Global Health and Emergency Care: A Resuscitation Research Agenda—Part 1

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Abstract

At the 2013 Academic Emergency Medicine global health consensus conference, a breakout session on a resuscitation research agenda was held. Two articles focusing on cardiac arrest and trauma resuscitation are the result of that discussion. This article describes the burden of disease and outcomes, issues in resuscitation research, and global trends in resuscitation research funding priorities. Globally, cardiovascular disease and trauma cause a high burden of disease that receives a disproportionately smaller research investment. International resuscitation research faces unique ethical challenges. It needs reliable baseline statistics regarding quality of care and outcomes; data linkages between providers; reliable and comparable national databases; and an effective, efficient, and sustainable resuscitation research infrastructure to advance the field. Research in resuscitation in low- and middle-income countries is needed to understand the epidemiology, infrastructure and systems context, level of training needed, and potential for cost-effective care to improve outcomes. Research is needed on low-cost models of population-based research, ways to disseminate information to the developing world, and finding the most cost-effective strategies to improve outcomes.
In May 2013, Academic Emergency Medicine hosted a global health and emergency care consensus conference that included a breakout session for creating a resuscitation research agenda. This is part one of the proceedings from that session.

Resuscitation is the act of attempting to maintain or restore life by establishing and maintaining the airway, breathing, and circulation through cardiopulmonary resuscitation (CPR), defibrillation, and other related techniques. We believe that the state of cardiac arrest and trauma resuscitation is a good reflection of the standard of prehospital and emergency care in any health system. While this report focuses on developed and newly developed countries, we hope that developing countries can use some of these principles to organize systems of resuscitation also.

This article will focus on cardiac arrest resuscitation and trauma resuscitation. Due to the limited time available at the conference, our group did not discuss resuscitation related to maternal and neonatal conditions, specifics of pediatric resuscitation, or resuscitation related to communicable diseases (sepsis, shock from diarrheal dehydration, etc.). We recognize that these conditions cause a huge burden of mortality and morbidity in the developing world. This is a key area for research in the future.

**BURDEN OF DISEASE AND OUTCOME**

**Trauma**

Traumatic injury is a leading cause of death and disability worldwide and disproportionately affects young, healthy, and productive individuals. The Global Burden of Disease study 2010 reported that injuries caused 5.1 million deaths, 9.6% of the entire mortality burden, an increase from 8.8% two decades earlier. Trauma accounted for 11% of disability-adjusted life-years (DALYs) in 2010. Estimates from the World Health Organization (WHO) for the year 2004 indicated that injury was responsible for 12.3% of all deaths of males and 7.1% of deaths of females and was the leading cause of death for men between the ages of 15 and 59 years in Latin America and in low- and middle-income countries (LMICs) in Europe.

Vehicular collisions emerged as an important cause of death with the introduction of motor cars in the 20th century. Advances in vehicle and road design, the introduction of mandatory safety devices such as seatbelts and airbags, and improvements in prehospital and in-hospital trauma care resulted in reduced rates of traffic fatalities in the developed world. However, in the developing world where many of these strategies are lacking, such collisions account for an increasing toll of preventable death and disability.

Timely transport to a qualified trauma center results in better outcomes for trauma victims. Core questions remain in both high-income countries and LMICs with respect to the transport, stabilization, and immediate management of acutely injured patients, including the optimal approach to early stabilization and triage, prehospital support, and immediate resuscitation.

**Cardiovascular Disease**

Cardiovascular disease remains the leading cause of death worldwide and is an increasing public health concern in LMICs. However, the methodologies used to estimate data are primitive and of limited quality. The global burden of cardiovascular and cerebrovascular disease is difficult to measure with precision, but it is estimated that it causes approximately 12.5 million deaths, or >22% of all deaths worldwide. The costs of both direct and indirect medical care of cardiovascular disease are likewise large. The estimated total costs of all cardiovascular and cerebrovascular disease in the United States alone were about $300 billion in 2008 ($180 billion in direct costs and $120 billion in indirect costs). This expenditure could triple by the year 2030.

**Need for Improved Resuscitation Care**

Globally there is a need for improved resuscitation care and focus on patient outcomes. This is not just in terms of mortality, but more importantly, functional outcomes. Research issues include the costs and benefits of interventions and how to allocate scarce resources.

Unfortunately, research investment does not match the public health impact of trauma and cardiovascular disease. A disproportionate share of resources is targeted to communicable disease. This seems particularly problematic when the noncommunicable diseases like cardiovascular disease, diabetes, respiratory disease, and cancer are noted to be surging in the developing world. For example, top health care funding organizations like the Gates Foundation and the WHO allocate only 2% of their budgeted funds to these noncommunicable diseases.

**RESUSCITATION RESEARCH IN RESOURCE-SCARCE SETTINGS**

Resuscitation research in LMICs must begin with understanding the epidemiology of diseases that require resuscitative efforts. These data are key to planning of resuscitation programs, as epidemiology may differ from that observed in high-income countries. Rao et al. reported that 10.3% of overall mortality in India was associated with sudden cardiac death, but victims were younger than those from the Western Hemisphere. In Nigeria only 4% of sudden cardiac deaths were due to acute myocardial infarctions. These studies demonstrate the importance of local epidemiologic research. The same applies to trauma: several single-center studies show the range of local epidemiology and mortality rates associated with trauma, but larger population studies are needed.

Assessment of outcomes of current resuscitation practices is also crucial. Prior to implementing
programs or training, baseline rates of survival after resuscitation must be described taking context into account. For example, in LMICs, almost all cardiac arrests that receive resuscitative efforts occur in the inpatient setting. Single-institution studies and registries can be informative, but larger studies are needed.\textsuperscript{19–21} Based on what is known about trauma outcomes in LMICs, Mock et al.\textsuperscript{22} estimated that between 1,730,000 and 1,965,000 lives could be saved if trauma fatality rates in LMICs were decreased to match those in high-income countries.

Similarly, basic infrastructure and capacity for resuscitation, such as the presence of designated resuscitation areas and emergency airway kits, must be examined. The WHO Global Initiative for Emergency and Essential Surgical Care\textsuperscript{23} has created a standard-ized and validated situational analysis tool that is used at the district hospital level to evaluate infrastructure. Although the primary focus is surgical capacity, many elements relate to resuscitation, such as the presence of an emergency care area and oxygen cylinders. The tool also contains a direct question on the ability to perform resuscitation, and this has been reported for several countries.\textsuperscript{24–27}

A prehospital system is another essential component in resuscitation. Since many LMICs have none, there is ample opportunity for research and program development. Nielsen et al.\textsuperscript{28} recently described the state of prehospital systems in 13 LMICs, found that prehospital systems were lacking, and suggested first aid training for commercial drivers and bystanders as an adjunct to formal systems. Hauswald and Yeoh\textsuperscript{29} described the economics of creating a U.S.-style prehospital system in Kuala Lumpur and estimated the cost at 2.5 million U.S. dollars per year for a benefit of approximately seven lives saved. They advocate looking beyond U.S.-style prehospital systems for more innovative and context-specific solutions. Their findings underscore the importance of careful study of the impact and implementation of prehospital systems in LMICs.

Resuscitation research in LMICs must include assessment of personnel across the entire health care system. Compared to research on neonatal and pediatric resuscitation training, there is a paucity of literature on training programs in adult trauma and cardiac arrest in LMICs. Many studies report only participant satisfaction or self-efficacy outcomes. More rigorous outcome measures of training efficacy should be sought.

Although health care workers in LMICs often lack knowledge and skills in adult resuscitation, they improve readily with training.\textsuperscript{30–32} Educational interventions in LMICs lead to improved operational performance in both simulated\textsuperscript{33,34} and clinical settings.\textsuperscript{35} A few studies have linked training programs to improved patient outcomes. Moretti et al.\textsuperscript{36} reported long-term survival gains following Advanced Cardiac Life Support certification training for prehospital providers in Mexico, underscoring the potential benefits of training programs for workers across the entire health care system.

While the research thus far is promising, there are important limitations. The bulk of the literature consists of single-center studies focused on low-level endpoints like knowledge and skills test results. Multicenter studies addressing more robust educational outcomes like simulated and real clinical performance are needed, remembering that patient outcomes are the ultimate metric of educational success.

A recent review by Meaney et al.\textsuperscript{38} noted that training programs were often modified to address local needs but often without input from local experts or needs assessment data. Clearly protocols used in high-income countries must be modified to be feasible and relevant in LMICs, and this should be done using evidence-based guidance, with the collaboration of local experts. Research regarding the appropriateness and feasibility of modifications to protocols for use in LMICs is needed. More importantly, this same review found no studies on cost-effectiveness of training programs,\textsuperscript{38} a crucial consideration.

Discussions of adult resuscitation in LMICs are often hampered by the misconception that critical care is always expensive and technologically advanced. The question should be framed as which forms of resuscitation are appropriate and under what conditions. Simple and inexpensive interventions such as oxygen, vascular access, fluid administration, and frequent reassessment fall squarely in the realm of resuscitation and are likely to be feasible and beneficial across a wide range of settings.

Additionally, as Riviello et al.\textsuperscript{39} point out, there is evidence that even resource-intensive interventions may prove cost-effective relative to public health initiatives such as vaccination and HIV care. Surgical care for trauma patients has often been deemed too costly for consideration in LMICs. However, a study of three Medecins Sans Frontieres hospitals reported costs of only $78 to $223 per DALY averted.\textsuperscript{40}

Critical care populations in LMICs are epidemiologically distinct from those in high-income countries, and are often comprised of patients who are younger and healthier.\textsuperscript{39,41} This suggests greater cost-effectiveness for critical care interventions in LMICs compared to in high-income countries, as resuscitated patients may have better functional outcomes over a longer future life span. It is also important to consider the broader societal effects of preventable adult deaths, particularly on the victims’ families.

GLOBAL TRENDS IN RESUSCITATION RESEARCH FUNDING PRIORITIES

North America

There is a relative paucity of research funding in the United States for cardiac arrest compared with other cardiovascular diseases.\textsuperscript{42} Between 1983 and 2009, there were 6,886 studies funded by the National Institutes of Health/National Heart, Lung, and Blood Institute (NHBLI) for research relating to myocardial infarction and 257 studies relating to cardiac arrest.\textsuperscript{42} When
considered as a rate of funded studies per 10,000 condition-specific deaths, this represents 439 per 10,000 deaths due to myocardial infarction, compared to eight funded studies per 10,000 deaths due to cardiac arrest.\textsuperscript{42}

Resuscitation Outcomes Consortium

The Resuscitation Outcomes Consortium (ROC) is an ongoing clinical research network conducting clinical research in the areas of cardiopulmonary arrest and traumatic injury.\textsuperscript{43} The principal funding agency is the NHLBI, partnering with the American Heart Association, the U.S. Army Medical Research and Material Command, the Canadian Institutes of Health Research, and the Heart and Stroke Foundation of Canada. The primary aim is to increase survival in the prehospital setting for trauma and cardiac arrest and to capitalize and expand on current resources of data by conducting high-quality clinical research on prehospital emergency interventions. The network includes nine regional clinical centers, three major satellites, and one central data and coordinating center. Participants include more than 260 emergency medical services (EMS) agencies in 10 sites, 36,000 EMS providers, and a combined population of nearly 24 million persons from diverse urban, suburban, rural, and frontier regions, which collectively represent 10% of the North American population.

Latin America and the Caribbean

The Emergency Cardiovascular Care Committee of the Inter-American Heart Foundation (IAHF) includes representatives from 12 countries with a total population of 500 million. Approximately 19,600 papers from these countries are published in peer-reviewed medical journals each year. Medical research accounts for a mean of 0.47% of the gross national product (max. = 1.08%; min. = 0.06%), but only a tiny proportion of this is invested in research in cardiovascular emergencies.

In a survey commissioned for this article by the IAHF network, responses supporting this assertion were received from six countries (Mexico, Peru, Brazil, Chile, Argentina, and Uruguay). Few groups have conducted studies or research related to cardiovascular emergencies, including CPR. There are no exact figures of contributions from other sources but it is clearly insufficient.

Europe

There are estimated to be 275,000 EMS-treated out-of-hospital cardiac arrests (OHCA)s in Europe each year.\textsuperscript{44} Most European countries have several funding bodies that could potentially provide grants for research relating to resuscitation. The European Commission Seventh Framework Program for Research and Technological Development (FP-7) is the EC’s main instrument for funding research in Europe. Of a total budget of US$66.7 billion, US$7.7 billion is allocated to health care research over the current 7-year period. There have been recent attempts to secure FP-7 funding for resuscitation related projects (e.g., to study postresuscitation hypothermia), but the process is highly competitive and so far no resuscitation program has successfully acquired this funding. Individual European countries provide resuscitation funding targeted at national projects. Many countries have charitable trusts (e.g., the British Heart Foundation). Although large grants are available from these organizations, applications to fund resuscitation research are not commonly successful because of the competition from “mainstream” cardiology teams.

The Resuscitation Council (UK) has a modest research budget of US$223,000 that it allocates each year. The UK National Health Service commissions and funds health care research through the National Institute for Health Research (NIHR). There are several NIHR funding programs, all of which could potentially fund resuscitation-related research: Health Technology Assessment, Research for Patient Benefit, Programme Grants for Applied Research, Programme development grants, and Invention for Innovation grants.

The Laerdal Foundation for Acute Medicine (www.laerdalfoundation.org) funds resuscitation and acute medicine projects worldwide. Funding levels recently reached about US$7 million annually and approximately half of this is allocated for projects to achieve the United Nations Millennium Goals 4 and 5, which are to reduce infant, child, and maternal mortality in the developing world. This recent change in the focus for research funding by the Laerdal Foundation is a good example of resuscitation research funding being prioritized and targeted at where it is likely to achieve the most effective change in outcomes. Other industrial partners have funded several large European multicenter trials.

Asia

Taiwan. Taiwan has a population of 23 million. With the rising burden of cardiovascular disease in the country, it is estimated that there are 20,000 cardiac arrests in Taiwan each year. EMS has developed rapidly in the past two decades, achieving a fivefold increase in the overall survival from cardiac arrest.\textsuperscript{45} Several characteristics of cardiac arrests and the community chain of survival warrant consideration before determining research priorities in this field in Taiwan:

- The incidence of ventricular fibrillation/pulseless ventricular tachycardia as the first monitored rhythm is low (Taipei = 8% vs. North America = 25%).\textsuperscript{46,47}
- The incidence of bystander-initiated CPR in Taiwan is lower than in western communities (10% to 20% in Taiwan,\textsuperscript{46} compared with 41% documented by the ROC consortium).\textsuperscript{47}
- Levels of advanced life support (ALS), including tracheal intubation and drugs, vary widely across different jurisdictions.\textsuperscript{48} Extracorporeal life support for in-hospital cardiac arrests developed in late 1990s and was implemented widely across most tertiary centers, achieving over 30% survival to discharge for selected patients.\textsuperscript{49}

Current areas of research include dispatcher CPR, dispatcher CPR assisted by video reminders/interactive audio-video instructions, effects from recent changes in citizen CPR format and Good Samaritan legislation, quality of CPR assessment, provision of prehospital ALS, sequence of CPR versus ECG analysis, and termination of resuscitation protocols.
Korea. The total national government budget for research and development in Korea was $15 billion in 2011. Of these funds, about $1.1 billion was given to health science and technology. Within this national budget, a total of approximately $1 million was spent by the Korea Centers for Disease Control and Preventions (KCDC) to support resuscitation research. KCDC has supported a nationwide cardiac arrest registry since 2008 (Cardio-Vascular Disease Surveillance, CAVAS project). The National Statistics Office accepted many of the indices regarding resuscitation as national statistics in 2010 and has published them every year since. Also, the National Emergency Management Agency provided $300,000 for OHCA research in 2011, focusing on the development of devices and clinical trials.

Korea has a special fund to improve EMS systems (founded in 2004) using approximately $40 million collected from traffic fines. The fund has supported public education, improvement of EMS organizations, and the operation of hospital emergency departments. The government plans to support public advocacy for CPR, public CPR education, and a public access defibrillation program costing $45 million over the next 5 years. Of the $1 billion in EMS funds, another 15% ($150 million over 5 years) will be used for EMS improvements, including education and training programs for EMS providers and support for EMS devices, some of which are used for EMS resuscitation.

Africa

According to WHO, sub-Saharan Africa shoulders 25% of the world’s disease burden, yet has only 3% of the world’s health workforce. Formal or structured emergency medical care is limited or nonexistent in many parts of Africa. Of particular concern is that almost half of the population of sub-Saharan Africa is under the age of 14 years old. Due to high rates of communicable diseases and malnutrition, children account for a large proportion of health care visits.

Widespread poverty and lack of public funding for higher education have limited the number of physicians produced. Prehospital standards of emergency care and rescue vary widely, from well-developed sophisticated “first-world” systems, to basic, rudimentary systems, even conveying patients with makeshift wheelbarrows, to places where prehospital service provision is totally nonexistent. Due to the severe shortage of medical practitioners, the responsibility of providing emergency and acute resuscitation care is frequently left to untrained or unprepared nurses. Training in emergency care is crucial for all nurses to cover emergencies from childbirth to the care of the elderly.

Major challenges facing the provision of care and research include low-income status (of both the population and the health care workers), lack of equipment, absence of qualified personnel, lack of funds, and inadequate training.

An African Federation for Emergency Medicine was formed in 2009. Similarly, 15 French-speaking African countries have formed a separate emergency care organization known as Societe Africaine Francophone de Medecine d’Urgence. In addition to the African Federation, other African countries developing residency training programs in emergency medicine include Ghana, Madagascar, Rwanda, Sudan, Uganda, and Zambia.

The need for systems-based research is extensive, particularly with regard to existing burdens, facilities, supply, and funding. A significant research priority for Africa is to determine what resuscitation training interventions would be deliverable and effective. Short-course resuscitation programs provided by the American Heart Association and European Resuscitation Council are now available throughout Africa and significant research could be done on memory retention, ease of adaptability, local modifications, accessibility, and improvisation.

Australia

The National Health and Medical Research Council (NHMRC) is the major funder of health and medical research in Australia, with the Heart Foundation and other nonprofit organizations providing smaller grants. Since 2003 the NHMRC has provided more than 731 million U.S. dollars for cardiovascular disease research. There has been an annualized increase of 8% over the decade, from 40 million in 2003 to 99 million in 2012. While the funds awarded annually to projects related to “cardiac arrest” have similarly increased, from US$754,000 in 2003 to US$2.7 million in 2012, the overall percentage of the cardiovascular research funds allocated to cardiac arrest projects hovered around 1% to 2% until 2012, when it rose to 2.9%.

The NHMRC cardiovascular disease funding data set lists 12 applications specifically related to cardiac arrest. These 12 included nine project grants, one Centre for Research Excellence grant, and two part-time Practitioner Fellowships. The nine ongoing projects comprised four epidemiologic studies (using linked data), three randomized controlled trials (therapeutic hypothermia and adrenaline), and two basic science studies.

The Australian Resuscitation Outcomes Consortium (Aus-ROC) is modeled on the North American ROC and brings together academic researchers, clinicians, ambulance service providers, and consumers with the common goal to improve outcomes in OHCA through the conduct of high-quality research. Aus-ROC funding will enable the establishment of infrastructure, train novice researchers, and build capacity to facilitate the conduct of multicenter clinical trials in OHCA, including the development of an Australia/New Zealand OHCA registry.

OTHER ISSUES IN RESUSCITATION RESEARCH

In Data Supplement S1 (available as supporting information in the online version of this paper), we discuss issues in resuscitation research regarding informed consent in resuscitation research and resuscitation research infrastructure.

Resuscitation Research Agenda for the Future

Globally, cardiovascular disease and trauma cause a high burden of disease but receive a disproportionately small amount of research funding. More investment is needed into real-world implementation trials of systems
of care and delivery of resuscitation therapy. There needs to be a focus on improving outcomes, the cost/benefit of interventions, how to allocate scarce resources, disparities in outcomes, and avoiding lost productivity. Maternal and neonatal resuscitation is also a large area for systematic research, especially in the developing world. We also need to address the ethical challenges of international resuscitation research, because issues with the current framework for exception to informed consent are a major obstacle and hindrance to research in the field.

There is a need for reliable baseline statistics regarding the quality of care and resuscitation outcomes globally. This includes establishing research infrastructure, data linkages between and across care providers, and using health outcomes to improve quality of care. Investment in reliable and comparable national databases, and in an effective, efficient, and sustainable resuscitation research infrastructure, are necessary to advance the field. Such improvements in research infrastructure will allow the effects of therapeutic trials and public health initiatives to significantly increase survival and quality of life as well as be quantified and replicated globally.

Research in resuscitation in LMICs is needed to understand the epidemiology, infrastructure and systems context, level of training, and potential for cost-effective care to improve outcomes. Research is needed regarding low-cost models of population-based research, ways to disseminate information to the developing world, and finding the most cost-effective strategies to improve outcomes.

CONCLUSIONS

While global priorities and opportunities for research funding vary, there is a need to develop research infrastructure and expertise in the international emergency medicine community to be successful in an increasingly competitive research environment. In the next article, we will discuss issues regarding data collection, management and analysis, regionalization of postresuscitation care, and resuscitation programs and research examples around the world.

References


Supporting Information
The following supporting information is available in the online version of this paper:

Data S1: Informed consent in resuscitation research.