

to strengthen the planning of the postauthorization phase and reduce preventable harm.

Once a product is on the market, new safety signals may emerge. Spontaneous reports of adverse reactions can be used to identify patterns of drug–drug and drug–disease interactions that were not apparent before authorization. Collection of data from all possible sources should be optimized, since adverse reactions in elderly populations are generally underreported. The risk-management plan for a drug — based on its risk profile — should be designed to fill knowledge gaps,

and targeted measures should be used to minimize risk.

Regulators must ensure that the development and evaluation of drugs take into account global demographic changes, so that safe and effective drugs reach the patients who ultimately use them.

The views expressed in this article are those of the authors and do not necessarily reflect those of the European Medicines Agency or its committees or working parties.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

From the European Medicines Agency, London (F.C., H.-G.E., G.R.), and the University of Rome Tor Vergata, Rome (G.R.).

1. European Medicines Agency. EMA geriatric medicines strategy (http://www.ema.europa.eu/docs/en_GB/document_library/Other/2011/02/WC500102291.pdf).

2. Cherubini A, Del Signore S, Ouslander J, Sem T, Michel P. Fighting against age discrimination in clinical trials. *J Am Geriatr Soc* 2010;58:1791-6.

3. European Medicines Agency. ICH harmonised tripartite guideline E7: studies in support of special populations: geriatrics questions and answers (http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/10/WC500005218.pdf).

4. Studenski S, Perera S, Patel K, et al. Gait speed and survival in older adults. *JAMA* 2011;305:50-8.

5. White paper: U.S. Food and Drug Administration (FDA) inventory of clinical trials protocols and clinical study data (www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/ConductingClinicalTrials/UCM309552.pdf).

DOI: 10.1056/NEJMp1209034

Copyright © 2012 Massachusetts Medical Society.

Intensive Care in Low-Income Countries — A Critical Need

Paul Firth, M.B., Ch.B., and Stephen Ttendo, M.B., Ch.B.

Mbarara is a small town in the rural southwest of Uganda, one of the poorest countries in the world. The per capita income in this equatorial East African nation is less than \$4 a day, and one third of the population lives below the poverty line.¹ When the Ugandan government and foreign donors recently committed to upgrading Mbarara Hospital's aging infrastructure, the hospital steering committee identified the expansion of the intensive care unit (ICU) as a critical objective.

At first glance, the provision of critical care may not appear to be a rational or cost-effective priority in a country where the annual health care expenditure is just over \$100 per person.¹ However, the inadequate basic medical infrastructure, the spectrum of diseases, and the demographic characteristics of Uganda, combined with the broader, less tangible benefits of an ICU, make critical care an essential component of

improved health care delivery in such a low-income setting.

The lack of access to early treatment means that many Ugandan patients present in critical condition, with late stages of disease. There is roughly one doctor for every 8500 people in Uganda, as compared with approximately one doctor for every 375 Americans.¹ In Mbarara's catchment area, this scarcity is exacerbated by the rural–urban maldistribution of health care professionals that is common to many countries around the globe. The paucity of community-based general surgeons, for example, has contributed to a situation in which approximately half the surgical operations performed at Mbarara Hospital are urgent or emergency procedures. By comparison, at Massachusetts General Hospital, an acute care referral hospital in Boston, less than 5% of surgical procedures are scheduled on a nonelective basis.

Although diseases faced by

Ugandans are usually advanced by the time patients are seen by a clinician, many of these diseases are acute, isolated problems that are possible to cure. The leading causes of premature death in low-income countries include obstetrical complications, traffic accidents, pneumonia, and malaria.² By contrast, in wealthier countries, people tend to die of acute exacerbations of chronic conditions such as vascular disease, cancer, or dementia — problems that are less amenable to cure.

Most of the patients admitted to Mbarara Hospital are young — in part because of the high population growth and young age distribution typical of sub-Saharan African populations. Almost half the surgical admissions, for example, are for patients under 30 years of age. Of these young patients, more than one third are children less than 10 years old.

The patient demographic characteristics and patterns of use in Mbarara's two-bed ICU reflect

the broader Ugandan population and burden of disease. The median age of patients in the ICU is approximately 27 years, and patients typically spend only 1 or 2 days in the unit. Sepsis, post-operative care, trauma, and obstetrical problems make up the bulk of indications for admission. Among the most common diagnoses are peritonitis from intestinal obstruction or other surgical condition; head trauma to drivers, passengers, or pedestrians involved in motor vehicle accidents; obstetrical complications, such as septic abortion and peripartum hemorrhage; and accidental or intentional (suicidal) organophosphate poisoning. Approximately half the patients require mechanical ventilation, but simple treatment such as close nursing care, intravenous antibiotic agents, and fluid resuscitation constitute much of the care for the others.

Clearly, there are marked differences between the critical care requirements of low-income and high-income countries. In the United States, patients in the ICU are typically older persons with multiple coexisting chronic diseases, who spend a longer period in the unit, often supported by complex technology. Common admission diagnoses frequently reflect new changes in long-standing diseases: exacerbations of emphysema, congestive cardiac failure caused by vascular disease, or recovery from vascular or oncologic surgery. In Mbarara, by contrast, the ICU functions largely as the site of basic rescue interventions for young patients who are acutely ill with curable diseases.

Given these differences, a basic utilitarian or public health argument can be made for specialized intensive care in low-income

settings. The average life expectancy is 53 years in Uganda; in the United States, it is 78 years.¹ A short period of critical care is a cost-effective and essential part of the treatment of the acute life-threatening conditions that affect the lives of millions of young people worldwide. Rescuing the critically ill from preventable deaths will ultimately improve overall life expectancy by decreasing the burden of death from treatable disease.

The practicalities of decreasing in-hospital death rates, however, even within a single institution, demand broader changes beyond the simple provision of ventilators and vasotropic drugs.³ A focus on both staff education and hospital functioning is needed to optimize use of the ICU.

Treatment of life-threatening illness does not start in a specialized unit but rather requires early detection and prompt intervention before the patient is transferred to an area with close monitoring. The development of critical care capacity should therefore not be limited to a single physical area but must involve the education of nurses and physicians hospital-wide. Recognition of the initial clinical syndromes of sepsis or hypovolemia, combined with an awareness that critical illness need not lead inevitably to fatal deterioration, is vital to ensuring early initiation of basic treatments such as antibiotic-agent administration and fluid resuscitation.

The Mbarara ICU is a mixed unit, with patients admitted from the surgical, obstetrical, medical, and pediatric wards. In order to justify and augment the use of this concentration of resources, it will be essential to determine the overall mortality rates in the various parts of the hospital, the

effects of various diseases, and the potential of critical care to improve outcomes. Consequently, an effort to track data on basic hospital admission and mortality in an electronic database is being initiated as the unit is being expanded. The availability of such data should improve health care providers' and policymakers' understanding of the overall challenges that the hospital faces and help them to identify impediments to better care.

Implementing the systemic changes required to effectively treat very sick patients may have a broader public health value beyond care of the critically ill. The massive migration of health care professionals from poorer countries to richer ones is a major impediment to improving health care in Africa.⁴ Although the causes and solutions are complex, the lack of educational and career opportunities and the personal and professional frustrations of working in systems where patients frequently die from treatable problems undoubtedly play a role in pushing clinicians out of African health systems. Improvement in hospital functioning combined with investment in clinician education and expertise may promote the retention of trained professionals and educators.⁵

Historically, Mbarara's pair of ICU beds and aging ventilators have been the sole ICU resources for the region's referral population of more than 3 million people. The hospital is now transitioning to an eight-bed unit, equipped with newer ventilators and a technical maintenance-support contract. Measured against the resources of richer countries, such a unit still seems unimaginably small. As a means of preventing avoidable deaths and catalyzing improvements in the

local health care system, it is an innovative step toward meeting a critical need.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

From the Department of Anesthesia, Critical Care and Pain Medicine, Massachusetts General Hospital, Boston (P.F.); and the Department of Anaesthesia and Critical Care,

Mbarara Regional Referral Hospital, Mbarara, Uganda (S.T.).

1. Central Intelligence Agency. The world factbook (<https://www.cia.gov/library/publications/the-world-factbook/geos/us.html>).
2. Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. *PLoS Med* 2006;3(11):e442.
3. Riviello ED, Letchford S, Achieng L, Newton MW. Critical care in resource-poor set-

tings: lessons learned and future directions. *Crit Care Med* 2011;39:860-7.

4. Mills EJ, Kanfers S, Hagopian A, et al. The financial cost of doctors emigrating from sub-Saharan Africa: human capital analysis. *BMJ* 2011;343:d7031.

5. Towey RM, Ojara S. Practice of intensive care in rural Africa: an assessment of data from Northern Uganda. *Afr Health Sci* 2008;8:61-4.

DOI: 10.1056/NEJMp1204957

Copyright © 2012 Massachusetts Medical Society.

Confronting the Social Determinants of Health — Obesity, Neglect, and Inequity

Jennifer K. Cheng, M.D., M.P.H.

Several months ago, I reluctantly participated in the filing of a Child Protective Services (CPS) report alleging the medical neglect of two young sisters. Lucy, a soft-spoken 13-year-old girl, and her rambunctious 10-year-old sister, Jackie, have a long history of medical nonadherence, progressive morbid obesity, and serious coexisting conditions including poorly controlled type 2 diabetes, hypertension, dyslipidemia, hepatic abnormalities, severe obstructive sleep apnea, poor psychosocial functioning, and chronic school absenteeism. Recently, Lucy and Jackie had missed multiple important appointments after their mother had agreed to an intensified in-clinic monitoring regimen, and repeated attempts to contact the family had been unsuccessful.

As the girls' latest pediatrician, I had recommended on several occasions sending a nurse to assist with home-based medical management, but the mother had declined each time, saying that she didn't want "strangers" in her home. With each missed appointment, our medical team felt a growing moral and professional responsibility to interrupt what we saw as a downward spiral for the girls' health. The deci-

sion to file a report in this case was based on three considerations: concerns that the severity and trajectory of the girls' medical problems portended life-threatening and potentially irreversible end-organ disease with lifelong sequelae; the hope that CPS involvement might bolster medical adherence by providing support services; and the dearth of other reasonable options for engaging the family in appropriate care.

As the obesity epidemic unfolds, increasing numbers of children with severe obesity might be referred for CPS adjudication. Indeed, some scholars have argued that "state intervention may serve the best interests of many children with life-threatening obesity [and is] the only realistic way to control harmful behaviors."¹ In practice, however, CPS agencies have limited ability to alter the milieu that shapes behavior among resource-poor families who are reported for medical neglect, particularly when the problem is refractory obesity. Such families face intransigent inequities throughout their lives that perpetuate cross-generational cycles of poverty and poor health and pose major challenges to the medical and welfare establishments.

Obesity stems from energy imbalance derived from a complex interplay of behavioral, genetic, environmental, and social factors. Children with obesity severe enough to warrant a report for medical neglect represent the tip of the iceberg and invariably come from impoverished families with chaotic lives fraught with social difficulties, including unfilled basic needs. Lucy and Jackie S. live in a crowded, run-down tenement in a high-crime neighborhood; they would like to ride their bikes but are often afraid even to step outside. Their single mother had long given up trying to find a job, and she battles bouts of depression as she struggles to provide for her children by piecing together supplemental security income and nutrition-assistance benefits. Recapitulating a cycle of indigence, Ms. S. grew up with few positive role models and faltered academically, dropping out of school in the 10th grade. She was never taught how to cook or keep a budget, and her meager supplemental income forces her to choose between food and utilities; in fact, the reason she had not responded to our calls was that her phone service had been disconnected for nonpayment. Ms. S. has also had difficulties