

development community in frugal design efforts. Efforts like The Gates Foundation's Reinvent the Toilet Challenge reflect the kind of integrative thinking that must occur at the beginning of a design initiative; support is being directed toward strategies to create a next-generation toilet that can not only manage waste but also harvest water and energy resources. The toilet will also need to operate without the usual infrastructure, be financially sustainable, and be valued by users. Although such competitions highlight important challenges, funders often solicit solutions with a high degree of technical innovation. An unintended consequence of this premium on innovation can be to complicate downstream implementation efforts. It is time for the engineering and international aid communities to adopt approaches that can improve global health in ways that can be sustained.

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ACKNOWLEDGMENTS

The authors gratefully acknowledge helpful discussions with P. Ondeng, E. Molyneux, and S. Hanson (National Academy of Sciences).

10.1126/science.1257085

PERSPECTIVE

Strengthening the evidence base for health programming in humanitarian crises

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Given the growing scale and complexity of responses to humanitarian crises, it is important to develop a stronger evidence base for health interventions in such contexts. Humanitarian crises present unique challenges to rigorous and effective research, but there are substantial opportunities for scientific advance. Studies need to focus where the translation of evidence from noncrisis scenarios is not viable and on ethical ways of determining what happens in the absence of an intervention. Robust methodologies suited to crisis settings have to be developed and used to assess interventions with potential for delivery at scale. Strengthening research capacity in the low- to middle-income countries that are vulnerable to crises is also crucial.

Health interventions in humanitarian crises—situations where disasters or conflicts constitute a critical threat to the health, safety, security, or well-being of a population—are an important focus within the broader field of global health. Such crises affect increasingly large numbers of people worldwide (1). There have been notable advances in programming, specifically in immunization and treatment of acute malnutrition, over the past 20 years. However, despite the increasing professionalization and standardization of humanitarian work (2), there is a consensus that the evidence base for much current practice remains weak (3, 4).

It is not coincidental that the evidence base for health programming is frail in crisis conditions that cause high mortality and morbidity. Such health care contexts also present many challenges to scientifically rigorous research. Prime among these challenges is the acute vulnerability of populations (5), which requires prompt intervention rather than exploration of the comparative benefits and limitations of alternative approaches. In the face of acute needs and against a typical backdrop

of limited funding, poor security, and shortages in human resources and logistics, simply providing immediate minimal standards of health services becomes an overriding concern. The space for research—particularly that involving experimental interventions or randomization or, more generally, offering different standards of care within the same population—dramatically shrinks (6, 7). Acutely vulnerable populations have a compromised capacity to give meaningful informed consent. Refusing study participation may be seen as rejecting vital medical assistance (8, 9).

The rapid response required in humanitarian crises contributes to an unpredictable programming environment. Although many health risks in the aftermath of disasters or conflict are predictable and minimum standards for response and best-practice interventions have already been established, health needs can evolve rapidly, and adaptable program strategies are required. Political sensitivities and security concerns may also have a substantial influence on the timing, coverage, and delivery of health interventions (10). Different sectorial interventions that affect health (including provision of shelter, water and sanitation, food security, livelihoods, nutrition, and vaccination) may be introduced with limited coordination and varying population coverage (11). This makes identification of comparison or control groups and attribution of outcomes to any single intervention methodologically challenging.

Difficulties in coordination are not only cross-sectoral but also reflect the more general complexity of multiple intervening actors and initiatives that characterize humanitarian responses. A population will typically receive services through a complex web of national and local governmental institutions, local civil society partners, United Nations agencies, nongovernmental organizations, and, in some emergencies, foreign

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medical teams (5). In coordination meetings, scores of agencies, each with discrete capacities and mandates, are often represented (10, 11). Many will have little expertise in research and a limited understanding of, or incentive to address, gaps in the evidence base in a coordinated fashion.

Research is also heavily constrained by fundamental data challenges (Fig. 1). There is frequently a lack of reliable preexisting data on disease burden and population demographics in humanitarian settings. Even where relevant data are present, the breakdown of health information systems and displacement of populations often mean that there is little access to these data for analysis or the data are no longer valid. When new data are collected, agencies may have little capacity or incentive to publicly share data on programming outcomes and even less to publish findings in peer-reviewed publications (5, 12). As a result, information and lessons learned on health interventions in crises often remain in reports that are not easily accessible to the broader humanitarian community.

Themes critical to scientific progress

Notwithstanding these challenges and given the growing scale and profile of humanitarian response, there is increasing interest in strengthening the evidence base for health interventions in such contexts. (3, 13). The authors serve as the funding committee of the Research for Health in Humanitarian Crises (R2HC) program (14). We were recently afforded the opportunity of reviewing preliminary expressions of interest and full proposals for funding for this initiative. By bringing us together as researchers and program managers from academic and humanitarian organizations across four continents, this process led us to formulate the following five themes as critical to scientific progress in this field.

Use of evidence from nonhumanitarian settings

Evidence from noncrisis settings serves as a fundamental basis for programming interventions in emergency contexts. For example, in most circumstances, evidence on drug efficacy or the effectiveness of insecticide-treated nets for malaria control can be appropriately generalized across populations. However, issues occurring rarely in noncrisis contexts, such as severe acute malnutrition, may require research to be conducted in a crisis setting. In addition, extrapolation from nonhumanitarian to humanitarian settings can overlook the many contextual factors that shape the particular vulnerability and fragility of humanitarian crisis conditions, requiring either different or modified interventions for such contexts. Acknowledging these alternative scenarios, researchers have an obligation to articulate the specific conditions where empirical work in the complex context of a humanitarian crisis is both adequately safe and evidentially necessary.

Identification of ethical bases of counterfactual analysis

To inform humanitarian programming, it is important not only to evaluate the outcomes of an intervention but also to understand what outcomes would be without the proposed intervention or with alternative interventions. Identifying ethical and rigorous means of such counterfactual analysis is crucial. Randomization to a control condition may be possible and appropriate. Where it is not, however, other means of attributing the effect of an intervention need to be adopted. Where operational constraints limit the initial coverage of an intervention, step-wedge designs and “waitlist controls” (15) may be considered. Changes in government policy, such as ages of vaccination, may allow a comparison of different interventions (16).

The development of robust methodologies appropriate to crisis settings

Although humanitarian contexts present many barriers to rigorous research, the same standards of methodological and statistical rigor used in other fields need to be adopted if a sound evidence base for response in crises is to be established. Meeting such standards in crisis settings requires methodological adaptation and evolution. Methodologies have to be matched not only with the specific practical and ethical constraints of a humanitarian setting but also with the current status of knowledge in their field of focus. A combination of studies is needed that address proof-of-concept research, acceptability and feasibility evaluations, and the creation of new tools, in addition to evidence of comparative effectiveness. For the latter, comparative clinical trials are required, but a range

of methodological approaches (e.g., time series analyses and rigorous observational studies) will also be relevant (17). Particular methodological innovation is required to tackle cross-cutting issues of access, capacity, accountability, and coordination (3).

Capacity and potential for scaling up of evidence-based intervention

Any research on humanitarian interventions must inform future practice, but this often requires consideration of a complex set of factors. Strong local engagement is important to ensure the specific demands of a humanitarian context are addressed and requires cultural adaptation and contextual sensitivity. The challenge with interventions suited to a unique context and the particularities of a single implementing agency is that they lack external validity and/or offer little prospect for wider scale-up. Interagency initiatives are strong candidates to shape wider practice. Strong local engagement, wide global ownership, and a detailed dissemination plan is a challenging prescription, but crucial to the translation of valid research evidence into accepted practice.

Research capacity development in countries vulnerable to emergencies

It is vital for donors and implementing agencies to establish effective engagement with research institutions from low- and middle-income countries (LMICs) to ensure ownership of the developing research agenda within settings vulnerable to humanitarian crisis. Although many research proposals include partnerships with LMIC institutions, established institutions from high-income countries still typically hold leadership. This requires sensitivity and commitment



Fig. 1. The REFAH AID director begins data collection procedures before aid distribution at Jalozai refugee camp, Peshawar, Pakistan. [Credit: Mukhtar Ahmad/REFAH AID (2009). Courtesy of Photoshare.]

to issues of both long-term research capacity development and means of ensuring that research initiatives respond to field-based challenges and concerns.

Conclusions

The circumstances of humanitarian crises present many barriers to the conduct of scientifically rigorous research, and yet these same circumstances shape the profound risks to the health of affected populations that make a solid evidence base for health programming in such settings crucial. There are clear opportunities for scientific advance. We consider that progress regarding the five themes elaborated above will be an important driver for assembling and using a more functional evidence base for future health programming and prioritization in humanitarian crises.

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ACKNOWLEDGMENTS

The authors are members of the funding committee responsible for review of submissions made in response to request for proposals from the R2HC program. The findings and conclusion of this report are those of the authors and do not reflect the official position of their organizations or of R2HC.

10.1126/science.1254164

PERSPECTIVE

Emerging, evolving, and established infectious diseases and interventions

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Planning, implementing, and evaluating interventions against infectious diseases depend on the nature of the infectious disease; the availability of intervention measures; and logistical, economic, and political constraints. Infectious diseases and vaccine- or drug-based interventions can be loosely categorized by the degree to which the infectious disease and the intervention are well established. Pertussis, polio, and measles are three examples of long-known infectious diseases for which global vaccination has dramatically reduced the public health burden. Pertussis vaccination was introduced in the 1940s, polio vaccination in the 1950s, and measles vaccination in the 1960s, nearly eliminating these diseases in many places.

Many known infectious diseases tend to be epidemic, but exactly when and where these epidemics will occur is uncertain. For such sporadic infectious diseases, it may be most efficient to implement a reactive vaccination campaign once an outbreak has begun. Planning for reactive vaccination requires keeping a mobile vaccine stockpile available that can be quickly moved for emergency vaccination. This strategy could be used for epidemic cholera, such as occurs in parts of Africa (1). When cholera was introduced into Haiti in 2010, such a stockpile did not exist. Limited supplies of cholera vaccine were scattered in different locations, and a decision was made not to vaccinate the local population, even though mathematical models showed that with limited quantities of vaccine, concentrating vaccination in high-risk areas would be most efficient (2). Now that such a stockpile of 2 million doses of oral cholera vaccine exists (3), it can be used for future cholera epidemics. Mobile stockpiles, such as the oral cholera vaccine, often have a finite shelf life, and their use can be valuable reassigned in endemic locations, such as Bangladesh, that experience annual cycles of high incidence.

For long-term intervention strategies, sustainability is an issue, and strategies can change as the economic constraints change or as new products become available. For example, a new product against meningococcal A meningitis was developed that overturned the reactive vaccination strategy in the meningitis belt of sub-Saharan Africa. An international commitment working through the Meningitis Vaccine Project developed an inexpensive vaccine against meningitis A (4)

that can be used in proactive vaccination. Initial introduction has been carried out or is planned in 26 African countries, with mass vaccination of people up to the age of 29 years to be followed by routine vaccination of young children.

Emerging infectious diseases sometimes lend themselves to effective vaccination. In light of the ongoing human cases of avian influenza A (H7N9) in China, the United States is preparing to stockpile vaccines for human cases of H7N9. When the pandemic influenza A (H1N1) emerged suddenly in 2009, influenza vaccine manufacturers turned their production lines to developing and producing appropriate vaccines for immediate administration. Yet for other emerging diseases like HIV/AIDS, which was discovered more than 30 years ago, no effective vaccine has successfully been developed for human use. For several newly emerging infectious diseases, it is questionable when or if vaccines or drugs can be developed at all. One example is Middle East respiratory syndrome (MERS), a viral respiratory illness caused by a coronavirus and first reported in Saudi Arabia in 2012. Another example is the arbovirus chikungunya, which is spreading explosively in the Americas, with 650,468 confirmed and suspected cases reported by the Pan American Health Organization as of 29 August 2014. Although antivirals, vaccines, and monoclonal antibodies are under early development, Anthony Fauci, Director of the National Institute of Allergy and Infectious Diseases, wrote that "in the meantime, we can only keep our fingers crossed" (5) that the epidemic in the Americas will decline on its own before becoming more widespread. According to (5), even if a vaccine were available, chikungunya outbreaks spread too rapidly for reactive vaccination to be effective. In the current Ebola outbreak in West Africa, there is no pharmaceutical intervention. For these newly emerging infectious diseases, surveillance and containment, education, and avoidance are the main responses available until vaccines or drugs may be developed.

Interventions in infectious diseases can have more than just direct protective effects in the

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Science **345**, 1290 (2014);

DOI: 10.1126/science.1254164

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