Ethical issues in Patient Safety Research

Interpreting existing guidance

World Health Organization

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Foreword

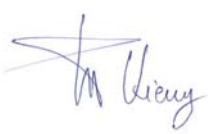
Research involving human participants must be conducted in a manner that respects the dignity, safety, and rights of research participants. This principle has formed the basis of ethically acceptable clinical and epidemiological research for decades. Research teams all over the world have increasingly recognized the need for external oversight in securing ethical advice, and independent ethics committees have been established to carry out this role. At the same time, significant scholarly work and international guidance have provided the philosophical and operational framework for improving the ethical conduct of research and building appropriate safeguards.

The recent expansion of research aiming to analyse the nature, behaviour and consequences of patient safety incidents and their surrounding circumstances, as well as the impact of innovative strategies to address patient safety problems, poses new research questions that raise new, and unresolved, ethical questions. For example, what does the ethical principle of "beneficence" require in studies that identify physician errors in on-going or recorded clinical practice? What does the principle of "respect for persons" require in studies that involve the observation of patients' and professionals' behaviour? When evaluating a strategy to reduce errors, is ethics committee review required when the only difference from usual practice is the collection of data to see if the strategy improves care? These and other challenges raised by patient safety research have been challenging ethics committees around the globe.

Tens of millions of patients worldwide suffer disabling injuries or death every year due to unsafe medical practices and care. As such, the World Health Organization (WHO) recognizes the ethical imperative to identify strategies that can improve the safety of patients as they receive care worldwide. In identifying ethical principles to guide this and other types of human research, WHO endorses the widely-used Council on International Organizations of Medical Sciences (CIOMS) "International Ethical Guidelines for Biomedical Research involving Human Subjects" (2002) and "International Ethical Guidelines for Epidemiological Research (2009)," and the World Medical Association (WMA) Declaration of Helsinki (2008). This report represents an important effort to apply the ethical guidance provided through these documents to the specific field of patient safety research. The report aims to help patient safety professionals, investigators, health-care institutions, ethics review committees, health authorities and others ensure the ethical conduct of patient safety activities. It synthesizes the organized deliberations of a highly respected group of research ethics and patient safety specialists from all over the world who, over the past years, have collaborated with WHO to produce this guidance. This document is especially important in resource-poor settings, where there is a pressing need to conduct more locally applicable research for health, including studies related to patient safety.

The guidance included in this report, is the first version of which we expect to be a continually maturing document. WHO, therefore, encourages readers and users of this document to provide feedback, allowing the continuous review and refinement of the guidance, based on additional input and new scholarly work.

This report represents the joint effort of the international experts who have provided their deliberations, together with the WHO Patient Safety Programme and the Secretariat of the WHO Ethics Review Committee, which steered and managed the process. I commend them all for taking on this important task.



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1. Introduction

This report responds to a request from patient safety researchers and research ethics committees (REC) for advice on how to interpret existing research ethics guidelines in the context of patient safety research. The report, which was produced by the WHO Patient Safety Programme and the WHO ERC Secretariat, builds on the reflections of an international expert group and was further enhanced by internal and external expert reviews by research ethics specialists and patient safety and quality improvement scientists from across the world. As explained in the foreword, this is the first version of this report, which will be revised to include future input, as evidence and scholarship in the area of patient safety research evolve.

This document is not intended to establish any new ethical principles. Rather, it represents an interpretation and application of existing, internationally accepted ethical principles to specific questions that arise in the context of patient safety activities. It is designed to be useful to patient safety professionals, investigators, health-care institutions, ethics review committees, health authorities and others aiming to ensure ethical conduct of patient safety research activities. It is hoped that the document will increase the attention given to ethical issues around patient safety research around the world, but particularly in resource poor-settings, where the need for locally applicable research findings is especially needed.

Ethical issues to consider when conducting patient safety research

WHO estimates that tens of millions of patients worldwide suffer disabling injuries or death every year due to unsafe medical practices and care. Nearly one in ten patients is harmed due to preventable causes while receiving health care in well-funded and technologically advanced hospital settings.[1] Much less is known about the burden of unsafe care in non-hospital settings, where most health-care services are delivered.[2] Furthermore, there is little evidence concerning the burden of unsafe care in developing countries, where the risk of harm to patients is likely to be greater, due to limitations in infrastructure, technologies, and human resources.[3] A retrospective analysis of medical records of patients admitted to 26 hospitals in eight developing and transitional countries estimated an incidence of preventable harm of almost 1 in 10.[4,5]

Research to understand the causes of unsafe care and to identify potential solutions involves diverse scientific designs and methodologies. For example, research may be based on a review of medical records, observations, surveys or interviews. It may use controlled randomized designs, allocating different hospitals or clinical units to alternative ways of delivering care, or it may use simulations. While patient safety studies share methodologies with many other types of health-related research, some aspects of patient safety research may appear different in ways that can have a bearing on the types and extent of ethical oversight that may be warranted.[6] For example, in patient safety research, the research "subject" who is targeted with a new intervention may be a health-care provider rather than a patient, even when outcomes are based on patient-related information, or the target may be a "system" of care rather than an individual. The issues raised by such methods are analogous to those raised in research using cluster designs.[7] In other studies, researchers identify errors that occurred during health-care, errors that may not have previously been known to patients or their families. Some tensions may arise between a researcher's duty of care to an individual patient and the aims of the research when clinically therapeutic results are withheld from individual subjects, particularly when this information is 'incidental' to the study's main outcomes measures.[8] Patient safety designs may also involve an individual simulating a patient, for example, someone who buys medicine from a pharmacy to determine whether a medicine's formulation is up to standard.

Patient safety activities can raise ethical issues even when those activities are not formally labelled as research. For example, quality assurance and audit programmes review how care is delivered and compare it to a set of explicit criteria to determine whether standards are being met and how care can be improved. Other programmes, often labelled as quality or patient safety improvement, may implement activities that alter how care is delivered in order to reduce problems or improve efficiencies. Many of these programmes address a defined question, systematically collect data, and/or evaluate new strategies to examine whether new approaches actually result in improvement.[9] Thus, they share several essential features with research, even though they may not always be explicitly labelled as such. These activities, therefore, raise similar ethical concerns as would research. For example, how can patients' privacy and confidentiality be ensured when examining records systematically? How can providers be protected from reprisals when patient safety efforts result in the documentation of health-care failures? (See Box 1) Additional complexities arise when such activities, not originally intended as research, are submitted for publication because the data, once analysed, appears to be of generalizable relevance. Finally, patient safety improvement programmes in hospitals and other health-care settings have purposes that extend beyond the immediate interests of the patients directly enrolled or affected by them, just as is true for activities more commonly viewed as research. These patients, too, deserve the health-care system's commitment to ensuring that their welfare and rights are protected.

Box 1: Some of the ethical questions raised by patient safety activities

- Which patient safety projects should be considered research requiring Research Ethics Committee (REC) review?
- What types of risks exist in patient safety research?
- What protections must be in place for patients and/or providers to reduce the risks from patient safety studies?
- Under what circumstances are informed consent or other forms of disclosure or permission needed from research participants?
- In particular, under what circumstances, if any, is deception allowable in patient safety research?
- What are the best practices for addressing privacy and confidentiality issues?
- Are there any potential direct or indirect benefits to, or incentives for, participating in patient safety research?
- Under what circumstances, if any, do researchers have a duty to intervene regarding past or imminent errors?

2. The application of research ethics principles to patient safety activities

EXISTING GUIDELINES

All proposals to conduct research involving human subjects must be submitted for review of their scientific merit and ethical acceptability to one or more scientific review and ethical review committees. The investigator must obtain their approval or clearance before undertaking the research.

CIOMS International Ethical Guidelines for Epidemiological studies, 2009 Guideline 2

It is conventional to define "research" as involving activities that are designed to develop or contribute to generalizable knowledge. Generalizable knowledge consists of theories, principles or relationships, or the accumulation of information on which they are based, that can be corroborated by accepted scientific methods of observation and inference.

CIOMS International Ethical Guidelines for Epidemiological Studies, 2009 Introduction

Research means a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge.

The "Common Rule" (USA)

Guidance point 1

Any patient safety activity that constitutes research, regardless of its methodology, should be submitted to a Research Ethics Committee (REC).

For purposes of REC oversight, patient safety activities constitute research when:

- they are aimed at addressing a specific question; and
- they use a predefined approach or method for collecting data in response to the question they intend to address; and
- their findings are intended to be applied to settings beyond those in which the activity or programme is implemented.

International guidelines define research as a systematic activity designed to develop or contribute to generalizable knowledge. Before conducting any study, researchers should consider whether the research is warranted and whether the selection and recruitment of participants is fair. There should be good reason to explore safety practice in research beyond routine evaluation. Furthermore, vulnerable populations should not be differentially exposed to any extra risks brought up by the research without good reason to avoid exacerbating pre-existing inequalities.[10] While health research has the potential to bring benefits to society and to the research communities, it can be associated with risks to the research participants. It is the obligation of those responsible for conducting the research to protect participants by minimizing those risks and seeking approval of an independent Research Ethics Committee (REC).

The rationale for requiring third party review of research is that the participants are often asked to undertake risks that are not offset by any potential personal benefit, in order to develop scientific knowledge that may benefit others in the future. REC review is designed to ensure that the risks assumed by the participants are carefully

examined and minimized to the extent that is reasonably possible, that the risks that remain are reasonable in relation to the potential benefits of the study, and that other ethical considerations, such as informed consent and confidentiality, are adequately addressed.

Patient safety research may entail potential risks to both patients and health-care providers, and like any other research activity must be submitted to a research ethics committee for review. Patient safety research must be distinguished from activities designed to provide benefits to an existing patient population, including activities characterized as "programme implementation or practice," such as surveillance or quality improvement. Such patient safety activities are in many instances mandated by regulatory or administrative authorities or units of health-care organizations, and are typically undertaken to serve the interests of the individuals who are cared for in these same organizations. In general, current regulations do not require these activities to be reviewed by an REC.

For instance, a hospital may implement a patient safety programme in which data are systematically collected from medical charts of surgery patients to better understand hospital-specific circumstances leading to infection (for example, staffing patterns, scheduling of procedures, or availability of equipment). The hospital's goal is to identify specific aspects of its organization or delivery of care aiming to reduce the risk of infection. When conducted as part of quality improvement practice, such activities are generally expected to quickly change clinical protocols and practices at the institution in question. Although patient data will be collected in a systematic way, the programme's focus on hospital-specific circumstances means that the data collected are unlikely to be generalizable beyond that particular setting. As such, many institutions would characterize the activity as quality improvement and thus, not require external ethics review, despite the fact that identifiable human data are being collected.

On the other hand, if a project abstracts data from medical charts in a series of hospitals to determine how infection rates can be reduced among hospitals more broadly, so that hospitals can learn more widely from the information, the project would generally fall within accepted definitions of research requiring REC review. In practice, however, there is a great variability in the interpretation of what constitutes research across different research committees and national legislations,[11] as illustrated in Case Study 1 and 2 and will be expanded in the next section. When in doubt, it is recommended that patient safety projects are submitted to ethics committees at an early stage, to determine whether or not they consider them as research that should receive their oversight.

An important criterion to bear in mind is whether or not the proposed intervention is evidence based. If it is not evidence-based, then it is recommended that the activity be developed within a research framework.

EXISTING GUIDELINES

The research protocol must be submitted for consideration, comment, guidance and approval to a research ethics committee before the study begins. This committee must be independent of the researcher, the sponsor and any other undue influence. It must take into consideration the laws and regulations of the country or countries in which the research is to be performed as well as applicable international norms and standards but these must not be allowed to reduce or eliminate any of the protections for research subjects set forth in this Declaration. The committee must have the right to monitor on-going studies. The researcher must provide monitoring information to the committee, especially information about any serious adverse events. No change to the protocol may be made without consideration and approval by the committee.

Ethical Principles for Medical Research Involving Human Subjects, World Medical Association Declaration of Helsinki, 2008 paragraph 15

Case study 1 – Obtaining research ethics oversight

Dovey S, Hall K, Makeham M, et. al.
Seeking ethical approval for an international study in primary care patient safety.
Br J Gen Pract 2011; 61: 197-204

Seeking ethics committee approval for research can be challenging even for relatively simple studies occurring in single settings. Complicating factors such as multicentre studies and/or contentious research issues can challenge review processes, and conducting such studies internationally adds a further layer of complexity. This paper drew on the experiences of the LINNAEUS Collaboration, an international group of primary care researchers, in obtaining ethics approval to conduct an international study investigating medical error in general practice in six countries. It describes the ethics review processes applied to exactly the same research protocol for a study run in Australia, Canada, England, the Netherlands, New Zealand, and the US. Wide variations in ethics review responses to the research proposal occurred, from no approval being deemed necessary to the study plan narrowly avoiding rejection. The ethics committees in each country had different concerns about the study protocol they were presented with, which was exactly the same in each country. The authors' experiences demonstrated that ethics committees operate in their own historical and cultural context, which can lead to radically different subjective interpretations of commonly-held ethical principles, and raised further issues such as 'what is research?'

Guidance point 2

Patient safety activities, even when they do not meet the definition of research requiring ethical review, may involve more than minimal risk to patients and health-care providers in some situations. It is the responsibility of those working in patient safety activities to be aware of ethical issues and seek guidance as needed.

Distinguishing between research and programme implementation is not always straightforward. For example, even though patient safety programmes are typically designed to improve care within a particular organization, their results may be disseminated to other organizations. Just as with research, the benefits of patient safety activities may ultimately extend beyond the population that was exposed to the risks. Moreover, the methodologies of many patient safety initiatives closely resemble those used in research, especially in cluster designs, including alterations to standard practice, use of randomization, and the systematic collection of data. Thus, as CIOMS has recognized in the context of epidemiology, and the Ottawa Statement in the context of cluster studies,[12] even activities that do not formally meet the definition of research may benefit from undergoing "careful ethical scrutiny or even reconsideration." Based on this principle, patient safety activities that do not constitute research may benefit from ethical oversight or advice whenever those activities involve greater-than-minimal risks.

For activities that do not formally meet the definition of research, this risk assessment may be made by a reference group that is independent of the activity and who are well versed in both ethics and the principles of patient safety improvement. Some institutions may choose to give this review authority to an REC. For those who may wish to publish the results of non-research activity, it would be advisable to obtain advice from a REC prior to starting the activity. Regardless of an activity's label, the most important question to consider when undertaking patient safety activities is whether the patients and providers who participate in these programmes will be subjected to any risks they would otherwise not assume.

EXISTING GUIDELINES

The "generalizable knowledge" definition works well for medical and behavioural studies pertaining to human health, which are commonly denominated "biomedical research" to indicate its relation to health. But the definition works less well in separating practice from research in the field of epidemiology. Many studies using the tools of epidemiology which are performed on a regular basis by public health agencies, such as routine surveillance for disease outbreaks, are correctly viewed as "practice" even though the information produced may contribute to generalizable knowledge. Thus, in carrying out their activities, epidemiologists (and others examining the activities) need to apply careful judgment to determine whether the activity should be classified as research or practice. Of course, it does not necessarily follow that everything placed in the former category is problematic or is even subject to all the requirements for advanced approval and individualized informed consent usually associated with research. Conversely, some activities that are routinely carried out by epidemiologists do raise ethical issues that may benefit from careful scrutiny or even reconsideration, even if they have long traditions and are sanctioned by regulations or statutes.

CIOMS International Ethical Guidelines for Epidemiological Studies, 2009 Introduction

Case study 2 – Distinguishing research from other programmes

Pronovost P, Needham D, Berenholz S, et. al. An Intervention to Decrease Catheter Related Bloodstream Infections in the ICU.
N Engl J Med, 2006, 355:272.

This patient safety project was implemented to determine the effectiveness of an evidence-based intervention aimed at reducing rates of catheter-acquired bloodstream infections in ICUs. The intervention aimed at improving physicians' use of five procedures that have been previously shown to reduce infections. These procedures include proper hand washing, full barrier precautions during insertion of the catheter, cleaning the patient's skin with chlorhexidine, avoiding the femoral site if possible, and removing unnecessary catheters. Agreement to participate was obtained from 108 ICUs from 67 hospitals in the state of Michigan, United States. Each of the ICUs implemented the evidence-based intervention, and infection rates before the implementation of the intervention were compared with infection rates after its implementation. Each ICU was responsible for reporting aggregate infection data back to the project staff. The project staff developed the intervention and conducted the evaluation but were not members of any of the ICUs involved in the study. The study was submitted to the REC of the home institution of the project staff before implementation.

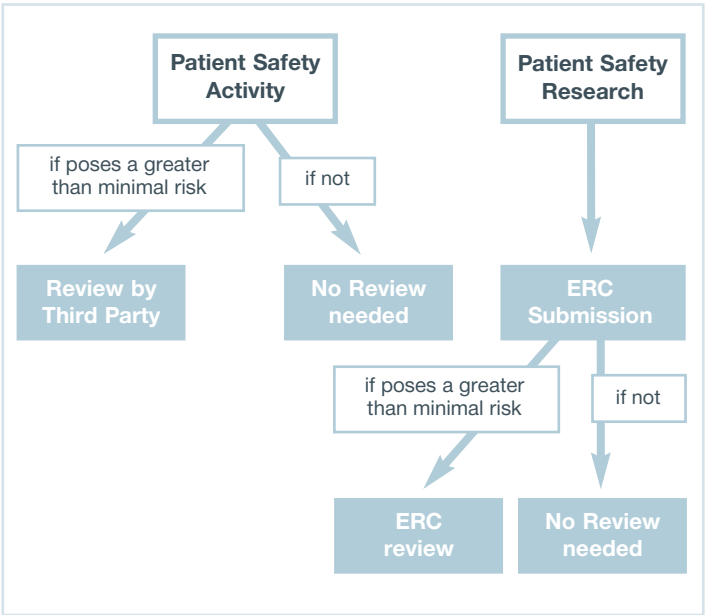
Indeed, confusion by experienced professionals about whether projects like this should be classified as research vs. quality improvement practice led to public controversy around this particular case, and questioning from government authorities, highlighting the need for clearer guidance around when projects such as this should be subject to ethical oversight and when they should not.

EXISTING GUIDELINES

The distinction between research and practice in public health does not correlate with the extent to which an activity carries risks for individuals and communities or otherwise raises ethical issues that would benefit from a prospective review process. The distinction has no bearing either on the ultimate question of whether a particular public health response is scientifically and ethically justifiable. ... Despite the conceptual problems of distinguishing between research and non-research, the distinction is deeply ingrained in many countries' regulatory structures and is unlikely to be changed any time soon. However, this does not mean that all research must undergo full REC review, nor does it mean that activities that fall outside local or international definitions of research should escape ethics review entirely.

WHO Technical Consultation on Research Ethics in International Epidemic Response

Figure 1. Suggested flow diagram



3. Understanding risk in patient safety research

Nature of the risks surrounding patient safety research
Patient safety research may involve the following types of risks:

Clinical risks: Clinical risks refer to the likelihood that patients may experience a worsening of their health status due to the conduct of the research study. Because patient safety studies do not generally modify the treatment plans for individual patients, they tend to involve considerably fewer clinical risks than other types of health-care research. However, the possibility of clinical risks should always be assessed. In many cases, patient safety studies may target *how* care is delivered, for example, through new reminder systems to avoid medication errors or testing the effect of different staffing ratios. These changes, while designed to improve the quality of care patients receive, could actually result in lower quality of care or could create errors rather than reduce them. This could happen due to inadequate training of staff on how to use the new systems, or by diverting staff attention to the new patient safety system at the expense of usual care responsibilities.

Social risks: Social risks are the risks that research participants encounter due to how others might treat them as a result of their participation in a study. While there may be minimal social risks for patients who take part in patient safety studies, medical providers or institutions may be concerned about social risks if they participate in research that exposes their own system failures or ineffectiveness. For example, research documenting the factors associated with significant health-care incidents that occurred in the past or rates of particular types of errors runs the risk that the providers involved with these incidents, or the institutions themselves, could suffer reputational and professional harm.

Psychological risks: Psychological risks include the possibility that research participants will become emotionally distressed, fearful or anxious as a result of their participation. For example, studies that interview patients or families about harmful incidents that occurred previously or about their perceptions of the quality of care may cause them to question the quality of their medical providers and to become anxious. Also, health providers may become anxious if they believe that researchers are evaluating their professional performance, particularly if they fear that the results may result in reprisals.

Economic risks: Economic risks refer to the possibility that research participants will be required to incur additional financial costs as a result of their participation in a study. For example, providers may have concerns about the economic implications of studies that uncover errors in how care is provided, including the possibility that negative information uncovered during a study could lead to litigation.

EXISTING GUIDELINES

Every medical research study involving human subjects must be preceded by careful assessment of predictable risks and burdens to the individuals and communities involved in the research in comparison with foreseeable benefits to them and to other individuals or communities affected by the condition under investigation.

Ethical Principles for Medical Research Involving Human Subjects, World Medical Association Declaration of Helsinki, 2008 paragraph 18.

For all epidemiological research involving human subjects, the investigator must ensure that potential benefits and harms are reasonably balanced and risks are minimized.

CIOMS International Ethical Guidelines for Epidemiological Studies, 2009 Guideline 8

The risks to which research subjects may be exposed have been classified as physical, psychological, social, and economic.

OHRP Institutional Review Board Guidebook

Determining the level of risk

Guidance point 3

Patient safety research may be considered of minimal risk if all of the following factors are present:

- The intervention does not modify clinical management or the treatment plan for the patient;
- Data are not individually identifiable, or adequate protections against breaches of confidentiality of data are in place;
- The intervention is unlikely to divert staff from existing responsibilities in ways that are likely to pose a risk to patient wellbeing and safety;
- Nothing in applicable laws, or institutional rules, or the local cultural context suggests that conducting the study in the particular environment would pose higher risks to the patient;
- No other features of the activity suggest an increased level of risk to patients, providers, or institutions, compared with the patient safety activity not being implemented.

International guidelines define minimal risk research as research that poses no greater risk than the risks attached to routine daily life or to routine medical or psychological examination. For providers, minimal risk might be defined as risks no greater than those encountered in conducting their usual practice.

Determining the level of risk posed by a study is important, because some countries' regulations state that research that poses no more than minimal risk may generally be reviewed using an expedited mechanism.[13] This means that RECs may choose to have only one or two members of the committee, rather than the full convened committee, review the protocol. In addition, international guidelines state that minimal risk studies may be eligible for a waiver of informed consent (see Guidance Point 6). While many patient safety studies are likely to pose minimal risk to patients, any study that poses higher risks to patients, providers, or institutions will require greater oversight and protections. Proportionate reviews are schemes that offer different forms of review in proportion to the risks and ethical issues involved in the research being undertaken.[14]

In Case Study 2, because the items on the checklist were based on established clinical practice recommendations and did not therefore create a risk of leading to substandard care, the risk to patients and providers was minimal. However, in Case Study 3, where providers were interviewed by researchers about why a patient safety incident may have occurred and about

EXISTING GUIDELINES

Minimal risk refers to "risk that is no more likely and not greater than that attached to routine medical or psychological examination."

CIOMS, International Ethical Guidelines for Epidemiological Studies, 2009 Commentary to Guideline 4 (Documentation of consent)

Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

The "Common Rule" (United States)

Physicians may not participate in a research study involving human subjects unless they are confident that the risks involved have been adequately assessed and can be satisfactorily managed. Physicians must immediately stop a study when the risks are found to outweigh the potential benefits or when there is conclusive proof of positive and beneficial results.

Ethical Principles for Medical Research Involving Human Subjects, World Medical Association Declaration of Helsinki, 2008 Paragraph 20

self-perceived competency and skills, providers might have potentially exposed some failures of their own or of their team or institution, thereby creating some level of social, psychological or even economic risks.The REC would have to determine, once safeguards have been put in place, whether a study like Case Study 3 poses more than minimal risks to the individuals involved.

Some types of studies are usually recognized as posing minimal risk. For example, research where individually identifiable human data are not collected, or when the data of the study is already in the public domain, tends to be considered of minimal risk and in many contexts may be exempt from a REC review altogether.[15] Similarly, projects that are randomized, whether at the clinic/institution level, or at the level of individual patients, may be considered minimal risk research if, based on best evidence, no study arms are considered therapeutically experimental and no study arms pose a significant deviation from the care usually received by patients in the study setting.

Certain projects may pose minimal risk when implemented in some settings, but may pose greater than minimal risk in other contexts, for example, in settings that are retributive towards providers or where confidentiality protections cannot be guaranteed. It is, therefore, important for those involved in patient safety research to understand the institutional culture, norms, laws and regulations where the research takes place, and identify those laws and regulations which are relevant to their work. For studies that document rates of errors, it may be especially important to know whether any local laws require the reporting of provider error to any authorities or licensing boards, as well as whether any exceptions to such policies exist for patient safety research. The existence of such laws may compromise the neutrality of researchers and pose risks to the participants in the study. Investigators documenting errors should also talk to trusted informants in local settings to know the chance of retribution for providers, if errors are found, as well as providers' anticipated anxiety about possible retribution. Patient safety professionals must also be sensitive to power relationships that exist between senior and junior hospital staff. In Case Study 3, those involved in the patient safety activity made clear to providers that all data would be kept confidential and therefore that no individual level data would be reported to hospital management. In settings where the local context could increase risks related to reporting or retribution, researchers may need to consider whether it would be ethically preferable to abandon the study, in order to prevent additional risks to participants, or whether it would be effective and feasible to build additional safeguards into the study. In some circumstances, collecting data anonymously (rather than confidentially) may be sufficient to protect against risk of harm.

Case study 3 – Assessing the level of risk and minimizing risk

Cullen DJ, Sweitzer BJ, Bates DW, et. al. Preventable adverse drug events in hospitalized patients: a comparative study of intensive care and general care units.
Crit Care Med, 1997, 25:1289-1297.

A patient safety project was implemented at 11 different ICUs and general care units in two tertiary care hospitals in the United States, with the objective of understanding the causes of adverse drug events (ADEs) resulting from human errors in drug use, so that they might be prevented in the future. Data on all ADEs that occurred in any of those 11 units over a six-month period were included in the project. Data on ADEs were collected in several ways: all nurses and pharmacists in those 11 units were asked to report all ADEs to nurse investigators involved in the project, a nurse investigator visited each unit twice a day on weekdays to obtain information from hospital staff on any ADEs that had recently occurred, and each day, the nurse investigator also reviewed all medical charts to collect information on reported and potential ADEs. All data were then reviewed by two physicians. These physicians judged the severity of the ADE and whether or not it had been preventable. For each ADE judged to have been preventable, the hospital staff involved in providing the patient with the medication were interviewed by a peer and asked to describe the circumstances surrounding the incident, to describe how the event had occurred, and to self-assess their competency and skills, decision-making style, openness to change, duration in the service or job, the amount and quality of supervision they had received, and the relationship of the incident to the timing of their shift. Consent was not obtained from patients within the unit. Project staff reported that several of the medical staff who had made errors did not want to discuss those errors with interviewers because they were scared about being reprimanded for their mistake. As stated by the project staff member, "We had to reassure them about the confidentiality issues and it worked most of the time." The project was approved by the REC at each of the two hospitals. During the review process, it was decided that if, during the course of the project, staff identified patterns of care that were harmful to a patient, it was the duty of the project staff to immediately inform the hospital staff and the appropriate authorities so that the recurring error could be corrected, but without retribution to any individual employees.

Minimizing social and psychological risk in patient safety studies

Guidance point 4

- Before conducting a study, researchers should consider discussing with leadership of the health-care institution under study the importance of avoiding a culture of blame with regard to patient safety.
- Patient safety researchers should also consider whether the political, social, institutional, or cultural context in which the project will be implemented could alter the project's risk profile.

Guidance point 5

Individuals involved in patient safety research who are interviewing or observing patients or providers should anticipate any distress participants may experience as a consequence of the conduct of the study and be prepared to offer solutions. Some options are:

- Be trained to ask participants if they would like to skip questions or stop the interview if they become distressed;
- Be equipped with referrals for supportive care or counselling in case participants become significantly distressed;
- Be equipped with the names of hospital authorities to whom participants and families can be referred if they have questions; and
- Ensure that all services and providers whose names will be given out as referrals have agreed to have their names provided to patients and families.

The following strategies can help minimize risks in patient safety research:

The "no blame" approach to patient safety improvement

Patient safety improvement is based on the understanding that most harmful incidents occur not because of negligent or unprofessional behaviour, but, instead, because of systemic problems with the manner in which health care is delivered. Strong evidence suggests that a culture of blame threatens the ability to learn from errors and understand why these occur, and thus threatens the ability to improve the public's health. It is important that institutions involved in patient safety research understand this fact, and that a no blame approach will actually increase the chances that practice improvements can ultimately occur and results can be used to make systemic improvements. Nonetheless, it is worth acknowledging that those exposed to harm have a right to accountability where harm occurs through negligence or unprofessional behaviour.

Decreasing the chances of identification of poorly performing individuals or institutions

If individuals or groups that consistently provide poor care are identified by patient safety research, there is a risk that the result will be punitive action. Because patient safety research is premised on a "no blame" approach, researchers should consider setting up firewalls to minimize this risk. Some suggestions in this regard include:

- Avoiding the use of names on data forms, aggregating data as soon as possible, and avoiding the identification of people or unique characteristics of cases in reports;
- Expanding the study population to include several different provider teams or several different institutions, in order to avoid inadvertent identification of particular institutions or groups, or to avoid the appearance of targeting; and
- Avoiding collecting data from providers or institutions in environments that seem likely to take retaliatory action. However, if by such avoidance, the result would be a biased sample, the researcher should consider redesigning the study.

Support for researchers facing complex and sensitive issues

A mechanism that might be a useful resource to advise on the course of action if uncovering possible evidence of intentional harm or incompetence or unethical practice, is to set up a "safety committee" of recognized expert clinicians who agree to review data and make a decision about the case and subsequent actions, including informing relevant hospital management or personnel about potential risks or unsafe providers. This safety committee may also advise health professionals reviewing health records who are in some cases compelled to report instances where they suspect incompetence and where intervention with the patient may still be beneficial. See Case Study 4 for an illustration of this.

Case study 4 – Providing neutral expert advice on the course of action

Baker GR, Norton PG, Flintoft V, et.al.
The Canadian Adverse Events Study:
the incidence of adverse events among hospital patients in Canada
CMAJ 2004; 170 (11): 1678-1686
This patient safety project involved the analysis for adverse events in a sample of 20 hospitals spread across five provinces in Canada. In this large and complex study, which involved the review of more than 3 700 medical charts, and where it would be possible to uncover some possible evidence of intentional harm or incompetence, the researchers set up a "safety committee" of recognized experts who agreed to provide back-up to the researchers and review data and make a decision about possibly informing the hospital or other relevant personnel about potential risks or unsafe providers. The researchers had to use the committee in one instance where a patient had been injured and provider actions were deemed worthy of further review.

General disclosure about the conduct of and findings from patient safety research
Institutions with more positive patient safety cultures are more likely to be open to the conduct of research studies that aim to improve patient safety. General awareness of patient safety principles in the institutions where research will take place can help to increase understanding of the issues involved and decrease concerns and stress related to the research study. Disclosing general details about the way the study will be conducted and disseminated may contribute to reducing anxiety. This sharing of information also demonstrates respect for the individuals involved in the research.

Anticipating risks from interviewing patients or their families
Some types of patient safety studies involve interviewing patients or family members after adverse incidents have occurred. These interviews are designed to learn more about the patients' and families' experience and understanding of the events that occurred, as well as about the background conditions associated with the incident.This information may provide important insights that can be useful for future prevention strategies. In some cases, patients or family members may become distressed during such interviews, either because they are asked to recall the harm that occurred, or they learn about or come to suspect errors or problems that had not been fully apparent to them previously. In other instances, patients may be asked about their doctors' performance (even in the absence of an incident) and this might lead to mistrust, concern or fear about the care they are receiving. Researchers should reassure participants that the information provided in the context of the research will be treated with the utmost confidentiality. Despite this, patients may still feel uncomfortable or fear retribution when disclosing aspects of the behaviour of providers. Those conducting interviews with patients and families must anticipate, and be prepared for such events and should have adequate responses and mechanisms in place in the form of referral or counselling for those that become distressed, as appropriate. Referral sites should be contacted in advance to ensure that they are willing and prepared to respond to requests.

Anticipating risks from interviewing or observing providers
Providers may be interviewed as part of patient safety research, to understand how systemic issues can contribute to harmful incidents. In the course of these interviews it is possible that providers may be questioned about their colleagues, their supervisors or hospital management. In such circumstances, providers may feel that they are at risk of repercussions if the information provided by them is not treated confidentially. In such cases they must know where they can ask questions, and feel comfortable with the interview, including the possibility that they can withdraw at any time or skip any question. Sometimes, providers may be distressed by the recollection of a harmful incident during the conduct of an interview, and it may be necessary to facilitate counseling or psychological support. On other occasions, research studies may involve the direct observation of provider behaviour and performance. Observing providers, even in the context of a research study, can often be perceived as a threat to the authority or the competence of the providers. In all of these cases, the research team must be sensitive to the concerns that may arise in these types of studies and anticipate such an event, having firewalls and referral mechanisms in place, and explaining the purpose of observations in advance. Referral sites should be contacted in advance to ensure that they are willing and prepared to respond to requests.

4. Informed consent

Waivers of informed consent from patients

Guidance point 6

Researchers conducting patient safety research studies must generally seek individual informed consent from patients. However, the requirement of obtaining individual informed consent from patients can be waived by an REC if

- The research does not directly inform or alter the individual patients' therapeutic or medical treatment plans; and
- Risks posed to patients by the research are minimal; and
- The research could not practically be carried out if individual informed consent were required; and
- The privacy and confidentiality or anonimity of individual patients are assured (see Guidance Point 8).

In cases where individual informed consent from patients will not be sought, general disclosure to patients about patient safety research is highly recommended.

As outlined in existing international ethical guidelines, voluntary, informed consent is generally required in research involving human participants. Informed consent involves informing potential participants, through documents and discussion, of the purpose, procedures, risks, potential benefits, and voluntary nature of the proposed research, and documenting the participant's agreement. According to international guidelines, RECs may waive the usual requirement of individual informed consent when the research involves no more than minimal risk, and a requirement of obtaining individual informed consent would make the research impracticable.[16]

EXISTING GUIDELINES

People have a right to know that their medical records or biological specimens may be used for research. …. Investigators should not initiate epidemiological research involving human subjects without first obtaining each subject's informed consent, unless they have received explicit approval to do so from an ethical review committee or the research activity is authorized by legislation or competent authorities in accord with the ethical principles in these Guidelines

CIOMS International Ethical Guidelines for Epidemiological Studies - 2009 - Commentary on Guideline 4

Consent may be indicated in a number of ways. The subject may imply consent by voluntary actions, express consent orally, or sign a consent form. As a general rule, the subject should sign a consent form, or, in the case of incompetence, a legal guardian or other duly authorized representative should do so. The ethical review committee may approve waiver of the requirement of a signed consent form if the research carries no more than minimal risk–that is, risk that is no more likely and not greater than that attached to routine medical or psychological examination–and if the procedures to be used are only those for which signed consent forms are not customarily required outside the research context. Such waivers may also be approved when the existence of a signed consent form would be an unjustified threat to the subject's confidentiality.

CIOMS International Ethical Guidelines for Epidemiological Studies - 2009 Commentary on Guideline 4

EXISTING GUIDELINES

In medical research involving competent human subjects, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail, and any other relevant aspects of the study. The potential subject must be informed of the right to refuse to participate in the study or to withdraw consent to participate at any time without reprisal. Special attention should be given to the specific information needs of individual potential subjects as well as to the methods used to deliver the information. After ensuring that the potential subject has understood the information, the physician or another appropriately qualified individual must then seek the potential subject's freely-given informed consent, preferably in writing. If the consent cannot be expressed in writing, the non-written consent must be formally documented and witnessed.

For medical research using identifiable human material or data, physicians must normally seek consent for its collection, analysis, storage and/or reuse. There may be situations where consent would be impossible or impractical to obtain for such research or would pose a threat to the validity of the research. In such situations, the research may be done only after the consideration and approval of a research ethics committee.

Ethical Principles for Medical Research Involving Human Subjects, World Medical Association Declaration of Helsinki, 2008 paragraphs 24 and 25

For example, reminding providers to follow evidence-based practices, and measuring the impact of the reminder on patient outcomes (based on review and confidential documentation of medical charts), may not require patient-level informed consent. This is because there are no experimental interventions administered to patients, the study does not alter the standard therapeutic plan, and the risks posed to patients by the research as a whole are minimal. In general consent is not ordinarily sought from patients when reminding providers about best practices.

When individual informed consent is required, it must usually be documented through the signature on a consent form. However, in some situations, RECs may approve other methods of documentation, such as allowing participants to express their willingness to participate orally, or allowing participants to imply consent through voluntary actions (such as completing a mailed questionnaire). RECs should not waive the requirement of obtaining written consent for research involving more than minimal risk, except in situations in which the principal risk to patients is the potential harm resulting from being linked to participation in the research, in which case oral consent should be sought. For example, in a study examining counselling services for women seeking abortions, an REC might conclude that the principal risk to participants is the stigma that could result if the fact that they were seeking abortion services was discovered, and that this risk could be minimized by allowing for an oral consent process.

Permission from patients

Some patient safety research studies involve the observation of health-care providers' behaviour and practices. In such studies, the researchers do not interfere with the practice other than by their presence in the health-care setting. When individual patient encounters are planned, as in observation of patient-physician interactions, requirements for obtaining the informed consent of patients may be waived if the object of study is the health-care staff and not the patient and the study does not involve changing the way that care is provided. In these cases, assuming it is feasible (i.e. that the patient is conscious and the situation is not an emergency), patients should be told that an observation will take place during their medical visit or interaction, as part of a larger effort to study how care works at that facility and to ensure that care is provided in the best possible way. Although patients need not be asked to provide prior informed consent to participate in these situations, they should be informed clearly that they have the right to opt out of the observation and any patient who expresses concerns should be helped to exercise this right. This right is not based on the principle of informed consent, but rather on the basic ethical importance of treating people with respect.

Group disclosure for patients
Even in circumstances where formal consent procedures have been waived, it is best practice to disclose to patients that patient safety research may be ongoing in the clinical setting, and to explain the implications of such activities on them. For example, a general disclosure may be provided by a poster or as leaflets either in waiting rooms or as part of patient information material during a medical consultation that states "As part of the quality improvement activities of our hospital, we periodically review patient charts, or observe doctors and nurses providing care to patients, to make sure that quality care is provided to patients and to examine which practices lead to optimal outcomes. Please let us know if you are uncomfortable with or unwilling to be part of any direct observational activities."

Waivers of informed consent for providers

Guidance point 7

Individual informed consent from providers participating in a research study must generally be obtained. However, the requirement of obtaining individual informed consent from patients can be waived by an REC if

- The research does not directly inform or alter individual patients' therapeutic or medical treatment plans; and
- Risks to the provider are minimal (see Guidance Point 3); and
- The research could not practicably be carried out with the consent of providers.

In cases where individual informed consent from providers will not be sought, general disclosure to providers about patient safety activities is highly recommended.

Even where studies pose minimal risks, it is a matter of basic respect to provide general disclosure to providers about patient safety research occurring in their clinical unit or setting, particularly when information from medical records identifies the providers, when team behaviour is observed, or when team results are recorded. Discussions with clinical staff about patient safety research can serve as an opportunity to raise the topic of patient safety more broadly, as well as to discuss strategies to improve patient safety and quality of care within the institution. Such discussions should include a focus on the fact that monitoring quality and evaluating new strategies to reduce incidents can help providers and institutions learn, through evidence, what is working and where improvements are needed. It must be stressed that the goal of such monitoring and evaluation is to improve the overall system and is *not* to implicate individual providers. Protections to ensure this (i.e. firewalls between individual data and authorities) should be communicated to providers. In addition, hospital, clinic, or facility staff should be informed about how results from patient safety activities will be reported to the hospital, clinic or facility leadership. Group disclosure and discussion can take place at staff meetings or through letters or emails. See Case Study 5 for an illustration.

Institutions participating in patient safety research activities for which individual consent of providers is not necessary should consider whether staff will

have the option of opting out. There could be some cases in which allowing individual staff members to opt out may not be feasible.

Sometimes, consent from providers might be waived, not because the risks are minimal but because the research could not practicably be carried out with their individual consent. This situation could arise, for example, because the research itself is likely to alter practice and so skew the results i.e. the Hawthorne Effect, or the effect of merely knowing one is being observed. This may be more likely for some research than for others, e.g. rates of hand washing to reduce infection rates.

Case study 5 – Group disclosure about patient safety activities

Donchin Y, Gopher D, Olin M, et al. A look into the nature and causes of human errors in the intensive care unit.
Qual Saf Health Care 2003, 12; 143-147

In a single hospital in Israel, a patient safety project was conducted to understand the causes of human errors in the intensive care unit (ICU) so that these errors could be prevented in the future. Data on human errors were reported by the hospital staff immediately after they were discovered. Information that was reported included the time that the error occurred, the time the error was discovered, the profession of the person who committed the error (physician, nurse, etc.), the profession of the person who reported the error and a short description of what happened and the presumed cause. Individuals involved in the project rated the severity of each of the error reports on a five point Likert scale. In addition, to understand the number of activities that occur in the ICU on a daily basis, 46 randomly selected patients were observed continuously for 24 hours by outside trained observers from the Israeli Institute of Technology. The observer recorded all encounters between the patient and his or her immediate bedside surroundings, including any human errors that occurred.

In a published article describing this project, the project team members indicated that all hospital ICU staff were informed about the project and its objectives and were excited to participate. In addition, project team members indicated that the need for ethical approval for this project was waived because "all that was done was observation". Names of hospital staff members and patients were not collected as part of this project. Data collection took place over a period of four months, during which time 554 human errors were reported by hospital staff. The results of this project cannot be directly applied to other ICUs at other hospitals, as the errors reported in this setting were almost certainly unique to this setting and the staff employed there. However, the project staff published this project because the methods used to complete it were innovative and it was felt that similar studies could be easily carried out in other settings.

5. Privacy and confidentiality

Guidance point 8

Staff involved in the conduct of patient safety research and patient safety activities should be aware of the principles and methods related to preserving privacy and confidentiality.

Privacy and confidentiality are two separate but related issues. The United States Office for Human Research Protections has stated that "Privacy can be defined in terms of having control over the extent, timing, and circumstances of sharing oneself (physically, behaviorally, or intellectually) with others. Confidentiality pertains to the treatment of information that an individual has disclosed in a relationship of trust and with the expectation that it will not be divulged to others in ways that are inconsistent with the understanding of the original disclosure without permission."[17]

As CIOMS has recognized, "patients have the right to expect that their physicians and other health-care professionals will hold all information about them in strict confidence and disclose it only to those who need, or have a legal right to, the information."[18] The medical profession sees confidentiality as essential, not only for successful health care, but more importantly to protect the trust that is placed in doctors by their patients.

There are many strategies for safeguarding the personal information of individuals involved in patient safety research. These include coding abstracted data with unique identifiers rather than names and masking features of specific cases, institutions, or settings that may make them recognizable even without names. Masking features of cases may be more challenging for sentinel events, such as a wrong site surgery or

EXISTING GUIDELINES

Research relating to individuals and groups may involve the collection and storage of information that, if disclosed to third parties, could cause harm or distress. Investigators should arrange to protect the confidentiality of such information by, for example, omitting information that might lead to the identification of individual subjects, limiting access to the information, anonymizing data, or other means.

CIOMS International Ethical Guidelines for Epidemiological Research 2009 Commentary on Guideline 18

Every precaution must be taken to protect the privacy of research subjects and the confidentiality of their personal information and to minimize the impact of the study on their physical, mental and social integrity.

Ethical Principles for Medical Research Involving Human Subjects, World Medical Association Declaration of Helsinki, 2008 paragraph 23

a patient death. Grouping similar cases together can help minimize the chance that individual providers or institutions will be identified.

In general, access to patient information before it is de-identified should be granted to as few individuals as possible. This might be achieved by assigning medical staff, who already have permission and confidentiality commitments to review patient charts, or asking data collectors to sign the same level of confidentiality agreement(s) required of hospital staff. Absent these safeguards, patients' consent to abstract data from hospital records, or a waiver of consent from a REC (see guidance point 6) should be sought. Where providers' behaviour is being analysed, by contrast, it may be more protective of privacy if outsiders, rather than colleagues, are the ones who document errors.

In some situations, such as when using a single case to illustrate some findings, confidentiality may be more difficult to ensure. Nevertheless, this principle must be respected even if to achieve it, some patients' details may need to be altered to protect the identity of individuals who would otherwise be identifiable based on the details of their case.

6. Duty to intervene or report

Guidance point 9

Individuals involved in patient safety research may, occasionally, observe practices that may put patients at risk. Researchers observing clinical encounters have a duty to intervene to protect these patients if all of the following are present and the research staff observing these events have sufficient expertise and experience to interpret these situations appropriately:

- they are highly suspicious that an error is imminent;
- they believe it is highly likely that the error will result in direct, severe or irreversible harm;
- their immediate action or intervention will prevent or reverse some of the negative effects of the error;

Where sufficient expertise and experience to interpret the situation is not present, staff should seek advice from more experienced professionals.

Guidance point 10

Similarly, researchers who are abstracting information from patient medical records have a duty to intervene if the research staff reviewing the records have sufficient expertise and experience to interpret the situation appropriately and all of the following are present:

- they are highly suspicious that an incident has occurred;
- they are confident that intervening could reverse some of the negative medical effects of the incident;
- there is no evidence to suspect that an intervention has already occurred in response to the (potential) incident;
- the consequences of the incident are of direct severe or irreversible harm;

Where sufficient expertise and experience to interpret the situation is not present, staff should seek advice from more experienced professionals.

EXISTING GUIDELINES

The WHO expert working group reviewed existing international ethical guidelines on research with human participants and found no discussion of researchers' duties to intervene when they observe practices that put patients at risk. In addition, a literature review conducted by WHO staff was "unable to identify literature that describes when or whether there is a duty to intervene when errors are observed either prospectively or as part of medical chart review."

The guidance set forth in this section of the report is based on the WHO expert working group's recommendations, which were developed through a process of group discussion.

Guidance point 11

Those involved in patient safety research have a duty to report the study results back to hospitals and units once the project is complete.

Patient safety studies sometimes involve observation of health care practices. Occasionally, researchers may face a situation in which they wonder if they should intervene with the care they are observing, in order to prevent a harmful incident they think may soon occur. Similarly, researchers who are reviewing medical records may come across an error or probable error that they believe was never reported. In such situations researchers must decide when, if ever, they should intervene.[19, 20] In general, the role of the researcher is different from the role of a clinician or hospital manager: researchers' primary role is to document the occurrence and nature of some features in order to identify better strategies in the future, or to measure rigorously whether new approaches to preventing harm are systematically better than older strategies. To intervene whenever they see a problem would almost certainly negate their ability to collect sound data, which are necessary for making more widespread progress in improving patient safety. Indeed, in some cases, part of the patient safety researcher's job is to document the rate and nature of substandard or unsafe practices in order to develop programmes to improve care. At the same time, researchers, as human beings and as professionals, cannot simply witness egregious, preventable, and imminent problems without intervening. Research teams must anticipate this problem and plan for the types of situations that may occur in studies, given their own methodology, setting, and population. In general, the expectation is that the above criteria would very rarely be met and researchers would very rarely be intervening. In rare cases, when researchers are qualified to assess risk, and if the risk of harm seems imminent, if the harm would be severe and irreversible, and if interfering could prevent the harm, then researchers should indeed intervene. To facilitate this process, the information sheet given to providers must mention the possibility of the observer commenting and intervening in such circumstances.

For example, if researchers are conducting a surgery checklist study, they should discuss at the protocol planning stage what types of possible incidents would count as highly likely to result in severe harm. An example might be awareness that the anaesthesiologist has included a life-threatening dose of a medication, and the observer is qualified to make such an assessment. In these extremely rare occurrences where a severe or irreversible incident may be imminent and the research staff have the experience and the knowledge to make such a critical observation, intervention should occur. The nature of the intervention will depend on the situation, but will probably involve asking the clinical staff a question related to confirming or double-checking the dose, or the surgical approach, or something similarly important. In case study 6, because the researchers observing the nurses were themselves nurses or pharmacy technicians, they had the expertise necessary to know when an error occurred. They were also instructed to intervene when errors that could cause harm to patients were made.

Case study 6 – Reporting serious errors that can cause direct and severe harm to patients

Greengold N, Shane R, Schneider P, et. al.
The Impact of Dedicated Medication Nurses on the Medication Administration Error Rate: A Randomized Controlled Trial.
Arch Intern Med, 2003:163:2359-2367

This patient safety project was implemented in two hospitals in the United States to understand if having a nurse dedicated to administering medications to patients would reduce the rate of medication administration errors. Four nursing units in each hospital were selected to participate in the project. Within those units, the project staff recruited nurses to participate in the project. Informed consent was obtained from each of the nurse participants and the REC at each of the hospitals approved the project. Once consent was obtained, the nurses were randomly assigned to the intervention or the control group. Those in the intervention group attended a medication safety programme and for two days each week for twelve weeks these nurses were exclusively responsible for administering medications to patients. Those in the control arm did not attend the programme and maintained all of their normal nursing activities.

The nurses in the intervention arm were observed by project staff the two days a week that they were exclusively responsible for administering medications. The nurses in the control arm were observed by the project staff the other three days of the week. The observers were all nurses or pharmacy technicians who attended an observer training session. They were responsible for "recording all aspects of drug retrieval, preparation, and administration" as well as "variations from safe medication practices". If, during the course of their observations, the observer recognized an error that could cause harm to a patient, the observer was instructed to intervene and prevent the error from occurring.

For incidents identified through chart reviews, or through any other mechanism, which are generally conducted retrospectively, any harm associated with the error is less likely to still be reversible. It may also be unclear from medical records alone whether the event was ever reported, whether others were aware of the event, whether any interventions have already occurred or whether, indeed, a harmful incident actually occurred. There will be a relatively small number of cases where intervention, after the fact, can change the clinical course. However, in such very rare cases, and if the patient can still be located, the hospital should be informed so that the patient can be contacted for further evaluation.

Nevertheless, researchers are not best placed to make judgements or take any action based on the findings of the research. Some groups have established "reference groups" or "safety committees" to provide advice on the adequate course of action in situations that may develop during patient safety research and where researchers may not have the expertise and capacity to manage the situation, as has been described under guidance points 4 and 5 (Case Study 4). These committees may constitute a good resource for researchers.

The purpose of patient safety research is to improve patient safety; therefore it is mandatory that the results of the research, in aggregate, be reported back to the hospital or department leadership so that appropriate corrective steps can be taken at the system level. The reporting back of research should be in aggregate form and be anonymized so that there is no way to identify individual providers or patients, as the purpose of reporting results is not to assign blame to individuals. Similarly, units participating in a study should have the opportunity to request that their unit's data not be reported to hospital leadership separately from the overall findings of the whole study. When publishing the outcome of such research, investigators should be particularly careful in situations where the specificities of the setting are so unique that even without the use of identifiers the health facility is easily identifiable.

7. Withholding information

Guidance point 12

Patient safety researchers who propose to withhold information from potential research participants as part of their research must do all of the following:

- Demonstrate to a research ethics committee that no other research method will suffice;
- Persuasively argue that significant advances could result from the research either for the local setting or more broadly;
- Consider whether asking participants to consent to participate, without disclosing the nature or precise timing of the intervention, is reasonable;
- Ensure that withholding information itself will not cause a study to involve greater than minimal risk.

Guidance point 13

In those cases where a research ethics committee approves an activity where information has been withheld from the participants, the committee must also:

- Ensure that nothing has been withheld that, if divulged, would cause a reasonable person to refuse to participate;
- Determine if debriefing of those who participated is possible or appropriate;
- Ensure that a general disclosure of the type of research that is proposed is in place, if possible.

EXISTING GUIDELINES

When deception is deemed indispensable to the methods of a study, the investigators must demonstrate to an ethical review committee that no other research method would suffice; that significant advances could result from the research; and that nothing has been withheld that, if divulged, would cause a reasonable person to refuse to participate. The ethical review committee should determine the consequences for the subject of being deceived, and whether and how deceived subjects should be informed of the deception upon completion of the research.

CIOMS International Ethical Guidelines for Epidemiological Studies 2009 – Commentary on Guideline.

Researchers have a commitment to telling the truth, but omission of some information (e.g. the specific purpose of the study) is considered acceptable in some situations. In general, the type of information that is withheld from participants may include not informing participants that they are in research, not informing them of the true purpose of the research, not informing them which behaviours or interventions are being studied, or taking on a false identity in order to gain additional research information. Such withholding of information from research participants is allowable in exceptional

circumstances, where projects are low risk, where it is necessary for obtaining the relevant data, where the project could significantly advance the field of patient safety, and where it does not change the overall risk profile of the study. For instance, in a study to determine the extent of a problem of fake or substandard quality drugs being sold by pharmacists, "mystery clients" were asked to go to public marketplaces for remedies for their children when they didn't really have a sick child, and the researchers then examined the pharmacological make-up of the products they were given. This study design was allowed by the local REC, because this was considered to be the only way of obtaining access to the pharmaceutical products actually being sold to patients and the study posed very few risks, if any, to those involved.

Case study 7 – Withholding information
(with permission for publication from author)

Counterfeit and substandard drugs have been increasingly recognized as a global public health threat. They impact health and the economy in many ways, including increased morbidity and mortality due to inadequate treatment; cause adverse effects from toxic ingredients; promote drug resistance; foster loss of confidence in the health system; and cause unnecessary suffering and economic hardship for patients and families. Previous studies in a landlocked central Asian country have found counterfeit and substandard drugs, but the extent of the problem is not known. In order to gain insight into the extent and nature of the problem of counterfeit and substandard drugs in the country and help efforts to ensure a safe and effective medication supply, a cross-sectional descriptive study was undertaken to determine the prevalence of selected counterfeit/substandard drugs in the capital city and determine the prevalence of drug outlets selling the selected counterfeit and substandard drugs in that city.

Drug outlets were randomly selected stratified by geographic setting and type of drug outlets. Nine drugs from 3 groups of medicines were selected for testing, based on their therapeutic importance, and earlier reports of being counterfeit or sub-standard. None of these drugs were prescription drugs and all can be purchased over the counter in that country.

A group of paid field workers, who acted as simulated customers, anonymously purchased the drug samples from drug outlets based in a district different from their home district. The field workers were trained to give a specified set of symptoms and ask the questions that usual patients normally would ask pharmacists (can you give me this antibiotic, is this a good brand, can you give me another brand, is this the brand that other people also purchase, etc.). Following appropriate training, the field workers were provided with a list of the drugs and amount needed of each one from the assigned drug outlet. The identity of the drug outlet or the field worker were not on the data collection form; instead a sample number was recorded by the PI when the field worker returned. This sample number was linked to a code for the drug unit known only to the PI. Any potentially identifying information about the drug outlets was coded and removed from samples and data collection tools prior to sample analysis so researchers involved in the analysis would not know the source of any of the samples. If a selected drug outlet did not have the required sample of a drug, the PI arranged for a repeat visit to this facility at a later time or substituted a different randomly selected drug outlet.

Results of the study were provided in an aggregated form to the National Drug Regulatory Authority and the Ministry of Health, in order to allow them to take further action, such as strengthening their regulations. Since the data were analysed anonymously, the Ministry did not receive any information about specific drug outlets, and no punitive action was possible as a result of this research study.

Since withholding information can lead to distrust, additional restrictions are placed on such studies. These include requirements that other designs not involving withholding information be used wherever possible to address the research question, that only minimal risk studies may withhold information, and that as much information about the study be provided as possible, even if one key element is not disclosed. The researcher should also consider whether disclosing information in a more general way (for example, "There will be some clients coming to your shop in the next six months, who may not be the 'real clients'") is possible, as a way of honouring commitments to truth telling while also trying to achieve important scientific ends. Another option is to ask participants to consent to research without knowing the full aspects of the study, with the assurance that the research intervention will not harm them and that a full disclosure will be made in a debriefing session.

Information should not be withheld solely because providing it might cause some individuals to refuse to participate. Withholding information is only appropriate if doing so is the sole way of addressing a socially important research question, and researchers and REC members should carefully consider the necessity of withholding or misleading participants about each aspect of the study. If some information could be provided without jeopardizing the study, that information should be provided.

Debriefing is a method of minimizing the infringement of subjects' right against experimentation without consent. In studies in which information is withheld, the REC should determine whether debriefing of participants should be required following data collection, taking into consideration factors such as the existence of an ongoing relationship between participants and researchers (which would favor debriefing) and whether debriefing would increase or decrease the likelihood that participants could experience psychological harm. The objective of debriefing participants involved in such research is to provide them with more complete information about the study and about why information was not provided to them upfront.[21] In general, debriefing involves explaining the purpose of the study, the social significance of the study, and why the particular study design was necessary. It also requires that the researchers identify and manage any harm that participants might have experienced as a result of having been involved in the study, and that researchers give participants the opportunity to withdraw their data from inclusion in the study. Although the right to withdraw data does not constitute informed consent, it allows participants to regain some control over how their private information is used. The risk of selection bias or having an underpowered study are not adequate reasons for choosing not to debrief study participants. If debriefing is to be performed, it should ideally occur immediately after data are collected.

8. Conclusions and way forward

The protection of research participants from harm caused by the conduct of research studies has become a central area of attention by researchers and ethicists worldwide. A vast corpus of scholarly debate has ensued thereafter, leading to widely accepted recommendations in general and as applied to various research disciplines. The general uptake and extension of research ethics committee reviews and of good practices by researcher bodies and scientific journals worldwide, promoting compliance with good ethical conduct in research, is proof of the commitment to and respect of these principles by professionals and institutions.

Nevertheless, new fields of research may challenge the application of existing ethical principles, if research questions or some specific circumstances of the conduct of particular studies lead to new situations for which there is no prior experience of ethical debate. This may be the case for patient safety research, quality improvement and in patient safety activities in general. These are still relatively new fields of enquiry, where some circumstances may seem to present new ethical questions and challenges. This is what led to the production of the guidance included in this report, in the expectation that some advice about the application of the existing ethical guidance to the field of patient safety research might help researchers and ethical review committee members in their ethical assessment and design of the studies.

As described in this report, there are a number of instances where researchers may be confronted with new situations and possibly with ethical controversies. The guidance provided in this report offers an initial response to many of the challenges faced by patient safety researchers and quality improvement professionals building from the existing corpus of ethical standards. Furthermore, this guidance also calls attention to the potential ethical risks that may be brought up by activities and programmes of patient safety or quality improvement, though usually not considered part of research and therefore not usually under the oversight of ethics review committees. This guidance raises the importance of considering potential risks inherent in such activities and suggests to institutions involved in such important activities to facilitate some level of ethical advice or oversight as feasible. The formation of a functional reference group, or patient safety committee, whether stable or ad-hoc, may represent a possible solution in these circumstances. Such a group or committee should be composed of respected professionals, able to provide their honest judgment to assist researchers and patient safety improvement bodies in solving issues of an ethical nature arising during the design or conduct of a given study.

This report could not possibly cover all ethical issues that could arise during the design and conduct of patient safety research and other related activities. Furthermore, the guidance provided here for the issues under consideration cannot be exhaustive. Instead it is a modest reflection of the discussions and debate held by its contributors. For this reason, this report aspires to be the first edition of a series, soon to be updated with new evidence and more elaborated debate. WHO encourages evaluation and feedback from the guidance described here, as well as increased and new discussion in this important field of ethics as applied to patient safety research.

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Appendix 1: How this guide was developed

The production of the "Ethical issues in patient safety research" included the following key steps:

1. Identification of ethical issues related to patient safety research, through an issue-spotting workshop with WHO staff and ERC members in March 2010.

2. Systematic review of the literature on ethical issues related to patient safety/quality improvement research, aiming to synthesize existing knowledge on the subject, in order to inform next steps in the process. Over 60 journal articles, monographs and other publications were reviewed to produce a synthesis of the state of knowledge. Results of the review are summarized in the manuscript "Ethical Issues in Patient Safety Research; A systematic review of the literature. Whicher DM, Kass NE, Audera-Lopez C, Butt M, Larizgoitia Jauregui I, Harris K, Knoche J, Saxena A. The list of the documents reviewed is provided at the end of this Appendix.

3. An International Expert Consultation held in May 2010 reviewed the set of ethical issues and initial synthesis of the literature. Experts were patient safety researchers, health facility managers, ethicists, ethics committee members, and patient advocate representatives. Using small group discussions and a case-based approach, the consultation identified a core set of issues that would benefit from further guidance and built consensus on the core concepts included in this guidance.

4. Two rounds of external reviewers, involving international academics with expertise in quality improvement, patient safety, research methods or ethics from all six WHO Regions, advised on the various iterations of the document.

5. Every external contributor in the working group and in the review process submitted a standard WHO "Declaration of Interests" form to the WHO Secretariat. None declared any conflicts or potential conflicts.

6. A drafting group produced the different iterations of this document, based on recommendations from the expert consultation and the two rounds of external review. The drafting group considered all suggestions made by the reviewers.

All participants in this process are listed in the Acknowledgements section that accompanies this document.

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Appendix 2: Summary of the ethical guidance related to patient safety research

Guidance point 1

Any patient safety activity that constitutes research, regardless of its methodology, should be submitted to a Research Ethics Committee (REC).

For purposes of REC oversight, patient safety activities constitute research when:

- they are aimed at addressing a specific question; and
- they use a predefined approach or method for collecting data in response to the question they intend to address; and
- their findings are intended to be applied to settings beyond those in which the activity or programme is implemented.

Guidance point 2

Patient safety activities, even when they do not meet the definition of research requiring ethical review, may involve more than minimal risk to patients and health-care providers in some situations. It is the responsibility of those working in patient safety activities to be aware of ethical issues and seek guidance as needed.

Guidance point 3

Patient safety research may be considered of minimal risk if all of the following factors are present:

- The intervention does not modify clinical management or the treatment plan for the patient;
- Data are not individually identifiable, or adequate protections against breaches of confidentiality of data are in place;
- The intervention is unlikely to divert staff from existing responsibilities in ways that are likely to pose a risk to patient wellbeing and safety;
- Nothing in applicable laws, or institutional rules, or the local cultural context suggests that conducting the study in the particular environment would pose higher risks to the patient;
- No other features of the activity suggest an increased level of risk to patients, providers, or institutions, compared with the patient safety activity not being implemented.

Guidance point 4

- Before conducting a study, researchers should consider discussing with leadership of the health-care institution under study the importance of avoiding a culture of blame with regard to patient safety.
- Patient safety researchers should also consider whether the political, social, institutional, or cultural context in which the project will be implemented could alter the project's risk profile.

Guidance point 5

Individuals involved in patient safety research who are interviewing or observing patients or providers should anticipate any distress participants may experience as a consequence of the conduct of the study and be prepared to offer solutions. Some options are:

- Be trained to ask participants if they would like to skip questions or stop the interview if they become distressed;
- Be equipped with referrals for supportive care or counselling in case participants become significantly distressed;
- Be equipped with the names of hospital authorities to whom participants and families can be referred if they have questions; and
- Ensure that all services and providers whose names will be given out as referrals have agreed to have their names provided to patients and families.

Guidance point 6

Researchers conducting patient safety research studies must generally seek individual informed consent from patients. However, the requirement of obtaining individual informed consent from patients can be waived by an REC if

- The research does not directly inform or alter the individual patients' therapeutic or medical treatment plans; and

- Risks posed to patients by the research are minimal; and
- The research could not practically be carried out if individual informed consent were required; and
- The privacy and confidentiality or anonimity of individual patients are assured (see Guidance Point 8).

In cases where individual informed consent from patients will not be sought, general disclosure to patients about patient safety research is highly recommended.

Guidance point 7

Individual informed consent from providers participating in a research study must generally be obtained. However, the requirement of obtaining individual informed consent from patients can be waived by an REC if

- The research does not directly inform or alter individual patients' therapeutic or medical treatment plans; and
- Risks to the provider are minimal (see Guidance Point 3); and
- The research could not practicably be carried out with the consent of providers.

In cases where individual informed consent from providers will not be sought, general disclosure to providers about patient safety activities is highly recommended.

Guidance point 8

Staff involved in the conduct of patient safety research and patient safety activities should be aware of the principles and methods related to preserving privacy and confidentiality.

Guidance point 9

Individuals involved in patient safety research may, occasionally, observe practices that may put patients at risk. Researchers observing clinical encounters have a duty to intervene to protect these patients if all of the following are present and the research staff observing these events have sufficient expertise and experience to interpret these situations appropriately:

- they are highly suspicious that an error is imminent;
- they believe it is highly likely that the error will result in direct, severe or irreversible harm;
- their immediate action or intervention will prevent or reverse some of the negative effects of the error;

Where sufficient expertise and experience to interpret the situation is not present, staff should seek advice from more experienced professionals.

Guidance point 10

Similarly, researchers who are abstracting information from patient medical records have a duty to intervene if the research staff reviewing the records have sufficient expertise and experience to interpret the situation appropriately and all of the following are present:

- they are highly suspicious that an incident has occurred;
- they are confident that intervening could reverse some of the negative medical effects of the incident;
- there is no evidence to suspect that an intervention has already occurred in response to the (potential) incident;
- the consequences of the incident are of direct severe or irreversible harm;

Where sufficient expertise and experience to interpret the situation is not present, staff should seek advice from more experienced professionals.

Guidance point 11

Those involved in patient safety research have a duty to report the study results back to hospitals and units once the project is complete.

Guidance point 12

Patient safety researchers who propose to withhold information from potential research participants as part of their research must do all of the following:

- Demonstrate to a research ethics committee that no other research method will suffice;
- Persuasively argue that significant advances could result from the research either for the local setting or more broadly;
- Consider whether asking participants to consent to participate, without disclosing the nature or precise timing of the intervention, is reasonable;
- Ensure that withholding information itself will not cause a study to involve greater than minimal risk.

Guidance point 13

In those cases where a research ethics committee approves an activity where information has been withheld from the participants, the committee must also:

- Ensure that nothing has been withheld that, if divulged, would cause a reasonable person to refuse to participate;
- Determine if debriefing of those who participated is possible or appropriate;
- Ensure that a general disclosure of the type of research that is proposed is in place, if possible.

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