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Jo CH, Jung HS, Cho GC, Oh YJ. Over-the-head two-thumb encircling technique as an alternative to the two-finger technique in the in-hospital infant cardiac arrest setting: a randomised crossover simulation study. Emerg Med J. 2014; 10.1136/emermed-2014-203873. [Epub ahead of print].

A simulated randomized controlled trial of a new method for lone rescuer infant CPR that attempts to harness the benefits of two-thumb encircling technique while minimizing hands-off time.

Summary: The authors conducted a simulated prospective randomized controlled trial comparing a new method for lone rescuer infant CPR, over-the-head two-thumbs encircling technique (OTTT), to the current standard, two-finger technique (TFT). The study was conducted among 50 ED and pediatric nurses at Hallyam University in Seoul, South Korea, and was a randomized crossover trial. Nurses were blinded to the study purpose, performed 2 minutes of each method and were evaluated by an automated manikin and participant questionnaire. OTTT had greater depth of compressions (42.1 vs. 37.0 mm, $p<0.001$) and greater proportion of effective compressions (95.3% vs. 61.5%, $p < 0.001$), but had a lower proportion of compressions with complete recoil (84.2% vs. 97.8%, $p = 0.001$). Mean hands-off time was not significantly different between the two methods. Participants reported less fatigue after OTTT than TFT; and that compression, ventilation, and changing positions were more difficult with TFT than OTTT.

Comments: This is the first evaluation of OTTT encircling technique in lone rescuer CPR for an infant, and demonstrates significant improvements to the standard TFT in a simulated setting. Over the head CPR has been studied in adult subjects, but had conflicting results due to physical difficulties in reach. This has obvious implications for infant cardiac arrest care in all resource level settings, and could potentially drive change in cardiac resuscitation of the infant. While the blinded prospective nature and numerous subjects are obvious strengths, the nature of observed simulation makes the conclusions imperfect, and human subject data would be a valuable next step.

Alexander Jenson, Gabrielle Jacquet

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Chisti MJ, Graham SM, Duke T, et al. Post-discharge mortality in children with severe malnutrition and pneumonia in Bangladesh. PLOS ONE. 2014;9(9):e107663.

Barriers to ongoing nutritional care and health care access as well as baseline nutritional status contribute significantly to mortality after hospital discharge for pneumonia.

Summary: This study sought to identify factors associated with post-discharge mortality in a cohort of under-5 children hospitalized with pneumonia and malnutrition in Dhaka, Bangladesh. Recruited patients met criteria for radiologically confirmed pneumonia and for severe malnutrition. Per protocol, all patients were transferred to an inpatient nutritional rehabilitation unit (NRU) after their recovery from pneumonia, and were only to be discharged after reaching targets for malnutrition improvement. Death at 3-month follow-up constituted the primary outcome. Follow-up was conducted by scheduled hospital visits, by phone, and by two attempts to visit a family's home. All families had access to a phone and were encouraged to call study staff if their children became ill. Verbal autopsies were conducted to determine the circumstances of death. After excluding inpatient deaths 369 patients were enrolled, of whom 29 were discharged against medical advice prior to NRU transfer, and of whom an additional 297 left "on risk bond" before meeting NRU discharge targets. There were 32 (8.7%) deaths and 54 (15%) losses to follow-up. Most deaths (59%) occurred within one month of discharge, and were associated with either gastrointestinal or respiratory symptoms on verbal autopsy (n = 25). Factors statistically associated with deaths included previous pneumonia, age less than 12 months, poor nutritional status at admission or discharge (severe wasting and severe underweight), non-completion of NRU treatment (left against medical advice or "on risk bond"), and poor medical follow-up (non-attendance to follow-up visits, no phone calls to study staff, use of traditional healers instead of medical professionals).

Comment: The study successfully selected children with pneumonia with a high risk of short-term mortality post-discharge, and conducted due diligence to establish outcome at 3 months. Despite these efforts, the study lost almost 15% to follow-up. While on the one hand the follow-up losses somewhat weaken the study's overall findings, they further highlight the challenges of ensuring appropriate post-discharge care to young children at high risk of death. Not surprisingly, and in keeping with previous literature, the study found younger and more malnourished children to be at higher risk of post-discharge death. More remarkable are the study's findings that less than 12% of the study cohort was able to adhere to full inpatient nutritional rehabilitation program, and that 0% of children later dying were able to attend any of the suggested post-discharge follow-up visits at the hospital. The authors mention pressure on mothers to return to their homes early to fulfill other household and childcare responsibilities. The study should remind emergency care and inpatient care providers worldwide to look beyond the acute illness and identify children with malnutrition. These children should be linked to locally appropriate community-based nutrition programs with the goal to reduce post-discharge mortality.

Andrew Kestler, Gabrielle Jacquet

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Ashley EA, Dhorda M, Fairhurst RM, et al. Spread of Artemisinin resistance in plasmodium falciparum Malaria. NEJM. 2014;371(5):411-23.

Despite widespread artemisinin resistance in mainland Southeast Asia, artemisinin-based combination therapy remains effective with a prolonged 6-day course.

Summary: Resistance to antimalarial medications is associated with increased morbidity and mortality, which preferentially afflict children. Artemisinin resistance to the standard 3-day course has recently emerged in Southeast Asia and is marked clinically by slowed parasite clearance and genomically by a mutation in the "propeller" region of *Plasmodium falciparum* kelch protein, *kelch13*. In order to map the extent and severity of resistance, researchers studied 1241 patients aged 6 months to 65 years with acute, uncomplicated *P. falciparum* malaria, a parasite count of 10,000 - 200,000 per cubic millimeter, and fever greater than 37.5 degrees Celsius or history of fever. There were 15 study sites in ten countries; at most sites, patients received oral artesunate at 2 mg per kilogram of body weight per day or 4 mg per kilogram per day, for three days, followed by three days of an artemisinin-based combination therapy. For patients with recurrent infection within the follow-up window, polymerase-chain-reaction genotyping was performed. Therapeutic response to treatment varied greatly across sites, with the highest rates of prolonged parasite clearance in western Cambodia and eastern Thailand (49% -73%). Nevertheless, a prolonged course of artemisinin-based combination therapy remained highly effective in these areas, with a cure rate of 97.7% in western Cambodia. In addition, single-nucleotide polymorphisms (SNPs) in the propeller of *kelch13* were associated with a 116% slower parasite clearance half-life across sites.

Comment: *P. falciparum* malaria resistance to the traditional 3-day course of artemisinin is an emergent problem in Southeast Asia. In this large, open label, multinational study, researchers found a geographic link between SNPs in the *kelch13* protein of *P. falciparum* and prolonged parasite clearance with artemisinin resistance in mainland Southeast Asia. Despite the SNP-associated resistance, treatment success was achieved with a longer 6-day course of artemisinin-based combination therapy. This study offers important data to support a 6-day rather than the typical 3-day course of artemisinin-based therapy to treat malaria in Southeast Asia.

R. Eleanor Anderson, Gabrielle Jacquet

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ECRLS

Carrasco LR, Leo YS, Cook AR, et al. Predictive Tools for Severe Dengue Conforming to World Health Organization 2009 Criteria. PLOS Negl Trop Dis. 2014;8(7):e2972.

A retrospective cohort study to create a predictive tool that identifies those most likely to develop severe dengue according to the new 2009 WHO dengue classification criteria.

Summary: This retrospective cohort study of confirmed adult dengue cases at Tan Tock Seng Hospital in Singapore was designed to identify predictors for the development of severe dengue among hospitalized patients. Data was collected for all adults with confirmed PCR or positive IgM/IgG for dengue but without severe dengue on admission over a three-year study period, 2006 to 2008. Laboratory data, pertinent history, and signs and symptoms were used to construct predictive tools for the development of severe dengue. These tools were constructed for both well-resourced settings (with clinical and laboratory variables) and resource-limited settings (with only clinical variables). Of the 596 cases, 96 developed severe dengue during admission. The model for well-resourced settings had 90% sensitivity and 29% specificity and included positive predictors of female sex, fever on admission, and abdominal distension and vomiting; and negative predictors of more years of age, longer fever duration, leucopenia, and a normal hematocrit. Without laboratory data (resource-limited settings), the model had 90% sensitivity and 27% specificity. The only WHO warning signs for severe dengue development that were significant in the model were abdominal pain and vomiting. Using this model, 19% of admissions could have been prevented, for a cost saving of $0.69 million at this hospital during the study period.

Comments: This study represents the first development of a prediction tool for severe dengue since the WHO released the 2009 classification criteria, and is the first step toward a valuable tool for practitioners to allocate scarce resources and potentially alleviate costs. The study benefits from complete records over a three-year study period. However, the development of these models in a well-resourced setting with optimal fluid therapy raises questions about the external validity of this model to predict severe dengue in resource-limited settings, where intravenous fluids, and even dengue diagnostic tests, may not be available. In addition, the study was conducted at a single site, and cost savings models were specific to Singapore hospitalization and health care costs. More studies are needed to validate this model in low-resource settings.

Alexander Jenson, Gabrielle Jacquet

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ECRLS

Andrews B, Muchemwa L, Kelly P, Lakhi S, Heimburger DC, Bernard GR. Simplified severe sepsis protocol: a randomized controlled trial of modified early goal–directed therapy in Zambia. Crit Care Med. 2014;42:2315-24.

A simplified protocol for the treatment of patients with severe sepsis in Zambia does not improve outcomes compared to usual care.

Summary: The objective of the study was to assess the efficacy of early goal-directed protocol-based treatment of patients with severe sepsis. From February – July 2012, patients with severe sepsis presenting to the University Teaching Hospital in Lusaka, Zambia, were randomly assigned to either usual care (56 patients receiving physician-directed amounts of IV fluids and antibiotics, with occasional use of non-titrated dopamine) or a Simplified Severe Sepsis Protocol (SSSP). Severe sepsis was defined as probable infection with SIRS criteria and evidence of end-organ dysfunction.

Each of the 53 patients in the SSSP group received a 2L bolus of IV fluids within the first hour, followed by an additional 2L over 4 hours if jugular venous pressure was less than 3 cm. Dopamine infusions were initiated and titrated to a mean arterial pressure > 65 mmHg, based on the study protocol. Study patients received antibiotics as soon as possible and transfusion of whole blood for hemoglobin less than 7 g/dL. 80.7% of the patients were HIV positive. Of these, 37.8% had blood cultures positive for tuberculosis mycobacteria. Overall, in-hospital mortality was 62.4% without a significant difference between the two groups (60.7% in the control group vs. 64.2% in the SSSP group, RR 1.05, 95% CI = 0.79 to 1.41). Only two patients, one in each group, were admitted to the ICU for mechanical ventilation. The study was stopped early due to increased mortality of patients with hypoxemic respiratory distress in the intervention group compared to the control group (100% vs 70%).

Comment: Sepsis is one of the leading global causes of death, especially in sub-Saharan Africa where infectious diseases and HIV are prevalent, and access to intensive care is very limited. While early goal–directed sepsis therapy protocols have been shown to decrease mortality in North America and Europe, a previous fluid-based intervention study in children with sepsis in sub-Saharan Africa found higher mortality in the intervention group. This new study provides evidence that this association may also be true in adults. As a randomized controlled trial, the study has a strong design and methodology. Unfortunately, its generalizability is limited by the very high prevalence of HIV and TB in the study population, which can cause subacute or chronic sepsis, potentially requiring different management. Additionally, the high burden of pulmonary infections (58%) may have led to worsening outcomes with volume resuscitation. The study's broad inclusion criteria, therefore, may have masked potential benefits in smaller patient population subsets. Ultimately, the study is unable to definitely provide an answer for the optimal management of volume status in all patients with sepsis in resource-poor settings, but does provide information on an important sub-group and raises questions for further research.

Sabrina Titze, Regan Marsh

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ECRLS

Bowen AC, Tong SYC, Andrews RM, et al. Short-course oral co-trimoxazole versus intramuscular benzathine benzylpenicillin for impetigo in a highly endemic region: an open-label, randomised, controlled, non-inferiority trial. Lancet. 2014;384:2132–40.

In the battle against neglected skin diseases such as impetigo, alternative approaches to standard treatment can provide a successful cure.

Summary: There is limited evidence for treatment options in the management of impetigo in resource-limited settings. This open-label, randomized controlled study sought to demonstrate the non-inferiority of oral co-trimoxazole (CTX) compared with a recommended standard of intramuscular benzathine benzylpenicillin (BPG). Children suffering with non-bullous impetigo between the ages of 3 months and 13 years were recruited over a 36-month period from 2009 to 2012 from seven remote indigenous communities in the Northern Territory of Australia. Following disease severity assessment, children were allocated to receive IM BPG, 3 days of oral CTX twice daily, or 5 days of oral CTX once a day. The primary outcome was treatment success at day 7 based upon scoring of digital images of impetigo sores by reviewers blinded to treatment allocation. Of the 508 children enrolled, 72% were classified as having severe impetigo. Within a 10% margin of consideration for treatment success, pooled results of both 3-day and 5-day regimens of co-trimoxazole showed non-inferiority compared to benzathine benzylpenicillin, with a reported absolute difference of 0.5% (95% CI = -6.2% to 7.3%). Furthermore, co-trimoxazole also demonstrated non-inferiority with regard to clearance of causative sore pathogens (*S. pyogenes* and *S. aureus*), as well as improved rates of adverse events.

Comment: Given the potential serious complications associated with untreated impetigo such as post-streptococcal glomerulonephritis, bacterial sepsis, and osteomyelitis, this study offers evidence for a genuine treatment alternative in the form of oral CTX. The study's randomization method, assurance of dose administration by means of direct observation, minimal loss to follow-up, and intention to treat analysis ensure the validity of reported findings. Importantly, although a non-blinded study, the reviewers of digital images responsible for determining the primary outcome were masked to treatment allocation, and this again strengthens the study findings. With as many as 140 million cases of impetigo at any one time infecting children in developing countries, this study adds important knowledge to the field of global EM, and also noted potentially improved compliance and decreased cost compared to BPG (although these issues were not specifically investigated). While this study may begin to influence prescribing behavior, it is important to recognize that further research is needed to examine the longer-term effect of oral antibiotics for the treatment of impetigo, as well as practical considerations such as compliance and total cost, given that in many resource-limited settings directly observed treatment by health care staff may not be feasible. This study builds on existing knowledge of impetigo and its management and should encourage further research about disease prevalence and local pathogen sensitivities, which can therefore guide local treatment guidelines that include oral treatment alternatives for impetigo.

Najeeb Rahman, Regan Marsh

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ECRLS

Kerr NL, Hauswald M, Tamrakar SR, Wachter DA, Baty GM. An inexpensive device to treat postpartum hemorrhage: a preliminary proof of concept study of health provider opinion and training in Nepal. BMC Pregnancy Childbirth. 2014;14:81-7.

Obstetric health care providers in Nepal are comfortable and confident using an inexpensive, locally sourced compression garment for postpartum hemorrhage.

Summary: This study evaluates a novel, inexpensive pneumatic anti-shock garment made of bicycle tires and locally available cloth for the treatment of postpartum hemorrhage. The authors sought to evaluate the acceptability of the CAPP (circumferential abdominal-pelvic pressure) device to obstetric nurses and midwives and the efficacy of a single three-hour training course in its use, as well as determine local production capacity and cost. Fifty-eight nurses and midwives were randomly selected from the 344 health posts in the catchment area of Kathmandu University Dhulikhel hospital, where the study was based, and attended three sessions over eight months. During the first session, participants learned to use the CAPP device; the second and third sessions evaluated opinions and skill maintenance. To determine efficacy of device placement, ultrasound measurements of distal aortic flow using the device on healthy participants were performed with an average of 39% (95% CI = 25% to 53%, $P < 0.001$), 28% (95% CI = 21% to 33%, $P < 0.001$) and 29% (95% CI = 24% to 34%, $P < 0.001$) reduction seen over each of the three sessions, respectively. At the 4- and 8-month follow-up sessions, all participants reported confidence in their ability to assemble and maintain the device and thought it would useful in the treatment of postpartum hemorrhage; all but one participant thought they could apply it alone. Ten of the 50 participants available at 8-month follow-up had used the device (each once) and all reported cessation of hemorrhage without major adverse effects. The device cost $40 to produce locally.

Comment: Postpartum hemorrhage is the leading cause of maternal mortality worldwide and a concern for public health practitioners and acute care providers alike, particularly in areas where definitive obstetric care may be delayed or unavailable. Significant research has been done on the emergent management of the condition. This article describes a creative intervention that can be used in resource-limited settings when standard measures have failed. The authors have taken the important first step of insuring that the device can be readily incorporated into practice, including issues of cost, education, acceptance, and clinical application. However, while the authors report on the decrease in distal aortic blood flow in healthy volunteers after application of the device and provide anecdotal evidence of 10 cases of its successful use, the device was not evaluated directly during postpartum hemorrhage. Additionally, patient acceptance was not assessed. Further analysis, including population-level studies or comparison with a criterion standard device, is necessary to fully evaluate the effectiveness of this promising intervention.

Karen Ekernas, Regan Marsh

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ECRLS

Thielecke M, Nordin P, Ngomi N, Feldmeier H. Treatment of Tungiasis with dimeticone: a proof-of-principle study in rural Kenya. PLoS Negl Trop Dis. 2014;8(7):e3058.

A new use for topical dimeticone against tungiasis parasite is more effective than standard treatment in a proof-of-principle study.

Summary: This proof-of-principle drug study presents positive results about dimeticone therapy for treatment of tungiasis (sand-flea) parasite in rural Kenya. Tungiasis is a neglected widespread parasitic disease that is usually self-limited, but can cause severe pain and inflammation, disfigurement of feet, and serious secondary infections from non-sterile removal attempts. Definitive treatment is surgical removal. Standard non-surgical treatment with potassium permanganate ($KMnO_4$) plus petroleum jelly is thought to be minimally effective. The authors sought to compare standard treatment with dimeticone, a silicone oil that has been effective in causing asphyxia in head lice.

Forty-seven children at one school, who had at least one tungiasis lesion per foot, were enrolled. Daily for 7 days, standard topical treatment of $KMnO_4$ plus Vaseline was applied to each child's right foot, and the left foot was treated with topical dimeticone. Outcomes were assessed using handheld digital video microscopes to assess viability of the parasite and local inflammation. On Day 7, dimeticone showed greater efficacy against parasites measured by presence/absence of parasite viability signs (78% efficacy vs 39%, $p < 0.001$). Significant improvement of inflammation scores was also seen in the dimeticone group, while inflammation worsened in the $KMnO_4$ group.

Comment: Tungiasis is a self-limited disease, but the use of photos and video demonstrate the morbidity caused by this parasite. Strengths of the study include: the case-control-type foot comparison method, documentation of stages using a simple but effective recording device, and use of the school as a location to run the study. At the end of the study, participants were compensated with definitive surgical removal of any remaining viable parasites and a pair of shoes. A notable limitation, the study could not be blinded as $KMnO_4$ causes temporary skin discoloration. Additionally, while all 47 enrolled children were assessed on the final day, there were missing data points mid-way when children were absent from school. Over 7 days, no adverse drug effects were reported, but no long-term follow up was done.

Given burden of disease, tungiasis and its complications (including secondary infection and tetanus) are important topics for the global EM provider. Dimeticone is a relatively inexpensive, safe, and easy treatment and has the potential to significantly reduce morbidity for affected patients. While there is a dearth of research on tungiasis, this paper provides preliminary data that will likely both improve disease treatment and support further studies.

Emily Grover, Regan Marsh

RE
ECRLS

World Health Organization. Antimicrobial Resistance: Global report on surveillance. April 2014. http://apps.who.int/iris/bitstream/10665/112642/1/9789241564748_eng.pdf

The first global survey of antimicrobial resistance describes an increasingly concerning reality and establishes a standard by which future resistance patterns can be monitored.

Summary: Data on antimicrobial resistance were collected from April to December 2013 using individual country reports, international surveillance networks, and literature review. Of 129 WHO member states, 114 submitted data on resistance rates for nine bacteria-antibacterial pairs. For countries lacking sufficient data, additional metrics were obtained via literature searches published reports, and international databases.

This 256-page report describes an established global epidemic of antimicrobial resistance and highlights a lack of regional surveillance infrastructure, especially in Africa and the Middle East. Resistance to individual pathogens is quantified in the second section of the report. Third-generation cephalosporins had high rates of resistance among *E. coli* and *K. pneumoniae* (30% to 60%*)*, with a predicted future dependence on carbapenems, although most countries also reported *K. pneumoniae* resistance to carbapenems (>50% in some groups). Penicillin resistance was reported worldwide and penicillin was less than 50% effective in some areas. Flouroquinalone resistance for *Salmonella* and *Shigella* was lower (often <5% to 10%), while rates of *S. aureus* resistance to beta-lactams and *S. pneumonia* resistance to penicillin were high and similarly widespread. The third section highlights health and economic burden of disease, and is derived mostly from an extensive literature review. Though resistant pathogens were found to result in worse clinical patient outcomes, insufficient data prohibited specific economic conclusions. The fourth section highlights surveillance in disease-specific programs such as HIV, malaria, tuberculosis, and influenza. Multi-drug resistant TB was described in 3.6% of new TB cases and 20.2% of previously treated cases while HIV resistance rates were as high as 10% to 17%. The authors conclude with recommendations to establish much-needed ongoing surveillance systems.

Comment: Representing the first time antimicrobial resistance data has been compiled on a global scale, this WHO report is essential for clinicians, health officials, and policy makers alike. The report's message is clear: antimicrobial resistance exists globally, affecting every country, and we are frighteningly close to what the authors call a "post-antibiotic era." Resistance was shockingly high to all nine pathogen-antibiotic pairs and was reported in specific diseases from HIV to urinary tract infections. The report would benefit from a more user-friendly format, as its statistical richness makes it sometimes challenging to digest. It is also limited by numerous and immense gaps in the surveillance data – in fact, this was a major conclusion of the report. However, the work clearly establishes an important baseline for future monitoring. This is not a report to be taken lightly – it paints a bleak future given our current antibiotic-driven approach to treating disease, and suggests that a new model for worldwide health care delivery is urgently needed, before even minor infections prove difficult or even impossible to treat.

Braden Hexom, Susan Bartels

OR
ECRLS

Duong YT, Mavengere Y, Patel H, et al. Poor Performance of the Determine HIV – 1/2 Ag/Ab Combo Fourth-Generation Rapid Test for Detection of Acute Infections in a National Household Survey in Swaziland. J Clin Microbiol. 2014;52(10):3743-8.

An evaluation of the utility of the Determine HIV-1/2 Ag/Ab combo fourth-generation rapid test for detecting acute HIV infections.

Summary: This cross-sectional household survey in Swaziland evaluated the performance of the Determine HIV-1/2 Ag/Ab combo fourth-generation rapid test (RT) for detecting acute HIV infections. A total of 18,172 individuals, aged 18 to 49 years received home-based HIV rapid testing using the Determine RT between 2010-2011. Antibody positive (Ab+) tests were confirmed by Uni-Gold testing. Individuals identified as having acute infections (Ag+/Ab -) were then tested for HIV-1 RNA quantification and followed up at 6 weeks. All RT-nonreactive samples were tested by nucleic acid amplification testing (NAAT) to identify any additional acute infections. Of the 18,172 participants, 5,802 (31.9%) were HIV-positive and 13 (0.1%) of 12,370 negative individuals were acutely infected by NAAT. The Determine combo test identified 12 individuals as having acute infections (Ag+/Ab-) but none had detectable HIV-1 RNA levels on confirmatory testing. In addition, the 8 subjects that followed up at 6 weeks remained HIV-negative (four lost to follow-up). Of the RT-nonreactive samples tested by NAAT, 13 (0.1%) were identified as having acute infections. None of these samples were Ag+ by Determine combo testing. Thus both the sensitivity and the positive predictive values were 0% for the Determine HIV-1/2 Ag/Ab combo RT for detecting acute HIV infections.

Comment: Findings from this study are congruent with previous findings with respect to the inability of the Determine combo RT to detect acute infections with high sensitivity. This was a nationally representative survey with a large sample size and was conducted in a high HIV prevalence and incidence area, which would be ideal for finding potential acute HIV infections. Follow-up testing of individuals identified as positive by both NAAT and Determine combo tests was conducted. One limitation of the study is that the Determine combo test is better at detecting sub-type B, while sub-type C is the predominant infecting strain of HIV in Swaziland. Another limitation is that the yield of true acute infections was very low, despite testing in a high incidence population. Prior research had been equivocal in terms of the utility of the Determine fourth-generation combo RT for detecting acute HIV infections. This study suggests that the Ag component of the Determine combo test in a high-prevalence and high-incidence setting is unable to detect acute infections reliably. The findings are important because they may refocus efforts to find an adequate rapid test for acute HIV infections.

Anand Selvam, Maxwell Osei-Ampofo

OR
ECRLS

Maude RJ, Silamut K, Plewes K, et al. Randomized controlled trial of levamisole hydrochloride as adjunctive therapy in severe falciparum malaria with high parasitemia. J Infect Dis. 2014;209:120-9.

Despite promising earlier work, levamisole provides no benefit when added to standard artesunate therapy in severe malaria.

Summary: Sequestration of infected erythrocytes in the microvasculature of various organs is believed to be an important part of the pathophysiology of severe falciparum malaria, including cerebral malaria. Binding sites on the vascular endothelium are thus a biologically plausible target for an adjunct to standard antimalarials. A common antihelminthic drug, levamisole, blocks adhesion of erythrocytes to the CD36 receptor in vitro, and in a pilot study by the authors, it appeared to decrease sequestration of infected erythrocytes in patients when added to standard treatment with intravenous quinine. Building on this experience, the authors randomized patients with WHO-defined severe malaria to standard treatment with artesunate versus artesunate plus a single dose of levamisole. Frequent blood samples allowed for measurement of clinically relevant values and calculation of parasite clearance, sequestration rate, and lactate clearance. Rectal mucosa was also examined with orthogonal polarizing spectroscopy (OPS) to measure microvascular flow. Parasite reduction rate was slightly and significantly faster in the levamisole group. However, sequestration rates were not improved. Measures of microvascular flow, including lactate clearance and the OPS measurements, showed no difference between groups. No significant difference in mortality between the groups was found.

Comment: Patient-centered outcomes are more common in EM research than the endpoints used in this clinical trial, but this study nevertheless makes an important contribution to our knowledge of malaria treatment. While the outcome was disappointing, it is heartening to see a negative trial published. As the authors themselves suggest, the salient difference between their previous study and this one is likely the change from quinine to artesunate in WHO guidelines and general practice. With the more rapid killing of more mature parasites, sequestration may be a less important mechanism to target. Although the sample size was small (n = 56), this was a carefully designed and conducted study, with computer-randomization of patients and blinding of patients, physicians, and laboratory personnel. Future studies focused on the role of sequestration would do well to emulate their methods.

Aislinn Black, Maxwell Osei-Ampofo

RE
ECRLS

Gupta S, Wong EG, Mahmood U, Charles AG, Nwomeh BC, Kushner AL. Burn management capacity in low and middle-income countries: a systematic review of 458 hospitals across 14 countries. Int J Surg. 2014;12(10):1070-3.

Given the disproportionate burden and prevalence of burn injury in low- and middle-income countries, a review was undertaken to assess capacity for burn management in these settings.

Summary: Health care facilities in low- and middle-income countries (LMIC) often lack the needed resources such as trained personnel and materials to provide adequate burn management. This review was performed to assess the capacity of such facilities to deal specifically with burn management. The reviewers searched for studies assessing seven criteria deemed critical for care of burn victims: the presence of a surgeon and an anesthesiologist, basic resuscitation and endotracheal intubation capacity, ability to manage acute burns and to provide skin graft and contracture release procedures. Data on 458 hospitals in LMICs was identified. The majority of hospitals for which this information was available were able to provide basic resuscitation services (over 80%). However, only a minority of these hospitals had the necessary skills and materials to provide endotracheal intubation, skin grafting, or contracture release for burn complications. Overall, only one surgeon and one anesthesiologist were available per hospital to provide care. No countries in the review were able to provide all key services, however, only two countries had full documentation of the presence or absence of each of the criteria.

Comment: This review highlights the dire need for increased capacity for burn management across LMICs, particularly in light of the burden of morbidity and mortality. Despite an increased prevalence and burden of disease, the resources available to address the problem fall far short of even the minimum required. The review was limited by lack of specific reported data on the criteria being used to measure capacity. Again, the authors did not count general medical practitioners who may have skills in burn care as potential human resources for burn management, which in the LMIC setting might have resulted in a significant underestimation of capacity.

Alison Schroth Hayward, Maxwell Osei-Ampofo

OR
ECRLS

Zhao QM, Ma XJ, Ge XL, et al. Pulse oximetry with clinical assessment to screen for congenital heart disease in neonates in China: a prospective study. Lancet. 2014;384:747–54.

Prospective screening study to determine the clinical usefulness of combining clinical examination with pulse oximetry testing of newborns to detect asymptomatic congenital heart disease.

Summary: This prospective multicenter screening study involving over 130,000 consecutive deliveries in 18 hospitals in China was designed to show that the routine use of pulse oximetry in addition to clinical assessment was feasible and accurate in detecting not just life-threatening congenital heart disease, but serious congenital heart disease with specific application to middle-income countries like China. The reference standard applied was echocardiography for every baby who screened positive by either method, in addition to clinical follow-up at 6 weeks and telephonic follow-up at one year. Of the 120,707 asymptomatic newborns assessed at a median age of 43 hours (range 6 to 72 hours), there were 3,582 who were screen-positive on a combination of clinical assessment and pulse oximetry, yielding a combined sensitivity and specificity of 90.2% (95% CI = 86.4% to 93.0%) and 97.3% (95% CI = 97.2% to 97.4%) respectively for major congenital heart disease, translating into a PPV of 7.9% (95% CI = 7.1% to 8.9%) and NPV of 99.97% (95% CI = 99.96% to 99.98%), or LR+ 32.9 (95% CI = 32.9% to 33.0%) and LR- 0.1 (95% CI = 0.10% to 0.11%). Similarly, 93% of asymptomatic critical congenital heart disease cases were detected.

Comments: The study achieved what it set out to do. Each identified consecutive newborn without a prenatal diagnosis of congenital heart disease received confirmatory screening, showing that the simple procedure of early clinical examination together with pulse oximetry proved to be superior to either modality on its own. In addition, the program could identify asymptomatic newborns early on, even in a middle-income setting. This is the largest such study to date, adding to the growing evidence that this is a useful screening tool in newborns. However, when considering external validity consider: 1) the critical timing of this examination and follow-up (see also the commentary in Ewer, AK. Pulse oximetry screening: do we have enough evidence now? Lancet 2014;384:725-726.); 2) the available resources that can be mustered both on confirmation testing as well as treatment. A screening program should not be implemented if the resources to confirm diagnosis or treatments for the conditions detected are not available. In many low-income and some middle-income countries, echocardiography is not freely available; neither is access to cardiothoracic surgery or interventional radiology. Spending resources on detection without recourse to intervention would be unethical. From an emergency medicine point of view, however, it means that for practitioners working in middle- and high-income countries, it is a worthwhile consideration to add pulse oximetry to a careful clinical examination when faced with a newborn within 24 to 48 hours of delivery.

Tyson Welzel, Bhakti Hansoti

RE
ECRLS

Saccone G, Berghella V. Antibiotic prophylaxis for term or near-term premature rupture of membranes: meta-analysis of randomized trial. Am J Obstet Gynecol. 2015;212:1.e1-9.

Antibiotic prophylaxis provided to gestations at 36 weeks or more presenting with premature rupture of membranes does not reduce the rate of chorioamnionitis or neonatal sepsis; however, there is a benefit to prophylactic antibiotics if latency is longer than 12 hours.

Summary: This article is a meta-analysis of five randomized controlled clinical trials including singleton gestations with premature rupture of membranes at 36 weeks or more gestational age randomized to the intervention of antibiotic prophylaxis compared to a control group (placebo or no intervention). The authors reviewed five trials, conducted in Mexico, Spain, Chile, Portugal, and Egypt, involving 2,699 women. There was no difference between the groups on primary outcomes of maternal chorioamnionitis or neonatal sepsis. Additionally, there was no difference on maternal secondary outcomes including latency, endometritis, postpartum septicemia, placental abruption, induction of labor, spontaneous labor, cord prolapse, days of hospitalization, and breast-feeding. Likewise, there was no difference in neonatal secondary outcomes including admission to the neonatal intensive care unit, respiratory complications, abnormality on cerebral ultrasound (either cystic periventricular leukomalacia or intraventricular hemorrhage), cerebral palsy, the rate of neonates who required antibiotics, neonatal infection/sepsis, Apgar score less than 7 at 5 minutes, and perinatal death. The rate of C-section was the only secondary outcome exhibiting a difference and was higher in women who received antibiotics (20.5% vs. 15.6%; RR, 1.32; 95% CI = 1.09 to 1.60). However, a subgroup analysis showed a 51% decrease in the rate of chorioamnionitis (2.9% vs. 6.1%; RR, 0.49; 95% CI = 0.27 to 0.91) and 88% decrease in the rate of endometritis (0% vs. 2.2%; RR, 0.12; 95% CI = 0.02 to 0.62) in women with a latency longer than 12 hours who received prophylactic antibiotics.

Comment: Longer latency is associated with higher rates of maternal and neonatal infections, but this difference is negated if prophylactic antibiotics are provided. This supports the recommendation of immediate induction of labor after term PROM. If it is anticipated that there will be a prolonged latency period, then prophylactic antibiotics should be administered to reduce the rate of chorioamnioitis and endometritis.

Michael Boyd, Kevin Lunney

OR
ECRLS

Gehani AA, Al-Hinai AT, Zubaid M, et al. Association of risk factors with myocardial infarction in Middle Eastern countries: the INTERHEART Middle East study. Eur J Prev Cardiol. 2014;4:400–10.

Based on the Middle East subset from the INTERHEART study, nine risk factors (tobacco use, ApoB/Apo1 ratio, psychosocial, abdominal obesity, diabetes, hypertension, lack of fruits and vegetables in the diet, lack of exercise, and tobacco consumption) constitute 97% of the population attributable risk of acute myocardial infarction in Middle Eastern countries.

Summary: Cardiovascular disease is the world's leading cause of morbidity and mortality, and 80% of cardiovascular disease burden occurs in middle- and lower-income countries. In particular, as Middle Eastern countries urbanize, cardiovascular disease is projected to increase substantially. The INTERHEART study enrolled 15,152 cases of acute MI and 14,820 controls in 52 countries and evaluated risk factors associated with acute myocardial infarction (AMI). This case-control study evaluates INTERHEART's subset of Middle Eastern subjects, using 1,364 cases and 1,525 controls. Data was gathered through structured questionnaires regarding socioeconomic status, ethnicity, lifestyle, dietary habits, tobacco use, personal and family history of cardiovascular disease, psychosocial factors, and risk factors such as diabetes, dyslipidemia, and hypertension. Physical exams were performed and blood was tested for total cholesterol, high density lipoprotein, and aoprotein (ApoB/Apo1 ratio). The authors found nine risk factors that accounted for 97% of the risk of AMI in Middle Eastern countries and ranked the severity of these risk factors by their odds ratios. Smoking (OR 3.63) and high ApoB/ApoA1 (OR 3.43) represent the two greatest risk factors for AMI. Psychosocial, abdominal obesity, diabetes, and hypertension were the next most important risk factors. Daily consumption of fruits and vegetables had a protective effect, and lack of exercise had an adverse effect. Smokers were also more likely to have AMI at a younger age than nonsmokers.

Comments: The Middle East had the lowest mean age of AMI (51.2) out of any of the regions in the INTERHEART study. Data regarding alcohol was subject to reporting bias and likely unreliable. The mean age of first AMI in the Middle East was 7 years lower in men than in women. From a public health perspective, this study shows that tobacco use and lipid control are the two highest yield targets to reduce AMI in Middle Eastern Countries. In fact, only 5% of cases who had AMI were on lipid lower drugs prior to their AMI. More aggressive cholesterol management and smoking cessation policies, in addition to targeting obesity, diabetes, and hypertension, could have a significant effect on the rate of AMI in Middle Eastern countries.

Michael Boyd, Kevin Lunney

OR
ECRLS

Means AR, Weaver MR, Burnett SM, Mbonye MK, Naikoba S, McClelland RS.Correlates of Inappropriate Prescribing of Antibiotics to Patients with Malaria in Uganda. PLOS ONE. 2014;9(2):e90179.

Antibiotics are inappropriately prescribed to malaria patients 42% of the time. This practice is associated with patients under 5 years of age, non-physician providers, and patient triage.

Summary: This study aims to identify the clinical and operational factors associated with inappropriate antibiotic use in malaria positive patients in Uganda. Understanding these factors can create targets for improving clinically appropriate antibiotic use. In this cross-sectional analysis, patient data was re-analyzed from a prior study to separate out those who received appropriate or inappropriate antibiotics. Malaria-positive patients were classified as either receiving antibiotics when not clinically indicated, or not receiving antibiotics when clinically indicated. Eight factors, three clinical (HIV status, triage level, age) and five operational (health practitioner professional level, repeat presentation for same chief complaint, <50% antimalarial availability, <50% antibiotic availability, rate of infected vector bites near health facility) were used in uni- and multivariate logistic regression models clustered by 36 facilities. Potential confounding factors were the type of facility (private vs public), patient sex, and month of visit. Of the 45,591 malaria-positive patients who presented, 90% did not have clinical indications to receive antibiotics; however, 42% (17,152) received antibiotic prescriptions. Of the 10% of malaria patients that did have clinical indications for antibiotics, 11% did *not* receive antibiotic prescriptions. The multivariate analysis for patients who received antibiotic prescriptions without clinical indications demonstrated that HIV-positive and emergency-level triage patients were less likely to receive inappropriate prescriptions. In contrast, children under the age of 5 years old were more likely to receive antibiotics without indications. Of the operational factors, lower skilled health care practitioners and a shortage of antimalarial treatments were correlated with an increased odds ratio of inappropriate antibiotic use. In patients who did not receive antibiotics when indicated, operational factors - specifically returning patients, and those visiting a facility in a medium to high malaria inoculation zone - were associated with patients not receiving clinically appropriate antibiotics.

Comments: The authors of this study importantly separate inappropriate antibiotic use into two practice patterns: antibiotics in the setting of no clinical indication, and no antibiotics despite an indication. They then identified the clinical and operational factors associated with each pattern to inform curriculum development focusing on improving antibiotic use. In particular, patient triage, clinical practice affecting children under 5 years, the assessment of returning patients and those in high malaria inoculation zones show opportunity for educational curricula and health systems development. HIV status is more likely correlated with appropriate treatment of HIV patients rather than appropriate antibiotic use in a malaria patient. The data set also realistically illustrates that non-medical officer providers see the bulk of the patients. As such, understanding the drivers of their practice patterns is an important area of future research to improve malaria patient management vis-à-vis antibiotic use.
Jacqueline Mahal, Kevin Lunney

RE
ECRLS

Zani B, Gathu M, Donegan S, Olliaro PL, Sinclair D. Dihydroartemisinin-piperaquine for treating uncomplicated *Plasmodium falciparum* malaria (Review). Cochrane Database Syst Rev. 2014;1.

When compared to artemether-lumefantrine and artesunate plus mefloquine, dihydroartemisinin-piperaquine is as good or better at preventing treatment failure of Plasmodium falciparum throughout Africa and Asia.

Summary: This review article, published by The Cochrane Collaboration, aims to compare dihydroartemisinin-piperaquine (DHA-P) to alternative World Health Organization approved artemisinin-based combination therapies for the treatment of uncomplicated *P. falciparum* malaria in both children and adults. The authors specifically focus on effectiveness and safety of various treatment strategies. Zani et al. conducted a broad search of the literature for randomized controlled trials comparing a three-day course of treatment with DHA-P to a three-day course with an approved alternative. The literature search included studies indexed through July 29, 2013. The primary outcome was PCR-adjusted and unadjusted treatment failure at 28, 42, and 63 days. Secondary outcomes were gametocyte carriage at day 7 or 14, gametocyte development, and change in hemoglobin from baseline. The authors also tracked treatment complications, including death and gastrointestinal complains, among other adverse events. Twenty-seven trials were included as primary references; an additional seven trials were included as secondary references. The 27 primary articles enrolled a total of 16,382 patients. Twelve studies were conducted in Africa; an additional 14 were conducted in Asia and Oceania, and 1 in South America. The authors concluded that while artemether-lumefantrine (AL6) performed well in Africa at 28 day follow-up, DHA-P is better at preventing further parasitemia, has lower treatment failure rates, and has a longer prophylactic effect. There was no difference among patients taking either medication in Asia. The side effect profile for both drugs was similar. Furthermore, the authors found both DHA-P and artesunate plus mefloquine (AS+MQ) perform well in Asia with respect to preventing treatment failure at 28-day follow-up. While both medications have long prophylactic effects, DHA-P is tolerated better than AS+MQ. Finally, while DHA-P can cause prolongation of the QTc interval, there were no cardiac arrhythmias reported.

Comment: Given the simplistic once-daily dosing of DHA-P, its strong performance in both Africa and Asia, and its limited side-effect profile, DHA-P is a reasonable first-line treatment for uncomplicated malaria due to *P. falciparum.* This is important due to the rise in resistance of *P. falciparum* to many antimalarial drugs, and the global burden of malaria. The authors conducted a thorough literature search, selecting only RCTs for inclusion in the review. The review is admittedly limited by the exclusion of infants less than 6 months old and pregnant women from the primary studies. These are two high-risk populations that will require further study in the future.

Alexis Kearney, Kevin Lunney

OR
ECRLS

Cavalcanti L, Mota LA, Lustosa GP, et al. Evaluation of the WHO classification of dengue disease severity during an epidemic in 2011 in the state of Ceará, Brazil. Mem Inst Oswaldo Cruz. 2013;109(1):93-98.

The 2009 WHO classification system for dengue disease more accurately predicts severe disease than the 1997 version. This improved accuracy may lead to earlier recognition of severe disease and positively affect patient care and early epidemic recognition.

Summary: This retrospective cross sectional study uses data from a large 2011 dengue outbreak in Brazil to compare the 2009 WHO classification of dengue disease with the previous 1997 WHO classification system. The 2009 system correctly identified 62% of the severe dengue cases versus only 37% identified with the 1997 system, and appears to identify severe disease with greater sensitivity and specificity than its predecessor.

Comment: Dengue is an important arthropod-borne infectious disease, with a wide spectrum of clinical severity ranging from mild systemic symptoms to severe hemorrhage, shock, and death. The disease is spreading to previously unaffected regions, and epidemics are on the rise. Cavalcanti et al. make an important contribution to the field of global emergency medicine literature by demonstrating the ability of the 2009 WHO dengue classification system to identify severe dengue disease more accurately, and potentially more rapidly. The article is limited by its retrospective nature, single-site setting, and small sample size (84 cases), but appears to set the stage for a prospective study to validate its findings. An additional limitation is that it attempts to compare two classification systems in terms of their ability to identify severe disease, without a clear gold standard. Despite this, the findings appear valid as they are in line with a 2012 study from Taiwan that also retrospectively compares the 1997 and 2009 WHO systems.

Daniel Millikan, Kevin Lunney

OR
ECRLS

Mueller T, Siv S, Khim N, et al. Acute Undifferentiated Febrile Illness in Rural Cambodia: A 3-Year Prospective Observational Study. PLOS ONE. 2014;4:1-10.

As the incidence of malaria continues to decrease in South East Asia and ease of its diagnosis improves, the appropriate diagnosis and management of non-malarial febrile illness has become increasingly important.

Summary: In Cambodia, advances in malaria control leading to decreased incidence, in conjunction with the advent of rapid malaria diagnostic testing (RDT), have highlighted the role of non-malarial febrile illness (NMFI). The authors suggest that there is data lacking regarding both the epidemiology and appropriate management of NMFI, which is especially challenging in peripheral or rural settings where diagnostic tools are scarce. The authors undertook a cross sectional prospective study over a period of three years in three geographically diverse peripheral health centers. One thousand one hundred ninety-three febrile participants aged 7 to 49 years were recruited, along with 282 non-febrile controls recruited from family members or accompanying persons. Clinical examination, RDT for malaria, and PCR for malaria species, leptospirosis, rickettsia, O. Tsutsugamushi, dengue virus and influenza virus were performed for all patients. PCR identified malaria in 56.7% of cases and in 27.7% percent of controls. All positive RDTs were in the case group, but 300 additional cases had negative RDT and positive PCR. RDT-negative cases were treated most often as acute upper respiratory infection, and most received amoxicillin. PCR revealed leptospirosis as the second most common pathogen (close to 9% in both case and control groups), followed by dengue virus and influenza A (both more frequent in the case group). Some geographical variation was noted for certain pathogens, and temporal epidemics were observed for dengue and influenza. In the discussion, the authors note that clinical exam and RDT missed a significant proportion of PCR-positive malaria cases. The authors also highlight that most RDT-negative cases were given amoxicillin for presumed acute upper respiratory infection, and that only 14% received treatment that would have been effective against the identified pathogen.

Comments: While limited in the scope of pathogens it sought to identify, this study highlights the need for understanding the epidemiology and incidence of NMFI in rural or peripheral settings, in order to guide management algorithms in areas with limited diagnostic capabilities to prevent misdiagnosis and prescription of incorrect medication. The findings also demonstrate that RDT does not identify all cases of PCR-proven malaria; however, some RDT-negative cases were still treated as malaria based on clinical suspicion, raising the important question of the clinical significance and management of low-density RDT-negative malaria. The study acts as a preliminary framework for future research aimed at examining a more diverse array of pathogens in NMFI, while being cognizant of regional variation and resource availability.

Kamna Balhara, Bhakti Hansoti

RE
DHR

Wuthisuthimethawee P, Lindquist SJ, Sandler N, et al. Wound management in disaster settings. World J Surg. 2015;3:9(4):842-53.

Guidelines for wound management in the acute aftermath of a disaster are created for first responders.

Summary: In an attempt to reduce infection rates and subsequently reduce morbidity and mortality, the authors conducted a systematic review of 62 articles to develop guidelines for first responders and non-expert health care providers on wound management in disaster settings. Important aspects addressed included types of wounds, infection rates, initial patient management, basic wound assessment and management, dressings, antibiotic use, tetanus prophylaxis, documentation, entrapment and extrication, crush injury, compartment syndrome, fractures, delayed amputation, extremity and head and neck wounds. Major disasters examined included earthquakes in Turkey, Pakistan, China, and Haiti; tsunami and terrorist bombings in Indonesia; and a tsunami in Thailand. A consensus panel, comprised of experts in surgery, disaster medicine, and anesthesia from Australasia, North America, South East Asia and the Indian subcontinent, collaborated at the Royal Australasian College of Surgeons to create guidelines for wound management in the acute aftermath of a disaster. The guidelines highlight ABCs, bleeding control, wound assessment, contamination control, dressing, documentation, medications, vaccinations, and follow-up and definitive management by a specialist and emphasize the cleaning, debridement, and avoidance of premature closure of contaminated wounds. Furthermore, the guidelines were created to be an easy reference that can be modified based on the location and specific needs. Ultimately, the goal was to provide first responders with a recommended consistent approach to wound care in the acute aftermath of a disaster.

Comments: The initial management of a patient and his or her wounds in a disaster setting is known to be a critical time for patient long-term outcome, morbidity, and mortality. The article successfully defines the problem, states its purpose, and organizes the characteristics of the types of wounds and their management. The authors illustrate a comprehensive guideline; however, the article does not indicate how it would disseminate the proposed guideline to ensure its international compliance. Additionally, non-expert health care responders may require further education and instruction about the guidelines in order use them correctly.

Tu Carol Nguyen, Gabrielle Jacquet

OR
DHR

Cooper L, Guan H, Ortiz-Hernandez AA, et al. Pediatrics in disasters: evaluation of a global training program. Adv Pediatr. 2014;61(1):245-60.

An educational intervention aimed at improving care of children in disasters was described and evaluated and serves as a model for high-impact short course development, implementation, and assessment across many LMICs.

Summary: A training course was developed to address needs of the vulnerable pediatric population in disaster events, and this article describes and presents evaluation data from the course. The Pediatrics in Disasters (PEDS) course consists of 10 modules over 2-4 days and was implemented in LMICs in Asia and Central & South America from 2008-2013, with 730 participants in 19 courses.

The aims of the course were to: 1) motivate LMIC providers to be more involved in disaster planning/response by providing useful training, 2) establish regional PEDS training centers to disseminate knowledge/skills in LMIC, and 3) facilitate collaboration across organizations regarding pediatric care in disasters. Evaluation methods included: 1) cognitive knowledge pre/post, 2) participant satisfaction and perception of course utility, 3) number of graduates who went on to participate in further disaster training/planning, and 4) course director survey. Results from the evaluations showed the course overall met its aims with an average increase in post-test score from pre-test of 20%, high scores on learner satisfaction items, and more than 50% of training centers doing (or planning) more PEDS trainings.

Comment: Disasters disproportionately affect children, and emergency providers in LMICs need critical knowledge and skills to improve their care in disasters. Strengths of the article include the course content and design, which appears to cover key topics of caring for children in disasters, and that they used several modes of content delivery. The evaluation methods were also multi-modal, with objective and subjective data from learners and trainers, immediately after the course and at longer-term follow-up. The authors faced challenges obtaining data from certain course centers, limiting the analysis and raising questions about confounders or bias, as well as limiting the study's power and forcing the authors to report more on trends than hard statistical tests. Courses were run only in Latin America and Asia, so generalizability to LMICs in Africa is unclear. Further, while the study met its defined aims, it is unknown if this corresponds to improved care of children in real disasters.

This article adds important knowledge about pediatric disaster training programs and supports that a short training course can be effective in increasing knowledge, participation, and collaboration. It also serves as a model of how to design, run, and evaluate a short educational intervention in resource-constrained settings.

Emily Grover, Regan Marsh

RE
DHR

World Health Organization. A Systematic Review of Public Health and Emergency Operations Centers. 2013.
http://apps.who.int/iris/bitstream/10665/99043/1/WHO_HSE_GCR_2014.1_eng.pdf

This manuscript presents peer-reviewed and grey literature on emergency operations centers (EOCs) in order to describe and benchmark best practices, with the goal of strengthening capacity to effectively respond to public health emergencies.

Summary: PubMed, EMBASE, Web of Science, IEEE Xplore, and ACM were searched for articles published between January 1993 and October 2013. The grey literature search included publications of the WHO, US CDC, academic research centers, and the Pan American Health Organization. Reference lists were hand-searched to identify other relevant articles. Best practices from the Cochrane Handbook for Systematic Reviews of Interventions, the Preferred Reporting of Items for Systematic Reviews and Meta-Analyses (PRISMA), and the WHO Handbook for Guideline Development were followed. The protocol was registered with PPROSPERO International and program quality was assessed using the Critical Appraisal Skills Programme (CASP).

The review included 291 articles describing EOCs. Nine EOC qualities were identified as important for effective emergency response: collaboration, coordination, communication, cooperation, harmonization, integration with vertical and horizontal programing, leadership, respect, and trust. Conversely, lack of communication and coordination were identified as the largest barriers to successful EOC function. The authors highlight legal and ethical issues surrounding EOCs as a priority for future research and call for international standards and guidelines on EOC operations, data collection, information management, risk communication, and training.

Comment: This was a well-designed and well-executed systematic review. Setting best practices and identifying features of successful EOCs are crucial to emergency response. Yet due to difficulties inherent in collecting data during emergencies, past mistakes are easily repeated and lessons learned may be lost. Major limitations of this work include the exclusion of non-English articles, the limitation on timeframe for article inclusion, the quality of studies available, and the challenges that arise when assessing a heterogeneous series of emergency events with varying descriptions of their EOCs. Additionally, there is a risk of publication bias, and lessons learned from poorly performing EOCs might be underreported in the literature. Nonetheless, this article provides an extensive summary of EOCs, defines qualities of EOCs that portend success, and attempts to set some best practice standards.

Mark Bisanzo, Susan Bartels

RE
DHR

Hayman KG, Sharma D, Wardlow RD, Singh S. Burden of cardiovascular morbidity and mortality following humanitarian emergencies: a systematic literature review. Prehosp Disaster Med. 2015;30(1):80-8.

Increased cardiac morbidity and mortality can be found in certain humanitarian emergencies.

Summary: The authors sought to evaluate the interaction between the increasing frequency of large-scale humanitarian emergencies and global burden of cardiovascular mortality. The authors performed a systematic review and searched electronic databases (PubMed, Scopus, CINAHL, and Global Health) for observational studies reporting the effect of natural disasters and conflict events on cardiovascular morbidity and mortality. Double-data extraction was used to abstract information on acute coronary syndrome, acute decompensated heart failure, and sudden cardiac death. 1,697 unique records were found, and among them 24 studies were included that involved 14,583 cardiac events.

The study concluded that conflicts are associated with an increase in long-term morbidity from acute coronary syndrome. However short-term effects of conflicts on cardiovascular disease vary by study.

Comment: This study used clear inclusion criteria and exclusion criteria in its review protocol. The bias within and across studies has been addressed. Although some limitations exist (the population prevalence of cardiovascular disease could not be explored, and most of the included studies are limited to Asia), the result is very supportive in that addressing chronic disease in disaster planning and response efforts may help mitigate long-term cardiac morbidity and mortality following a disaster.

Leon Li, Bhakti Hansoti

RE
EMD

Evans JA, Shim J-M, Ioannidis JP. Attention to local health burden and the global disparity of health research. PLOS ONE. 2014 April;9(4):e90147.

Worldwide, the volume of disease-specific research does not parallel global burden of disease, and instead mirrors the total economic market for treatment for each disease—reflecting a provincial research focus by all countries, with wealthy nations dominating in productivity.

Summary: Wide global health disparities between high-income and low- and middle-income countries remain, and are well known. In this environment, authors evaluate the extent to which the volume of disease-specific *research* worldwide parallels the illness burden at both global and national levels. Using NLM Medical Subject Headings (MeSH) corresponding to 111 disease categories from the World Health Organization Global Burden of Disease (GBD) Project, the authors identified 3,771,604 distinct disease-related articles from two years (2002, 2004) for which corresponding country-specific GBD data was also uniformly available. They analyzed the association between each disease's publication volume and its corresponding burden (in disability-adjusted life years) and "market for treatment"—defined per disease as the product of Gross National Income and disease-specific DALYs summed across each of 192 countries. Worldwide, the authors found *no* correlation between disease-specific research volume and corresponding illness burden, and instead found a strong association between diseases' global market for treatment and corresponding publication volume. Conversely, within any given country, publication volume from that country *does* parallel local disease burden. From this, the authors conclude that the global mismatch between health care research and illness burden is fueled by national differences in research productivity and local disease burden. The few wealthy nations that dominate health research focus on locally important conditions, leaving other diseases with large global burdens scientifically under-represented due to weaker research capacity in the low-income settings where these diseases predominate.

Comment: This article sheds light on both the extent and possible underlying causes fueling the mismatch in worldwide health research and disease burden. The study's review methodology is novel, clearly described, and generally appropriate to study aims. The authors appropriately call attention to several limitations implicit in their methods, including the unclear degree to which peer-reviewed publications can be used as a proxy for aggregate disease knowledge. Moreover, by ignoring publications generated in years (or decades) prior, the authors limit their ability to detect whether gaps in research produced during the study period reflect true disparities in disease-specific knowledge or are simply the result of longstanding and mature lines of scientific inquiry. Finally, although its general conclusions are interesting, the article remains slightly out-of-touch to those interested in the balance between emergency care research and disease burden, as the GBD disease categorization scheme it employs does not individually differentiate emergency disease.

David Silvestri, Bhakti Hansoti

OR
EMD

Seidenberg P, Cerwensky K, Brown RO, et al. Epidemiology of injuries, outcomes, and hospital resource utilisation at a tertiary teaching hospital in Lusaka, Zambia. Afr J Emerg Med. 2014;4:115-22.

An urban African hospital trauma registry provides epidemiologic and clinical data to help guide emergency systems planning.

Summary: This was a prospective observational study conducted over 6 months at an urban teaching hospital in Lusaka, Zambia. Nearly 3,500 patients were enrolled in a registry designed to evaluate the epidemiology and injuries of patients presenting due to trauma. The study was conducted at the primary trauma facility for Lusaka and the major referral hospital for all of Zambia. All patients with traumatic injuries were enrolled 24 hours a day, and data such as patient age, sex, mechanism of injury, means of transportation to hospital, alcohol use, injuries, vital signs, injury severity score, and disposition were collected for each patient. Approximately half of these patients were admitted to the hospital, and for them additional data were collected to explore resource utilization, including the need for blood transfusions, HIV status, surgical procedures, and duration of hospitalization. The vast majority of patients were male (72%) and relatively young (median age 24 years old). Approximately one quarter of patients were children under 12 years of age; children were noted to have a disproportionately high percentage of burns. Very few patients (less than 6%) were brought to the hospital by EMS. Importantly, nearly two thirds of the patients arrived within 6 hours of their injuries, and less than one quarter arrived within 1 hour. The three most common mechanisms of injury included falls, road traffic accidents, and assaults. Of the patients admitted, more than half required surgical intervention; mostly laceration repairs and orthopedic interventions. Approximately 5% required blood transfusions and approximately 3% died. Important findings about risk factors for injury were also identified, including inadequate usage of seatbelts and child safety seats, and a high percentage of alcohol usage and interpersonal violence.

Comment: As trauma and emergency care systems evolve and mature globally, a more thorough understanding of the epidemiology of traumatic injuries will be necessary to improve patient care, especially as global mortality from trauma has now exceeded mortality from the "Big Three" infections (HIV, TB, malaria). Defining risk factors and outcomes of trauma patients is important for local health systems to plan resource allocation, both in the prehospital and hospital settings. The identification and enumeration of specific risk factors (such as alcohol use and insufficient seatbelt) use in this study may help public health systems prepare educational and intervention campaigns to decrease traumatic injuries. This study was well conducted, comprehensive, and free from any obvious bias. The findings will provide important information and guidance to emergency providers in urban centers in Zambia and, likely, throughout sub-Saharan Africa. One major limitation was that the registry was only collected over 6 months, potentially skewing results towards certain types of injuries but missing others that may have a more seasonal predilection. Despite this, the study demonstrates that comprehensive prospective data can indeed be collected in this setting and used for the improvement of emergency medical services.
Indi Trehan, Maxwell Osei-Ampofo