

## **Gender/Equity**

#### 5. BMJ 2019;367:l5825 Practice Clinical Update

#### Caring for long term health needs in women with a history of sexual trauma

Veronica Ades, et al., NYU School of Medicine, Department of Obstetrics & Gynecology, New York, NY, USA <a href="mailto:Veronica.Ades@nyumc.org">Veronica.Ades@nyumc.org</a>

#### What you need to know

Trauma focused cognitive behavioural therapy interventions in the acute phase after sexual assault can potentially prevent development of post-traumatic stress disorder

Some people are hesitant to disclose a history of sexual trauma and may avoid routine medical care because of fear of retraumatisation

Some groups recommend routinely screening women for a history of sexual trauma, but you may individualise this and ask if specific concerns arise during the consultation

Exercise additional sensitivity during examination and explain the steps so the patient knows what to expect and can request to defer examination at any point

Annual pelvic examination may be avoided in people who express anxiety or discomfort; a thorough review of symptoms may suffice in these patients if they have no related symptoms Globally, about 30% of women report intimate partner violence (physical, sexual, or both) (95% confidence interval 27.8% to 32.2%) and about 7.2% (95% confidence interval 5.3% to 9.1%) of women face non-partner sexual violence in their lifetime. Sexual violence in men is less studied. In the United States, the National Intimate Partner and Sexual Violence Survey determined a lifetime prevalence of contact sexual violence (including forced penetration and fondling) of 36.3% (95% confidence interval 35.3% to 37.2%) among women and 17.1% (95% confidence interval 16.3% to 17.9%) among men.

Experiences of sexual violence negatively affect a person's long term physical and psychological wellbeing as well as their interaction with the healthcare system.

Most guidelines focus on treatment in the acute setting in the immediate aftermath of sexual assault, and rarely address long term care. Box 1 lists key aspects of acute medical care for people who have experienced sexual violence.

## **Health Financing/ Health Policy**

6. Lancet 2019;394(10204):1132

World Report

## Cuba's doctors-abroad programme comes under fire

Alves, L

Disapproval of the assistance programme that sends hundreds of Cuban doctors to foreign countries has been building.

The Cuban Government has strongly denied recent allegations by the USA that Cuba is violating human rights by exploiting medical professionals it sends abroad to help those in need. From Brazil to Kenya to Angola, criticism ranges from the reduced wages these doctors receive while abroad, to Cuban doctors taking positions that could have been given to local doctors.

Data from Cuba's Foreign Affairs Ministry show that since the 1960s, more than 600 000 Cuban medical professionals have been sent to over 160 countries. In 2018, approximately 55 000 Cuban medical specialists were working in 67 countries.

"Cuba has deceived many countries for years, presenting these missions as humanitarian, when in reality they are a big business for the island", stated Cuban-Spaniard Javier Larrondo, founder of human rights organisation Prisoners Defenders, during a confer- ence in May in Miami, FL, USA. "We are talking about earnings of US\$8 billion a year", said Larrondo, adding that approximately 56% of professionals declared they did not go on the missions voluntarily and 39% said they had been coerced for having an education debt to the Cuban Government.

According to USAID, the Cuban regime "exploits its medical professionals, teachers, and other workers, using them to buy international financial and political support and keep its struggling economy afloat, while pocketing the majority of these workers' salaries and subjecting them to poor living conditions, constant surveillance, and threatening those who wish to leave their mission".

#### 7. BMJ 2019;366:l5327 Feature Essay

# How moves towards universal health coverage could encourage poor quality drugs: an essay by Elizabeth Pisani

Elizabeth Pisani, associate professor, epidemiology. Erasmus School of Health Policy and Management, Rotterdam, The Netherlands, and King's College London, UK pisani@ternyata.org

Universal health coverage depends on affordable medicines. But pushing down prices without also investing in quality assurance will increase the sale of substandard and falsified drugs, warns Elizabeth Pisani

Many governments in middle income countries are working hard to deliver on political promises that all their citizens will have access to quality health services, without being impoverished. They are finding that universal health coverage (UHC) doesn't come cheap.

Indonesia's national health insurance scheme, for example, has given out 223.4 million health cards since its inception in 2014. Nationwide, 73% of households said at least one household member had some health insurance in 2018, up from 52% in 2013. Yet the scheme has been in permanent deficit; by 2018 it had a shortfall of 23 trillion rupiah (£1.3bn; €1.5bn; \$1.6bn.

Such deficits lead to belt tightening. Globally, about a quarter of all health spending is on drugs. In poorer countries the proportion is higher, and patients typically foot more of the bill. As governments move towards UHC, they increasingly pay for drugs that used to be paid for by patients—and look for ways to push prices down.

Cheaper drugs should mean more people effectively treated for the same budget, taking countries towards UHC. There's plenty of room for belt tightening. Generic and branded drug makers often charge whatever they can. Inefficient procurement and plain old corruption push prices up; some poorer countries pay 30 times more than the international reference price for basic generic drugs. But countries with under-resourced health budgets seeking to push down prices should be careful what they wish for. Recent research in China, Indonesia, Romania, and Turkey found evidence that drug manufacturers and distributors react quickly to keep profits as high as possible, potentially leaving patients exposed to substandard drugs, and creating opportunities for criminals to sell fake drugs.

The downside of cheap drugs

One way to maintain profits is to cut production costs—for example, by shifting manufacturing to cheaper locations or increasing worker productivity. Some manufacturers also mentioned more worrying measures, such as switching to cheaper ingredients or packaging, or skipping some quality assurance steps.

The result can be drugs that are so sloppily made that they don't dissolve properly in the body; that degrade before the patient takes them, sometimes because of cheap but inappropriate packaging or handling; or that are dangerously lacking in active ingredients. Similar problems have been reported from India, one of the biggest producers of cheap drugs.

#### 8. BMJ 2019;366:l5664 News

#### Increase investment in primary healthcare by 1% of GDP, says WHO

Joanne Silberner

Governments around the world should invest significantly more in primary healthcare, the World Health Organization has said in a new report.

The report coincides with a high level meeting of the United Nations on 23 September on universal health coverage, a system where all people get the healthcare they need without financial hardship. The meeting, the first of its kind, is billed by the UN as "an opportunity to mobilise the global community and secure political commitments."

Countries must increase spending on primary healthcare by at least 1% of their gross domestic product (GDP) if the world is to close glaring coverage gaps and meet health targets agreed in 2015, says a new report from the World Health Organization and partners on the eve of a UN General Assembly high-level meeting on Universal Health Coverage.

They must also intensify efforts to expand services countrywide.

The world will need to double health coverage between now and 2030, according to the Universal Health Coverage Monitoring Report. It warns that if current trends continue, up to 5 billion people will still be unable to access health care in 2030 – the deadline world leaders have set for achieving universal health coverage. Most of those people are poor and already disadvantaged.

#### 9. bmjgh-2019-001788 Research

# Effects of appointment scheduling on waiting time and utilisation of antenatal care in Mozambique

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Abstract

Background Poor patient experience, including long waiting time, is a potential reason for low healthcare utilisation. In this study, we evaluate the impact of appointment scheduling on waiting time and utilisation of antenatal care.

Methods We implemented a pilot study in Mozambique introducing appointment scheduling to three maternity clinics, with a fourth facility used as a comparison. The intervention provided women with a return date and time for their next antenatal care visit. Waiting times and antenatal care utilisation data were collected in all study facilities. We assessed the effect of changing from first come, first served to scheduled antenatal care visits on waiting time and complete antenatal care (≥4 visits during pregnancy). Our primary analysis compared treatment facilities over time; in addition, we compared the treatment and comparison facilities using difference in differences.

Results We collected waiting time data for antenatal care from 6918 women, and antenatal care attendance over the course of pregnancy from 8385 women. Scheduling appointments reduced waiting time for antenatal care in treatment facilities by 100 min (95% CI –107.2 to -92.9) compared with baseline. Using administrative records, we found that exposure to the scheduling intervention

during pregnancy was associated with an approximately 16 percentage point increase in receipt of four or more antenatal care visits during pregnancy.

Conclusions Relatively simple improvements in the organisation of care that reduce waiting time may increase utilisation of healthcare during pregnancy. A larger scale study is needed to provide information about whether appointment scheduling can be sustained over time.

## 10. bmjgh-2019-001809 Research

#### The catastrophic and impoverishing effects of out-of-pocket healthcare payments in Kenya, 2018

Paola Salari et al.,

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#### **Abstract**

Introduction Progress towards effective service coverage and financial protection—the two dimensions of Universal Health Coverage (UHC)—has been limited in Kenya in the last decade. The government of Kenya has embarked on a highly ambitious reform programme currently being piloted in four Kenyan counties and aiming at national rollout by 2022. This study provides an updated assessment of the performance of the Kenyan health system in terms of financial protection allowing to monitor trends over time. In light of the UHC initiative, the study provides a baseline to assess the impact of the UHC pilot programme and inform scale-up plans. It also investigates household characteristics associated with catastrophic payments.

Methods Using data from the Kenya Household Health Expenditure and Utilization Survey (KHHEUS) 2018, we investigated the incidence and intensity of catastrophic and impoverishing health expenditure. We used a logistic regression analysis to assess households' characteristics associated with the probability of incurring catastrophic health expenditures.

Results The results show that the incidence of catastrophic payments is more severe for the poorest households and in the rural areas and mainly due to outpatient services. Results for the impoverishing effect suggest that after accounting for out-of-pocket(OOP) payments, the proportion of poor people increases by 2.2 percentage points in both rural and urban areas. Thus, between 1 and 1.1 million individuals are pushed into poverty due to OOP payments. Among the characteristics associated with the probability of incurring OOP expenditures, socioeconomic conditions, the presence of elderly and of people affected by chronic conditions showed significant results. Conclusion Kenya is still lagging behind in terms of protecting its citizens against financial risks associated with ill health and healthcare seeking behaviour. More effort is needed to protect the most vulnerable population groups from the high costs of illness.

## 11. bmjgh-2019-002151 Editorial :https://gh.bmj.com/content/4/6/e002151

## Poor-quality medical products: social and ethical issues in accessing 'quality' in global health

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Assuring access to medicines, vaccines and medical devices of adequate quality is a key pillar of any well-functioning health system and a prerequisite to achieving universal health coverage. However, high prevalence of substandard and falsified (SF) medical products, particularly in low-income and middle-income countries (LMICs), and widespread inadequate practices in the management, prescription and use of medical products along their life cycle, all undermine access to

quality-assured medical products and the performance of health systems. In addition, what counts as 'quality' can be highly variable and greatly contested, with perceptions of what constitutes 'good standards' shaped by a range of geographical, contextual, sociopolitical and cultural factors. This Special Issue seeks to highlight the ethical and social challenges that shape universal access to quality-assured, adequately used medical products throughout their full-life course. We aim to pursue an in-depth and interdisciplinary exploration of the structural, political, economic and ethical factors that influence the detection and prevention of SF medical products, the access to quality-assured medicines and their adequate use along their full life cycle, that is, from manufacturing sites until completion of a treatment course.

This collection is open to research papers on subjects including the ethical challenges in medicines regulation, procurement, supply, rational use and health-seeking behaviour; the social life of medicines (uses and perceptions of quality and effectiveness of interventions); and the determinants of trust in medicine and in medical products. While we will examine global health and feature several examples from LMICs, we consider the discussion relevant to all countries and at the global level. This Special Issue will promote dialogue between researchers in different disciplinary communities whose work touch on the ethical and social dimensions of achieving universal access to quality-assured, adequately used medical products, throughout their full-life course. We look forward to considering your papers, dedicated to offering novel and timely insights into an important but still sidelined issue in global health. Papers should be submitted by 15 April 2020. The usual article processing charges and waiver policy will apply. However, authors who require but are unable to obtain waiver through the regular BMJ Global Health processes are welcome to contact the corresponding author of this editorial for additional considerations.

#### **HIV/AIDS**

## 12. TMIH 2019;24(10):1221-8

Safety and efficacy of Option B+ ART in Malawi: few severe maternal toxicity events or infant HIV infections among pregnant women initiating tenofovir/lamivudine/efavirenz

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Objectives: Malawi's Option B+ universal antiretroviral therapy (ART) program for pregnant and breastfeeding women does not include routine laboratory monitoring. We report safety outcomes of pregnant women who initiated ART through Option B+.

Methods: We analysed 12-month data from an observational cohort study on Option B+ among women newly initiating tenofovir/lamivudine/efavirenz (TDF/3TC/EFV) at a government antenatal clinic in Lilongwe, Malawi. Proportions of women engaged in care, incidence of DAIDS grade  $\geq 2$  laboratory toxicity, grade  $\geq 3$  adverse events (AEs), viral suppression (<1000 copies/mL), birth outcomes and infant HIV infections are reported.

Results: At ART initiation, participants (n = 299) had a median age of 26 years (IQR 22-30), median CD4 count of 352 cells/µl (IQR 231-520) and 94% were in WHO Stage 1. We noted 76 incident DAIDS Grade  $\geq$  2 laboratory results among 58 women, most commonly elevated liver function tests (n = 30 events) and low haemoglobin (n = 27). No women had elevated creatinine. Clinical AEs (n = 45) were predominantly infectious diseases and Grade 3. Five participants (2%) discontinued TDF/3TC/EFV due to virologic failure (3) or toxicity (2). Twelve months after ART initiation, most women were engaged in care (89%) and had HIV RNA < 1000 copies/ml (90%). 8% of pregnancies resulted in preterm birth, 9% were low birthweight (<2500 g), and 2% resulted in infant HIV infection at 6 weeks post-delivery. Conclusion: Most women remained on ART and were virally suppressed 12 months after starting Option B+. Few infants contracted HIV perinatally. While some women experienced adverse laboratory events, clinical symptom monitoring is likely reasonable.

#### **Infectious diseases**

13. Lancet 2019;394(10205):1217

World Report

## Polio returns to the Philippines

#### Thornton J.

Cases of the illness have re-emerged in the country for the first time in 19 years.

Two cases of vaccine-derived poliovirus infection have been confirmed by the Philippines Department of Health (DoH), 1400 km apart. The first was in a girl aged 3 years from Lanao del Sur, on the island of Mindanao, reported on Sept 19; the second was in a boy aged 5 years from Laguna province, 100 km southeast of Metro Manila, which was reported a day later.

The cases are being investigated by the DoH and local governmental units, with support from WHO and UNICEF. The DoH is planning a mass oral poliovirus immunisation programme for children younger than 5 years for mid-October and increased surveillance of acute flaccid paralysis, a symptom of infection.

The last known case of wild poliovirus was recorded in the Philippines in 1993, and the country was declared polio-free in 2000. Oyun Dendevnorov, the UNICEF Philippines representative, said these new cases were "deeply disconcerting".

It is of particular concern, said UNICEF, that the infections are of vaccine-derived poliovirus type 2. Vaccine-derived cases tend to occur in places with low vaccination cov- erage and poor sanitation. People who have been vaccinated excrete the weakened virus, which further circulates and can mutate over time into the vaccine-derived form, which can cause illness and paralysis. In 2018, there were vaccine-derived poliovirus outbreaks in DR Congo, Papua New Guinea, Kenya, Somalia, Mozambique, Indonesia, Niger, and Nigeria.

Wild poliovirus type 2 was globally eradicated in 2015 and, as a result, the trivalent oral polio vaccine (OPV) in the Philippines immunization schedule was replaced with a bivalent OPV against type 1 and 3, giving no protection against type 2. WHO has agreed to send a supply of monovalent type 2 vaccine from a stockpile in Geneva to be used in Mindanao, where the first case occurred. UNICEF said that polio vaccination coverage has been "steadily declining" in the Philippines, with subnational gaps in coverage. In 2018, coverage with the OPV was 66%. Coverage with the injectable inactivated polio vaccine, which protects against all three polio types, was 41%.

This shortfall is due to several factors, including inadequate delivery at the community level, too few primary care immunisation sessions, and difficulties in accessing hard-to-reach areas in the archipelago. The Philippines has 7641 islands, some of which are mostly mountainous. But anxiety about vaccines generally has increased sharply in the Philippines following the withdrawal of the dengue vaccine, Dengvaxia, in 2017, 1 year after its introduction, over fears about the risks it posed to health. A study published last year found that the proportion of Filipinos who believe "that vaccines are important, are safe and are effective" decreased from about 100% in 2015, to 60–80% in 2018.

#### Malaria

## 14. Am J Trop Med Hyg. 2019 101 (6), 1434-1441 Dec 2019

Spatial Effects of Permethrin-Impregnated Bed Nets on Child Mortality: 26 Years on, a Spatial Reanalysis of a Cluster Randomized Trial.

Jarvis CI, et al. MRC London Hub for Trials Methodology Research, London, United Kingdom.

In addition to the direct effect of insecticide-treated nets (ITNs), there has been evidence for spatial indirect effects. Spatial analyses in cluster randomized trials (CRTs) are rare, but a large-scale CRT from 1993 was one of the first to conduct a spatial analysis of ITNs in CRTs. We revisit these data by applying a broader range of contemporary spatial methods to further explore spatial spillover. We conducted three analyses: 1) exploratory spatial analysis, considering spatial patterns and spillover in the data; 2) spatial modeling, estimating the intervention effect considering spatial effects; and 3) analysis of distance-based spillover and interaction with the intervention, characterizing the functional distance over which the spillover effect was present. There were consistent indications of spatial patterns from the exploratory analysis. Bed nets were associated with a 17% reduction in allcause mortality for children aged 6-59 months, and the intervention estimate remained robust when allowing for the spatial structure of the data. There was strong evidence of a spatial spillover effect: for every additional 100 m that a control household was from an intervention household (and vice versa), the standardized mortality ratio (SMR) increased by 1.7% (SMR 1.017, 95% credible interval 1.006-1.026). Despite evidence of a spatial spillover effect, the conclusions of the trial remain unaffected by spatial model specifications. Use of ITNs was clearly beneficial for individuals, and there was compelling evidence that they provide an indirect benefit to individuals living nearby. This article demonstrates the extra utility that spatial methods can provide when analyzing a CRT.

## 15. Am J Trop Med Hyg. 2019 101 (6), 1416-1423 Dec 2019

Direct Estimation of Sensitivity of Plasmodium falciparum Rapid Diagnostic Test for Active Case Detection in a High-Transmission Community Setting.

Taylor SM, et al. Division of Infectious Diseases, Duke University Medical Center, Durham, North Carolina.

Community-based active case detection of malaria parasites with conventional rapid diagnostic tests (cRDTs) is a strategy used most commonly in low-transmission settings. We estimated the sensitivity of this approach in a high-transmission setting in Western Kenya. We tested 3,547 members of 912 households identified in 2013-2014 by index children with (case) and without (control) cRDT-positive malaria. All were tested for Plasmodium falciparum with both a cRDT targeting histidine-rich protein 2 and with an ultrasensitive real-time PCR. We computed cRDT sensitivity against PCR as the referent, compared prevalence between participant types, and estimated cRDT detectability as a function of PCR-estimated parasite density. Parasite prevalence was 22.9% by cRDTs and 61.5% by PCR. Compared with children aged < 5 years or adults aged > 15 years, geometric mean parasite densities (95% CI) were highest in school-age children aged 5-15 years (8.4 p/uL; 6.6-10.6). The overall sensitivity of cRDT was 36%; among asymptomatic household members, cRDT sensitivity was 25.5% and lowest in adults aged > 15 years (15.8%). When modeled as a function of parasite density, relative to school-age children, the probability of cRDT positivity was reduced in both children aged < 5 years (odds ratio [OR] 0.48; 95% CI: 0.34-0.69) and in adults aged > 15 years (OR: 0.35; 95% CI: 0.27-0.47). An HRP2-detecting cRDT had poor sensitivity for active P. falciparum case detection in asymptomatic community members, and sensitivity was lowest in highly prevalent low-density

infections and in adults. Future studies can model the incremental effects of high-sensitivity rapid diagnostic tests and the impacts on transmission.

## 16. Am J. 2019 101 (6), 1204-1211 Dec 2019 Trop Med Hyg

# Origin and Spread of Evolving Artemisinin-Resistant Plasmodium falciparum Malarial Parasites in Southeast Asia.

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In this review, we provide an epidemiological history of the emergence and ongoing spread of evolving Plasmodium falciparum artemisinin resistance (ARTR). Southeast Asia has been the focal point for emergence and spread of multiple antimalarial drug resistance phenomena, and is once again for evolving ARTR, also known as the "delayed clearance phenotype" (DCP). The five countries most impacted, Cambodia, Thailand, Myanmar, Laos, and Vietnam, each have complex histories of antimalarial drug use over many decades, which have in part molded the use of various artemisinin combination therapies (ACTs) within each country. We catalog the use of ACTs, evolving loss of ACT efficacy, and the frequency of pfk13 mutations (mutations associated with ARTR) in the Greater Mekong Subregion and map the historical spread of ARTR/DCP parasites. These data should assist improved surveillance and deployment of next-generation ACTs.

## 17. Am J Trop Med Hyg. 2019 101 (6), 1405-1415 Dec 2019

#### The Economic Burden of Malaria: Revisiting the Evidence.

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A portion of the economics literature has long debated about the relative importance of historical, institutional, geographical, and health determinants of economic growth. In 2001, Gallup and Sachs quantified the association between malaria and the level and growth of per capita income over the period 1965-1995 in a cross-country regression framework. We took a contemporary look at Gallup and Sachs' seminal work in the context of significant progress in malaria control achieved globally since 2000. Focusing on the period 2000-2017, we used the latest data available on malaria case incidence and other determinants of economic growth, as well as macro-econometric methods that are now the professional norm. In our preferred specification using a fixed-effects model, a 10% decrease in malaria incidence was associated with an increase in income per capita of nearly 0.3% on average and a 0.11 percentage point faster per capita growth per annum. Greater average income gains were expected among higher burden countries and those with lower income. Growth of industries with the same level of labor intensity was found to be significantly slower in countries with higher malaria incidence. To analyze the causal impact of malaria on economic outcomes, we used malaria treatment failure and pyrethroid-only insecticide resistance as exogeneous instruments in two-stage least squares estimations. Despite several methodological challenges, as expected in these types of analyses, our findings confirm the intrinsic link between malaria and economic growth and underscore the importance of malaria control in the agenda for sustainable development.

## 18. Am J Trop Med Hyg. 2019 Nov 4[Online ahead of print]

# Estimation of Malaria-Attributable Fever in Malaria Test-Positive Febrile Outpatients in Three Provinces of Mozambique, 2018.

Plucinski MM, et al. United States President's Malaria Initiative, Centers for Disease Control and Prevention, Atlanta, Georgia.

Like most malaria-endemic countries, Mozambique relies on tabulation of confirmed malaria test-positive febrile patients to track incidence of malaria. However, this approach is potentially biased by incidental malaria parasitemia in patients with fever of another etiology. We compared pan-Plasmodium aldolase and lactate dehydrogenase and Plasmodium falciparum HRP2 antigen concentrations measured using a laboratory bead-based assay of samples collected from 1,712 febrile and afebrile patients of all ages in Maputo, Zambézia, and Cabo Delgado provinces. We used a Bayesian latent class model to estimate the proportion of malaria-attributable fevers in malaria test-positive febrile patients. Depending on the antigen, estimated rates of malaria-attributable fever in malaria test-positive febrile patients were 100% in Maputo, 33-58% in Zambézia, and 63-74% in Cabo Delgado. Our findings indicate that most malaria test-positive febrile patients in the three provinces of Mozambique had a fever that was likely caused by the concurrent malaria infection. Counting malaria test-positive febrile patients for estimation of malaria incidence appears to be appropriate in this setting.

## 19. Lancet 2019;394(10203):1056-1112

# Malaria eradication within a generation: ambitious, achievable, and necessary Feachem RGA et al.

50 years after a noble but flawed attempt to eradicate malaria in the mid-20th century, the global malaria community is once again seriously considering eradication. Momentum towards eradication has been building for decades, and more than half of the world's countries are now malaria free. Since 2000, a surge of global progress has occurred, facilitated by the roll-out of new technologies and the substantial growth in political and financial commitment by countries, regions, and their global partners. Annual domestic and international spending on malaria increased from roughly US\$1.5 billion in 2000 to \$4.3 billion in 2016. Simultaneously, the number of countries with endemic malaria dropped from 106 to 86, the worldwide annual incidence rate of malaria declined by 36%, and the annual death rate declined by 60%.

Inspired by these outstanding achievements, and troubled by a stagnation in progress that saw 55 countries report an increase in cases between 2015 and 2017, the Lancet Commission on Malaria Eradication (the Commission) was convened to consider whether malaria eradication is feasible, affordable, and worthwhile. In this report of the Commission, we synthesise existing evidence and new epidemiological and financial analyses to show that malaria eradication by 2050 is a bold but attainable goal, and a necessary one given the never-ending struggle against drug and insecticide resistance and the social and economic costs associated with a failure to eradicate.

Global social, economic, and environmental trends are, in most places, reducing malaria. Our models show that these trends alone will lead to greatly reduced but still widespread malaria by 2050. When the effects of enhanced access to high-quality diagnosis, treatment, and vector control are factored in, the 2050 projections show a world largely free of malaria, but with pockets of low-level transmission persisting in a belt across Africa, from Senegal in the northwest to Mozambique in the southeast. In view of these projections, we explore the responses to the operational, biological, and financial challenges that are required to bend the curve (ie, to accelerate the decline in malaria cases and deaths) and achieve elimination everywhere outside of Africa by 2030 and worldwide eradication by 2050.

Operational obstacles limit the success of malaria programmes in many countries, including ineffective management, inadequate use of data to inform strategies, poorly incentivised staff, and disengaged communities. Solutions to most of these challenges are available and inexpensive but require access to management training and tools, which many malaria programmes do not have. Strengthening programme management and improving the availability and use of data for decision making are operational priorities which, if addressed, would enhance programme effectiveness and accelerate the path to malaria eradication. Leveraging the expertise and comparative advantages of the private sector and forming close partnerships with private health-care providers will further strengthen performance.

Multiple challenges arise from the complexity of malaria biology: malaria parasites and their mosquito vectors are constantly evolving resistance to widely used drugs and insecticides, the most common methods of parasite detection are not sensitive enough to identify all infections, simian malaria is now common in humans in parts of southeast Asia, and the effectiveness of standard vector control interventions is low in areas with the highest transmission intensity and where outdoor biting is common. Encouragingly, the research and development pipeline for drugs, insecticides, diagnostics, and vector control tools is robust. Promising new products with strong potential to overcome existing challenges have become available in the past 5 years or are scheduled to roll out over the next decade. Continued investment in research and development will be essential, with prioritisation of technologies that provide long durations of efficacy, do not require difficult or protracted compliance from individuals and households, and drive down malaria in high-transmission or otherwise problematic settings.

The cost of malaria eradication is not known and will be highly dependent on managerial efficiency, the efficacy and cost of new tools, and the degree to which interventions can be targeted. Estimates suggest that annual spending of \$6 billion or more is required; current global expenditure is approximately \$4·3 billion. The Commission believes that an additional investment of \$2 billion per year is necessary, with a quarter of that coming from increased development assistance from external donors and the rest from government health spending in malaria-endemic countries. Securing additional funding will not be easy. Development assistance for health has plateaued since 2011, but opportunities exist for new and smaller donors to step in and fill the gap. In addition, our analyses show that government spending on malaria in high-burden countries has increased faster than their growth in gross domestic product, indicating that health in general, and malaria specifically, is a high priority. The opportunities for increased public expenditure on malaria and reduced reliance on donor funds need to be assessed and acted upon country by country. For both donors and countries, a shared and time-bound commitment to eradication will catalyse enthusiasm and financial support.

Strong and committed leadership and governance, reinforced through transparency and independent accountability mechanisms, are essential to ensure that eradication is achieved. Leadership and ambition are increasingly coming from the national and regional levels. Global malaria eradication will be achieved through regional elimination. Global organisations should focus on supporting and enabling countries and regions by developing guidance, coordinating across stakeholders, and advocating for sustained investment and research. There is value in closer collaboration and clearer definition of roles between the two apex organisations, WHO and the RBM Partnership to End Malaria. Opportunities also exist for greater alignment of policies and investment strategies between The Global Fund to Fight AIDS, Tuberculosis and Malaria and the US President's Malaria Initiative, the two major malaria funders. Finally, the Commission recommends the creation of an independent monitoring board for malaria eradication.

Beyond the obvious benefits of eradicating a disease that has caused untold morbidity and mortality throughout human history, malaria eradication also contributes to broader health and development goals. Strengthening global health security and meeting many of the Sustainable Development Goals—including achieving universal health coverage, promoting equity, and reducing poverty—are all supported and reinforced by progress towards malaria eradication, and vice versa. Malaria

eradication has multiple benefits for human welfare and prosperity, the value of which will greatly exceed the investment required to get the job done.

In this report, the Commission concludes that malaria eradication is possible, worthwhile, and affordable, and that the alternatives to eradication are untenable. We identify opportunities for specific actions that will overcome challenges and accelerate progress, starting with an immediate, firm, global commitment to achieving eradication by 2050.

#### **Non Communicable Diseases**

## 20. Am J Trop Med Hyg. 2019 Nov 25. [Online ahead of print]

Integrated Cross-Sectional Multiplex Serosurveillance of IgG Antibody Responses to Parasitic Diseases and Vaccines in Coastal Kenya.

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Accurate and cost-effective identification of areas where co-endemic infections occur would enable public health managers to identify opportunities for implementation of integrated control programs. Dried blood spots collected during cross-sectional lymphatic filariasis surveys in coastal Kenya were used for exploratory integrated detection of IgG antibodies against antigens from several parasitic infections (Wuchereria bancrofti, Schistosoma mansoni, Plasmodium spp., Ascaris lumbricoides, and Strongyloides stercoralis) as well as for detection of responses to immunizing agents used against vaccine-preventable diseases (VPDs) (measles, diphtheria, and tetanus) using a multiplex bead assay (MBA) platform. High heterogeneity was observed in antibody responses by pathogen and antigen across the sentinel sites. Antibody seroprevalence against filarial antigens were generally higher in Ndau Island (P < 0.0001), which also had the highest prevalence of filarial antigenemia compared with other communities. Antibody responses to the Plasmodium species antigens CSP and MSP-119 were higher in Kilifi and Kwale counties, with Jaribuni community showing higher overall mean seroprevalence (P < 0.0001). Kimorigo community in Taita-Taveta County was the only area where antibody responses against S. mansoni Sm25 recombinant antigen were detected. Seroprevalence rates to Strongyloides antigen NIE ranged between 3% and 26%, and there was high heterogeneity in immune responses against an Ascaris antigen among the study communities. Differences were observed between communities in terms of seroprevalence to VPDs. Seroprotection to tetanus was generally lower in Kwale County than in other counties. This study has demonstrated that MBA holds promise for rapid integrated monitoring of trends of infections of public health importance in endemic areas.

#### 21. TMIH 2019;4(9):1032-41

#### Methotrexate exposure and risk of strongyloidiasis

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Objective: Rheumatologic disease patients receiving immunomodulating drugs such as methotrexate (MTX) have increased infection rates. Strongyloides, a global endemic intestinal parasite, can cause significant or fatal disease in immunocompromised patients. The risk of serious Strongyloides infection with MTX dosed for rheumatologic disease is unknown.

Methods: We performed a systematic literature review searching EMBASE, Medline and Web of Science databases. All studies reporting humans exposed to MTX and tested for Strongyloides were reviewed. Exclusion criteria were bone marrow transplantation, intrathecal route and MTX exposure completed >1 year prior to clinically apparent Strongyloides disease.

Results: After excluding duplicates, 294 articles were reviewed. Of these, 29 cases were described in 27 papers. Twenty cases (69%) had an underlying rheumatologic or dermatologic disease, the rest had a haematologic disease. Hyperinfection or dissemination was found in 59% of cases (52% low-dose MTX; 75% high-dose MTX). Death occurred in 34% of cases (19% low-dose MTX; 75% high-dose MTX, P < 0.01). All eight patients on high-dose MTX received other immunosuppressants. Corticosteroids were taken in 18/21 patients on low-dose MTX. One of the three patients on MTX monotherapy had hyperinfection syndrome. None had disseminated Strongyloides. Conclusions: Serious Strongyloides infection can occur with low-dose MTX particularly when given with other immunosuppression. Global travel and greater awareness of rheumatologic conditions in low- to middle-income countries will increase the exposure of individuals prescribed MTX (with or without corticosteroids) to Strongyloides. Strongyloides screening and treatment should be considered for individuals receiving low-dose MTX therapy, particularly if combined with additional immunosuppression.

## **Sexual and Reproductive Health**

## 22. Lancet 2019;394(10210):1750-63

How women are treated during facility-based childbirth in four countries: a cross-sectional study with labour observations and community-based surveys

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Background. Women across the world are mistreated during childbirth. We aimed to develop and implement evidence- informed, validated tools to measure mistreatment during childbirth, and report results from a cross-sectional study in four low-income and middle-income countries. Methods. We prospectively recruited women aged at least 15 years in twelve health facilities (three per country) in Ghana, Guinea, Myanmar, and Nigeria between Sept 19, 2016, and Jan 18, 2018. Continuous observations of labour and childbirth were done from admission up to 2 h post partum. Surveys were administered by interviewers in the community to women up to 8 weeks post partum. Labour observations were not done in Myanmar. Data were collected on sociodemographics, obstetric history, and experiences of mistreatment.

Findings. 2016 labour observations and 2672 surveys were done. 838 (41·6%) of 2016 observed women and 945 (35·4%) of 2672 surveyed women experienced physical or verbal abuse, or stigma or discrimination. Physical and verbal abuse peaked 30 min before birth until 15 min after birth (observation). Many women did not consent for episiotomy (observation: 190 [75·1%] of 253; survey: 295 [56·1%] of 526) or caesarean section (observation: 35 [13·4%] of 261; survey: 52 [10·8%] of 483), despite receiving these procedures. 133 (5·0%) of 2672 women or their babies were detained in the facility because they were unable to pay the bill (survey). Younger age (15–19 years) and lack of education were the primary determinants of mistreatment (survey). For example, younger women with no education (odds ratio [OR]  $3\cdot6$ , 95% CI  $1\cdot6$ – $8\cdot0$ ) and younger women with some education (OR  $1\cdot6$ ,  $1\cdot1$ – $2\cdot3$ ) were more likely to experience verbal abuse, compared with older women ( $\geq$ 30 years), adjusting for marital status and parity.

Interpretation. More than a third of women experienced mistreatment and were particularly vulnerable around the time of birth. Women who were younger and less educated were most at risk, suggesting inequalities in how women are treated during childbirth. Understanding drivers and structural dimensions of mistreatment, including gender and social inequalities, is essential to ensure that interventions adequately account for the broader context.

#### Miscellaneous

#### 23. Lancet 2019;394(10203):997-8

World Report

#### Blood transfusion in Kenya faces an uncertain future

Adepoju, P.

By the end of September, 2019, PEPFAR will stop supporting blood transfusion in Kenya, with no clear plan for the future.

Throughout its 25-year history, the Kenya National Blood Transfusion Service (KNBTS) has received financial support from the US Government—at various times through the US Agency for International Development, Centers for Disease Control and Prevention (CDC), and, presently, the US President's Emergency Plan for AIDS Relief (PEPFAR). But it could be without direct US funding from September, 2019, because the PEPFAR fund for the country's blood transfusion service is projected to run out. For 2019, PEPFAR has budgeted US\$350 million as new funding for Kenya, a reduction of nearly \$95 million from the year before. To ensure that the treatment of Kenyans living with HIV/AIDS is not affected by the shortfall, cuts were made elsewhere and funding for blood transfusion services was stopped outright, with the US Government expecting that the Kenyan Government would take over from PEPFAR. A PEPFAR spokesperson said that their substantial support has positioned Kenya to be able to control the HIV/AIDS epidemic by 2020, including its 15-year support for the national blood safety programme.

However, the Kenyan Government is yet to announce any concrete plans to safeguard the country's transfusion service. While refusing to give specific details, the government told The Lancet it is "doing everything possible to ensure there is no disruption in the activities of KNBTS". But experts said disruption is inevitable, and the government has failed to act early and swiftly enough. PEPFAR said that the Kenyan Government had year-on-year notices to plan for the transition and avert crisis. A spokesperson told The Lancet that "planned transition of this modest assistance to [Kenyan Government] responsibility has been underway for several years, through our close consultation with relevant [Kenyan Government] partners, and will be fully completed by Sept 30, 2019. Thanks to long-standing US Government technical assistance and financial support for Kenya's blood safety programme, including the KNBTS, the [Kenyan Government] possesses the necessary technical capacity to effectively manage this programme autonomously". Joseph Wang'endo, CEO of the Bloodlink Foundation, a non-profit trust that is striving to ensure sufficient and safe blood transfusion services in Kenya, said "the reality is that the blood banking system in Kenya has been heavily reliant on PEPFAR, which was not the plan initially. From 2014, the government was expected to increasingly take over the funding of the KNBTS as PEPFAR transitioned. But this has not happened."

In the short term, the government is aiming to avoid a significant drop in the number of blood units by implementing a monthly routine blood drive programme, while for the long term, Kariuki said the health ministry plans to develop a robust legislative and regulatory framework "that will strengthen Kenya's blood transfusion governance structures".

# 24. bmjgh-2019-001853 Research

Stuck in the middle: a systematic review of authorship in collaborative health research in Africa, 2014–2016

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#### Abstract

Background Collaborations are often a cornerstone of global health research. Power dynamics can shape if and how local researchers are included in manuscripts. This article investigates how international collaborations affect the representation of local authors, overall and in first and last author positions, in African health research.

Methods We extracted papers on 'health' in sub-Saharan Africa indexed in PubMed and published between 2014 and 2016. The author's affiliation was used to classify the individual as from the country of the paper's focus, from another African country, from Europe, from the USA/Canada or from another locale. Authors classified as from the USA/Canada were further subclassified if the author was from a top US university. In primary analyses, individuals with multiple affiliations were presumed to be from a high-income country if they contained any affiliation from a high-income country. In sensitivity analyses, these individuals were presumed to be from an African country if they contained any affiliation an African country. Differences in paper characteristics and representation of local coauthors are compared by collaborative type using  $\chi^2$  tests. Results Of the 7100 articles identified, 68.3% included collaborators from the USA, Canada, Europe and/or another African country. 54.0% of all 43 429 authors and 52.9% of 7100 first authors were from the country of the paper's focus. Representation dropped if any collaborators were from USA, Canada or Europe with the lowest representation for collaborators from top US universities—for these papers, 41.3% of all authors and 23.0% of first authors were from country of paper's focus. Local representation was highest with collaborators from another African country. 13.5% of all papers had no local coauthors.

Discussion Individuals, institutions and funders from high-income countries should challenge persistent power differentials in global health research. South-South collaborations can help African researchers expand technical expertise while maintaining presence on the resulting research.