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## International Health Alerts 2018-1 Abstracts

### Child Health / iCCM

1. Trop Med Int Health 2018 Jan;23(1):10-25

#### **Comparing the behavioural impact of a nudge-based handwashing intervention to high-intensity hygiene education: a cluster-randomised trial in rural Bangladesh**

Grover E et al., Department of Civil Engineering and Environmental Science/Center for Applied Social Research, University of Oklahoma, Norman, OK, USA

#### **OBJECTIVE:**

To determine the impact of environmental nudges on handwashing behaviours among primary school children as compared to a high-intensity hygiene education intervention.

#### **METHODS:**

In a cluster-randomised trial (CRT), we compared the rates of handwashing with soap (HWWS) after a toileting event among primary school students in rural Bangladesh. Eligible schools (government run, on-site sanitation and water, no hygiene interventions in last year, fewer than 450 students) were identified, and 20 schools were randomly selected and allocated without blinding to one of four interventions, five schools per group: simultaneous handwashing infrastructure and nudge construction, sequential infrastructure then nudge construction, simultaneous infrastructure and high-intensity hygiene education (HE) and sequential handwashing infrastructure and HE. The primary outcome, incidence of HWWS after a toileting event, was compared between the intervention groups at different data collection points with robust-Poisson regression analysis with generalised estimating equations, adjusting for school-level clustering of outcomes.

#### **RESULTS:**

The nudge intervention and the HE intervention were found to be equally effective at sustained impact over 5 months post-intervention (adjusted IRR 0.81, 95% CI 0.61-1.09). When comparing intervention delivery timing, the simultaneous delivery of the HE intervention significantly outperformed the sequential HE delivery (adjusted IRR 1.58 CI 1.20-2.08), whereas no significant difference was observed between sequential and simultaneous nudge intervention delivery (adjusted IRR 0.75, 95% CI 0.48-1.17).

#### **CONCLUSION:**

Our trial demonstrates sustained improved handwashing behaviour 5 months after the nudge intervention. The nudge intervention's comparable performance to a high-intensity hygiene education intervention is encouraging.

### Communicable Diseases

2. BMJ 2017;359:j5759 News

#### **Philippines halts dengue immunisation campaign owing to safety risk**

Owen Dyer

The Philippines has halted a dengue immunisation campaign and all marketing of the world's first approved dengue vaccine, Sanofi Pasteur's Dengvaxia, after post-market testing confirmed that it can increase the risk of severe dengue in people who have never been exposed to the virus.

The vaccine is at the centre of a growing political scandal in the Philippines, where 830 000 schoolchildren have already been vaccinated in a campaign that continued unmodified despite a World Health Organization warning in July 2016 that Dengvaxia may pose a threat to people who had never been infected.

### 3. [Lancet 2018 Jan 6;391\(10115\):82-94](#)

#### **Chagas disease**

Pérez-Molina JA et al., National Referral Centre for Tropical Diseases, Infectious Diseases Department, Hospital Universitario Ramón y Cajal, Instituto Ramón y Cajal de Investigación Sanitaria, Madrid, Spain <jperezm@salud.madrid.org>

Chagas disease is an anthroponosis from the American continent that has spread from its original boundaries through migration. It is caused by the protozoan *Trypanosoma cruzi*, which was identified in the first decade of the 20th century. Once acute infection resolves, patients can develop chronic disease, which in up to 30-40% of cases is characterised by cardiomyopathy, arrhythmias, megaviscera, and, more rarely, polyneuropathy and stroke. Even after more than a century, many challenges remain unresolved, since epidemiological control and diagnostic, therapeutic, and prognostic methods must be improved. In particular, the efficacy and tolerability profile of therapeutic agents is far from ideal. Furthermore, the population affected is older and more complex (eg, immunosuppressed patients and patients with cancer). Nevertheless, in recent years, our knowledge of Chagas disease has expanded, and the international networking needed to change the course of this deadly disease during the 21st century has begun.

### 4. [Lancet 2017;391\(10117\):252-65](#)

#### **Soil-transmitted helminth infections**

Jourdan PM et al., Schistosomiasis Control Initiative, Imperial College London, St Mary's Campus, London, UK; DEWORM3, Natural History Museum, London, UK; Norwegian Centre for Imported and Tropical Diseases, Department of Infectious Diseases, Oslo University Hospital, Ullevål, Oslo, Norway

More than a quarter of the world's population is at risk of infection with the soil-transmitted helminths *Ascaris lumbricoides*, hookworm (*Ancylostoma duodenale* and *Necator americanus*), *Trichuris trichiura*, and *Strongyloides stercoralis*. Infected children and adults present with a range of medical and surgical conditions, and clinicians should consider the possibility of infection in individuals living in, or returning from, endemic regions. Although safe and effective drugs are donated free to endemic countries, only half of at-risk children received treatment in 2016. This Seminar describes the epidemiology, lifecycles, pathophysiology, clinical diagnosis, management, and public health control of soil-transmitted helminths. Previous work has questioned the effect of population-level deworming; however, it remains beyond doubt that treatment reduces the severe consequences of soil-transmitted helminthiasis. We highlight the need for refined diagnostic tools and effective control options to scale up public health interventions and improve clinical detection and management of these infections.

### 5. [Am J Trop Med Hyg. 2018 Jan;98\(1\):203-206. Epub 2018 Jan 1.](#)

#### **Emergence, Epidemiology, and Transmission Dynamics of 2009 Pandemic A/H1N1 Influenza in Kampala, Uganda, 2009-2015**

Cummings MJ et al; Division of Pulmonary, Allergy, and Critical Care Medicine, Columbia University Medical Center, New York.

In sub-Saharan Africa, little is known about the epidemiology of pandemic-prone influenza viruses in urban settings. Using data from a prospective sentinel surveillance network, we characterized the

emergence, epidemiology, and transmission dynamics of 2009 pandemic A/H1N1 influenza (H1N1pdm09) in Kampala, Uganda. After virus introduction via international air travel from England in June 2009, we estimated the basic reproductive number in Kampala to be 1.06-1.13, corresponding to attack rates of 12-22%. We subsequently identified 613 cases of influenza in Kampala from 2009 to 2015, of which 191 (31.2%) were infected with H1N1pdm09. Patients infected with H1N1pdm09 were more likely to be older adult (ages 35-64) males with illness onset during rainy season months. Urban settings in sub-Saharan Africa are vulnerable to importation and intense transmission of pandemic-prone influenza viruses. Enhanced surveillance and influenza pandemic preparedness in these settings is needed.

6. *Am J Trop Med Hyg* 2017 Dec 26. [Epub ahead of print]

### **A Combined Syndromic Approach to Examine Viral, Bacterial, and Parasitic Agents among Febrile Patients: A Pilot Study in Kilombero, Tanzania**

Hercik C et al; Georgetown University, Washington, DC

The use of fever syndromic surveillance in sub-Saharan Africa is an effective approach to determine the prevalence of both malarial and nonmalarial infectious agents. We collected both blood and naso/oro-pharyngeal (NP/OP) swabs from consecutive consenting patients  $\geq 1$  year of age, with an axillary temperature  $\geq 37.5^\circ\text{C}$ , and symptom onset of  $\leq 5$  days. Specimens were analyzed using both acute febrile illness (AFI) and respiratory TaqMan array cards (TAC) for multiagent detection of 56 different bloodstream and respiratory agents. In addition, we collected epidemiologic data to further characterize our patient population. We enrolled 205 febrile patients, including 70 children ( $1 < 15$  years of age; 34%) and 135 adults ( $\geq 15$  years of age; 66%). AFI TAC and respiratory TAC were performed on 191 whole blood specimens and 115 NP/OP specimens, respectively. We detected nucleic acid for *Plasmodium* (57%), *Leptospira* (2%), and dengue virus (1%) among blood specimens. In addition, we detected 17 different respiratory agents, most notably, *Haemophilus influenzae* (64%), *Streptococcus pneumoniae* (56%), *Moraxella catarrhalis* (39%), and respiratory syncytial virus (11%) among NP/OP specimens. Overall median cycle threshold was measured at 26.5. This study provides a proof-of-concept for the use of a multiagent diagnostic approach for exploratory research on febrile illness and underscores the utility of quantitative molecular diagnostics in complex epidemiologic settings of sub-Saharan Africa.

## **Emergency Medicine**

7. *Trop Med Int Health* 2017 Dec;22(12):1464-1492

### **Impact of nutrition interventions on pediatric mortality and nutrition outcomes in humanitarian emergencies: A systematic review**

Balhara KS et al., Department of Emergency Medicine, University of Texas Health Science Center at San Antonio, San Antonio, TX, USA

#### **OBJECTIVES:**

Malnutrition contributes to paediatric morbidity and mortality in disasters and complex emergencies, but summary data describing specific nutritional interventions in these settings are lacking. This systematic review aimed to characterise such interventions and their effects on paediatric mortality, anthropometric measures and serum markers of nutrition.

#### **METHODS:**

A systematic search of OVID MEDLINE, Cochrane Library and relevant grey literature was conducted. We included all randomised controlled trials and observational controlled studies

evaluating effectiveness of nutritional intervention(s) on defined health outcomes in children and adolescents (0-18 years) within a disaster or complex emergency. We extracted study characteristics, interventions and outcomes data. Study quality was assessed using Grading of Recommendations Assessment, Development and Evaluation (GRADE) criteria.

### **RESULTS:**

A total of 31 studies met inclusion criteria. Most were conducted in Africa (17), during periods of conflict or hunger gaps (14), and evaluated micronutrient supplementation (14) or selective feeding (10). Overall study quality was low, with only two high and four moderate quality studies. High- and medium-quality studies demonstrated positive impact of fortified spreads, ready-to-use therapeutic foods, micronutrient supplementation, and food and cash transfers.

### **CONCLUSION:**

In disasters and complex emergencies, high variability and low quality of controlled studies on paediatric malnutrition limit meaningful data aggregation. If existing research gaps are to be addressed, the inherent unpredictability of humanitarian emergencies and ethical considerations regarding controls may warrant a paradigm shift in what constitutes adequate methods. Periodic hunger gaps may offer a generalisable opportunity for robust trials, but consensus on meaningful nutritional endpoints is needed.

## **Health Financing / Health Policy**

### **8. BMJ 2018;360:k270 News**

#### **Indian clinical guidelines lack scope, rigour, and quality, study finds**

Dinsa Sachan

Most clinical practice guidelines in India do not meet international standards in either their scope, the way they were developed, or the independence of their authors, a study has found.

Indian guidelines should be better regulated by introducing a central approval system, said lead researcher Soumyadeep Bhaumik, a former student of international public health at Liverpool School of Tropical Medicine, UK, and a former associate editor of The BMJ.

For the study, researchers examined 11 clinical practice guidelines for the four conditions that account for the highest disease burden in India—*ischaemic heart disease, lower respiratory infections, chronic obstructive pulmonary disease, and tuberculosis.*

### **9. Trop Med Int Health 2017 Dec;22(12):1533-1541**

#### **Who accesses surgery at district level in sub-Saharan Africa? Evidence from Malawi and Zambia**

Gajewski J et al., Royal College of Surgeons in Ireland, Dublin 2, Ireland

### **OBJECTIVES:**

To examine age and gender distribution for the most common types of surgery in Malawi and Zambia.

### **METHODS:**

Data were collected from major operating theatres in eight district hospitals in Malawi and nine in Zambia. Raw data on surgical procedures were coded by specialist surgeons for frequency analyses.

### **RESULTS:**

In Malawi female surgical patients had a mean age of 25 years, with 91% aged 16-40 years. Females accounted for 85%, and obstetric cases for 75%, of all surgical patients. In Zambia, female surgical patients had a mean age of 26, with 75% aged 16-40 years. They accounted for 55% of all cases, 34% being obstetric. Male surgical patients in Malawi were on average older (33 years) than in Zambia (23 years). General surgical cases in men and women, respectively, had a median age of 42 and 32 in Malawi and 26 and 30 in Zambia. The median age of trauma patients was 12 in males and 10 in females in both countries. Children aged 0-15 years accounted for 64-65% of all trauma cases in Malawi and 57-58% in Zambia, with peak incidences in 6- to 10-year-olds.

### **CONCLUSIONS:**

Women of reproductive (16-45 years) mainly undergoing Caesarean sections and children aged 0-15 years who accounted for two-thirds of trauma cases are the main patient populations undergoing surgery at district hospitals in Zambia and Malawi. Verification and analysis of routine hospital data, across 10-30% of districts countrywide, demonstrated the need to prioritise quality assurance in surgery and anaesthesia, and preventive interventions in children.

10. *Lancet* 2017 Dec 9;390(10112):2595-2601. Epub 2017 Dec 8

### **China's Silk Road and global health**

Tang K et al; Department of Global Health, School of Public Health, Peking University, Beijing, China. <tangkun@hsc.pku.edu.cn>

In 2013, China proposed its Belt and Road Initiative to promote trade, infrastructure, and commercial associations with 65 countries in Asia, Africa, and Europe. This initiative contains important health components. Simultaneously, China launched an unprecedented overseas intervention against Ebola virus in west Africa, dispatching 1200 workers, including Chinese military personnel. The overseas development assistance provided by China has been increasing by 25% annually, reaching US\$7 billion in 2013. Development assistance for health from China has particularly been used to develop infrastructure and provide medical supplies to Africa and Asia. China's contributions to multilateral organisations are increasing but are unlikely to bridge substantial gaps, if any, vacated by other donors; China is creating its own multilateral funds and banks and challenging the existing global architecture. These new investment vehicles are more aligned with the geography and type of support of the Belt and Road Initiative. Our analysis concludes that China's Belt and Road Initiative, Ebola response, development assistance for health, and new investment funds are complementary and reinforcing, with China shaping a unique global engagement impacting powerfully on the contours of global health.

## **HIV / AIDS**

11. *BMJ* 2017;359:j5011 Clinical Review State of the Art Review

### **Recent advances in pre-exposure prophylaxis for HIV**

Monica Desai, et al., [desai.monica@gmail.com](mailto:desai.monica@gmail.com)

Although pre-exposure prophylaxis (PrEP)—the use of antiretroviral drugs by non-infected people to prevent the acquisition of HIV—is a promising preventive option, important public health questions remain. Daily oral emtricitabine (FTC)-tenofovir disoproxil fumarate (TDF) is highly efficacious in preventing the acquisition of HIV in people at risk as a result of a range of different types of sexual exposure. There is good evidence of efficacy in women and men, and when men who have sex with men use event based dosing. Studies have been conducted in several countries and epidemics. Because adherence to this treatment varies greatly there are questions about its public health benefit. Oral FTC-

TDF is extremely safe, with minimal impact on kidney, bone, or pregnancy outcomes, and there is no evidence that its effectiveness has been reduced by risk compensation during open label and programmatic follow-up. It is too early to assess the impact of this treatment on the incidence of sexually transmitted infections (STIs) at a population level. Many challenges remain. Access to pre-exposure prophylaxis is limited and disparities exist, including those governed by race and sex. Different pricing and access models need to be explored to avoid further widening inequalities. The optimal combination prevention program needs to be defined, and this will depend on local epidemiology, service provision, and cost effectiveness. This review updates the evidence base for pre-exposure prophylaxis regarding its effectiveness, safety, and risk compensation.

12. *Trop Med Int Health* 2017 Dec;22(12):1493-1504

**Is hearing impairment associated with HIV? A systematic review of data from low- and middle-income countries**

Ensink RJH et al., Gelre Hospital, Zutphen, The Netherlands

**OBJECTIVES:**

To systematically review evidence on the prevalence and characteristics of hearing impairment among children and adults living with HIV in low- and middle-income countries (LMIC).

**METHODS:**

Articles were identified up to January 2016 through searching four electronic databases. Epidemiological studies conducted in LMIC that explored the association between HIV status and hearing loss, with or without an HIV-uninfected comparison group, were eligible for inclusion. Results were screened and assessed for eligibility, and data were extracted by two reviewers, with discussion in the case of disagreement. Findings were narratively synthesised.

**RESULTS:**

The search identified 638 unique references, of which 21 studies were included in the review, including 3491 people with HIV from 13 LMIC. There was lack of consistency in the definition used for hearing loss, making comparability across studies difficult. Among children with HIV, across the three studies that used a cut-off of >15 dB in either ear, the prevalence of hearing loss ranged from 22 to 37%. Among the three studies that used >25 dB in either ear, the prevalence ranged from 32 to 39%. Among adults with HIV, for the five studies that used a threshold of >25 dB for either ear, the prevalence ranged from 10 to 43%. The prevalence of hearing impairment was significantly higher among people with HIV than in controls in eight of the ten studies that assessed this comparison. Conductive hearing loss was the most common type of hearing loss in children with HIV, while sensorineural hearing loss was more common in adults with HIV. There was a lack of evidence for an association between ART use and hearing loss, although there was some suggestion that late stage of HIV disease or low CD4 count was related to hearing loss. There were concerns about the quality of the studies included in the review.

**CONCLUSIONS:**

The current evidence is suggestive of a high prevalence of hearing loss among people living with HIV compared to people without HIV, or to WHO estimates for the general population. More research is needed to better understand the aetiology of hearing loss in relation to HIV, and whether screening for and treatment of hearing loss can be effectively integrated into HIV treatment services needs further research.

13. *Trop Med Int Health* 2018 Jan;23(1):79-91

**Viraemia before, during and after pregnancy in HIV-infected women on antiretroviral therapy in rural KwaZulu-Natal, South Africa, 2010-2015**

Chetty T et al., Africa Health Research Institute, KwaZulu-Natal, South Africa

## **OBJECTIVES:**

Pregnancy and post-partum viral load suppression is critical to prevent mother-to-child HIV transmission and ensure maternal health. We measured viraemia risk before, during and after pregnancy in HIV-infected women.

## **METHODS:**

Between 2010 and 2015, 1425 HIV-infected pregnant women on lifelong antiretroviral therapy (ART) for at least six months pre-pregnancy were enrolled in a cohort study in rural KwaZulu-Natal, South Africa. Odds ratios were estimated in multilevel logistic regression, with pregnancy period time-varying.

## **RESULTS:**

Over half of 1425 women received tenofovir-based regimens ( $n = 791$ ). Median pre-pregnancy ART duration was 2.1 years. Of 988 women (69.3%) with pre-pregnancy viral loads, 82.0%, 6.8% and 11.2% had VL  $<50$ , 50-999 and  $\geq 1000$  copies/ml, respectively. During pregnancy and at six, 12 and 24 months, viral load was  $\geq 1000$  copies/ml in 15.2%, 15.7%, 17.8% and 16.6% respectively; viral load  $<50$  was 76.9%, 77%, 75.5% and 75.8%, respectively. Adjusting for age, clinical and pregnancy factors, viraemia risk (viral load  $\geq 50$  copies/ml) was not significantly associated with pregnancy [adjusted OR (aOR) 1.31; 95% CI 0.90-1.92], six months (aOR 1.30; 95% CI 0.83-2.04), 12 months (aOR 0.96; 95% CI 0.58-1.58) and 24 months (aOR 1.40; 95% CI 0.89-2.22) post-partum. Adjusting for ART duration-pregnancy period interaction, viraemia risk was 1.8 during pregnancy and twofold higher post-partum.

## **CONCLUSIONS:**

While undetectable viral load before pregnancy through post-partum was common, the UNAIDS goal to suppress viraemia in 90% of women was not met. Women on preconception ART remain vulnerable to viraemia; additional support is required to prevent mother-to-child HIV transmission and maintain maternal health.

## **Malaria**

14. *Am J Trop Med Hyg.* 2017 Dec 18. [Epub ahead of print]

### **Impact Evaluation of Seasonal Malaria Chemoprevention under Routine Program Implementation: A Quasi-Experimental Study in Burkina Faso**

Druetz T et al; Department of Tropical Medicine, School of Public Health and Tropical Medicine, Tulane University, New Orleans, Louisiana

Seasonal malaria chemoprevention (SMC) for children  $< 5$  is a strategy that is gaining popularity in West African countries. Although its efficacy to reduce malaria incidence has been demonstrated in trials, the effects of SMC implemented in routine program conditions, outside of experimental contexts, are unknown. In 2014 and 2015, a survey was conducted in 1,311 households located in Kaya District (Burkina Faso) where SMC had been recently introduced. All children  $< 72$  months were tested for malaria and anemia. A pre-post study with control group was designed to measure SMC impact during high transmission season. A difference-in-differences approach was coupled in the analysis with propensity score weighting to control for observable and time-invariant nonobservable confounding factors. SMC reduced the parasitemia point and period prevalence by 3.3 and 24% points, respectively; this translated into protective effects of 51% and 62%. SMC also reduced the likelihood of having moderate to severe anemia by 32%, and history of recent fever by 46%. Self-reported coverage for children at the first cycle was 83%. The SMC program was successfully added to a package of interventions already in place. To our knowledge, with prevalence

< 10% during the peak of the transmission season, this is the first time that malaria can be reported as hypo-endemic in a sub-Saharan setting in Burkina Faso. SMC has great potential, and along with other interventions, it could contribute to approaching the threshold where elimination strategies will be envisioned in Burkina Faso.

15. *Am J Trop Med Hyg* 2017 Dec 18. [Epub ahead of print]

### **Impact of Sick Cell Trait and Naturally Acquired Immunity on Uncomplicated Malaria after Controlled Human Malaria Infection in Adults in Gabon**

Lell B et al; Centre de Recherches Médicales de Lambaréné (CERMEL), Lambaréné, Gabon

Controlled human malaria infection (CHMI) by direct venous inoculation (DVI) with 3,200 cryopreserved *Plasmodium falciparum* sporozoites (PfSPZ) consistently leads to parasitemia and malaria symptoms in malaria-naïve adults. We used CHMI by DVI to investigate infection rates, parasite kinetics, and malaria symptoms in lifelong malaria-exposed (semi-immune) Gabonese adults with and without sickle cell trait. Eleven semi-immune Gabonese with normal hemoglobin (IA), nine with sickle cell trait (IS), and five nonimmune European controls with normal hemoglobin (NI) received 3,200 PfSPZ by DVI and were followed 28 days for parasitemia by thick blood smear (TBS) and quantitative polymerase chain reaction (qPCR) and for malaria symptoms. End points were time to parasitemia and parasitemia plus symptoms. PfSPZ Challenge was well tolerated and safe. Five of the five (100%) NI, 7/11 (64%) IA, and 5/9 (56%) IS volunteers developed parasitemia by TBS, and 5/5 (100%) NI, 9/11 (82%) IA, and 7/9 (78%) IS by qPCR, respectively. The time to parasitemia by TBS was longer in IA (geometric mean 16.9 days) and IS (19.1 days) than in NA (12.6 days) volunteers ( $P = 0.016$ ,  $0.021$ , respectively). Five of the five, 6/9, and 1/7 volunteers with parasitemia developed symptoms ( $P = 0.003$ , NI versus IS). Naturally acquired immunity (NAI) to malaria significantly prolonged the time to parasitemia. Sick cell trait seemed to prolong it further. NAI plus sickle cell trait, but not NAI alone, significantly reduced symptom rate. Twenty percent (4/20) semi-immunes demonstrated sterile protective immunity. Standardized CHMI with PfSPZ Challenge is a powerful tool for dissecting the impact of innate and naturally acquired adaptive immunity on malaria.

16. *Am J Trop Med Hyg* 2018 Jan 22. [Epub ahead of print]

### **The Effectiveness of Community Bed Net Use on Malaria Parasitemia among Children Less Than 5 Years Old in Liberia**

Stebbins RC et al; Department of Epidemiology, Gillings School of Global Public Health, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina

In 2013, the under-5 mortality rate in Liberia was 71 deaths per 1,000 live births, with malaria responsible for 22% of those deaths. One of the primary existing control tools, long-lasting insecticide-treated bed nets (LLINs), is thought to be dually effective, acting as a physical barrier but also decreasing the mosquito population in communities. However, there has been little investigation into the protective effects of community-wide bed net use above and beyond the individual level. Using data from the population-representative 2011 Liberia Malaria Indicator Survey, we estimated the association between proportion of a community using LLINs and malaria in children using multi-level logistic regression. To investigate the potential effect measure modification of the relationship by urbanicity, we included an interaction term and calculated stratum-specific prevalence odds ratios (PORs) for rural and urban communities. We calculated a POR of malaria for an absolute 10% increase in community bed net use of 1.13 (95% confidence interval [CI]: 0.91, 1.41) and 0.35 (95% CI: 0.13, 0.92) for rural and urban communities, respectively, indicating a strong, though imprecise, protective effect within urban communities only. Our results indicate that bed net use has an indirect protective effect in urban areas, above and beyond individual use. Little or no such effect of community-wide use is seen in rural areas, likely because of population density factors. Therefore,

although all control efforts should be multifaceted, promotion of bed net use in urban areas in particular will likely be a highly effective tool for control.

## Mental Health

17. *BMJ* 2017;359:j5621 Feature Christmas 2017:

### **Time and Place Different shell, same shock**

Stoyan Popkirov, et al., [popkirov@gmail.com](mailto:popkirov@gmail.com)

One hundred years on from the first world war, Stoyan Popkirov and colleagues review the German and British medical films that tell the same story of illness and healing.

In both war and illness, we tell stories to frame our suffering. We create cultural narratives of national ideology or neurophysiology to cope with adversity. And those stories are not always beholden to history or histology but instead to creating meaning. One narrative with cultural tremors that reverberated throughout the 20th century, sparking changes in politics and medicine alike, was that of shell shock during the first world war.

Never fully defined, at times overused, and even banned, shell shock became as much a story as a diagnosis. Its causes and presentations varied greatly, from blasts to breakdowns and from blindness to paralysis, shaped as much by the terror of those affected as by the conceptual frameworks of the times. The incomprehensible new horror of industrialised warfare manifested itself in a severe and mysterious epidemic affecting tens of thousands of soldiers on both sides of the war. It was a medical conundrum that led to a crisis in military personnel and needed to be understood urgently given the ongoing deadlocked war. Initial theories of blast related neuropathology were soon abandoned in favour of psychological aetiologies. The presentations of shell shock were recognised as functional disorders, highlighting beyond any doubt that “hysteria” could affect men too, and in large numbers.

## Non-Communicable Diseases

18. *BMJ* 2018;360:j5295 Research

### **Incidence of type 1 diabetes in China, 2010-13: population based study**

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**Objective:** To estimate the incidence of type 1 diabetes in all age groups in China during 2010-13.

**Design:** Population based, registry study using data from multiple independent sources.

**Setting:** National registration system in all 505 hospitals providing diabetes care, and communities of patients with diabetes in 13 areas across China, covering more than 133 million person years at risk, approximately 10% of the whole population.

**Participants:** 5018 people of all ages with newly diagnosed type 1 diabetes and resident in the study areas from 1 January 2010 to 31 December 2013.

**Main outcome measures:** Incidence of type 1 diabetes per 100 000 person years by age, sex, and study area. Type 1 diabetes was doctor diagnosed and further validated by onsite follow-up. Completeness of case ascertainment was assessed using the capture mark recapture method.

**Results:** 5018 cases of newly diagnosed type 1 diabetes were ascertained: 1239 participants were aged <15 years, 1799 were aged 15-29 years, and 1980 were aged ≥30 years. The proportion of new onset cases in participants aged ≥20 years was 65.3%. The estimated incidence of type 1 diabetes per 100 000 persons years for all ages in China was 1.01 (95% confidence interval 0.18 to 1.84). Incidence per 100 000 persons years by age group was 1.93 (0.83 to 3.03) for 0-14 years, 1.28 (0.45 to 2.11) for 15-29 years, and 0.69 (0.00 to 1.51) for ≥30 years, with a peak in age group 10-14 years. The incidence in under 15s was positively correlated with latitude ( $r=0.88$ ,  $P<0.001$ ), although this association was not observed in age groups 15-29 years or ≥30 years.

**Conclusion:** Most cases of new onset type 1 diabetes in China occurred among adults. The incidence of type 1 diabetes in Chinese children was among the lowest reported in the study.

International studies of type 1 diabetes, such as the DiaMond (Diabetes Mondiale) Project and European Community Concerted Action Programme in Diabetes (EURODIAB) study have shown wide variation in the incidence of type 1 diabetes among children. According to the DiaMond Project, China had one of the lowest incidences of type 1 diabetes in children—0.51 per 100 000 person years during 1985-94. A nationwide registry of type 1 diabetes in China does not exist.

The incidence of type 1 diabetes in children has been increasing worldwide. Recent results of the SEARCH for Diabetes in Youth study from the United States suggest that environmental or behavioural factors, or both, play larger parts in the increased incidence of type 1 diabetes compared with decades ago. The study of type 1 diabetes in a low incidence region such as China may help advance the understanding of the contribution of varying combinations of genetic and environmental factors to the development of the disease. Moreover, most epidemiological studies of type 1 diabetes focused on childhood onset type 1 diabetes. Although type 1 diabetes most often develops in children, it can occur at any age. Our previous study also indicated that the onset of type 1 diabetes in adulthood is not rare in China. Yet little is known about its incidence in adults aged more than 20 years.

19. *Trop Med Int Health* 2017 Dec;22(12):1599-1608

### **Cardiopulmonary ultrasound for critically ill adults improves diagnostic accuracy in a resource-limited setting: the AFRICA trial**

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#### **OBJECTIVE:**

To assess the effects of a cardiopulmonary ultrasound (CPUS) examination on diagnostic accuracy for critically ill patients in a resource-limited setting.

#### **METHODS:**

Approximately half of the emergency medicine resident physicians at the Komfo Anokye Teaching Hospital (KATH) in Kumasi, Ghana, were trained in a CPUS protocol. Adult patients triaged to the resuscitation area of the emergency department (ED) were enrolled if they exhibited signs or symptoms of shock or respiratory distress. Patients were assigned to the intervention group if their treating physician had completed the CPUS training. The physician's initial diagnostic impression was recorded immediately after the history and physical examination in the control group, and after an added CPUS examination in the intervention group. This was compared to a standardised final diagnosis derived from post hoc chart review of the patient's care at 24 h by two blinded, independent reviewers using a clearly defined and systematic process. Secondary outcomes were 24-h mortality and use of IV fluids, diuretics, vasopressors and bronchodilators.

#### **RESULTS:**

Of 890 patients presenting during the study period, 502 were assessed for eligibility, and 180 patients were enrolled. Diagnostic accuracy was higher for patients who received the CPUS examination (71.9% vs. 57.1%,  $\Delta$  14.8% [CI 0.5%, 28.4%]). This effect was particularly pronounced for patients with a 'cardiac' diagnosis, such as cardiogenic shock, congestive heart failure or acute valvular disease

(94.7% vs. 40.0%,  $\Delta$  54.7% [CI 8.9%, 86.4%]). Secondary outcomes were not different between groups.

### **CONCLUSIONS:**

In an urban ED in Ghana, a CPUS examination improved the accuracy of the treating physician's initial diagnostic impression. There were no differences in 24-h mortality and a number of patient care interventions.

20. [Lancet 2018 Jan 3. pii: S0140-6736\(18\)30001-1. \[Epub ahead of print\]](#)

### **Perioperative patient outcomes in the African Surgical Outcomes Study: a 7-day prospective observational cohort study**

Biccard BM et al; African Surgical Outcomes Study (ASOS) investigators

**BACKGROUND:** There is a need to increase access to surgical treatments in African countries, but perioperative complications represent a major global health-care burden. There are few studies describing surgical outcomes in Africa. **METHODS:** We did a 7-day, international, prospective, observational cohort study of patients aged 18 years and older undergoing any inpatient surgery in 25 countries in Africa (the African Surgical Outcomes Study). We aimed to recruit as many hospitals as possible using a convenience sampling survey, and required data from at least ten hospitals per country (or half the surgical centres if there were fewer than ten hospitals) and data for at least 90% of eligible patients from each site. Each country selected one recruitment week between February and May, 2016. The primary outcome was in-hospital postoperative complications, assessed according to predefined criteria and graded as mild, moderate, or severe. Data were presented as median (IQR), mean (SD), or n (%), and compared using t tests. This study is registered on the South African National Health Research Database (KZ\_2015RP7\_22) and ClinicalTrials.gov (NCT03044899). **FINDINGS:** We recruited 11 422 patients (median 29 [IQR 10-70]) from 247 hospitals during the national cohort weeks. Hospitals served a median population of 810 000 people (IQR 200 000-2 000 000), with a combined number of specialist surgeons, obstetricians, and anaesthetists totalling 0.7 (0.2-1.9) per 100 000 population. Hospitals did a median of 212 (IQR 65-578) surgical procedures per 100 000 population each year. Patients were younger (mean age 38.5 years [SD 16.1]), with a lower risk profile (American Society of Anesthesiologists median score 1 [IQR 1-2]) than reported in high-income countries. 1253 (11%) patients were infected with HIV, 6504 procedures (57%) were urgent or emergent, and the most common procedure was caesarean delivery (3792 patients, 33%). Postoperative complications occurred in 1977 (18.2%, 95% CI 17.4-18.9) of 10 885 patients. 239 (2.1%) of 11 193 patients died, 225 (94.1%) after the day of surgery. Infection was the most common complication (1156 [10.2%] of 10 970 patients), of whom 112 (9.7%) died. **INTERPRETATION:** Despite a low-risk profile and few postoperative complications, patients in Africa were twice as likely to die after surgery when compared with the global average for postoperative deaths. Initiatives to increase access to surgical treatments in Africa therefore should be coupled with improved surveillance for deteriorating physiology in patients who develop postoperative complications, and the resources necessary to achieve this objective.

## **Research Ethics**

21. [Trop Med Int Health 2017 Dec;22\(12\):1505-1513](#)

### **Exogenous factors matter when interpreting the results of an impact evaluation: a case study of rainfall and child health programme intervention in Rwanda**

Mukabutera A et al., School of Public Health, University of Rwanda College of Medicine and Health Sciences, Kigali, Rwanda

**OBJECTIVE:**

Public health interventions are often implemented at large scale, and their evaluation seems to be difficult because they are usually multiple and their pathways to effect are complex and subject to modification by contextual factors. We assessed whether controlling for rainfall-related variables altered estimates of the efficacy of a health programme in rural Rwanda and have a quantifiable effect on an intervention evaluation outcomes.

**METHODS:**

We conducted a retrospective quasi-experimental study using previously collected cross-sectional data from the 2005 and 2010 Rwanda Demographic and Health Surveys (DHS), 2010 DHS oversampled data, monthly rainfall data collected from meteorological stations over the same period, and modelled output of long-term rainfall averages, soil moisture, and rain water run-off. Difference-in-difference models were used.

**RESULTS:**

Rainfall factors confounded the PIH intervention impact evaluation. When we adjusted our estimates of programme effect by controlling for a variety of rainfall variables, several effectiveness estimates changed by 10% or more. The analyses that did not adjust for rainfall-related variables underestimated the intervention effect on the prevalence of ARI by 14.3%, fever by 52.4% and stunting by 10.2%. Conversely, the unadjusted analysis overestimated the intervention's effect on diarrhoea by 56.5% and wasting by 80%.

**CONCLUSION:**

Rainfall-related patterns have a quantifiable effect on programme evaluation results and highlighted the importance and complexity of controlling for contextual factors in quasi-experimental design evaluations.

22. *Am J Trop Med Hyg* 2018 Jan;98(1):95-99

**Pilot Study of the Addition of Mass Treatment for Malaria to Existing School-Based Programs to Treat Neglected Tropical Diseases**

Cohee LM et al; Division of Malaria Research, Institute for Global Health, University of Maryland School of Medicine, Baltimore, Maryland

Malaria and neglected tropical diseases (NTDs), including schistosomiasis and soil transmitted helminths, threaten the health of school aged in sub-Saharan Africa. Established school-based mass drug administration (MDA) programs are used to control NTDs. Recent clinical trials have shown benefit of mass treatment of malaria in schools. The potential of adding malaria treatment to existing NTD programs has not been thoroughly evaluated. We offered malaria treatment with artemether-lumefantrine during routine NTD MDA and developed peer education programs in two primary schools in southern Malawi. We assessed participation, safety, and tolerability of coadministration of artemether-lumefantrine with praziquantel and albendazole. Results were compared with two schools conducting standard NTD MDA with additional monitoring by study staff. A total of 3,387 students (68%) received the standard NTD MDA. Among parents who came to schools on the day of the MDA, malaria treatment was well accepted; 87% of students who received the standard NTD MDA in intervention schools also consented for treatment with artemether-lumefantrine. The most frequent treatment emergent adverse events (AEs) were headache and vomiting. However, AEs were rare and were not more frequent in students who received artemether-lumefantrine in addition to praziquantel and albendazole. In this study, we found that the addition of malaria treatment to NTD MDA is well-received and safe. Such integrated programs may leverage existing infrastructures to reduce intervention costs and could become the framework for further integrated school-based health programs.

## Sexual and Reproductive Health

### 23. BMJ 2018;360:j5737 Practice 10-Minute Consultation

#### Birth options after a caesarean section

Jane E Norman, Sarah J Stock, [jane.norman@ed.ac.uk](mailto:jane.norman@ed.ac.uk)

Either vaginal birth or elective repeat caesarean section are reasonable options, and adverse outcomes are rare in most uncomplicated pregnancies in women with a previous caesarean section

Around 50% of women with one previous caesarean section attempt a vaginal birth in their second pregnancy, and of these nearly two thirds are successful

Explore the woman's concerns, preferences, reasons for previous caesarean section, and plans for future pregnancies to inform the choice of mode of delivery

A 30 year old woman at 36 weeks' gestation in her second pregnancy asks about her options for delivery. Her previous baby was born by emergency caesarean section at 39 weeks, after breech presentation was diagnosed in labour.

Birth options after an earlier caesarean section include

- A trial of labour after caesarean: allowing spontaneous labour to occur, anticipating a vaginal delivery (known as vaginal birth after caesarean section, or VBAC)
- Planned elective repeat caesarean section (ERCS).

Both are reasonable options for most women. The rates of serious maternal and neonatal adverse outcomes with either of the strategies are low. Pregnancy complications might alter the risks and benefits of each delivery strategy. ERCS is recommended in some scenarios, but an exploration of the woman's wishes and shared decision making is vital. Women attribute different values to the benefits and risks of either approach. Studies from the UK and US show that around 50% of women attempted a vaginal birth after one previous caesarean section.

Indications for elective caesarean section:

Fetal complications

Breech presentation at term; offer elective caesarean section if external cephalic version is unsuitable or unsuccessful

Other non-vertex presentations, including transverse lie

Twin pregnancy if the first twin is breech

Maternal complications

Placenta praevia (covering or less than 2 cm from the internal orifice)

Maternal viral infections:

- Primary genital herpes simplex virus infection occurring in the third trimester
- HIV: if the woman is on any antiretroviral therapy and the viral load is 400 copies per ml or more, OR if the woman is not on antiretroviral therapy

Obstruction to pelvic outflow such as a pelvic fibroid, or a bony pelvic deformity

Maternal conditions rendering labour unsafe, such as substantial dilation of the aortic root (eg, >4 cm with Marfan's syndrome)

Women with uterine scars other than those associated with lower segment caesarean section, such as women with a myomectomy or classic caesarean section scar

#### 24. *BMJ* 2018;360:k55 Research

##### **Within country inequalities in caesarean section rates: observational study of 72 low and middle income countries**

Adeline Adwoa Boatman, et al., Correspondence to: A R Hosseinpoor [hosseinpoora@who.int](mailto:hosseinpoora@who.int)

**Objective:** To provide an update on economic related inequalities in caesarean section rates within countries.

**Design:** Secondary analysis of demographic and health surveys and multiple indicator cluster surveys.

**Setting:** 72 low and middle income countries with a survey conducted between 2010 and 2014 for analysis of the latest situation of inequality, and 28 countries with a survey also conducted between 2000 and 2004 for analysis of the change in inequality over time.

**Participants:** Women aged 15-49 years with a live birth during the two or three years preceding the survey.

**Main outcome measures:** Data on caesarean section were disaggregated by asset based household wealth status and presented separately for five subgroups, ranging from the poorest to the richest fifth. Absolute and relative inequalities were measured using difference and ratio measures. The pace of change in the poorest and richest fifths was compared using a measure of excess change.

**Results:** National caesarean section rates ranged from 0.6% in South Sudan to 58.9% in the Dominican Republic. Within countries, caesarean section rates were lowest in the poorest fifth (median 3.7%) and highest in the richest fifth (median 18.4%). 18 out of 72 study countries reported a difference of 20 percentage points or higher between the richest and poorest fifth. The highest caesarean section rates and greatest levels of absolute inequality were observed in countries from the region of the Americas, whereas countries from the African region had low levels of caesarean use and comparatively lower levels of absolute inequality, although relative inequality was quite high in some countries. 26 out of 28 countries reported increases in caesarean section rates over time. Rates tended to increase faster in the richest fifth (median 0.9 percentage points per year) compared with the poorest fifth (median 0.2 percentage points per year), indicating an increase in inequality over time in most of these countries.

**Conclusions:** Substantial within country economic inequalities in caesarean deliveries remain. These inequalities might be due to a combination of inadequate access to emergency obstetric care among the poorest subgroups and high levels of caesarean use without medical indication in the richest subgroups, especially in middle income countries. Country specific strategies should address these inequalities to improve maternal and newborn health.

#### 25. *Trop Med Int Health* 2018 Jan;23(1):106-119

##### **The association between female genital fistula symptoms and gender-based violence: A multicountry secondary analysis of household survey data**

Mallick L et al., The DHS Program/Avenir Health, Rockville, MD, USA

##### **OBJECTIVE:**

The Demographic and Health Surveys (DHS), which include standardised questions on female genital fistula symptoms, provide a unique opportunity to evaluate the epidemiology of fistula. This study sought to examine associations between self-reported fistula symptoms and experience of gender-based violence (GBV) among women interviewed in DHS surveys.

##### **METHODS:**

This study used data from thirteen DHS surveys with standardised fistula and domestic violence modules. Data from the most recent survey in each country were pooled, weighting each survey equally. Multivariable logistic regressions controlled for maternal and demographic factors.

##### **RESULTS:**

Prevalence of fistula symptoms in this sample of 95 625 women ranges from 0.3% to 1.8% by country. The majority of women reporting fistula symptoms (56%) have ever experienced physical violence, and more than one-quarter have ever experienced sexual violence (27%), compared with 38% and 13% among women with no symptoms, respectively. Similarly, 16% of women with fistula symptoms report recently experiencing sexual violence—twice the percentage among women not reporting symptoms (8%). Women whose first experience of sexual violence was from a non-partner have almost four times the odds of reporting fistula symptoms compared with women who never experienced sexual violence. These associations indicate a need to investigate temporal and causal relationships between violence and fistula.

### **CONCLUSIONS:**

The increased risk of physical and sexual violence among women with fistula symptoms suggests that fistula programmes should incorporate GBV into provider training and services.

## **Miscellaneous**

### **26. BMJ 2017;359:j5926 Feature The BMJ charity appeal Christmas 2017**

#### **The BMJ charity appeal Christmas 2017: help Médecins Sans Frontières' volunteer doctors help the Rohingya people**

Jane Feinmann, journalist [jane@janefeinmann.com](mailto:jane@janefeinmann.com)

“Médecins Sans Frontières make it possible for you to do your job as a doctor, as well as you can, in the most difficult circumstances imaginable,” says Ian Cross, a retired Leicester GP and one of the first MSF doctors to respond to the recent emergency in Bangladesh as more than 600 000 Rohingya, mostly women and children, fled violence in Myanmar.

“I saw an appeal for doctors at the end of August, just as the news of the exodus was emerging,” he recalls. At the MSF health facility in Kutupalong, close to the Bangladesh border, he was one of 43 expatriate employees and volunteers organising medical facilities for refugees.

Working with another UK doctor and 12 Bangladeshi doctors, the MSF team were treating an average of 400 new outpatients a day, with 100 inpatients crammed into 80 beds.

#### **Gunshot and landmines**

“A third of the patients were children, some so malnourished that they had barely any resistance to disease. I learnt quickly how to manage gunshot wounds and landmine injuries. Each bed in the birthing unit was occupied 24 hours a day. The neonatal unit was filled with critically ill and premature babies with neither incubators nor ventilators. Dying patients became part of normality.”

But Cross has returned anything but defeated, acknowledging the team and MSF's logisticians. “They did an astonishing job ensuring we had an adequate drugs supply, building two extra wards with bamboo and plastic sheeting when they were needed, constructing a new incinerator away from the inpatient wards, and working out the best places to site tube wells and latrines,” he says. As well as doctors, the team recruited extra midwives, nurses, laboratory technicians, cleaners, and crowd controllers. Another 300 Rohingya volunteer outreach workers identified health problems, educated patients, and helped with vaccine campaigns.

The MSF inpatient unit was built at Kutupalong in 2008 to serve the steady trickle of Rohingya refugees that began leaving Myanmar two decades ago, many settling in the massive refugee camp nearby. “That background enabled MSF to understand the scope of the crisis and what needed to be done quickly,” explains Cross.

What he offers MSF, he says, is, “above all, the experience of 25 years as a GP.” Working abroad, he says, is “general practice with knobs on: conditions you might see in UK practice but much more advanced and which you have to manage with fewer resources—with a bit of tropical stuff thrown in

for good measure.” One thing that surprised him was the number of vaccine preventable diseases, including tetanus and measles, “because the Rohingya have been denied immunisations in Myanmar,” he says.

## 27. *BMJ* 2018;360:j5773 Practice Clinical Updates

### **Fever in the returning traveller**

Doug Fink, Robert Serafino Wani, Victoria Johnston, [douglas.fink@nhs.net](mailto:douglas.fink@nhs.net)

Malaria is the most common specific diagnosis in febrile returning travellers and must be excluded using peripheral blood smear testing for the malarial parasite

To protect yourself and prevent an outbreak, always ask yourself, “Does this patient need to be isolated?”

Consider the possibility of antimicrobial resistance if a patient with fever has recently travelled to Africa, Asia, or the Middle East, particularly if they were hospitalised

Sources and selection criteria

We searched the Medline database (1994–2017) using the terms “fever,” “travel,” and “travel medicine.” The search was limited to English language articles. Given the absence of randomised controlled trials in this field, we focused on observational studies in adult travellers (>16 years). Studies of infection in endemic populations were excluded. Appropriate publications were selected from the abstract list by two authors, with additional relevant articles included from their references. We have reviewed guidelines from the World Health Organization, Centers for Disease Control and Prevention, Public Health England, and the European Society for Clinical Microbiology and Infectious Diseases, and have compiled key recommendations from these.

International travel is increasingly common. The United Nations World Tourism Organisation estimates that by 2030, nearly 2 billion people will travel internationally each year, most of them to emerging economies. In the UK alone, there were more than 70 million visits abroad by UK residents in 2016, and 37 million overseas residents visiting the UK.

Illness associated with travel is common. Most infections are mild or self limiting, however their non-specific presentations make them challenging to distinguish from life threatening infections such as malaria.

## 28. *Am J Trop Med Hyg.* 2018 Jan 8. [Epub ahead of print]

### **The Quality of Medicines Used in Children and Supplied by Private Pharmaceutical Wholesalers in Kinshasa, Democratic Republic of Congo: A Prospective Survey**

Schiavetti B et al; Department of Public Health, Institute of Tropical Medicine, Antwerp, Belgium

Poor-quality medicines are a threat to public health in many low- and middle-income countries, and prospective surveys are needed to inform corrective actions. Therefore, we conducted a cross-sectional survey on a sample of products used for children and available in the private market in Kinshasa, Democratic Republic Congo: amoxicillin (AX) and artemether/lumefantrine (AL), powders for suspension, and paracetamol (PC) tablets 500 mg. Overall, 417 products were covertly purchased from 61 wholesalers. To obtain a representative sample, the products were weighted on their market shares and a subset of 239 samples was randomly extracted to undergo in-depth visual inspection locally, and they were chemically assessed at two accredited laboratories in Belgium. Samples were defined of “poor-quality” if they failed to comply with at least one specification of the International Pharmacopoeia (for AL) or United States Pharmacopoeia 37 (for AX and PC). Results are reported according to the Medicine Quality Assessment Reporting Guideline. The visual inspection detected nonconformities in the aspects of antimalarial powders for suspension, and poor-quality labels across all medicine types. According to chemical analysis, 27.2% samples were of poor quality and 59.5% of

AL samples were underdosed in artemether. Poor quality was more frequent for locally manufactured antimalarials (83.3%,  $P = 0.021$ ; 86.4%,  $P = 0.022$ ) and PC (4.8%,  $P = 0.000$ ). The poor quality of the surveyed products may decrease the treatment's efficacy and favor the development of resistances to antimalarials. It is hoped that these findings may guide the corrective actions of the Democratic Republic of Congo Regulatory Authority, which was the main partner in the research.