

**WORLD ALLIANCE FOR PATIENT SAFETY**

# **SUMMARY OF THE EVIDENCE ON PATIENT SAFETY: IMPLICATIONS FOR RESEARCH**

**The Research Priority Setting Working Group of the World Alliance for Patient Safety**



**World Health  
Organization**



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# Preface



This publication of the World Health Organization aims to outline the future direction of patient safety research across the globe. Patient safety research does not have the benefit of the well-established approaches available to other fields of medical study. Multiple hurdles and challenges will need to be faced when designing trials, conducting audits and making

use of novel techniques, such as those that directly involve the patient as a partner in risk identification and problem resolution. This is partly related to the fact that patient safety research is a new field of study and that traditional research methods may therefore need to be suitably adapted.

We must develop a better understanding of adverse events in health care: their causes, how they are reported, how to learn from them and prevent them. Setting nationally and internationally recognized research priorities enables the selection of areas for research that are not only important for individual countries, but also allow collaboration and sharing of findings across geographical borders. This publication outlines the areas that the World Alliance for Patient Safety recommends for urgent attention, through a rigorous consensus process by international experts. Priorities should then be set by researchers and research leaders, according to the preference of countries.

Understanding the complexities of the academic, external funding and peer review systems will require a great deal of energy and a steadfast belief that the results will justify the efforts. We will need courage to promote our area of research and lift it to the forefront of scientific thinking.

My hope is that the material contained here will contribute to the development of research agendas globally, help to define the scope of the problem more accurately, measure its magnitude with renewed precision, elicit fully the appropriate policy and clinical solutions, and close the gap in knowledge that still prevails today.

Sir Liam Donaldson  
Chair, WHO World Alliance for Patient Safety  
Chief Medical Officer for England



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# Abbreviations used



<b>AIDS</b>	acquired immunodeficiency syndrome
<b>HIV</b>	human immunodeficiency virus
<b>ICD</b>	<i>International Classification of Diseases and Causes of Death</i>
<b>OECD</b>	Organisation for Economic Co-operation and Development
<b>WHO</b>	World Health Organization



# Executive summary



Unsafe medical care is a major source of morbidity and mortality throughout the world. In order to understand the scope of the issues facing policy-makers and researchers involved in improving the safety of health care, the World Health Organization (WHO) World Alliance for Patient Safety convened an ad-hoc expert working group to advise on the priorities for research on patient safety. To facilitate this work, the group used a framework for identifying topics in patient safety and the clinical and organizational issues that are central to improving it. As patient safety is a critical component of the quality of health care and is often described as a prerequisite for high-quality care, the group chose a framework that has been used previously to describe the three components of quality: structure, process and outcomes.

The aim of the report was to summarize existing research on patient safety and to set priorities on that basis. The group identified specific clinical outcomes (such as health care-associated infections), underlying structural problems (such as lack of a trained workforce) and procedural mechanisms (such as poor communication between clinicians) that contribute to unsafe care. On the basis of the epidemiology of patient safety and expert opinion, the group identified 23 topics that have a substantial impact on the safety of medical care and asked experts to describe how each issue affects patient safety.

This report contains several key findings. First, the available data suggest that harm from medical care poses a substantial burden in terms of morbidity and mortality on people around the world. Second, much of the evidence base has been created in the developed nations; although there is some epidemiological evidence of poor clinical outcomes due to unsafe medical care in developing countries and countries with economies in transition, the information on structural and process factors that contribute to unsafe medical care is derived almost entirely from a small number of developed countries. Their applicability to patient safety in other countries is not well known. Finally, although some of the means for reducing harm are known, large gaps in knowledge need to be filled before comprehensive solutions can be found.

In the light of these findings, the Working Group made several recommendations. First, better understanding is required of the causes, frequency and harm of adverse events in developing countries and those with economies in transition. Secondly, special focus should be placed on understanding the underlying processes of care that lead to adverse events. As the epidemiology and causes of adverse events become better known, it will become possible to find the solutions that are most likely to reduce harm.

This report was prepared as a complementary input to the deliberations of the expert group. Its goal is to summarize current knowledge and highlight major gaps in the main areas associated with patient safety. It is meant to serve as a basis for discussions about priorities. Current knowledge suggests that substantial harm can occur from medical care, but limitations in knowledge, especially for developing countries, make it difficult to recommend strategies for reducing that harm. The next generation of research should therefore focus on demonstrating reductions in harm from medical care, to ensure that health care is a balm for human suffering and not a contributor to it.







# SECTION I

## BACKGROUND AND MAIN FINDINGS

### Introduction

‘Adverse events’ are injuries due to medical care. They probably represent a major source of morbidity and mortality throughout the world. Although estimates of the size of the problem are imprecise, it is likely that millions of people suffer disabling injuries or death directly attributable to medical care. Injuries can occur in association with many medical interventions, from tainted blood supplies to health care-associated infections to substandard drugs. Many of the injuries are preventable and are therefore particularly troubling because of the longstanding medical principle to ‘First, do no harm.’

Understanding the types of adverse events that occur, their scope, frequency and preventability is critical for devising policies to reduce harm from medical care. As part of this goal, the World Health Organization (WHO) launched a series of activities to define topics for research into patient safety in order to identify interventions to reduce harm and improve the care of the billions of people across the globe who come into contact with health-care systems. The main objective of this report is to provide guidance for setting WHO’s priorities for patient safety research, by summarizing the available information on unsafe care in clinical contexts in various countries and the underlying causes of unsafe care.

The types and causes of adverse events that are particularly harmful to patients were identified. Avedis Donabedian’s widely used quality-of-care framework was used to frame the issues that contribute to unsafe care (1). The framework comprises three dimensions: outcome, structure and process. The Agency for Healthcare Research and Quality in the United States of America (the United States) has defined ‘outcomes’ as the results or consequences of clinical activities by physicians and other providers, ‘structure’ as the resources and organizational arrangements in place to deliver care or influence care delivery and ‘process’ as the activities of physician and other provider for delivering care (2). Specific consequences, such as health care-associated infections and adverse drug events, can be categorized as outcomes of unsafe care. Mechanisms such as latent failures in organizational structure reflect poor structures; whereas the underlying mechanisms in patient safety problems, such as poor communication between clinicians, reflect poor processes.

This report provides a ‘snapshot’ of the state of patient safety in the world today. There is a greater knowledge base for the section on ‘outcomes’ than that for the other aspects, as much more is known about the consequences of unsafe medical care than the structural and process factors that underlie them. The structural and process issues that affect patient safety are, however, critical. As stated by the Agency for Healthcare Research and Quality, there is “an obvious lack of information about the prevalence and etiology of medical errors, as well as the effects of these errors. It is impossible to design intelligent systems, protocols, or processes to reduce errors if we do not first know where errors are occurring and why.” (3). Meaningful data require better measures. The indicators that providers and policy-makers use (if they use indicators at all) have major limitations of reliability, validity and generalizability, limiting their usefulness for tracking adverse events or understanding the mechanisms that contribute to unsafe patient care.

# Methods

The Working Group began by identifying major patient safety-related outcomes, such as health care-associated infections, and the underlying mechanisms, such as poor communication, through literature searches, discussions within the Group and external sources, such as the National Patient Safety Foundation in the United States, which has created similar lists. Reviews on patient safety (e.g. those of the Agency for Healthcare Research and Quality (4) and the Quality in Australian Health Care Study (5), Table 1) were also identified to ensure that topics identified by others as causes of morbidity and mortality associated with unsafe medical care were at least considered. Experts in the Working Group and external experts were asked to report on specific topics in patient safety and to report

what is not known but would be helpful for better understanding of the issue and for designing solutions to reduce harm. Each section was reviewed by other members of the Working Group for completeness and balance. Finally, the entire report underwent external review by several international experts in patient safety.

Although some topics might appear to be disconnected from others, they are held together by the underlying factors, delineated in the sections on structural factors and processes of care, that are at the root of many of the outcomes. Many of the discussions overlap, not by design but because many factors contribute to unsafe care, and addressing one of them, such as provider fatigue, without addressing others, such as safety culture, would be inadequate to change health care.

**Table 1. Comparison of patient safety issues identified in this report with the 20 most frequent categories of adverse events in the Quality in Australian Health Care Study (5)**

Top 20 Principal category (of adverse events in the QAHCS)	Equivalent patient safety issue (in this report)
Catheter-related urinary tract infection	Iatrogenic infections and adverse events due to medical devices
Wound infection after an abdominal, retroperitoneal or pelvic procedure	Injuries due to surgical and anaesthesia errors
No, delayed or inadequate investigation of ischaemic heart disease	Misdiagnosis
Pressure sore or decubitus ulcer	Pressure sores and decubitus ulcers
Wound infection after peripheral procedure	Injuries due to surgical and anaesthesia errors
Post-procedural incisional hernia	Injuries due to surgical and anaesthesia errors
Inadequate reduction of a fracture or poor alignment	Injuries due to surgical and anaesthesia errors
Ongoing pain or restricted movement after back surgery	Injuries due to surgical and anaesthesia errors
Postoperative pulmonary embolism	Injuries due to surgical and anaesthesia errors
Gastrointestinal bleeding secondary to non-steroidal anti-inflammatory drug	Adverse events due to drug treatment
Postoperative bowel obstruction or adhesions	Injuries due to surgical and anaesthesia errors
Wound infection after lower segment caesarean section	Injuries due to surgical and anaesthesia errors
Recurrent incisional hernia	Injuries due to surgical and anaesthesia errors
Postoperative nausea and vomiting	Injuries due to surgical and anaesthesia errors
Injury due to fall in nursing home	Injuries due to falls in hospitals; safety of the elderly
Failed, blocked or ruptured aneurysm, vascular graft	Not covered in this report
Acute pain after surgery or procedure	Injuries due to surgical and anaesthesia errors
Problems after radiation therapy	Not covered in this report
Injuries due to fall in hospital	Injuries due to falls in hospitals
Postoperative atelectasis or health-care associated pneumonia	Iatrogenic infections

## Identification of topics

The topics were identified through literature reviews and by consensus among internationally recognized experts. Each outcome topic was chosen because it represents a major cause of harm from medical care for patients around the world. We compared our list of issues with those recognized in other studies and found substantial overlap. We also compared our list of topics with events identified by the Agency for Healthcare Research and Quality as 'patient safety indicators', which are used to identify adverse events that occur during hospitalization (4). We again found substantial overlap. On the basis of these comparisons, we considered that we had a reasonable list of topics to focus on. Individual issues of patient safety were addressed by identifying the scope of the problem, its severity and, when the information was available, potential structural or procedural interventions.

## Preparation of reports on topics

Experts in patient safety were asked to write reports on specific topics. Each author was given the freedom to choose a method of collecting data and describing the relevance of the topic to patient safety globally. They were given broad guidelines to include sections on clinical outcomes (such as adverse drug events), epidemiology (how often events occur, their severity and their preventability) and underlying causes. The economies of countries were categorized according to the World Bank 2006 classification on the basis of gross national income (6) into developing ('low income'), transitional ('medium income') and developed ('high income'), and the authors were asked to seek information for countries in all three categories. Finally, the authors were asked to identify the gaps in knowledge on their topic that might be addressed in future research.

## Main findings

Our findings suggest that unsafe patient care is ubiquitous, that it is associated with significant morbidity and mortality throughout the world, and that much of it might be amenable to intervention. Much of the evidence on the burden of harm from medical care is from developed nations, although enough evidence exists from developing countries and countries with economies in transition to suggest that unsafe medical care is a major problem in those nations as well. The data on structural and process factors that affect patient safety come almost exclusively from a small number of developed nations; however, there are still substantial gaps in knowledge about patient safety in developed countries and sizeable gaps in understanding about the relevance and impact of these issues in other countries.

On the basis of the evidence reviewed, it is likely that a combination of efforts to improve patient safety is needed. Focus is required not only on individual topics, such as health care-associated infections, but also on underlying structural or process mechanisms that contribute to suboptimal care. Interventions specific to a particular problem will probably have a more immediate impact, but interventions that target structures or processes, such as improving communication and the culture of safety, will probably have a broad, lasting impact on the delivery of safe, high-quality, efficient care.

## Adverse events due to drug treatment

Adverse events due to drug treatment include errors of commission and errors of omission, the latter meaning that a patient fails to receive a medication that is both indicated and necessary. Estimates from developed nations suggest that between 7.5% and 10.4% of patients in acute care settings experience an adverse drug event (7–9). Adverse drug events cost billions of dollars to

health-care systems around the world and result in 140 000 deaths annually in the United States alone (10, 11). No estimates exist of the cost or causes of or effective solutions for adverse drug events in developing countries. An estimated 28–56% of adverse drug events are preventable (12). Computerized physician prescribing has been proposed as a possible remedy (13, 14) and could be implemented in most developed countries. Research is needed on the prevention of adverse drug events in ambulatory settings and in specific populations, such as the elderly and children, which has not been described in the literature. Focus on developing countries and those with economies in transition will be critical.

## **Adverse events and injuries due to medical devices**

Adverse medical device events resulting in patient harm can be categorized into manufacturer-related errors, user errors and use or design errors (15–22). In the United States, more than 1 million events occur annually, at a rate of 6.3 events per 1000 patient-days (23). WHO has suggested that adverse events might be a particular problem in developing countries, where medical equipment is often unusable owing to lack of resources (24, 25). Effective, comprehensive surveillance programmes to detect adverse events are needed in both developed and developing countries. High-quality surveillance programmes to track the types, frequency and clinical settings of events would be a first step towards better understanding of their impact on patient safety. Better data are needed from countries at all stages of development in order to reduce the frequency of such events or mitigate the harm they cause.

## **Injuries due to surgical and anaesthesia errors**

Surgical errors, many of which are preventable, result in reduced patient safety

during perioperative care and while the patient is under the responsibility of the surgical team. They can be attributed to structure and process failures. In developed countries, estimates suggest that adverse events in the operating room account for 48% of all adverse events, affect about 2% of all hospitalized patients and are preventable 74% of the time (26). In many developing countries, the quality of surgical care is often constrained by lack of trained staff, poor facilities, inadequate technology and limited supplies of drugs and other essential materials (27). A systems approach to reducing surgical errors must take into account the highly complex, interdisciplinary, high-pressure environment of surgery (28). Given the budgetary constraints and differing priorities in resource allocation in developing countries, the focus should not be on complex system redesign but on evaluation and implementation of basic measures of hygiene and maintenance of instruments. Sources of finance for education and training of nurses and surgeons on safe practices should be assessed. Sensitivity to local practices, the culture of health-care delivery, hierarchical structures and channels of communication is essential, as is a non-punitive environment for reporting. Research is needed to explore the reasons for geographical differences in adherence to evidence-based guidelines and barriers to their implementation.

## **Health care-associated infections**

Health care-associated infections are infections that occur in the health-care setting, often due to the care itself. Worldwide, at least one in four patients in intensive care will acquire an infection during a stay in hospital, and this estimate may be doubled in developing countries (29), where the proportion has been estimated to be from 25% (30) to 40% or more (29). In developed countries, 5–10% of patients admitted to hospitals acquire an infection (30). The costs associated with health care-associated infections vary from US\$ 7–8.2 billion annually in the United States (30) to

€ 800 million in the United Kingdom and France (31) and US\$ 48 million in Turkey (32). Essential elements of an infection control programme include education of health-care workers, a well-organized surveillance system, appropriate legislation and consistent implementation of basic control measures, such as hand hygiene (33, 34). Research should be focused on investigating antimicrobial resistance and the spread of multiresistant microorganisms (35).

## Unsafe injection practices

In 2000, WHO estimated that some 16 billion injections are administered each year in developing countries and those with economies in transition, about 95% of which are for curative care. Worldwide, 39.6% of injections are given with syringes and needles reused without sterilization, and in some countries this proportion is as high as 70% (36). In some countries, unsafe disposal can lead to re-sale of used equipment on the black market. The proportion of non-industrialized countries that still reported open burning of syringes (considered unacceptable by WHO) was 50% in 2004 (37). Each year, unsafe injections cause an estimated 1.3 million early deaths, a loss of 26 million years of life and an annual burden of US\$ 535 million in direct medical costs (38). Changing the behaviour of health-care workers and patients, ensuring the availability of equipment and supplies and managing waste safely and appropriately could improve injection safety significantly. Future research should be directed to evaluating the impact of these strategies and activities on the burden of disease transmitted through unsafe injections as well as their cost-effectiveness, in terms of infections averted.

## Unsafe blood products

In developed countries, blood and blood products are used mainly in complex medical and surgical procedures, trauma care and the

treatment of patients with haematological disorders or leukaemia, whereas in developing countries a greater proportion of transfusions are prescribed for the treatment of complications of pregnancy, severe childhood anaemia and trauma. In a study by WHO, 59% of the countries that responded to a questionnaire had no established quality system, and at least 21.6% of donations were not screened for human immunodeficiency virus (HIV) in a quality-assured manner. It has been estimated that 5–15% of HIV infections in developing countries are due to unsafe blood transfusion (39, 40). Severe bleeding accounts for up to 44% of maternal deaths in Africa, where the risk for maternal death is 1 in 16. Unsafe blood also poses a high risk for transmission of other bloodborne infections, including hepatitis B, hepatitis C, syphilis, malaria, Chagas disease and West Nile fever. Best practice has shown that, even in countries with a high prevalence of infections such as HIV, a well-organized programme of voluntary blood donation and effective procedures for assessing the suitability of donors can lower the prevalence of infections. Important gaps in knowledge include: lack of information about the burden of infections averted by specific blood safety strategies, behavioural risk factors among blood donors and residual risks from transfusions even when screening programmes are in place.

## Safety of pregnant women and newborns

Improving patient safety among pregnant women and newborns is critical to reducing morbidity and mortality rates peripartum in women and newborns. With an estimated 7.6 million infant deaths during the perinatal period each year and over 500 000 deaths in women due to pregnancy or childbirth, of which 99% occur in developing countries, maternal and child health remains a concern for clinicians, researchers and policy-makers worldwide (41–43). High maternal and infant mortality rates can be attributed largely to lack of access to medical facilities and

inadequate medical care. Few women receive care of an adequate standard, and referral services are often of poor quality (44). Poor health care can also create distrust in the health-care system, further exacerbating the problem of access by decreasing patients' incentive to seek medical attention, even when competent staff and facilities are available (45). Social determinants of health and fundamental patient safety factors such as hygiene, blood safety, a trained workforce and adequate medical supplies further contribute to disparities in maternal and infant mortality between the developed and developing countries. This multifaceted problem requires an integrated solution; effective intrapartum care strategies should incorporate reproductive health while improving the quality of intrapartum care given to reduce pregnancy-related risks, from conception to delivery. Research must be broadened to address conditions such as pre-eclampsia, eclampsia and preterm delivery, which disproportionately affect women in developing countries and remain poorly understood. Targeting research to the needs of all populations, especially the most vulnerable, could result in significant reductions in overall maternal and perinatal mortality, with the added benefit of reducing health-care costs in the more developed countries.

## **Safety of the elderly**

Older adults are at increased risk for adverse events in every clinical setting because of atypical presentation of disease, the propensity of the central nervous system to act as the 'final common pathway' for medical problems affecting other organ systems, and reduced physiological reserve. Adverse drug events disproportionately affect the elderly, with an estimated rate of 50 per 1000 person-years in the United States (46). Of these events, 27% were considered preventable. The excess cost associated with preventable events in this population approached US\$ 2000 per event (47). Nursing homes often house some of the frailest patients in the population who, in

the United States, experience a rate of 10 adverse drug events per 100 resident-months, of which 40% were considered to be preventable (48). The use of multidisciplinary teams to care for frail elderly patients receiving complex medication regimens might be the best opportunity to improve the quality and safety of medical care in this high-risk population. Computerized physician order entry systems have been promoted to improve medication safety for older patients (49). Future research should focus on more efficient, less costly, less labour-intensive approaches to identifying preventable adverse events in older adults in all clinical settings.

## **Injuries due to falls in hospitals**

Patient falls in hospitals are the commonest patient safety injury reported and often lead to negative outcomes for practitioners and patients alike, including injuries, prolonged hospitalization and legal liability (50). The most serious complications of falls among the elderly arise from hip fractures, after which up to 20% of patients become non-ambulatory, and only 14–21% recover the ability to perform daily activities (51). Estimates from the United Kingdom suggest that falls account for two in five patient safety events, accruing annual costs of £ 92 000 annually for an average 800-bed acute hospital trust with an average of 24 falls weekly (52). The overall rate in the hospital patient population was 4.8–8.4 falls per 1000 patient-days, an estimated 30% of which resulted in an injury (53). Decreased use of physical restraints has been shown to reduce both the incidence of falls and the severity of injury (54). Reducing the use of psychoactive drugs in the elderly, which requires few additional resources, is likely to be cost-effective in most nations of the world. Research should be conducted to identify new means of preventing falls and to evaluate the efficacy of known techniques to minimize the incidence and morbidity. Further information is also needed on the incidence and severity of patient falls in developing countries.



## Decubitus ulcers

Risk factors for decubitus ulcers include immobility, friction, incontinence, cognitive impairment and poor nutritional status (55–57). In the United States between 1990 and 2001, decubitus ulcers were reported to be the cause of death of 114 380 persons (age-adjusted mortality rate, 3.79 per 100 000 population) (58). Estimates of prevalence in developed countries range from 10.1% to 14.8% (59). Less information is available for developing countries and those with economies in transition. In the United Kingdom, the treatment of decubitus ulcers was estimated to cost £ 1.4–2.1 billion annually, which represented up to 4% of total National Health Service spending in 2000 (60). Certain foam bedding and alternating pressure beds can reduce the risk for decubitus ulcers, especially for high-risk patients (61–63). Other interventions, such as routine skin inspection, improved nutrition, routine repositioning and increased mobility, have shown varying degrees of success but can be implemented in a variety of settings worldwide (14). Whether interventions to prevent decubitus ulcers would be cost-effective in developed countries and feasible in other countries is not known.

## Organizational determinants and latent failures

Catastrophic breakdowns of complex, well-defended systems have been termed ‘organizational accidents’ because they arise from factors originating at different levels of the system and can involve various processes, latent failures or poor supervision (64). If health care can be said to have a culture, it incorporates at least two obstacles to improving safety: first, a belief in trained perfectibility (after long, arduous training, health-care professionals expect—and are expected—to get it right); and, second, a tendency to stigmatize and sanction fallibility (error is equated to incompetence). Together, these pervasive influences make it difficult for

health-care providers to admit their errors or to learn from them collectively. Such learning is a prerequisite for a safety culture. A number of auditing techniques, such as proactive process measures, have been designed to identify those organizational dimensions that are currently most in need of remediation and to track subsequent progress. The dimensions vary from one situation to another but generally include such generic issues as teamwork, communication, protocols, rostering and scheduling, design and maintenance management. Research should be directed to how organizational factors combine with provider factors, such as fatigue or lack of adequate training, to affect patient safety.

## Structural accountability: use of accreditation and regulation to ensure patient safety

Accreditation is a formal process through which an external entity assesses whether a health-care organization meets published, specified standards. Regulation is the governmental establishment of standards to which health-care providers must adhere. Accreditation, which can have significant market value, has become the preferred method for driving patient safety. Accrediting organizations now exist in at least 39 countries, and the number is expected to grow. Regulation, although more widespread than accreditation, generally sets only the minimum provider requirements for practice. Future areas of research should include determining what accrediting and regulatory standards best improve safety, the cost-effectiveness of accreditation and regulation, and how multiple accrediting and regulatory efforts can be coordinated.

## Safety culture

A patient safety culture comprises shared attitudes, values and norms related to patient safety. Attributes such as open communication about safety problems, effective teamwork and

support by local and organizational leaders who make safety a priority characterize a positive patient safety culture. In health-care and other high-hazard industries, a positive safety culture is a fundamental determinant of safety: researchers seeking to quantify its importance have reported a relationship between safety culture and clinical outcomes, such as hospital-acquired infections (65). Interventions designed to improve aspects of safety culture include executive walk rounds (66, 67), teamwork training exercises (68) and a 'comprehensive' unit-based programme (69). A requirement to measure and report safety culture with standardized instruments can improve safety. The multidimensional nature of safety culture means that interventions that address only certain aspects might have a limited impact. Improved understanding of the factors involved in patient safety culture and interventions to improve it are topics for further research. A better understanding of safety culture in developing countries and countries with economies in transition is also needed.

## **Training, education and human resources**

The main threats to patient safety worldwide are inadequate numbers of equitably distributed, qualified health-care providers and incomplete knowledge about safe practice. The global health-care workforce, which comprises more than 100 million persons, including 24 million doctors, nurses and midwives, is the primary resource for making care safer (70). The deficit in 57 countries is estimated to be 2.4 million doctors, nurses and midwives (71), and these countries are therefore unlikely to meet the health-related Millennium Development Goals or to be in a position to improve safety. Preventing 'burnout' and improving training can help reduce deficits in the health-care workforce. In developed countries, little is known about the appropriate levels of staffing in different clinical contexts that would minimize adverse events, and little is known about the training and staffing necessary

to optimize patient safety in ambulatory care. The gaps in knowledge about manpower training and staffing are even more substantial in other countries. While there is compelling evidence that inadequate training and poor staffing levels are probably important components of unsafe care, little is known about the magnitude of these risks for patient safety.

## **Stress and fatigue**

Extended shifts greatly increase the risk that physicians and nurses will make errors in patient care and suffer occupational injuries; similarly, excessive nurse workloads are associated with increased risks for adverse outcomes. In comparison with physicians who do not work 24-h shifts, physicians in training who frequently work 24-h shifts make 36% more serious medical errors in the care of patients, make five times as many serious diagnostic errors, suffer twice as many motor vehicle crashes, suffer 61% more occupational injuries and report making four times as many fatigue-related errors that lead to a patient's death. Nurses working more than 12 h likewise make up to three times as many medical errors as those working less than 12 h. In addition, the risks for patient mortality and failure to rescue have been found to increase as nurses' patient loads become excessive. Limiting physicians' shifts to 16 consecutive hours has been shown to substantially decrease the risk for serious medication errors. Less substantive reductions in work hours (for example, the professionally mandated limit in the United States of 30 consecutive hours for physicians in training) appear to be less effective. Further studies are needed of how to optimize continuity of care and medical education while reducing work hours to safe levels, and comparative studies should be conducted of various circadian-based scheduling solutions. Research on other work conditions, such as physician:patient ratios, nurse and physician work acuity and the physical environment are needed.



## Production pressure

Production pressures occur when the optimal capacity of a health-care system or an individual health-care provider to care for patients has been exceeded. Although little empirical evidence exists, it is likely that excessive production pressures will adversely affect patient care. It is difficult to quantify the effect of production pressures on health outcome, as there is no standard measure of workloads; in most studies, a cross-sectional design has been used. A single longitudinal study indicated that the incidence of falls, urinary-tract infections and decubitus ulcers might be lower in hospitals with a high nurse: patient ratio, although a second longitudinal study found no correlation. To date, no intervention studies have been completed. Further work will be necessary to characterize the effect of production pressures on patient safety. Although much work has been done with respect to nurse staffing, most is of poor quality and the results inconsistent. Future work will require standard measures of staffing and overcrowding and more rigorous, prospective studies.

## Lack of appropriate knowledge and transfer of knowledge

The existence of knowledge at different levels affects how it is transferred, with communication and handovers between providers remaining central to optimizing patient safety. In an analysis in 2005, communication problems were identified as the cause of nearly 70% of sentinel events (72). Effective communication and teamwork are often assumed, and there has been little formal training and evaluation in these areas (73). Many institutions are advocating techniques such as read-back confirmation, interruption-free 'time-outs' and cross-monitoring (74, 75). Adoption of these methods has been slow, as one study showed that hospital emergency rooms regularly use only 8 of 21 best-practice handover strategies (76). What are the most effective knowledge management tools and practices to ensure that

the content of clinical decision support systems is valid? What is the effect of decision support on actual outcomes, rather than just process measures? How can communication sciences that address beliefs and misunderstandings in oral, written and electronic messages be applied in health care to make handovers less error-prone?

## Devices and procedures with no human factors

Human factors engineering is an important means of understanding the hazards of medical care and how to reduce those hazards. Problems in human factors design are pervasive in health-care devices, work areas and processes. Laboratory evaluations of various types of devices have shown error rates of over 10% (77). Human factors engineering can be used to investigate adverse events (78), to make decisions about procurements (79), and to improve design issues involving architecture, devices and clinical procedures (77), such as in anaesthesiology (80), surgery (81) and nursing (82). It will be important to identify the most efficient tools for investigating device safety, prospectively assessing risks associated with devices and for assisting procurement. Interdisciplinary research centres of excellence should be set up for clinicians who seek human factors engineering expertise and vice versa.

## Misdiagnosis

Misdiagnosis is a huge, unexplored aspect of patient safety, with widely ranging rates of delays and erroneous diagnosis. Our ignorance stems is due to the difficulty of studying the problem and the complex causes and consequences of diagnostic error. Six areas in which research could be concentrated are: misdiagnosis of major infectious diseases in developing countries; failure to diagnose life-threatening medical, surgical and trauma

emergencies in time; delays and misdiagnosis of cancer; errors in interpreting radiological images, pathology specimens or skin lesions; cognitive failures in making the correct diagnosis; and follow-up on the results of diagnostic tests. Potential strategies for minimizing the frequency and impact of diagnostic errors include: re-designing health-care systems to decrease dependence on human memory; providing a better infrastructure for learning from diagnostic outcomes and blame-free learning from errors that are identified; processes to minimize the harmful impacts of diagnosis errors and delays; and training to improve clinicians' cognitive skills and their awareness of common biases and disease-specific pitfalls.

## Poor test follow-up

The rates of test follow-up remain suboptimal worldwide, resulting in serious lapses in patient care (83). In developing countries, the rates of follow-up of tests for infectious diseases are variable, while in developed countries, numerous lapses in the follow-up of test results have been reported in inpatient, transition to outpatient and outpatient settings. Patient and provider perspectives on the communication of test results reveal confusion and miscommunication, especially in developing countries. Rapid diagnostic testing has alleviated some barriers to follow-up care, by allowing providers to discuss test results with patients at the same clinical encounter. The consequences of poor test follow-up are substantial, as delayed or incomplete follow-up after an abnormal screening result can adversely affect patient outcome. Delays also contribute to increased litigation: in the United States, one-fourth of diagnosis-related malpractice suits have been attributed to avoidable failures in the follow-up system (84). Improving test follow-up requires use of health information techniques to streamline communication between diagnostic laboratories and physicians and rapid, efficient delivery of test results and management recommendations to patients. Patients should also express clear

preferences about how providers should contact them, and they should contact providers directly if delivery of test results is delayed. Research is needed to improve communication, evaluate social and clinical workflows to increase the number of return patient visits, design remote communication of test results for patients who are unable to return for a follow-up visit and assess rapid diagnostic tests.

## Counterfeit and substandard drugs

Counterfeit drugs are those 'produced with an intention to cheat', which can include mislabelling, missing or wrong active ingredients or insufficient quantities of a correct ingredient. They pose a serious health risk, as repeated use can result in therapeutic failure, drug resistance or even death (85, 86). Counterfeit drugs account for more than 10% of the global medicines market and up to 30% of medicines consumed in developing countries (85, 87). A study in the United States predicted that the income generated by sales of counterfeit drug would reach US\$ 75 billion globally in 2010, an increase of over 90% from 2005. Deterrent legislation, an official supply chain and lower costs of legitimate drugs could reduce this burden. Consistent, systematic efforts are needed at the international level; at the national level, competent national drug regulatory authorities with the necessary resources to control the manufacture, importation, distribution and sale of medicines are needed (85). Research is needed to determine the most effective regulatory mechanisms for reducing the number of substandard drugs and to find other solutions to reduce the harm from substandard drugs.

## Inadequate measures of patient safety

Measures of patient safety could be used to quantify and improve medical care by giving providers and policy-makers insight into the

safety of medical care being provided and possible targets for improvement (88). Safety measures can be classified in Donabedian's domains of structure, process and outcomes (89). The Institute of Medicine in the United States has estimated that 44 000–98 000 preventable deaths occur annually in that country (90). An analysis based on the patients' safety indicators of the Agency for Healthcare Research and Quality in the United States showed that at least 32 000 persons in that country die each year due to 18 types of medical injuries (91). The cost of medical errors to the United States, in lost income, disability and health-care costs, has been estimated to be at least US\$ 29 billion annually (90). Most safety measures, including surveys, process measures and automated trigger tools on computers, are relatively inexpensive and can be used widely (92). Given the paucity of existing tools, more instruments should be created and validated, and existing measures should be refined and further validated and spread to health-care organizations.

future mitigation are some of the interventions that should be explored. Research areas include determining the effect of patient- and family-centred care on patient safety, eliciting patient perceptions of safety and quality, observing the usefulness of conflict resolution in bridging gaps between providers and patients and their families and gauging the effect of educational programmes for patients and their families on patient safety.

## **Lack of involvement of patients in patient safety**

Patients and family members have an increasingly important role to play not only in protecting themselves from breakdowns of the health-care system but also in contributing to lessons to help mitigate future events. Most of the focus in improving patient safety has been at the institutional level, and information about the burden of adverse events in health-care systems has not been shared publicly in a transparent manner. Increasing public awareness about their contribution to reducing preventable harm might result in new, more effective measures. Improving health literacy, involving patients and their family members in analysing medical system breakdowns, providing information to the general public in an understandable format, involving patients and families in improving quality and safety, holding councils for collaboration and educating health-care staff by telling stories to provide lessons for





# SECTION II

## OUTCOMES OF UNSAFE MEDICAL CARE

### 1 Adverse events due to drug treatment

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#### Scope of the problem

Adverse events due to drug treatment include errors of commission and errors of omission, the latter meaning that a patient fails to receive a medication that is both indicated and necessary. Table 2 lists some errors in each category.

**Table 2. Causes and types of errors of commission and omission**

Errors of commission	Errors of omission
<b>Health system level</b>	
Necessary information for safe use of drug lacking	Drug not available
Substandard drug	Drug too expensive be used
Counterfeit drug	
Error-prone conditions	
Look-alike medication	
Sound-alike medication	
Process organization and resources	
<b>Provider level</b>	
<b>Physicians</b>	<b>Physicians</b>
Inadequate prescription	Failure to prescribe drug
Lack of knowledge about drug	
Lack of information on patient	
Lack of medical knowledge	<b>Other professionals</b>
Failure to apply medical knowledge	Failure to administer drug
Failure of follow-up	
Failure to recognize drug side-effects	
<b>Other professionals</b>	
Failure to administer drug correctly	
Failure of patient identification	
<b>Patient level</b>	
Intentional or unintentional lack of adherence	Intentional or unintentional lack of adherence

Adverse drug events are usually considered errors of commission and are the commonest cause of serious patient safety issues in developed countries (9). The attention paid to patient safety issues in these countries has led to a significant body of literature about the causes, frequency and consequences of adverse drug events and strategies for preventing them. While the information from developed countries is hardly complete, adverse drug events are one of the better understood topics in patient safety. In contrast, little is known about such events in developing countries, probably because of more pressing issues, such as lack of access to providers and high-quality drugs (partly due to the existence of counterfeit and substandard drugs, see below).

Most studies have addressed prescribing errors, which are the single most relevant cause of adverse drug events. A study of general practices in Australia showed that approximately 10% of patients had experienced an adverse drug event in the preceding months, about 50% of the events being moderate to severe (7). In the United Kingdom, 216 claims against general practitioners handled by the Medical Defense Union between 1995 and 2001 were directly related to errors in prescribing, monitoring or administering medicines, and of 1000 consecutive claims reported to the Medical Protection Society, 193 (19.3%) were associated with medication and prescribing errors (93). The Canadian Adverse Events Study (8) showed that 7.5% of patients admitted to acute care hospitals in Canada experienced at least one adverse event in 2000, drug- or fluid-related events being the second commonest type of adverse event after surgical procedures. Of the adverse events, 37% were judged to have been preventable.

A study in the United States showed that medication errors were common (about 5 per 100 medication orders), although only 7 of 100 medication errors had significant potential for harm and 1 of 100 actually resulted in injury (94). Another study found 6.5 adverse drug

events for every 100 hospitalized patients; 45% of the serious and life-threatening events were preventable (9). These findings are consistent with those of other studies in the United States, showing that injuries due to drugs are common among hospitalized patients, although the true incidence varies significantly (from 1.5% to 35%) (9), owing to the operational definition of adverse drug event and the detection method used.

Detection and underreporting are major problems, however. In hospitals in the United States, only 1–5% of adverse drug events are identified (95). Research on underreporting of serious adverse drug events in Canada and the United States suggests that the formal reporting rate may be as low as 1.5% of all events (8). In one study, it was estimated that only about 1% of serious events are reported to the Food and Drug Administration in the United States (96).

A study in the ambulatory care setting in the United States showed that 1.4% of hospital admissions were for adverse drug events (97). A more recent examination indicated that 25% of patients who had received a prescription from a primary care provider experienced an adverse drug event, nearly one in seven of which were serious (98). Yet another study showed that 5% of elderly residents of the United States who attended ambulatory care suffered an adverse drug event in any given year, 42% of which were considered preventable (46).

## Severity of the problem

The consequences of adverse drug events in developed countries are substantial. In Australia, such events are one of the most important causes of morbidity (7), with substantial financial implications: adverse drug events cost the Australian health care system over US\$ 500 million each year, which represents 1% of the total amount spent on health nationally (10).

In the United States, adverse drug events



have also been found to exact a large human toll. Studies suggest that adverse drug events may contribute to as many as 140 000 deaths annually, occurring in about 1 of 16 hospitalized patients (11). The financial impacts are also substantial. In one study, the cost attributable to a preventable adverse drug event was estimated to be US\$ 4685 (1996 value) (99). In another study, the additional cost of hospitalization of patients with an adverse drug event was estimated to be US\$ 2000, excluding malpractice costs and the cost of injury to the patient (11). It was estimated in a 700-bed teaching hospital in the United States that the cost attributable to all adverse drug events was US\$ 5.6 million per year, and that for preventable events was US\$ 2.8 million per year (99).

No information is available for developing countries and those with economies in transition; however, as access to medications improves, it is reasonable to assume that adverse drug events will also become an important source of morbidity, mortality and financial liability in those countries, which already have resource-strapped health systems.

## Possible interventions

A systems analysis of serious medication errors showed that almost half were associated with insufficient information about the patient and the drug (100). An estimated 28–56% of adverse drug events are preventable, and the commonest ones result from errors in order writing (12). Computerized physician order entry and clinical decision support have been proposed as possible remedies for adverse drug events (13, 14) and could be implemented in most developed countries. For example, computerized order checking can potentially prevent ordering errors, such as wrong dose, known allergy, wrong frequency and drug interactions (9). Further, the use of clinical information technology could eliminate reliance on handwriting for ordering medications (101).

One study showed that computerized physician order entry reduced serious medication errors by 55% (102). Whether this technology would be feasible or cost-effective in resource-poor settings is unknown.

Several interventions have been successful. For example, the error rate in anaesthesia was reduced by nearly sevenfold, from 25–50 per million to 5.4 per million, by instituting standardized guidelines and protocols and by standardizing equipment. In a study conducted in 1999 in which a pharmacist was included on medical rounds, medication ordering errors were reduced by 66%, from 10.4 to 3.5 per 1000 patient-days. Avoidance of similar-sounding and similar-looking names and packages of medication can also reduce the potential for error (101). Such interventions require less capital expenditure than a computerized physician order entry system and are more likely to be applicable in developing countries and those with economies in transition.

Several international efforts have been started to promote drug safety. In 1968, WHO initiated the International Drug Monitoring Programme (103), which currently involves 81 countries and in which data on adverse drug reactions are collected. The programme is administered by the Uppsala Monitoring Centre in Sweden.

## Gaps in knowledge

There are critical gaps in knowledge about adverse drug events in developed countries. While the best current evidence for the causes of these events is from these countries, much of it is for the hospital setting; relatively few studies have examined why adverse drug events occur in ambulatory care, how often they occur and the impact they have on patient well-being. The studies were generally carried out in large urban settings and might not be fully generalizable to other settings, such as rural areas. Furthermore, the consequences of medication errors in

specific populations, such as the elderly and children, have not been described.

The epidemiology and causes of adverse drug events in countries with economies in transition, including the drugs involved, the frequency of events, their severity and the amenability of these events to prevention, are generally unknown. Studies under way of adverse events in resource-poor settings will help fill some of the gaps, but these incidence studies might not be adequate to understand the events fully and to find ways to reduce their frequency. Further, given that several strategies (e.g. computerized physician order entry, pharmacists' involvement) have been found to reduce medication errors and adverse drug events in developed countries, it will be important to investigate which can be transferred and be cost-effective in developing countries and those with economies in transition.

## 2 Adverse events and injuries due to medical devices

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### Scope of the problem

A medical device is an item used to cure, mitigate, treat, diagnose or prevent disease or affect the structure or function of the body; it does not achieve this action through chemical action or metabolism (104). The definitions used in Australia (105), Canada (106), the European Union (107) and by the World Bank (25) are similar.

Medical devices are used in every setting (e.g. hospitals, physician offices, nursing homes and private homes) throughout the world.

Devices have many features that affect the design of surveillance or studies of safety. There is no universally recognized nomenclature or identification system that provides the optimal level of detail for all applications, although the Universal Medical Device Nomenclature System™ (108) has been used in many countries, and the Global Medical Device Nomenclature has been adopted by a number of major stakeholders (109). Devices can be simple or complex, and continual redesign can result in devices with the same model name but a mix of features in use at any one time. Furthermore, during routine maintenance or updating, new components from the original or another manufacturer might be installed. Some devices are used in conjunction with others and with drugs, which can interfere or interact, resulting in injuries associated with magnetic resonance imaging (110), misconnection of medical gas (111) and drug-mediated sensitivity to devices (112). Environmental conditions can also adversely affect the functioning of devices; for example, extreme heat can break down latex (113), humidity can result in inaccurate blood glucose readings (114), and mobile radios can disturb medical telemetry equipment (115). Devices may also be reused, for the same or different patients; cleaning and sterilization can degrade device materials and might not be effective (23). Reuse of devices intended for only one use has been reported in developing countries (25, 116–118), and used implants have been found for sale on the Internet (119).

Adverse medical device events have been defined as 'patient harm caused by device-related medical or nursing management rather than the patient's illness' (120). The Global Harmonization Task Force was formed in 1992 by Australia, Canada, the European Union, Japan and the United States to ensure the safety, effectiveness and quality of medical devices while also promoting technological innovation and



facilitating international trade. The Task Force for medical devices has described adverse events in detail on their website <http://www.ghtf.org/index.html>, without defining them. These events can be categorized into manufacturer-related errors (e.g. inappropriate sterilization or design errors such as inappropriate device layout), user errors (due to factors such as fatigue, stress, insufficient dexterity, incorrect training and negligence) and use errors (when deficiencies in design facilitate or provoke user error) (15–22). It can be difficult to determine which of the three categories applies, as the sponsor, device, training, labelling and use conditions are interrelated and interactive (23, 121). Human factors are inherent in the use of virtually every device (122), and infusion pumps have attracted particular interest in this respect (123, 124).

Little information is available on adverse device events, as most of the literature refers to topics covered in other sections of this report, such as surgical errors and health care-associated infections. WHO studies have suggested that adverse events might be a particular problem in developing countries, where medical equipment is often unusable or only partly usable owing to a lack of resources for maintenance or replacement (24, 25). Adverse medical device events also occur in developed countries, however. In neonatal and paediatric intensive care units, more than 16 such events per 1000 patients days were reported in Switzerland (125) and more than 19 in the United States (126), with 20 and 3 adverse events per 1000 patient days, respectively. In a tertiary-care hospital in the United States, the overall incidence of adverse medical device events was 83.7 per 1000 discharges (120), and, nationally, more than 1 million events occurred annually, at a rate of 6.3 events per 1000 patient-days (23). In the period July 1999 to June 2000 in the United States, there were an estimated 454 383 emergency department visits for an injury associated with a medical device, and 58 000 of the patients died in the emergency department or were hospitalized (127).

In 2004, the United States Food and Drug Administration received about 53 000 individual and 104 000 summary reports of adverse medical device events from manufacturers, user facilities and importers and an additional 3400 voluntary reports from health-care professionals and the public (128); however, reports from another section of the United States Government indicate severe underreporting to the Food and Drug Administration (129). The main problems reported were aortic connector device failure leading to haemorrhage and death, thrombus and reactions associated with coronary stents, meningitis associated with cochlear implants, aneurysm-related deaths associated with endovascular grafts, hospital-bed fires, toxic shock syndrome associated with a particular brand of tampon, off-label use of an adhesion barrier and saline leakage into the access port of an adjustable gastric band (130). Some adverse events with major impacts on public health were reported to newspapers rather than to the Food and Drug Administration, such as sudden cardiac deaths associated with an implantable “cardioverter” defibrillator (131), which resulted in many recalls (132). A recent report on the epidemiology and surveillance of medical devices, the first of its kind, describes many adverse medical device events, including infections related to endoscopy and haemodialysis; prion transmission from surgical instruments; latex allergy; silicone gel breast implant ruptures; failure of abdominal aortic aneurysm stents, artificial aortic valves and cochlear implants; and adverse events related to electromagnetic interference, ear candles, drug-eluting stents, haemostasis devices, contact lenses, artificial joints, intervertebral discs and intrapartum fetal monitoring devices (23).

In developing countries with budgetary constraints, equipment is often used well beyond its intended life, without appropriate maintenance. This situation increases the risk for harm of both patients and health-care workers. Poorly maintained infrastructure and equipment also result in a higher probability of adverse events. Adverse event reporting systems do

not exist in most developing countries, as no definition of a medical device exists.

Trends in the use of medical devices, such as an extension from specialized health-care settings to community care and homes, use by untrained and unskilled persons, use under pressure of time and the increasing complexity of devices (21), suggest that the problem of adverse events will not improve soon in the absence of interventions.

## Severity of the problem

Little information is available on the severity of harm due to non-infectious complications of faulty medical devices. Many of the studies are narrowly focused, and the results might not be generalizable. Between June 1985 and January 1987 in Canada and the United States, a computer-controlled radiation therapy machine massively overdosed six people, resulting in several deaths, in an event that has been called the worst accident in the history of medical accelerators. When the machines were recalled for significant design changes, investigators found both hardware and software problems (133).

Faulty medical devices often result in product recall, which is costly for manufacturers. In January 2001, one company recalled hip implants after it was found that they could loosen. Over 2760 of the 31 000 patients who had received the implants had them replaced, and the company settled a class action lawsuit for the defective implants for US\$ 1 billion in 2002 (134).

## Possible interventions

An effective intervention to improve anaesthesia safety involved clinicians, experts in human factors, medical device manufacturers and regulators (135). The persistence of adverse events related to infusion pumps led to published analyses (136–141) and redesign by the manufacturer (124, 142).

Effective, efficient interventions will, however, require knowledge of the range, frequency, rates and causes of adverse medical device events.

Effective, comprehensive surveillance programmes to detect such events are lacking (143). Underreporting has been severe because of lack of recognition of the relation between devices and adverse events, lack of recognition that such events should be reported to health-care entities or agencies, lack of time to prepare reports and fear of being held responsible. A significant hindrance to reporting is lack of documentation about device use and adverse events in medical records (120, 144). The lack of standardized nomenclature for devices further hampers good written documentation.

Even when adverse medical device events are detected, follow-up investigations are often insufficient. Many investigations are described as ‘superficial’ or ‘fail to conduct ... an in-depth analysis of the error’, and ‘the finger of blame is simply pointed at the device user, masking other reasons behind the error’ (20, 21, 145).

With over 100 000 brands of medical devices in 1700 product categories (or 8000 Global Medical Device Nomenclature generic device terms), ranging from simple tongue depressors to ventilators and other complex devices, regulation has proved to be challenging. The Global Harmonization Task Force has encouraged a convergence of regulatory practices for medical devices across the globe (146). As a result, for example, Australia’s regulatory framework is similar to that adopted by the European Union, although the two systems still have some differences (147).

## Gaps in research

Little is known about adverse medical device events. Better data are needed from countries in all stages of economic development on the frequency of these events, their causes and

potential means to reduce their frequency or mitigate the harm they cause. High-quality surveillance programmes to track the types of events, their frequency and their clinical settings would be a first step to better understanding the impact of adverse medical device events on patient safety. Effective surveillance programmes will require a universally acceptable nomenclature and complete documentation of both device use and adverse events in health-care records.

### 3 Injuries due to surgical and anaesthesia errors

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#### Scope of the problem

The operating room is one of the most complex work environments in health care, with sophisticated technology and the involvement of persons from multiple disciplines, besides surgeons, such as anaesthetists, operating-room nurses and preoperative consultants. Procedures are often performed in high-risk situations and under time pressure, requiring rapid responses to changing conditions and unforeseen challenges.

The main aspect of surgical care is of course the operation, although establishing a correct diagnosis leading to the correct procedure, continuous monitoring, adequate medication and rehabilitation must also be taken into account in analysing patient safety in surgical care.

Surgical errors are defined here as errors that

endanger patient safety during perioperative care and management, while the patient is the responsibility of the surgical team. Surgical errors can be attributed to structure and process failures, which are reflected in outcomes (1). Like medical errors in general, not all surgical errors result in complications, and many complications are not due to errors; although some complications or adverse events are not preventable, preventable adverse events are, by definition, due to errors.

Surgical management of disease is difficult. System failures due to human factors and organization probably contribute to preventable adverse events and poor surgical outcomes in general (148). Low hospital volume of procedures (149, 150), surgeon inexperience (151), inadequate supervision of trainees (152), fatigue and excessive workload (153, 154) probably all contribute to errors and harm. Other sources of error have been reported to be deficits in hospital process and administration (155, 156) and insufficient communication and team skills (157–161). These areas are ones that could be improved by clinicians, administrators and regulatory bodies, with clear targets for effective interventions and policies.

The aim of this section is to review the topic of surgical and anaesthesia errors. Much of the discussion is based on the assumption that a certain level of infrastructure and services is available. This level might not exist in many parts of the world, where more fundamental issues of basic resources and access to health care are priorities. Many developing countries have a shortage of health-care workers, limited training and limited services. Health systems are strained by treatment of malaria and HIV/AIDS, and migration of health-care staff to developed countries. Furthermore, financial instability and an insecure environment due to conflicts compound the problems in many countries. Health care might not be a priority in decisions about resource allocation (71). Research currently undertaken in more developed countries might still provide guidance on avoiding potential risks

to surgical safety and may aid in designing and implementing a better health infrastructure, with safety measures, while the levels of service and infrastructure improve.

This section does not describe specific procedural errors or threats to safety in subspecialties but discusses general conceptual deficits that affect all surgical fields. Safety issues due to deficits in infrastructure, infection at the surgical site, venous thromboembolism, surgery at the wrong site and retained objects are addressed, and possible solutions and policies to solve these prevalent problems are proposed.

## **Severity of the problem and possible interventions**

### **Infections at surgical sites**

Infections at surgical sites make a heavy contribution to patient injury and mortality and to health-care costs. Their prevalence in the United States is more than 2% (162–165). Mortality rates, length of stay, readmission rates, use of health-care services and the total cost of care are all substantially higher for patients with infections at surgical sites than for uninfected patients (166–168). Reports from developing countries indicate an even higher incidence of infections at surgical sites than in developed countries, three studies showing rates of 10.9%, 12% and 26.7% (169, 170). Overall, infection control practices were considered to be poor as a result of deficient facilities, inadequate surgical instruments and lack of proper supplies for wound care and personal hygiene. While records of surgical site infections are rare and few studies are available, rates of 40–70% have been reported (171). Lack of adequate decontamination, non-functioning sterilization equipment, reuse of limited sets of equipment and improperly reprocessed surgical drapes pose threats to hygiene (172). These issues should be addressed in conjunction with adequate perioperative antibiotic prophylaxis.

The effectiveness of preoperative administration of antimicrobial agents to prevent infection has been established and confirmed (162, 173–175). Therapeutic levels of antibiotics must be present at the time of the incision to achieve effective prophylaxis, and the timing of administration is critical. Despite the existence of guidelines, however, adherence is frequently inadequate (176, 177), as evident in inadequate timing of antimicrobial administration, inappropriate choice of antibiotics and inadequate duration of prophylaxis (178–180). Few studies have been reported on prophylaxis for infections at surgical sites in developing countries, and a quality improvement programme to reduce the incidence of these infections in low- and middle-income countries has been proposed (181). Although an estimated 40–60% of infections at surgical sites could be prevented by administration of proper prophylactic antibiotics, over-use, under-use and misuse of antibiotics have been estimated to occur in 20–50% of operations (162). The timing of administration is critical, and both early and late administration are associated with increased rates of infection (175).

Improving adherence to evidence-based practice, as determined by national experts and representatives of major surgical professional organizations, can reduce the incidence of surgical infections. The guidelines include three main performance measures for antibiotic administration: selection of appropriate drugs, administration 60 min before incision to achieve therapeutic levels, and discontinuation within 24 h of surgery (162, 176). In one study, anaesthetists were identified as the practitioners most likely to administer antibiotics within 60 min of the incision. Changes were made accordingly in ordering, documentation and antibiotic preparation, and education sessions were held with all operating-room staff at meetings and grand-round presentations. The results of these changes were prominently displayed, and feedback was provided. The surgical site infection rate was significantly reduced (182).

For a lasting reduction in the rate of infections at surgical sites, the process of antibiotic prophylaxis administration must be analysed, and all departments providing care must participate in implementing change (27, 183–185). Appropriate use and administration of prophylactic antibiotics can also be improved by standing orders, computerized reminders, defined location of antibiotic administration, proper documentation and identification of accountable providers (186–188). Adoption of a uniform institutional practice for antibiotic administration can decrease variations in performance, in both developed and developing countries. The more pressing issue in health-care systems in developing countries, however, is ensuring a constant supply of antibiotics for prophylaxis. Because of different hygiene and disinfection procedures and potentially different infectious disease profiles, the needs for specific types and classes of antibiotics might be different from that in developed countries. Research is needed to evaluate feasible supply channels and cost-effective application and distribution, taking into account the local culture and needs. The focus should be on establishing efficient, cost-effective, sustainable strategies for financing and implementation.

Prophylactic administration of antibiotics is not the only means for reducing infections at surgical sites: other means are antisepsis, optimal surgical technique, patient temperature maintenance, glucose control and the use of clippers instead of razors (182).

## **Venous thromboembolism**

Postoperative thromboembolic events are among the main causes of morbidity and mortality after surgery (189, 190). Patients undergoing certain types of surgery, such as orthopaedic and abdominal operations, are at highest risk (191, 192); postoperative pulmonary embolism is the single most important cause of death after surgery such as hip replacement. The extent of this type of complication in resource-poor settings is unknown

and might be difficult to assess because of lack of consensus on diagnosis and because a substantial number of incidents occur after discharge from the hospital and are therefore not recorded. Even though most countries might not have access to advanced surgical interventions such as joint replacement, the preventable nature of venous thromboembolism as a post-surgical complication underlines the importance of raising awareness of prophylactic measures. The assessment below is based on a systematic review of studies on the risk for venous thromboembolism and its prevention (193).

Most hospitalized patients have one or more risk factors for venous thromboembolism (194, 195), which are usually cumulative. For example, patients with fractures of the hip are at particularly high risk because of their advanced age, the presence of a proximal lower extremity injury and its operative repair and a frequent marked reduction in mobility for weeks after surgery. If cancer is also present, the risk is even greater.

The use of thromboprophylaxis is based on solid scientific evidence. Without prophylaxis, the incidence of objectively confirmed, hospital-acquired deep-vein thrombosis is 10–40% among medical and general surgical patients and 40–60% after major orthopaedic surgery (196). In many of these patient groups, venous thromboembolism is the commonest serious complication (197, 198), and about 10% of hospital deaths are attributed to pulmonary embolism (199), making it the commonest preventable cause of hospital death. Although better patient care might attenuate some of the risk factors for venous thromboembolism, hospitalized patients might now be at greater risk than those studied in the past because of more advanced age, a greater prevalence of cancer and intensive cancer therapy, more extensive surgical procedures and prolonged stays in critical care units.

While groups at high risk for venous thromboembolism can be identified, it is not

possible to predict which patients in a given risk group will have a clinically important thromboembolic event. Furthermore, massive pulmonary embolism usually occurs without warning, and patients with this complication often cannot be resuscitated. Routine screening of patients for asymptomatic deep-vein thrombosis is logistically difficult and is neither effective in preventing clinically important venous thromboembolism nor cost-effective (200–203). The objective of thromboprophylaxis is not only to prevent fatal pulmonary embolism but also to prevent symptomatic deep-vein thrombosis and pulmonary embolism, which are associated with considerable short- and long-term morbidity and use of resources (204).

Most cases of symptomatic venous thromboembolism associated with hospital admission occur after hospital discharge (205, 206). When symptomatic hospital-acquired venous thromboembolism is suspected, extensive diagnostic testing is necessary. If the condition is confirmed, therapeutic anticoagulation therapy, with its potential for serious bleeding complications, must be initiated, resulting in a longer hospital stay or readmission. Furthermore, the risks for post-thrombotic syndrome and for recurrent thrombosis are increased (207–209).

Prophylaxis against venous thromboembolism remains the most appropriate strategy for reducing the sequelae described above, and primary thromboprophylaxis reduces the rates of deep-vein thrombosis, pulmonary embolism and fatal pulmonary embolism (193, 210). In a systematic review by the Agency for Healthcare Research and Quality in the United States, in which interventions for patient safety were ranked on the basis of the strength of the evidence (14), the safety practice with the highest rank was appropriate use of prophylaxis to prevent venous thromboembolism in patients at risk. The recommendation was based on overwhelming evidence that thromboprophylaxis reduces adverse patient outcomes, while, at the same time, decreasing overall costs (211, 212).

Prevention of thromboembolic events with anticoagulants, early mobilization and mechanical devices (i.e. compression stockings) are also known to be effective (193). Many of these treatments, such as warfarin and compression devices, are known to be cost-effective in high-income countries. Whether they are readily available, cost-effective and likely to be used in middle- or low-income countries is not known. The limited publications available for review indicated that the rate of postoperative thromboembolic complications is higher in developing than in developed countries. As in developed countries, there appears to be no clear consensus about prevention strategies (213–215). The same issues and barriers as those described above with regard to a sustainable supply of antibiotics apply to pharmaceutical thromboprophylaxis. In resource-poor settings, early mobilization of patients and cheaper alternatives, such as intermittent pneumatic calf compression, might also be useful.

## Infrastructure

In many developing countries, the quality of surgical care is often constrained by lack of trained staff, poor facilities, inadequate technology and limited supplies of drugs and other essential materials (27). Challenges at various levels of infrastructure in developing countries and possible approaches to overcoming them are outlined below. Basic supplies for preoperative disinfection at standards considered acceptable in developed countries are often lacking, probably resulting in higher rates of preventable infection. In order to formulate sustainable, feasible approaches to these issues, it is important to understand the local infrastructure. A local response to restricted supplies of standard preparations from developed countries can be to use cheaper, locally available preparations that are equally effective. This would be a cost-effective option, and the funds saved could be used to improve preoperative antibiotic administration or hospital infrastructure (216). Improving access to basic preoperative disinfectants and sterile



equipment and ensuring that they are used is a critical challenge which needs further study.

The different levels of infrastructure in developing countries also affect use of newer surgical techniques with potentially better outcomes, lower complication rates and lower use of resources in the long run. Aside from the initial investment in equipment and training for these techniques, a new infrastructure for care support might be required for successful implementation, and this and resistance from local surgeons might be substantial barriers to safer patient treatment and care. Use of some techniques, however, might be feasible even in settings lacking the optimal infrastructure (217).

Adequate infrastructure includes not only equipment and facilities but also qualified medical personnel and specialists, who are lacking in vast regions of developing countries, representing a major cause of morbidity and mortality in those areas. The impossibility of being seen by a qualified surgeon in a timely manner almost surely contributes to death and disability across the world. Improved training and more surgeons are the solution but are costly. Advances in communication and information technology might extend specialist coverage to underserved rural regions, and telemedicine can provide local medical personnel with specialist advice on diagnosis, management and monitoring of treatment (218). This concept could also be extended to include the participation of international experts. Virtual consultations could thus improve patient safety by widespread dissemination and access to expert medical and surgical care.

## **Surgery at the wrong site**

Although rare, cases of surgery at the wrong site receive wide media coverage when they occur. Surgery at the wrong site can be defined as surgery on the wrong person, on the wrong organ or limb or at the wrong vertebral level

(219). The incidence of such errors has been difficult to assess. In a review of 10 years of data from medical malpractice insurers, claims related to surgery at the wrong site comprised 1.8% of all orthopaedic surgical claims (220). In an analysis of the causes of 126 cases by the Joint Commission on Accreditation of Healthcare Organizations in the United States, surgery on the wrong patient accounted for 13% of cases, use of the wrong procedure for 11% and surgery on the wrong body part or site for 76% (220).

Possible risk factors include emergency operations, unusual time pressures to start or complete a procedure and the involvement of many surgeons or procedures at a single surgical visit. Surgery at the wrong site is unacceptable but rare, and serious injury attributable to it is even rarer. One study showed that surgery at the wrong site serious enough to result in a report to risk managers or a lawsuit occurred about once every 5–10 years in a single large hospital (219). Cases of surgery at the wrong site reported in the media might exaggerate the incidence and harm.

No single protocol will prevent all cases. An optimal reduction in the number of cases requires safe, simple, efficient, pragmatic measures, and various systematic approaches to prevention have been proposed (219, 221). Communication failure has been identified as a leading cause of operations at the wrong site (222). Teamwork is central to a culture of effective communication in the operating room and is a surrogate marker for patient safety (223, 224). A number of team-based approaches have been proposed over the past few years, which could be used in tackling this and other sources of surgical errors (160, 161, 225). Effective team communication can provide an additional safeguard against surgery at the wrong site. Even if multiple layers of checks and controls are in place in a coordinated health-care team, however, the ultimate responsibility for ensuring the correct site of operation in every case is that of the surgeon.

## Retained objects

Like surgery at the wrong site, leaving sponges or instruments inside patients is rare but can result in major injury (226) and often results in wide media coverage and lawsuits. The incidence of these errors has not been determined, but estimates suggest that they comprise one case out of every 1000–1500 intra-abdominal operations (227). It is unclear why these incidents occur and how to prevent them (228). As is the case in wrong-site surgery, the lack of information on this error makes it difficult to assess the prevalence of this error in resource poor settings accurately. The possible catastrophic consequences and readily preventable nature of this error merit an evaluation.

The established standards require that only sponges detectable on radiography be used for surgery; they should be counted once at the start and twice at the end of surgery. Instruments should be counted in all cases involving open cavities. If the count is incorrect, radiography or a manual search should be performed. Some reported incidents appear to have resulted from failure to adhere to these standards (229). In most cases, however, foreign bodies go undetected, despite proper procedures. Even if counts are done properly, one-third of the time they are not documented because of the emergency nature of an operation or an unexpected change in procedure (228).

It has been proposed that hospitals should monitor compliance with the existing standard of counting sponges and counting instruments in every operation involving an open cavity. Radiographic screening of high-risk patients before they leave the operating room should be considered even when the counts are documented as correct. Routine intraoperative radiographic screening in selected, high-risk categories of procedures has been proposed for detecting retained foreign bodies (228).

## Insufficient communication

Surgery at the wrong site or with the wrong procedure, retained sponges, unchecked blood transfusions, mismatched organ transplants and overlooked allergies are all potentially catastrophic events, which, in certain circumstances, can be prevented by improved communication and safer hospital systems. In the analysis of causes submitted to the Joint Commission on Accreditation of Healthcare Organizations in the United States, communication was identified as the commonest cause of sentinel events (222). Creating a culture of safety is therefore a high priority for surgeons and hospitals. Several interventions to improve patient safety in surgery have been introduced, including additional checks to confirm procedures and new policies for operating rooms. In addition, many hospitals are investing in safety training programmes for their staff (224).

System factors have been identified that change the expected course of care and compromise patient safety. Some relate to communication and information flow, particularly in the context of handover of patients, competing tasks and a high workload. Like other complex systems, operating rooms rely on information: performance and safety depend on how information is forwarded between phases, physical locations and providers.

Team instability—for example, different scrub nurses—can result in inferior outcomes in terms of care, indicating the importance of human resource management to ensure good teamwork, where members know and understand each other well. Organizational and team policies for communication are also important (148). A policy that disallows distraction in the operating room appears to be beneficial, probably because of the inevitable effects on communication.

Another systemic cause, which is often ignored by researchers, is resources. If there is more than minimal staffing—known in



highly reliable organizations as ‘redundancy’—people have time to communicate properly. Communication is not simply transmitting but also receiving, including confirmation that the transmission has been understood in the way intended. Team meetings can engender rapport and improve communication (230). Personality may also be a factor: leaders should foster active communication among team members even when it results in constructive criticism of the leader (224). The encouragement of open communication and constructive criticism has been used in aviation safety and could be applied to surgical teams as well (159). Miscommunication can also arise from the power relationships that exist in health care as a result of the traditionally different status of different professional groups. More than any other medical specialty area, the culture in surgery is one in which the hierarchy is still close to the traditional military model (157).

## Anaesthesia errors

Deficiencies in a number of activities before surgery can endanger patients, particularly when health personnel are inadequately trained and in emergency situations. New techniques used by anaesthesiologists in developed and, increasingly, developing countries have led to dramatic reductions in untoward events from anaesthesia. These include preoperative anaesthetic check-up, appropriate preparation before a surgical procedure, choice of appropriate anaesthetic technique for a coexisting medical condition, use of sterile techniques and checking of anaesthesia machines before use. Intra-operative complications, such as hypothermia, burns, oversedation without pain relief and undetected respiratory and cardiac arrest, still occur however. Inadequate monitoring and management of hypotension and bleeding also pose risks to patients. Inadequate positioning can result in decubitus ulcers. Additional technical errors include incorrect intubation, overdose or wrong administration of anaesthetic drugs and gases and malfunctioning anaesthetic monitors

and machines. Many of these potential problems can be avoided or reduced with appropriate training of health personnel. Clinical awareness and vigilance (visual, verbal and skin contact with the patient) are often replaced by a reliance on high-technology monitoring devices.

Major improvements in quality and safety in anaesthesia can be attributed to technological improvements and enhancements in anaesthesia equipment and drugs. An emphasis on education, training, communication and teamwork also has a positive impact. All these improvements require significant commitment of resources. In large parts of developing countries, even the basic equipment is lacking, and millions of people do not have access to the resources that should be considered a basic human right, including safe anaesthesia and pain relief during surgery and childbirth. A recent report pointed out that the lack of even basic theatre facilities, such as reliable electricity, running water and oxygen, and shortages of drugs, equipment and personnel exemplify the extreme challenges of running a safe basic health-care system under these conditions (231). The increasing demand for anaesthesia in remote locations other than conventional operating rooms indicates the need for research on morbidity and mortality at such sites (232).

## Gaps in knowledge

In order to assess the scope of surgical errors, comprehensive data must be collected and analysed. This requires a change in reporting, one approach being a non-punitive environment, possibly complemented by incentives to report. Except in cases of blatant disregard of established standards of care or malicious intent, departmental responsibility could be assumed, rather than blaming individuals. Besides addressing cultural impediments to detailed reporting, data collection could be enhanced by applying modern information technology, resulting in use of Internet-based reporting portals at the level of the national

health system and could include regional, risk-adjusted benchmarking. A reduction in the technical and cultural barriers to reporting is a prerequisite for creating evidence-based guidelines.

Validated questionnaires to elucidate the epidemiology of surgical errors would make it possible to define safety indicators. On that basis, the reporting of case series and anecdotal evidence in the literature could be replaced by studies with scientifically sound research designs.

Health services might evaluate the use of safety practices used in industry, the military and aviation, not merely by transferring the measures but by analysing the differences from health systems and the processes of health-care delivery. The reasons for geographical differences in adherence to evidence-based guidelines and barriers to their implementation should also be evaluated.

The issues facing developing countries in combating the causes of surgical errors should also be analysed. Given budgetary constraints and differing priorities in resource allocation, the focus should not be on complex system redesign but on evaluation and implementation of basic measures of hygiene and maintenance of instruments. Sources of finance to provide education and training for nurses and surgeons on safe practices should be assessed, with a focus on long-term sustainability for maintaining changes in care delivery. Sensitivity to local practices, the culture of health-care delivery, hierarchical structures and channels of communication is essential. The cooperation of local champions could facilitate the analysis and implementation of measures. Once basic measures of hygiene are in place, further measures proven to be successful in the developed world could be evaluated. A tiered approach of applying methods to local settings would allow for flexible adaptation to regional preferences and constraints.

## Conclusion

Many complications and errors in surgery and anaesthesia can be prevented. A study in the United States in 1999 showed that 54% of surgical errors were preventable (233). The Harvard Medical Practice Study showed that adverse events in the operating room accounted for 48% of all adverse events, occurred in about 2% of all hospitalized patients and were preventable 74% of the time (26). The most effective strategy might be to plan interventions for the operations most likely to result in adverse events: the study of surgical adverse events in the United States in 1992 showed that 15 types of operations accounted for 58% of surgical adverse events and for 37% of all hospital adverse events (233). Guidelines for the prevention of surgical-site infections such as those established by the United States Centers for Disease Control and Prevention, might be useful (177). Modifiable risk factors for surgical and anaesthesia errors should be identified in order to design targeted interventions to improve patient safety.

Reducing surgical errors and improving patient safety are essential for improving health care and should be included in research and implementation in this area. Ideally, safe standards of care with a focus on better outcomes should be founded on the principles of evidence-based medicine. Implementation of and adherence to safety guidelines should be monitored, possibly with financial incentives.

A systems approach to reducing surgical errors must take into account the highly complex, interdisciplinary, high-pressure environment of surgery (28). One aim would be to modify the professional culture prevalent in surgery, addressing the leadership style of surgeons (234). A positive, non-punitive reporting culture could build the basis for assessing the incidence and scope of surgical errors and allow the design of further measures to decrease the rate. A systems approach should also emphasize team training and improved communication

(235). Methods used in industry, aviation and the military could be applied to surgery (161), including human factor engineering (236–238), crew resource management (239) and simulation training (240, 241). Experience in improving reliability (242–244) could be applied as well.

Integrating patient safety and error reduction into the curriculum of medical education, postgraduate medical education, board certification, re-certification and continuing medical education could raise awareness about these issues and perhaps modify the practice of clinical care.

## 4 Health care-associated infections

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### Scope of the problem

Health care-associated infections are infections that occur in the health-care setting, often due to the care itself. The WHO definition of health care-associated infection (245) is ‘an infection occurring in a patient in a hospital or other health care facility in whom the infection was not present or incubating at the time of admission. This includes infections acquired in the hospital but appearing after discharge, and also occupational infections among staff of the facility (246)’.

The problem is far-reaching: worldwide, at least one in four patients in intensive care will acquire an infection during a stay in hospital, and this estimate may be doubled in developing countries. This unacceptable type of adverse event occurs in all countries, regardless of development

status, although the rate is probably much higher in developing countries, where health systems deliver care to populations with poorer health status and lack human and technical resources (29). The proportion of patients with health care-associated infections in developing countries has been estimated to be 25% (30) to 40% or more (29), and the problem appears to be worsening, as the past two decades have seen the greatest increase in hospitals in those countries. Surgical-site infections are leading causes of illness and death in certain hospitals in sub-Saharan Africa. In the overcrowded, understaffed health services common in resource-poor settings, incorrect use of medical techniques is common, increasing the risk for infection associated with the process of care. The contrast between developed and developing countries is often stark: the rate of health care-associated infections among neonates in developed countries is 12-fold lower than that in developing countries, and, in this age category, the rate of infections associated with vascular devices is 3–20 times higher in developing than in developed countries (29).

Health care-associated infections also occur in modern, technologically advanced health systems in developed countries, even if the burden of disease is generally lower. It has been estimated that 5–10% of patients admitted to hospitals in developed countries acquire an infection (30). National surveys of health care-associated infection rates in hospitals in high- and middle-income countries in Europe over the past 20 years showed overall rates of 3.5–14.8% (31).

Often, infections are attributable to medical devices. In a study in Turkey, the mean overall rate of infections associated with devices was 29.1 infections per 100 patients, and the mean infection rate was 34.2 per 1000 patient-days. The rate of ventilator-associated pneumonia was 20.8 infections per 1000 ventilator-days, that of catheter-associated urinary-tract infection was 13.6 infections per 1000 urinary catheter-days, and that of catheter-associated

bloodstream infection was 9.7 infections per 1000 central line-days (247). More than 40% of health care-associated infections in adults are in the urinary tract and at surgical sites (248), suggesting areas in which targeted interventions might be effective. A study of Mexican public hospitals showed an overall health care-associated infection rate of 24.4%, or 39.0 per 1000 patient-days, the commonest being catheter-associated bloodstream infection, followed by ventilator-associated pneumonia and catheter-associated urinary-tract infection (249). A study in Colombia showed an overall health care-associated infection rate of 12.2%, or 18.2 infections per 1000 patient-days, central venous catheter-related bloodstream infection again being the commonest, followed by ventilator-associated pneumonia and catheter-associated urinary-tract infection (250).

## Impact of the problem

The costs associated with health care-associated infections vary from country to country but substantially affect health budgets everywhere. Such infections cost US\$ 7–8.2 billion every year in the United States alone (30). Not only do they generate additional costs, but they also substantially increase morbidity and mortality (31). Health care-associated infections prolong hospital stays by an average of 10–15 days per infection. They also often form the basis for litigation against physicians, nurses and hospitals (251). In Europe, 2–3 million people are estimated to be affected by health care-associated infections annually, with a corresponding economic burden of € 800 million, and about 5000 deaths are estimated to be attributable to these infections annually in France and the United Kingdom (31).

In 1995, the hospital sector in Turkey spent an additional US\$ 48 million for medical management of health care-associated infections (32). In Mexico, the cost of such infections represents 70% of the entire budget

of the Ministry of Health, and they are the third commonest cause of death (29), with an estimated 450 000 cases and 32 deaths per 100 000 inhabitants each year (252). In Trinidad and Tobago, the annual cost of health care-associated infections in a rural Government hospital providing primary and tertiary care in 1992–98 was estimated to be US\$ 697 000 (253), representing 5% of the annual health budget (29). In Thailand, some hospitals spend 10% of their annual budget on the management of health care-associated infections (29).

## Possible interventions

Health care-associated infections can be prevented by several evidence-based interventions. Most interventions have, however, been studied only in developed countries, and their applicability to developing countries and those with economies in transition is unknown. Infection control programmes can be cost-effective, at least in developed countries (254, 255), although more sophisticated measures might be required for specific sites of infection, particular devices or specific pathogens. Nevertheless, the most effective control measures consist of simple, well-known precautions, such as hand hygiene (33, 34). The essential elements of an infection control programme include education of health-care workers, a well-organized surveillance system, appropriate legislation and consistent implementation of basic control measures.

As demonstrated in a study of the efficacy of health care-associated infection control in the United States (254), surveillance is an essential element of hospital control programmes, especially in developed countries, so that the problem can be quantified and identified and the basis for tackling it established. It is unknown if surveillance is equally necessary or cost-effective in developing countries. Efforts to improve surveillance have been made in a number of countries, including creation of a standardized surveillance system for health care-associated

infections in surgery patients in Spain, the National Nosocomial Infection Surveillance Service in the United Kingdom and the National Nosocomial Infection Surveillance System in the United States. Also in the United States, the Joint Commission on Accreditation of Healthcare Organizations has required surveillance and reporting of health care-associated infections for hospital accreditation for over two decades. In Germany, it was found that focusing on device-associated infections, as opposed to hospital-wide surveillance, allowed for cost-effective surveillance of health care-associated infections (256). Another study showed that decision support can help reduce health care-associated infection rates (175).

Contact transmission is the route most frequently used by infectious pathogens. As health-care workers can facilitate the spread of health care-associated microorganisms through contaminated hands, hand hygiene is the single most effective infection control measure. It is the core of conventional 'standard precautions', including appropriate handling and disposal of equipment. The application of such measures should extend to the care of every hospitalized patient, regardless of their diagnosis, risk factors and presumed infection status, to reduce the risk of both the patient and the staff for acquiring an infection. Standard precautions provide for a clean environment and promote patient safety at a basic level. Transmission precautions for preventing contact and airborne and droplet spread are used for patients who are known or suspected to be infected or colonized with highly infectious pathogens, according to their mode of transmission (257). As such precautions are generally expensive and require special facilities and equipment, they are often not achievable in most developing countries.

The four commonest health care-associated infections in developed countries are associated with an invasive procedure or device (258). Preventive measures for urinary-tract infections, surgical-site infections, pneumonia and

bloodstream infections have been validated in clinical trials and are available. International guidelines for best practice of these procedures are being drawn up to minimize the risk for a preventable health care-associated infection. Additional effort is needed to translate the recommendations into effective implementation strategies, especially in settings with limited resources. It is important that standard, transmission-based, site-specific or device-related precautions be integrated into routine patient care (257) and solutions be sought to overcome behavioural determinants of poor compliance by health-care workers. Promising perspectives include a campaign organized by the Institute for Healthcare Improvement in the United States, which is based on several interdependent interventions to prevent device-associated infections (<http://www.ihl.org/IHI/Programs/Campaign/Campaign.htm?TabId=2>). At a global level, the World Alliance for Patient Safety has launched the 'global patient safety challenge', called 'Clean care is safer care', to address health-care associated infections. The aim is to strengthen integrated infection control in relation to blood and blood products, injections, clinical procedures and water, sanitation and waste management, with the promotion of hand hygiene in health care as the cornerstone. The new evidence-based WHO *Guidelines on hand hygiene in health care (advanced draft)* (available at: [http://www.who.int/patientsafety/information\\_centre/ghhad\\_download/en/index.html](http://www.who.int/patientsafety/information_centre/ghhad_download/en/index.html)) have been released, in which a multimodal implementation strategy is proposed to translate the evidence-based recommendations into practice. Improving hand hygiene in health care can be expected to save millions of lives by reducing health care-associated infections.

## Gaps in knowledge

The challenges for professionals in infection control are many and varied, and a number of areas require study. As in many fields, the gaps in knowledge differ according to the level of

development and the resources available, and so the research objectives and needs of developed, developing countries and those with economies in transition are not the same.

Surveillance systems and laboratory standards for quantifying the burden of health care-associated infections in developing countries and those with economies in transition require improvement. In particular, standardized, feasible methods of study and case definitions applicable in these settings must be identified and validated. Research is also needed on the specific risk factors for health care-associated infections under conditions of poor hygiene, understaffing and inadequate equipment.

Although most precautions against infection are relatively simple, they are not applied globally. Promoting clean care in developing countries is essential, and identifying effective strategies for minimum infection control in all countries should be a priority on the research agenda. Health-care facilities must strive to implement standard precautions satisfactorily in daily practice, to foster advocacy and adequate resource allocation and to be prepared for unexpected epidemics (257). In particular, given the financial constraints and other major health priorities in developing countries and those with economies in transition, research on the cost-effectiveness of interventions is important in order to make infection control a reality.

In countries where basic infection control systems are in place and function well, advanced measures can be introduced. Tackling antimicrobial resistance and the spread of multiresistant microorganisms will remain a priority for all health-care facilities (35). Those with policies for prudent use of antibiotics and good infection control practices will be in a better position to optimize patient safety in the face of the emergence of new pathogens. Computerization of patient records can enhance the efficiency of surveillance, and use of sophisticated software to identify patients at risk for health care-associated infection will

result in earlier intervention. Studies are needed to determine whether this is a feasible, cost-effective strategy for resource-poor countries. To improve device safety, new materials must be developed and tested. Furthermore, multicentre clinical trials should be conducted to provide the basis for revision of infection control guidelines (33).

A further challenge for professionals in infection control is to prevent infection during transgenic therapy and in patients with massive or complete immunosuppression induced to avoid organ transplant rejection. Modification of the behaviour of health-care workers is another challenge, which will require an innovative approach to alter the complex, interdependent, multidimensional variables involved (33). Composite interventions are considered the most effective approach for substantial changes in practice and structure for infection control; however, the design of such investigations does not allow determination of the effectiveness of individual interventions. Therefore, further research on this topic should be conducted in randomized clinical trials.

## 5 Unsafe injection practices

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Injections are among the commonest health-care procedures. In 2000, WHO estimated that some 16 billion injections are administered each year in developing countries and those with economies in transition, about 95% for curative care. Immunization accounts for about 3% of all injections, and the remainder for other indications, including injection of blood and blood products and contraceptives.

In certain regions of the world, use of injections



has completely overtaken the need, reaching proportions no longer based on rational medical practice. In some situations, as many as nine of ten patients presenting to a primary health-care provider receive an injection, over 70% of which deliver treatments that are unnecessary or could be given in an oral formulation (36, 259). Injection safety assessments by WHO in 80 countries showed that injections are overused in the curative sector, up to 70% of the injections prescribed in some countries being considered unnecessary in comparison with treatment guidelines (260). Patients tend to prefer injections because they believe them to be stronger and faster. They also believe that doctors regard injections as the best treatment. In turn, doctors overprescribe injections because they believe that they best satisfy patients, even though patients are often open to alternatives. In addition, prescription of an injection allows the doctor to charge a higher fee for service. Better communication between patients and providers could clarify such misunderstandings and help to reduce injection overuse.

Most injections, if given with sterile techniques by competent practitioners, are relatively safe. When safety control practices are not respected, however, severe complications can result, putting human lives at risk. Reuse of syringes and use of needles without sterilization expose millions of people to infection. Assessments made in numerous countries have revealed that syringes and needles are often just rinsed in a pot of tepid water between injections. Worldwide, 39.6% of injections are given with syringes and needles reused without sterilization, and in some countries this proportion is as high as 70% (36).

Other unsafe practices, such as poor collection and disposal of dirty injection equipment, expose health-care workers and the community to the risk for needle-stick injuries. In some countries, unsafe disposal can lead to re-sale of used equipment on the black market. The proportion of non-industrialized countries that still reported open burning of syringes (considered

unacceptable by WHO) was 50% in 2004 (37).

## **Burden of disease associated with unsafe injection practices**

Each year, unsafe injections cause an estimated 1.3 million early deaths, a loss of 26 million years of life and an annual burden of US\$ 535 million in direct medical costs (38). Unsafe injection practices are a powerful means for transmission of bloodborne pathogens, including hepatitis B virus, hepatitis C virus and HIV. As infection with these viruses initially does not result in symptoms, the epidemic is a silent one. Its consequences are, however, being increasingly recognized.

Hepatitis B virus is highly infectious and causes the largest number of infections. In developing countries and those with economies in transition, 33% of the 21.7 million new cases of hepatitis B infection occurring each year are due to unsafe injections. Unsafe injections are the commonest cause of hepatitis C virus infection in developing countries and those with economies in transition, causing 2 million new infections each year and accounting for 42% of new cases. Globally, nearly 2% of all new HIV infections are caused by unsafe injections, a total of 260 000 people being infected annually. In South Asia, up to 9% of new cases may be caused in this way (36). Hepatitis B virus, hepatitis C virus and HIV cause chronic infections that lead to disease, disability and death a number of years after the unsafe injection. Persons infected with hepatitis B virus in childhood typically present with chronic liver disease by the age of 30 years, at the prime of life, with dramatic effects on national economies.

## **Potential solutions**

Unsafe injection practices are often viewed as a chronic problem with no easy solution. Safe and appropriate use of injections can, however, be achieved by adopting a three-part strategy.

- (1) *Changing the behaviour of health-care workers and patients:* 20 years into the HIV pandemic, knowledge about HIV among patients and health-care workers in some countries has led to consumer demand for safe injection equipment, which has irreversibly improved injection practice. With better knowledge about hepatitis C and hepatitis B viruses, similar consumer demand should emerge. HIV prevention programmes could be expanded to include injection safety.
- (2) *Ensuring the availability of equipment and supplies:* Simply increasing the availability of safe injection equipment can stimulate demand and improve practices. As the cost of safe, disposable syringes is lower (less than US\$ 0.05 per unit) than the fee paid for receiving an injection (US\$ 0.50 on average), patients are usually willing to pay a little extra for safety once they understand the risk.
- (3) *Managing waste safely and appropriately:* As waste disposal is frequently not an integral part of health planning, unsafe waste management is common. When it is appropriately planned, significant results ensue. National strategies require a national policy for managing health-care waste, a comprehensive system for implementation, improved awareness and training of health workers at all levels and selection of appropriate options for local solutions.

## Gaps in research

Since injection safety first became a priority in 1998, many activities have been implemented, and tools, guidelines and training materials have been developed. Now, it is time to evaluate the impact of these strategies and activities on the burden of disease transmitted through unsafe injections as well as their cost-effectiveness in terms of infections averted. Another research topic should be how to improve the access of developing countries to safe injection devices.

Research is also needed to identify the best methods for changing the behaviour of health-care workers, in order to change unsafe practices, such as two-hand recapping of used injection equipment and the proper disposal of sharps.

## 6 Unsafe blood products

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### Scope of the problem

Transfusion of blood and blood products is an essential support in health-care systems, saving millions of lives each year. In countries with developed health-care systems, blood and blood products are used mainly in complex medical and surgical procedures, trauma care and the treatment of patients with haematological disorders and leukaemia. The pattern of blood usage is different in countries where diagnostic facilities and treatment options are more limited, a greater proportion of transfusions being prescribed for the treatment of complications during pregnancy and childbirth, severe childhood anaemia and trauma.

In developing countries, maternal conditions are the third leading cause of death among women aged 15–44 years. Each year, more than 500 000 women die needlessly during pregnancy or childbirth, 99% of them in the developing world. Severe bleeding can kill even a healthy woman within 2 h if she is unattended; it accounts for up to 44% of maternal deaths in Africa, where the risk for maternal death is 1 in 16, which should be compared with 1 in 65 in Asia and 1 in 3700 in North America. Up to one-fourth of all maternal deaths could be saved by access to safe blood transfusion. Malaria, a major cause of life-threatening anaemia, is one of the main



causes of mortality among children aged 0–4, causing 8% of all deaths in that age group (261, 262). Globally, road traffic injuries are the second leading cause of death for males and females aged 5–29 years (263). Blood transfusions are frequently central to the management of all these conditions.

The safety of blood transfusion is therefore important for avoiding morbidity or mortality. Blood safety is an integral part of any strategy to reduce the disease burden and loss of life due to HIV and other bloodborne pathogens such as hepatitis B and C viruses. Systems to ensure the availability and safety of blood should be integrated into the overall health-care system.

Crucial safety issues in blood transfusion are poor access to blood and blood products when required; unsafe blood and blood products, carrying the risk for transfusion-transmissible infections, such as with HIV and hepatitis B and C viruses; serious or fatal transfusion reactions; poor laboratory procedures for testing donated blood for markers of infection and blood group and for compatibility testing between the donor and the recipient; gross misuse of blood and blood products; and unsafe transfusion practices at the patient's bedside.

### **Poor access to blood and blood products**

While the need for blood is universal, there is a major imbalance between developing and developed nations in access to blood and blood products. Every second, somewhere in the world, someone needs a blood transfusion, but millions of patients do not have access to safe blood. About 81 million units of whole blood were donated annually during 2001–2002, but less than 40% of this global blood supply was collected in developing countries, which are home to more than 80% of the world's population (264) and where people still die due to a lack of blood and blood products. In sub-Saharan Africa, fewer than 3 million units of blood are collected each year for a population of more than 700

million. The average number of blood donations per 1000 population is 12 times higher in high-income than in low-income countries (264). The main reasons for poor access to blood are fragmented, uncoordinated blood transfusion services and lack of integration of transfusion services into the health-care system. Low blood donation rates and high discard rates, due either to positive infection markers in blood collected from unsafe donors or to expiry of blood because of poor blood stock management, contribute to the lack of universal access to safe blood and blood products.

### **Unsafe blood and blood products**

Transfusion of blood infected with HIV probably exposes the recipient to more infectious material than any other route (265). Transfusion of unsafe blood and blood products therefore poses a much higher risk for transmission of HIV (95–100%) than other common routes, the risk being 11–32% for perinatal HIV transmission and 0.1–10% for sexual contact (266). It has been estimated that 5–15% of HIV infections in developing countries are due to unsafe blood transfusion (39, 40). These new HIV infections, in turn, contribute to the widening pool of infection in the general population due to sexual and mother-to-child transmission. An epidemiological review suggested that, although there is considerable regional variation, as much as 25% of HIV-infected women and children in some areas of Africa acquired their infection from blood transfusion (246). Unsafe blood also poses a high risk for transmission of other bloodborne infections, including the causative agents of hepatitis B, hepatitis C, syphilis, malaria, Chagas disease and West Nile fever.

The safety of blood and blood products varies widely among countries, and developing countries continue to face the greatest risks (39). Blood transfusion services in many developing countries rely predominantly on donations from family members or paid donors, who have a higher incidence of transfusion-transmissible

infections than voluntary donors, and there are few organized, community-based blood donor programmes. Only 39 countries in the world have established, sustainable blood donor programmes based entirely on voluntary blood donation (267).

Although it is recommended that all donated blood be screened for at least four important transfusion-transmissible infections—HIV, hepatitis B virus, hepatitis C virus and the causative agent of syphilis—most countries do not have reliable systems for screening donated blood due to shortages of trained staff, unreliable supplies of test kits and lack of basic quality systems. Of the 2.7 million units of blood collected in 40 sub-Saharan countries in 2004, 88.5% were not tested for HIV in a quality-assured manner (268). In 2001–2002, the WHO Global Database on Blood Safety showed that 97 (59%) of the 164 countries that responded had no established quality system and at least 21.6% of donations were not screened for HIV in a quality-assured manner; and 39 countries (22%) reported that blood was issued without testing when reagents or test kits were unavailable (264). Serious blood shortages also contribute to increased risks for transmission of HIV and hepatitis viruses because blood transfusion services have to rely on unsafe donors and are under increased pressure to issue blood without testing.

The safety of blood transfusion is particularly threatened in emergency situations, due to weakening or collapse of health systems as a result of complex emergencies such as armed conflicts and disasters, and among refugee populations. In these circumstances, an adequate number of safe blood donors and quality-assured testing of all donated blood are especially difficult to maintain.

### **Unsafe blood transfusion practices**

During the past three decades, most global efforts have been directed at enhancing the

quality and safety of blood and blood products, and the transfusion process has received less attention. Two critical factors in ensuring rational, safe transfusion are the clinical decision for transfusion and the process of administration of blood. Poor practices and procedures during these steps lead to gross misuse of blood, unnecessary transfusions and unsafe transfusion practices at the patient's bedside.

Up to 50% of transfusions have been shown to be unnecessary (269–271). Most developing countries have no national policies or guidelines on clinical use of blood, and persons who prescribe blood and blood transfusion services staff often have little understanding of the appropriate clinical use of blood. Unnecessary transfusions are therefore attributable to lack of training, poor implementation of guidelines and the absence of functioning hospital transfusion committees.

Throughout the world, transfusion of blood into the wrong recipient remains the single most common, serious hazard of transfusion and the most likely cause of death due to transfusion, and this error occurs at a much higher rate than transfusion-transmitted hepatitis C virus and HIV combined (272–274). Serious errors in the administration of blood are due mainly to inadequate procedures, leading to misidentification of patients or samples. The rates of incorrectly labelled and collected samples are high, and the final bedside checks to ensure that a blood unit is intended for the recipient are often performed either incompletely or incorrectly (275).

Best practice has shown that, even in countries with a high prevalence of infections such as HIV, a well-organized programme of voluntary blood donation and effective procedures for assessing the suitability of donors can lower the prevalence of infections among blood donors. South Africa and Zimbabwe are currently able to maintain an HIV infection rate in blood donors below 0.5%, even

though the HIV rate in the general population exceeds 20% (264). Creation of national blood programmes and intense media campaigns increased the rate of voluntary donations in Bolivia from 10% in 2002 to 50% in 2005 and in China from 45% in 2002 to 91.3% in 2004 (252).

## Gaps in research

The gaps in knowledge about issues in unsafe blood and blood products, unsafe transfusion practices, patient misidentification and lack of recognition of adverse events include lack of information about the epidemiology, impact and potential solutions. The extent of these gaps depends on the level of development of the health-care system. Important gaps include lack of information about the burden of infections averted by specific blood safety strategies, about factors in the lifestyle and behaviour of various populations of blood donors associated with high risks for infection, and about the possible residual risk for transmission of infections due to transfusion of unsafe blood products even when screening programmes are in effect. Retrospective studies are needed to determine the effectiveness of existing systems for blood safety. The risk for transmission of viral infections due to unsafe blood can be assessed by following-up blood donors and recipients; however, lack of an effective mechanism for follow-up in most developing countries and lack of donor database obviate a proper evaluation of seroconversion rates and assessment of the real risk for transmission of infections from unsafe blood. Knowledge about the extent of unnecessary transfusions is still in its infancy. The complex events at the patient's bedside that can lead to misidentification of patients at the time of sample collection or transfusion have still not been identified. We also need better understanding of the factors that lead to lack of recognition and inadequate management of adverse events associated with blood, leading to serious or fatal reactions.

# 7 Safety of pregnant women and newborns

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## Scope of the problem

An estimated 7.6 million infants die in the perinatal period each year, and more than 500 000 women die during pregnancy or childbirth, of whom 99% are in developing countries (41–43). While maternal and child health has remained a chief concern for policy-makers worldwide, little is known about the role of poor-quality, unsafe care. High maternal and infant mortality rates can be attributed mainly to lack of access to medical facilities and inadequate care. Access to care should be addressed by capacity-building, improved transport and increased numbers of health facilities and health-care providers. This section focuses primarily on the impact of poor-quality, unsafe care; however, it is important to understand that lack of access to care and poor care when accessible are linked: when local health-care providers give poor care, the population is less likely to seek that care.

Lack of access to basic prenatal care, safe pregnancy procedures and skilled birth attendants underlie the huge disparity in maternal and infant mortality between developed and developing countries. Approximately 1 in 48 women in developing countries and only 1 in 1800 in developed countries dies of complications of pregnancy, delivery, puerperium or abortion (276). The main causes of maternal death in the developing world are unsafe abortions, haemorrhage, hypertensive disorders of pregnancy, sepsis, obstructed and prolonged

labour and infections (277). The consequences of maternal death permeate the family, deeply influencing children, as the likelihood of death among children under the age of 5 is as high as 50% in some developing countries (278).

Most maternal deaths occur during or immediately after labour and delivery; for instance, in rural Bangladesh 40% of deaths occur during labour or within 48 h of delivery, primarily due to eclampsia and postpartum haemorrhage, and 30% between 3 and 42 days after delivery, often due to sepsis and associated diseases (279). The Egyptian Ministry of Health documented similar trends, indicating that 39% of deaths took place during delivery or within the first 24 h, and 36% occurred within 42 days postpartum; only 25% took place during pregnancy (280).

Most neonatal deaths occur at home in low- and middle-income countries, against a backdrop of poverty, suboptimal access to care and weak health systems. Preterm delivery, birth asphyxia and infection account for most newborn mortality (42). In low-resource countries, lack of access to reproductive health services and antenatal care and poor-quality maternity care when available have been identified as the main reasons for under-use of services (44). Reports from several countries suggest increasing access to obstetric care; however, maternal and infant mortality rates continue to be problems, with wide disparities among countries.

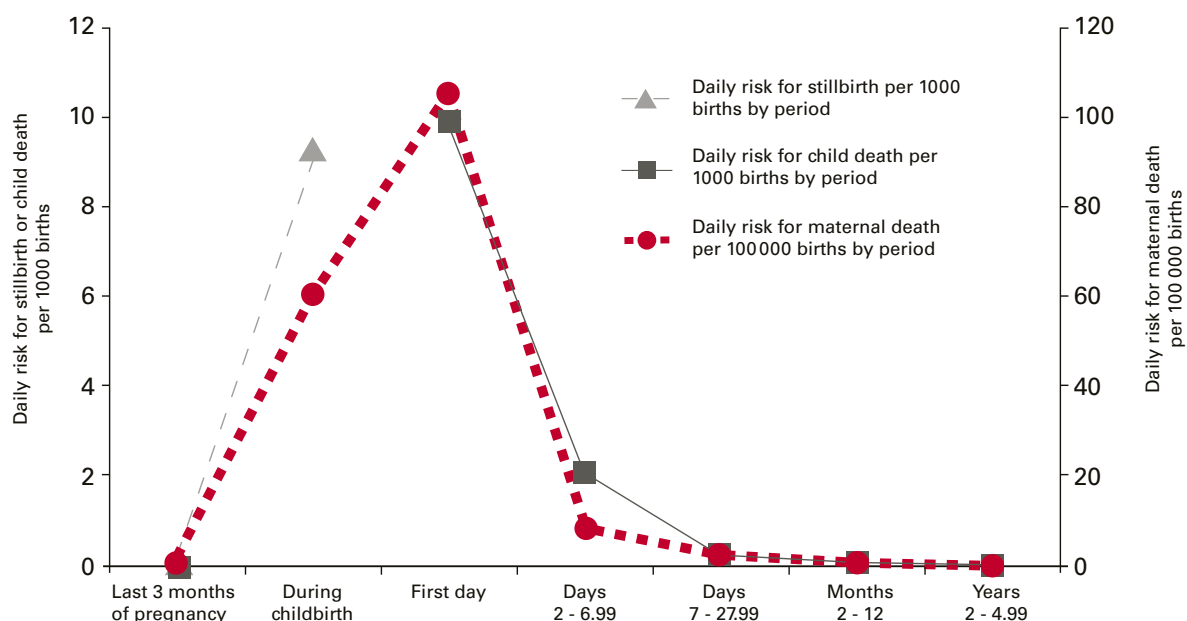
Few women receive care of an adequate standard (44). Factors that contribute to poor patient management include delays and errors in diagnosis, treatment and referral, personnel and equipment shortages and health facilities that cannot manage and properly treat even the small proportion of women who reach health facilities before delivery (281). In the developing world, these easily preventable shortcomings affect patient outcomes adversely. A study in Viet Nam of 22 health-care institutions showed that 96 of 128 (75%) maternal deaths occurring during 1984–1985 resulted from delays or errors in diagnosis (281). Additional studies show that

lack of medical infrastructure adversely affects patient outcomes: 70% of the 152 maternal deaths that occurred in three hospitals in Senegal in 1986–1987 were linked to lack of equipment and facilities (281).

These alarmingly high mortality rates directly affect not only the persons who receive care from poor health systems but also the rest of the population, by diminishing their confidence that they will receive safe medical care. Patients have little incentive to seek medical attention if they believe that it will be ineffective (45). Improving access to high-quality health care is thus a key contribution to reducing maternal mortality rates. Access alone may not be adequate: ensuring high-quality, safe care will also have an important impact on mortality rates and indirectly increase consumer confidence in the health-care system. Validation of the health-care system through positive patient outcomes should increase motivation to access medical treatment.

Referral services are also often of poor quality, exacerbating the problems of limited access and poor quality of health care (44). This is particularly striking with regard to newborn care, as few centres have adequately trained staff or resources for neonatal emergencies, and 75% of all newborn deaths take place within the first week of life. Furthermore, newborn care in hospital settings does not guarantee decreased rates of perinatal mortality. Over 90% of all deliveries in Brazil take place in a hospital, yet the estimated infant mortality rate in 1995–1997—37.5 per 100 000 births—was six times higher than that in countries with the lowest rates (282). Lack of good perinatal care directly affects newborn mortality rates, as seen from a study at the Mexican National Institute of Perinatology in 1988–1991, which showed that the perinatal mortality rate of 24.8 per 1000 births could be reduced by 35% if all avoidable perinatal deaths were prevented (283). Given that referral systems and high-quality care are often inaccessible because of inadequate transport, many newborns remain at high risk.

**Figure 1.** Daily risks for death of children, women (maternal deaths) and last-trimester fetuses from late pregnancy to 5 years after birth, showing the convergence of risk during childbirth and the early postnatal period



Overuse and misuse of clinical interventions can also harm mothers and infants. Use of caesarean section is a typical example. While in low-resource countries lack of access to maternal health services and underuse of caesarean section underlie the high rates of maternal and newborn mortality, in many more developed countries caesarean section is overused. Strategies are being sought to reduce the use, because of concern that higher rates do not confer additional health gains and burden the health services. The results of two recently published studies suggest a strong inverse association between caesarean section rates and maternal, infant and neonatal mortality in countries with high mortality levels (284, 285). In addition, there is some suggestion of a direct association at lower levels of mortality (285).

## Severity of the problem

Although there are still lapses in the safety of pregnancy procedures in some developed countries, in developing countries there are

inadequate safety protocols, limited access to services and poor-quality care. The current lifetime risk of dying from complications of pregnancy or childbirth is 1 in 60 worldwide, 1 in 1800 in more developed countries and 1 in 48 in developing countries. The rates vary by region, with the highest maternal mortality rates in Africa, where 1 in 16 women will die, the rates being 1 in 65 in Asia and 1 in 3700 in North America (276). Most of these deaths could be averted with timely medical attention and adherence to basic patient safety measures, such as antibiotics, emergency obstetric care and safe transfusions (276).

The causes of maternal mortality can be divided into direct causes during pregnancy and in the peripartum period and indirect causes that may be present before but become more severe during pregnancy, including diabetes, malaria and hepatitis (286). About 80% of all maternal deaths are due to direct causes (286), and five direct complications account for over 70% of maternal deaths: haemorrhage (25%), infection (15%), unsafe abortion (13%), eclampsia (12%)

and obstructed labour (8%). While haemorrhage is a major cause of maternal death in developing countries, most maternal deaths in developed countries are due to other direct causes, mainly complications of anaesthesia and caesarean section (287). Nevertheless, the real source of morbidity and mortality of pregnant women remains unavailable, inaccessible, unaffordable or poor-quality care. Each year, an estimated 1 million children lose their mothers, resulting not only in isolation but also in diminished life chances, as these children are 10 times more likely to die within 2 years of their mothers' death (288).

Of the 20 countries with high neonatal mortality rates, 16 (80%) are in sub-Saharan Africa; however, because the Asian population is increasing, with a large number of births, Asia has the highest absolute toll of infant mortality. Over one-fourth of the world's neonatal deaths (1.09 million) occur in India alone. Figure 1 shows the estimated daily risks for stillbirth and maternal and under-5 deaths during various periods. The risk for death on the first day of life is very high, but declines over succeeding days and weeks. The daily risk for maternal death also peaks during and immediately after childbirth, and there is a marked increase in the risk for stillbirth at the time of birth.

Disability from pregnancy is also a serious concern, as 42% of the 129 million women who give birth annually experience some complications during pregnancy. About 15% of women worldwide develop potentially life-threatening complications, which include chronic pain, impaired mobility, obstetric fistula, prolapse, severe anaemia, pelvic inflammatory disease, reproductive-tract infections and infertility (289). Furthermore, in developing countries, pregnancy and complications from childbirth account for 18% of disease among females (289). WHO estimates that about 12.5 million women have associated illnesses that are aggravated by pregnancy, including anaemia, malaria, cardiac disease, hepatitis, tuberculosis and diabetes, which can indirectly cause death or disability for both the mother and her newborn (290).

Social determinants of health and fundamental patient safety factors, such as hygiene, blood safety, a trained workforce and an adequate supply of medical treatments, are at the heart of disparities in maternal and infant mortality. Women in both developed and developing countries are often unable to make informed decisions about their health and nutrition owing to lack of economic resources and education. Lack of access to reproductive health information and services due to financial, logistical, social or cultural barriers further complicates the situation. Proper medical attention, hygienic conditions and safe transfusions during delivery can substantially reduce the risk for complications and infection. Slightly over half (53%) of deliveries in developing countries are attended by a health professional, of which only 40% take place in medical centre. According to WHO, training skilled attendants to prevent, detect and manage obstetric complications and provide equipment, drugs and other supplies is the single most important means of preventing maternal deaths. Inadequate use of prenatal care has also been associated with increased risks for maternal mortality. In developing countries, 70% of births are preceded by at least one antenatal visit, while 38 million women receive no antenatal care. Additional factors that prevent women in developing countries from receiving the life-saving health care they need include distance from health services, cost, poor quality of available services and substandard treatment by health providers.

## Possible interventions

Implementation of an effective intrapartum care strategy is the best means for reducing both maternal and newborn mortality (291, 292). Second-level priorities are postpartum care, family planning, safe abortion and proper nutrition and protection from infection (291). As epidemiological information is lacking on many developing countries, efforts should be made to increase their capacity for data collection and for reporting vital statistics (287). Trends in



caesarean section rates should be monitored, even if interventions to reduce overuse have had limited success (44).

In an effort to identify cost-effective, evidence-based interventions, 16 interventions have been tested in three service delivery modes: outreach, family and community, and facility-based clinical care (293–295). It has been estimated that universal (99%) coverage with these interventions could avert 41–72% of neonatal deaths worldwide. Coverage by 90% with a combination of universal (i.e. for all settings) outreach and family and community care would avert 18–37% of neonatal deaths. Most of the benefit is found with family and community care, and rapid success in averting neonatal deaths can be achieved in settings with high mortality and weak health systems, through health education to improve home care, create demand for skilled care and increase care-seeking. Simultaneous expansion of clinical care for newborns and mothers, which is more costly but highly effective, is essential to achieve the reduction in neonatal deaths required to meet Millennium Development Goals 4 and 5, which are to reduce by two-thirds the mortality rate among children under 5 and reduce by three-fourths the maternal mortality ratio.

## Gaps in research

Although research on maternal and perinatal health has made significant progress in recent years, most has been driven by the needs of health systems operating in the richest countries. This has resulted in interventions in pregnancy and childbirth that are difficult to reproduce in low-resource settings, exacerbating the gaps in women's reproductive health conditions around the world.

The paucity of research on conditions that disproportionately affect women in developing countries has prevented the development of effective, affordable, feasible preventive

strategies. Pre-eclampsia, eclampsia and preterm delivery are pregnancy-related conditions that are still poorly understood, receive little international funding and greatly contribute to the high maternal and perinatal morbidity and mortality rates in many developing countries. Therefore, the research and development agenda for maternal and perinatal health should have a broader focus, to target the needs of populations that are more vulnerable and in greater need of affordable preventive and therapeutic interventions. Implementation of such an agenda could lead to significant reductions in maternal and perinatal mortality, a goal that has not been reached despite decades of international commitment. This new focus could have the added benefit of significantly reducing the underlying causes of morbidity and disability and the associated health-care costs in the developed world.

The main objective of a research programme for maternal and newborn health should be to improve sexual and reproductive health, as indicated by the International Conference on Population and Development (Cairo 1994) (296) and the World Conference on Women's Health (Beijing 1994) (297). These conferences addressed themes of social equity, poverty, gender, development and education as fundamental prerequisites for horizontally integrated health interventions and family planning. These lines of action were reiterated in the Reproductive Health Strategy adopted by the World Health Assembly in 2004 (43) and are implicit in at least three of the Millennium Development Goals (improving maternal health, reducing child mortality and combating HIV/AIDS) (298).

Two main strategies can be used to reduce the risk for pregnancy-related mortality and morbidity (299): spacing and limiting pregnancies through family planning and providing safe, accessible obstetric and perinatal services. Integration of these strategies could provide great benefits for maternal and perinatal health. For example,



family planning programmes and policies include addressing the rates of adolescent pregnancy and designing measures to increase the age at first pregnancy, thereby ensuring that first pregnancies occur after full pelvic maturation is achieved. In addition, sexually transmitted infections, which can contribute to maternal and perinatal mortality and morbidity, can be controlled by providing education and screening during maternal and perinatal care and suitable conditions for offering contraceptives and services for the prevention and treatment of sexually transmitted infections. How to best integrate these activities into antenatal, delivery and postnatal care represents a research challenge in itself (299).

Research in maternal and newborn health conducted so far has focused mainly on biomedical clinical, epidemiological and operational studies to test the efficacy of prevention and treatment interventions; evidence-based guidelines for the provision of essential, comprehensive obstetric care; and evaluation of the cost-effectiveness of interventions. Present evidence indicates that further research is needed in the following areas (299, 300):

- implementation of effective interventions;
- feasible interventions for low-resource settings;
- the causes of the pathological conditions mainly responsible for maternal and perinatal mortality and morbidity, such as hypertensive disorders of pregnancy, preterm births and intrauterine growth restriction, in order to design effective prevention and treatment; and
- identification of obstacles in health systems and at community level, including recruitment, training and retention of qualified staff, acceptance of best practices and removal of harmful beliefs and practices at family and community levels.

In order to avoid compartmentalization, fragmentation and duplications of efforts,

future research in the biomedical, clinical and epidemiological fields and operational, social science and health system and policy research should be coordinated. Collaborative strategies and partnerships represent the best approach to improving maternal and newborn health.

## 8 Safety of the elderly

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### Scope of the problem

In most developed countries, the size of the geriatric population will increase enormously over the coming decades. For example, the fastest growing segment of the elderly population in the United States is persons aged 85 or older. Any issue of patient safety or quality relating to the geriatric population—for example, adverse drug events, falls and fractures and decubitus ulcers—is magnified by virtue of the large projected increases in the numbers of older persons over the coming years.

Older adults are at increased risk for adverse events in every clinical setting, including hospitals, the ambulatory setting and nursing homes, due to a number of factors, including the atypical presentation of disease in the elderly, the propensity of the central nervous system to act as the 'final common pathway' for medical problems affecting other organ systems and reduced physiological reserve. Elderly persons are also more likely to have multiple chronic medical conditions, to be functionally impaired, to lack economic resources, to be burdened by cognitive deficits and to be cared for by many health-

care providers, further complicating medical management and care planning.

With regard to drug therapy, pharmacokinetics and pharmacodynamics change with age; for example, older persons have an increased proportion of body fat and reduced muscle mass, which, together with reduced drug clearance, can result in markedly longer drug half-lives and serum concentrations. They may also be more intrinsically sensitive to some medications. Together, these factors place elderly persons at potentially greater risk for drug-related injury than any other patient population.

Medication is the commonest medical intervention used in the care of elderly patients. In the ambulatory setting in the United States, 40% of all elderly persons use more than five different drugs per week, and 12% use 10 or more (301). In nursing homes, even more medication is used, posing particular risks for these very frail patients. While high levels of medication use are often appropriate and necessary, the sheer degree of exposure places older patients at particularly high risk.

Adverse drug events are the most serious consequence of suboptimal medication in the elderly. These effects can include confusion, falls and hip fractures related to the use of antipsychotic medications and sedatives. Incontinence, constipation, blurred vision and dry mouth are potential side-effects of anticholinergic medications. Renal impairment and upper gastrointestinal bleeding are potential adverse effects of therapy with nonsteroidal anti-inflammatory drugs. Hypoglycaemia is the most common and serious side-effect of diabetes medication. Excessive anticoagulation with warfarin has been associated with major bleeding events, including intracranial bleeding. While some of these adverse events are unavoidable, they are often associated with errors in medication management, including errors in prescribing, monitoring and using drugs.

## Severity of the problem

Most studies of the incidence and preventability of adverse drug events among older adults have been conducted in developed countries. One study of 30 000 adults aged 65 or older followed over 12 months identified 1523 adverse drug events, for a rate of 50 per 1000 person-years (46). Of these events, 27% were considered preventable, for a rate of 14 per 1000 person-years. Errors associated with preventable adverse drug events occurred most often during prescribing and monitoring, although 21% were associated with patient adherence. Patients at highest risk for an adverse drug event were female and aged 80 or older, and there was a dose-response relation with comorbidity and the number of medications used (302). Elderly persons taking non-opioid analgesics, anticoagulants, diuretics and anti-seizure medications were at increased risk for a preventable adverse drug event. The excess cost associated with preventable events in this population approached US\$ 2000 per event (47).

Nursing homes, in which 1.6 million elderly persons live in the United States, house some of the frailest patients in the population. Nursing home residents are far likelier than non-institutionalized elderly persons to be chronically ill, be functionally impaired, lack economic resources and family caregivers, be over the age of 85, have cognitive deficits and take large numbers of medications. Several studies of adverse drug events in nursing homes have shown that many are preventable; a recent study showed a rate of 10 adverse drug events per 100 resident-months, of which 40% were considered to be preventable (i.e. associated with errors) (48). Errors leading to preventable events in nursing homes occur primarily during the ordering and monitoring of medication.

Non-medication-related safety issues in hospitals, such as falls, decubitus ulcers and delirium, are of special relevance for the elderly,

especially for frail elderly patients with multiple morbidities and functional deficits (303). Some of these issues, such as falls and decubitus ulcers, are addressed in other sections of this report.

## Possible interventions

The underlying cause of many of the prescribing and monitoring errors identified in clinical settings appears to be lack of information at the time of ordering, including information on relevant conditions, other medications, recent laboratory test results and dosing history. Particular problems are related to the complexity of medication regimens and the involvement of multiple providers. Transitions between home, hospital, subacute, and long-term care facilities are frequent in this population and add to the complexity. This range of problems can be addressed by interventions such as enhanced inter-provider and provider–patient communication, medication reconciliation protocols and clinical decision support, in addition to computerized provider order entry systems.

The use of multidisciplinary teams to care for frail elderly patients receiving complex medication regimens might be the best way to improve the quality and safety of medical care in this high-risk population. Such teams can include nurse specialists, clinical pharmacists and other health professionals who complement and extend the work of the physician. Such collaborative programmes are generally implemented for a single disease; for example, disease management programmes specifically for the care of older patients with heart failure have been shown to be extraordinarily effective in reducing hospitalization rates and the costs of care (304). Disease management programmes have not, however, always proven to be more effective than usual care for other conditions, such as anticoagulation management in patients with atrial fibrillation and the care of patients with reactive airways disease (305, 306). Furthermore, simultaneous enrolment in several

disease management programmes might not be the best option for caring for elderly patients with a number of chronic conditions, as a fragmented approach might place these patients at further risk for adverse drug events. Innovative programmes, such as the Program of All-inclusive Care for the Elderly in the United States, have shown promise for providing comprehensive care for very frail elderly persons, emphasizing an interdisciplinary approach to care (307).

Computerized physician order entry systems have been promoted to improve medication safety for older patients (49). At present, however, most hospitals in the United States have not established these systems, and the challenges to their broad implementation in ambulatory and long-term care remain formidable.

While a variety of preventive approaches have been proposed to address problems such as falls, decubitus ulcers and delirium in hospitals, the strength of the available evidence is limited (308). Interventions to improve safety for which there is substantial evidence of benefit have still not been widely adopted (309, 310).

## Gaps in research

Future research efforts should focus on more efficient, less costly, less labour-intensive approaches to identifying preventable adverse events in older adults in all clinical settings. Characterization of such events in near ‘real time’ would facilitate the design and rapid implementation of systems approaches to improving patient safety. Information is also needed on the incidence and preventability of adverse clinical events among older adults receiving care in countries other than the United States, both developing and developed, as the challenges to providing health care to the elderly are global.

More creative approaches are needed for improving the safety of older patients,

including interventions with high- and low- (or no-) technology components. Testing new strategies for improving communication among the members of a health-care team should be a priority. For example, the situational briefing model SBAR (situation, background, assessment, recommendation) (73) might be a promising framework for structuring critical communication among health-care personnel providing care for older patients with multiple medical problems who are receiving complex treatment.

## 9 Injuries due to falls in hospitals

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### Scope of the problem

Falls in hospital are a significant issue in patient safety worldwide, often resulting in severe injuries to patients, an increased workload for hospital staff and greater financial costs. While hospital falls can occur at any stage of life, they are most prevalent among older patients and, given the demographic trends, will become an increasing problem. Ageing is quickly becoming a global concern, with elderly populations increasing most rapidly in Asia, Latin America, the Middle East and Africa. Developing countries will continue to undergo rapid population ageing in the coming decades, with a projected 839 million older adults living in developing countries by 2025, exceeding the elderly population in developed countries by nearly 500 million (311). If these trends are extended to falls, developing countries will experience the vast majority of the expected burden associated with hip fractures by the year 2050 (312–314).

Most of the available information on in-hospital falls comes from research conducted in developed countries. The National Patient Safety Agency in the United Kingdom reported that falls account for two in five patient safety events, representing the commonest patient injury reported. The overall rate in the hospital patient population was 4.8–8.4 falls per 1000 patient-days. Most falls were due in part to the effects of the patient's illness rather than to hazards in the hospital per se; however, one could argue that the failure of hospitals to anticipate such falls and to prevent them is a major deficiency. Not surprisingly, patients over 80 years and those who had fallen previously were the most vulnerable (52). In a study in the United Kingdom, it was estimated that 30% of falls resulted in an injury, but only 2.1% of falls were associated with severe injuries (53) leading to death or permanent disability. A study in the United States showed a rate of 6.6 falls and 0.4 injurious falls per 1000 admissions (315), while an Irish study reported a fall rate of 13.2 per 10 000 patient-days. In all studies, fall rates were strongly correlated with age, while the severity of injury was higher in institutions that used restraints (316). Sicker patients and confused persons were more likely to have an injurious fall (315).

The incidence of falls in hospitals in developing countries has not been adequately studied, although there are increasing efforts to do so. The available information is for the ambulatory care setting, where elderly patients were asked whether they had fallen in the previous year. In one study, 28.5% of Turkish patients aged 65 years and older had fallen within the year preceding their outpatient visit, and this rate was estimated to be comparable to those in developed countries (317). Other studies in developing countries provide prevalence rates of falls, although most were conducted in non-health-care settings. In analyses by the Salud, Bienestar y Envejecimiento en América Latina y el Caribe, the prevalence rates of falls were 21.6% in Bridgetown, Barbados, 29% in

Havana, Cuba, 33% in Mexico City, Mexico, and 34% in Santiago, Chile (314, 318). In a study in Hong Kong, 19.3% of elderly persons reported having fallen within a year, in accordance with the range for developed countries (319). In a study in the United Republic of Tanzania, falls accounted for about 35% of reported injuries among persons over 60 years of age in urban and rural settings (320). Although these rates do not represent falls in health-care establishments and are therefore not true patient safety events, they do demonstrate that fall rates are high in developing countries and countries with economies in transition and suggest that they are likely to be at least as prevalent as in developed countries. According to estimates from the American Geriatrics Society, the British Geriatrics Society and the American Academy of Orthopedic Surgeons Panel on Falls, the rates of falls in hospitals and long-term care facilities exceed that in communities for the elderly by several fold (321). There is therefore a growing need for research and interventions on falls, not only in hospitals but also in long-term care facilities.

## Severity of the problem

Patient falls in hospitals are common and often lead to poor outcomes, including injuries, prolonged hospitalization and even death (50). The most serious complications of falls among the elderly arise from hip fractures, after which up to 20% of patients become non-ambulatory and only 14–21% recover the ability to perform all their daily activities (51). Falls are also associated with a greater chance for unplanned readmission or discharge to residential or nursing home care (322). A study in the United States showed that falls in hospital were associated with a 61% longer hospital stay and 71% higher total cost, after adjustment for potential clinical and non-clinical confounders (315, 323). Estimates from Australia suggest that over 40% of patients with specific clinical problems experience one or more falls during hospitalization, and 38% of all patient incidents

involve a fall (324). A study in the United Kingdom showed rates of in-hospital falls of 2.9–13 per 1000 hospital bed-days, with up to a third resulting in injury (325). It is difficult to estimate the direct costs of falls to the health system, as they are generally absorbed into the operational costs and are not itemized; however, the National Patient Safety Agency estimated that an average 800-bed hospital trust with an average of 24 falls weekly will accrue a cost of £ 92 000 annually (52).

## Possible interventions

It has been shown that restraints should not be used to prevent falls as they often result in more serious injuries (316): programmes for decreased use of physical restraints have been shown to reduce both the incidence of falls and the severity of injury (54). Other interventions, such as identification bracelets for high-risk patients, vision correction, physiotherapy, bed alarms, hip protectors and special flooring materials, have all been tested, with varying degrees of success (326–328). Whether these interventions would be cost-effective in developing countries and countries with economies in transition is unknown. One study showed that adjusting the initial dose of psychoactive medications for patient age resulted in a 50% decrease in the fall rate (329). Techniques like reducing the use of psychoactive drugs in the elderly, which requires few additional resources, would probably be cost-effective in most countries of the world.

## Gaps in research

Much remains to be known about the risk factors for falls in the health-care setting. Research is needed to identify new means of preventing falls and for evaluating the efficacy of known techniques to minimize the incidence and morbidity of falls. Interventions should be cost-effective, easy to adopt and implement without unnecessarily disrupting or hindering the patient or the workflow of the



provider. Further information is also needed on the incidence and severity of patient falls in developing countries.

## 10 Decubitus ulcers

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### Scope of the problem

Decubitus ulcers, also known as pressure sores or pressure ulcers, are an important source of morbidity and mortality and a key issue in patient safety in hospitals. In the United States between 1990 and 2001, decubitus ulcers were reported to be the cause of death of 114 380 persons (age-adjusted mortality rate, 3.79 per 100 000 population) (58). A national survey in acute-care hospitals in the United States revealed an overall prevalence of approximately 10%, while a 1-day survey showed a prevalence of 15% (330). These rates are similar, the differences probably due to the lack of standardized methods for determining prevalence rates and differences in the patient populations studied (331). The rates are similar in other developed countries, with an 11% incidence rate in German hospitals (332), 12% in a Swedish hospital (333), 13% in Israel (59) and 17% on lower extremities in adults confined to bed in Japan (334). The risk factors for decubitus ulcers include immobility, friction, incontinence, cognitive impairment and poor nutritional status (55–57).

Less information is available on developing countries and those with economies in transition. Limited studies have shown rates of 11.2–43% in hospitalized Thai patients (335) and 8.7–10.8% in Thai hospitals (336, 337), 39.8% in Brazil (338) and 4.9% in an academic teaching hospital in India, where the incidence among certain subgroups of patients was reported to be as high as 40.9% (339). Although

the incidence of ulcers increases with longer stays and more comorbidity, it is not known whether these factors vary substantially among countries.

Many of the cases of decubitus ulcer reported in prevalence studies occur outside hospital and are therefore often considered not to be a patient safety problem. This ignores the fact that most cases occur in patients who live in long-term care facilities and therefore continue to represent injuries in the health-care setting. Therefore, it is important that healthcare systems take responsibility for these events and address them across the spectrum of care, if this important source of morbidity and mortality is to be eliminated.

### Severity of the problem

Decubitus ulcers are a major health-care concern because of their impact on patient morbidity and suffering and their economic impact (331). Without proper treatment, decubitus ulcers can lead to cellulitis, osteomyelitis, sepsis and death (340). A study in Australia showed that having a decubitus ulcer resulted in a median increase in the length of hospital stay of 4.3 days (341). In Australian public hospitals, a median of 95 695 cases of decubitus ulcer resulted in a median of 398 432 bed-days lost, incurring median opportunity costs of AU\$ 285 million (342). In the United Kingdom, the treatment of decubitus ulcers was estimated to cost £ 1.4–2.1 billion annually, or approximately 4% of total National Health Service spending in 2000 (60).

Little information is available on decubitus ulcers in developing countries; however, the situation can be expected to be comparable to, if not worse than, that in developed countries owing to even greater resource constraints. Furthermore, given that poor nutrition is a significant risk factor for decubitus ulcer, the rates might be expected to be higher in developing countries where adequate, nutritional food is either unavailable or prohibitively expensive.

## Possible interventions

Most of the information on interventions to reduce the prevalence of decubitus ulcers comes from developed countries and refers to types of mattresses. Several studies (61–63) have shown that certain foam bedding and alternating pressure beds can reduce the risk for decubitus ulcers, especially for high-risk patients (343). Other interventions, such as routine skin inspection, good nutrition, routine repositioning and increased mobility, have had varying degrees of success but can be implemented in a variety of settings worldwide (14). Potential interventions, such as improved nursing care through better staffing and training and ulcer-prevention beds, have not been evaluated in developing countries or countries with economies in transition. While they are likely to be beneficial everywhere, it is not clear that they would be cost-effective in developing countries.

## Gaps in research

Whether interventions to prevent decubitus ulcers would be cost-effective in developed countries and feasible in developing countries or countries with economies in transition remains unknown. The prevalence and consequences of interventions for decubitus ulcer must be determined before cost-effectiveness can be considered.









# SECTION III

## STRUCTURAL FACTORS THAT CONTRIBUTE TO UNSAFE CARE

### 11 Organizational determinants and latent failures

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#### Background

When a patient is harmed nosocomially, the main objective of the subsequent enquiry is usually to identify the health-care professionals whose unsafe acts made the immediate, local contribution to the adverse event. More often than not, these persons are then named, blamed, shamed and disciplined. While this method is managerially and legally convenient, it has little or no remedial value, not least because it isolates the errant individual from the situation in which the unsafe acts occurred. One of the basic facts of human fallibility is that the same circumstances continue to result in the same types of error by different people (64). In short, some tasks and some workplaces constitute recurrent error traps. It is often the situation rather than the person that is error-prone.

Over the past 20–30 years, detailed investigations of major accidents in a variety of hazardous domains (though very rarely in health care) have made it clear that the errors of individuals are both consequences and causes. Rather than being the sole instigators, these individuals have usually inherited workplace and organizational ‘pathogens’.

#### Nature of organizational accidents

Catastrophic breakdowns of complex, well-defended systems (e.g. in aviation, railways, power plants and health-care facilities) have been termed ‘organizational accidents’ because they arise from a combination of factors originating at different levels of the system. The etiology of an organizational accident has been summarized as follows (64).

- The adverse event sequence begins with negative consequences of organizational processes (e.g. decisions on planning, scheduling, forecasting, designing, rostering, specifying, communicating or maintaining).
- The latent failures so created are transmitted along various organizational and departmental pathways to the workplace (the operating theatre, pharmacy, ward or intensive care unit), where they create the local conditions that promote the commission of errors and procedural violations (e.g. understaffing,

fatigue, technical problems, high workload, poor communication, inadequate supervision, training deficiencies, inexperience, poor teamwork and unnecessary distractions).

- While errors occur quite frequently, most are inconsequential and are caught by defences, controls and good teamwork. A very few, however, can penetrate these defences to cause harm. The fewer or weaker the defences, the greater the probability that proximal errors will have an adverse impact.

At first sight, this model might appear to shift the 'blame' from the front line to the upper reaches of the organization. There are three reasons why this should not be the case. First, a few unsafe acts are indeed egregious and deserve sanctions. Second, blame and disciplinary action are wholly inappropriate if the individuals concerned did not recklessly choose to act in a manner likely to provoke error. Third, organizational decisions are shaped by economic, political and financial constraints; like designs, they are always a compromise. Moreover, it is not just bad decisions that have bad outcomes. All high-level judgements are likely to have potential disadvantages for someone somewhere in the system. All systems have resident 'pathogens', and the more they have, the fewer local events are needed to complete an adverse event scenario.

Errors are here to stay, but they rarely equate to incompetence. They simply confirm the maker's humanity. The capacity to go wrong is an unavoidable part of the human condition. We cannot change the human condition, but we can modify the local and organizational conditions under which people work so as to make them less provocative and more forgiving of the inevitable errors.

## **Safety culture**

An organization's culture with regard to patient safety—its safety culture—is important because

it is probably the one factor that can affect all the system's processes and defences for good or ill. Culture is a product of the organization's attitudes, beliefs and practices.

If health care can be said to have a culture, it contains at least two obstacles to improving safety: first, a belief in trained perfectibility (after long, arduous training, health-care professionals expect—and are expected—to get it right); and, second, the tendency to stigmatize and sanction fallibility (error equates to incompetence). Together, these pervasive influences make it difficult for health-care providers either to admit their errors or to learn from them collectively. Such learning is a prerequisite for a safety culture. A safe culture is made up of a number of components: a just culture (agreeing on the difference between unacceptable unsafe acts and 'honest' errors), a reporting culture (collecting, analysing and disseminating information about adverse events and near misses) and a learning culture (once the organization has acquired a memory of past events, it can set about learning from them). The interventions summarized below are designed to promote the progression from a vulnerable culture to a resilient one. More information about safety culture is given in another section of this report.

## **Possible interventions**

Attempts to identify and correct latent failures before they combine with local triggers to cause harm are mostly derived from the social sciences and humanities. As such, they tend to be less expensive than technological solutions, although they can be fairly labour-intensive. As these organizational issues are universal, the possible interventions considered below are, in principle, applicable across the economic spectrum. There is no one best technique: the various countermeasures can be mixed and matched to suit the local culture.

- The Incident Decision Tree is a web-based tool created by the United Kingdom's National Patient Safety Agency to give managers and clinicians a principled basis for deciding whether to suspend or otherwise sanction staff who have been involved in a serious patient safety incident. It, together with detailed instructions on its use, is available online at: [http://www.npsa.nhs.uk/health/resources/incident\\_decision\\_tree](http://www.npsa.nhs.uk/health/resources/incident_decision_tree).
- The Root Cause Analysis toolkit was also developed by the National Patient Safety Agency to guide a retrospective analysis of a patient safety incident, so as to identify the workplace, organizational and systemic factors that contributed to it. Details of the toolkit and the associated training are available online at: [http://www.npsa.nhs.uk/health/resources/root\\_cause\\_analysis](http://www.npsa.nhs.uk/health/resources/root_cause_analysis).
- Incident reporting systems exist in various forms throughout the world. Each incident, once reported, contributes to our understanding of latent failures and organizational risk. For each event, particularly inconsequential ones, the important question is: Could the contributions to this occurrence have combined with other factors to penetrate or bypass the system's safeguards to cause a catastrophic patient safety incident?
- While it is difficult to predict errors, the latent failures that give rise to them are present within the system. A number of auditing techniques, such as proactive process measures, have been designed to identify those organizational dimensions that are currently most in need of remediation and to track subsequent progress. The dimensions vary from one situation to another but generally include such generic issues as teamwork, communication, protocols, rostering and scheduling, design and maintenance management. Persons on the front line make regular assessments (weekly or monthly) of the extent to which these factors impinge on their work and on safety. The results are summarized as bar

charts. In any one testing session, two or three dimensions will stand out as requiring attention. Instead of dwelling on the last event and struggling to find local solutions for what was probably an organizational malaise, the attention of managers is directed towards eliminating the worst of the current latent problems (64, 344).

## Gaps in research

While it is clear that organizational factors affect patient safety, the factors that are most important is less clear. Further, more research is needed on how organizational factors mix with provider factors, such as fatigue or lack of adequate training, to cause patient safety incidents. These questions remain unanswered, not just in the developing world but also in developed countries. Finally, an important part of the research agenda should focus on how best to change organizational factors to optimize patient safety.

# 12 Structural accountability: use of accreditation and regulation to ensure patient safety

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Accreditation and regulation in health care, by the very nature of their design, appear to

be well-suited catalysts for patient safety (345). Accreditation is a formal process in which a recognized entity assesses whether a health-care organization meets published, specified standards (346). Regulation is governmental establishment of standards to which organizations and providers must adhere if they wish to avoid legal penalties (347). Both can effectively direct how patient care is given (347), despite the voluntary nature of accreditation, as its market value can lead to provider action on a level with governmental regulation.

An increasing number of countries have begun to use accreditation and regulation, with an emphasis on the former, to improve patient safety (348–350), due to the logical consensus that countries can improve patient safety by increasing awareness about critical issues, increasing education and changing the provision of care by using process or outcome standards. More countries continue to consider adoption of standards as a matter of sound health-care policy. The present and contemplated levels of activity in this area merit an assessment of current use of accreditation and regulation, identification of key issues that have arisen as a result, and potential areas of research that would help guide future policy.

Accreditation is a relatively young tool in health care. It was first used in 1955, when the Joint Commission on Accreditation of Healthcare Organizations was formed in the United States (351). Today, at least 39 countries have at least one accrediting body, and 33 having a system that functions at national level (349, 352). The accrediting organizations are concentrated in European countries but are also present in Africa, Asia and South America (353). In some instances, accreditation crosses international borders. For example, to provide evidence of the safety of their care to foreign entities whose business is being sought, health-care institutions have sought approval from accrediting organizations in the respective countries (354).

Regulation has a longer history than accreditation and is more frequently used throughout the world (352). It has usually been used to set minimum requirements for promoting public welfare, as licensing and reporting are the common requisites of practice (355). Although regulation will clearly have an expanding role in patient safety, accreditation appears to remain the preferred option, in accordance with the notion that regulation should set the basic standards and accreditation should set the highest practice standards feasible (349).

Countries sometimes use accreditation and regulation together. In at least 11 countries, accreditation is covered by legislation (349). In addition, countries sometimes use regulation—either by direct statute or de facto—to require providers to obtain accreditation (352). For example, France, Italy and Scotland all require accreditation by law (353). The United States Government requires either accreditation by the Joint Commission on Accreditation of Healthcare Organizations or direct regulatory review for Medicare payments. As Medicare can account for 40% of revenue and Government review is often undesired, accreditation by the Joint Commission is ostensibly mandatory for many providers (347).

## **Issues in accreditation and regulation**

Does accreditation or regulation actually improve patient safety? The answer to this question is relevant because of the high institutional value placed on accreditation and regulation, for activities undertaken as a result of Government mandates or voluntarily. Unfortunately, direct scientific answers to the question have not yet been provided (351, 356, 357), although it remains important for international quality improvement (353, 358).

The absence of evidence is not surprising, given the difficulty of testing the effects of

implemented standards rigorously, because rarely, if ever, can standards be tested in a randomized or controlled design (359). Moreover, accreditation often involves multiple standards. Implementation has so far been based on the logical perception that setting minimum practitioner training requirements or requiring adoption of evidence-based interventions will result in patient safety. It is considered that setting new standards will also heighten awareness of, and lead to education about, critical patient safety issues.

Nevertheless, rigorous demonstration of the empirical benefits of accreditation and regulation and identification of the most effective standards would clearly be of value. The former would justify further use of accreditation and regulation, and the latter would help focus efforts most effectively. In trying to determine what is known about the use of accreditation and regulation, a number of observations arise (357).

First, the choice of standard, based on 'process' or 'outcome', is important. Choosing process standards can be difficult, as evidence of efficacy is lacking for many safety interventions, partly due to the relative novelty of the study of patient safety. This limitation can make outcome standards tempting, but a shift from process standards might result in failure to provide the procedural guidance that institutions most need. In practice, accreditation standards involve both types of measures, although most are based on process. All standards must remain responsive and not static, because of the rapidity with which medical practice changes (355, 360).

Second, costs are an important consideration (356). Accreditation and regulation are well placed to make improvements that would have a net social benefit, but they might not be cost-effective for the provider (361). Thus, even though regulators can bring about desired improvements, they must consider the costs of compliance (362). The direct financial costs and the opportunity costs of meeting the standard

and the cost of demonstrating compliance should not be underestimated and should be taken into account in choosing a standard.

Third, accreditation and regulation standards are often mandated by different entities, leading to overlapping or conflicting requirements. The standards might actually conflict and thus create competing incentives, forcing institutions to choose among them. Even if there is no conflict in standards, overlapping standards can result in unnecessary duplication of work for both providers and regulators. In addition, an excessive number of standards and agencies can dilute the importance of individual standards. Consequently, better coordination of accreditation and regulation has been proposed, including efforts that cross national borders (357).

## Gaps in research

Potentially informative areas of research would answer three questions. The first is: 'What standards work best?' Research would involve identifying which process or outcome standards are most effective and the best mix of standards; a related area of research would be to find how best to identify these combinations. The second question is: 'Are accreditation and regulation cost-effective?' Research should address not only the cost of using the standard but also that of demonstrating compliance. The last question is: 'What is the right amount of accreditation and regulation, and how best are multiple efforts coordinated?' The answers to this and the previous questions are becoming more important as use of accreditation and regulation expands across the world.

Many gaps still exist in patient safety research. Questions on the efficacy of accreditation and regulation, such as the most effective standards and how they are best implemented still have no clear, evidence-based answers. The gaps exist uniformly across countries, regardless of how long accreditation has been used.



# 13 Safety culture

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## Patient safety culture

Organizational culture is typically described as a set of shared beliefs among a group of individuals in an organization. Safety culture was introduced as a specific concept of organizational culture in the wake of the Chernobyl nuclear reactor accident in 1986, which was subsequently found to have been caused primarily by human rather than technical failures. Importantly, investigators of the disaster saw the human failures not as shortcomings of the individuals but rather as a failure of the culture of encouraging an approach to safety that reflects understanding of the inevitability of human error. Similar conclusions were reached about the *Columbia* and *Challenger* space shuttle accidents in the United States (363). While the proximal causes of the shuttle disasters were technical failures, the roots of both accidents were believed to lie in the culture of safety at the National Aeronautics and Space Administration.

A large body of research supports the concept that a key condition for safety in high-hazard industries, including health care, is a set of shared beliefs that support safe practices among individuals working in an organization. Such a culture is marked by open communication, teamwork, acknowledged mutual dependency and the primacy of safety as a priority at all levels.

## Cultural challenges to improving safety

The delivery of medical care has changed dramatically in the past four to five decades.

Throughout most of its history, medical care was a 'cottage industry', in which practitioners worked autonomously with a few truly dangerous tools, like surgery, that were used only when circumstances warranted the high risks involved. Today, innumerable therapies and interventions are deployed, with relatively high risks for morbidity and mortality. Despite these dramatic changes in the delivery of medical care, the culture of medicine has not kept pace. The literature on safety usually refers to four categories of shared beliefs that affect safety in medicine.

First, health-care workers are usually more interested in the accountability of individuals, assigning 'blame' for mistakes to persons working on the front lines (the so-called 'sharp end') of care delivery (244). Most safety experts consider that this focus is poorly suited to substantial improvements in safety. Instead, a systems approach to patient safety, one that addresses the latent factors that allow an error to occur (or fail to prevent it), is required.

Second, clinicians often encounter numerous errors during clinical practice, leading to the impression that such problems are inevitable. For example, most physicians accept a modest rate of catheter-related bloodstream infections, although such infections can virtually be eliminated by scrupulous adherence to insertion and maintenance protocols (364). This perception, sometimes referred to as the 'normalization of deviance', appears to be widespread in health-care organizations.

Third, medical care is typically organized hierarchically. Organizational hierarchies of responsibility and accountability frequently suppress communication about safety, because reporting 'problems' is viewed as a personal attack rather than an effort to improve. As was shown in the Toyota automobile production system, an organizational commitment to treating problems as opportunities to improve can reverse the effect of organizational hierarchies on safety culture.

Finally, there has been little emphasis on organizational learning in health care. Front-line workers often note that the same problems occur repeatedly and may be confronted by persons in many organizations around the globe. Capturing and communicating information that facilitates and demonstrates improved outcomes or a reduction in errors has usually been given less priority than information on new products or interventions. Such intra- and inter-institutional learning needs an environment of value for the effort necessary to identify solutions and to communicate them widely.

## Measuring patient safety culture

It is important to measure safety culture in order to understand and improve patient safety. Shared beliefs are usually measured by qualitative methods, such as interviews and observations, or quantitative methods, such as surveys. Most studies of safety culture have been based on collecting data from persons who provide care or persons who organize and direct care or both. Qualitative data collected from focus groups, interviews and direct observation are valuable for a contextual understanding of safety culture, although they do not allow comparison of groups.

Quantitative approaches do allow comparisons among groups, and this approach is becoming increasingly common in the United States. In a recent review, 13 surveys of patient safety culture were identified, some of which have been used extensively (365). The surveys addressed many aspects, including overall perceptions of safety, management and institutional commitments to safety, reporting practices, organizational learning, teamwork and communication, use of a just or non-punitive response to error, adequacy of staffing, job satisfaction and working conditions, handover of patients from one provider to the next, transitions and recognition of stress. The surveys differ in the specific items addressed,

the number and type of dimensions, the subjects and their length. While most of the surveys have face validity, few have been validated against actual adverse events or errors, or against other measures of patient safety culture, such as in-depth interviews or observation.

## Patient safety

Although the logic of a relation between culture and safety is compelling, the literature supporting such a link in health care remains limited. Sexton has suggested an association between culture and medication errors, length of stay and bloodstream infection rates (65, 366), but on the basis of cross-sectional and observational studies, thus leaving room for uncertainty about the exact nature of the relations.

While efforts to define the relation more clearly are under way, measurement of the effect of culture on patient safety is challenging. A key challenge is establishing a summary estimate of safety culture. A single organization can have multiple microcultures and internal geographical variation and thus might have a high score on one aspect of safety culture (e.g. reporting) but a poor score on another (e.g. handover of a patient from one provider to the next). Some groups are experimenting with various approaches to determining how the measures should be combined to create a summary score, but no clear consensus has emerged.

## Patient safety culture in the developing world

Safety culture is being assessed throughout the world, with reports from Canada, Japan, New Zealand, the United Kingdom and the United States, among others (367–370). Nonetheless, limited information is available about safety culture in developing countries. While it is likely that similar cultural challenges face health-care delivery throughout the world, it is reasonable

to expect that individual societies have unique problems (371). In order to measure the culture of patient safety in developing countries, the existing tools and methods might have to be modified to take into account different economic and sociocultural aspects.

## **Gaps in research and opportunities**

Future research and practical application of what is known about safety culture present a number of opportunities. Several important questions with regard to measurement and best practices remain unanswered. First, rigorous studies are required to validate the available instruments for measuring safety culture; little information is available on the relation between culture and patient outcomes. Second, there is little information to support the choice of an intervention for improving safety culture, although there are some novel approaches, such as safety rounds (372), teamwork training (68) and 'executive walk rounds' (66, 67). It is not known whether these approaches will change the culture of safety. A multifaceted programme designed to be implemented at the unit level appears promising, but it is complex and the essential components of the intervention are unclear (69). Third, there is no clear consensus about the essential dimensions of safety culture or their relative importance; many dimensions have been proposed, some of which may overlap. Fourth, most published data on the culture of patient safety were collected in the inpatient acute-care setting. Given the high volume of ambulatory and post-acute care, more information on safety culture and patient safety in these settings would be important.

On a more practical level, administrators need guidance about the best practices for creating a culture of patient safety. There will be continuing tension between systems

approaches and individual responsibility in patient safety. Organizational leaders who embrace a systems approach should be aware that individual responsibility cannot be ignored. At the same time, leaders who follow an individual approach to patient safety should be aware that this focus can result in less safety if the organization is seen as punitive and unresponsive to individual needs for support.

## **14 Training, education and human resources**

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Human resources are the most valuable asset in health care and, in some locations, practically the only one. The major threats to patient safety worldwide are inadequate numbers of equitably distributed and qualified health-care providers and incomplete knowledge about safe practices. The health-care workforce, which comprises more than 100 million persons worldwide, including 24 million doctors, nurses and midwives, is the primary global resource for making care safer (70). Numerical sufficiency, adequate geographical distribution and an appropriate mix of skills and qualifications are critical for achieving safer care. Yet, all countries have deficits in their health workforce. Some 57 countries have such critical shortages of doctors, nurses and midwives that they are unlikely to meet the health-related Millennium Development Goals or to be in a position to improve safety. These 57 countries together have an estimated deficit of 2.4 million doctors, nurses and midwives (71). Patient safety and health workforce adequacy are inextricably linked.

## Workforce adequacy and patient outcomes

The relation between the density of physicians and nurses and safety is difficult to determine, partly because the available data are limited. In addition, at both global and local levels, there is a general relation between the supply of physicians and nurses and economic development (373), and, as economic development influences a range of other social activities that affect health, it is difficult to reach unequivocal conclusions. Despite these limitations and despite contrary views (374), the weight of evidence leads to the conclusion that physicians and nurses add to quality and safety and that, except when there is an excess capacity, more physicians and nurses and better-trained physicians and nurses add more.

It is easiest to measure the effects on health of greater numbers of physicians and nurses among countries with widely different economic status because the outcomes are vividly apparent. For example, in comparing the mortality of mothers, infants and children under 5 years in almost 200 countries, WHO found that each 1% increase in the density of physicians yielded an improvement of approximately 0.30% in outcomes, similar to the independent effects of gross national product (0.45%) and female literacy (0.39%) (375).

Fundamental health outcomes such as these are profoundly influenced in poor countries, but they are not the principal reason for improving safety and quality in developed countries, where medicine has reached a higher technological plane and patients' expectations are higher. Nonetheless, similar observations have been made in these countries, where a 1% increase in the number of physicians per capita was associated with a 0.40% decrease in premature mortality among women and 0.30% among men (376). Jarman *et al.* (377) found a strong inverse association between mortality in hospital and

the number of physicians per bed in hospitals in the United Kingdom. The relation was similar in magnitude to that observed in the international comparison cited above, each 1% increase in doctors being associated with a 0.12% decrease in hospital mortality and each 1% increase in general practitioners being associated with a 0.37% decrease. Baicker *et al.* (378) reached similar conclusions when they compared the number of general practitioners in various states of the United States with the quality and costs of care. They found that a larger number of general practitioners was associated with higher quality and lower costs. Although they reported an inverse relationship for specialists (more specialists being associated with lower quality and higher costs), direct analysis of the data on specialist supply (379) and quality (380) showed that the opposite is true, i.e. that more specialists also yield better outcomes.

## Patient safety in hospitals

Many studies have shown that better nurse and physician staffing and qualifications are associated with better outcomes among hospitalized patients. Florence Nightingale reported in 1855 that more patients died in British military hospitals in the Crimea from preventable causes associated with hazards in the care environment than from wounds received in battle, and that the introduction of trained nurses substantially reduced the number of preventable deaths (381). Surveys of health-care consumers and practising physicians indicate that nurse understaffing in hospitals and 'burnout' (physical or emotional exhaustion, especially as a result of long-term stress or dissipation) and fatigue of health-care providers are the main causes of medical errors in today's hospitals (382). Research in a variety of developed countries shows that patients cared for in hospitals in which professional nurses comprise a greater share of the hospital staff and take care of fewer patients have lower risk-adjusted mortality

(383, 384). Similarly, hospitals that have better educated nurses—a greater proportion of nurses with baccalaureate degrees—have lower rates of mortality and failure to rescue patients with complications (383, 385).

The hospital characteristics associated with favourable patient outcomes have been studied extensively over the past 20 years. The most commonly studied outcome has been mortality. In a series of such studies, major teaching hospitals have consistently been distinguished by lower severity-adjusted mortality (386–388). While such hospitals have more physicians per patient, including resident physicians, they also have more nurses, more of whom hold baccalaureate degrees (383), and other characteristics, thereby making it difficult to infer the basis for the better outcomes. For example, in a study of patients admitted for myocardial infarct, in which a lower mortality rate was found in major teaching hospitals, the better outcomes were attributed to more frequent prescription of aspirin, beta blockers and angiotensin I-converting enzyme inhibitors (389). In another study, however, the percentage increase in use of these drugs was less than the percentage decrease in mortality, leading the authors to suggest that the better mortality rates of teaching hospitals might be due to better training of their medical staffs (390). This conclusion is consistent with the observation that a prominent aspect of the better quality of teaching hospitals is higher scores on the ‘explicit physician cognitive scale’, a measure of the thoroughness of clinical examinations (391).

## Physician credentials and quality

The association between the level of training of physicians and the quality and safety of the care they give has been addressed in a number of studies. Better physician staffing in hospitals is associated with lower mortality and better patient outcomes (377, 392), and physicians with board certification are associated with better patient

outcomes (383). In one study, hospitals with a higher percentage of board-certified specialists had lower mortality rates (386). In a second study, an even stronger relation was found with board certification when the mortality associated with complications of surgery (failure to rescue) was measured (383). In intensive care units, the lowest severity-adjusted mortality was found in units staffed by fully trained specialists (393).

Brennan *et al.* (394) observed that studies of quality have tended to ignore the density of physicians and the quality of care that individual physicians provide, in favour of safety, effectiveness, efficiency, timeliness and equity. The emphasis has been on continuous quality improvement by changing systems of care (395), and the autonomous professional behaviour of physicians has been viewed as a barrier to achieving safe health care (234). The studies cited above offer another perspective: that the density and level of training of physicians, and not simply the standards that the new, industrialized medicine is attempting to create, are fundamental to the safety and quality of patient care.

## Gaps in knowledge

Critical gaps exist in current knowledge of the role of human resources in patient safety. In developed countries, for which most data are available, little is known about the appropriate level of staffing in different clinical contexts that is necessary to minimize adverse events. Further, much of the information applies to the hospital setting, and the minimal levels of training and staffing necessary to optimize patient safety in ambulatory care are unknown. Other important gaps in knowledge in developed countries include information on how best to improve staffing levels in various clinical setting and the most cost-effective approach for improving provider coverage.

More substantial gaps in knowledge about human resources training and staffing exist for

developing countries and those with economies in transition. While there is compelling evidence that inadequate training and poor staffing levels are probably important components of unsafe care, little is known about the magnitude of these risks for patient safety. Further, little is known about the types of providers (nurses, doctors, community workers) and the level of training that might be optimal for providing clinical care in communities or hospitals in these countries. Finally, given that these countries often lack resources, cost-effective strategies are needed to improve the training of the current health-care workforce and to ensure that staffing levels are optimized to reduce unsafe care and improve patient outcomes.

## Application of research to policy-making

Many studies have demonstrated a link between health-care workforce capacity and patient safety. Most decision-makers are not, however, aware of the existing research, and workforce policies and safety initiatives are largely developed in isolation, with conflicting objectives and poor results. Additionally, important gaps in knowledge hamper efforts to improve patient safety by workforce-related strategies. Such gaps are greatest in developing countries.

# 15 Stress and fatigue

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## Scope of the problem

Working conditions affect providers' ability to provide safe, high-quality care. The factors include staffing levels, workload, working hours,

shift rotation patterns, physical environment, workflow design and organizational culture. As working conditions differ significantly among countries, the results of studies are usually country-specific.

A study in the United States detected an inverse relation between registered nurse staffing and the post-surgical adverse event of pneumonia, suggesting that staffing levels should be taken into consideration in efforts to minimize adverse events (396). Fatigue and sleep deprivation often play a key role in errors. Resident physicians in a large teaching hospital in the United States attributed mistakes to excessive work hours, inadequate supervision and problems with handing over to the next provider (397). Another study found that interns made significantly more serious errors when they worked frequent extended shifts (of 24 h or more) than when they worked shorter shifts, suggesting that decreasing interns' working hours could reduce serious medical errors in intensive care units (398). Several countries have implemented measures to reduce work hours. For example, the European Working Time Directive requires European Union Member States to limit the number of hours a resident can spend in hospitals to 56 h per week and to limit standard shifts to 10 h per day.

## Severity of the problem

### Stress and fatigue

Working conditions, including consecutive and weekly work hours, staffing levels and workload, affect the ability of providers to give safe, high-quality care. As working conditions can affect the ability to deliver care in any setting (medical, surgical, inpatient and outpatient), interventions to improve working conditions can broadly reduce the risks for many types of clinical error, including misdiagnoses, surgical errors, medication errors and health care-associated infections.

Stress and fatigue resulting from health-care workers' working conditions are widespread.



While further data are needed on the prevalence of sleep deprivation among licensed physicians, the large majority of physicians-in-training (residents) in the United States routinely experience sleep deprivation. A national prospective study showed that three-fourths of interns (first-year residents) work one or more shifts of more than 24 h in any given month (399) and most do so recurrently. On average, interns have only about 2.5 h of sleep during these shifts. In addition, long work hours and fatigue are highly prevalent among nurses; about 40% of all shifts recorded in one large study exceeded 12 h and led to fatigue and adverse consequences (400). Long work hours have been shown to lead to decrements in alertness, mood and performance across a range of tasks, as described below. In developing countries, where residents and nurses also have long working hours, fatigue can be expected to be widespread, although direct data for the developing world are lacking.

‘Burnout’ and depression, indicators of job stress, have also been found to be widespread. Burnout, a syndrome of emotional exhaustion and detachment due to chronic stress in the workplace, has been estimated to affect 41–76% of residents (401), while depression appears to affect a slightly larger proportion of residents than persons in the general population (402). Studies are needed to determine the rates of depression and burnout in health-care providers in developing countries.

## **Sleep deprivation**

Sleep deprivation has been shown to be an important, under-recognized source of a wide range of safety hazards in health care. Sleep deprivation is ubiquitous in the medical profession and might have far more serious consequences than most providers realize.

The traditional 24-h shifts of resident physicians have been shown to pose a danger to patients, themselves and the general public. In a randomized trial, the Harvard Work Hours, Health

and Safety Group in the United States found that medical interns working traditional 30-h shifts experienced twice as many physiologically documented attention failures while working at night; made 36% more serious medical errors overall; made 21% more serious medication errors; and made five times as many serious diagnostic errors as interns whose scheduled work was limited to 16 consecutive hours (398, 403). In a nationwide prospective cohort study in the United States, it was further found that interns working more than 24 h had more than twice the risk for crashing their cars when driving home after work (399) and 61% had increased odds of suffering an occupational percutaneous injury after 20 h at work (404), injuries that expose providers to a risk for bloodborne infections.

These field studies of the relation between sleep deprivation and safety have been supplemented by many laboratory and simulator studies, which also demonstrated hazards associated with sleep deprivation. Arnedt *et al.* found that working a traditional schedule that included shifts longer than 24 h every four or five nights impaired residents’ neurobehavioural and simulated driving performance to the same degree as a blood alcohol level of 0.04–0.05%, even though the residents had an average of 3 h of sleep during their overnight shifts (405); 24 h with no sleep has been shown to induce impairment commensurate with a blood alcohol level of 0.10% (406). While not every laboratory or simulation study of residents has shown that sleep deprivation decreases performance, most have shown a decline in performance in one or more domains. In a meta-analysis of 60 studies of physicians’ and non-physicians’ performance when sleep-deprived, the mean performance of resident physicians on clinical tasks after 24 h of sleep deprivation decreased by an average of nearly two standard deviations overall, to the 7th percentile of the level at which they performed when rested (407).

Sleep deprivation has also been shown in a series of cohort studies to affect nurses’ risk for



motor vehicle crashes and self-reported medical errors. Nurses working rotating shifts were twice as likely in one study to report an accident or error as those working day or evening shifts. Those who rotated had 2.5 times the odds of reporting a near-miss motor vehicle crash and 2.2 times the risk of making medication errors (408). Rogers *et al.* found in a survey of 393 nurses that about 40% of all nursing shifts exceeded 12 h and that the risk for nurses of making an error increased significantly when their shift exceeded 12 h (400). These and similar studies led the Institute of Medicine in the United States to recommend that nursing shifts be limited to a maximum of 12 h (409), but adoption of this recommendation has been limited.

Many developed countries have implemented regulations to reduce working hours, but the stringency, effectiveness and enforcement of these regulations varies widely. In the United States, residents cannot work more than 80 h per week (averaged over 4 weeks) or more than 30 h in a row (including time for education and handing over of patient care), according to professional regulations implemented in 2003. Unfortunately, compliance with even these modest limits—which greatly exceed those in other safety-sensitive industries in the United States—is poor (410). The European Working Time Directive requires that all European Union Member States limit the weekly work of physicians and nurses to 48–56 h and limit consecutive work to 13 h; these regulations are enforced by law (411). In New Zealand, the work of junior doctors has been limited by contractual agreement for over 20 years to 72 h per week and 16 consecutive hours (412).

## Workload

Nurse workload and nurse–patient ratio have also been found to affect patient safety. In a large study based on an administrative database, the risk for 30-day mortality and for failure-to-rescue for each additional patient assigned to a nurse increased by 7% (413). Similarly, a higher

proportion of hours of care provided by registered nurses and a greater absolute number of hours of care per day were found in a second large study based on an administrative database to be associated with decreased hospital stay and decreased rates of urinary-tract infections, upper gastrointestinal-tract bleeding, pneumonia, shock, cardiac arrest and failure to rescue (414). These and related findings led the Institute of Medicine in the United States to recommend minimum nurse staffing levels in intensive care units and nursing homes and to set priorities on formal monitoring of nurse workload and staffing in order to ensure safe care (409).

## Other working conditions

Research on other working conditions, such as the physician–patient ratio, nurse and physician work acuity and the physical environment (including physical barriers to care, noise levels, lighting and ergonomic design of workspace) is in its infancy, and solutions to extreme work hours and overwork in all settings should be evaluated. Nevertheless, studies conducted to date show that working conditions can have an important effect on safety and that efforts to improve conditions should be pursued at the same time as efforts to reduce the rates of specific types of clinical errors.

## Gaps in research

Given the heterogeneous working conditions in different countries, a common terminology is needed, with standards for studies on stress and fatigue. Proposing what to measure and how to measure it might help to design studies that can be compared with those in other countries and settings. ‘Long shifts’ has a different meaning in Europe and in the United States, and the training and tasks of e.g. nurses might differ among countries. Applying agreed definitions to the available studies would indicate which data can be transferred between countries and which questions still require study.

Questions to be considered are as follows:

- What is known about the short-term (e.g. errors) and long-term consequences (e.g. burnout) of stress and fatigue? Is the level of stress and fatigue that causes short-term consequences the same as that which causes long-term consequences?
- Various kinds of error have been defined. Are they differently sensitive to induction by stress and fatigue?
- What effect do stress and fatigue have on performance other than inducing error? For example, how do they affect the relationship between caregiver and patient and relatives?
- Is there a linear relation between stress and fatigue and induction of errors, or can significant thresholds be identified. How do age, gender, job experience and job satisfaction modify this relation?
- Do age, gender and job experience modify the error-inducing effect of stress and fatigue?
- From the point of view of error prevention, what are the ideal working conditions?
- To what extent can breaks during a shift prevent the adverse effects of stress and fatigue?

## 16 Production pressure

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At the level of systems, production pressures are situations in which the optimal capacity of a health-care system to care for patients is exceeded, due to unexpectedly large numbers of patients or a reduction in health-care workers or physical space available to provide care. At the level of the provider, this results in an increased

cognitive workload. In industries other than health care, there is a clear relation between a high workload and human error (22). In the health-care industry, concern has been expressed about the effects of production pressures on patient care; however, little empirical evidence is available to guide policy-makers (90, 409). Studies are now being conducted to determine the effect of patient overcrowding in emergency departments (415), but most of the evidence pertains to nurse staffing levels in acute-care hospitals (416, 417) and facilities with long-term, skilled nursing (418).

During the past two decades, the results of a number of observational studies on the relation between nurse staffing levels and patient outcomes were reported. The evidence has, however, several limitations, including heterogeneous definitions of staffing levels. The commonest methods used to calculate nurse staffing are nurse:patient ratios and hours per patient-day. The nurse:patient ratio is simply the number of patients a nurse cares for at any one time, while hours per patient-day are calculated by dividing the average number of patients in a facility by the number of nursing staff hours. Both methods suffer from a similar constraint, that it is often not known whether the nurses with the highest volume of patients are the same as those who take care of the patients experiencing adverse outcomes. For practical reasons, these studies had an ecological approach, limiting the possibility of drawing causal inferences.

A major concern about the literature is the adequacy of the adjustment for case mix. It might be that if hospitals with a high nurse:patient ratio has a healthier patient population, there could be an erroneous assumption that the nurse staffing level is beneficial, unless adjustments are made to account for the patients' severity of illness. The literature has been quite inadequate in this area. Further, few of the studies addressed how patient turnover might affect patient outcomes in the context of staffing levels. Admitting and discharging a patient can use up a tremendous

amount of nursing resources, which is overlooked when a study is confined to a patient census. One study indicated that failure to adjust for patient turnover might result in a significant bias (419).

Three systematic reviews have been published on the association between nurse staffing and patient outcomes (416–418). Owing to differences among the studies, meta-analysis could not be used. Most of the studies covered in all three of the reviews were cross-sectional; only two longitudinal studies have been conducted on nurse staffing levels and patient care outcomes (420, 421). Two of the reviews included studies of acute-care hospitals (416, 417), and the third included studies of nursing homes (418).

The first systematic review, published in 2004, included citations since 1980, with 43 studies eligible for inclusion (416). The authors concluded that there was no evidence for a specific minimal nurse:patient ratio in acute-care hospitals. Of 12 studies in which falls were an outcome, 10 had null findings; in one study, increased nursing hours were associated with a statistically significant reduction in falls, while a second study showed that increased nursing hours were statistically significantly associated with an increase in falls. Of six studies in which treatment errors were an outcome, five had null findings or effects judged to be unimportant (422–426), and the remaining study showed a statistically significantly increased rate of medication errors (427).

In the second systematic review, Lankshear *et al.* identified 22 studies published since 1990 in which adjustment had been made for both case mix and hospital characteristics (study inclusion criteria) (417). To account for the different measures used for nurse staffing, data presented as nurse:patient ratios or 'full-time equivalents' were transformed into 'converted hours per patient day'. The studies covered a wide range of outcomes, including mortality, pneumonia, urinary-tract infections, falls,

decubitus ulcers and medication errors. Three studies showed statistically significant relations between total nursing hours and medication errors; however, two showed a direct correlation. In both of the latter studies, however, medication errors were self-reported; thus, the positive association might have been due to more reporting rather than to an increase in events (427, 428). Another study showed an inverse relation between nursing hours and medication errors, which was significant only in cardiac care units (429). Three studies showed a significant association between falls and nursing hours, but two additional studies could not replicate these findings. In one of the two longitudinal analyses, Mark *et al.* found no consistent effect of nurse staffing on complications of pneumonia, urinary-tract infections or decubitus ulcers in 422 hospitals (420). The second longitudinal study showed that acute-care hospitals with higher nurse:patient ratios had statistically significant decreases in the rates of decubitus ulcers, falls and urinary-tract infections; however, the effects were small and of questionable clinical significance (421).

Bostick *et al.* reported a systematic review of nurse staffing in skilled care facilities (418), covering 87 studies published since 1975 that met the authors' inclusion criteria. They included many different patient outcomes. The authors concluded that most of the evidence supported a relation between staff levels and decubitus ulcers, but the effects were modest.

Emergency room overcrowding has also been identified as a potential safety concern (415), although limited evidence exists to support such concern. Most of the published studies are surveys of self-reported errors, with no objective measure of adverse events. Schull *et al.* evaluated the effect of emergency department crowding on door-to-needle time for intravenous thrombolysis in cases of suspected myocardial infarct (430). Retrospective data were obtained from 25 emergency departments in four geographical networks (all in Ontario, Canada),

and crowding was defined as the percentage of network hospitals that diverted ambulances. In comparison with emergency departments with no crowding (no network diversion), those with high levels of crowding (> 60% network diversion) had a 40% greater odds for significant delay.

This review demonstrates that little work has been done on production pressures for physicians and other clinicians (apart from nursing). Furthermore, nearly all the data come from developed countries. Production pressures for clinicians, especially physicians, are likely to be a major source of unsafe medical care in developing countries and those with economies in transition, where anecdotal evidence suggests that physicians have substantially larger patient loads (both in ambulatory care and in hospitals) than physicians in developed countries. There is no information on the extent to which this pressure compromises patient safety.

## Gaps in research

Several gaps remain with regard to the effect of production pressures on patient safety. First, it is unclear how best to measure production pressures. Simple statistics such as nurse:patient ratios discount potential confounders such as patient homogeneity, the skill of the provider and the effect of time-intense functions, such as patient transfers (admissions and discharges). Research should initially be focused on methodological issues, including a definition of 'workload' and identification of the most appropriate, valid tools to measure it. Although several studies have been conducted on nurse staffing, their heterogeneity hinders interpretation. Workload measures can vary, depending on the context, and additional

measures are needed, such as for the ambulatory setting and for different specialties (surgical or medical). Research on patient safety is also limited by a lack of models to simulate health-care encounters in various settings and workloads. More comprehensive patient-system modelling might help to determine an equitable workload distribution. More sophisticated models could incorporate provider-specific workload measures and determine the effects of physician and ancillary staff levels on health-care delivery and performance. Finally, additional research must be performed in settings other than those for acute care, such as outpatient clinics. Emergency department overcrowding is an increasing problem, and its effect on patient safety is a high research priority.

The current body of literature must be expanded to include more types of health-care systems. Research with standardized measures for production pressures should be conducted in both developed countries (single-payer systems, employer-based plans) and developing countries. Compensation strategies to address work inequities might be substantially different and offer important insights into effective safety interventions.

## Conclusion

Limited information exists on the effect of production pressures on patient safety, especially in developing countries and those with economies in transition. Although much attention has been paid to nurse staffing in developed countries, much of the work is of poor quality and the results are inconsistent. Research in these areas requires standardization of measures of staffing and overcrowding and more rigorous, prospective study designs.

# 17 Lack of appropriate knowledge and its transfer

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The existence of knowledge at different levels affects how it is transferred. For example, a clinician brings to bear knowledge of the practice of medicine when taking care of a patient and transfers knowledge about the patient to another clinician to provide contiguous care. Medical knowledge as a whole gradually improves over time and must be disseminated globally. This section deals with the availability and transfer of the first and second types of knowledge: 'practice knowledge' and 'patient information'.

## Availability and transfer of knowledge about practice

In 2006, almost 2000 articles were added every day to the corpus of published biomedical literature (431), and the rate is growing linearly (432). Unfortunately, the lag time before research findings are translated into clinical practice does not keep up (433). In many jurisdictions, health professionals are required to accrue regular continuing medical education credits, but this strategy does not allow health-care providers to keep up, even within a narrow specialty. Health-care providers must also separate proven research findings from those that have been refuted (434).

Practice guidelines are one way of transferring research findings for adoption. Professional societies often draw up and promulgate best practice standards. Nevertheless, such standards are limited by issues of timeliness

(recommendations that are out of date by the time they are published) and bias (for example, financial support from a pharmaceutical company) and meet significant barriers to dissemination (435) and adoption (436). Methods to increase their adoption are often based on the carrot-and-stick model: naming the provider (and sometimes patients) when compliance is poor (437) or giving incentives to the provider (or patient) for good compliance, such as 'pay for performance' (438).

In practices with computerized medical records, such as provider order entry, a more effective mechanism for bringing the latest evidence to the bedside is clinical decision support (439, 440). Ideally, decision support makes it easy to do the right thing and hard to do the wrong thing. It is either active, giving 'alerts' about potential errors of commission (e.g. drug allergies and drug-drug interactions) or reminders to reduce errors of omission. Less interruptive forms of decision support that are integrated into the work flow are usually more acceptable to clinicians, such as algorithms to calculate safe doses for elderly patients (329) or for ordering medications for patients with renal impairment (441), as opposed to presenting all possible doses and then alerting the clinician when an unsafe dose is selected. The use of computerized physician order entry with decision support to reduce errors is reviewed in another section of this report.

Entirely passive forms of decision support require the user to ask for help, such as using reference materials to look things up. As noted previously, almost half of all medication errors are associated with insufficient information about the patient and the drug; this knowledge gap could often have been closed simply by consulting a reference (100). Although clinicians generate one to three patient-related questions for every one to three patients (442, 443), the answers to the questions are sought less than half the time (444), and the commonest source is colleagues. This method of decision support might appear

obvious, but it should not be underestimated as a mechanism for transferring knowledge, as it is used at the time the recipient is most motivated to learn. Many barriers exist, however, including the time, effort and experience needed to formulate a question explicitly, the choice of the most appropriate resources and locating the answer within the resource (445). Another barrier is the lack of convenient, up-to-date information. The traditional bookshelf of textbooks, although convenient, quickly becomes outdated (446). Electronic references are updated regularly and are widely available via local area networks or the worldwide web.

The most effective references are those that are conveniently integrated into the electronic clinical applications that health-care providers use for patient care, such as electronic medical records and provider order entry. 'Infobuttons', which are being used to support such integration (447–449), take into account all the context available about the search (for example, clinician characteristics, such as role, degree or specialty; patient characteristics, such as age, gender, comorbidity and concurrent medications; and setting, such as the activity being undertaken by the provider when the search was requested) to return specific, useful results.

## **Availability and transfer of patient information**

A type of knowledge transfer that is often underestimated is the handing over of patient information from an outgoing provider to an incoming one. Such handovers are coming under increasing scrutiny as potential sources of error (450). For example, an analysis by the Joint Commission on Accreditation of Healthcare Organizations in 2005 identified communication problems as a major cause of nearly 70% of sentinel events (72). Effective communication and teamwork are often assumed, and formal training and evaluation in these areas has been largely absent (73). Although there are few

published studies of the optimal method for transmitting patient information in this setting (76, 451–454) or of the consequences of poor communication (235, 453), many institutions (including the Agency for Healthcare Research and Quality (74) and the Joint Commission on Accreditation of Healthcare Organizations (75)) are advocating techniques used in the nuclear, defence, aviation, aeronautics and even commercial sectors, such as read-back confirmation, interruption-free 'time-outs' and cross-monitoring. Adoption of these methods has been slow, as one study showed that hospital emergency rooms regularly use only 8 of 21 best-practice handover strategies (76).

## **Gaps in research**

For all forms of knowledge transfer—institution to clinician, clinician to clinician or clinician to patient—significant questions remain unanswered. For example, what are the barriers to translating new research results into altered clinician behaviour, and how can they be overcome? What are the most effective knowledge management tools and practices to ensure that the content of clinical decision support systems is valid? What is the effect of decision support on actual outcomes, rather than just process measures? Specifically for 'infobuttons', how can reference resources be more optimally organized, indexed and linked to specific information deficits? With respect to handovers, what are the minimal requirements for effective transfer of knowledge from clinician to clinician and clinician to patient? How can the communication sciences, which address beliefs and misunderstandings in oral, written and electronic messages, be applied in health care to make handovers less error-prone?

Because of the differences in available resources and technological infrastructure between developed and developing countries, it should not be assumed that the answers to these questions are the same in all circumstances.



Research findings in one setting must be validated in the other before they are transferred and applied globally.

## 18 Devices and procedures with no human factors

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Human factors engineering, also known as ergonomics or 'usability engineering', is an important means of understanding the hazards of medical care and how to reduce those hazards. As problems with the design of equipment and procedures in both hospitals and clinics contribute to adverse events, increasing appreciation of design problems and how they could be remedied is important for ensuring patient safety.

Other industries in which safety is critical, such as aviation and nuclear power, have reduced design hazards by focusing on human factors engineering, namely, the interaction between technology, people and the work context (18, 455). Over the past three decades, some attention has been paid to human factors in the health-care setting (19, 456–458), and empirical evidence for the potential benefits of applying human factors to medicine has increased in recent years (459, 460). Human factors engineering can be used to improve patient safety in a variety of ways, including checklists, forcing functions and better design of medical devices (461).

In applying human factors engineering to medical devices and procedures, it is important

to understand how the device will be used, with a clear understanding of the device users (e.g. patient, family member, physician, nurse, professional caregiver), typical and atypical use, device characteristics, characteristics of the environments in which the device will be used and the interaction between users, devices and the use environments (462). Next, ways in which the devices could constitute hazards should be identified, analysed and tested. Once hazards have been identified, they should be addressed by modifying the device–user interface (e.g. control or display characteristics, logic of operation, labelling) or the users' capacity to use the device (e.g. training, limiting use to qualified users) (463).

The principles of human factors engineering include consistent design of controls and displays, readable and understandable warnings and labels, and fail safe design which lead to intuitive device operation and improved situational awareness. The United States Food and Drug Administration has a website describing the importance of human factors engineering in medical devices: <http://www.fda.gov/cdrh/humanfactors/index.html>.

### Examples of research and application

Human factors engineering can be used in many ways to address patient safety in clinical care: teaching and raising the awareness of health-care personnel about patient safety (464), investigating the causes of adverse events (78) and making decisions about procurements, such as choosing the least troublesome vendors (79). Human factors engineering can also be used to analyse integrated design issues involving architecture, devices and clinical procedures (77), for instance, in anaesthesiology (80) and more recently in surgery (81). Much of the literature on human factors engineering and medicine has direct implications for device companies but also for the design of protocols, work processes and paper or computer forms (82). Professionals in human



factors engineering and health care are forming partnerships to address complex devices, software and clinical care management (459, 465).

Human factors engineering can be used in design and redesign, which has implications for the interrelated interests of industry, regulators, standards groups and health-care providers. Standards groups for the medical device industry (e.g. the Association for Advancement of Medical Instrumentation in the United States) and regulators (e.g. Health Canada) have worked for years to understand the type and severity of medical device hazards. While much progress was made on hard engineering flaws (e.g. malfunction) and reducing biological contamination, use error has become a focus only recently (462). The literature in this area is mainly conceptual and provides general descriptions of how human factors engineering tools and principles can be used (466). Many design-related experiments are proprietary, although this situation is changing with new ways of sharing best practices (467).

Health-care organizations and academia have begun programmes to apply the ideas and methods of human factors engineering to the procurement of medical devices and software. The University Health Network and the University of Toronto in Canada have formed a Healthcare Human Factors Group to evaluate competing products before purchase (<http://www.ehealthinnovation.org/hhf>). In one example, seven pacemaker programmers were compared by the Group for several dimensions of usability before the purchasing decision was made (468). The Cognitive Engineering Research Group at the University of Queensland in Australia is also studying the attributes of medical devices from the point of view of human factors engineering. They have found that consideration of design issues in medical alarms can help in decision-making about cardiac monitors (469). Health-care organizations in the United States (and probably elsewhere in the world) are investing in human factors engineering testing sites, to ensure that

purchasing decisions lead to less error in the choice of products (e.g. Beaumont Technology Usability Center, Detroit, Michigan; <http://www.beaumontusability.com/>).

## Gaps in research

The research gaps in human factors engineering and patient safety have recently been summarized (470). The conclusions of a symposium on human factors and health care in 1974 are, however, still applicable today (456). Proposals for better reporting and analysis might be helpful, but reporting should be done carefully with a focus on human factors engineering. In general, it is more important to design and test methods and applications that can be used in the urgent, complex setting of health care.

Specific recommendations to fill research gaps include:

- finding the most efficient ways of rating human hazards in existing devices and device classes (not more reporting);
- identifying the most efficient human factors engineering tools for investigating the safety (e.g. root cause analysis) of devices for patients and prospectively assessing the risk associated with devices;
- finding effective human factors engineering processes to provide practical advice about hazards during procurement, also for developing countries where refurbished (older) equipment is often used;
- setting up interdisciplinary research and application centres of excellence for:
  - clinicians who seek human factors engineering expertise,
  - human factors engineers and
  - innovative research on special requirements of home care, miniaturization and integration with computing and telecommunication; and
- understanding the role of human factors engineering design in health care, including patient adherence, guideline implementation and decision-support systems.







# SECTION IV

## PROCESSES THAT CONTRIBUTE TO UNSAFE CARE

### 19 Misdiagnosis

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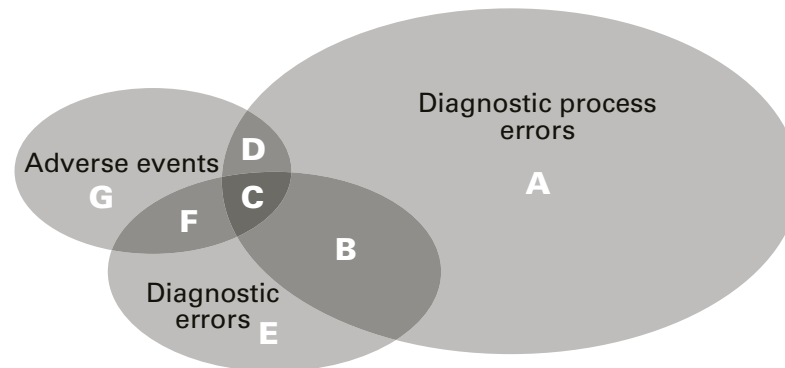
#### Scope and definition of the problem

The problem of misdiagnosis (incorrect diagnosis), delayed diagnosis and missed diagnosis (detected only at autopsy) looms large in both developed and developing countries. Even in the most highly developed countries with sophisticated technology, it has been conservatively estimated that 10–15% of diagnoses are erroneous (471). A review of three large series of malpractice claims showed that diagnostic errors are the leading cause of malpractice suits, comprising 26–58% of identified errors (472, 473).

Diagnostic errors are more difficult to study than areas of patient safety that are well defined, such as medication and surgical errors, because the 'error' is often distributed over time and place. It is easy, for example, to pinpoint exactly when and where a patient who is allergic to penicillin erroneously received the drug and had a fatal anaphylactic reaction or when the wrong limb was amputated, but defining when and how someone's cancer should have been diagnosed or determining whether a practitioner who mistakenly diagnosed malaria (in an area endemic for malaria) in a febrile child with bacterial sepsis has committed an error is more difficult (474).

While much research is needed to untangle and quantify these issues, a Venn diagram model (Figure 2) is suggested to represent the relations between errors in diagnostic process (which are relatively common although often of little consequence, circle A), missed, delayed or misdiagnoses (which may or may not result from a process error and may or may not be harmful to the patient, circle B) and adverse outcomes (which result only occasionally from a wrong diagnosis, circle C). Not only does such a scheme help sort out the issues and direct patient safety efforts towards preventable, consequential errors in diagnosis (within zone C), but it also avoids the narrowly directed impulse to blame practitioners solely because they arrived at a wrong diagnosis even though there is no harmful consequence (circle B, zone E) (475).

**Figure 2.** Relations between diagnostic process errors, misdiagnosis and adverse events



Adapted from reference 475

Group A, errors in diagnostic process (e.g. blood samples of two patients switched; physician does not examine a patient with abdominal pain physically); group B, error in diagnostic process with resulting misdiagnosis (e.g. wrong diagnosis because blood sample switched); group C, adverse outcome resulting from misdiagnosis due to error (e.g. patient given toxic treatment with adverse effect as a result of switched samples; failure to diagnose appendicitis because of failure to examine abdomen, with resulting rupture and patient death); group D, harm due to error in diagnostic process (e.g. colon perforation during colonoscopy on wrong patient); group E, mis-, delayed or missed diagnosis but no error or care and no harm (e.g. incidental prostate cancer found at autopsy); group F, adverse event due to misdiagnosis but no identifiable process error (e.g. death from acute myocardial infarct but no chest pain or other missed symptom); group G, adverse event unrelated to misdiagnosis or delay or error in diagnostic process (e.g. death due to correctly diagnosed disease complication or unpreventable drug reaction, such as penicillin anaphylaxis in patient who has never been exposed)

An important issue in thinking about diagnostic errors, and particularly assessing similarities and differences between diagnostic errors in developed and developing countries, is the role of diagnostic testing. Testing issues include access to and availability of tests, appropriateness of testing resource allocation and available technology in different settings, regulation and monitoring of test quality, expertise and training in test performance, interpretation and follow-up, as well as appropriate selection of tests for particular patients, situations or populations (476). It would be pointless to fault a village health worker working in a setting with no electricity or microscope for overdiagnosing and overtreating patients with fever as malaria (see below) or for missing a lung or liver tumour detectable only by computed tomography scanning (477). The real power of the patient safety movement has been to look beyond blaming individual practitioners for inevitable errors to identifying how the reliability and accuracy of diagnosis can be improved in ways that do not necessarily depend on more technology and resources.

## Nature and magnitude of diagnostic error

To illustrate ways in which diagnostic problems can most productively be identified and overcome, six areas in which progress can and should be made have been chosen as examples.

### 1. Misdiagnosis of major infectious diseases in developing countries

*Malaria* is the most important parasitic disease worldwide, causing an estimated 1.5–2.7 million deaths annually (478). In both developing and developed countries, misdiagnosis of malaria remains a serious problem. Little information is available on underdiagnosis, but it probably represents a substantial burden in endemic countries. Its consequences are obvious, as patients can die of this highly curable disease. Underdiagnosis of malaria can also be a problem in developed, non-endemic countries, where practitioners' lack of familiarity with or failure to suspect this disease can lead them to miss imported cases

(479). For example, in Canada, 59% of cases of malaria were missed on first presentation, and in the United States, fatal malaria was not diagnosed in 40% of patients at first presentation (479). Overdiagnosis is also a problem, as other conditions are overlooked, and individuals with a wrong diagnosis of malaria are exposed to unnecessary side-effects of drugs. Overreporting of malaria incidence leads to underreporting of diseases with symptoms similar to malaria, and, perhaps most seriously, overdiagnosis and overtreatment contribute to higher rates of resistance to malaria drugs and misallocation of resources (480).

One-third of the world's population is latently infected with the *tuberculosis* bacillus, and this treatable disease kills nearly 2 million people annually, many because of lack of diagnosis or treatment (481). The rates of underdiagnosis of tuberculosis are difficult to estimate because of the huge numbers of infected patients, the various organ systems affected, the diverse spectrum of clinical manifestations of the disease and the large numbers of cases that are undiagnosed *ante mortem* but are not examined *post mortem*. There have been many reports of cases of pulmonary, spinal, gastrointestinal, central nervous system, cutaneous and miliary tuberculosis that were initially misdiagnosed and sometimes found only at autopsy (482–484). In one study of the diagnosis of tuberculosis in public hospitals in New York City, patients had no better than a '50–50 chance' of a correct diagnosis during their initial hospitalization (485). A report from Ho Chi Minh City, Viet Nam, documented an average delay of more than 2.5 months, and 58% of patients presented to physicians who initially failed to diagnose this clinically critical disease correctly (486).

More than 80% of cases of infection with *HIV* are undiagnosed; even in the United States, one-fourth of the more than 1 million people with HIV infection are unaware of their diagnosis (487). While this could be construed as a public health failure, many persons with HIV infection are in

contact with the health-care system, so that the inability of that system to recognize, educate and screen the vast numbers of infected persons represents a failure of the system as well. Trivial in comparison numerically, although devastating in their consequences, are isolated case reports of uninfected patients erroneously given a diagnosis of HIV infection, usually as a result of a misinterpreted result or other laboratory, technical or clerical error (e.g. the specimens of two patients mixed up) (488–490). Precise categorization of diagnostic error in this disease is further complicated (as for other infectious and noninfectious diseases) by the fact that tests for HIV are not 100% specific and sensitive and the results depend on the timing of the test in relation to infection. Fortunately, current HIV tests are more accurate, with lower rates of false-positive and false-negative results than many other diagnostic tests.

This focus on failures of HIV testing does not include other diagnostic errors for AIDS, such as patients presenting with syndromes that mimic other diseases; neither does it include the erroneous attribution of symptoms in an AIDS patient to HIV, missing a different, potentially treatable condition or complication (491–493). While such situations are probably less common, there is virtually no published information. Studies are needed to gauge the prevalence, patterns and means of preventing such diagnostic failures.

## **2. Failure of timely diagnosis in life-threatening medical, surgical and trauma emergencies**

A variety of critical conditions require urgent diagnosis so that rapid intervention can prevent more severe morbidity and mortality. These diagnoses cover a number of specialties, age groups and types of interventions and include acute appendicitis and other causes of acute surgical abdominal emergencies (such as gangrenous bowel obstruction or perforation); obstetrical emergencies (such as ectopic pregnancy); neurosurgical emergencies (such as



subdural haematoma) and spinal cord compression (e.g. due to epidural abscess, tumours and haematomas); vascular emergencies (thoracic or abdominal aortic dissection); and various necrotizing soft-tissue infections. Some of the published evidence suggests shockingly high rates of diagnostic error and delay, estimates ranging from 5% to up to 70% of cases (475). Timely diagnosis is, however, unhelpful in many instances unless it is linked to access to life-saving care, further complicating this paradigm, as surgical and trauma services are often limited in developing countries, and, where they are available, there is often poorer access in rural than in urban settings (494, 495).

### **3. Delays in diagnosis and misdiagnosis of cancer**

Given the rising incidence of cancer worldwide, the evidence for better survival from various cancers when they are diagnosed at an early stage (496–498) and the clinical, technical and organizational challenges in diagnosing cancer, it is not surprising that minimizing errors and delays is an important priority for patient safety (499). While controversies about the role of and strategies for cancer screening complicate discussion of this problem, there is unfortunately compelling evidence of shortcomings and errors resulting in unacceptably long delays in diagnosis for patients who present with cancer symptoms. For example, in one British hospital, the mean time after patients' first presentation until surgical treatment for lung cancer was 109 days, due largely to 'inefficiency and delays' in the diagnostic process (500). In a Finnish study of lung cancer, the median 'symptom-to-treatment' delay was nearly 4 months, due largely to delays in diagnostic logistics (501). In a study in the United States of 250 malignant neoplasms found at autopsy, 111 had been either misdiagnosed or undiagnosed, and the cause of death in 57 of the cases was judged to be related to the misdiagnosed cancer (502). In other studies, cancer was the diagnosis that led to 59% (106 of 181) of outpatient malpractice

claims, breast and colorectal cancers being most often involved (472, 503).

### **4. Errors in interpreting radiology images, pathology specimens or skin lesions**

While diagnostic errors are encountered in every medical specialty, they can be studied most easily in fields such as radiology, pathology and dermatology, because the actual diagnostic material can be re-reviewed by other observers, uncovering errors and allowing discrepancy rates to be measured. The overall rates cited generally range from 2% to 5% missed or misdiagnosed, although a rate of 10% was recently reported (504). A classic, often tragic example is misdiagnosis of cancer, either false-positive or false-negative, both being associated with potentially devastating medical, psychological and legal consequences. The rates of misdiagnosis identified by re-reading pathology slides in several studies at major teaching institutions ranged from 1.4% to 5.8% (505, 506). A large multi-institutional study showed a 5.3% rate of errors that had a 'moderate or marked' impact on patient care (504). A study of X-rays read by emergency medicine physicians when a staff radiologist was unavailable and later re-read by a radiologist showed error rates in up to 16% of plain films and 35% of cranial computed tomography scans (507). Misreading of pathology slides, X-rays and other such tests can be related to training and interpretive skills or to factors such as the quality of the specimens or images (508), production pressure and other factors (as discussed elsewhere in this report).

### **5. Cognitive failures in making the correct diagnosis**

Human reasoning is susceptible to predictable errors, and most people make certain mistakes repeatedly (509–511). Psychological studies and studies of human factors show that individuals can be misled by a variety of situational constraints and cognitive biases, in ways that can cause them to overlook a correct diagnosis or fix on one that is incorrect. Many aspects of this



problem and possible remedial strategies have been explored in the medical and non-medical literature. Biases such as anchoring (one form of which is premature closure, which is a tendency to focus on one diagnosis that appears to explain all the symptoms and therefore stop considering other possibilities), availability (unconsciously placing disproportionate weight on a rare but recently encountered, vividly recalled diagnosis, such as one that the clinician recently missed) or confirmation (tendency to seek information that confirms a preconception of the diagnosis and to ignore or undervalue evidence that does not support the preconception) (512, 513). A study of 90 cases of suspected diagnostic errors in internal medicine identified 320 cognitive errors in relation to 74 patients. In this study and others, most of the diagnostic errors were multifactorial, cognitive errors often being associated with system problems, which also contributed to the errors (475, 513, 514).

## **6. Reliable follow-up of critical diagnostic test results**

This area is perhaps that in which the most productive and concrete steps can be taken to improve diagnosis. It is dealt with in a separate section of this report.

## **Possible interventions**

Although there is no shortage of advice on ways to minimize diagnostic error, no randomized trials of successful interventions were found. In a study of malpractice claims for missed or delayed diagnosis in an ambulatory setting, Gandhi *et al.* concluded that each diagnostic error represents numerous system and latent failures, indicating that complicated, multifaceted interventions are needed (472). In both developed and developing countries and health-care systems, practitioners try, at times against great odds, to diagnose their patients' problems and diseases, but the practical interventions that can best advance this essential health-care function remain to be identified.

General approaches that have been proposed by experts and that common sense suggests might bring about improvement are listed below, although these ideas must be tested in both small-scale, local projects for rapid improvement (515) and in more rigorously designed trials.

### **Better infrastructure for feedback and calibration of diagnostic decisions**

How often, when an incorrect diagnosis is found and a correct diagnosis subsequently made, does the practitioner who initially saw that patient have the opportunity to learn about the mistaken diagnosis? Even when this does occur, the feedback is rarely given in a systematic, timely or optimal fashion for learning (475). Post-mortem examinations used to serve this function, but only for the small numbers of fatal cases; furthermore, in most countries, autopsies are now rarely performed. Care delivery systems should be redesigned to provide feedback, so that both clinicians and institutions can learn systematically. Formal feedback mechanisms for laboratory quality control created by pathologists could serve as models for such change (504, 516).

### **Create and enhance 'blame-free' venues for case review and improvement**

Every health centre, laboratory, hospital and training programme needs better mechanisms for reviewing and discussing diagnostic errors. Particularly because of the multifactorial, complex nature of diagnostic problems, such discussions are essential, both to draw the correct conclusion and to understand system failures. Feedback surveillance mechanisms that support learning should be combined with personally engaging cases to bring about curiosity, learning and change (517).

### **Strategies to minimize harm from errors**

Because of the complexity of diagnosis and the inevitability of human error, paying more attention

to ensuring that patients are not harmed even when mistakes occur might be the best means to protect them. Simple measures, such as involving patients in follow-up (especially if they are not responding or improving as expected), soliciting second opinions when uncertainty or risks are greatest, or creating back-up systems to identify overlooked abnormal laboratory test results are essential (518).

### **Disease-specific measures**

Measures are needed to quantify the rates, types and causes of errors in particular diagnoses and interventions in order to target weak links in the chain of events. What are the common pitfalls in diagnosing the disease, and how can recurring errors be overcome? What high-risk, critical diagnoses should be targeted? Are there simple, cost-effective tests that could be used at a particular point of care to overcome the existing limitations of diagnostic testing?

### **Leveraging information technology to overcome human memory and communication limitations**

Health workers in poorer countries can now access up-to-date information of the highest quality via Internet textbooks and references. One example is a website set up by a physician in India, Dr Kakkilaya, on pitfalls in diagnosing malaria (519). Other online resources include expert diagnostic aids, such as validated questionnaires and prediction instruments (e.g. questionnaires based on symptoms and signs), some of which can approach the accuracy of laboratory diagnostic tests (520, 521). Expert telemedicine diagnostic consultations can in theory now be made for patients in even the remotest villages of the world. It should also be possible to use information technology to track patients more effectively, document findings, construct differential diagnoses, match patterns (e.g. skin lesion, symptom complex) and give reminders of questions or laboratory results to be followed-up. Online information technology

can also help in collecting a patient's records, test results, diagnoses and assessments from earlier visits more easily and reliably and even identify exposures and other risk factors (522). Many of the potential solutions in this domain require additional testing, however, as few have been proven to be effective.

### **Cognitive training and better tools to arm practitioners against well-known pitfalls in diagnostic reasoning**

'Metacognition' training is advocated by people such as Crosskerry, who, as discussed above, focus on the mental processes involved in diagnostic decision-making and error (523). They postulate that increased awareness of hazards can help prevent clinicians from blindly falling into traps. It will be important to determine whether such training can create general knowledge and behaviour to overcome the wide array of diagnostic errors (and hence have a potentially broad impact) or would be most valuable if applied to particular diagnostic situations in which biases have been shown to adversely affect thinking and outcomes.

## **Gaps in research**

Large gaps exist in current knowledge about the role of misdiagnosis in adverse events and unsafe patient care in developing countries. One of the most critical is the extent of underdiagnosis of important diseases and the extent to which that contributes to the burden of illness. Other important areas for developing countries and those with economies in transition are to determine which conditions are underdiagnosed or undertreated and the impact on patients' lives and well-being.

In developed countries, there have been a few studies on the role of information technology in reducing misdiagnosis, especially as these systems become more sophisticated and provide more feedback to clinicians. It is also unclear

what kinds of training physicians and nurses need to improve their diagnostic capability.

## 20 Poor test follow-up

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### Scope of the problem

The rates of test follow-up remain suboptimal across the globe, resulting in serious lapses in patient care (83). In developing countries, the rates of follow-up of testing for infectious diseases are variable. A study in the Central African Republic in 2002 showed that a high percentage of persons (89%) returned to obtain the results of HIV testing, consistent with previous reports from West Africa, East Africa and South Africa, perhaps stemming from a strong motivation to seek testing and counselling (524). In Abidjan, Côte d'Ivoire, women who tested positive for HIV were three times more likely to fail to return for their test results than women who tested negative, consistent with reports from Kenya and Rwanda but in contrast to the results of studies in industrialized countries, where no difference was reported (525).

In developed countries, numerous lapses in follow-up of test results have been reported, in both inpatient and outpatient settings. A retrospective evaluation of critical laboratory test results for inpatients showed that the median time to appropriate treatment was 2.5 h, over 25% of treatment being delayed by at least 5 h (526). Another study showed that only 51% of laboratory results indicating potentially

life-threatening conditions were followed-up by appropriate treatment (527). The problem extends to the transition between inpatient and outpatient care. One survey of primary-care providers of patients discharged with potentially actionable test results showed that 61% of the test results had not been forwarded to the provider, although 37% required outpatient follow-up and management (528).

Evaluation of the follow-up of outpatient test results pertains mostly to cancer screening, because of the strong benefits of early detection for survival and because missed diagnoses of cancer are the commonest cause of litigation (472). Several studies showed that 18–39% of women failed to receive recommended short-term follow-up after an abnormal mammogram (529–531). The rate was as high as 60% among medically underserved ethnic minority women with low incomes (532); and, in a study in Connecticut, United States, pain during the mammogram and lack of a usual provider were significant independent predictors of inadequate follow-up among African-Americans (531). Another study showed that lower estimated household income and no previous mammogram were predictors of inadequate follow-up (531). Poor patient comprehension of the results of mammograms and cervical smears and of the resulting recommendations was also found to be a significant barrier (533, 534). In one study, 87% of women with inadequate follow-up of mammogram results reported that they had been notified of their results (531).

Patient and provider perspectives and expectations with regard to the communication of test results also play a significant role. In a survey of clinical physicians, 17–32% reported that they had no reliable method for ensuring that test results had been received, even though they spent an average of 74 min per day managing test results (533). As a result, one-third of the surveyed physicians reported that they did not always notify patients of abnormal results (534). The surveyed patients reported that they did not

usually discuss their preferences for notification with their providers (535). Many studies have shown, however, that patients prefer to receive notification of both normal and abnormal test results, with recommendations for management after abnormal results (536–543).

Developing countries face a number of additional barriers to the communication of test results, such as delays in test processing due to a scarcity of adequate laboratory resources, lower rates of correct specimen collection because of lack of training, and delays in communication of results from laboratories to providers due to poor methods of communication. The lack of reliable or regular means of direct communication with patients at home by post or telephone (544) further exacerbates this problem. In such settings, more emphasis is placed on rapid testing, so that clinicians can convey test results to patients and give therapy at the same clinical encounter.

## Severity of the problem

The consequences of poor test follow-up are substantial. Delayed or incomplete follow-up after abnormal screening results can compromise the effectiveness of breast cancer screening programmes (545). A meta-analysis of 87 studies in various countries in 1999, comprising over 100 000 breast cancer patients, showed that women who had experienced a delay of 3–6 months between symptom identification and start of treatment, representing both patient and provider delays, had a 12% lower 5-year survival rate than women with a delay of less than 3 months (546). Poor follow-up of tests for other malignancies and cardiovascular disease are probably important causes of higher rates of morbidity and mortality from these conditions than would be necessary, although quantification of the impact of poor test follow-up is still in its infancy. Poor test follow-up is also a major contributor to litigation, as one-fourth of diagnosis-related malpractice suits have been

attributed to avoidable failures in the follow-up system (84).

## Possible interventions

Improving test follow-up requires a multifaceted approach, including empowering patients to take a more active role. In most parts of the world, however, empowering patients would require a major culture shift and, even in the developed world, such a culture shift has been slow in coming. Therefore, most of the interventions in this area focus on practitioners.

In the developing world, significant barriers to communication have resulted in the use of rapid laboratory tests, which allow clinicians to perform the tests, discuss the results and form a plan with the patient at the same clinical encounter. Examples of such innovations include rapid HIV testing, rapid cervical cancer screening and rapid tuberculosis testing (547–549). Not all tests can be performed rapidly, however, and communication between the source laboratory and physicians, documentation by physicians and communication between physicians and their patients should be improved. Recent studies have addressed physician-centre barriers, such as use of electronic health records, Internet access and improved communication with laboratories, but little has been done to evaluate communication of test results between physicians and patients in remote areas (550).

A number of interventions in the developed world have been shown to improve test result follow-up and compliance with follow-up recommendations. For example, giving the responsible physician critical test results for inpatients directly resulted in a 38% shorter median time for ordering the appropriate treatment (526), and electronic mail alerts have been shown to reduce the time for adjustment of doses of medications with toxic renal effects (551). A meta-analysis showed that cognitive interventions, such as education of patients

about abnormal results through interactive telephone counselling, were effective, improving compliance by 24–31%, and that behavioural interventions such as patient reminders increased follow-up by 18% (552). Direct posting of mammography results to patients resulted in a significantly smaller number of patients who were dissatisfied with the communication of test results (553). Studies evaluating follow-up of cervical smear testing showed significantly improved follow-up rates after telephone reminders, an education programme with slides and tapes and vouchers to pay for transport to receive follow-up (554, 555). Transport incentives had the strongest effect among patients who were socioeconomically disadvantaged or lacked health insurance (555).

Health information technology, such as automated systems to track test results, can provide solutions. In a survey of physicians, over 90% of respondents considered that such a system would be useful (534). Most systems have been used for inpatient care, such as delivering abnormal laboratory values to the ordering physician's pager (556, 557) or providing reminders after the physician has viewed a patient's chart, which has been shown to reduce the time to appropriate withdrawal of medications (558) and ordering other recommended therapies (557). Systems specifically designed for managing outpatient test results (559) have been shown to improve patient satisfaction with the communication of test results.

One of the most important interventions must be to change the culture and expectations regarding test result follow-up. The responsibility for communicating test results should be clearly delegated, with emphasis on the ordering provider, as there are numerous means to help providers give higher-quality, more efficient delivery of results to patients. In addition, patients should clearly discuss their preferences and be willing to contact their provider directly if they do not receive their test results in a timely fashion.

## Gaps in research

There are a number of outstanding research questions with regard to the communication of test results to patients. First, further work is needed to evaluate social and clinical workflow interventions that could increase the proportion of patients who return to discuss the results of tests that cannot be performed at the same visit. Also, the communication of test results to patients by remote means should be evaluated as a means of reducing the need to return to the clinic to discuss follow-up. In addition, techniques for rapid testing, which allow communication of test results at the same visit, should be evaluated.

All countries could benefit from sophisticated clinical information technology systems, which can ensure that every abnormal clinically significant result has a clear, documented follow-up plan. Future work should focus on identifying communication infrastructure needs in various environments to determine which interventions would be most effective. Identification of the types of test results that are most likely to be inadequately communicated to patients could provide direction and focus for ways to circumvent barriers and educate clinicians.

## 21 Counterfeit and substandard drugs

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### Scope of the problem

Counterfeit and substandard medicines are a serious, pervasive problem throughout the

world. Counterfeit drugs are those 'produced with an intention to cheat', which can include mislabelling, missing or wrong active ingredients or insufficient quantities of a correct ingredient. Substandard drugs are 'genuine medicines produced by legitimate manufacturers that do not meet the quality specifications that the producer says they meet'; their production 'may not be an intention to cheat, but may be due to problems with the manufacturing process' (86).

Counterfeit drugs account for more than 10% of the global medicines market in both industrialized and developing countries (85). In poor countries, it has been estimated that up to 30% of the medicines consumed are counterfeit or substandard, although this proportion varies from country to country (85, 87). In Peru, for example, the Ministry of Health estimated that illegal or counterfeit medicines accounted for 20% of the local market (85). Poor-quality drugs have been widely reported in Africa, Asia and Latin America, often where there is a weak drug regulatory system (560). In developing countries, most of the counterfeited medicines are those used to treat life-threatening conditions, such as malaria, tuberculosis and HIV/AIDS (85). The situation does not appear to be improving. In the Democratic Republic of Congo, antidepressants are sold as antiretroviral drugs, which is especially worrying given that the overall prevalence of HIV infection among adults 15–49 years old is about 5% (561). The appearance of counterfeit malaria medications is also increasing in Cambodia, the Lao People's Democratic Republic and Viet Nam (562). Additionally, drugs that are banned in industrialized countries often continue to be manufactured and sold in countries such as India (563).

In contrast, the most frequently counterfeited medicines in wealthier countries are new, expensive lifestyle drugs, such as hormones, steroids and antihistamines (85). In early 2006, the Netherlands, the United Kingdom and the United States all experienced issues with a

counterfeit influenza remedy (85). Today, Viagra is one of the most widely counterfeited drugs in the developed world (85), and it has been estimated that 50% of all Viagra sold online is fake (564). Other counterfeited pharmaceuticals found in developed countries include such drugs as Lipitor, Procrit and Epogen (565–567), which are often purchased from vendors abroad and then imported. A customs laboratory in the United States found that 67% of drugs sampled from parcels in the post had not been approved by the Food and Drug Administration or had been withdrawn from the United States market for safety reasons; 5% contained no active ingredient, and 28% contained controlled substances prohibited from importation (568). Increasing numbers of medicines are being counterfeited, including expensive anti-cancer drugs and antiviral drugs. The Center for Medicines in the Public Interest in the United States predicted that the income generated by sales of counterfeit drug would reach US\$ 75 billion globally in 2010, an increase of over 90% from 2005 (85).

Drug counterfeiters are a loosely organized group of people who work in the shadows of the legitimate pharmaceutical industry. In the developed world, the pharmaceutical industry and wholesalers have made it more difficult for counterfeiters to get their products into the distribution system, but drug counterfeiters have developed alternative systems, through a global network of Internet pharmacy operations, mail systems and credit card financial institutions, to deliver counterfeit drugs to consumers at home. Deceptive websites are often nearly identical to authentic primary sites, and many consumers cannot discern between the authentic and the rogue sites. The dangers of counterfeit drugs have been exacerbated by the counterfeiting of active ingredients. Verifying the authenticity of the active primary ingredient has become a serious problem for the pharmaceutical industry since recent events in which key ingredients were diluted or contaminated.



## Severity of the problem

Counterfeit and substandard drugs pose a serious health risk, as repeated use of such medicines can result in therapeutic failure, drug resistance or even death (85). For example, access to high-quality antimalarial drugs is crucial for the safe treatment of malaria (560), and it has been estimated that, if malaria medicines were effective, of better quality and used properly, as many as 200 000 of the 1 million deaths that occur from malaria annually could be prevented (85). Another example of the adverse effects of poor monitoring of drug quality is the epidemic of meningitis in Niger in 1995, where over 50 000 people were inoculated with fake vaccines from another country and 2500 people died as a result (85). In 1999, counterfeit antimalarial agents killed at least 30 people in Cambodia (85). Paracetamol cough syrup prepared with a toxic chemical resulted in 89 deaths in Haiti in 1995 and 30 infant deaths in India in 1998 (85).

Recently, highly toxic diethylene glycol was mixed into 260 000 bottles of cough syrup in Panama, leading to hundreds of deaths, especially among children, and similar poisoning events occurred in Argentina, Bangladesh, Haiti and India. In this case, diethylene glycol, much of which was made in China by counterfeiters, was added instead of glycerine.

## Possible interventions

Several measures can be taken to limit the number of counterfeit and substandard drugs on the market. Factors that encourage the counterfeiting of drugs include the absence of deterrent legislation, a combination of high demand for a medicine and low production costs, poverty, the lack of an official supply chain, high cost of the legitimate drug, and the fact that the drug can be produced in small cottage industries (85). At the international level, consistent, systematic efforts are needed; at the national level, structures such as competent national drug regulatory authorities with the

necessary resources to control the manufacture, importation, distribution and sale of medicines are needed (85). Trade in counterfeit medicines is more prevalent in countries that have weak drug regulation and enforcement, scarce or erratic supplies of basic medicines, unregulated markets and unaffordable prices (85). In the United Republic of Tanzania, one explanation for the presence of substandard malarial drugs may be the inexperience of the national drug regulatory enforcement body; therefore, collaboration with academic institutions involved in pharmaceutical research is encouraged in order to increase expertise and technical support (560). Implementing routine quality testing of drugs throughout the drug supply chain might be effective. Additionally, examples of successful national regulation should be studied. In China, for example, the State drug administration closed 1300 illegal factories and investigated cases of counterfeit drugs worth US\$ 57 million in 2002 (85).

Collaboration between national and international organizations will be crucial. WHO has created an International Medical Products Anti-counterfeiting Task Force to disseminate information and devise strategies to combat counterfeit drugs worldwide. Other organizations should continue to promote rigorous structures, such as strengthening pharmaceutical legislation and improving processes by promoting good manufacturing practice. In 2005, WHO's Western Pacific Regional Office established the first web-based system to track the activities of drug counterfeiters; WHO plans to extend this system to other regions (85).

Additional measures that have been taken include providing simple, inexpensive markers of authenticity and educating patients and health-care workers (85). For example, the Peruvian Ministry of Public Health has begun education campaigns to persuade people to purchase medicines only at registered pharmacies (85). Other potential solutions include improving inspection at all steps of the drug distribution



chain and regular testing of local and imported products (569). In Nigeria, the National Agency for Food, Drug Administration and Control has banned imports from 30 countries and maintains inspectors in importing countries to ensure that drugs entering Nigeria meet the required standards (85).

Technology should also play a role; for example, health information systems are essential for monitoring the safety of vaccines, especially in developing countries (570). Other new techniques, which vary in sophistication and cost, include simple colorimetric assays to identify fake antimalarial agents, radio-frequency identification and bar codes to track drugs, holograms and watermarks to authenticate packages and tamper-resistant packaging tape (85).

## Gaps in research

In 2001, WHO established a prequalification project to facilitate access to drugs for HIV/AIDS, malaria and tuberculosis that meet unified standards. As part of the prequalification process, a manufacturer must provide comprehensive data about the quality, safety and efficacy of the product and open its manufacturing sites to inspectors, who can assess compliance with WHO Good Manufacturing Practice in order for the product to be included in the prequalified products list (571). It will be important to determine the extent to which this project has affected the supply of unsafe or counterfeit medications.

Critical questions from the developing world include understanding which regulatory mechanisms are most effective for reducing the number of substandard drugs and whether other solutions exist to reduce the harm from substandard drugs.

# 22 Inadequate measures of patient safety

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## Background

Patient safety measures are universally inadequate (90). Even in countries that have fundamental health-care delivery systems, patient safety has encountered several barriers. First, creating a common nomenclature has been difficult (572). Second, experts advocate various approaches to improving patient safety and to the factors that should be measured: some advocate reducing all medical injuries, while others suggest focusing on preventable medical errors (573, 574). Third, there is a lack of evidence about many patient safety practices that are commonly believed to be beneficial (14, 575).

Despite these obstacles, there are increasing efforts to create and validate patient safety measures. Zhan *et al.* stressed the importance of classifying and designing such measures within each of Donabedian's domains—structure, process and outcomes (572). Countries in the Organisation for Economic Co-operation and Development selected 21 measures for gauging patient safety in their health systems (Table 3) (576), although all those selected were outcome measures.

Some state-of-the-art patient safety measures in each of Donabedian's domains and their potential application internationally are described below. Several conventional techniques, such as voluntary reporting, morbidity and mortality conferences, autopsies, manual chart review

and malpractice litigation review, are often prohibitively expensive or have poor sensitivity for detecting adverse events and are therefore not covered (577). As there is overlap between the health-care domains of quality and safety, measures specifically related to patient safety are described and more general quality measures, such as risk-adjusted mortality rates, are not.

## Patient safety measures

### Structure

As in other industries, safety events in health care are considered to be due primarily to system failures. Thus, several surveys have been made of the safety 'climate' in different health-care settings (90). Nine surveys were recently reviewed and were found to have identified five common dimensions: leadership, policies

and procedures, staffing, communication and reporting (578). Some of the surveys are applicable to any health-care setting, while others focus on specific departments (e.g. pharmacy). Better performance in some instruments, such as the safety attitudes questionnaire, is associated with better outcomes (shorter stay, fewer medication errors, lower ventilator-associated pneumonia rates and lower bloodstream infection rates) (367, 579); however, it is unclear whether interventions for improving the safety culture lead to better outcomes.

The safety attitudes questionnaire has been translated into numerous languages, including Chinese, Dutch, French, German, Greek, Portuguese and Spanish. Research in those countries demonstrated a clear correlation between safety performance and safety attitude, supporting the measure's cross-cultural validity

**Table 3.** Health-system level safety indicators selected for use by members of the Organisation for Economic Co-operation and Development

Area	Indicator
Hospital-acquired infection	Ventilator pneumonia
	Wound infection
	Infection due to medical care
	Decubitus ulcer
Operative and post-operative complications	Complications of anaesthesia
	Postoperative hip fracture
	Postoperative pulmonary embolism or deep venous thrombosis
	Postoperative sepsis
	Technical difficulty with procedure
Sentinel events	Transfusion reaction
	Wrong blood type
	Wrong-site surgery
	Foreign body left in during procedure
	Medical equipment-related adverse events
	Medication errors
Obstetrics	Birth trauma, injury to neonate
	Obstetric trauma, vaginal delivery
	Obstetric trauma, caesarean section
	Problems with childbirth
Other care-related adverse effects	Patient falls
	In-hospital fractures

(580). When translating a safety survey, countries should consider the setting for which the survey was designed (e.g. inpatient, pharmacy), reliability testing of individual questions and ensuring that the intended meaning of the questions is preserved.

## Process

The National Quality Forum in the United States, comprising over 260 groups, has identified 30 evidence-based safety practices for improving patient safety in hospitals (581). Some of the practices involve structure, such as safety culture, staffing and medication storage; however, most involve processes of care, such as the participation of a pharmacist in medication prescription, recording of verbal orders, use of standardized abbreviations and use of computerized physician order entry. The Leapfrog Group, a coalition of purchasers in the United States, has attempted to spread use of these practices by reimbursing hospitals that implement them and has graded hospitals according to their implementation of each of the safety practices. Although the Leapfrog Group surveys only hospitals in the United States, hospitals in other countries could improve their use of the patient safety practices outlined by the National Quality Forum. Countries can choose to create their own surveys or audit hospitals and grade them on the basis of their performance within each domain.

The Surgical Care Improvement Project in the United States is a partnership of several health-care organizations whose aim is to reduce complications of surgery (582). Within the Project, processes for preventing postoperative infection, venous thromboembolism, cardiac events and respiratory complications are measured. Although the processes were selected by experts, it is not known whether better compliance with these processes is associated with fewer complications. Developing countries and those with economies in transition might

have difficulty in measuring implementation of the processes, as this requires adequate nursing and information.

## Outcomes

Computerized rules or triggers to screen for adverse events have become increasingly popular, as they are relatively inexpensive and lead to identification of many more events than voluntary reporting (92). *International Classification of Diseases and Causes of Death*, 9th revision (ICD-9) codes, Current Procedural Terminology codes and data from pharmacies and clinical laboratories have been used in automated detection. The Institute for Healthcare Improvement in the United States has been a pioneer in the development and use of automated triggers to detect adverse medication events, adverse events in medical care and events in intensive care units (583). Bates *et al.* concluded from a review that computerized techniques for identifying adverse events, drug events and health care-associated infections are sufficiently developed for broad use (92). This is probably true for most developed countries, and other countries might also benefit from trigger tools, provided they have adequate data sources. Table 4 lists some of the triggers commonly used in automated detection tools.

Although most triggers have been designed for hospital use, several that rely on pharmacy and laboratory data have been used in ambulatory care. Providers who use electronic medical records also have sophisticated screening tools for analysing physicians' notes and discharge summaries to detect adverse events (584). These tools are useful only in countries with electronic medical records.

Patient safety indicators are special automated trigger tools based on billing data from hospital discharges to identify potential preventable adverse events (585). They involve use of ICD-9 codes, demographics, length of stay, vital status

at discharge and other variables to identify medical, surgical and obstetrical complications. They were created by the Agency for Healthcare Research and Quality in the United States to help hospitals identify the causes of disease and to improve internal quality. Many of the safety indicators selected by OECD countries (Table 3) are based on patient safety indicators. Most of the indicators are derived from prior work (586, 587). They have not yet been validated extensively, although they have been found useful in several studies for estimating rates, identifying risk factors and tracking trends in inpatient safety events (91, 588). The Veterans Health Administration in the United States has modified and used patient safety indicators (589, 590), and many developing countries and those with economies in transition, particularly those in which ICD-9 codes are used, could easily modify and use these indicators.

The adverse outcomes index is a composite measure of obstetrical safety, calculated as the percentage of deliveries with one or more adverse events (591). Complications are identified from administrative data and include maternal death, uterine rupture, maternal admission to an intensive

care unit, birth trauma, blood transfusion and third- or fourth-degree tear. The index was created by a panel of experts, but it has not been validated. Further, it has several limitations: there is no mechanism to adjust for the severity of illness, and some practices identified as complications probably represent appropriate clinical practice in a particular situation (e.g. blood transfusion or transfer to an intensive care unit). In its current state, the measure might be most useful for identifying hospitals with extremely high or low event rates. After validation, it could be used in other countries, as it is based on administrative data.

### Gaps in research

Patient safety measures are still in an early stage of development. There are currently few tools that could be used easily and in all health-care settings. Given the paucity of existing tools, more instruments should be created and validated, and existing measures should be refined and further validated.

Many patient safety practices, such as those endorsed by the National Quality Forum, are based on some evidence or have expert

**Table 4. Examples of automated triggers for detecting adverse events**

Type of alert	Automated trigger *	Potential adverse event
Medication use	Use of Flumazenil	Overdose of a benzodiazepine
	Use of Naloxone	Overdose of a narcotic
	Use of anti-diarrhoeal agents	Medication induced diarrhoea
Laboratory	Partial thromboplastin time > 100 s	Overdose of heparin
	International normalized ratio > 6	Overdose of warfarin
	Glucose < 50 mg/dl	Overdose of a hypoglycaemic agent
	Haemoglobin decrease	Iatrogenic bleeding
Microbiological	Clostridium difficile in stools	Infection due to antibiotic or chemotherapy agent
	Bacteraemia in blood culture	Health care-associated infection
Procedural	Endotracheal intubation	Iatrogenic respiratory failure
	Chest tube insertion	Iatrogenic pneumothorax
	Pulmonary embolism tests	Iatrogenic thromboembolism
	New-onset dialysis	Iatrogenic renal failure

\*Trigger operates in response to predetermined terms or keywords that alert the clinician to the occurrence or potential occurrence of certain adverse events

endorsement but are not routinely used in most hospitals. Use of opinion leaders to disseminate safety practices in health care would be one way of improving implementation rates (592). Ways must be found to disseminate innovations in health-care safety (593).

As patient safety measures are developed and matured, developing countries should make investments to improve their patient safety. International data standards, electronic data sources and electronic medical records are key components of this strategy (572). Cost-benefit analyses of these practices could provide an impetus and help countries make the necessary investments.

In addition to research on the use of information technology in patient safety, its use should also be studied in the broader framework of occupational health, as it is important to understand how working conditions, ward design, work flow and staffing relate to patient safety. Interventions are needed to improve the structural dimensions of health care, such as a safety culture, and to determine its effect on outcomes.

Although many countries do not have an advanced infrastructure for medical data or electronic medical records, most of the measures described above could be adapted and used by other countries. Most electronic detection tools are based on basic pharmacy or laboratory data, are inexpensive and greatly improve the rates of detection of adverse events. Patient safety indicators can be adapted easily in countries where ICD-9 or ICD-10 codes are used for hospitalizations. The safety attitudes questionnaire has already been translated into several languages. Safety process measures, such as those suggested by the National Quality Forum and in the Surgical Care Improvement Project, require more resources, although they would probably be a worthwhile investment.

Although patient safety measures are still in their infancy, countries would benefit greatly from

implementing them. Many of them have been useful in developed countries for understanding the extent of preventable safety events occurring in health care. Identifying problems, measuring progress and demonstrating that improvement has been achieved all depend on use of the most robust measures possible (594).

## 23 Lack of involvement of patients in patient safety

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The challenges posed by 'patient safety' have been addressed mainly from a system perspective. That is, clinicians and policy-makers increasingly recognize that many errors and adverse events are linked to the design of health-care systems and their features, such as poor communication, lack of human factors engineering and a poor safety culture (90, 595). Understanding the role of patient safety from the perspective of patients and their family members is, however, essential to a holistic understanding of adverse events and the elements required for improvement and change (90, 596–598). Further, the involvement of patients and family members as fully contributing members of the health-care team is increasingly recognized as an additional, necessary systemic safeguard as the complexity of health care continues to increase (595, 597–600). Bringing together groups of patients and their families in advisory councils in partnership with health-care administrators and providers is increasingly showing its value and importance for changing the health-care system (597–599).

Deconstructing processes in health care to their constituent parts has helped understanding of the epidemiology of disease and for devising successful medical interventions. This logic fails, however, when it comes to communication, and “the patient safety movement...is in danger of over-promising and under-delivering unless it includes a focus on the *relationship* between the caregiver and the patient as a core and critical piece of the puzzle” (601).

Providers in the health-care system should tailor their approaches to patients and their families (599, 600). What level of involvement does this particular patient and family member want? What is their relative level of health literacy? It is essential that such an approach be used: many patients are comfortable in assigning all the responsibility for treatment decisions to health-care professionals, while, at the other end of the spectrum, a technologically knowledgeable, proficiently health-literate individual might know more about current trends in a given epidemiological area than health-care professionals, including evidence-based scepticism about the appropriateness of certain medications or surgical interventions, on the basis of sources varying from papers in peer-reviewed medical journals to dubiously factual websites that prey on the fears and hopes of people seeking succour. This spectrum implies that the roles of patients and family members and their ‘volume of voice’ will necessarily differ from one individual and family to another. No one quantitative, universal standard would allow meaningful assessment of whether the indicator of patient or family involvement decreases the likelihood of harmful adverse events. While evidence exists that persons with low literacy and lower socioeconomic status, recent immigrants, elderly people, visible minorities and women experience a statistically significantly higher incidence of medical errors, little validated research indicates why this should be so (602). This could be an illuminating area of research, not only in respect of the apparently inequitable distribution of medical errors in the

health-care system but for society as a whole. Methods for increasing the knowledge and confidence of individuals should be evaluated, as well as the most time-effective methods for the health-care system.

It has been said, in many different ways and languages, that people who consider themselves unheard cannot hear. Thus, the culture of health care must change to a safety culture, in which a preoccupation with failure is emphasized and individuals throughout the health-care team, including patients and families, have the opportunity to be heard and can stop the process at any time for further clarification or to air concerns (596, 599, 600). Health-care providers should be implicitly curious about the perspectives of patients and their families and have enough humility to say, for example, “I made a mistake in thinking that this medication would be the best one for you, and I am sorry for that. I think this (different) medication will probably be better. What do you think?” Many providers will balk at such an idea, quoting the warnings of their insurance lawyers about liability issues associated with apologizing to the fellow human being whom the provider has wronged, inadvertently and unintentionally. Morally right actions are rarely without their opponents, but the ethical guidelines of various health professional licensing bodies and health-care organization accreditation bodies on disclosure of adverse events are clear: disclosure must be made, as a moral duty. Patients and their families must also be fully transparent about actions affecting the health status of the patient, including compliance with prescribed medication regimens, physical activity and diet (599). This is an individual and social responsibility necessary for exercising the ‘right’ to safe health care.

The main reason for the current lack of a loud patient or family voice in patient safety is fear. In addition, we continue to focus on outcomes of the health-care interaction, as opposed to the patterns that exist therein. Until we achieve



widespread understanding and accounting for such issues as conflict, power, decision-making, relationships and learning, our efforts will remain incomplete in important ways (595). Health-care providers, administrators and the patients and families themselves must have courage. Collectively, there are entrenched problems to be solved with a health-care system that was largely conceived and created by health-care providers. A truly patient- or family-centred system should be created, in which the patient or family member is the centre of a concentric circle of people working together to improve individual and public health (596–600).

## Gaps in knowledge

Most of the peer-reviewed and other research being published is focused on purely institutional responses or initiatives that usually do not include the contribution that patients and families can play in identifying issues to be solved and coming up with creative solutions from their own perspective. A fundamental power imbalance remains between providers or researchers and consumers in the system. This balance must be shifted, with transparent communication of the issues to be solved in health care, how and where patients and families can make an immediate contribution (e.g. hand hygiene by providers, patients and families) and rebuilding relationships to address the mistrust created by information control and fear of financial penalty subsequent to adverse events.

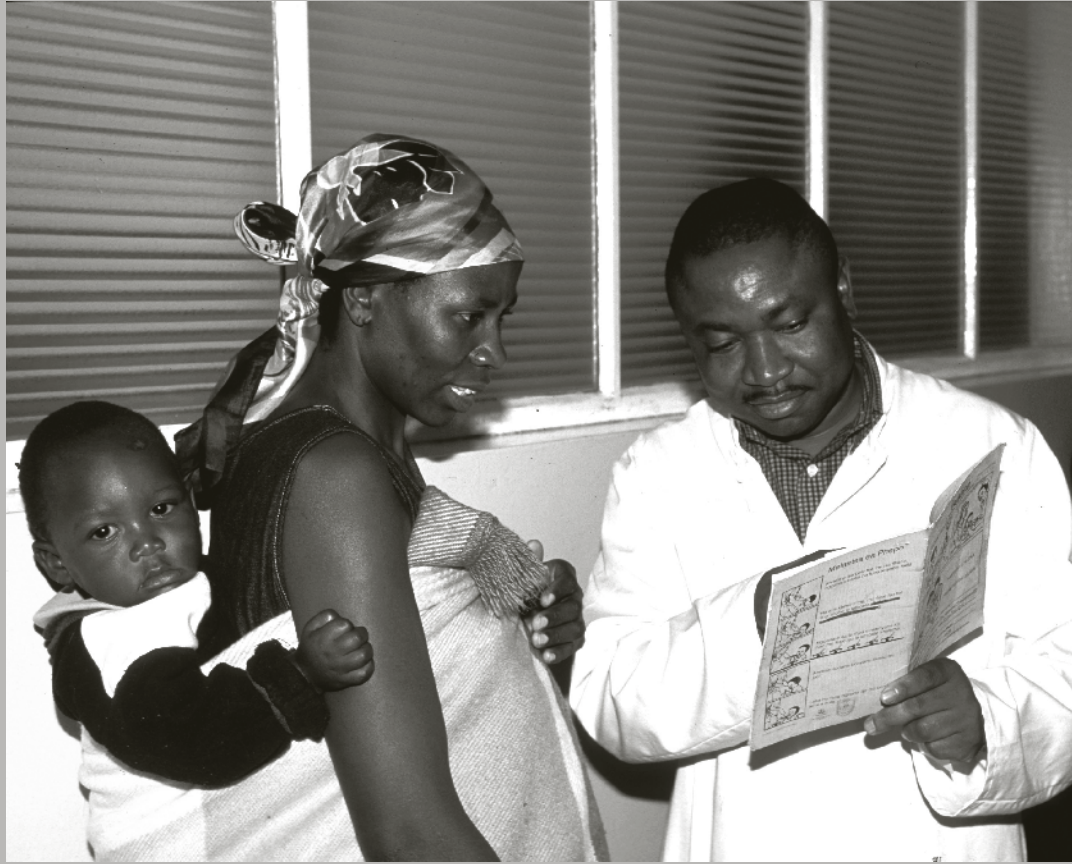
While the programme of ‘expert patients’ has been in existence in various forms for over

a decade, little has been written about the role of an informed consumer who is aware of the systemic flaws in health care, where such things as communication breakdowns can lead to inadvertent harm to the patient. An initial step would be a ‘safe patient curriculum’ reflecting the characteristics of various national health systems. The information would be collected by health-system researchers, providers and policy-makers and by consumer groups, such as Consumers Advancing Patient Safety in North America. It should be written in plain language and include such topics as health literacy, medication reconciliation, sharing test results directly with patients in hard copy with clear language about what the results actually mean, reputable web and print resources for information, knowledge-building and support, and, most importantly, assertive communication augmented by effective conflict resolution skills. Such a programme would probably be effective in shifting the culture of health care from information control and blame to one of a generative nature, in which assumptions can be challenged and refined for the benefit of all persons within the system.

Methods should be designed to explore qualitative, phenomenological processes in which the perceptions of patients and their families are used for better understanding and system improvement. This could be followed by data on the incidence (qualitative) of adverse events among ‘safety-educated’ patients and what types of events were successfully avoided because of new knowledge, to building numerical support for spread.









# SECTION V

## DISCUSSION, RECOMMENDATIONS AND CONCLUSIONS

### Discussion

A major goal of this report was to identify key aspects of patient safety and create a framework for approaching those issues. We identified 23 outcomes of unsafe patient care, the structural features of health systems and the processes of care that lead to adverse events. These areas span inpatient hospital care to outpatient ambulatory care. While this list is hardly exhaustive, it represents many of the main issues relevant to improving the delivery of health care.

Our review suggests that certain clinical areas, such as health care-associated infections, unsafe blood products and unsafe medications, are the major causes of morbidity and mortality and are thus the main challenges for persons wishing to improve the safety of medical care. While there is some information about the incidence and severity of adverse events in countries at all stages of economic development, the most reliable information on most of the topics is for developed countries. Therefore, more information is needed about these clinical issues in developing countries and those with economies in transition. Given the recent emphasis on community-based approaches to care and outreach programmes involving community health workers, more research is needed on patient safety in those circumstances. In particular, little is known about the engagement of civil society in such measures and in strategies for creating demand for research on issues of safety by patients and other recipients of care.

### Recommendations

As this report shows, current understanding of the extent of unsafe care and its causes is still in its infancy. This is especially true for developing countries and those with economies in transition, where the vast majority of the world's population lives and receives health care. There are even larger gaps in our knowledge about how to improve the safety of health care. Although some solutions are available, we know little about how to address many of the problems identified. The first step will be better data collection. Currently, potential or actual adverse events are substantially underreported, and health-care organizations continue to rely on spontaneous reporting, assuming that more systematic approaches to monitoring these events are too expensive (92). The next generation of solutions will need to rely on better analysis of the epidemiology of adverse events; for that, high-quality data on the underlying incidence and causes of adverse events are needed. Individualized solutions that take into account both local culture and customs must be devised. Another area for research is translating knowledge into practice, which is being addressed by a long-standing programme of the Agency for Healthcare Research and Quality in the United States and other organizations. Work is also needed

on understanding how solutions for safety, identified by careful research at high-quality institutions, can be translated into better care for other organizations throughout the world.

The research agenda for improving patient safety will vary substantially by and within countries. Routine use of quality improvement strategies, such as practice guidelines, benchmarking, auditing and reminders, can help to mitigate medical errors in the developed world; however, the extent to which such strategies will help in developing countries and those with economies in transition is unclear.

Several organizations, such as the Joint Commission on Accreditation of Healthcare Organizations and the Institute of Healthcare Improvement in the United States, are trying to focus the attention of health-care providers on real solutions to patient safety. The Joint Commission, for example, launched a programme for reducing medication errors, surgical errors and several of the other adverse events discussed in this document. The World Alliance for Patient Safety designated the Joint Commission and the Joint Commission International as the WHO Collaborating Centre for Patient Safety (Solutions). The Collaborating centre has proposed nine solutions for 2007, including communication during handover of a patient and best practices for needle reuse. These initiatives, while preliminary, can help to set priorities and persuade providers to adopt simple (and later, more complex) strategies to reduce harm. It is not known, however, how applicable these solutions will be in developing countries and those with economies in transition and how much harm they will reduce in the developed ones.

Other industries can provide model solutions to safety issues, and the nuclear power and aviation industries are often invoked as models for the health-care system. These industries are less complex than health care, and the lessons learnt from them might have limited application;

however, they might provide insights that could be useful for health-care providers.

Other possible solutions to unsafe care, such as greater use of health information technology and reducing the working hours of medical staff, might be more applicable initially in developed than in developing countries or countries with economies in transition. There is no reason to believe, however, that many of the latter countries will not be able to use these solutions in the near future, at least in parts of the health-care sector. The adoption of other technologies, such as cellular telephones, suggests that many developing countries and those with economies in transition might bypass developed nations in the use of health information technology to improve quality and safety. Many of the solutions, such as computerized prescribing by providers, will require adaptation to local cultural practices. The extent to which adaptation will be needed and the feasibility of the solutions for different countries are important research questions.

A critical target in improving patient safety throughout the world is the culture of health care, which often results in blame without an examination of the underlying systemic factors. Several sections of this report tackle these issues. Solutions that address organizational and cultural factors will have to be tested rigorously in various clinical settings (ambulatory, hospital and long-term care facilities) and will also probably require adaptation in different countries. Research is needed on how these issues can be most effectively addressed in developing countries and those with economies in transition.

## Gaps in research

This report has shown the need for better data in many areas of patient safety research, and, before meaningful advances can be made, major gaps in knowledge must be filled. Knowledge is lacking in all three of the domains of safety

identified: poor outcomes of care due to adverse events, structural contributors to unsafe care and processes of care that lead to safety issues. Some of the key deficiencies in each of these areas are outlined below.

## Outcomes

While more and more is known about the epidemiology and severity of adverse events and lapses in patient safety, much of the knowledge pertains to developed countries. For five of the patient safety areas—adverse drug events, adverse medical device events, surgical errors, falls and decubitus ulcers—almost all the available information is for developed countries and occasionally for those with economies in transition. Nevertheless, when these events have been studied in developing countries, their rates are comparable to those in developed countries, suggesting that the burden posed by these adverse events is just as substantial in those areas.

Even when information is available from developing countries, important aspects of their epidemiology remain unknown. For example, although there is information about health care-associated infections in developing countries, the types of infection and their frequency in hospitalized patients are largely unknown. In other contexts, issues that are important for developed countries, such as missed or inadequate diagnoses of ischaemic heart disease, basic epidemiology and cost estimates, are lacking for developing countries. Another topic that has received surprisingly little attention is the safety of paediatric patients. Research specific to safety issues in the paediatric setting clearly needs attention. Although adverse events in children might be less common, their effects can be devastating.

The data that are often readily available to identify patient safety lapses have limitations. Use of administrative data, such as diagnosis and procedure codes and diagnosis-related groups,

is tempting but their usefulness is unknown. One study showed that using administrative data as the sole source for quantifying hospital-acquired decubitus ulcers gave estimates that were substantially different from the true rate, shown by chart abstraction (603). Administrative data are generally collected for the purposes of reimbursement and legal documentation and are therefore limited for identifying adverse events and medical errors. Additionally, they often contain coding inaccuracies due to variations between coders and institutions, and there is limited scope for risk adjustment, among other problems (604).

Relatively little high-quality information is available about means for reducing adverse events and improving patient safety, for several reasons. First, the database of known interventions that can reduce errors and improve the safety of care is still being assembled. Second, many of the interventions will require programmes that are beyond the purview of a single health-care provider. For example, removing counterfeit medications will require both commitment from health-care providers and support from governments for better regulation of medication production and better enforcement of laws against counterfeits. Third, many of the solutions will come from improvements in the culture of patient safety, human factors re-engineering and other system redesign. Such programmes will probably affect many areas of patient safety but could not be implemented by a single provider organization. Finally, as indicated above, many solutions have been designed and evaluated in developed countries, and it will be important to understand how they can be transferred to developing countries and countries with economies in transition.

## Structures

Basic information is lacking on the optimal activities of national regulatory and accreditation bodies responsible for patient safety, especially in developing countries and those with economies

in transition. Little is also known about how factors such as workplace culture, resources or regulations influence behaviour. In the United States, some health-care organizations are starting to use safety culture assessment to measure organizational factors that might contribute to patient harm and to design and evaluate safety improvement interventions (605). Whether this will be effective is unknown. As mentioned above, individual provider organizations can address structural aspects of safety, but many efforts will require broader societal commitment.

## Processes

The examination of processes provides information that can be acted upon, as data can be collected more quickly than data on outcomes, and process measures generally require less risk adjustment than outcomes (606). Some processes have been shown to improve patient safety, such as making routine quality checks of medications or creating structured handovers between providers. Much remains to be learnt about how certain processes contribute to unsafe patient care. A major challenge in research on processes of care is the difficulty in establishing strong relations between processes and outcomes, given that studies often focus on only one component of the care process (606). Studies in which several processes are

analysed simultaneously (e.g. reducing fatigue and improving handovers between providers) might be valuable. Ensuring that processes are tied directly to favourable patient outcomes is another critical area of research.

## Conclusions

Patients come to the medical system to reduce their suffering from illness. In the past two decades, it has become clear that the health-care system not only cures disease and alleviates pain but also often causes harm and suffering. This is not an acceptable cost of providing health care. Our review suggests that harm occurs too often and much of it is preventable. Reducing harm will require greater understanding of the causes of these events, especially in developing countries and those with economies in transition.

WHO can help to expand knowledge about the causes of such harm and its impact on the world's population and can help promote safe practice around the world. It can also promote strategic collaborations among countries so that they can learn from each other's strengths and weaknesses, minimize redundancy and find the most effective solutions to reducing harm. With a concerted effort, we can ensure that health care is a balm to human suffering and less often a cause.







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