

Ethical considerations

for health policy and
systems research

A publication from the Alliance for Health
Policy and Systems Research (WHO) with the
Global Health Ethics Unit (WHO)

Two decades of advancing and supporting health policy and systems research

The Alliance for Health Policy and Systems Research (the Alliance) works to improve the health of those in low- and middle-income countries by supporting the generation and use of evidence that strengthens health systems. As an international partnership hosted by the World Health Organization, we work together with organizations around the world to:

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- Support institutional capacity for the conduct and uptake of health policy and systems research;
- Stimulate the generation of knowledge and innovations to nurture learning and resilience in health systems; and
- Increase the demand for and use of knowledge for strengthening health systems.

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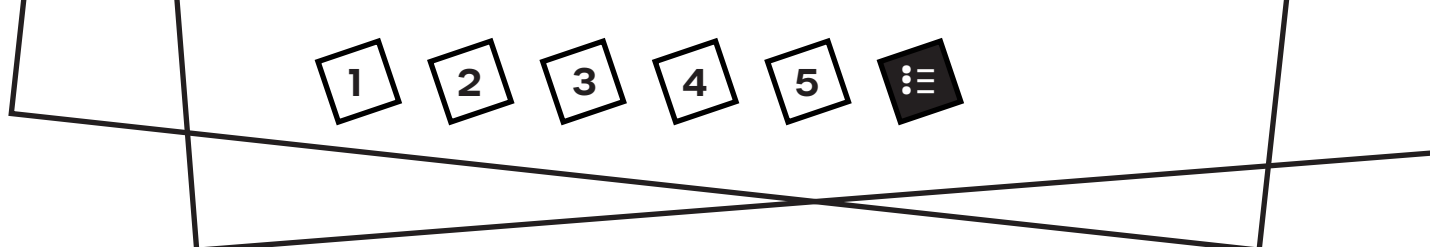
This document is a synthesis of the report of the 'Experts Meeting on Ethical Review for Health Policy and Systems Research' held in Zurich on 23 and 24 July 2015 and a scoping review on the topic commissioned by WHO (1).

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* indicates that the person attended the meeting in Zurich.

Abbreviations & acronyms

CIOMS	Council for International Organizations of Medical Sciences
HPSR	Health policy and systems research
LMICs	Low- and middle-income countries
REC	Research ethics committee



Preface

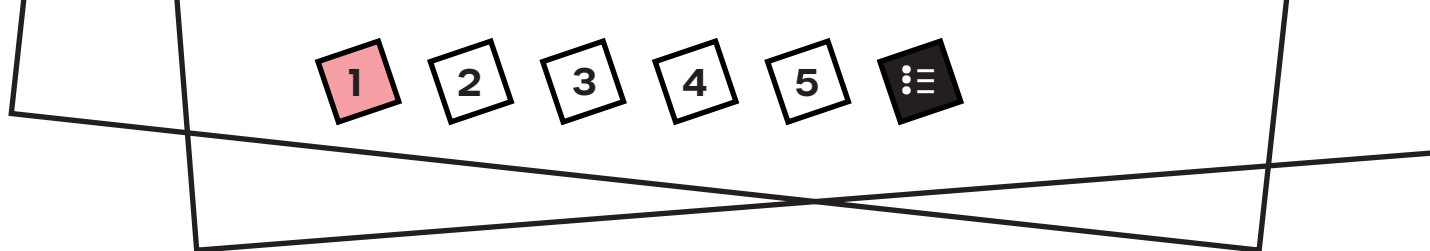
Over the last century, research has contributed to significant improvements in health and well-being for populations around the world. New technologies and medicines have saved millions of lives, but as we work to achieve universal health coverage (UHC), we need to also recognize the importance of research on the politics, policies and systems that shape our ability to reach our collective health goals. The field of health policy and systems research (HPSR) aims to do exactly that.

HPSR is a relatively young and emerging field that draws from diverse public health and social science research approaches to respond to the complex challenge of strengthening health systems. Practitioners of HPSR grapple with a distinct set of ethical issues reflecting the multidisciplinary nature of the field. For instance, when is a project considered health research versus practice? When researchers are studying policy decisions that have already been made, is research ethics review required?

This document shines a light on these ethical issues and offers a series of considerations for all those involved in HPSR. It is an important first step in thinking about developing clear research ethics guidelines for HPSR that are distinct from guidelines targeted at traditional health, biomedical and epidemiological research. While the principles for the ethical conduct of HPSR are not different, how those principles are interpreted and applied can vary widely – which ultimately leads to inconsistent application of ethical reviews in the field.

This document will be of value to all involved in undertaking or using HPSR, including researchers, educators and students, as well as policy-makers and practitioners involved in co-producing research on health policy and systems. Research ethics committees – especially those that have limited experience of dealing with HPSR – will find it particularly helpful, as it illustrates the points made with clear and relevant examples. I hope that the contents will stimulate further thinking and development of guidance in this field.

Dr Soumya Swaminathan
Chief Scientist, World Health Organization



1. Introduction

Achievement of universal health coverage requires well-functioning health systems, with evidence-based policies and programmes (2). Health policy and systems research (HPSR) is essential for generating evidence that is sensitive to context, informed by multiple disciplines and focused on changing policy and practice to strengthen health systems. The field of HPSR and its conduct pose important challenges for both researchers and research ethics committees (RECs) about the interpretation and application of the principles for ethical conduct of health research to policy and systems research. For instance, when is a project health research and when is it health practice? Is research ethics review required for studies of existing policy decisions? In HPSR, to what extent could the risks to individuals be considered secondary to the risks to populations, and how should that decision be made? Are the risks to patients more important than the risks to health care providers or policy-makers? Who are the participants in HPSR, and who should be asked for consent? Currently, there is no guidance to help ethics committees and researchers address these complexities and nuances. The available guidelines for ethical conduct of research remain applicable to traditional health, biomedical and epidemiological research. While the principles for the ethical conduct of health systems research are not different, their interpretation and application may be. The outcomes of reviews provided by different ethics committees can therefore vary widely.

This document, prepared by the Global Health Ethics team at WHO in collaboration with the Alliance for Health Policy and Systems Research, responds to a request from researchers and RECs for advice on interpreting existing research ethics principles in the context of HPSR. It lists the ethical challenges encountered in HPSR and provides a framework to guide researchers and RECs in answering some of the questions posed above when reviewing or conducting HPSR. This document is a necessary, critical first step towards raising awareness about the unique ethical challenges that HPSR poses and advocates for comprehensive ethical guidance in HPSR for both RECs and researchers.

The document provides researchers and RECs with a series of “points to consider” for clear identification, consideration and communication of ethical issues in HPSR. It builds on a scoping review of the literature on ethics of health policy and systems research prepared by B. Pratt and colleagues for WHO (1), the reflections of an international expert group (3) and comments by international expert reviewers.

Broadly, the aim of the document is to promote clear thinking and communication about the ethical issues in HPSR study protocols and REC review. It is intended that, after reading this document, researchers will better understand relevant



ethical issues in their HPSR study protocols and respond effectively to REC comments and questions; and REC members will be better able to identify aspects of an HPSR project that fall within its purview, identify ethical issues raised by the study and better communicate comments and questions to researchers.

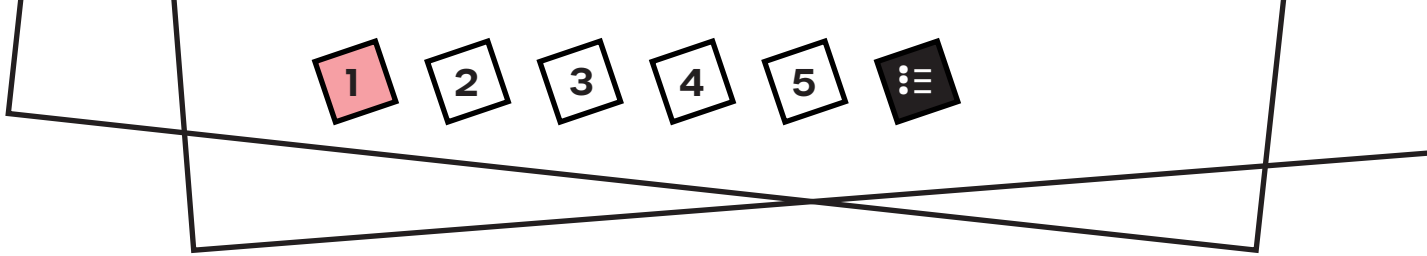
This is not a guidance document, nor does it establish any novel ethical principles. Rather, it provides points to consider in the application of existing ethical principles to HPSR and could form the basis for future comprehensive ethical guidance for HPSR. The document is not intended to override any applicable national regulations or laws.

The aim of HPSR is to generate knowledge to improve “how societies organize themselves to achieve health goals” (4). It addresses socially important questions on the “coverage, quality, efficiency and equity of health systems” (4). It is interdisciplinary, blending economics, sociology, anthropology, political science, public health and epidemiology to draw a comprehensive picture of how health systems respond and adapt to health policies and how health policies can shape and be shaped by health systems and the broader determinants of health. The focus of the research is therefore on policies and programmes and not on the clinical management of patients or the development of new therapeutics. While rigorous evidence to inform policy and programmes is relevant to all health systems, the potential impact of HPSR is greatest in the world’s poorest nations (5).

All research involving or affecting human participants must conform to high scientific and ethical standards. Internationally accepted ethical principles are articulated in a number of documents, including the International Ethical Guidelines for Health-related Research Involving Humans of the Council for International Organizations of Medical Sciences (CIOMS) (6) and the Declaration of Helsinki of the World Medical Association (7). These international statements have been supplemented with useful guidance specific to the ethics of cluster randomized trials (8) and research on patient safety research (9).

As in many new areas of research, HPSR raises some difficult issues because of the questions asked and the methods used to answer them. The main purpose of current ethical guidelines is to seek to protect the liberty and welfare interests of individual research participants. HPSR, however, also includes health systems and organizations and entire communities (4). For example, when a research project involves a policy change that alters service delivery in health institutions and thus the outcomes of patients, who should be considered research participants and from whom should consent be obtained? Who protects group or institutional interests in such research? How does one ensure that the potential benefits of a study outweigh the risks to both individuals and groups? Must changes in service delivery be sustainable?

It is our hope that the points to consider listed in this report will guide researchers and RECs in identifying, considering and communicating ethical issues in HPSR.



We further hope that the document will inform a broader range of stakeholders, including health institutions, government agencies and funding agencies, about the ethical issues raised by this socially important research. Finally, we hope that the document will promote dialogue about ethical issues on HPSR and that consensus can be captured in formal ethical guidance in the near future.

The document comprises three sections: a brief overview of the field and the ethical challenges of HPSR, 14 considerations about the ethical dimensions of HPSR and six case studies in which the considerations are applied.



2. Health policy and systems research

2.1 Definition

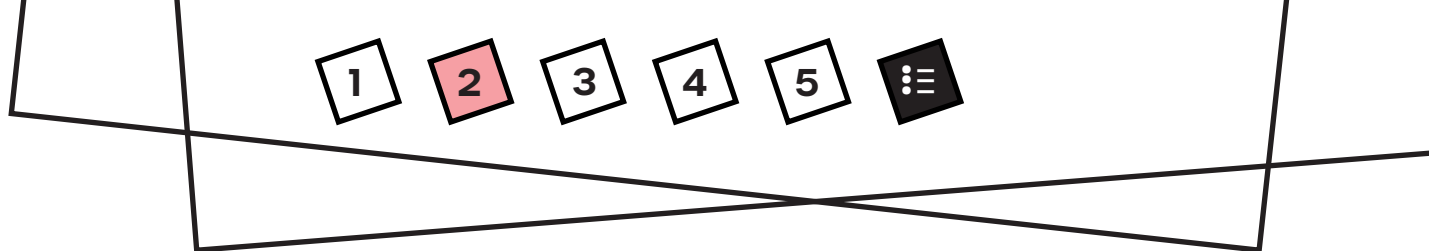
Health policy and systems research is understood as the “production of new knowledge to improve how societies organize themselves to achieve health goals” (4), with the primary goal of promoting the generation, dissemination and use of research for improving the health systems of low- and middle-income countries (3, 10). A health system consists of all the organizations, institutions, resources and people with the primary purpose of improving the health of populations (11). HPSR covers a broader terrain, including the policy process, the health system and global influences (10).

HPSR is defined by the types of research questions it addresses and the context of the research and not by specific research methods. The questions it addresses are relevant to real-world issues and settings. It involves applied research that can support implementation of health policies and health system development, drawing on methods and perspectives from a range of disciplines, including anthropology, economics, epidemiology, geography, history, medicine, nursing, political science, sociology and statistics (12). HPSR encompasses diverse research methods, including descriptive, explorative, explanatory, emancipatory and predictive types. Finally, HPSR engages and involves communities and health care providers in the co-production of knowledge and its use in practice.

For a more detailed description of HPSR, its defining features, steps in conducting HPSR studies, types of studies and research design and methods, refer to Gilson (10).

2.2 Ethical challenges

The aim of establishing ethical principles for health research is first and foremost to protect the liberty and welfare interests of individual participants (13). The ethical principle of respect for persons is grounded in the general requirements of informed consent for autonomous people and protection for those who cannot make their own decisions. The ethical principle of beneficence requires that the potential benefits and risks of a study are in reasonable relation to one another. Thus, patients participating in research must be protected from interventions known to be inferior and benefit from interventions (when possible), and the risk to participants must be generally minimized and reasonable in relation to



the potential benefits. The ethical principle of justice requires that the potential benefits and burdens of study participation be distributed equitably. Vulnerable participants – understood to be those who cannot protect their own interests through the informed consent process or who are at “identifiably increased likelihood of incurring additional or greater wrong” (14) for other reasons – are entitled to additional protection, including a surrogate decision-maker, and limits to the risks to which they may be exposed. An exception to the largely individualistic focus of ethical principles is the requirements that the research have social value and that researchers protect and promote the interests of communities in research.

HPSR raises difficulty in interpretation of these accepted ethical principles because of the questions addressed and the methods used (15). First, in HPSR, research and practice are commonly intertwined. As explained above, HPSR is conducted to understand what systems are in place in a setting, the interactions among the components of those systems, what can be done to influence policy agendas and improve their implementation and what can be done to improve health outcomes. In order to achieve these goals, HPSR commonly involves close collaboration with policy- and decision-makers. Further, studies are often embedded within policy-making and delivery at the level of the (health) system, organization or practice. As Luyckx and colleagues (3) explain: “Given the embedding of [HPSR] in real-world contexts, there is a need to separate what should be governed by the ethics of health systems practice and policy making and what should be governed by the ethics of research.” Accurate identification of the elements that constitute research and are thereby subject to research ethics principles challenges both researchers and RECs.

Secondly, HPSR affects stakeholders at several levels, complicating the identification of research participants (16,17,18). In a cluster randomized trial of a novel method of service delivery, hospitals may be randomized, health providers affected and data collected from patients. In such complex studies, who should be considered participants: patients or health providers? Are hospitals “nonhuman research participants”? From whom is informed consent required? Under what conditions might the consent requirement be waived?

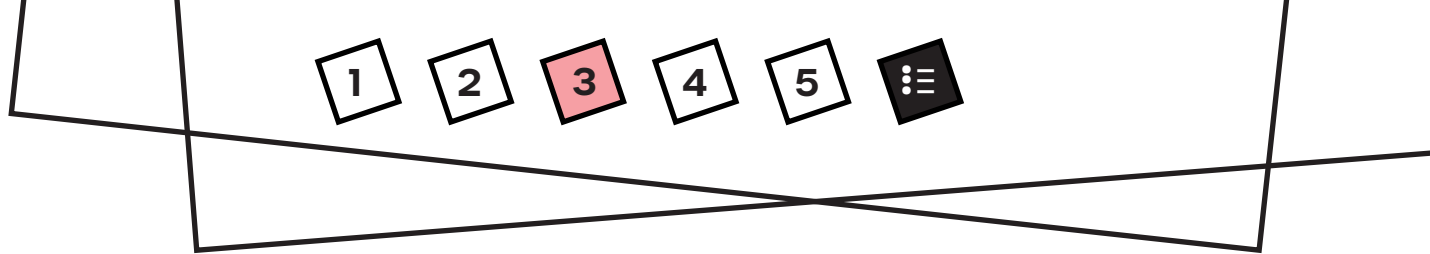
Thirdly, as pointed out by Hyder and colleagues (16), “[g]iven the macro focus of [HPSR], the participants and beneficiaries are often communities, hospitals, and health care institutions, as opposed to individuals.” Group and institutional interests are commonly implicated in HPSR, and it is important that these interests be adequately accounted for in research ethics review. This raises the question of whether the permission of groups or institutions is required and, if so, who speaks on their behalf? Are other mechanisms, such as group consultation, effective in protecting group interests and, if so, when should they be used?

Fourthly, harm-benefit analysis is complicated in HPSR studies that involve both individuals and groups. According to Luyckx and colleagues (3), “Often in [HPSR], one group is subject to an intervention, but the benefits and risks of that intervention may accrue in separate groups. Additional groups potentially placed



at risk may not be obvious.” Such questions may be particularly difficult to answer when individual and group interests conflict. Further, the applicability of key concepts in harm-benefit analysis to HPSR is unclear. The ethical requirement of clinical equipoise – that there be genuine uncertainty in the expert community about the preferred health intervention – protects patients in clinical research from knowingly being exposed to substandard medical treatment. HPSR interventions are not, however, conducted to test medical treatments but to analyse changes in policy, implementation or service delivery. How, if at all, does clinical equipoise guide the choice of interventions in HPSR? Is equipoise for a context or process acceptable as grounds for testing an intervention that could include a control group that does not receive the optimal clinical treatment or for whom the “standard of care” is suboptimal?

Fifthly, researchers are widely acknowledged to have an obligation to consider providing access to interventions after a study. As the goal of HPSR is to strengthen health systems, there may be a stronger obligation to ensure that health service interventions that are proved to be effective are rolled out and are sustainable (4).



3. Ethical considerations

Researchers and RECs need guidance in applying accepted ethical principles to HPSR. To that end, we offer 14 considerations for clear identification, reflection and communication of ethical issues in HPSR (Table 1). These considerations interpret the existing international research ethics guidelines (Declaration of Helsinki, the CIOMS guidelines etc.) for domains that are specific to HPSR, and do not exclude the application of other guidance points common to health research, but not mentioned here. They build on the eight domains of ethical relevance in health systems research proposed by Hyder et al. (16), and those identified through the scoping review (1). The questions are ordered sequentially to assist the reader in identifying research elements, the study interventions and data collection tools and applying relevant ethical principles to those elements. The column “challenges in HPSR” lists features that exemplify the pertinence of the question. The column “specific questions” provides a number of probes or prompts to assist researchers and RECs in addressing the question in a specific case. As HPSR can be very complex, judgement is required in applying ethical principles.

To illustrate application of the points, section 4 provides six cases that illustrate diverse examples of HPSR and an ethical analysis of each.

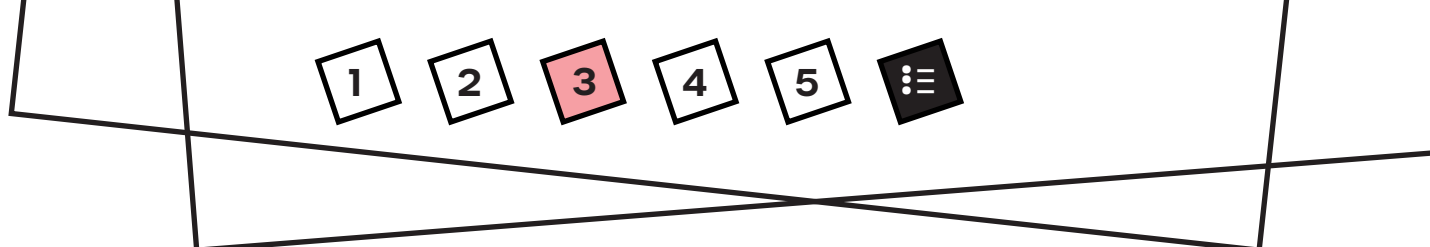
Table 1: Considerations about the ethics of HPSR

Point to consider	Challenges in HPSR	Specific questions
1. Is it research?	Studies are complex, and research and practice may be intertwined.	In the study protocol, are practice and research elements clearly identified?
	Quality improvement is the primary goal of most HPSR.	Is the project as a whole rightly classified as programme evaluation?
	A distinction between research and quality improvement is not helpful.	Is there uncertainty? If yes, a written determination from an REC may be required.

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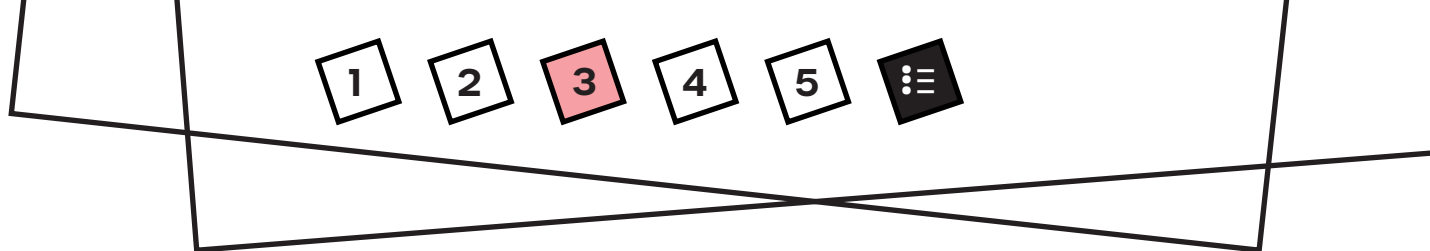


Point to consider	Challenges in HPSR	Specific questions
2. Which aspects are research?	Research and practice are intertwined, and it may be difficult to clearly identify research and practice elements.	<p>Are practice elements (activities that are part of routine delivery of care) clearly identified? One way of identifying practice elements might be to determine whether activities are under the control and direction of the ministry of health, health administrators or a health organization and whether they preserve the role of provider judgement in providing care.</p> <p>Are research elements clearly identified?</p>
3. Is research ethics committee review required?	<p>Studies may have multiple levels, complicating identification of participants.</p> <p>Research involving human participants must be reviewed by an REC.</p>	<p>If the project involves research, does it involve human participants (see point to consider 7)?</p> <p>Is there uncertainty about whether an REC review is required? A written determination from an REC may be required.</p>
4. Are there adequate plans to manage any conflicts of interest?	Conflicts of interest may occur when an agency or institution evaluates its own performance.	Are there adequate plans in place to ensure the independence of the study and disclosure of results?
5. Where relevant, what is the study intervention ?	<p>Study interventions are diverse.</p> <p>The study may be administered at different levels.</p>	<p>What action is to be evaluated in the study? Actions may involve policy change, educational interventions or reorganization of care delivery.</p> <p>Is the action administered at the level of the community or organization, health professional or citizen?</p>



Point to consider	Challenges in HPSR	Specific questions
6. What are the procedures for data collection?	<p>A single study may involve various types of data collection, including desk reviews, primary data collection and use of routinely collected data.</p> <p>Data may be collected at various levels (e.g. individual, aggregated).</p>	<p>By what means is information collected for research purposes?</p> <p>Is it collected at the level of the cluster, health professional or patient?</p>
7. Who are the research participants?	<p>Studies commonly involve stakeholders at various levels, including the health system, hospital, health provider and citizen.</p> <p>Within one study, an intervention may target one group but the outcomes may be measured in a different group.</p>	<p>In the context of the study, who is manipulated, intervened upon, observed or otherwise interacted with by researchers or whose private health information is collected?</p> <p>Are policy-makers, decision-makers or health providers research participants?</p> <p>Is there uncertainty about the identifiability of samples or data that would require a written determination from an REC?</p>
8. From whom is informed consent required, or is a waiver of consent appropriate?	<p>Different groups of participants may be exposed in different aspects of the study.</p> <p>Policy-makers, decision-makers and health providers may have a prima facie ethical duty to continually improve the delivery and outcomes of health care.</p> <p>Intervention at cluster level may be difficult or impossible to avoid, making refusal of consent meaningless.</p>	<p>Will research participants provide informed consent?</p> <p>Will research participants be provided with information relevant to their involvement in the study?</p> <p>If policy-makers, decision-makers or health providers are research participants, will their informed consent be obtained?</p> <p>Do the conditions for a waiver of consent apply?</p> <p>If consent is waived, will staff, patients or members of the public be notified that a research study is being conducted?</p>

Point to consider	Challenges in HPSR	Specific questions
9. Is permission from a “gatekeeper” required?	<p>Studies commonly involve groups as well as individuals, and there may be an impact on group or institutional interests.</p> <p>A variety of gatekeepers may be involved, including the ministry of health, hospital administrator or data custodians.</p> <p>The authority of the gatekeeper to give permission may be unclear.</p>	<p>Does the conduct of the study substantially implicate group or institutional interests?</p> <p>Does the gatekeeper have the legitimacy to give permission?</p> <p>For what aspects of the study is the gatekeeper giving permission?</p>
10. Is group or community engagement required?	<p>Engagement with communities in activities that involve them is good practice.</p> <p>Some studies may substantially affect the interests of groups or communities.</p>	<p>Are there adequate plans to engage with relevant groups or communities before initiation of the study?</p>
11. Are there adequate plans for protection of privacy and confidentiality?	<p>Data collection procedures may include use of routinely collected data and individual and aggregated data.</p> <p>Data may be collected on patients, health providers or institutions.</p>	<p>Has use of identifiable data been adequately justified?</p> <p>Are adequate procedures in place to protect the confidentiality of patients and health providers?</p> <p>Are institutions or communities identifiable, and, if so, is there risk to their reputations?</p>



Point to consider	Challenges in HPSR	Specific questions
12. Are the potential benefits and risks of the study acceptable?	<p>Benefit-risk analysis is complicated by potential impacts on group and individual interests.</p> <p>Application of clinical equipoise to studies involving policy or care delivery is not straightforward.</p> <p>Different groups of participants may be exposed in different aspects of the study, and separate benefit-risk analyses may be required.</p> <p>Improvement of the health system or human and material capacity building are not necessarily benefits but the central aims of the HPSR.</p>	<p>Is the study intervention consistent with competent practice in the relevant field?</p> <p>Will the control condition deprive participants of effective care or programmes to which they would have access?</p> <p>Are the risks of data collection minimized and reasonable in relation to the importance of the knowledge to be gained?</p> <p>Does the study discuss benefits that are more appropriate to HPSR, such as equitable distribution of existing resources? This is also a justice issue.</p>
13. Are concerns about justice and equity adequately addressed?	<p>The research question must address a local health priority in context.</p> <p>Studies may be conducted to evaluate interventions in people who are socially disadvantaged or to explore differences in the effects of interventions in subgroups with different levels of social disadvantage.</p> <p>Studies commonly involve health providers and other employees in health institutions.</p> <p>Health providers and employees may be exposed to social risks, including reputational or professional harm.</p>	<p>Does the research project address a local health priority?</p> <p>Does the study protocol ensure the participation of hard-to-reach and “hidden” groups and those that are often left out?</p> <p>Are any groups unfairly excluded?</p> <p>Are some participants vulnerable and at increased likelihood of incurring additional or greater wrongs?</p> <p>Is adequate protection in place for vulnerable participants?</p> <p>If the study involves employees, are procedures in place to promote free and informed participation?</p> <p>Are procedures in place to protect the interests of participating groups, health facilities or organizations?</p>



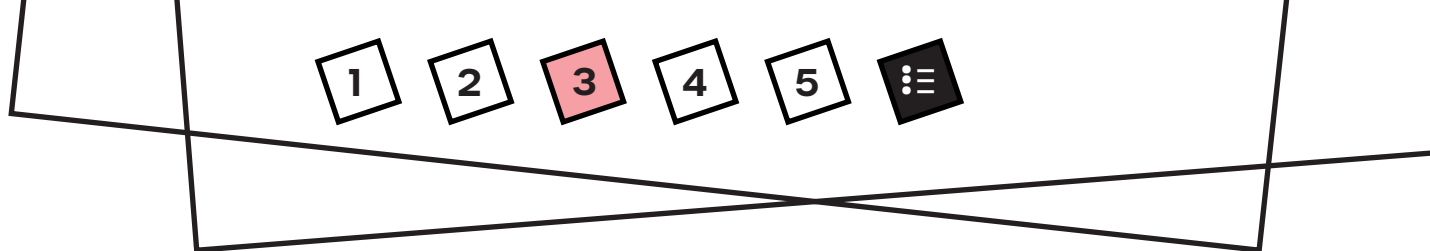
Point to consider	Challenges in HPSR	Specific questions
14. Where relevant, are there satisfactory plans for access to interventions after the study, and roll-out of successful interventions on a wider scale?	<p>The aim of HPSR is to strengthen health systems through research. It therefore has a greater responsibility to ensure that when interventions are studied, they are sustainable, and efforts are made to develop plans for wider roll-out of the successful interventions.</p> <p>Multiple actors are commonly involved, and it may be unclear where the researcher's obligation ends and that of others, including the State, begins.</p>	<p>Who is funding the study, and who is responsible for implementing its results?</p> <p>Are there adequate plans to ensure that the intervention is sustainable and the government is committed to incorporate the successful interventions into the health systems programmes and policies?</p>

3.1 Is it research?

Many, if not all, human activities imply ethical questions. As the aim of our analysis of HPSR is to describe the application of widely accepted ethical principles for research with human beings, we discuss only research that involves human participants. In restricting our focus, we do not imply that non-research activities do not raise ethical issues. The day-to-day functioning of health systems, health organizations and medical practice are replete with ethical issues that require further consideration (19).

Research may be defined as a systematic activity "designed to develop or contribute to generalizable health knowledge" (6). Generalizable knowledge has been defined as "theories, principles or relationships, or the accumulation of information on which they are based related to health, which can be corroborated by accepted scientific methods of observation and inference" (6). Research is usefully distinguished from non-research for quality improvement, which is designed only to inform a change in local practice or policy. "Such[...] 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" (9).

In some sense, the aim of most HPSR is to improve the quality and efficiency of the provision of health care. As a result, an appeal to distinguish between "research" and "quality improvement" is unhelpful; however, any systematic



activities designed to produce generalizable knowledge must be considered research. We examine the complex disentanglement of research and practice in HPSR in more detail under point to consider 2.

Programme evaluation that is not designed to contribute to generalizable knowledge but merely to inform local policy or practice does not fulfil the definition of research, and ethical principles for research do not apply (see case 6 for an instance of programme evaluation that is not research). In view of the perceived inconvenience of research ethics review, researchers may unwittingly classify research as non-research for quality improvement. As there may be a conflict of interest in such judgements, researchers should consult an appropriate REC for a written determination that the activity in question is in fact not research. It does not follow, however, that non-research should not be subject to ethical scrutiny; however, the form that it takes may differ from REC review. For example, principles applicable to research may also be applicable to non-research quality improvement or programme evaluation. In case 6, we illustrate how issues of privacy and confidentiality are considered in programme evaluation.

3.2 Which aspects are research?

In HPSR, research and practice are commonly intertwined, and it may be difficult to clearly distinguish the two. Nonetheless, Luyckx and colleagues (3) conclude that it is “important in [HPSR] to establish boundaries between research and practice.” Case 1 provides a real instance of this challenge. In brief, the study was conducted to evaluate the introduction of a new, integrated medical record for ante-, peri- and postnatal care of women in three Jordanian hospitals in the context of introduction of an electronic health record throughout the health system. Clinical data on women and newborns are routinely collected in Jordanian hospitals. The researchers initiated activities including training for health professionals, audit of health records and weekly visits by one of the researchers to health providers in order to improve the uptake and quality of the integrated medical record. Which aspects of this study should be considered practice and which research? Accurate identification of research elements is important, as ethical principles and regulations for research apply only to these elements.

What distinguishes practice and research elements in HPSR? Practice elements may be thought of as those that are part of the routine delivery of care. At the level of a health system or health organization, they are activities that are under the control and direction of a ministry of health or health organization. At the level of the individual medical practitioner, they are activities for the care of patients and those that preserve the role of health provider judgement. In the above example, introduction of an electronic health record and routine collection of data on women and newborns are under the control and direction of the ministry of health and the hospitals and should thus be considered practice.



Practice is not a research element. Research elements are part of a systematic investigation designed to produce generalizable knowledge and may include novel policies, methods of health service delivery or treatments. They are typically under the control of the researchers and may involve protocolized care. In the above example, the training programme, record audits and weekly visits by a researcher were all part of an “action research” approach to improve the uptake and quality of a health system policy. As the example illustrates, identification of research and practice elements of HPSR is complex and a matter of judgement.

3.3 Is review by a research ethics committee required?

All research involving human participants must be reviewed and approved by an REC. This requirement is widely acknowledged in international ethics documents. For instance, the CIOMS International Ethical Guidelines (6) stipulate that,

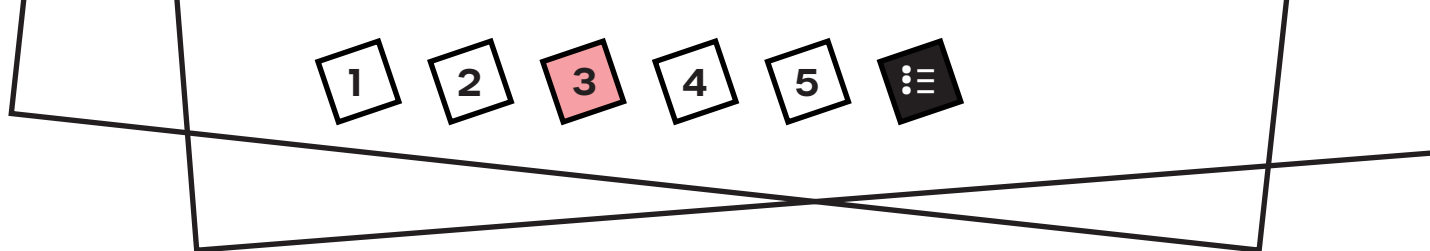
All proposals to conduct health-related research involving humans must be submitted to a [REC] to determine whether they qualify for ethical review and to assess their ethical acceptability.... The researcher must obtain approval or clearance by such a committee before beginning the research.

REC review ensures that a proposed study meets the standards for scientific and ethical acceptability set out in international documents, such as WHO’s Standards and Operational Guidance for Ethics Review of Health-related Research with Human Participants (20). REC review has been described as an important mechanism to preserve the public’s trust in the research enterprise (21).

Human participants research is any research in which human beings are intervened upon or interacted with or in which their private information is collected or used for research purposes. The difficulty of identifying human participants for HPSR studies is discussed in detail in point to consider 7. (See case 4 for an instance of research that does not involve human participants.) When there is doubt about whether REC review is required, (e.g. if there is doubt about whether an activity is practice or research or whether it involves human participants) researchers should consult an appropriate REC for a written determination.

3.4 Are there adequate plans to manage conflicts of interest?

The aim of health research is to provide the knowledge necessary to promote people’s health. Researchers, health institutions and funders, however, may have other interests. A conflict of interest exists “when there is a substantial risk that secondary interests of one or more stakeholders in research unduly influence their judgment and thereby compromise or undermine the primary goal of the



research” (6). Conflicts of interest may jeopardize the scientific validity of a study and the ethical protection of research participants. Accordingly, the CIOMS International Ethical Guidelines require that research institutions “develop and implement policies and procedures to identify, mitigate, eliminate, or otherwise manage such conflicts of interest” (6). Researchers must fully disclose conflicts of interest to the REC, which, in turn, must ensure that appropriate measures are in place to mitigate the conflicts.

In HPSR, interests may conflict when an agency or institution evaluates its own performance or practices. This may also occur in the context of ownership or publication of analyses or when the funding or employing institution is required to authorize or approve publication (see case 5 for a discussion of complexities in publication). Secondary interests of government agencies and health institutions include financial benefit, such as cost savings, and reputation. Where applicable, researchers must disclose such conflicts of interest to the REC. The REC must ensure that adequate plans are in place to ensure the independence of the study and of disclosure of result.

3.5 What is the study intervention?

A study intervention is a component of research, which is the action to be evaluated in the study. In the context of HPSR, study interventions may include a policy change, education or reorganization of care delivery. Study interventions may be conducted at the level of the cluster (e.g. health system, community or hospital), health professional or patient. Accurate identification of the study intervention is important for analysis of the potential benefits and harms of the study, as discussed in point to consider 12.

The cases illustrate the wide diversity of study interventions in HPSR, including those in which researchers:

- evaluated a novel voluntary health insurance scheme administered at cluster level, in villages in rural China (case 2);
- used action research, including a training programme, record audit and weekly visits by a researcher, to target health providers to improve the uptake and quality of an integrated health record (case 1); and
- tested the effectiveness of provision of a clean delivery kit to women before home delivery in the United Republic of Tanzania (case 5).

Some HPSR studies involve no study intervention but are designed to evaluate a government programme or the way in which care is routinely delivered. Three of the examples involve no study intervention (cases 3, 4 and 6). Even in the absence of a study intervention, however, a study might involve exposure of participants to risks by collection of their data from medical records or through observation (see points to consider 6 and 12).

3.6 What are the procedures for collecting data?

Data collection procedures are components of research. They are the means by which information is collected for research purposes. In HPSR studies, data collection may involve a review of policies, abstracting data from medical or other confidential records, questionnaires, focus groups or interviews. Data may be collected at different levels, including clusters, health professionals or patients. Additionally, data may be aggregated or individual. The cases illustrate the diversity of data collection procedures in HPSR:

- Researchers in Brazil conducted a secondary analysis of data on population health in geographical clusters to assess the effects of an integrated primary care programme (case 4).
- Researchers in Ghana interviewed hospital management and staff and reviewed employment records to identify good human resource management practices (case 3).
- Community health workers in the United Republic of Tanzania administered a questionnaire to mothers and examined newborns for signs of infection to assess the effectiveness of clean delivery kits (case 5).

Accurate identification of data collection procedures for research is important for analysis of the potential benefits and harms of studies, as discussed under point to consider 12.

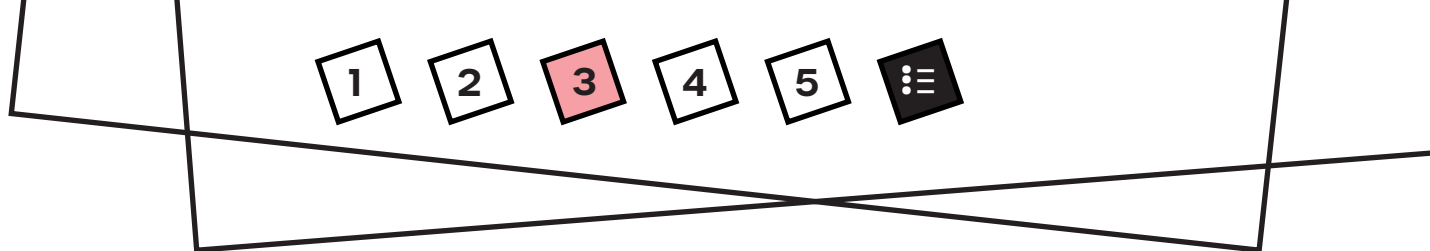
3.7 Who are the research participants?

Identification of participants for HPSR may be difficult. Such studies commonly involve stakeholders at a variety of levels, including the health system, hospital, health provider, patients or healthy individuals in the community. Additionally, within a single study, the intervention may target one group of individuals, while the outcomes might be measured for a different group. Accurate identification of research participants is important, as the REC's first task is to protect their liberty and welfare interests.

WHO's guidance document for RECs (20) defines research participants as human beings who, in the context of a research study,

(1) [A]re exposed to manipulation, intervention, observation or other interaction with investigators, either directly or through alteration of their environment; or (2) become individually identifiable through investigators' collection, preparation or use of biological material or medical or other records.

When policy-makers, decision-makers, health providers or patients are directly manipulated, intervened upon, interacted with or observed for research purposes, they should be considered research participants. Researchers and RECs should,



however, exercise caution in interpreting the phrase “through alteration of their environment”. Some environmental manipulations, such as alterations in fee schedules to change health provider behaviour or health messages to change patient behaviour, directly target individuals. In these cases, health providers and patients should both be considered research participants. In other cases, environmental manipulations are too indirect to meaningfully confer the status “research participant”. For instance, a strategy to increase uptake of evidence-based practice may target health providers and indirectly affect patients. To ascertain who should be classified as a research participant, researchers and RECs should consider whether the “manipulation, intervention, observation or other interaction” is direct or not and the degree to which the interests of individuals are meaningfully affected by such actions.

For example, in the study by Naughton and colleagues to promote prescription of drugs known to reduce the risk of cardiovascular events in patients with heart disease or diabetes (22), family doctors were randomized to receive either an audit of their prescriptions plus an educational session or audit alone. The data collected were practice-level data from a national pharmacy database and did not include identifiable information on patients. In this study, physicians were directly intervened upon by education and audit in an attempt to change their behaviour. The aim of the intervention was to align physician prescribing with evidence-based practice recommendations; importantly, the role of physician judgement in determining appropriate treatment was preserved. Accordingly, the physicians were research participants. Although the impact of the research will ultimately be on patients, they should not be considered research participants, because the impact is both indirect and aligned with their interests.

When identifiable biological samples (e.g. blood samples with patient identifiers) or private information (e.g. data abstracted from patients’ medical records) are collected for research purposes, the relevant individuals are research participants. Caution should be exercised in determining whether samples or private information are identifiable. The use of sophisticated genetic technology or a combination of two or more datasets may unwittingly make samples or information identifiable. Thus, linkages between anonymized data sets may inadvertently create identifiable data by aligning variables such as age and postal code that identify an individual within a population. Secondary analysis of data involves no research participants if the data are collected anonymously, rigorously anonymized or available to researchers only as grouped data.

When there is doubt about the identifiability of samples or data, researchers should seek a written determination from the REC. In some cases, such as when routinely collected data are obtained and analysed solely at group level, the data are truly anonymous and their use does not confer status as a research participant. Cases 4 and 6 illustrate the use of grouped data.



3.8 From whom is informed consent required, or is a waiver of consent appropriate?

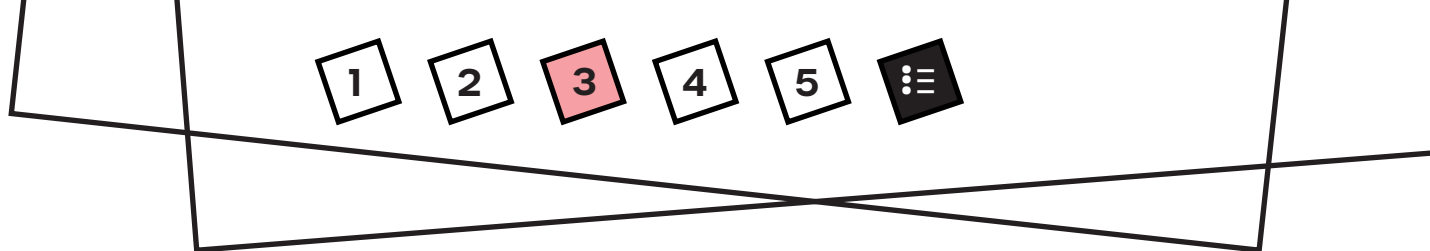
It is generally presumed that informed consent must be obtained from research participants (6). The ethical principle of respect for persons requires that the choices of autonomous people, that is, people who can responsibly make their own decisions, be given due regard (20). The principle of respect for persons is the source of the ethical obligation to obtain the informed consent of research participants. For informed consent to be valid, the research participant must have the cognitive capacity to make the choice, be so situated as to choose freely, have adequate information and understand what is at stake in the decision. International ethical documents list detailed requirements for disclosure in the informed consent process¹. While requirements vary somewhat, researchers must generally disclose:

- the fact that the activity is research,
- the voluntary nature of study participation,
- the right to withdraw from the study at any time,
- the aim(s) of the research study,
- the methods to be used,
- sources of funding and possible conflicts of interest,
- the institutional affiliation(s) of the researcher,
- the study intervention(s),
- the data collection procedure(s),
- the potential benefits and risks associated with the study intervention(s) and data collection procedure(s),
- steps taken to protect the confidentiality of private information,
- alternatives to study participation,
- the availability of compensation for research-related injury, and
- access to the intervention after the study.

It has been argued (23) that “disclosure” in itself is insufficient for optimal informed consent and that researchers and research staff should “educate” research participants to ensure that they understand the research and the consequences of participation.

The principle of respect for persons further stipulates that adults who lack decision-making capacity, such as people with advanced dementia, or young children who legally lack decision-making capacity are entitled to additional protection (6). First, the inclusion of incapable individuals must be justified by the study hypothesis. Secondly, decisions “to provide informed consent” should be made by an authorized surrogate decision-maker (20). Thirdly, in the case

1. This is a non-exhaustive list of common requirements. Full guidelines can be found from, inter alia, the Council for International Organizations of Medical Sciences (<https://cioms.ch/wp-content/uploads/2017/01/WEB-CIOMS-EthicalGuidelines.pdf>), the US Department of Health & Human Services (<https://www.hhs.gov/ohrp/regulations-and-policy/guidance/checklists/index.html>) and the National Human Genome Research Institute (<https://www.genome.gov/about-genomics/policy-issues/Informed-Consent-for-Genomics-Research/Required-Elements-of-Consent-Form>).



of studies that have no direct benefit for vulnerable groups, the risk of study participation should be no more than a minor increase above the minimal risk, whereby “minimal risk” is understood as the risks of daily life. The risks of daily life may, however, be higher in circumstances of poverty and political strife. Accordingly (6), RECs

[M]ust be careful not to make such comparisons in ways that permit participants or groups of participants from being exposed to greater risks in research merely because they are poor, members of disadvantaged groups or because their environment exposes them to greater risks in their daily lives.

The ethical principle of respect for persons may be more difficult to uphold in HPSR than in clinical research (3). As we have seen, the same HPSR study may involve research participants belonging to different groups, such as policy-makers, decision-makers, health providers and patients. A distinguishing feature of HPSR is that these different groups of participants may be exposed in different aspects of the study. For instance, health providers may be the targets of the intervention, while health outcome data are collected for patients. The informed consent procedure must provide prospective participants with information relevant to their participation. It must answer the question: “If I participate in the study, what difference will it make to me?” In all cases, the aim of the study and other basic elements of informed consent must be disclosed. Beyond this, however, in HPSR, the details of disclosure may differ by group. In our example above, details of the study intervention, including the procedures involved, the potential benefits and harm and alternatives, must be disclosed to health providers but not to patients. Even if patients will not receive the study intervention, details of data collection procedures, including potential benefits and harms and steps taken to protect the confidentiality of the data must be disclosed as part of the informed consent procedure. The possibility of different consent procedures for different groups of research participants is a novel aspect of HPSR.

While the requirement for informed consent of patients in research is well accepted, it has been suggested that informed consent is not required from health providers, as they have a duty to participate in quality improvement research (18). This argument may extend to policy-makers and other decision-makers in HPSR. We consider that policy-makers, decision-makers and health providers have a *prima facie* ethical duty to seek to continually improve the delivery and outcome of health care. This does not create an ethical duty to take part in specific research studies, nor does it support the claim that researchers do not have an obligation to seek consent for research participation. Researchers and RECs must proceed on the presumption that the informed consent of policy-makers, decision-makers and health providers in HPSR studies is required. Two of the cases (1 and 3) involved research on health providers or other hospital employees in which informed consent was required for at least some aspect of study participation.



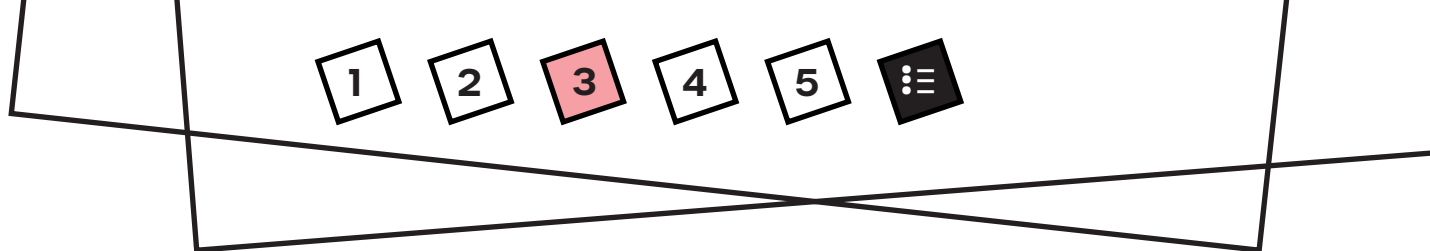
Although informed consent is important to ethical conduct of research, there are exceptions. According to international ethical guidelines (6), an REC may waive the requirement for informed consent when:

- the study is socially valuable;
- it would be infeasible or impracticable to conduct the study if informed consent was required; and,
- participation involves no more than minimal risk to participants.

Waiver of consent reflects the *prima facie* nature of the ethical principles underlying research. Thus, if a study seeks to achieve socially important ends, if those ends cannot be met with the informed consent requirement and study participation poses only minimal risk to participants, the requirement for informed consent may be waived. The case for a waiver of informed consent must be made by researchers and accepted by the REC. When a waiver is made for consent, the REC may require that staff, patients or members of the public in the health system or institution be notified that a research study is being conducted. Notification may include advertisements in clinic waiting rooms, media announcements or letters to patients.

Informed consent may be waived in many HPSR studies. When HPSR involves an intervention such as a policy change or alteration in the delivery of health services, administered at the level of a group or institution, it may be difficult or impossible for health providers or patients to avoid the intervention. For instance, in the Flexibility In duty hour Requirements for Surgical Trainees (FIRST) trial, two policies were compared, and resident well-being and patient safety were evaluated (24). Short of withdrawing from their training programme, residents could not avoid exposure to the intervention. In such cases, refusal of informed consent would be meaningless; even if a participant refused to be enrolled in the study, he or she would nonetheless be exposed to the intervention. Thus, a waiver of consent is an important mechanism for HPSR involving a group intervention.

In other cases, the practicability of informed consent depends on factors including group size, the ease with which research participants can be contacted, research infrastructure (such as the availability of local research staff) and research funding. When requiring informed consent would make a study impracticable, consideration should be given to waiving consent. For instance, in case 3, researchers described effective human research management practices in a well-performing hospital in Ghana. They made a realistic evaluation, including review of employee records. Requiring informed consent from all employees for review of their records would probably have made the study impracticable because of the large number of employees involved. Provided that adequate measures are in place to protect confidentiality, the review poses only minimal risk and, accordingly, a waiver of consent may be appropriate. In all cases in which a waiver is contemplated, researchers and RECs must ensure that all the ethical requirements for a waiver of consent are fulfilled.



3.9 Is permission from a “gatekeeper” required?

HPSR studies commonly involve groups – health systems, communities or health institutions – as well as individuals. As Hyder and colleagues (16) rightly observe,

[I]t may be challenging for RECs to assess what role various actors should play in the authorization and implementation of the study. For instance, when schools or hospitals are the unit of allocation, how should the employees of these institutions factor into the ethical analysis?

Recognition that group or institutional interests may be implicated in the conduct of HPSR is recent and has led to the involvement of “gatekeepers” in study design and approval. A “gatekeeper” has been defined as “an individual, body, or mechanism that can represent the interests of the cluster” (25). In a health system, the gatekeeper is most commonly the minister of health or a delegate; in a community, it is the mayor or other community leader; and, in a hospital, it is the chief executive officer or a delegate. In some settings, there may be multiple gatekeepers. For example, in a hospital, permission of both the chief executive officer and the relevant department head may be required. Gatekeepers can play an important role in ensuring that the interests of groups and institutions are adequately considered and protected in the conduct of research. When a study substantially affects such interests, gatekeepers can protect those interests. When appropriate, the gatekeeper may provide permission for inclusion of the group or institution in the study; or the gatekeeper may organize and participate in consultations between researchers and group members on the design and conduct of the study (see point to consider 10).

Gatekeeper permission is appropriately sought when a study is likely to affect group or organizational interests substantially and when the gatekeeper has the legitimacy and political authority to provide such permission. For instance, in a study of changes in care delivery in hospitals, the hospital chief executive officer or a delegate will review the implications of participation in the study on hospital staffing, finances, legal liability and conformity with other policies and practices, such as access to confidential records. Only when he or she is satisfied that institutional interests are adequately protected should permission for enrolment be provided on behalf of the hospital. Nevertheless, the potential conflicts of interest of gatekeepers must be acknowledged and managed (see point to consider 4). Gatekeepers should recognize that the conduct of high-quality HPSR will improve the quality and efficiency of health care. Accordingly, they should not unreasonably withhold their permission for participation, for instance, out of concern that poor practices or patient outcomes will be revealed. Researchers and RECs must recognize that gatekeeper permission does not weaken or replace the requirement for informed consent from individual research participants.

Gatekeeper permission may involve various decision-makers, including health authorities, hospital administrators and data custodians. In case 5, clean delivery

kits were given to expectant mothers by a maternal and child health aide, and data were collected by a village health worker. As the study had a substantial impact on the activities of community health workers, the permission of the local health authority was required. In case 1, uptake of an integrated medical record was promoted by engagement with clinicians and records staff and by health record audits. The permission of the senior hospital administrator was required because of the impact on employee time and access to confidential records. In case 4, the impact of community-based primary care was evaluated in a secondary analysis of population health data collected by the Brazilian Ministry of Health and Institute of Geography and Statistics. Permission from both organizations was required to ensure that use of the data was in accordance with their policies.

3.10 Is group or community engagement required?

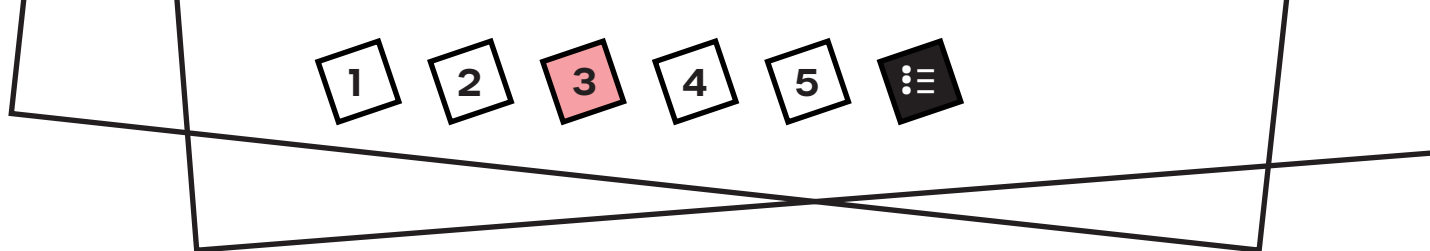
The importance of community engagement in research is now widely recognized. For instance, the WHO guidance document for RECs (20) recommends that “[r]esearchers should actively engage with communities in decision-making about the design and conduct of research (including the informed consent process).” When research is likely to have a substantial impact on group or community interests:

Researchers, sponsors, health authorities and relevant institutions should engage potential participants and communities in a meaningful participatory process that involves them in an early and sustained manner in the design, development and implementation of the informed consent process and monitoring of research, and in the dissemination of its results.

Successful community engagement strategies (6):

- begin at the earliest opportunity;
- are fully collaborative and transparent;
- seek diverse views;
- elicit the community’s health priorities, preferred (research) designs and willingness to be involved in research;
- ensure continual communication;
- involve the community in the conduct of the study, when possible; and
- negotiate recruitment, data-sharing, ancillary care and access after the study.

Researchers should communicate their community engagement strategy to the REC. Extending consultation and engagement beyond communities to include other social groups (such as civil society, mother’s groups, patient advocacy groups) and institutions involved in HPSR is relatively new. Often



called stakeholder engagement, such consultations and engagements should also include policy-makers, health administrators, physicians and health care workers and are a useful means for identifying both stakeholders and “potential burdens, barriers, relevant practices and beliefs” to explore the impact of a study on groups and institutions and to collaborate in solutions to minimize their risks (3). Gatekeepers may protect group or organizational interests by organizing and participating in consultations between researchers and group members (see also point to consider 9). Given the novelty of the practice, researchers and RECs should share their experiences on ways of engaging gatekeepers and other stakeholders in the design and conduct of HPSR.

3.11 Are there adequate plans for protection of privacy and confidentiality?

Researchers and sponsors have an ethical obligation to protect the confidentiality of private health information. “Identifiable health information” may be defined as information that could be used alone or with other information to identify, contact or locate a single person or to identify an individual in context. The use of identifiable health information in research must be justified, and researchers must submit plans for ensuring its confidentiality to the REC for approval. Steps taken to protect confidentiality should be disclosed to research participants in the consent process.

HPSR may raise particular challenges to privacy and confidentiality because of the “multiple layers of data collection, analysis of many different kinds of data, feedback loops and macro-scale monitoring” (3). As data may be collected on patients, health providers, institutions and health systems, researchers and RECs must ensure adequate protection of data from multiple sources and on multiple entities. As HPSR may reveal poor performance or patient outcomes, researchers and RECs should be cognizant of the risk of stigmatization of practitioners or institutions due to the results of the studies.

3.12 Are the potential benefits and risks of the study acceptable?

A central responsibility of researchers and RECs is to uphold the ethical principle of beneficence and to ensure that the potential benefits of study participation outweigh the risks. Accordingly, the CIOMS International Ethical Guidelines (6) state that,

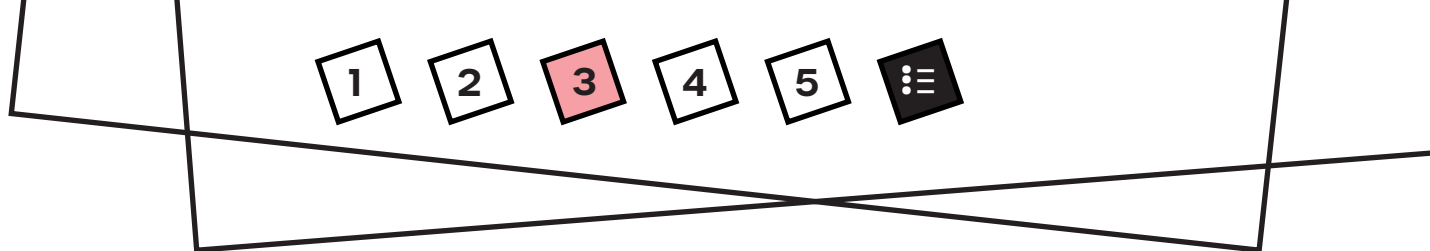
Before inviting potential participants to join a study, the researcher, sponsor and the [REC] must ensure that risks to participants are minimized and appropriately balanced

in relation to the prospect of potential individual benefit and the social and scientific value of the research.

In clinical research, procedures may be classified in terms of the prospect of direct benefit to the research participant. “Therapeutic procedures” are interventions, such as drugs, surgery or diagnostic tests, that hold the prospect of direct benefit. Therapeutic procedures must satisfy the ethical requirement of clinical equipoise, that is, there must be uncertainty about the comparative merits of the intervention(s) within the community of expert practitioners. “Non-therapeutic procedures” do not hold out the prospect of direct benefit for research participants; these include study procedures such as questionnaires or blood tests that are not clinically indicated but that further the scientific ends of the study. The risks of procedures must be “minimized and appropriate in relation to the social and scientific value of the knowledge to be gained (expected benefits to society from the generalizable knowledge)” (6).

Benefit-harm analysis is complicated in HPSR. As Hyder and colleagues observed (16), “[t]he current norm for reviewing research focuses on the individual, but this ... is not well suited for assessing [HPSR], in which group-level interventions and impacts require a much broader lens.” Group interventions may affect the interests of a health system, community, other social group or health institution (26). For instance, an evaluation of the quality of care delivered at hospitals may create the perception that a particular hospital delivers low-quality care, thereby harming the reputation of that institution. Further, the participation of different stakeholders in a study may mean that the potential benefits and harms are not the same for all participants (16). Thus, “one group is subject to an intervention, but the potential benefits and risks of that intervention may accrue in separate groups ... [and] groups potentially placed at risk (of harm) may not be obvious” (3). Indeed, groups placed at risk may include “health professionals or community workers especially if functioning outside their usual roles in a study” (3). As study interventions in HPSR are not treatments but changes in policy, implementation strategies or service delivery, application of clinical equipoise is not straightforward.

To evaluate the potential benefits and harm of HPSR, researchers and the REC should address three issues. First, they must ensure that the study intervention (if any) is justified, i.e. that it is consistent with competent practice in the relevant field of study. The central insight of clinical equipoise is that the legitimacy of study interventions derives from uncertainty in a domain of practice. In the case of medical treatment, the relevant expert community is physicians; however, in the case of a policy change or change in service delivery, the relevant expert community is policy- and decision-makers (27). Ideally, a novel policy or change in service delivery should be supported by evidence that suggests it has advantages over current practice. In HPSR, evidence is not always available. In these cases, researchers and RECs may appeal to expert opinion about the study intervention. They should understand that clinical equipoise depends on the context. Thus, even if a health intervention is known to be effective



in one setting, clinical equipoise may nonetheless support evaluation of its effectiveness or implementation in another setting, for which evidence is lacking.

Secondly, the control condition (if any) must be justified, and researchers and the REC must ensure that it does not deprive participants of effective care or programmes to which they would have access. HPSR studies generally have a pragmatic orientation: they seek to evaluate interventions in real-world conditions. Thus, control conditions are typically usual practice rather than placebo. The question is whether control conditions should be augmented to compensate those in the control group for not having access to the study intervention. We urge caution in the use of augmented controls: their use is not required by clinical equipoise, and they may bias the study towards a null result. The choice of control condition in low- and middle-income countries raises ethical issues due to lack of adequate access to health care. Researchers and RECs should consult guidance on the choice of control conditions in these settings (6). HPSR studies commonly seek to improve care delivery at a local level. In case 5, researchers evaluated the effectiveness of providing women with a clean delivery kit to prevent neonatal infection in rural United Republic of Tanzania, where neonatal infection due to unhygienic conditions in childbirth is common. The effectiveness of providing clean delivery kits to pregnant women has not been evaluated in this setting; thus, there is clinical equipoise for the intervention and control in this context. Researchers chose a stepped wedge design so that all communities would eventually have access to the kits. Furthermore, women in the study were not denied access to any effective care programmes. For these reasons, use of a usual care control condition in this case appears to be appropriate.

Thirdly, researchers and the REC must ensure that the risks of data collection procedures are justified, although they must be minimized, consistent with sound scientific design. Researchers and RECs should construe the risks of data collection broadly and give due consideration to the burden (of collecting data) on health care staff. Further, the risks must be deemed reasonable in relation to the importance of the knowledge to be gained. When the study population includes vulnerable participants, the risks of data collection procedures are typically capped at a minor increase above the minimal risk, defined as the risk of daily life.

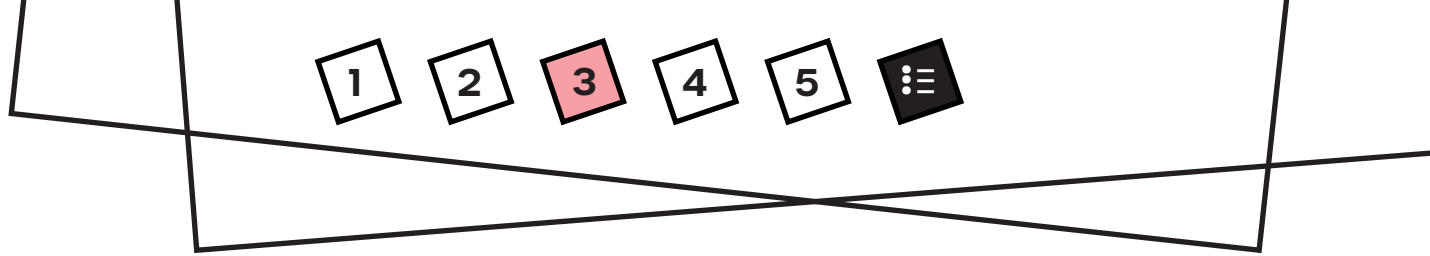
When data collection procedures involve access to patient health records or other confidential records, researchers must ensure that collection of patient data with identifiers is justified and that adequate protection is in place to preserve the confidentiality of personal information (point to consider 11). Research staff who have access to confidential records must be adequately trained and should agree in writing to maintain the confidentiality of personal information. Unless required by the study, the data collected should not include identifying information, such as patient name or health insurance number. Researchers should additionally ensure that access to health records complies with relevant institutional policies.

3.13 Are concerns about justice and equity adequately addressed?

The ethical principle of justice requires that the burdens and benefits of research participation are distributed equitably. When research involves vulnerable people, researchers and RECs have an obligation to “ensure that specific protections are in place to safeguard the rights and welfare of these individuals and groups in the conduct of the research” (6). “Vulnerability” is “an identifiably increased likelihood of incurring additional or greater wrong” as a result of research participation (14). Thus, assessing vulnerability involves “judgments about both the probability and degree of physical, psychological or social harm, as well as a greater susceptibility to deception or having confidentiality breached” (6). Vulnerability must be assessed case by case. Factors that potentially contribute to vulnerability include diminished decision-making capacity, illness, incarceration, marginalization, stigmatization, poverty and lack of access to adequate health care.

Generally, the inclusion of vulnerable participants should be promoted to ensure that they have access to the benefits of study participation. Some HPSR may seek to mitigate the social causes of vulnerability, such as in studies to inform “strategies to reduce health care disparities ... [by] testing established interventions in a new context with a strong focus on advancing equity” (3). When HPSR studies involve vulnerable participants, additional protection should be provided, which may include ensuring that the study hypothesis requires their inclusion and research procedures that have no prospect of direct benefit generate no more than minimal risk. Community engagement, as discussed in point to consider 10, is a useful mechanism for addressing the potential impact of study participation on vulnerable participants. One aim of engagement and consultation is to ensure that research is consistent with the health needs and priorities of the group or community. It also allows examination and discussion of the study by those whose interests may be affected and may reveal ways of reducing risks and promoting benefits to participants.

HPSR studies commonly involve health providers and other employees in health institutions, who may be concerned about social risks, including reputational or professional harm. Employees within a hierarchical institution may be pressured overtly or unintentionally to participate in HPSR. As a result, “their agreement to volunteer may be unduly influenced, whether justified or not, by the expectation of preferential treatment if they agree to participate in the study or by fear of disapproval or retaliation if they refuse” (6). For these reasons, health providers and other employees in health institutions may be regarded as vulnerable participants. Researchers and the REC should ensure that prospective participants are recruited in the absence of their supervisor (28), and supervisors should not be informed of the names of those who have agreed or refused to participate in a study.



3.14 Are there satisfactory plans for access to interventions after the study?

The ethical principle of justice requires equitable distribution of the benefits of research, including access to the intervention after the study. As pointed out by the CIOMS (6), “[e]ven if research addresses a question that has social value for the community or population in which it is carried out, the community or population will not benefit from successful research unless the knowledge or interventions that it produces are made available to them.” Thus, researchers should submit to the REC a plan to ensure reasonable access to the results of the study and any beneficial interventions.

The goal of HPSR is to strengthen health systems through research. Accordingly, the obligation to ensure the sustainability of successful interventions is a highlight of HPSR. Generally, “[t]he responsibility for the scale-up and roll-out of successful interventions should fall to the State, which is often involved from the planning stages, and interventions should be integrated into health policy” (3). The most difficult cases are in low- and middle-income countries, where the long-term sustainability of an intervention may be uncertain. In such cases, it may be unreasonable to burden researchers with a long-term commitment to provide the intervention after the study. In all cases, researchers should “clearly communicate the long-term implementation strategies (if applicable) to the [REC]” (3).



4. Case examples

4.1 Introduction of a new birth record in three hospitals in Jordan: a study of health system improvement (29)

Ethical issues

- Is this research or practice?
 - Are health staff research participants? Is their consent required?
 - Is permission required from the chief administrators of the hospitals?
-

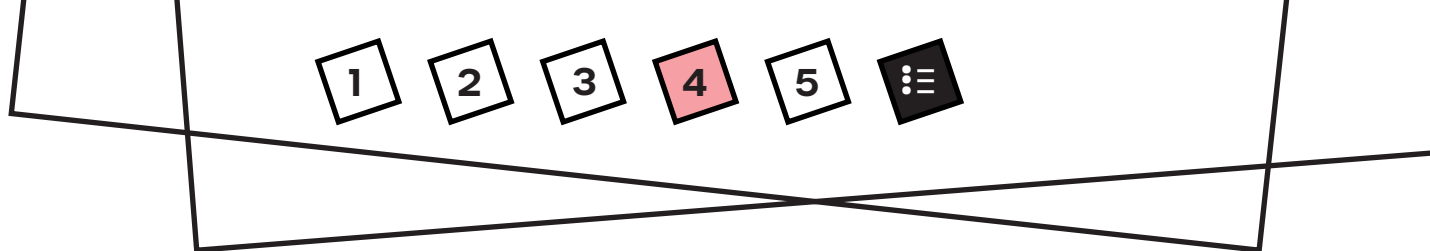
Summary

Background and objectives

WHO has led the development of minimum datasets for perinatal medical records, and a number of countries use such records. In this study, a new, integrated medical record system for recording antenatal, birth and postnatal care data for women was introduced at three hospitals in Jordan to improve the continuity of patient care and allow studies of national trends or assessment of hospital performance. The aim of the study was to assess the feasibility of introducing the new record system, which is shared between the hospital and community practitioners, and its impact in improving the quality of reporting and enhancing continuity of patient care by linking records throughout the perinatal period. Specifically, the potential utility of the record in a national data system for monitoring and benchmarking maternity care was considered.

Methods

The study involved introduction of a consolidated maternity record and training of health providers. The record was based on that of an Australian perinatal data collection system that has been used for national reporting and benchmarking, which was modified for use in Jordan. Practice-research engagement was used to connect clinicians to the research and use of the new birth record. Training was provided to health professionals as part of a “participant-researcher interaction” designed to engage staff in quality improvement, and one of the researchers made weekly visits to the three hospitals to audit 10 randomly selected files for completeness and accuracy and to provide feedback and



review to the health providers. The audits were also used to collect data on the characteristics of those who completed the record as well as clinical data on randomly selected women who gave birth at the participating hospitals before and immediately after introduction of the record and up to seven months afterwards. Interviews and focus groups with key informants at different levels of the health system were undertaken before and after introduction of the record. Quantitative descriptive analysis and qualitative data analysis were used. The study was approved by the Ministry of Health of Jordan and the Ethics Committee of the University of Technology, Sydney, Australia. Local and national leaders helped to manage and lead the project in an unspecified capacity.

Results

Improved clinical reporting, organizational development and sustained commitment to the new record from clinicians, managers and policy leaders were found. The action research approach led to professional dialogue among doctors, nurses and midwives towards the common goal of improving health care for mothers and infants. The new record continues to be used in the three hospitals, and statistical summaries are sent to the researchers for analysis.

Ethical analysis

1. Is it research?

The researchers used mixed methods, involving practice–research engagement to investigate the feasibility of using a new birth record that was shared between the hospitals and communities, and the associated outcomes. The aim was to improve care locally and to determine whether the new birth record could be used nationally. As the study was a systematic investigation designed to produce generalizable knowledge, it is research.

2. Which aspects are research?

The study was conducted in a country in which the health system is introducing an online clinical data entry system. Data are collected routinely on women and newborns, and the online system allows hospitals to create an integrated perinatal health record. These aspects should be considered part of the health system and not part of the research. The research included both an intervention and data collection. The intervention was a training programme designed to increase the commitment of health professionals to recording data in a timely, accurate manner. Data collection, described in more detail below, involved three record audits, interviews and focus groups.



3. Is review by a research ethics committee required?

This research study involved various human participants, and thus REC review was required.

4. Are there adequate plans to manage conflicts of interest?

The study was reviewed by two separate committees. The two researchers were based at academic institutions independent of the Ministry that was introducing the record. Local and national leaders helped to manage and lead the project, but their roles and potential conflicts of interest were not reported.

5. What is the study intervention?

The study intervention is a consolidated birth record and associated training programme to prepare health professionals and encourage timely, accurate recording of data into an integrated perinatal health record. The training programme is an instance of “action research” or “participant-researcher interaction”, which involved weekly visits to the three hospitals by one of the researchers and review of 10 randomly selected files for completeness and accuracy. The study included engagement of participants (health care providers) in analysing the results and improving practice.

6. What are the data collection procedures?

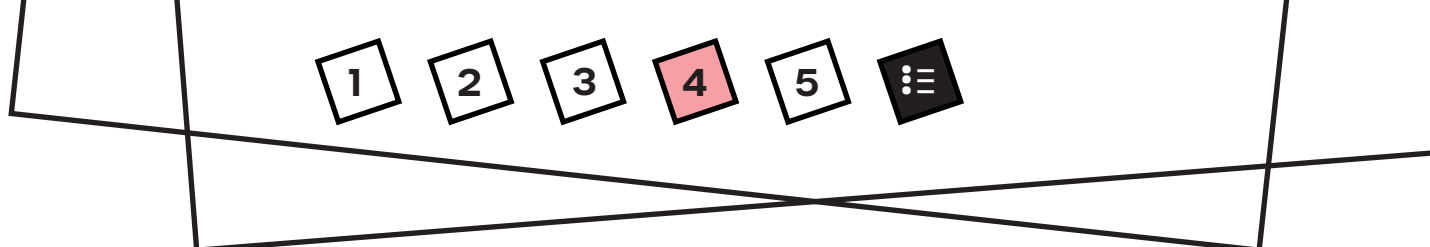
The completeness and accuracy of clinical records were audited three times: before the study intervention, immediately after it and seven months later. All patient data were de-identified. Interviews and focus groups were conducted with managers, clinicians, medical records staff and mothers, who had access to their birth record.

7. Who are the participants?

Health professionals targeted by a training programme were the research participants. Managers, clinicians, medical records staff and mothers who participated in interviews and focus groups for data collection purposes were also research participants. As the records audited had only de-identified data, the patients whose medical records were audited were not research participants.

8. From whom is informed consent required, or is a waiver of informed consent appropriate?

As the training intervention and weekly audits were conducted in the hospitals, informed consent would have been required from all health care providers, which could have made the study impracticable. As the intervention – training and introduction of the new record – poses only minimal risk to the daily lives of health providers working in hospitals, a waiver of consent was probably appropriate; complete information about the study and the study procedures should, however, be provided to them.



The informed consent of clinicians, medical records staff and mothers who participated in interviews and focus groups was required. The informed consent of patients for access to their medical records was not required, as the data were de-identified.

9. Is permission from a “gatekeeper” required?

The training had implications for the participating institutions, including health providers and medical records staff. Hospital participation in the study thus required the permission of the relevant senior administrator.

10. Is group or community engagement required?

Consultation on the content of the medical record was held with Ministry of Health officials before its introduction. In view of the different levels of intervention, multiple groups or communities were involved. Group or community engagement with health professional societies might be required because of the potential implications for workloads and patient safety or if audit data for the hospital were to be made publicly available. Public consultation might have been warranted on use of de-identified data for research and quality assurance and to maintain trust.

11. Are there adequate plans for protection of privacy and confidentiality?

As noted in question 7, data were examined on patients, physicians and hospitals. Patient data were appropriately de-identified to maintain their privacy and confidentiality. Physician data on practice and completeness of records was not de-identified but kept confidential and was fed back to the individual health providers. Privacy cannot be preserved in focus groups, as participants occupy a shared space; however, confidentiality should be maintained and the resulting transcripts de-identified, including redaction of comments that may lead to re-identification of an individual.

12. Are the potential benefits and risks of the study acceptable?

The case for the study intervention has been well articulated. The study is in keeping with international initiatives to improve patient safety and quality by maintaining national sets of minimum perinatal data. While perinatal surveillance programmes are routine in developed countries, they have not been instituted in many developing countries. Training health providers in timely, accurate recording of data in the integrated perinatal health record would probably improve care. The data collection procedures appear to be appropriate. De-identification of patient data in the audits minimizes the risk of breaches of confidentiality. Risks associated with records audits, interviews and focus groups are outweighed by the potential for important knowledge from effective implementation of a new birth record.

13. Are concerns about justice and equity adequately addressed?

The participant-action component of the study provided information on health provider compliance with the new birth record. When individual informed consent can be obtained from health providers, negotiations should be conducted in the absence of organizational leaders, who should not be informed of the names of individuals who agree to or refuse study participation. A range of stakeholders were involved in introduction of the new record, as were mothers as recipients of care. A universal record with associated benchmarking and audit may identify inequities in care. The action-research approach appeared to foster closer collaboration among professionals throughout the medical hierarchy. Mothers were also given a copy of the record, which may facilitate communication and empower them in the physician-patient relationship. The study did not consider equity in the analyses of the audit data.

14. Are there satisfactory plans for access to interventions after the study?

Plans were not specified. The intervention included the new health record, professional training, audit and feedback. Training was not discussed in the publication, and probably ceased at the end of the study, but the new health record was made available to the participating hospitals for continued use even after the study ended.

4.2 Impact of rural mutual health care on health status: evaluation of a social experiment in rural China (30)

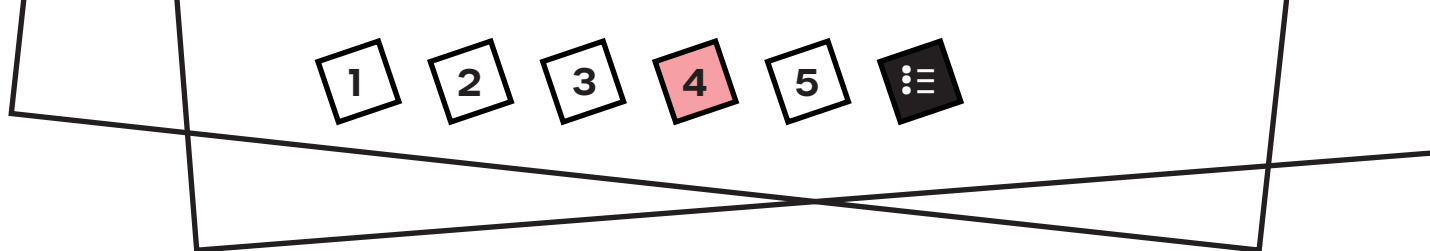
Ethical issues

- Is the voluntary health insurance scheme a research intervention?
- Is it ethical not to offer health insurance to the control communities?
- Are there vulnerable participants in the study? If so, how can they be protected?

Summary

Background and objectives

In 2003, the Chinese Government introduced a voluntary health insurance scheme (rolled out over a five-year period) to cover partly outpatient visits and the costs of hospitalization. However, the scheme did not improve hospitalization rates as anticipated, as there was no supply-side intervention to deal with the problems of waste caused by unnecessary treatment and drugs, and insurance



benefits were capped, indicating limited direct benefit for most people. The aim of this study was to evaluate whether extending health insurance to cover outpatient and inpatient services and strengthen the supply side of health systems improved community health. If found to be successful, the model could be used to expand rural health care systems. In particular, the authors evaluated the impact of the modified community health insurance scheme in one Chinese province between 2003 and 2006. The hypothesis was that decreased costs and better quality at points of care would increase use of services and improve access for the sick elderly, women and low-income families.

Methods

A new community-based health insurance scheme was modelled on the Government-sponsored scheme but with several improvements, including free outpatient and hospital services; physician enrolment in the scheme on a competitive basis, with those selected receiving a bonus according to the health outcomes of the patients and pre-defined performance measures; and de-linking village doctors from drug dispensing and other measures to reduce over-prescribing and ensure better quality and safety. The study had a quasi-experimental design. An intervention site was selected at random, and a control site was identified that matched the intervention site according to socio-economic conditions, the availability of health facilities and the distance to health centres. The control site received no new health insurance scheme or other new policy. Six villages in the intervention site and four in the control area were selected randomly. Within each intervention and control village, longitudinal surveys of individuals in randomly selected households were conducted to collect data on self-rated health status one year before and two years after the intervention. Health status was rated with two validated measures: the Categorical Rating Scale and EQ-5D (a standardized instrument used to measure health outcomes). Only individuals aged 15 years and older were asked to self-rate their health status. Propensity matching was used to create comparable groups of villagers who did and who did not enrol in the scheme. The difference-in-difference method was used to estimate the effect of the intervention. Subgroup analyses by age, gender and socio-economic status addressed differential effects of the intervention on these groups.

Results

A positive effect was found on the health status of villagers, with significantly less pain, discomfort, anxiety and depression. Sub-group analyses indicated that the effect of the intervention varied by age but not by income or gender.

Ethical analysis

1. Is it research?

A quasi-experimental design was used to evaluate a novel community-based health insurance scheme and to develop a sustainable rural health care system tailored to Chinese conditions. As the study was a systematic investigation designed to produce generalizable knowledge, it was research.



2. Which aspects are research?

The study was conducted in a changing environment of the provision of rural health services in China. The Chinese Government announced the introduction of a voluntary health insurance scheme to cover the costs only of hospitalization, except for deductible costs. The study involved villages that had not yet been included in the Government programme. The study intervention included aspects of the Government programme but with novel elements of design to increase use and efficient delivery. Longitudinal health surveys were conducted in both intervention and control villages. Both the novel health insurance scheme and the surveys should be considered parts of the research study.

3. Is review by a research ethics committee required?

This research study involved human participants and, as such, required REC review.

4. Are there adequate plans to manage conflicts of interest?

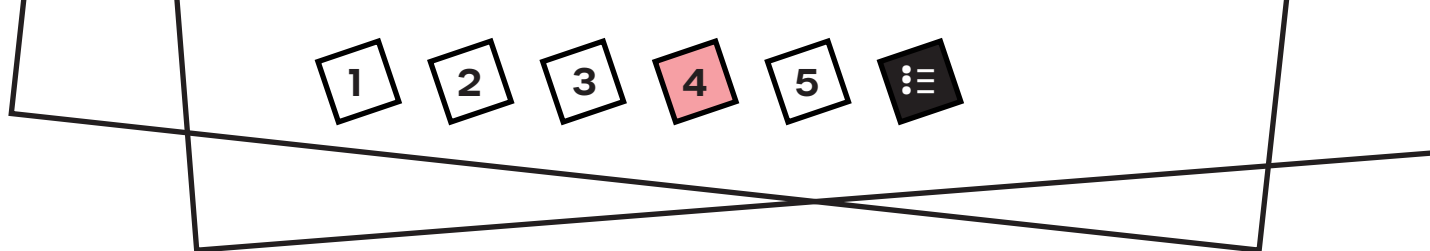
The authors included a specific conflict of interest statement. The scheme had the potential for introducing conflicts of interest as it offered incentives for health care professionals, including a bonus based on selected health outcomes and performance measures, but data were not collected from health care professionals.

5. What is the study intervention?

The study intervention is the voluntary health insurance scheme in which both the study sponsor and participants contribute to insurance to cover the costs of health care. While the scheme simulated the planned Government scheme, there were a number of differences: the benefits included both outpatient services and hospital services with no deductible expenses; physicians were selected on a competitive basis and given a salary and a bonus according to the health outcomes of patients and performance measurements; medications were purchased in bulk by the village; and review of prescription purchases and costs was introduced. These elements were designed to improve health care use and to promote more efficient delivery.

6. What are the data collection procedures?

Two questionnaires were used, the Categorical Rating Scale of overall health status and the EQ-5D for five dimensions of health (mobility, self-care, usual activities, pain or discomfort and anxiety or depression). Questionnaires were administered to a random sample of one in three households in intervention and control villages one year before and two years after the intervention. Additional demographic and socioeconomic variables were collected.



7. Who are the study participants?

People who were approached for enrolment in the health insurance scheme were research participants because they were the targets of the study intervention. People in the intervention and control communities who completed the study questionnaires were research participants because the researchers interacted with them, and their private information was collected for research purposes. Physicians who participated in the new insurance scheme were part of the intervention itself and opted voluntarily into the scheme. They were therefore not research participants. However, the intervention itself could raise ethical concern because of the inclusion of bonuses and physician performance appraisals and should be carefully evaluated by an ethics committee.

8. From whom is informed consent required, or is a waiver of informed consent appropriate?

The health insurance scheme in this study is voluntary and requires individuals to sign up for it and contribute to it financially. Thus, informed consent for study participation was practicable and should be obtained. Informed consent for data collection requires a separate process. Health questionnaires were administered at different times, and participation in the health insurance scheme was not a requirement to complete the questionnaires.

9. Is permission from a “gatekeeper” required?

As the study intervention required substantial changes to the provision of health services in the participating villages, permission from the relevant health authorities was required.

10. Is group or community engagement required?

Given the potential changes in the availability of prescriptions and changes to health care delivery, the communities should be engaged. Stakeholder engagement should include prior and on-going engagement with the physicians, and with officials of the ministry of health, and the local health authorities in order to ensure the implementation of the study findings on a wider scale if found to be successful.

11. Are there adequate plans for protection of privacy and confidentiality?

Only aggregate survey data were analysed; individual patient data remained confidential.

12. Are the potential benefits and risks of the study acceptable?

The study intervention was appropriate. Provision of health insurance to people who previously had none has been associated with decreased mortality and morbidity. In this case, the study intervention was similar to the planned Government programme but included a number of changes



designed to improve its scope, uptake and efficiency. Control communities were not denied access to programmes to which they already had access. The data collection procedures were appropriate. Standard health questionnaires were used, and steps were taken to protect the confidentiality of the data collected.

13. Are concerns about justice and equity adequately addressed?

Equity is implicitly addressed by identification of vulnerable populations – women, low-income groups and the elderly – who might benefit from study participation. The subgroup analyses of these groups explicitly examined differential effects of the intervention and therefore directly addressed questions of justice.

14. Are there satisfactory plans for access to interventions after the study?

The outcome of the study had important policy implications for the government. From the publication, it is not clear if the researchers engaged with the policy-makers to share the research results and support the modifications to policy based on the successful intervention.

4.3 A realist evaluation of the management of a well-performing regional hospital in Ghana (31)

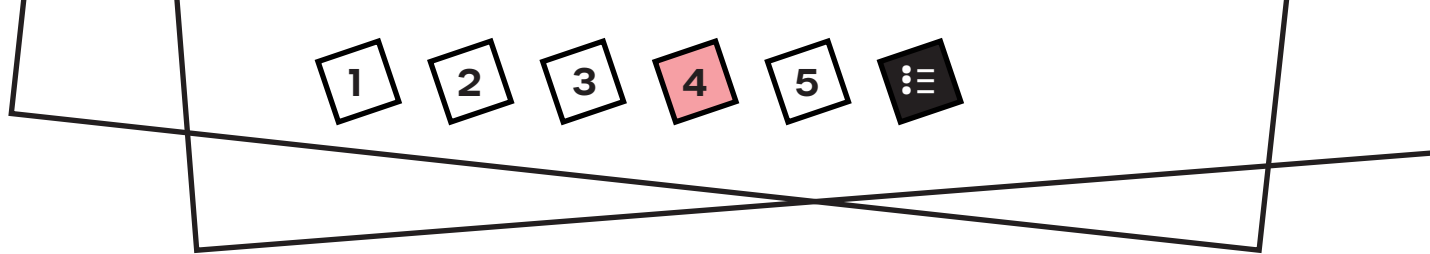
Ethical issues

- Is this research or non-research quality improvement?
 - Is the hospital's human resource management approach a research intervention?
 - How should recruitment of hospital employees be handled?
-

Summary

Background and objectives

A realist case study was conducted of a well-performing hospital in Ghana as part of a longitudinal study on the role of management in the success of hospitals that ensure equitable access to high-quality care and efficient service. The objective of the study was to determine links between human resource management and performance. The hospital selected was recognized for its research and patient care and had received a "best hospital" award.



Methods:

A realist evaluation framework was developed for hypothesis formulation, data collection, data analysis and synthesis of findings. A case study design was used, with individual and group interviews, participant observations and document reviews to collect data. During the preparatory phase, a self-assessment was undertaken, including risk minimization, consent and post-study feedback. Informed consent was obtained from all interviewees, and steps were taken to protect confidentiality and anonymity.

Results

Human resource management included effective induction of new staff, training and personal development, communication and information-sharing and decentralized decision-making. Additional components included: ensuring optimal physical working conditions, ensuring access to managers and involving managers in daily work. Teamwork, recognition and trust emerged as key elements of the organizational climate. Interviewees reported high levels of organizational commitment.

Ethical analysis

1. Is it research?

The study was a realist evaluation of the management approach at a single regional hospital. It was part of a longitudinal study that went beyond individual cases and local knowledge. As the study was a systematic investigation designed to produce generalizable knowledge, it is research.

2. Which aspects are research?

The approach allowed the researchers to gain deep understanding of the successful management strategies used at an award-winning hospital. Although the published report refers to the hospital's management approach as the intervention, routine administrative practice at the hospital was the subject of study. The data collection procedures included interviews, group discussions and document review. As this is not routine practice and involved systematic collection of data from human participants, they are research.

3. Is review by a research ethics committee required?

This research study involved human participants and, as such, requires REC review.

4. Are there adequate plans to manage conflicts of interest?

The report included a declaration by the study authors that they had no competing interests. Given the purposive sampling of interviewees, the research team should remain distant from the health authority.



5. What is the study intervention?

There was no study intervention.

6. What are the data collection procedures?

The researchers collected both quantitative and qualitative data.

Quantitative data were collected by review of documents, including hospital policies and employee records. The qualitative data included in-depth interviews with six members of the hospital management team and 11 staff members and three group discussions with unit heads and staff.

7. Who are the participants?

Hospital managers and staff who participated in interviews or group discussions were interacted with by researchers and were thus research participants. Researchers reviewed staff employment records containing private information. Staff whose records were reviewed were therefore also research participants.

8. From whom is informed consent required, or is a waiver of informed consent appropriate?

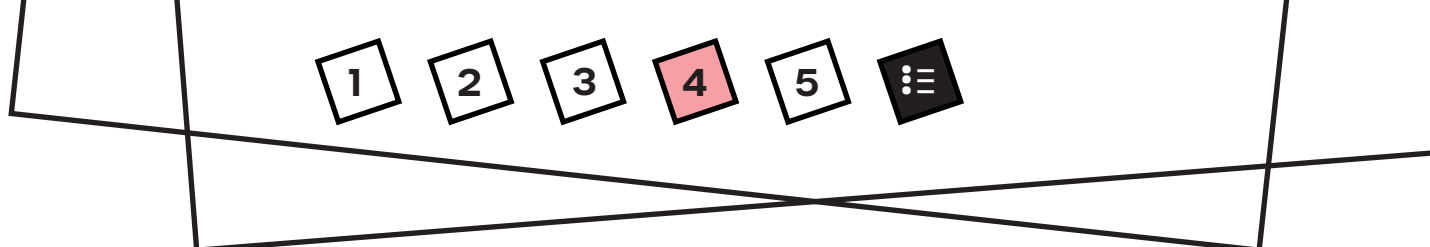
Informed consent should be obtained from all participants in interviews or group discussions. Requiring informed consent for the review of hospital employee records would probably have made the study impracticable. Provided that adequate measures are in place to protect employee confidentiality and records are anonymized before they are given to researchers, the records review probably poses only minimal risk, and, accordingly, the REC may grant a waiver of consent. Information should nevertheless be provided to all staff about the evaluation and the procedures being used, and they should be given ample opportunities to ask questions and raise any concerns.

9. Is permission from a “gatekeeper” required?

As the study required access to hospital employees and confidential employment information, institutional interests are at stake. The researchers therefore required the permission of the hospital’s chief administrator.

10. Is group or community engagement required?

Consultation with professional societies may be required, given that there are implications for practice. Engagement with different cadres of hospital staff, and with the ministry of health prior to the study may have been useful to guide the study design, and to gain acceptability of the study procedures.



11. Are there adequate plans for protection of privacy and confidentiality?

Because the name of the hospital is revealed, individuals in the hospital are potentially identifiable. This includes members of the hospital management team, all of whom were interviewed. The permission from the hospital's chief administrator presumably took this into consideration.

12. Are the potential benefits and risks of the study acceptable?

Data collection procedures were appropriate. Steps were taken to safeguard confidentiality and anonymity. The REC must examine carefully confidentiality procedures for the review of employment records (including who has access to the records, the training they receive and the form in which data are recorded) as well as procedures for storing (and ultimately disposing of) recordings or transcripts containing identifiable information.

13. Are concerns about justice and equity adequately addressed?

As the study involved employees of the hospital, negotiations for consent should be conducted in the absence of organizational leaders, and such leaders should not be informed of the names of individuals who agree to or refuse study participation. The identification of a well-performing hospital, explicitly defined as a hospital that ensures equitable access to high-quality care, indicates that equity of patient care was considered during selection of cases.

14. Are there satisfactory plans for access to interventions after the study?

The report states that feedback from the study will be presented to the team, allowing them to reflect and act on the findings. It is not clear whether the study results will be used to improve management approaches in similar hospitals in the country.

4.4 Extension of community-based primary care: analysis of the family health programme and infant mortality in Brazil, 1999–2004 (32)

Ethical issues

- When does secondary analysis of data require REC review?
 - Does data linkage affect the identifiability of data in such studies?
 - Is REC review required?
-

Summary

Background and objectives

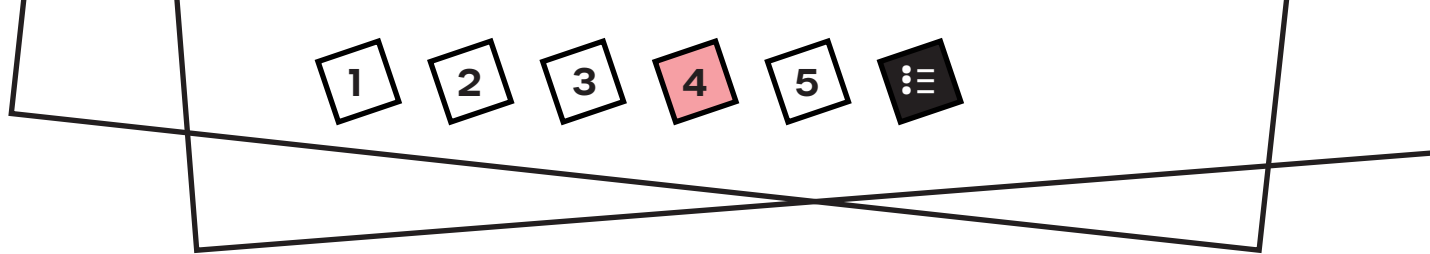
The rates of infant and child mortality in Brazil are higher than in similar countries. The authors of this study assessed the effects of an integrated community-based primary care programme, the Family Health Programme, on infant, neonatal and post-neonatal mortality rates between 1999 and 2004 and conducted an ecological analysis of the effect of the programme on these parameters. The Family Health Programme funds primary care services within Brazil's national health system. Despite the ambitious scope of the programme, changes at national level have been evaluated rarely and in only one peer-reviewed publication. In this analysis, local outcomes were analysed.

Methods

The programme comprises a decentralized approach to primary care, which includes responsibility for the organization of services, financing and delivery, with teams that may include dentists and social workers in addition to physicians and nurses. Each municipality in Brazil adopted the programme at a different time, and coverage increased at different rates. In this quasi-experimental study, a pooled, cross-sectional time series approach was used to assess relations between dependent and independent variables over six years. The unit of analysis was the "micro-region", and 557 micro-regions encompassing all of Brazil's 5564 municipalities were analysed. The analysis included control for independent variables known to influence infant mortality, which were poverty (proportion of the population in the lowest income quintile), women's health and development (proportion of women with no prenatal care and proportion of women aged > 15 years with no formal schooling), child health (proportion of children vaccinated against hepatitis B or with low birth weight, defined as percentage weighing < 2500 g at birth) and health services (numbers of physicians and hospital beds per 1000 population). Data on programme coverage, health resources and outcomes were obtained from the Brazilian Ministry of Health, while data on the variables known to influence infant mortality were derived from representative population surveys conducted by the Brazilian Institute of Geography and Statistics.

Results

Poverty, female illiteracy, lack of prenatal care and low rates of vaccination against hepatitis B were all found to be associated with higher rates of infant mortality, and the analysis showed that the rates decreased as programme coverage increased. After control for other health determinants, a 10% increase in coverage was associated with a 0.45% decrease in infant mortality, a 0.6% decrease in post-neonatal mortality and a 1% decrease in diarrhoea-related mortality. Extension of the programme to the north and north-east of the country may have contributed to reducing interregional inequalities in infant mortality associated with primary care. Coverage was not associated with any change in



neonatal mortality rates. Because of the ecological nature of the study (i.e. data and analysis at regional level), it was not possible to test whether the reductions in infant mortality and other outcomes occurred in families that actually used the Family Health Programme. This study was partially supported by the Brazilian Ministry of Health; however, the paper includes a statement that the conclusions presented represent the opinion of the authors alone.

Ethical analysis

1. Is it research?

The study was an ecological analysis of the effects of the Brazilian Family Health Programme on child health. To date, there has been limited evaluation and only at national level. As the study is a systematic investigation designed to produce generalizable knowledge, it is research.

2. Which aspects are research?

The Family Health Programme is the main means of providing primary care services in Brazil's national health system. The Government provides funds to municipalities to organize primary health care for residents, including access to medical care, coordination of care between providers and health promotion. Extension of the programme during the five-year study period provided an opportunity to study effects on child health. As the programme and its extension were entirely under the control of the Brazilian Government and municipalities, it is part of routine delivery of health services in the country. The research component of the study is use of data on programme coverage, outcomes and relevant variables from a variety of sources, including the Ministry of Health and the Institute of Geography and Statistics.

3. Is review by a research ethics committee required?

This study probably does not involve human participants, as data are aggregated by micro-region. Therefore, REC review may not be required although a privacy review may be, particularly if data sets are being linked. In complex or unclear cases, researchers should seek a written determination from an REC as to whether review is required.

4. Are there adequate plans to manage conflicts of interest?

Funding of the research by the Ministry of Health presents a potential conflict of interest. Researchers should retain independence in the design, analysis and publication of results.

5. What is the study intervention?

There is no study intervention.



6. What are the data collection procedures?

The study is a secondary analysis of data collected by several organizations. Data on programme coverage, health resources and outcomes were administrative data from the Brazilian Ministry of Health. Data on factors known to influence infant mortality, including poverty, women's health and development, child health and health services, were from population surveys.

7. Who are the participants?

Use of existing data in a secondary analysis involves no research participants if the data were collected anonymously, rigorously anonymized or available to researchers only at group level. Linkages among anonymized data sets may inadvertently create identifiable data by aligning variables (such as age and postal code) that pick out an individual within a population. As the unit of analysis was the micro-region and not the individual, it is likely that only group data were provided to the researchers. The study therefore did not involve individuals whose private information was collected for research purposes. Researchers and RECs should carefully consider the identifiability of data to determine whether review is required.

8. From whom is informed consent required, or is a waiver of informed consent appropriate?

Secondary use of data does not usually require informed consent. If the study does not involve human participants, no informed consent is required. If the study does involve human participants, the conditions for a waiver of consent probably apply. The study was based on a national sample and, provided adequate measures were in place to protect confidentiality, probably posed only minimal risk.

9. Is permission from a "gatekeeper" required?

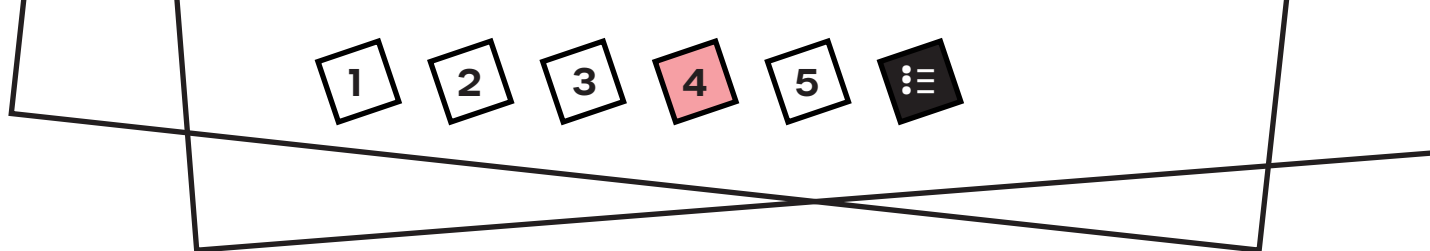
As the study was based on data collected by the Department of Health and the Institute of Geography and Statistics, their permission and compliance with their data policies was required.

10. Is group or community engagement required?

While there was no study intervention, municipalities received financial incentives to adopt the programme, and they were being evaluated. Continuing consultation and engagement with the public and municipalities may be required.

11. Are there adequate plans for protection of privacy and confidentiality?

All data were analysed at aggregate level as rates or proportions. Nevertheless, attention should be paid to data on area units, which might be identifiable if the cells are very small. For counts of small



cells, approaches such as aggregation of categories or suppression of cells below a certain threshold might be considered. Publication and dissemination of results must not harm the reputations of regions.

12. Are the potential benefits and risks of the study acceptable?

The study involved no intervention or control condition. The data collection procedures were appear to be appropriate. Secondary data were analysed. Careful attention should be paid to inadvertent creation of identifiable data by linkage of different databases. Rigorous procedures to protect the confidentiality of data should be in place and described in detail in the study protocol. Procedures to guard against reputational harm to regions must also be included in the protocol.

13. Are concerns about justice and equity adequately addressed?

No additional protection is required. The analyses only at local level allow for consideration of equity by region and geography.

14. Are there satisfactory plans for access to interventions after the study?

There is no study intervention. The results of the evaluation should be made public in an ethical manner to keep the public informed about the outcome of the policy.

4.5 Use of a clean delivery kit and factors associated with cord infection and puerperal sepsis in Mwanza, United Republic of Tanzania (33, 34)

Ethical issues

- Should access to the study intervention (if found successful) be an ethical requirement?
- Whose responsibility is it to provide access to the intervention after the study?
- Is gatekeeper permission required? If so, from whom?

Summary

Background and objectives

Unclean birth practices increase the likelihood of puerperal sepsis or cord infection. Previous studies in the United Republic of Tanzania implicated puerperal sepsis in 17% of all maternal deaths. WHO advocates the concept of “six cleans” during delivery: clean hands, a clean delivery surface, clean perineum, nothing unclean inserted into the vagina, a clean cord-cutting tool and a clean cord



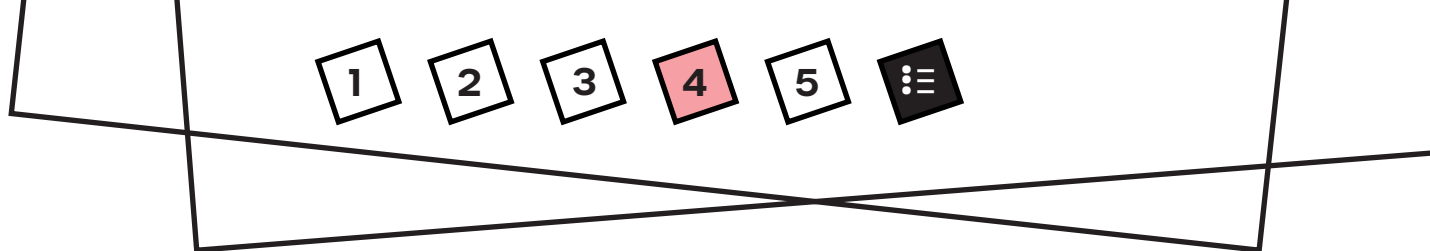
tie. Basic clean delivery kits are designed to ensure these “six cleans”, but their use has not been evaluated in rural United Republic of Tanzania. The aim of this study was to determine the effectiveness of clean delivery kits given to pregnant women in preventing cord infection and puerperal sepsis and to provide qualitative information on community acceptability, correct use and the appropriateness of the kits. The study was a collaboration between a nongovernmental organization (the Program for Appropriate Technology in Health (PATH), Seattle, WA, USA), the Tanzanian Ministry of Health and National Institute of Medical Research and the London School of Hygiene and Tropical Medicine.

Methods

A stepped-wedge cluster randomized design was intended, although the study was reported as a cross-sectional observational study. Two study sites (districts) were sectioned into 10 clusters in total, a cluster being defined as a dispensary or health centre that provided antenatal care to its population. The sites were selected if they had a community maternal and perinatal health care surveillance system that included registration of pregnant women and antenatal and postnatal consultations by trained health volunteers. The surveillance system included site visits, data reviews and training. Pregnant women aged 17–45 years who intended to give birth within the study area were eligible for inclusion. The intervention comprised a free clean delivery kit and health education to pregnant women on the principles of the “six cleans” by village health workers. During the first week after delivery, village health workers visited the households of mothers who had delivered and administered questionnaires about the delivery to the mother and birth attendant. Information collected in the questionnaires included use of the kit, bathing, shaving, place of delivery and any substance put on the umbilical cord. The health worker also examined the mothers and infants physically and evaluated use of the clean delivery kit. A woman was defined as having used a kit if she reported having used at least one of the items in the kit for cord disinfection (e.g. methylated spirit) or to prevent puerperal sepsis (e.g. clean plastic sheet). Written consent was obtained from all participants. For those who were illiterate, the information sheet was read aloud in its entirety, the woman stamped her thumbprint to signify her consent, and a witness signed the form. Institutional review boards of PATH and the Tanzanian National Institute of Medical Research approved the study protocol.

Results

Two sets of study results were published, in 2005 and 2007. In the first, the study was described as a stepped-wedge cluster randomized trial (33), while the second report suggested that randomization was not used (34). The authors of the two studies were different. The second manuscript was preceded by a “notice of duplicate publication”, indicating that the earlier publication was deemed to be a “preliminary evaluation” and was “published without consent of the research group.” Both sets of study results indicated that the clean delivery kits provided to pregnant women reduced the incidence of cord



infection and puerperal sepsis. In low-resource settings, where home birth is common and clean delivery supplies are scarce, disposable kits can be made available through health clinics, markets, pharmacies or other channels to help reduce rates of infection. Funding was provided by the United States Agency for International Development. The second manuscript included a statement that the opinions expressed were those of the authors and did not necessarily reflect those of the Agency.

Ethical analysis

1. Is it research?

The aim of the study was to determine the effectiveness of clean delivery kits provided to pregnant women in preventing cord infection and puerperal sepsis in United Republic of Tanzania. As the study was a systematic investigation designed to produce generalizable knowledge, it was research.

2. Which aspects are research?

The study was conducted in two districts of the country, in which a nongovernmental organization managed a system for active community care and perinatal surveillance. Home visits by community health workers were part of routine care, but the provision of clean delivery kits and associated education were not part of routine practice either in these districts or elsewhere in the country. Provision of clean delivery kits and education was therefore the study intervention. The data collection procedures included a questionnaire administered to mothers and birth attendants.

3. Is review by a research ethics committee required?

This research study involved human participants and, as such, required REC review.

4. Are there adequate plans to manage conflicts of interest?

While no statement of conflict of interest was included in the first publication, in 2005, such a statement was provided in the second publication, in 2007. The authors included employees of the programme being evaluated. When authors are involved in both the development and evaluation of a policy, there is a potential conflict of interest.

5. What is the study intervention?

The study intervention is the provision of a clean delivery kit and education on its use to pregnant women. A community health worker provided the kits to pregnant women at their first antenatal visits and explained proper use of the kit and the principle of the "six cleans."



6. What are the data collection procedures?

Community health workers made two visits to the mothers' homes in the week after delivery to check for signs of infection in the mother and child. They also administered the questionnaire to the mother and birth attendant. The information collected included use of the kit, bathing, shaving, place of delivery and any substance put on the umbilical cord.

7. Who are the participants?

Pregnant women were targeted by the study intervention, and pregnant women and birth attendants were administered questionnaires and interacted with researchers. As such, the pregnant women and birth attendants were research participants.

8. From whom is informed consent required, or is a waiver of informed consent appropriate?

Informed consent of pregnant women should be obtained at the time of study enrolment. Informed consent for administration of the questionnaires should be obtained from both mothers and birth attendants.

9. Is permission from a "gatekeeper" required?

As the study had a substantial impact on the activities of community health workers, permission is required from the local health authority.

10. Is group or community engagement required?

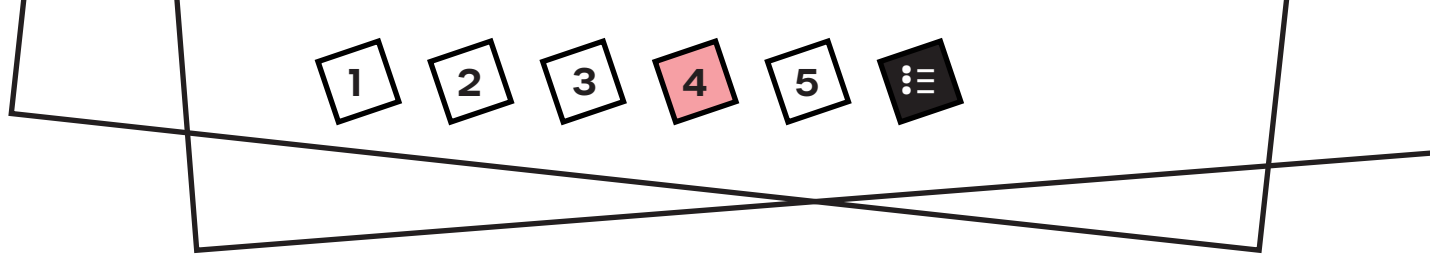
As the study affects health system delivery (including costs and provision after the study), engagement with the communities, the health care workers and stakeholder engagement with relevant health administrative bodies is appropriate.

11. Are there adequate plans for protection of privacy and confidentiality?

Health information was collected on questionnaires, and health data were collected from an existing surveillance system. The study was reviewed by two ethics committees, which presumably reviewed privacy and confidentiality issues.

12. Are the potential benefits and risks of the study acceptable?

The study intervention was justified. Cord infection and puerperal sepsis are both common after childbirth in sub-Saharan Africa. The effectiveness of clean delivery kits provided to pregnant women had not been evaluated in the region. The data collection procedures were adequate. The REC should ensure that adequate measures are in place to protect the confidentiality of the data collected.



13. Are concerns about justice and equity adequately addressed?

In the United Republic of Tanzania, the adult illiteracy rate is 32.2% and may be higher in rural communities. Researchers should ensure that informed consent documents are available in both written and verbal formats, that adequate steps are taken to ensure that participants understand the content and that their comprehension is confirmed by witnesses. Participants should not be excluded because of their level of literacy or because they are hard to reach.

14. Are there satisfactory plans for access to interventions after the study?

The surveillance system includes an education component on clean delivery and care. The second manuscript includes a statement that kits should be made available, which may indicate that they were not provided after the study. The Tanzanian Ministry of Health, which was listed as a collaborator, had an obligation to do so. Continuing education and awareness of the “six cleans” could nevertheless improve outcomes.

4.6 Evaluation of the national yellow fever surveillance programme in Cameroon (35)

Ethical issues

- Is this research or non-research quality improvement?
 - Is REC review required?
 - Is gatekeeper permission required?
-

Summary

Background and objectives

WHO has estimated that 200 000 cases and up to 30 000 deaths are caused by yellow fever each year in Africa. Most occur in 12 countries, including Cameroon. In 2002, the Government of Cameroon issued a five-year strategic plan to control yellow fever, which included routine vaccination, regular preventive mass vaccination campaigns and national case-based yellow fever surveillance with laboratory confirmation and a rapid mass vaccination response when an outbreak occurred. The study is an evaluation of the national immunization programme.

Methods:

The study involved secondary analysis of data on vaccination collected in the public health surveillance programme. Routine childhood vaccinations are offered in both public and private health centres, which compile monthly syntheses. Written procedures were prepared for yellow fever surveillance, including case definitions, case investigation forms and detailed instructions for specimen collection and outbreak investigations and response. Regular supportive supervision and meetings were used to monitor and improve the quality of data collection, analysis and reporting during both routine and supplementary activities. Data on vaccination and surveillance from each level of the national health system were analysed, including monthly syntheses of routine vaccination and any supplementary activities. Three indicators were used: the proportion of reported yellow fever cases for which there was a blood specimen, the proportion of districts that provided at least one blood specimen in a year and the proportion of yellow fever outbreaks investigated. Data on vaccination and surveillance reported between 2003 and 2006 were analysed. The sustainability of yellow fever control activities was discussed.

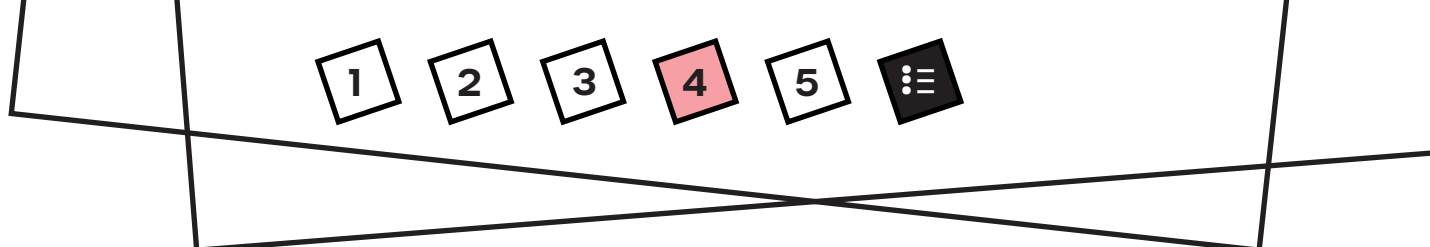
Results

Between 2004 and 2006, the national coverage rate of routine yellow fever vaccination rose from 58.7% to 72.2% and reached parity with the vaccination coverage rate for measles. Variation in coverage across the country was reduced, and parity was maintained with measles coverage. During this period, the number of suspected cases of yellow fever increased substantially, as did the proportion of districts that reported at least one suspected case per year. The number of confirmed cases remained stable. Yellow fever outbreaks occurred in several districts, but, because of constraints on rapid mobilization of resources, reactive supplementary vaccination activities were conducted in only two of the districts several months after confirmation of the outbreak. No serious adverse events were reported after vaccination. The authors concluded that Cameroon successfully planned and implemented evidence-based strategies for preventing yellow fever outbreaks and for detecting and responding to outbreaks when they occur.

Ethical analysis

1. Is it research?

In 2002, Cameroon adopted a five-year strategic plan for yellow fever control. In this observational study, routinely collected public health data were analysed to assess the impact of the programme. As the study sought only to inform local policy or practice, it is a non-research quality improvement study and not research.



2. Which aspects are research?

Yellow fever is a significant cause of morbidity and mortality in low- and middle-income countries. Most of the 200 000 cases each year in Africa occur in 12 countries, of which Cameroon is one. Starting in 2002, Cameroon implemented a public health strategy to control the disease, which involved routine vaccination of children, mass vaccination of children and adults in high-risk areas and case-based surveillance with mass vaccination in outbreaks. Routine data are collected from vaccination programmes, and demographic and clinical information and a blood sample are collected from each yellow fever case. The aim of this observational study was to evaluate retrospectively the effectiveness of the plan during the first four years of its implementation. The study is thus programme evaluation and not research.

3. Is review by a research ethics committee required?

As the study is non-research for quality improvement, it is not human participants research. Accordingly, REC review is not required.

4. Are there adequate plans to manage conflicts of interest?

The study was conducted by individuals who participated in or coordinated the yellow fever control programme. Independent review of the study design and analyses would be beneficial.

5. What is the study intervention?

There is no study intervention.

6. What are the data collection procedures?

All the data collected and analysed were obtained during routine conduct of a public health programme. No data were collected or analysed for the purposes of this project.

7. Who are the participants?

As the activity is not research, there are no research participants.

8. From whom is informed consent required, or is a waiver of informed consent appropriate?

As there are no research participants, informed consent is not required; however relevant groups and communities must be informed about the activity.

9. Is permission from a “gatekeeper” required?

The programme was evaluated within the Ministry of Public Health, the agency responsible for the yellow fever control strategy. All data were collected on behalf of the Ministry.



10. Is group or community engagement required?

Given the stated goal of achieving sustainability of the yellow fever control programme, engagement with the communities and relevant stakeholder groups is warranted.

11. Are there adequate plans for protection of privacy and confidentiality?

While the study was conducted as evaluation of a public health prevention and surveillance system, relevant privacy protection should be in place. Identification of very few cases in certain years and specific districts could potentially allow identification of individuals (see point to consider 7). Techniques to ensure anonymity (for example, suppression of case data or aggregation of small cell counts) should be used.

12. Are the potential benefits and risks of the study acceptable?

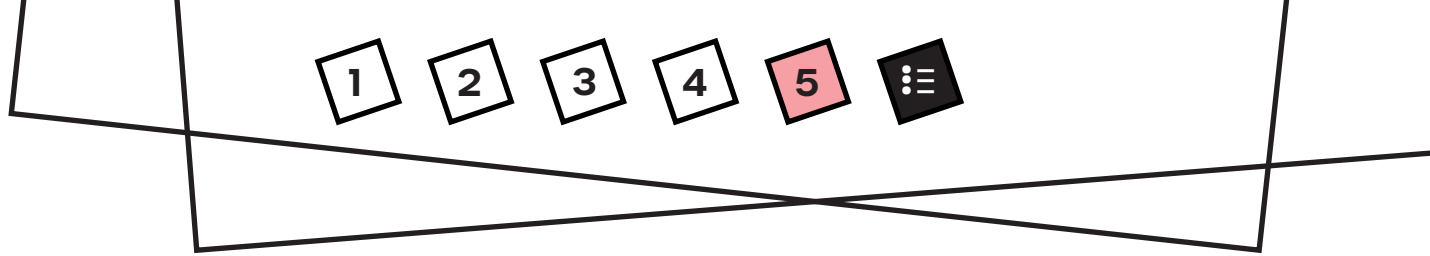
As there is no study intervention or data collection additional to routine collection of data, there is no benefit or harm from data collection. Due consideration should be given to potential harms to individuals as a result of this evaluation.

13. Are concerns about justice and equity adequately addressed?

Aspects of equity and justice were addressed by considering geographical variations in coverage and the incidence of cases. Reduction of inequality of coverage is emphasized in the analyses. As there were no vulnerable participants, additional protection was not required. As mentioned above, however, consideration should be given to suppressing case data, in view of the small cell sizes of confirmed cases. Publication of the names of districts with confirmed cases and cell sizes ≤ 3 may allow identification of individuals.

14. Are there satisfactory plans for access to interventions after the study?

There was no specific study intervention. Rather, an implemented programme of vaccination was assessed retrospectively. Programme sustainability is being discussed.



5. Conclusion

HPSR raises difficult questions in the application of accepted ethical principles for research. This document was prepared in response to a request from researchers and RECs. In it, we reviewed and interpreted ethical principles in order to provide useful “points to consider” in HPSR. The document does not represent the final word on the ethics of HPSR but is a first step towards formal guidance. Accordingly, feedback and suggestions for improvement are welcomed.

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The field of HPSR and its conduct pose important challenges for both researchers and research ethics committees (RECs) about the interpretation and application of the principles for ethical conduct of health research to policy and systems research. For instance, when is a project health research and when is it health practice? Is research ethics review required for studies of existing policy decisions?

This document provides researchers and RECs with a series of “points to consider” for clear identification, consideration and communication of ethical issues in HPSR.

It is intended that, after reading this document, researchers will better understand relevant ethical issues in their HPSR study protocols and respond effectively to REC comments and questions; and REC members will be better able to identify aspects of an HPSR project that fall within its purview, identify ethical issues raised by the study and better communicate comments and questions to researchers.

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