International Health Alerts 2015 Contents

IHA 2015-2

Child Care

1. Am J TMH 2015;92(5):1053-8

Maji: a new tool to prevent overhydration of children receiving intravenous fluid therapy in low-resource settings

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We designed and evaluated the accuracy and usability of a device to regulate the volume of fluid dispensed during intravenous drip therapy. The mechanical system was developed in response to a pressing need articulated by clinicians in pediatric wards throughout sub-Saharan Africa, who require a tool to prevent overhydration in children receiving intravenous fluid in settings that lack burettes or electronic infusion pumps. The device is compatible with most intravenous bags and limits the volume dispensed to a preset amount that can be adjusted in 50 mL increments. Laboratory accuracy over a range of clinically-relevant flow rates, initial bag volumes, and target volumes was within 12.0 mL of the target volume. The ease of use is "excellent," with a mean system usability score of 84.4 out of 100. Use of the device limits the volume of fluid dispensed during intravenous therapy and could potentially reduce the morbidity and mortality associated with overhydration in children receiving intravenous therapy.

2. Lancet 2015;385(9975):1315-23

Effect of early neonatal vitamin A supplementation on mortality during infancy in Ghana (Neovita): a randomised, double-blind, placebo-controlled trial

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Background: Results of randomised controlled trials of newborn (age 1-3 days) vitamin A supplementation have been inconclusive. The WHO is coordinating three large randomised trials in Ghana, India, and Tanzania (Neovita trials). We present the findings of the Neovita trial in Ghana.
Methods: This study was a population-based, individually randomised, double-blind, placebo-controlled trial in the Brong Ahafo region of Ghana. The trial participants were infants aged at least 2 h, identified at home or facilities on the day of birth or in the next 2 days, able to feed orally, and likely to stay in the study area for at least 6 months. They were randomly assigned (ratio 1:1) to receive either one oral dose of vitamin A (50,000 IU) or placebo immediately after recruitment. The research team and parents of the infants were masked to treatment assignment. Follow-up home visits were undertaken every 4 weeks, when data were recorded for deaths, facility use, and care seeking. The primary outcome was post-supplementation mortality to 6 months of age. Analysis was by intention to treat. Potential adverse events were recorded at 1 and 3 days after supplementation. This trial is registered with the Australian New Zealand Clinical Trials Registry (ANZCTR)CTRN12610000582055.
Findings: We assessed 26,414 livebirths for eligibility between Aug 16, 2010, and Nov 7, 2011. We recruited 22,955 newborn infants, with 11,474 randomly assigned to receive vitamin A and 11,481 to receive placebo. Loss to follow-up was low with vital status at 6 months of age reported for 22,698 (98·9%) infants. We recorded 278 post-supplementation deaths to 6 months of age in the vitamin A group (mortality risk 24·5 in 1000 supplemented infants) and 248 deaths in the placebo group (mortality risk 21·8 per 1000 supplemented infants), relative risk (RR) 1·12 (95% CI 0·95-1·33; p=0·183) and risk difference (RD) 2·66 (95% CI -1·25 to 6·57; p=0·18). Adverse events within 3 days of supplementation did not differ by trial group. 122 infants died in the first 3 days after supplementation; 70 (0·6%) in the vitamin A and 52 (0·5%) in the placebo group (risk ratio [RR] 1·35, 95% CI 0·94-1·93, p=0·102). 53 infants were reported to have a bulging fontanelle; 32 (0·3%) in the vitamin A group and 21 (0·2%) in the placebo group (RR 1·53, 0·88-2·62, p=0·130).
Interpretation: The results of this trial do not support inclusion of newborn vitamin A supplementation as a child survival strategy in Ghana.

3. Lancet 2015;385(9975):1324-32

Effect of neonatal vitamin A supplementation on mortality in infants in Tanzania (Neovita): a randomised, double-blind, placebo-controlled trial

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Background: Supplementation of vitamin A in children aged 6-59 months improves child survival and is implemented as global policy. Studies of the efficacy of supplementation of infants in the neonatal period have inconsistent results. We aimed to assess the efficacy of oral supplementation with vitamin A given to infants in the first 3 days of life to reduce mortality between supplementation and 180 days (6 months).
Methods: We did an individually randomised, double-blind, placebo-controlled trial of infants born in the Morogoro and Dar es Salaam regions of Tanzania. Women were identified during antenatal clinic visits or in the labour wards of public health facilities in Dar es Salaam. In Kilombero, Ulanga, and Kilosa districts, women were seen at home as part of the health and demographic surveillance system. Newborn infants were eligible for randomisation if they were able to feed orally and if the family intended to stay in the study area for at least 6 months. We randomly assigned infants to receive one dose of 50,000 IU of vitamin A or placebo in the first 3 days after birth. Infants were randomly assigned in blocks of 20, and investigators, participants' families, and data analysis teams were masked to treatment assignment. We assessed infants on day 1 and day 3 after dosing, as well as at 1, 3, 6, and 12 months after birth. The primary endpoint was mortality at 6 months, assessed by field interviews. The primary analysis included only children who were not lost to follow-up. This trial is registered with the Australian New Zealand Clinical Trials Registry (ANZCTR), number ACTRN12610000636055.
Findings: Between Aug 26, 2010, and March 3, 2013, 31,999 newborn babies were randomly assigned to receive vitamin A (n=15,995) or placebo (n=16,004; 15,428 and 15,464 included in analysis of mortality at 6 months, respectively). We did not find any evidence for a beneficial effect of vitamin A supplementation on mortality in infants at 6 months (26 deaths per 1000 livebirths in vitamin A vs 24 deaths per 1000 livebirths in placebo group; risk ratio 1·10, 95% CI 0·95-1·26; p=0·193). There was no evidence of a differential effect for vitamin A supplementation on mortality by sex; risk ratio for mortality at 6 months for boys was 1·08 (0·90-1·29) and for girls was 1·12 (0·91-1·39). There was also no evidence of adverse effects of supplementation within 3 days of dosing.
Interpretation: Neonatal vitamin A supplementation did not result in any immediate adverse events, but had no beneficial effect on survival in infants in Tanzania. These results strengthen the evidence against a global policy recommendation for neonatal vitamin A supplementation.

4. Lancet 2015;385(9975):1333-42

Efficacy of early neonatal supplementation with vitamin A to reduce mortality in infancy in Haryana, India (Neovita): a randomised, double-blind, placebo-controlled trial

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Background: Vitamin A supplementation in children aged 6 months to 5 years has been shown to reduce mortality. The efficacy of neonatal supplementation with vitamin A to reduce mortality in the first 6 months of life is plausible but not established. We aimed to assess the efficacy of neonatal oral supplementation with vitamin A to reduce mortality between supplementation and 6 months of age.
Methods: We undertook an individually randomised, double-blind, placebo-controlled trial in Haryana, India. We identified pregnant women through a surveillance programme undertaken every 3 months of all female residents in two districts of Haryana, India, aged 15-49 years, and screened every identified livebirth. Eligible participants were neonates whose parents consented to participate, were likely to stay in the study area until at least 6 months of age, and were able to feed orally at the time of enrolment. Participants were randomly assigned to receive oral capsules containing vitamin A (retinol palmitate 50,000 IU plus vitamin E 9·5-12·6 IU) or placebo (vitamin E 9·5-12·6 IU) within 72 h of birth. Randomisation was in blocks of 20 according to a randomisation list prepared by a statistician not otherwise involved with the trial. Investigators, participants' families, and the data analysis team were masked to treatment allocation. The primary outcome was mortality between supplementation

and 6 months of age. Analysis included all participants assigned to study groups. This trial is registered with ClinicalTrials.gov, number NCT01138449, and the Indian Council of Medical Research Clinical Trial Registry, number CTRI/2010/091/000220.
Findings: Between June 24, 2010, and July 1, 2012 we screened 47,777 neonates and randomly assigned 44,984 to receive vitamin A (22,493) or placebo (22,491). Between supplementation and 6 months of age, 656 infants died in the vitamin A group compared with 726 in the placebo group (29·2 per 1000 vs 32·3 per 1000; difference -3·1 per 1000, 95% CI -6·3 to 0·1; risk ratio 0·90, 95% CI 0·81 to 1·00). We noted no significant interactions between the intervention effect and sex on mortality at 6 months (p=0·409). Supplementation with 50,000 IU vitamin A within the first 72 h of life was generally safe and well tolerated, with the exception of a small excess risk of transient bulging fontanelle (205 cases in the vitamin A group confirmed by physician vs 80 cases in the placebo group, risk ratio 2·56 [95% CI 1·98-3·32]).
Interpretation: The findings of this study, done in a population in which vitamin A deficiency is a moderate public health problem, are consistent with a modest reduction in mortality between supplementation and 6 months of age. These findings must be viewed together with similar trials in other populations to enable determination of appropriate public health policy.

5. Lancet 2015;385(9979):1758-66
Oral amoxicillin compared with injectable procaine benzylpenicillin plus gentamicin for treatment of neonates and young infants with fast breathing when referral is not possible: a randomised, open-label, equivalence trial
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Background: WHO recommends referral to hospital for possible serious bacterial infection in young infants aged 0-59 days. We aimed to assess whether oral amoxicillin treatment for fast breathing, in the absence of other signs, is as efficacious as the combination of injectable procaine benzylpenicillin-gentamicin.
Methods: In a randomised, open-label, equivalence trial at five sites in DR Congo, Kenya, and Nigeria, community health workers followed up all births in the community, identified unwell young infants, and referred them to study nurses. We randomly assigned infants with fast breathing as a single sign of illness or possible serious bacterial infection, whose parents did not accept referral to hospital, to receive either injectable procaine benzylpenicillin-gentamicin once per day or oral amoxicillin treatment twice per day for 7 days. A person who was off-site generated randomisation lists using computer software. Trained health professionals gave injections, but outcome assessors were masked to group allocations. The primary outcome was treatment failure by day 8 after enrolment, defined as clinical deterioration, development of a serious adverse event including death, persistence of fast breathing on day 4, or recurrence up to day 8. The primary analysis was per protocol and we used a prespecified similarity margin of 5% to assess equivalence between regimens. This study is registered with the Australian New Zealand Clinical Trials Registry, number ACTRN12610000286044.
Findings: From April 4, 2011, to March 29, 2013, we enrolled 2333 infants aged 0-59 days with fast breathing as the only sign of possible serious bacterial infection at the five study sites. We assigned 1170 infants to receive injectable procaine benzylpenicillin-gentamicin and 1163 infants to receive oral amoxicillin. In the per-protocol analysis, from which 137 infants were excluded, we included 1061 (91%) infants who fulfilled predefined criteria of adherence to treatment and adequate follow-up in the injectable procaine benzylpenicillin-gentamicin group and 1145 (98%) infants in the oral amoxicillin group. In the procaine benzylpenicillin-gentamicin group, 234 infants (22%) failed treatment, compared with 221 (19%) infants in the oral amoxicillin group (risk difference -2·6%, 95% CI -6·0 to 0·8). Four infants died within 15 days of follow-up in each group. We detected no drug-related serious adverse events.
Interpretation: Young infants with fast breathing alone can be effectively treated with oral amoxicillin on an outpatient basis when referral to a hospital is not possible.

6. Lancet 2015;385(9979):1767-76

Simplified antibiotic regimens compared with injectable procaine benzylpenicillin plus gentamicin for treatment of neonates and young infants with clinical signs of possible serious bacterial infection when referral is not possible: a randomised, open-label, equivalence trial

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Background: WHO recommends hospital-based treatment for young infants aged 0-59 days with clinical signs of possible serious bacterial infection, but most families in resource-poor settings cannot accept referral. We aimed to assess whether use of simplified antibiotic regimens to treat young infants with clinical signs of severe infection was as efficacious as an injectable procaine benzylpenicillin-gentamicin combination for 7 days for situations in which hospital referral was not possible.
Methods: In a multisite open-label equivalence trial in DR Congo, Kenya, and Nigeria, community health workers visited all newborn babies at home, identifying and referring unwell young infants to a study nurse. We stratified young infants with clinical signs of severe infection whose parents did not accept referral to hospital by age (0-6 days and 7-59 days), and randomly assigned each individual within these strata to receive one of the four treatment regimens. Randomisation was stratified by age group of infants. An age-stratified randomisation scheme with block size of eight was computer-generated off-site at WHO. The outcome assessor was masked. We randomly allocated infants to receive injectable procaine benzylpenicillin-gentamicin for 7 days (group A, reference group); injectable gentamicin and oral amoxicillin for 7 days (group B); injectable procaine benzylpenicillin-gentamicin for 2 days, then oral amoxicillin for 5 days (group C); or injectable gentamicin for 2 days and oral amoxicillin for 7 days (group D). Trained health professionals gave daily injections and the first dose of oral amoxicillin. Our primary outcome was treatment failure by day 8 after enrolment, defined as clinical deterioration, development of a serious adverse event (including death), no improvement by day 4, or not cured by day 8. Independent outcome assessors, who did not know the infant's treatment regimen, assessed study outcomes on days 4, 8, 11, and 15. Primary analysis was per protocol. We used a prespecified similarity margin of 5% to assess equivalence between regimens. This study is registered with the Australian New Zealand Clinical Trials Registry, number ACTRN12610000286044.
Findings: In Kenya and Nigeria, we started enrolment on April 4, 2011, and we enrolled the necessary number of young infants aged 7 days or older from Oct 17, 2011, to April 30, 2012. At these sites, we continued to enrol infants younger than 7 days until March 29, 2013. In DR Congo, we started enrolment on Sept 17, 2012, and continued until June 28, 2013. We randomly assigned 3564 young infants to either group A (n=894), group B (n=884), group C (n=896), or group D (n=890). We excluded 200 randomly assigned infants, who did not fulfil the predefined criteria of adherence to treatment and adequate follow-up. In the per-protocol analysis, 828 infants were included in group A, 826 in group B, 862 in group C, and 848 in group D. 67 (8%) infants failed treatment in group A compared with 51 (6%) infants in group B (risk difference -1·9%, 95% CI -4·4 to 0·1), 65 (8%) in group C (-0·6%, -3·1 to 2·0), and 46 (5%) in group D (-2·7%, -5·1 to 0·3). Treatment failure in groups B, C, and D was within the similarity margin compared with group A. During the 15 days after random allocation, 12 (1%) infants died in group A, compared with ten (1%) infants in group B, 20 (2%) infants in group C, and 11 (1%) infants in group D. An infant in group A had a serious adverse event other than death (injection abscess).
Interpretation: The three simplified regimens were as effective as injectable procaine benzylpenicillin-gentamicin for 7 days on an outpatient basis in young infants with clinical signs of severe infection, without signs of critical illness, and whose caregivers did not accept referral for hospital admission.

7. TMIH 2015;20(4):484-92

Implementing WHO hospital guidelines improves quality of paediatric care in central hospitals in Lao PDR

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Objectives: To evaluate the impact of implementing a multifaceted intervention based on the WHO Pocketbook of Hospital Care for Children on the quality of case management of common childhood illnesses in hospitals in Lao PDR
Methods: The quality of case management of four sentinel conditions was assessed in three central hospitals before and after the implementation of the WHO Pocketbook as part of a broader mixed-methods study. Data on performance of key steps in case management in more than 600 admissions were collected by medical record abstraction pre- and post-intervention, and change was measured according to the proportion of cases which key steps were performed as well as an overall score of case management for each condition.
Results: Improvements in mean case management scores were observed post-intervention for three of the four conditions, with the greatest change in pneumonia (53-91%), followed by diarrhoea and low birthweight. Rational drug prescribing, appropriate use of IV fluids and appropriate monitoring all occurred more frequently post-intervention. Non-recommended practices such as prescription of antitussives became less frequent.
Conclusions: A multifaceted intervention based on the WHO Pocketbook of Hospital Care for children led to better paediatric care in central Lao hospitals. The degree of improvement was dependent on the condition assessed.

Communicable diseases

8. BMJ 2015;350:h1394

Practice: Pityriasis versicolor

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Pityriasis versicolor is a superficial fungal infection of the skin. It is caused by Malassezia, a lipophilic dimorphic fungus. This fungus is part of the normal skin flora but can cause disease when it converts to its pathogenic hyphal form. Certain environmental, genetic, and immunological factors can predispose to this pathogenic conversion and contribute to the development of disease.
The fungus grows best in warm and humid conditions, explaining the higher prevalence of pityriasis versicolor in humid tropical climates. A survey in central Sweden found a 0.5% prevalence of pityriasis versicolor, whereas the prevalence is as high as 50% in tropical countries. There is a significant increase in disease prevalence between childhood and adolescence, probably due to hormonal changes that increase sebum production and allow for a more lipid-rich environment in which the fungus can grow. The disease is also more common among adolescents and young adults who are physically active.3 Although effective oral and topical treatment options exist, disease recurrence is common and pityriasis versicolor can have an impact on quality of life.
The bottom line.
Pityriasis versicolor is a superficial fungal infection of the skin caused by Malassezia species that induces a characteristic rash of well demarcated, thin, scaly plaques that can be hypopigmented, hyperpigmented, or erythematous.
Diagnosis is usually made clinically, based on characteristic skin lesions and the “evoked scale sign” (when stretching or scraping the skin makes the fine scale of lesions more apparent).
Diagnosis is aided by microscopic examination of potassium hydroxide treated or stained skin scrapings, which reveal numerous spores and hyphae.
First line topical treatments include ketoconazole, selenium sulphide, or zinc pyrithione shampoo.
Systemic treatment is limited to use in extensive disease.
Disease recurrence is common; options for prophylaxis include topical ketoconazole, selenium sulphide, or zinc pyrithione shampoo.

9. BMJ 2015;350:h2105

Editorial: Ebola and ethics: autopsy of a failure

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Thousands died while we argued over the wrong questions.
The current epidemic of Ebola virus disease has attracted medical ethics commentators like bees to a honey pot. No previous infectious disease epidemic has elicited such a flurry of articles on the ethical challenges associated with infection control and treatment in such a short time. Has this been of any use?
The ethical questions raised by various authors broadly fall into three categories. The first relates to questions of individual medical ethics, in particular surrounding the compassionate use of experimental drugs and vaccines. The second concerns allocation of resources to these experimental treatments versus infection control. And the third centres on how resources should be spent in the long term—on building a public health and clinical infrastructure that can cope in an epidemic instead of propping up a weak infrastructure during a humanitarian crisis.
The tension between these moral challenges can be grouped along two axes: individual versus public health, and short term versus long term.

10. Lancet 2015;385(9973):1136-45

Typhoid fever

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Control of typhoid fever relies on clinical information, diagnosis, and an understanding for the epidemiology of the disease. Despite the breadth of work done so far, much is not known about the biology of this human-adapted bacterial pathogen and the complexity of the disease in endemic areas, especially those in Africa. The main barriers to control are vaccines that are not immunogenic in very young children and the development of multidrug resistance, which threatens efficacy of antimicrobial chemotherapy. Clinicians, microbiologists, and epidemiologists worldwide need to be familiar with shifting trends in enteric fever. This knowledge is crucial, both to control the disease and to manage cases. Additionally, salmonella serovars that cause human infection can change over time and location. In areas of Asia, multidrug-resistant Salmonella enterica serovar Typhi (S Typhi) has been the main cause of enteric fever, but now S Typhi is being displaced by infections with drug-resistant S enterica serovar Paratyphi A. New conjugate vaccines are imminent and new treatments have been promised, but the engagement of local medical and public health institutions in endemic areas is needed to allow surveillance and to implement control measures.
(Paragraphs: Introduction, Typhoid fever in Asia, Typhiod fever in Africa, Antimicrobial drug resistance, Conclusions.)

11. TMIH 2015;20(5):638-642

Prevalence of hepatitis C virus in mothers and their children in Malawi

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Objectives: Hepatitis C virus (HCV) prevalence is poorly mapped in the East African region; with the advent of novel HCV therapies, better epidemiological data are required to target the infection. We sought to estimate HCV prevalence in healthy Malawian mothers and assess mother-to-child transmission (MTCT); context is provided by reviewing previously published HCV prevalence data from the region.
Methods: Using ELISA screening and confirmatory blot, serological testing of 418 healthy Malawian mothers for HCV was performed. To examine MTCT, the children of any positive women were also tested for HCV; all children had malignant disease unrelated to hepatocellular carcinoma. We compared our results to published literature on HCV prevalence in Malawi and its neighbouring countries.
Results: Three of 418 women were HCV reactive by ELISA; two were confirmed positive by immunoblot (0.5%). One child of an HCV-infected mother was HCV seropositive. The literature review revealed HCV prevalence ranging from 0 to 7.2% in the region, being highest in Tanzania and specifically for cohorts of inpatients and HIV-co-infected people. The overall estimated prevalence of

HCV in Malawi was 1.0% (95%CI 0.7-1.4) when all studies were included (including this one), but lower in healthy cohorts alone at 0.3% (95%CI 0.1-1.2).
Conclusions: This is the first study using confirmatory tests to examine HCV prevalence in healthy Malawian mothers; the prevalence was low. Future studies need to address the source of infection in healthy women.

HIV / AIDS

12. TMIH 2015;20(4):430-47
Reframing HIV care: putting people at the centre of antiretroviral delivery
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The delivery of HIV care in the initial rapid scale-up of HIV care and treatment was based on existing clinic-based models, which are common in highly resourced settings and largely undifferentiated for individual needs. A new framework for treatment based on variable intensities of care tailored to the specific needs of different groups of individuals across the cascade of care is proposed here. Service intensity is characterised by four delivery components: (i) types of services delivered, (ii) location of service delivery, (iii) provider of health services and (iv) frequency of health services. How these components are developed into a service delivery framework will vary across countries and populations, with the intention being to improve acceptability and care outcomes. The goal of getting more people on treatment before they become ill will necessitate innovative models of delivering both testing and care. As HIV programmes expand treatment eligibility, many people entering care will not be 'patients' but healthy, active and productive members of society. To take the framework to scale, it will be important to: (i) define which individuals can be served by an alternative delivery framework; (ii) strengthen health systems that support decentralisation, integration and task shifting; (iii) make the supply chain more robust; and (iv) invest in data systems for patient tracking and for programme monitoring and evaluation.

13. TMIH 2015;20(4):518-26
Renal impairment in HIV-infected patients initiating tenofovir-containing antiretroviral therapy regimens in a Primary Healthcare Setting in South Africa
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Objective: Long-term use of tenofovir disoproxil fumarate is associated with declines in glomerular function and chronic kidney disease in HIV-infected patients. We aimed to assess the prevalence and incidence of renal impairment in a primary care setting in sub-Saharan Africa.
Methods: We analysed data from 1092 HIV-infected patients initiating tenofovir at a primary care clinic in Cape Town, South Africa. Renal function was assessed for the first 12 months on ART by estimating glomerular filtration rate (eGFR) calculated using the Cockroft-Gault equation categorised into normal, mild, moderate and severe reduction in renal function based on values >90, 60-89, 30-59 and <30 ml/min/1.73 m(2) , respectively. Associations were assessed using logistic regression, and average GFR trajectory over time was modelled using linear mixed-effects models.
Results: The cohort consisted of 62% women; median age was 34 years (IQR 29; 41 years). The majority had normal renal function pre-ART (79%), 19% had mildly reduced GFR, and 2% had moderate renal impairment. Older age, more advanced WHO stage and anaemia were independently associated with prevalent renal impairment. On average, estimated glomerular function improved over the first year on tenofovir [1.10 ml/min/1.73 m(2) average increase over 12 months (95% CI: 0.80; 1.40)]. Male gender, anaemia and immunosuppression (WHO Stage III/IV and CD4 cell counts <100 cells/mm(3)) were associated with lower average eGFR levels over time. Overall, 3% developed eGFR <50 ml/min/1.73 m(2) during this period. Serum creatinine tests conducted before 4 months on ART had low predictive value for predicting change in eGFR after a year on ART.

Conclusion: Generally, renal function improved in HIV-infected adults initiating ART in this primary healthcare setting during the first year on ART. While monitoring of renal function is recommended in the first 4 months on ART, renal impairment appears uncommon during the first 12 months of tenofovir-containing ART in primary care populations.

14. TMIH 2015;20(6):791-6

Improvement in mortality and retention among adult HIV-infected patients in the first 12 months of antiretroviral therapy in Dodoma urban district,Tanzania

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Objective: To determine mortality and retention in ART programmes in Tanzania, between 2010 and 2013.
Methods: Retrospective routinely collected data were analysed from people starting ART in the period 2010-2013. Mortality and retention over the first 12 months on ART were compared across the 4 years, and adjustment was made for individual level potential confounders.
Results: Data from 3844 people (70.6% female) starting ART were analysed. Mortality in the first year declined from 11.4% in 2010 to 4.9% in 2013, and retention after 12 months increased from 77.8% in 2010 to 98.1% in 2013. Mortality was inversely associated with CD4 count, lowest among those with CD4 350+ cells/μl [adjusted odds ratio (AOR) = 0.03, 95% CI 0.01-0.03], associated with male sex (AOR = 1.79, 95% CI 1.39-2.31), but not age. Lost to follow-up (LTFU) was lowest among those with CD4 = 350+ cells/μl AOR = 0.20, 95% CI 0.10-0.30), but not associated with age or sex, and higher in urban health facilities (AOR = 1.88, 95% CI 1.15-3.09). After adjustment for individual level characteristics, there was a statistically significant yearly improvement in mortality (AOR = 0.31, 95% CI (0.21-0.44) and LTFU (AOR = 0.06, 95% CI 0.04-0.10).
Conclusion: Mortality and retention in the first 12 months on ART have significantly improved over the 4 years from 2010 to 2013. These improvements may indicate better services, earlier initiation on ART, and strengthened systems to provide ART in Tanzania. These results refute the worries that earlier initiation on ART might lead to lower retention in the ART programme

Malaria

15. Am J TMH 2015;92(5):933-40

Sociocultural and structural factors contributing to delays in treatment for children with severe malaria: a qualitative study in southwestern Uganda

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Malaria is a leading cause of pediatric mortality, and Uganda has among the highest incidences in the world. Increased morbidity and mortality are associated with delays to care. This qualitative study sought to characterize barriers to prompt allopathic care for children hospitalized with severe malaria in the endemic region of southwestern Uganda. Minimally structured, qualitative interviews were conducted with guardians of children admitted to a regional hospital with severe malaria. Using an inductive and content analytic approach, transcripts were analyzed to identify and define categories that explain delayed care. These categories represented two broad themes: sociocultural and structural factors. Sociocultural factors were 1) interviewee's distinctions of "traditional" versus "hospital" illnesses, which were mutually exclusive and 2) generational conflict, where deference to one's elders, who recommended traditional medicine, was expected. Structural factors were 1) inadequate distribution of health-care resources, 2) impoverishment limiting escalation of care, and 3) financial impact of illness on household economies. These factors perpetuate a cycle of illness, debt, and poverty consistent with a model of structural violence. Our findings inform a number of potential interventions that could alleviate the burden of this preventable, but often fatal, illness. Such interventions could be beneficial in similarly endemic, low-resource settings.

16. BMJ 2015;350:h1019

Research: The impact of providing rapid diagnostic malaria tests on fever management in the private retail sector in Ghana: a cluster randomized trial

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Objective: To examine the impact of providing rapid diagnostic tests for malaria on fever management in private drug retail shops where most poor rural people with fever present, with the aim of reducing current massive overdiagnosis and overtreatment of malaria.
Design: Cluster randomized trial of 24 clusters of shops.
Setting: Dangme West, a poor rural district of Ghana.
Participants: Shops and their clients, both adults and children.
Interventions: Providing rapid diagnostic tests with realistic training.
Main outcome measures: The primary outcome was the proportion of clients testing negative for malaria by a double-read research blood slide who received an artemisinin combination therapy or other antimalarial. Secondary outcomes were use of antibiotics and antipyretics, and safety.
Results: Of 4603 clients, 3424 (74.4%) tested negative by double-read research slides. The proportion of slide-negative clients who received any antimalarial was 590/1854 (32%) in the intervention arm and 1378/1570 (88%) in the control arm (adjusted risk ratio 0.41 (95% CI 0.29 to 0.58), P<0.0001). Treatment was in high agreement with rapid diagnostic test result. Of those who were slide-positive, 690/787 (87.8%) in the intervention arm and 347/392 (88.5%) in the control arm received an artemisinin combination therapy (adjusted risk ratio 0.96 (0.84 to 1.09)). There was no evidence of antibiotics being substituted for antimalarials. Overall, 1954/2641 (74%) clients in the intervention arm and 539/1962 (27%) in the control arm received appropriate treatment (adjusted risk ratio 2.39 (1.69 to 3.39), P<0.0001). No safety concerns were identified.
Conclusions: Most patients with fever in Africa present to the private sector. In this trial, providing rapid diagnostic tests for malaria in the private drug retail sector significantly reduced dispensing of antimalarials to patients without malaria, did not reduce prescribing of antimalarials to true malaria cases, and appeared safe. Rapid diagnostic tests should be considered for the informal private drug retail sector.

17. Lancet 2015;385(9976):1436-46

Efficacy of indoor residual spraying with dichlorodiphenyltrichloroethane against malaria in Gambian communities with high usage of long-lasting insecticidal mosquito nets: a cluster-randomised controlled trial

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Background: Although many malaria control programmes in sub-Saharan Africa use indoor residual spraying with long-lasting insecticidal nets (LLINs), the two studies assessing the benefit of the combination of these two interventions gave conflicting results. We aimed to assess whether the addition of indoor residual spraying to LLINs provided a significantly different level of protection against clinical malaria in children or against house entry by vector mosquitoes.
Methods: In this two-arm cluster, randomised, controlled efficacy trial we randomly allocated clusters of Gambian villages using a computerised algorithm to LLINs alone (n=35) or indoor residual spraying with dichlorodiphenyltrichloroethane plus LLINs (n=35). In each cluster, 65-213 children, aged 6 months to 14 years, were surveyed at the start of the 2010 transmission season and followed in 2010 and 2011 by passive case detection for clinical malaria. Exposure to parasite transmission was assessed by collection of vector mosquitoes with both light and exit traps indoors. Primary endpoints were the incidence of clinical malaria assessed by passive case detection and number of Anopheles gambiae sensu lato mosquitoes collected per light trap per night. Intervention teams had no role in data collection and the data collection teams were not informed of the spray status of villages. The trial is registered at the ISRCTN registry, number ISRCTN01738840.
Findings: LLIN coverage in 2011 was 3510 (93%) of 3777 children in the indoor residual spraying plus LLIN group and 3622 (95.5%) of 3791 in the LLIN group. In 2010, 7845 children were enrolled, 7829 completed passive case detection, and 7697 (98%) had complete clinical and covariate data. In 2011, 7009 children remained in the study, 648 more were enrolled, 7657 completed passive case

detection, and 7545 (98.5%) had complete data. Indoor residual spraying coverage per cluster was more than 80% for both years in the indoor residual spraying plus LLIN group. Incidence of clinical malaria was 0.047 per child-month at risk in the LLIN group and 0.044 per child-month at risk in the indoor residual spraying plus LLIN group in 2010, and 0.032 per child-month at risk in the LLIN group and 0.034 per child-month at risk in the indoor residual spraying plus LLIN group in 2011. The incident rate ratio was 1.08 (95% CI 0.80-1.46) controlling for confounders and cluster by mixed-effect negative binomial regression on all malaria attacks for both years. No significant difference was recorded in the density of vector mosquitoes caught in light traps in houses over the two transmission seasons; the mean number of A gambiae sensu lato mosquitoes per trap per night was 6.7 (4.0-10.1) in the LLIN group and 4.5 (2.4-7.4) in the indoor residual spraying plus LLIN group (p=0.281 in the random-effects linear regression model).
Interpretation: We identified no significant difference in clinical malaria or vector density between study groups. In this area with high LLIN coverage, moderate seasonal transmission, and susceptible vectors, indoor residual spraying did not provide additional benefit.

18. TMIH 2015;20(6):744-56
Availability and price of malaria rapid diagnostic tests in the public and private health sectors in 2011: results from 10 nationally representative cross-sectional retail surveys
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Objectives: To describe the state of the public and private malaria diagnostics market shortly after WHO updated its guidelines for testing all suspected malaria cases prior to treatment.
Methods: Ten nationally representative cross-sectional cluster surveys were conducted in 2011 among public and private health facilities, community health workers and retail outlets (pharmacies and drug shops) in nine countries (Tanzania mainland and Zanzibar surveyed separately). Eligible outlets had antimalarials in stock on the day of interview or had stocked antimalarials in the past 3 months.
Results: Three thousand four hundred and thirty-nine rapid diagnostic test (RDT) products from 39 manufacturers were audited among 12 197 outlets interviewed. Availability was typically highest in public health facilities, although availability in these facilities varied greatly across countries, from 15% in Nigeria to >90% in Madagascar and Cambodia. Private for-profit sector availability was 46% in Cambodia, 20% in Zambia, but low in other countries. Median retail prices for RDTs in the private for-profit sector ranged from $0.00 in Madagascar to $3.13 in Zambia. The reported number of RDTs used in the 7 days before the survey in public health facilities ranged from 3 (Benin) to 50 (Zambia).
Conclusions: Eighteen months after WHO updated its case management guidelines, RDT availability remained poor in the private sector in sub-Saharan Africa. Given the ongoing importance of the private sector as a source of fever treatment, the goal of universal diagnosis will not be achievable under current circumstances. These results constitute national baselines against which progress in scaling-up diagnostic tests can be assessed.

Tuberculosis

19. BMJ 2015;350:h882
Clinical Review: Multidrug resistant tuberculosis
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Tuberculosis remains a major cause of morbidity and mortality globally, with an estimated nine million people developing the disease and 1.5 million deaths in 2013; equating to 4100 deaths a day.1 Nevertheless, considerable gains have been made in international tuberculosis control; incidence rates are decreasing (albeit slowly) and mortality has been reduced by 45% worldwide. The advent of multidrug resistant tuberculosis threatens this progress. In this review we detail the challenges faced globally in the diagnosis, treatment, and control of multidrug resistant tuberculosis and why this matters to high and low burden multidrug resistant tuberculosis settings alike.

The bottom line. Multidrug resistant tuberculosis refers to tuberculosis with resistance to at least rifampicin and isoniazid. Multidrug resistant tuberculosis is increasingly common; however, there is a large shortfall between the estimated total number of cases and the numbers diagnosed and treated Diagnosis is hampered by lack of access to quality assured diagnostics, although newer, rapid molecular and phenotypic methods may go some way to improving this situation
Compared with drug susceptible tuberculosis, treatment for multidrug resistant tuberculosis requires the use of drug regimens that are prolonged (18-24 months), less efficacious, and noticeably more toxic; new drugs and regimens are becoming available for the first time in decades and ongoing trials should define how best they should be used Worldwide, treatment success is only around 50%; however, several settings, including some low income countries, have proved that higher success rates are achievable.

20. BMJ 2015;350:h108

Editorial: Tuberculosis in India

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An ancient enemy just gets stronger.
Twenty years ago it was widely believed that India was successfully on its way to controlling its alarming tuberculosis (TB) epidemic. The country's massive scale-up and implementation of directly observed treatment short course (DOTS) therapy under the Revised National Tuberculosis Control Program (RNTCP) was lauded internationally as a global model of excellence.
Yet this represented only half of the story of TB in India. A terrifying picture of the death, devastation, poverty, and suffering caused by TB began to emerge almost two decades later, when it became apparent that TB in India was not just a national crisis but a global one. Each year India has 2.2 million new cases, more than 300 000 deaths, and economic losses of $23bn (£14.9bn; €20.3bn) from TB, making it India's biggest health crisis. At the heart of this crisis is the failure of India's RNTCP to engage and monitor the country's large and unregulated private sector. This is where most patients with TB seek initial care despite extensive evidence of inaccurate diagnostics and inappropriate treatment. Despite positive developments the general perception remains that India's TB programme has failed to control disease and to reach out to poor and marginalised people who need its help most. India needs to do much more if it seriously wants to control its TB epidemic. This will require immediate and massive investment in public health infrastructure, particularly new diagnostics and treatment. It also needs to tackle the long neglected social determinants of TB. A group of experts recently put together recommendations for India's prime minister, urging him to tackle TB as a national emergency. In particular, these experts focused on issues of public awareness, diagnosis, treatment, drug resistance, nutritional support, and private sector engagement. This was a reminder that effective TB control needs more than new strategies: it needs political will and commitment, backed by sufficient resources. Unless this happens, TB will continue to be India's silent epidemic and a death sentence for poor people.

21. BMJ 2015;350:h1235

Views & Reviews Personal View: India should screen all tuberculosis patients for drug resistant disease at diagnosis

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Inadequate screening for drug resistance.
A first step in prevention is early screening for drug resistance in all patients with TB. With improved screening from 2011 to 2013 the number of notified cases of MDR TB in India each year increased nearly sixfold to 25 244. However, this is still far short of the estimated 62 000 incident cases of MDR TB each year.

India plans to offer drug susceptibility testing, first to patients with presumptive MDR TB, such as those who have previously received treatment, and by 2015 to all adult patients with pulmonary disease. Adults with extrapulmonary disease and children are not yet included in the patients to be investigated.
Only 248 341 of 1 415 617 patients (17.5%) who were registered with the national programme up to 2013 underwent drug susceptibility testing; this needs to be scaled up much more quickly. A diagnostic strategy that investigates only presumptive MDR cases will miss out as much as half of patients with MDR TB. Screening should be offered to all patients with TB at the time of diagnosis and not only when they fail to improve.
The World Health Organization recommends testing for drug resistance either to isoniazid and rifampicin or to rifampicin alone. In many countries, including India, the current focus is on promoting cartridge based nucleic acid amplification tests (CBNAATs) to pick up rifampicin resistance alone as a surrogate for MDR TB . This strategy misses out isoniazid monoresistance.

22. TMIH 2015;20(4):537-45

Identifying locations of recent TB transmission in rural Uganda: a multidisciplinary approach

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Objectives: Targeting high Tuberculosis (TB) transmission sites may offer a novel approach to TB prevention in sub-Saharan Africa. We sought to characterise TB transmission sites in a rural Ugandan township.
Methods: We recruited adults starting TB treatment in Tororo, Uganda, over 1 year. Fifty four TB cases provided names of frequent contacts, sites of residence, health care, work and social activities, and two sputum samples. Mycobacterium tuberculosis (MTB) culture-positive specimens underwent spoligotyping to identify strains with shared genotypes. We visualised TB case social networks, and obtained, mapped and geo-coded global positioning system measures for every location that cases reported frequenting 1 month before treatment. Locations of spatial overlap among genotype-clustered cases were considered potential transmission sites.
Results: Six distinct genotypic clusters were identified involving 21 of 33 (64%) MTB culture-positive, genotyped cases; none shared a home. Although 18 of 54 (33%) TB cases shared social network ties, none of the genotype-clustered cases shared social ties. Using spatial analysis, we identified potential sites of within-cluster TB transmission for five of six genotypic clusters. All sites but one were healthcare and social venues, including sites of drinking, worship and marketplaces. Cases reported spending the largest proportion of pre-treatment person-time (22.4%) at drinking venues.
Conclusions: Using molecular epidemiology, geospatial and social network data from adult TB cases identified at clinics, we quantified person-time spent at high-risk locations across a rural Ugandan community and determined the most likely sites of recent TB transmission to be healthcare and social venues. These sites may not have been identified using contact investigation alone.

Farmaceuticals

23. Am J TMH 2015; Apr 20. pii: 15-0221

The Global Pandemic of Falsified Medicines: Laboratory and Field Innovations and Policy Perspectives: Summary

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This supplement to the American Journal of Tropical Medicine and Hygiene, entitled "The pandemic of falsified medicines: laboratory and field innovations and policy perspectives," showcases 17 articles on detection technologies and methods, field surveillance data, multisectorial perspectives, and policy interventions and recommendations needed to create a coordinated and effective response to curb the pandemic of poor-quality medicines. The goal of this special issue is to alert scientists, public health

authorities, and decision makers to the problem of poor-quality drugs and to take prompt actions to mitigate and resolve the growing peril.

- Responding to the Pandemic of Falsified Medicines. Am J TMH 2015; Apr 20. pii: 14-0393
- Monitoring the Quality of Medicines: Results from Africa, Asia, and South America. Am J TMH 2015; Apr 20. pii: 14-0535
- Stopping Murder by Medicine: Introducing the Model Law on Medicine Crime. Am J TMH 2015; Apr 20. pii: 15-0154
- Collaborative Health and Enforcement Operations on the Quality of Antimalarials and Antibiotics in Southeast Asia. Am J TMH 2015; Apr 20. pii: 14-0574
- Estimated Under-Five Deaths Associated with Poor-Quality Antimalarials in Sub-Saharan Africa. Am J TMH 2015 ;Apr 20. pii: 14-0725
- Quality of the Antibiotics-Amoxicillin and Co-Trimoxazole from Ghana, Nigeria, and the United Kingdom. Am J TMH 2015; Apr 20. pii: 14-0539
- Integration of Novel Low-Cost Colorimetric, Laser Photometric, and Visual Fluorescent Techniques for Rapid Identification of Falsified Medicines in Resource-Poor Areas: Application to Artemether-Lumefantrine. Am J TMH 2015; Apr 20. pii: 14-0832
- Quality of Artemisinin-Containing Antimalarials in Tanzania's Private Sector-Results from a Nationally Representative Outlet Survey. Am J TMH 2015; Apr 20. pii: 14-0544
- Quality of Antimalarials at the Epicenter of Antimalarial Drug Resistance: Results from an Overt and Mystery Client Survey in Cambodia. Am J TMH 2015; Apr 20. pii: 14-0391
- A Repeat Random Survey of the Prevalence of Falsified and Substandard Antimalarials in the Lao PDR: A Change for the Better. Am J TMH 2015; Apr 20. pii: 15-0057
- Rapid and Specific Drug Quality Testing Assay for Artemisinin and Its Derivatives Using a Luminescent Reaction and Novel Microfluidic Technology. Am J TMH 2015; Apr 20. pii: 14-0392
- Counterfeit Drug Penetration into Global Legitimate Medicine Supply Chains: A Global Assessment. Am J TMH 2015; Apr 20. pii: 14-0389
- Chemical and Bioassay Techniques to Authenticate Quality of the Anti-Leishmanial Drug Miltefosine. Am J TMH 2015; Apr 20. pii: 14-0586

24. BMJ 2015;350:h2178

Feature Generic Drugs: Can (and should) Africa make its own medicines?

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Africa has a huge burden of disease but makes few of its own drugs. Mara Kardas-Nelson reports on the region's nascent pharmaceutical industry and its chances of success.

Support for Africa producing medicines is in vogue these days. The World Health Organization executive director, Margaret Chan, supports it. So does Michel Sidibé, head of UNAIDS. "The goal is to address health inequities and build capacity to meet supply shortages for essential health commodities that cannot be sourced reliably and sustainably from outside the continent," they wrote last year. Major international organisations and donors, from the UN Industrial Development Organization (Unido) to the German Federal Enterprise for International Cooperation, are providing technical assistance to make local production happen, and the African Union has put together a business plan to spur its implementation.

The rationale for local production is simple: it is assumed that big donors bankrolling many of Africa's programmes for HIV, tuberculosis, and malaria, three of the continent's biggest killers, won't stick around forever. Africa imports 70% of its drugs, and if African countries have to pick up more of the tab, some drugs could instead be produced at home, bolstering local economies. Local production might also provide a more steady supply of medicines, ensuring that drugs are immediately available during local health emergencies and even in the face of international shocks, such as when the Chinese government closed down its chemical companies during the Beijing Olympics, leading to shortages of active pharmaceutical ingredients used by some African countries.

Local production could also give greater control to overstretched African regulators, which are battling against low quality drugs, sometimes made in far-off factories that are difficult to monitor.

25. TMIH 2015;20(6):797-806

Adverse Drug Reaction reports for cardiometabolic drugs from sub-Saharan Africa: a study in VigiBase

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Objective: Identifying key features in individual case safety reports (ICSR) of suspected adverse drug reactions (ADRs) with cardiometabolic drugs from sub-Saharan Africa (SSA) compared with reports from the rest of the world (RoW).
Methods: Reports on suspected ADRs of cardiometabolic drugs (ATC: A10[antidiabetic], B01[antithrombotics] and C[cardiovascular]) were extracted from WHO Global database, VigiBase(®) (1992-2013). We used vigiPoint, a logarithmic odds ratios (log2 OR)-based method to study disproportional reporting between SSA and RoW. Case-defining features were considered relevant if the lower limit of the 99% CI > 0.5.
Results: In SSA, 3773 (9%) of reported ADRs were for cardiometabolic drugs, in RoW for 18%. Of these, 79% originated from South Africa and 81% were received after 2007. Most reports were for drugs acting on the renin-angiotensin system (36% SSA & 14% RoW). Compared with RoW, reports were more often sent for patients 18-44 years old (log2 OR 0.95 [99 CI 0.80; 1.09]) or with non-fatal outcome (log2 OR 1.16 [99 CI 1.10; 1.22]). Eight ADRs (cough, angioedema, lip swelling, face oedema, swollen tongue, throat irritation, drug ineffective and blood glucose abnormal) and seven drugs (enalapril, rosuvastatin, perindopril, vildagliptin, insulin glulisine, nifedipine and insulin lispro) were disproportionally more reported in SSA than in the RoW.
Conclusions: 'In recent years, the number of adverse drug reactions (ADRs) reported in Sub-Saharan Africa (SSA) has sharply increased. The data showed the well-known population-based differential ADR profile of ACE inhibitors in the SSA population.

Gender

26. Lancet 2015;385(9977):1555-66

Prevention of violence against women and girls: what does the evidence say?

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In this Series paper, we review evidence for interventions to reduce the prevalence and incidence of violence against women and girls. Our reviewed studies cover a broad range of intervention models, and many forms of violence--ie, intimate partner violence, non-partner sexual assault, female genital mutilation, and child marriage. Evidence is highly skewed towards that from studies from high-income countries, with these evaluations mainly focusing on responses to violence. This evidence suggests that women-centred, advocacy, and home-visitation programmes can reduce a woman's risk of further victimisation, with less conclusive evidence for the preventive effect of programmes for perpetrators. In low-income and middle-income countries, there is a greater research focus on violence prevention, with promising evidence on the effect of group training for women and men, community mobilisation interventions, and combined livelihood and training interventions for women. Despite shortcomings in the evidence base, several studies show large effects in programmatic timeframes. Across different forms of violence, effective programmes are commonly participatory, engage multiple stakeholders, support critical discussion about gender relationships and the acceptability of violence, and support greater communication and shared decision making among family members, as well as non-violent behaviour. Further investment in intervention design and assessment is needed to address evidence gaps.

27. Lancet 2015;385(9977):1567-79

The health-systems response to violence against women

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Health systems have a crucial role in a multisector response to violence against women. Some countries have guidelines or protocols articulating this role and health-care workers are trained in some settings, but generally system development and implementation have been slow to progress. Substantial system and behavioural barriers exist, especially in low-income and middle-income countries. Violence against women was identified as a health priority in 2013 guidelines published by WHO and the 67th World Health Assembly resolution on strengthening the role of the health system in addressing violence, particularly against women and girls. In this Series paper, we review the evidence for clinical interventions and discuss components of a comprehensive health-system approach that helps health-care providers to identify and support women subjected to intimate partner or sexual violence. Five country case studies show the diversity of contexts and pathways for development of a health system response to violence against women. Although additional research is needed, strengthening of health systems can enable providers to address violence against women, including protocols, capacity building, effective coordination between agencies, and referral networks.

28. Lancet 2015;385(9977):1580-9

From work with men and boys to changes of social norms and reduction of inequities in gender relations: a conceptual shift in prevention of violence against women and girls

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Violence perpetrated by and against men and boys is a major public health problem. Although individual men's use of violence differs, engagement of all men and boys in action to prevent violence against women and girls is essential. We discuss why this engagement approach is theoretically important and how prevention interventions have developed from treating men simply as perpetrators of violence against women and girls or as allies of women in its prevention, to approaches that seek to transform the relations, social norms, and systems that sustain gender inequality and violence. We review evidence of intervention effectiveness in the reduction of violence or its risk factors, features commonly seen in more effective interventions, and how strong evidence-based interventions can be developed with more robust use of theory. Future interventions should emphasise work with both men and boys and women and girls to change social norms on gender relations, and need to appropriately accommodate the differences between men and women in the design of programmes.

Health Policy

29. BMJ 2015;350:h225

Feature Spotlight: Patient Centred Care: Patient communities reform healthcare in India

Jain A.

Public disillusionment with health service provision has led patient advocates in India to mobilise and push for change. India presents a classic paradox. At one end patients receive the best of advanced medical care, and at the other millions lack access to basic services. The public health sector is neglected, and patients have to rely on a private sector that is commercialised and unregulated. Corruption is pervasive, resulting in exploitation of patients and irrational care. Yogesh Jain, a public health advocate, puts it plainly, “With the discourse on primary healthcare hovering around access, cost, and sometimes quality, patient centred care seems like a futuristic thing in this country.” Disillusionment with the status quo has given rise to vibrant examples of patients mobilising to safeguard their right to health. A vision for a better future is driving communities to organise so that

they can collectively influence health outcomes, as the following examples of patients with HIV and patients with chronic disease show.
Healthcare in India: a snapshot.
Financing—Public expenditure on health is 1.2% of GDP, which is among the lowest in the world. Costs are largely borne by patients through out of pocket payments, making it a major cause of household debt and impoverishment.
Privatisation—93% of all hospitals and 80-85% of all doctors are in the private sector, which provides for 80% of outpatient care episodes and 60% of inpatient care. The sector is largely exempt from regulatory oversight.
Access to medicines—Often called the developing world's pharmacy, India is the world's third largest producer of drugs and exports medicines to over 200 countries. Yet, over half of its population lacks access to medicines they need; 74% of out of pocket expenditure is on drugs.
Workforce—India has the largest number of medical colleges in the world yet faces a workforce crisis. India has seven doctors and 17 nursing and midwifery staff per 10 000 population. The global averages are 14 and 29 respectively. Urban density of health workers is four times that in rural areas.
Infrastructure—The third national District Level Household and Facility Survey in 2007-08 showed that out of 4535 community health centres, only 754 are functional as per the Indian Public Health Standards.

30. Lancet 2015;385(9980):1902-9

A retrospective and prospective analysis of the west African Ebola virus disease epidemic: robust national health systems at the foundation and an empowered WHO at the apex

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The Ebola virus disease outbreak in west Africa is pivotal for the worldwide health system. Just as the depth of the crisis ultimately spurred an unprecedented response, the failures of leadership suggest the need for innovative reforms. Such reforms would transform the existing worldwide health system architecture into a purposeful, organised system with an empowered, highly capable WHO at its apex and enduring, equitable national health systems at its foundation. It would be designed not only to provide security against epidemic threats, but also to meet everyday health needs, thus realising the right to health. This retrospective and prospective analysis offers a template for these reforms, responding to the profound harms posed by fragile national health systems, delays in the international response, deficient resource mobilisation, ill defined responsibilities, and insufficient coordination. The scope of the reforms should address failures in the Ebola response, and entrenched weaknesses that enabled the epidemic to reach its heights.

31. Lancet 2015; May 14. pii: S0140-6736(15)60574-8

Financing universal health coverage-effects of alternative tax structures on public health systems: cross-national modelling in 89 low-income and middle-income countries

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Background: How to finance progress towards universal health coverage in low-income and middle-income countries is a subject of intense debate. We investigated how alternative tax systems affect the breadth, depth, and height of health system coverage.
Methods: We used cross-national longitudinal fixed effects models to assess the relationships between total and different types of tax revenue, health system coverage, and associated child and maternal health outcomes in 89 low-income and middle-income countries from 1995-2011.
Findings: Tax revenue was a major statistical determinant of progress towards universal health coverage. Each US$100 per capita per year of additional tax revenues corresponded to a yearly increase in government health spending of $9·86 (95% CI 3·92-15·8), adjusted for GDP per capita. This association was strong for taxes on capital gains, profits, and income ($16·7, 9·16 to 24·3), but not for consumption taxes on goods and services (-$4·37, -12·9 to 4·11). In countries with low tax

revenues (<$1000 per capita per year), an additional $100 tax revenue per year substantially increased the proportion of births with a skilled attendant present by 6·74 percentage points (95% CI 0·87-12·6) and the extent of financial coverage by 11·4 percentage points (5·51-17·2). Consumption taxes, a more regressive form of taxation that might reduce the ability of the poor to afford essential goods, were associated with increased rates of post-neonatal mortality, infant mortality, and under-5 mortality rates. We did not detect these adverse associations with taxes on capital gains, profits, and income, which tend to be more progressive.
Interpretation: Increasing domestic tax revenues is integral to achieving universal health coverage, particularly in countries with low tax bases. Pro-poor taxes on profits and capital gains seem to support expanding health coverage without the adverse associations with health outcomes observed for higher consumption taxes. Progressive tax policies within a pro-poor framework might accelerate progress toward achieving major international health goals.

32. Lancet 2015;385(9974):1230-47
Health-system reform and universal health coverage in Latin America
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Starting in the late 1980s, many Latin American countries began social sector reforms to alleviate poverty, reduce socioeconomic inequalities, improve health outcomes, and provide financial risk protection. In particular, starting in the 1990s, reforms aimed at strengthening health systems to reduce inequalities in health access and outcomes focused on expansion of universal health coverage, especially for poor citizens. In Latin America, health-system reforms have produced a distinct approach to universal health coverage, underpinned by the principles of equity, solidarity, and collective action to overcome social inequalities. In most of the countries studied, government financing enabled the introduction of supply-side interventions to expand insurance coverage for uninsured citizens--with defined and enlarged benefits packages--and to scale up delivery of health services. Countries such as Brazil and Cuba introduced tax-financed universal health systems. These changes were combined with demand-side interventions aimed at alleviating poverty (targeting many social determinants of health) and improving access of the most disadvantaged populations. Hence, the distinguishing features of health-system strengthening for universal health coverage and lessons from the Latin American experience are relevant for countries advancing universal health coverage.

33. Lancet 2015;385(9974):1248-59
Overcoming social segregation in health care in Latin America
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Latin America continues to segregate different social groups into separate health-system segments, including two separate public sector blocks: a well resourced social security for salaried workers and their families and a Ministry of Health serving poor and vulnerable people with low standards of quality and needing a frequently impoverishing payment at point of service. This segregation shows Latin America's longstanding economic and social inequality, cemented by an economic framework that predicted that economic growth would lead to rapid formalisation of the economy. Today, the institutional setup that organises the social segregation in health care is perceived, despite improved life expectancy and other advances, as a barrier to fulfilling the right to health, embodied in the legislation of many Latin American countries. This Series paper outlines four phases in the history of Latin American countries that explain the roots of segmentation in health care and describe three paths taken by countries seeking to overcome it: unification of the funds used to finance both social security and Ministry of Health services (one public payer); free choice of provider or insurer; and expansion of services to poor people and the non-salaried population by making explicit the health-care benefits to which all citizens are entitled.

Non-communicabel diseases

34. BMJ 2015;350:h1510

Editorial: Air pollution, stroke, and anxiety

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Particulate air pollution is an emerging risk factor for an increasing number of common conditions
The effects of air pollution on the lungs and heart are now widely appreciated, with expanding evidence for an important role in cardiac disease. The Global Burden of Disease Study identified fine particulate matter (PM2.5) in outdoor air and household air pollution from use of solid fuels as the ninth and fourth leading risk factors, respectively, for disease worldwide, and the World Health Organization attributes one in every eight deaths to air pollution. The effects of air pollution are not limited to cardiopulmonary diseases. Recent evidence suggests a role in diverse outcomes, including diabetes, low birth weight, and preterm birth. This research stems from improved understanding of the role of air pollution in initiating systemic inflammation, a response that may affect multiple organ systems. Two linked studies (doi:10.1136/bmj.h1295, doi:10.1136/bmj.h1111) add to growing evidence that air pollution is an important risk factor for an increasing number of common diseases.
In the first of the two papers, Shah and colleagues systematically reviewed and meta-analysed 103 studies conducted in 28 countries and including 6.2 million events to assess the role of short term fluctuations in air pollution as a trigger for stroke. Although evidence from several cohort studies of long term exposure to particulate matter indicates associations with stroke mortality, such findings are not universal.
The role of air pollution as a possible trigger for stroke has important implications for disease burden, especially in China where air pollution and the incidence of (especially haemorrhagic) stroke are high. In their analysis, Shah and colleagues found that increases in each of the common gaseous and particulate air pollutants were significantly associated with admission to hospital for stroke or stroke related mortality, with associations strongest for strokes on the same day as exposure; increased ozone was only weakly associated with cerebrovascular events.
The findings of these two studies support a sharper focus on air pollution as a leading global health concern. They also suggest opportunities for reducing the prevalence of two debilitating and common diseases. One of the unique features of air pollution as a risk factor for disease is that exposure to air pollution is almost universal. While this is a primary reason for the large disease burden attributable to outdoor air pollution, it also follows that even modest reductions in pollution could have widespread benefits throughout populations. The two linked papers in this issue confirm the urgent need to manage air pollution globally as a cause of ill health and offer the promise that reducing pollution could be a cost effective way to reduce the large burden of disease from both stroke and poor mental health.

35. TMIH 2015;20(5):581-588

Heart failure in sub-Saharan Africa: review of the aetiology of heart failure and the role of point-of-care biomarker diagnostics

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Within Africa, the burden of heart failure is significant. This arises from the increase in cardiovascular disease and associated risk factors such as hypertension and diabetes, as well as causes of heart failure which are particular to sub-Saharan Africa, such as endomyocardial fibrosis. The lack of access to echocardiography and other imaging modalities, from a cost and technical perspective, combined with the predominantly rural nature of many countries with poor transport links, means that the vast majority of people never obtain an appropriate diagnosis. Similarly, research has been limited on the causes and treatment of heart failure in Africa and in particular endemic causes such as EMF and rheumatic heart disease. This review outlines the burden of heart failure in Africa and highlights the opportunity to expand diagnosis through the use of biomarkers, in particular natriuretic peptides. This

builds on the success of point-of-care testing in human immunodeficiency virus and tuberculosis which have been extensively deployed in community settings in Africa.

Sexual and Reproductive Health

36. Am J TMH 2015;92(4):838-47

Geographic variation of female genital mutilation and legal enforcement in sub-saharan Africa: a case study of Senegal

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This paper draws on household data to examine the prevalence of female genital mutilation (FGM) in Senegal and the effectiveness of the country's anti-FGM law in dealing with actual breaches and providing protection to the victims. The 2010-2011 Senegal Demographic Health Survey and Multiple Indicators Cluster Survey (SDHS-MICS) covers 14,228 women and their daughters. Logistic regression was used to investigate the geographic distribution of FGM across regions. For the enforceability of anti-FGM, desk research was used. Overall prevalence among women and daughters was 28.1% and 6.2%, respectively. Significant factors were sociodemographics, ethnicity, and region. This analysis shows both advantages and vulnerabilities of the anti-FGM law in relation to the issue of enforcement. It indicates that the law falls short of offering adequate protection to potential victims. FGM is a cultural and social norm imbedded predominantly in rural settings and as such, drives resistance to jettisoning FGM. Legislation has been one of the driving forces behind the eradication of the practice.

37. Lancet 2015; Mar 26. pii: S0140-6736(14)61935-8

Comparison of treatment of incomplete abortion with misoprostol by physicians and midwives at district level in Uganda: a randomised controlled equivalence trial

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Background: Misoprostol is established for the treatment of incomplete abortion but has not been systematically assessed when provided by midwives at district level in a low-resource setting. We investigated the effectiveness and safety of midwives diagnosing and treating incomplete abortion with misoprostol, compared with physicians.
Methods: We did a multicentre randomised controlled equivalence trial at district level at six facilities in Uganda. Eligibility criteria were women with signs of incomplete abortion. We randomly allocated women with first-trimester incomplete abortion to clinical assessment and treatment with misoprostol either by a physician or a midwife. The randomisation (1:1) was done in blocks of 12 and was stratified for study site. Primary outcome was complete abortion not needing surgical intervention within 14-28 days after initial treatment. The study was not masked. Analysis of the primary outcome was done on the per-protocol population with a generalised linear-mixed effects model. The predefined equivalence range was -4% to 4%. The trial was registered at ClinicalTrials.gov, number NCT01844024.
Findings: From April 30, 2013, to July 21, 2014, 1108 women were assessed for eligibility. 1010 women were randomly assigned to each group (506 to midwife group and 504 to physician group). 955 women (472 in the midwife group and 483 in the physician group) were included in the per-protocol analysis. 452 (95·8%) of women in the midwife group had complete abortion and 467 (96·7%) in the physician group. The model-based risk difference for midwife versus physician group was -0·8% (95% CI -2·9 to 1·4), falling within the predefined equivalence range (-4% to 4%). The overall proportion of women with incomplete abortion was 3·8% (36/955), similarly distributed between the two groups (4·2% [20/472] in the midwife group, 3·3% [16/483] in the physician group). No serious adverse events were recorded.
Interpretation: Diagnosis and treatment of incomplete abortion with misoprostol by midwives is equally safe and effective as when provided by physicians, in a low-resource setting. Scaling up

midwives' involvement in treatment of incomplete abortion with misoprostol at district level would increase access to safe post-abortion care.

38. TMIH 2015;20(5):554-568

Rehabilitation experiences after obstetric fistula repair: systematic review of qualitative studies

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Objectives: To synthesise evidence on women's experiences surrounding rehabilitation and reintegration after obstetric fistula repair in sub-Saharan Africa and explore recommendations from women and health service providers.
Methods: Systematic literature review of qualitative studies surrounding rehabilitation experiences of women in sub-Saharan Africa who have undergone obstetric fistula repair. Using a pre-defined search strategy, seven databases, relevant source publications and grey literature were searched for primary qualitative studies. Data from ten studies were collected, and thematic analysis based on the framework approach was used to analyse the findings.
Results: The most important rehabilitating factor for women was fulfilment of social roles. Health service perspectives were more frequent than women's perspectives. Counselling and health education were the most common recommendations from both perspectives.
Conclusion: Little qualitative evidence is available on rehabilitation after obstetric fistula repair in sub-Saharan Africa. Counselling services and community health education are priorities. Further research should emphasise women's perspectives to better inform interventions aimed at addressing the physical and social consequences of obstetric fistula.

39. TMIH 2015;20(6):813-9

Good clinical outcomes from a 7-year holistic programme of fistula repair in Guinea

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Objectives: Female genital fistula remains a public health concern in developing countries. From January 2007 to September 2013, the Fistula Care project, managed by EngenderHealth in partnership with the Ministry of Health and supported by USAID, integrated fistula repair services in the maternity wards of general hospitals in Guinea. The objective of this article was to present and discuss the clinical outcomes of 7 years of work involving 2116 women repaired in three hospitals across the country.
Methods: This was a retrospective cohort study using data abstracted from medical records for fistula repairs conducted from 2007 to 2013. The study data were reviewed during the period April to August 2014.
Results: The majority of the 2116 women who underwent surgical repair had vesicovaginal fistula (n = 2045, 97%) and 3% had rectovaginal fistula or a combination of both. Overall 1748 (83%) had a closed fistula and were continent of urine immediately after surgery. At discharge, 1795 women (85%) had a closed fistula and 1680 (79%) were dry, meaning they no longer leaked urine and/or faeces. One hundred and fifteen (5%) remained with residual incontinence despite fistula closure. Follow-up at 3 months was completed by 1663 (79%) women of whom 1405 (84.5%) had their fistula closed and 80% were continent. Twenty-one per cent were lost to follow-up.
Conclusion: Routine programmatic repair for obstetric fistula in low resources settings can yield good outcomes. However, more efforts are needed to address loss to follow-up, sustain the results and prevent the occurrence and/or recurrence of fistula.

Miscellaneous

40. BMJ 2015;350:h1975

Feature Rural Health: Can mobile phones transform healthcare in low and middle income countries?

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Mobile technology has the potential to put rural populations in touch with formal health services for the first time, but is the buzz around mobile health justified, asks Sophie Arie
More than 21% of new HIV infections in Zambia arise from mother to child transmission. Specialised treatment can increase chances of survival by up to 75% if started before the baby is 12 weeks old. But until recently it took almost that long (66 days on average) to send blood samples from rural areas to a laboratory and to get the test results back.
Thanks to mobile phones the situation is changing. Under a government programme called Mwana, supported by Unicef and other international organisations, newborn babies in Zambia can be tested for HIV in half that time. It can still take some 30 days for blood samples to reach the laboratory, but now it takes only a few seconds for results to come back, by text message, to rural health clinics.
Mobile phone use has spread fast in Africa, with more than 80% of households now having access. Millions of geographically isolated people in low and middle income countries, many of whom have never seen a doctor, can now contact the health services they need when they need them, at least in theory. As call prices fall and network coverage improves, can mobile health, or m-health, transform some of the world's weakest health systems, saving millions of lives?

41. TMIH 2015;20(4):493-500
Compounding diagnostic delays: a qualitative study of point-of-care testing in South Africa
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Objectives: Successful point-of-care (POC) testing (completion of test-and-treat cycle in one patient encounter) has immense potential to reduce diagnostic and treatment delays, and improve patient and public health outcomes. We explored what tests are done and how in public/private, rural/urban hospitals and clinics in South Africa and whether they can ensure successful POC testing.
Methods: This qualitative research study examined POC testing across major diseases in Cape Town, Durban and Eastern Cape. We conducted 101 semi-structured interviews and seven focus group discussions with doctors, nurses, community health workers, patients, laboratory technicians, policymakers, hospital managers and diagnostic manufacturers.
Results: In South Africa, diagnostics are characterised by a centralised system. Most tests conducted on the spot can be made to work successfully as POC tests. The majority of public/private clinics and smaller hospitals send samples via couriers to centralised laboratories and retrieve results the same way, via internet, fax or phone. The main challenge to POC testing lies in transporting samples and results, while delays risk patient loss from diagnostic/treatment pathways. Strategies to deal with associated delays create new problems, such as artificially prolonged turnaround times, strains on human resources and quality of testing, compounding additional diagnostic and treatment delays.
Conclusions: For POC testing to succeed, particular characteristics of diagnostic ecosystems and adaptations of professional practices to overcome associated challenges must be taken into account.