An Ethical Framework for the development and review of health research proposals involving humanitarian contexts

Project Final Report
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Context Note

This final report discusses a proposed ethical framework addressing research on health interventions in humanitarian crises. The framework is intended to support and help ensure that health research conducted in such crises is ethically sound by providing guidance and a review process for research protocols and their refinement. While the primary intent is to provide a tool for the R2HC Funding Committee and its review of grant applications to support such research, the larger effective audience includes researchers and their organizations (academic, NGO, agency, governmental, private); research ethics boards (REBs/IRBs) and similar review bodies; regulatory agencies; funders and sponsors, and the interested public.

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Disclaimer

The ethical framework discussed here and all supporting work was developed by the authors/investigators. They are solely responsible for the content of this paper. Observations, arguments and conclusions contained herein are not necessarily those of ELRHA, DFID or the Wellcome Trust.

1.0 Abstract

The authors propose an ethical framework to 1) guide development of research designs and protocols intended for implementation in humanitarian crises and complex emergency contexts to help ensure their ethical viability, and 2) support ethical review of such protocols by independent ethical review bodies (REBs, IRBs), funders, and other organizations of interest, and 3) serve general educational purposes and enhance public understanding of the issues involved in and ethical principles guiding research in such settings. The framework is designed as a tool – offering a practical and easily implementable approach in which key ethical principles are considered in a clustered, hierarchical order. Implementation and assessment of the utility of this approach by researchers and by REBs/IRBs considering research protocols involving humanitarian crisis setting will guide further refinement of this ethical framework.

Contents

2.0 Project Context/Background

The overall aim of the Research for Health in Humanitarian Crises (R2HC) programme is to improve health outcomes by strengthening the evidence base for public health interventions in humanitarian crises. The specific outcome of the programme will be to directly increase the quality and quantity of collaborative research on recognised public health challenges in humanitarian crises, leading to improved health outcomes through evidence-based and cost-effective humanitarian interventions.

The R2HC programme will:

- Undertake a system wide Evidence Review to identify major challenges/evidence needs associated with public health interventions in humanitarian contexts in order to inform the shaping of the research calls.
- Facilitate research collaborations between public health researchers and either NGOs, multilateral agencies or both.
- Establish a rapid response facility set aside for pre-approved research projects/consortia to be set up and undertaken in the acute phase of an emergency. The facility will allow research to commence in the immediate aftermath of a humanitarian crisis and enable the gathering of rich data and trialling of specific interventions developed for acute disaster situations.

In order to guide the R2HC programme and its Funding Committee on ethical dimensions of research the programme might fund, a decision was taken to commission development of an ethical framework and guidelines. More here.

The Terms of Reference for the ethical framework notes:

"…There is considerable inconsistency in the quality and extent of the evidence base that informs public health interventions in the aftermath of disasters. There are two main reasons for this: firstly, it is challenging, but not impossible, to conduct quality research in such settings. Secondly, three groups – non-governmental organisations (NGOs), multilateral agencies, and academics have traditionally worked in relative isolation from each other in response to such crises.

"Added to this, the ethical challenges of conducting public health research in disaster settings and/or alongside operational humanitarian programmes are a major consideration for research teams and academic institutions seeking to work in this field. Prior consultation on this issue by the Wellcome Trust identified that while some good research on ethics has been conducted by individual agencies and universities, the lack of comprehensive research or widely agreed guidance on the issue is a major problem and a potential risk for research programmes and funders.

"ELRHA is therefore commissioning work to develop and agree a guiding framework for use by the R2HC programme. This work will include broad consultation and the identification and collation of existing frameworks, research and good practice. A new framework for use within the R2HC programme will be developed out of this process and be widely circulated for consultation. It is important to note that this framework does not intend to take the place of established ethical review processes within academic institutions and other organisations which undertake research. The R2HC framework and guidelines will be used principally to inform potential applicants to the programme on the standards DFID and the Wellcome Trust expect to be adhered to in funded research and which will be referred to during the proposal appraisal and selection process.

"Further research and testing of the utility of the framework in operational contexts will be conducted through the funded research programmes. It is intended that a final review of the framework will lead to it being published and potentially recognised internationally as a best practice standard…"

The authors of this paper note the R2HC programme definitions for "humanitarian public health", "humanitarian crisis" and "research" are intentionally broad and therefore the ethical framework discussed here is intended to address a wide spectrum of research opportunities. Humanitarian public health is defined for the purposes of the R2Hc programme as:

> *Interventions that contribute collectively, in combination or singularly to saving lives, building resilience and promoting better health outcomes in humanitarian emergencies. In this approach public health interventions should be considered in their broadest scope including all relevant practice areas including water, sanitation, nutrition and mental health.*
> *R2HC Programme, June 2013*

The graphic below, developed by the authors, is a depiction of the range of health interventions and issues which are understood to be included by the definition above and is derived from the scope of health intervention areas considered as part of the Evidence Review commissioned by the R2HC programme.

Conceptual Framework 1.0:
Health Interventions in Humanitarian Crises/Contextual Factors
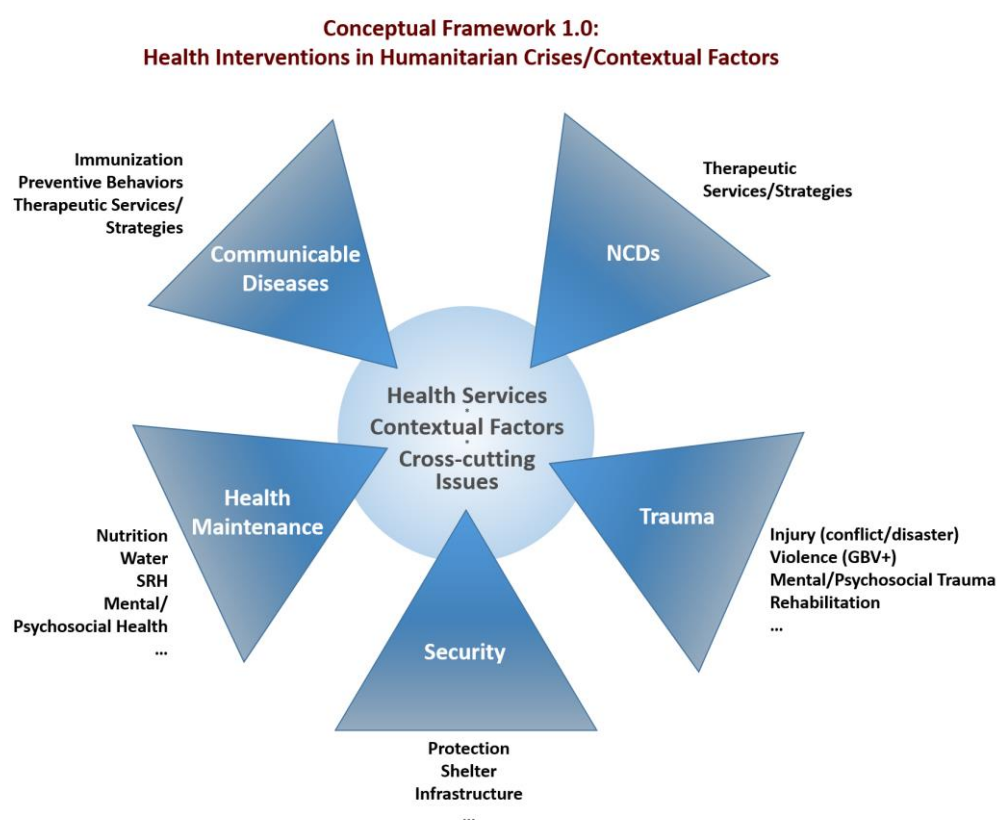
This work – led by Dr Karl Blanchett and Dr Bayard Roberts of the London School of Hygiene & Tropical Medicine – conducted "a system-wide Evidence Review to identify major challenges/evidence needs associated with public health interventions in humanitarian contexts." An overview of the Evidence Review is available here and its final report is available here.

We include below two key slides from this review from a June 2013 presentation. They depict the "state of evidence" supporting the field in this area. The data underscores the relative paucity of "strong" evidence in the literature in a broad range of contextual factor and health interventions.
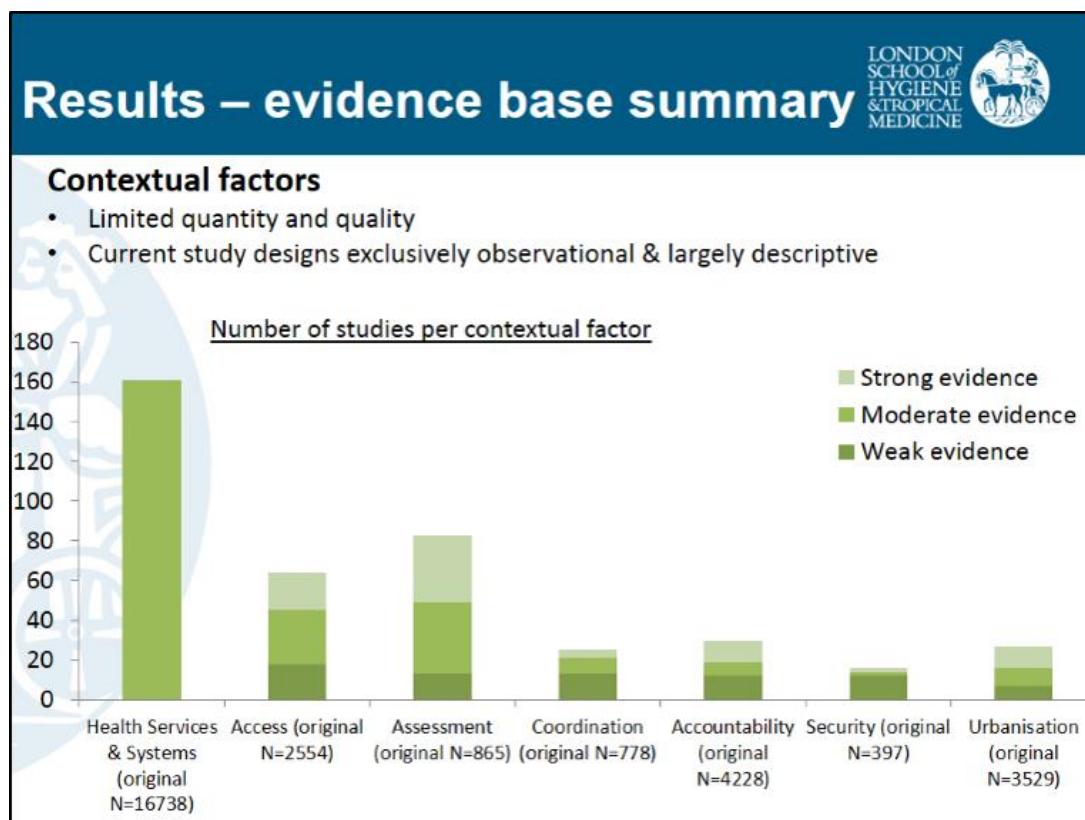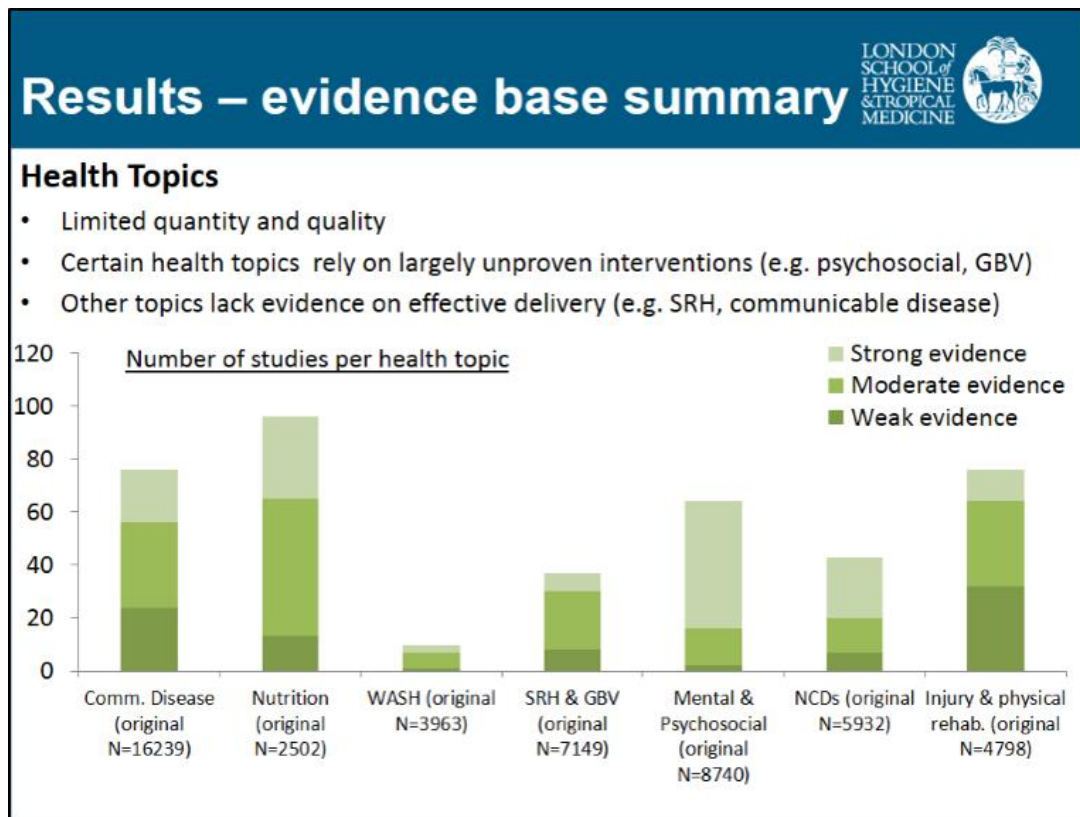
3.0 Literature Review

The project team conducted a set of literature searches using a range of literature databases to identify substantive literature focused on ethical considerations surrounding health research in humanitarian settings. This specific strategies and databases employed are summarized in Annex C.

Important additions were suggested by informants who identified journal articles, other published materials, and programs/projects relevant to these themes. Additionally, some informants shared manuscripts and ethical frameworks in development by their organizations on a confidential basis. Finally, the authors utilized a visit to the WHO archives to determine what historical anchorage there might be around ethical frameworks as they might apply to research on such health interventions.

We highlight here selected literature from the process above and included in the project bibliography in Annex A. Our principal rationales for inclusion here include: 1) the article or document contributes to a high-level chronology on how thinking has evolved on these themes over the last twenty five years, and/or 2) the article or document aggregates and structures its discussion of ethical principles and themes in a way which is supportive of *framework* thinking.

[1988]

We begin by documenting the earliest example found from a WHO Archives "hand-search" of relevant printed indexes and finding aides to identify references to research, ethics, policies or standards around health interventions in disaster and humanitarian settings.

The Asian-Pacific Conference on Disaster Medicine, held 24 to 26 November 1988, under the sponsorship of the Japanese Association for Acute Medicine and the Japan International Cooperation Agency, resulted in The Osaka Declaration on Disaster Medicine [see full text in Annex E and excerpt in Text box 1 below]. The declaration does not address ethics per se, but does recognize the role of regional and international cooperation at the time of disasters, "in order to develop smooth cooperation mechanisms and to formulate study programs for disaster relief medicine."

Text box 1

The Osaka Declaration on Disaster Medicine

Excerpt [Accessed via index in paper-only compilation, WHO Archives, September 2013]

PREAMBLE

…CONVINCED that to strengthen medical relief in order to minimize the amount of suffering and the number of victims, it is important to promote international cooperation both at ordinary times with preventative systems, and at actual disaster times with concerted relief actions;

WE REPRESENTATIVES of twenty nations and major international relief organizations herewith make the following

DECLARATION

1. We shall continue our efforts to develop and fortify emergency medical systems for large scale disasters worldwide by recognizing the problems associated with such disasters and discovering effective countermeasures.
2. We shall make effort to improve in particular the Asian and Pacific countries' capability of disaster medicine by developing channels of information exchange among such countries of the region regarding disaster countermeasures.
3. We shall internationally promote studies related to disaster prevention in collaboration with specialists in non-medical fields and related sectors of science and technology, so that results can be properly reflected in the administrative policies and multidisciplinary measures of each country.
4. We shall deepen our understanding of the importance of regional and international cooperation at the time of disaster, in order to develop smooth cooperation mechanisms and to formulate study programs for disaster relief medicine…

[1990]

The second example from the WHO Archives review comes from a 1990 meeting of EuroActDis which, in part, took up ethical issues surrounding research in disaster settings. This language {Text box 2] from the minutes presents an interesting indicator of the thinking at that time.

<div style="border:1px solid #000; padding:10px;">

Text box 2

Concerted European Action for Coping with Disaster
Minutes of the EuroActDis Meeting, Paris, 19-20 April 1990
[Accessed via index in paper-only compilation, WHO Archives, September 2013]
II. Summary
2) Ethical Issues and Ways of Intervention
"It is unethical to withhold any intervention from victims of disasters. We must therefore conduct standard controlled trials, rather than placebo controlled trials or no-treatment controlled trials. The two questions we have to define are first, what is the minimal ethical intervention; and second, what special risk procedure can be offered to any participant in a trial who becomes suicidal, violent, psychotic, risk addicted or substance dependent."

</div>

[1995]

We believe the first milestone discussion in the literature addressing ethical concerns was generated by WHO's then operative Division of Emergency and Humanitarian Action (EHA). In 1995, EHA published WHO/EHA 95.1 - ***Coping with major emergencies: WHO strategy and approach to humanitarian action***. 22 pages. WHO, Geneva, 1995 [available here].

This document is an important, first articulation of WHO's emerging role in complex emergencies and proceeds from WHA and WHO Executive Board resolutions and other actions. It does not address research about health interventions that might be engaged in such emergencies or the field practice standards that might be operative. It provides a useful snapshot of "early thinking" on these larger themes.

[1997]

We see the first significant contribution to the *ethics* of research on health interventions in humanitarian contexts in the 1997 report ***Consultation on Applied Health Research Priorities in Complex Emergencies***. WHO/EHA 98.1 30 pages. WHO, Geneva; Limited distribution. [available here]

We regard this as a seminal document that captures the health research dimension of the problem and primarily addresses health research priorities. But there is a strong treatment of ethics of such research including a brief to the consultation group on the then relevant "globally applicable ethical and scientific standards" for biomedical research on human subjects (p. 4), and a briefing on the decades of preceding work by the WHO Advisory Committee on Health Research (ACHR), although not specific to such research in emergency settings (p.5). General criteria for research in emergency settings were laid out which resonate well some 16 years later (p.6).

In "4.7 Ethics" (p.15) the core set of ethical foundation documents are referenced (Helsinki, CIOMS, etc.) and a few statements are worth presenting here [Text box 3].

<div style="border:1px solid #000; padding:10px;">

Text box 3

"…It is the duty of relief agencies who take care of such victims to make sure that any research proposal which includes them is approved by an ethical committee"
"..Beneficence, autonomy (informed consent and confidentiality) and justice are the key elements in ethical evaluation of research on human subjects and must also be the reference framework for research in complex emergencies…"
Cont.

</div>

Among six recommendations made by the group were two of specific relevance to this project.

The first involved developing guidance "on the need to establish an ethical review committee, specific to research on complex emergencies…"

The purpose of the committee "could be (to provide a) voluntary peer review process of research proposals…" and "advocacy: the committee would act as an advocacy group for raising ethical awareness among scientists and humanitarian agencies who design and implement medical research in refugee settings…"

A companion recommendation was that WHO and UNHCR "set up an ethical expert group to prepare a template of ethical guidelines reflecting the overarching need to protect the rights, dignity and autonomy of research subjects in emergencies"

Finally, in the Conclusions section, the report notes: "An ethical framework for conducting research in emergencies should be based on existing clauses and instruments. The (additional) need was expressed to establish fact track procedures to disseminate information through publications and journals."

[2000]

The next milestone is the paper by Emanuel, Wendler and Grady in 2000: ***What Makes Clinical Research Ethical?*** (JAMA, 2000; 283: 2701-2711) [available here].

This paper's abstract helpful summarizes one of the first "frameworks" we encountered [Text box 4].

> *Text box 4*
>
> Abstract (formatting added)
>
> Many believe that informed consent makes clinical research ethical. However, informed consent is neither necessary nor sufficient for ethical clinical research. Drawing on the basic philosophies underlying major codes, declarations, and other documents relevant to research with human subjects, we propose 7 requirements that systematically elucidate a coherent framework for evaluating the ethics of clinical research studies:
>
> (1) value—enhancements of health or knowledge must be derived from the research;
>
> (2) scientific validity—the research must be methodologically rigorous;
>
> (3) fair subject selection—scientific objectives, not vulnerability or privilege, and the potential for and distribution of risks and benefits,
> should determine communities selected as study sites and the inclusion criteria for individual subjects;
> *Cont.*

(4) favorable risk-benefit ratio—within the context of standard clinical practice and the research protocol, risks must be minimized, potential benefits enhanced, and the potential benefits to individuals and knowledge gained for society must outweigh the risks;

(5) independent review—unaffiliated individuals must review the research and approve, amend, or terminate it;

(6) informed consent—individuals should be informed about the research and provide their voluntary consent; and

(7) respect for enrolled subjects—subjects should have their privacy protected, the opportunity to withdraw, and their well-being monitored.

Fulfilling all 7 requirements is necessary and sufficient to make clinical research ethical. These requirements are universal, although they must be adapted to the health, economic, cultural, and technological conditions in which clinical research is conducted.

[2001]

In 2001, Leaning proposed robust guidelines limiting such research in ***Ethics of research in refugee populations***. The Lancet. Vol 357, May 5, 2001 [available here]

Leaning's guidelines are presented below [Text box 5]:

Text box 5

Proposed guidelines for research in refugee and internally displaced populations
:: Undertake only those studies that are urgent and vital to the health and welfare of the study population
:: Restrict studies to those questions that cannot be addressed in any other context
:: Restrict studies to those that would provide important direct benefit to the individuals recruited to the study or to the population from which the individuals come
:: Ensure the study design imposes the absolute minimum of additional risk
:: Select study participants on the basis of scientific principles without bias introduced by issues of accessibility, cost, or malleability
:: Establish highest standards for obtaining informed consent from all individual study participants and where necessary and culturally appropriate from heads of household and community leaders (but this consent cannot substitute for individual consent)
:: Institute procedures to assess for, minimise, and monitor the risks to safety and confidentiality for individual subjects, their community, and for their future security
:: Promote the well-being, dignity, and autonomy of all study participants in all phases of the research study

[2004]

Forward to 2004, we note the special section – ***The ethics of disaster research*** –Journal of Traumatic Stress, October 2004, Volume 17, Issue 5, 361–448. [available here]

This special section includes the following articles, helping move the discussion forward:
- ***Ethical issues pertaining to research in the aftermath of disaster*** (pages 363–372), Lauren K. Collogan, Farris Tuma, Regina Dolan-Sewell, Susan Borja and Alan R. Fleischman, Abstract
- ***Decision-making capacity and disaster research*** (pages 373–381), Donald L. Rosenstein, Abstract
- ***The risks and benefits of participating in trauma-focused research studies*** (pages 383–394), Elana Newman and Danny G. Kaloupek, Abstract

- **The concept of vulnerability in disaster research** (pages 395–402), Carol Levine, <u>Abstract</u>

[2009]
We judge the next milestone to be 2009 with three papers of significance.

The first is **Conducting Research in Disease Outbreaks**. Macklin and Cowan (2009) PLoS Negl Trop Dis 3(4): e335. doi:10.1371/journal.pntd.0000335 [available <u>here</u>]. The authors explore the forms and depth of ethical review around research on disease outbreaks, a subset of the larger sphere of humanitarian crises and complex emergencies.

They argue that "some form of ethical oversight is needed to conduct an investigation of a disease outbreak" but that the specific mechanism and procedures "can vary" depending on the circumstances and context. We see a balance being explored to enable appropriate and timely research to proceed on outbreaks, while helping ensure that the "rights and welfare of individuals are protected in disease outbreaks and that communities maintain trust in public health research and practice."

The second and third papers listed just below are linked insofar as they both address, overall, the MSF ethical framework applied by its internal research ethics board against research proposed by MSF staff in various roles:
- **Research Ethics Review in Humanitarian Contexts: The Experience of the Independent Ethics Review Board of Médecins Sans Frontières.** Schopper D, Upshur R, Matthys F, Singh JA, Bandewar SS, et al. (2009). PLoS Med 6(7): e1000115. doi:10.1371/journal.pmed.1000115 [available <u>here</u>]
- **Ethics of conducting research in conflict settings.** Nathan Ford, Edward J Mills, Rony Zachariah and Ross Upshur. Conflict and Health 2009, 3:7 doi:10.1186/1752-1505-3-7 [available <u>here</u>]

The Schopper paper's "Summary Points" note that in 2001, the international humanitarian aid organisation Médecins Sans Frontières decided to constitute an independent ethics review board to ensure that the increasing amount of operational and clinical research it undertakes is scientifically valid and ethical. This article describes the functioning of this ethics review board and the challenging ethical issues that it has discussed since its inception.
The Ford paper provides a specific discussion of the MSF ethical review framework in place at the time and now refined (see 2013 discussion following). We excerpt the elements of this framework and the initial description below [Text box 6].

Text box 6

:: Collaborative Partnership Researchers should engage in partnership with national and/or international research institutions as relevant and appropriate…

:: Community engagement Researchers should respect the community's values, culture, traditions, and social practices; involve the community in the design and implementation of research through a consultative process; and share fairly any financial and other rewards of the research…

:: Social value Beneficiaries should be clearly specified, and the importance of the health problems being investigated and the prospect of value of the research for the beneficiaries made clear…Efforts should be made to avoid diverting resources from health services for the conduct of research…

:: Scientific Validity Research design should optimize possibilities of achieving the social value requirements. Research should be feasible given the social, political, and cultural environment and with sustainable improvements in the local health care and physical infrastructure…

Fair selection of participants Study population should be selected in such a way as to ensure scientific validity of the research and minimize the risks of the research…

Favourable Harm-Benefit Ratio Protocol should clearly assess potential harms and benefits to the study participants and the harm-benefit ratio for the community.

Informed consent Study community should be involved in establishing appropriate recruitment procedures and incentives for the participants. Consent procedures should be acceptable and practical within the study community…

Also in 2009, a WHO consultation added perspectives to the issues involved in **Research ethics in international epidemic response : WHO technical consultation**, Geneva, Switzerland, 10-11 June 2009 [available here]. We excerpt extensively from the Executive Summary reflecting its relevance to this project [Text box 7].

Text box 7

:: In many countries, most research with human participants must undergo prospective ethical review by a research ethics committee (REC), while activities characterized as public health or clinical practice are not subject to this requirement. However, distinguishing between research and practice is complicated by the fact that there is a significant area of overlap in these activities in terms of methodology, systematization of investigation, and the outcome of producing generalizable knowledge…

:: The ultimate goal for public policy should be to ensure that most, if not all, emergency public health activities are subject to some form of ethical oversight, whether or not those activities are formally characterized as research. The specific nature of the oversight should be commensurate with the activity's objectives, methods, risks and benefits, as well as the extent to which the activity involves vulnerable groups.

:: To achieve this goal, it is crucial to streamline the ethics review process and to establish appropriate, flexible mechanisms and procedures for ethical oversight not limited to traditional REC systems.

:: While some crucial emergency health research should still undergo full REC review because of significant risks to individuals or populations under study, a "fast-track" review approach should also be adopted. However, review should not be expedient to the point of dropping or narrowing ethical principles.

:: Options for promoting fast-track review of emergency research include adjusting the balance between in-person and electronic communications by REC members; the use of pre-emergency repositories of study protocols or protocol parts which could be submitted to RECs for ethical pre-screening; the creation of special emergency research RECs, perhaps on a national or regional level; and, where there is no other feasible option, greater reliance on retrospective rather than prospective ethics review, with safeguards to address non-compliant or sub-standard research ethics conduct.

:: Public health activities that are classified as practice may raise important ethical issues. Stakeholders should formulate plans to ensure that such activities receive appropriate and timely ethical review. One option to consider, at least in some situations, is review by special committees with appropriate expertise and experience to examine procedures and methods specific to a public health practice. For activities that do not warrant committee review, or in countries that choose not to institute a committee review structure, public health practitioners can be equipped with tools to help them assess whether their planned activities comport with principles of public health ethics. Training modules for research ethics committees and public health professionals should be created to support this goal.

:: There is a critical need for capacity building in the ethical review of public health research and practice. Researchers, public health agencies and other stakeholders should work together to develop short courses, degree programmes and other training modalities. Funding agencies should direct appropriate support to these efforts.

[2010]

In 2010, there were two important contributions to thinking about health research in post-disaster and humanitarian settings. The first was **Ethical Issues in Post-Disaster Clinical Interventions and Research: A Developing World Perspective:** *Key Findings from a Drafting and Consensus Generation Meeting of the Working Group on Disaster Research and Ethics (WGDRE) 2007.* Sumathipala, Athula; Jafarey, Aamir. Asian Bioethics Review 2.2 (Jun 2010) [available here].

In Appendix 2 of this report, the Working Group presents its "Draft Statement/Guidelines for Disaster Research" with the opening context below [Text box 8].

In addition to the accepted national and international ethical guidelines for the conduct of research, we urge researchers to pay particular attention to the following ethical principles when conducting research in disaster-affected situations. These guidelines are meant to supplement the relevant existing national and international documents and not to replace them. The areas which these guidelines address include the potential for harm resulting from the research process and its socio-political implications, and the potential for the exploitation of the research participants as well as the affected community. They also look at conflicts of the researchers' interests with that of the community being studied, and the process of recruitment of survivors as participants with a particular emphasis on obtaining valid and truly informed consent. These guidelines also emphasise gender and cultural sensitivity, and the need for research to contribute to the healing and empowerment of the disaster-affected community.

The Guidelines are organized around 12 themes which we list below. Each theme includes a series of clarifying points presenting normative dimensions which is too lengthy for inclusion here. The themes are:

1. Relevance to disaster situations
2. Informed consent and voluntariness
3. Community consultation and participation
4. Non-exploitation
5. Dignity, privacy and confidentiality
6. Risk Minimization
7. Institutions arrangements
8. Professional Competence
9. Public interest and distribution justice
10. Dissemination of results
11. Ethics review
12. International collaborative research

The second contribution took the form of a review article on these issues titled ***Conducting research in the aftermath of disasters: ethical considerations*** O'Mathúna, Dónal P., Journal of Evidence-based Medicine, May 2010, Volume 3, Issue 2, Pages 61–138. [available here]

[2011]

We note the important milestones represented by the collaboration that supported WHO's ***Standards and Operational Guidance for Ethics Review of Health-Related Research with Human Participants***. WHO, 2011; 43 pages ISBN: 9789241502948 [available here]

As described, this document compiles "…10 standards that are applicable to the ethics review of health related research with human participants. This document is intended to provide guidance on the research ethics review process, not to take a substantive position on how particular ethical dilemmas in health-related research should be resolved…"

We include the summary listing of guidelines, codes, statutes and regulations as a way to acknowledge that this project is not attempting to create "new " principles, but rather fashion a tool incorporating these established norms to make ethical review more practical and effective [Text box 10]

Annex 1 (pp 28-18)
Guidelines and codes of best practice:
1. Nuremberg Code (Available at: http://ohsr.od.nih.gov/guidelines/nuremberg.html , accessed 17 January 2009
2. Declaration of Helsinki (Available at http://www.wma.net/en/30publications/10policies/b3/index.html , accessed 05 October 2011)
3. CIOMS: International Ethical Guidelines for Biomedical Research Involving Human Subjects (2002) available at http://www.cioms.ch/publications/layout_guide2002.pdf , accessed 05 October 2011)
4. CIOMS: International Ethical Guidelines for Epidemiological Research Involving Human Subjects (2009) (For more information click http:// www.cioms.ch/frame_ethical_guidelines_2009.htm)
5.UNAIDS/WHO, Ethical Considerations in Biomedical HIV Prevention Trials (2007) (Available at http://data.unaids.org/pub/Report/2007/JC1399_ethical_considerations_en.pdf , accessed 05 October 2011)
6. UNESCO Universal Declaration on Bioethics and Human Rights (2005) (Available at http://portal.unesco.org/en/ev.php-URL_ID=31058&URL_DO=DO_TOPIC&URL_SECTION=201.html
7. Nuffield Council on Bioethics: the Ethics of Research related to Healthcare in Developing Countries (2002) (Available at http://www.nuffieldbioethics.org/sites/default/files/Ethics%20of%20research%20related%20to%20healthcare%20in%20developing%20countries%20I.pdf

Statutes and regulations
1. The Universal Declaration of Human Rights Available at http://www.un.org/en/documents/udhr/ accessed on 05 October 2011)
2. ICH Good Clinical Practice Guidelines (1996) (Available at http://www.ich.org/fieadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6_R1/Step4/E6_R1__Guideline.pdf
3. ICH Guidelines on Choice of Control Groups and Related Issues in Clinical Trials (2000) (Available at http://www.ich.org/fi leadmin/Public_Web_Site/ICH_Products/Guidelines/
4. Council of Europe. Convention on Human Rights and Biomedicine, 1997 (Available at http://conventions.coe.int/treaty/EN/Treaties/Html/164.htm , accessed 05 October 2011)
5. Council of Europe. Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Biomedical Research, 2005 (Available at http://conventions.coe.int/treaty/EN/Treaties/Html/195.htm , accessed on 05 October 2011))
6. Directive of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use. Official Journal of the European Communities, 2001: L121/34. (Available at http://www.eortc.be/Services/Doc/clinical-EUdirective-04-April-01.pdf , accessed 05 October 2011)
7. The Common Rule (45 CFR Part 46) (Available at http://www.hhs.gov/ohrp/policy/ohrpregulations.pdf accessed 05 October 2011)
8. United States Food and Drug Administration regulations for the protection of human subjects CFR—Code of Federal Regulations Title21, Part50 (Available at http://www.accessdata.fda.gov/scripts/

[2013]

Providing an important case study is the recently published: ***Ethical considerations for vaccination programmes in acute humanitarian emergencies***. Keymanthri Moodley, Kate Hardie, Michael J Selgelid, Ronald J Waldman, Peter Strebel, Helen Rees & David N Durrheim **WHO Bulletin,** 2013;91:290-297. [available here]

We provide the full text of the abstract below [Text box 11]:

Text box 11

Humanitarian emergencies result in a breakdown of critical health-care services and often make vulnerable communities dependent on external agencies for care. In resource-constrained settings, this may occur against a backdrop of extreme poverty, malnutrition, insecurity, low literacy and poor infrastructure. Under these circumstances, providing food, water and shelter and limiting communicable disease outbreaks become primary concerns.

Where effective and safe vaccines are available to mitigate the risk of disease outbreaks, their potential deployment is a key consideration in meeting emergency health needs. Ethical considerations are crucial when deciding on vaccine deployment. Allocation of vaccines in short supply, target groups, delivery strategies, surveillance and research during acute humanitarian emergencies all involve ethical considerations that often arise from the tension between individual and common good.

The authors lay out the ethical issues that policy-makers need to bear in mind when considering the deployment of mass vaccination during humanitarian emergencies, including beneficence (duty of care and the rule of rescue), non-maleficence, autonomy and consent, and distributive and procedural justice.

We note that an updated **WMA Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects** [64th WMA General Assembly, Fortaleza, Brazil, October 2013] was released recently which clarifies and strengthens various principles and is available here:

Further, we note that MSF has recently released **MSF ERB Research Ethics Framework Template and Guidance Documents, v1 Nov 2013,** a revision to its ethical framework discussed in the two papers referenced earlier by Schopper et al, and Ford, et al.

The new framework, excerpted just below, includes this context statement [Text box 12]:

Text box 12

"…Based on the experience of the past ten years, it was decided to move away from the Emanuel* framework in form and in content. While most of the benchmarks of the Emanuel framework are retained in some form, the framework is more practical by formulating explicit questions following a temporal logic of research development. An alternative format focused on principles or statements has been avoided, as it can suggest that ethics is a series of inflexible and absolute rules, and it can be unclear how the different elements relate to each other. In contrast, a series of questions are open-ended and invite discussion and engagement. They seek to encourage researchers to think critically about their proposed protocols and justify their methods, think about possible harms and benefits, and consider what the implications of their research might be. Additional considerations particularly relevant to MSF's research were added, such as conflict of interest, securing resources for research, use of biological material, dissemination of research findings."

In 2003, in order to provide structured advice to field researchers and to facilitate standardized reviews, the ERB decided to adapt a draft framework for clinical research in the developing world developed by the National Institute of Health in the United States. (Emanuel EJ, Wendler D, Killen J, Grady C. What makes clinical research in developing countries ethical? The benchmarks of ethical research. JID 2004;189:930-7.)

We have excerpted the core question structure from the new MSF ethical framework below [Text box 13]. We note that the Guidance document also presents a number of "sub-questions" under headings which, while stated as not exhaustive, are helpful to understand the nuance and intent of the ERB. This fuller treatment is presented as Annex E in this document. The authors urge a full reading of the MSF documentation as cited.

Important to this revision of the MSF framework in our view is the shift to a question-based approach for researchers and the arrangement of the questions in a temporal order.

[2014]

Just published at this writing is an important book titled **Disaster Bioethics: Normative Issues When Nothing is Normal** by editors Dónal P. O'Mathúna, Bert Gordijn, and Mike Clarke [Springer, Public Health Ethics Analysis Series, Volume 2, 2014. More here]. While the entire book is informative and extends the literature in important ways, its second half focuses on research ethics and disasters with contributions as below (see initial content and abstracts from links).

Overall, these chapters explore the special ethical challenges involved in health research in disaster settings and we believe the insights to be generalizable to humanitarian crises of all descriptions which result in vulnerable individuals and populations. We urge readers to further explore the book overall and these chapters in particular. We found them to further validate our project findings and the foundations underpinning our proposed ethical framework discussed below [Text box 14]

Text box 14

Research Ethics and Disasters
Book Chapter Interests Divided: Risks to Disaster Research Subjects vs. Benefits to Future Disaster Victims
Pages 109-127
Evelyne Shuster
Book Chapter Purple Dinosaurs and Victim Consent to Research in Disasters
Pages 129-141
George J. Annas
Book Chapter Setting Disaster Research Priorities
Pages 143-157
Virginia Murray, Anthony Kessel
Book Chapter Studying Vulnerable Populations in the Context of Enhanced Vulnerability
Pages 159-173
Ruth Macklin
Book Chapter Research Ethics Governance in Disaster Situations
Pages 175-190
Doris Schopper
Book Chapter Ethical Concerns in Disaster Research—A South African Perspective
Pages 191-204
Keymanthri Moodley

[Summary]

We have used these milestone articles, wider readings (see Project Bibliography as Annex A), and extensive interactions with humanitarian response practitioners, academics, ethicists, NGO leaders, government and agency heads, and other informants to ground our development of the ethical framework below.

4.0 Scoping Observations

Framework as Tool, Structure, Process

The TOR for this project specifies that an "ethical framework" be developed, with the stated intent that this work "…*will provide the required tools to ensure rigorous and appropriate ethical approval for new research that will be funded through the R2HC programme."* [TOR, p.1]

Therefore, we took as our departure point that the commissioned ethical framework should function *as a tool*, and that both structure and process would be important dimensions of such a tool.

The preceding literature review does identify important and useful discussions of ethical issues involved in health research in humanitarian crises, and references the set of codes and relevant statutes that underpin current ethical norms. But overall, these papers present *inventories* of ethical principles arranged in different formulations. In our view, they do not present – with the exception of the temporal structure of the new MSF framework – examples of systematic *processes* or *structures* which could be used as effective tools by the research community, research ethics boards (REBs/IRBs) or other organizations of interest for effective engagement of research protocols for humanitarian contexts.

Equally, our engagement of the humanitarian, health and development communities through our interviews, meetings and correspondence corroborated the above: the foundation set of ethical norms is largely "accepted" as a corpus to guide action, but without systematic processes or structures to inform their efficient or effective use.

Expert Interviews and Interactions: Insights and Perspectives

The R2HC Ethical Framework project has included over 60 direct interviews, small meetings and conference calls, complemented by hundreds of emails involving a range of informants from various contexts including UN agencies, NGOs, international organizations, academia, industry, and government. Many of these exchanges have continued as we refined the proposed ethical framework and requested additional feedback. An inventory of informants is provided as Annex B.

Through these interactions, we confirmed that there is broad recognition that ethical parameters should and do guide "formal" research and general understanding of the importance of independent ethical review and the role played by REBs/IRBs.

Equally, we encountered a reasonably consistent view that "research" is defined to be that work undertaken to establish generalizable knowledge and similar ideas around "intent" as establishing the threshold for research. This proceeds from practice as well as various statutory foundations.

So in many cases, informants assigned their "assessment" work – even when it involved vulnerable populations – to a category "below" research based on their assertions about *intent*. Typically, such work was described as "normal program evaluation" or "standard follow-up" and therefore "exempt" from ethical review.

Equally, a number of organizations noted that where such assessment activity might involve ethical issues that suggested independent review, the expectation was that such matters would be addressed by the academic partner or contractor they may have retained to conduct the work through their institutional review bodies, and/or through their management of such processes with relevant national and local REBs.

Based on our work, we believe that the classification of much assessment work as "normal" and "routine" in the NGO and humanitarian response community is likely resulting in REBs/IRBs granting

"exempt" status for ethical review when they are presented with such protocols. See further discussion below on REB/IRB processes.

Even when organizations have ethical codes and policies in place – some specifying appropriate independent ethical reviews for research conducted under its purview – we encountered unexpected candor in our discussions about how such requirements can be and often are "gamed" (or even ignored) to avoid the process and time delays involved.

The authors view these findings as perhaps understandable but troubling. We assert that any work – however termed – which involves interaction with vulnerable individuals or populations should be considered for ethical review, and most such work should involve some form of independent ethical review. We are not moved by arguments about the intent to generalize knowledge or other classification approaches which allows such interventions to be, a priori, exempt from ethical review.

Through the project term, we have continued to refine the graphic below to depict the range of "research" that might qualify in the R2HC programme context. It intends to depict a broad range of research "modes" (formats/strategies/conventions). While the scale of effort (and cost) may vary considerably ("Y" axis), and the impact of such research on the health intervention underway and the formality of ethical review indicated may vary ("X" axis), we argue that in humanitarian crises and emergency contexts, no research mode is justifiably "exempt" from appropriate ethical review.
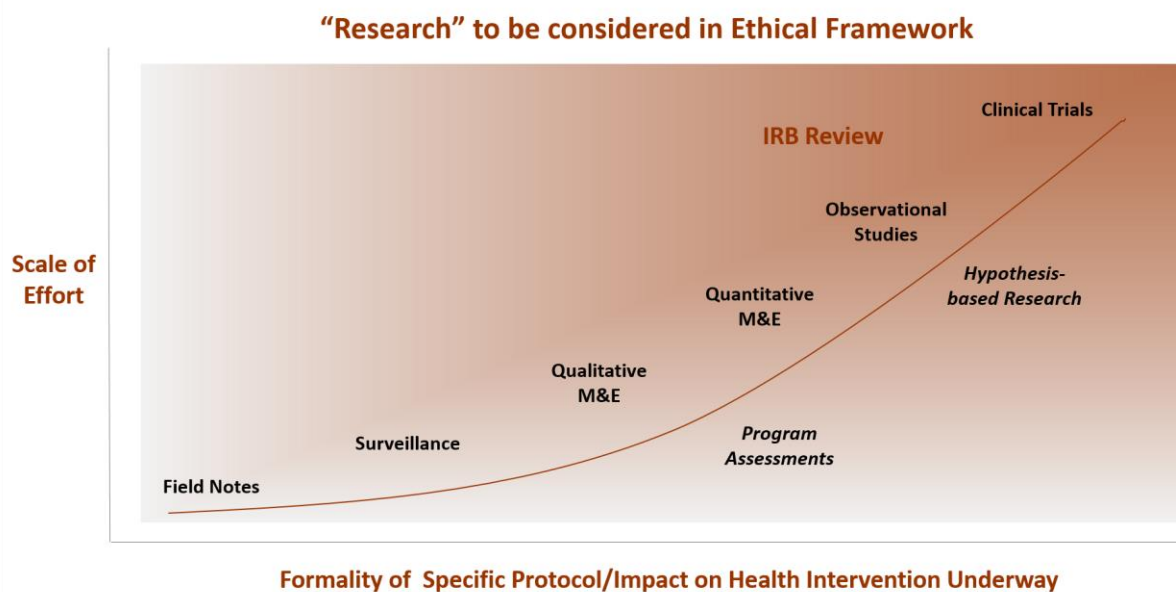
Current Process Standards for REBs/IRBs
While the earlier referenced *Standards and Operational Guidance for Ethics Review of Health-Related Research with Human Participants.* (WHO, 2011) does specify documentation of processes used by REBs/IRBs in their work, we recognize that there is no accepted procedural standard under which ethical review bodies use specific ethical frameworks to conduct their deliberations.

This guidance presents "…10 standards that are applicable to the ethics review of health related research with human participants. This document is intended to provide guidance on the research ethics review process, not to take a substantive position on how particular ethical dilemmas in health-related research should be resolved…"

Indeed, the term "framework" appears only once in this core document in reference to an "adequate legal framework" in Standard 1:

> Standard 1: Responsibility for establishing the research ethics review system Relevant authorities ensure that ethics review of health-related research is supported by an adequate legal framework that is consistent with the standards set forth in this document…[p.4]

Standard 9 and Annex 3 do refer to written policies which include "review procedures" but do not discuss any normative dimension for such procedures or make reference to specific "ethical frameworks" which might be considered beyond the general set of codes summarized in the document:

> Standard 9: Written policies and procedures
> Written policies and procedures specify the REC's membership, committee governance, review procedures, decision-making, communications, follow-up, monitoring, documentation and archiving, training, quality assurance, and procedures for coordination with other RECs.
>
> > 4. Submissions, documents required for review, review procedures, and decision-making [p.21]
> > The REC's policies and procedures describe the requirements for submitting an application for review, including the forms to be completed and the documents to be submitted. They also specify the process and procedure for review, process for coordinating review with other committees, process for setting up meetings, circulating documentation for the meetings, inviting non-members of the REC, approving the meeting minutes, and any related process issues. Procedures for deliberation and decision-making are clearly established and described. Specific quorum requirements for reviewing and making decisions or taking actions are clearly established in the standard operating procedures.
>
> Annex 3
> Guidance for developing written procedures for the research ethics committee
> REC written procedures address the following issues:
>
> > c) Review procedures [p.33]
> > The REC's written procedures specify the process by which the REC will decide which projects should be reviewed by the full convened committee and which projects may be reviewed through an expedited procedure. The written procedures address who will have the responsibility of making this determination, as well as the number of reviewers required for expedited review and how those reviewers will be selected. The Chair regularly notifies the REC members of expedited reviews that have been conducted between convened REC meetings. The REC's written procedures state the procedures for coordinating with and/or relying on the reviews and decisions of other domestic RECs or RECs in other countries.

Despite these standards requiring *documentation* of processes, our work did not identify evidence (or sources of evidence) that aggregated examples of such documented processes or which suggested any best practices. We did not learn – from the literature review or expert interviews across the field – that there is any adherence by REBs/IRBs to *specific* review processes or decision-making structures in general, or that any "ethical frameworks" which specifically address health research in humanitarian crises are in use.

Indeed, one important implication of the evidence review work just concluded for ELRHA by Karl Blanchet and Bayard Roberts referenced earlier is that the modest volume of health research conducted in these settings underscores that the REB/IRB community has had little collective experience in reviewing and monitoring such protocols.

We also explored the state of efforts to inventory national and local ethics review bodies and associated regulatory bodies to determine what evidence there might be of transparent reporting on review processes and decision procedures, specifically regarding research proposed for humanitarian contexts.

We note here three inventory efforts for reference, but they are either still in a formative or restorative state, and did not offer a level of completeness or transparency that could ground any conclusions:

- Health Research Web effort
  http://www.healthresearchweb.org/en/regulation_and_ethics_review_of_research.
- UNESCO Global Ethics Observatory (GEObs)
  http://www.unesco.org/new/en/social-and-human-sciences/themes/global-ethics-observatory/access-geobs/
- The Harvard Global Research Ethics Map which is being refreshed after a hiatus of effort
  https://webapps.sph.harvard.edu/live/gremap/index_main.cfm?CFID=10146416&CFTOKEN=58788028

Formation of Framework Process/Structure/Clusters

As the context above became clearer during our work, we used our continuing series of expert interviews and meetings to informally explore whether and how the ethical principles embodied in the various codes and regulations, and issues engaged in the literature, might be organized, clustered, or ordered. The end point would be an ethical framework that would function *as a process,* reflective of the specific considerations of research in humanitarian contexts.

We fashioned and refined a working set of "clusters" which grouped the relevant ethical principles and "ordered" them in a process. We presented these clusters, the proposed order of consideration, and also developed a graphical structure to present the trial framework as a tool in a number of the interviews and group meetings conducted we conducted.

<div style="border:1px solid maroon; padding:1em;">

R2HC Ethical Framework – Parameter Clusters

A. **- Scientific Requirement to Conduct Protocol in Emergency Setting**
   - Clear Articulation of Benefits/Risks/Harms

B. **- Protocol Design: Scientific Validity/Feasibility**
   - Research Focus: Relative Priority

C. **- Team Strength: Competence/Collaborative Structure/**
   - Declared Interests

D. **- Quality of Community Engagement**
   - Respect for Cultural Context/Norms/Values

E. **- Community and Individual Benefit**
   - Confidentiality/Data Security

F. **- Informed Consent**

</div>

What resulted was an iterative process, refining these clusters and their ordering. The summary above also reflects our intent that this ethical framework strike an appropriate balance between *enabling* needed research to build the evidence base to inform practice, and an overarching ethical imperative to *assure very robust protections and safeguards* for individuals and groups in humanitarian crises and emergency contexts.

We recognize that such protections are needed to address the special vulnerabilities of these populations, including the extraordinary power imbalance between those *providing* protection, health interventions, sustenance and support, and those *in need and receiving it* in these contexts.

We elected to avoid establishing "bright lines" which researchers "must not cross" (or, conversely, specific thresholds they must achieve or surpass) as a test of whether their protocols should receive ethical approval.

Rationale for a Graphical Device to Present Framework

As the notion of ethics clusters emerged and a step-wise approach to considering them in reviewing a research protocols for implementation in a humanitarian crises evolved, the authors also began exploring how these ideas might best be presented to and easily engaged by the intended audiences.

We considered that the ethical framework should be "packaged" in a form that was also useful in educational settings, and that would ideally support public understanding of this area of research and the ethical parameters that guide it – especially the protection of and consideration for the vulnerable populations involved.

In short, we recognized that the framework should also have mnemonic utility, approachable by a range of audiences, and considered various graphic metaphors (forms and shapes) to provide "structure" for the ethical clusters and the proposed process order in order to aid and enhance understanding.

Our solution evolved to a graphic form which might suggest a "winnowing" of some theoretical group to protocols which might be under consideration for a given humanitarian crisis, or by a specific IRB/REB. The winnowing would occur through application of the ethical clusters and the "knock-out" of protocols at the various stages, yielding an ethically viable group of protocols.

This led to sketches of pyramidal forms to suggest that winnowing phenomenon and which might also accommodate the six steps or thresholds associated with the ethical clusters. In the end, we applied the ethical clusters to an inverted pyramidal form and began to use it to present our thinking as expert interviews and meetings continued.

Our experience has been that informants engage the ethical framework graphic and the ideas it organizes straightforwardly. Only a few informants in these settings questioned why a visual device was needed, but accepted the clustering and step-wise process. Beyond expert interviews and meetings, the authors have presented the ethical framework graphic in PowerPoint presentations to university undergraduate, graduate and medical student groups with positive response.

In addition, earlier drafts of this thinking in white paper form are in wide circulation in the humanitarian response community, and a draft is in use by those research teams invited to apply for the second review round for the initial cycle of the R2HC grant process.

In summary, the ethical framework tool utilizes an inverted pyramidal form to present "clusters" of ethical parameters in a visually coherent way to suggest an order of engagement. Each ethics cluster is labeled (A-F) to further establish the process steps. We have structured a set of study questions and guidance supporting the framework. These are discussed below and are intended to invite the research team to clearly articulate how their protocol addresses the ethical parameters of the framework, and support REBs/IRBs in their work of reviewing and monitoring research protocols which are implemented in these settings.

Integration of Ethical Clusters into Framework Graphic

We elected to integrate the draft ethical clusters to a graphical structure to support the presentation and utility of the ethical framework as a working tool. We recognize that alternate graphical devices might serve this purpose but have tested the solution below in a number of the project interviews and group meetings. The solution below has been refined based on feedback received to date.

R2HC Ethical Framework – Parameter Clusters

A
- Scientific Requirement to Conduct Protocol in Emergency Setting
- Articulation of Benefits/Risks/Harms

B
- Protocol Design: Scientific Validity/Feasibility
- Research Focus: Relative Priority
- Team Strength: Competence/Collaboration

C
- Independent Ethical Review & Oversight
- Strategies for Safeguards, Security, Exits

D
- Quality of Community Engagement
- Respect for Cultural Context/Norms/Values

E
- Community and Individual Benefit
- Confidentiality/Data Security

F
- Informed Consent

**R2HC Research Protocols –
Pool for Funding Consideration**

The limitation of this approach, at present, is that it is a *process hypothesis* – to be tested and refined by use and assessment, and not yet an evidence-based process in the ELRHA/R2HC sense. To address this, the authors have made recommendations to ELRHA regarding various opportunities to present the framework to relevant REBs/IRBs, support its deployment, and refine it further based on its use in ethical review processes.

5.0 R2HC Ethical Framework and Key Questions

We present below a discussion of the ethical framework by considering a set of relevant questions that researchers developing protocols, and those conducting ethical reviews of such protocols, might utilize. A fuller discussion of these questions is presented in the next section.

R2HC Ethical Framework – Parameter Clusters

A
- Scientific Requirement to Conduct Protocol in Emergency Setting
- Articulation of Benefits/Risks/Harms

B
- Protocol Design: Scientific Validity/Feasibility
- Research Focus: Relative Priority
- Team Strength: Competence/Collaboration

C
- Independent Ethical Review & Oversight
- Strategies for Safeguards, Security, Exits

D
- Quality of Community Engagement
- Respect for Cultural Context/Norms/Values

E
- Community and Individual Benefit
- Confidentiality/Data Security

F
- Informed Consent

*R2HC Research Protocols –
Pool for Funding Consideration*

Cluster A: Emergency Context Requirement/Benefits-Harms-Risks

:: Why must this research must be conducted in a humanitarian crisis or emergency context – in short, explain why the expected evidence and benefit cannot be gained from implementation of the protocol in more stable (non-emergency) settings?
:: What are the known and potential harms and risks to individuals and the subject population overall by involvement in the proposed research?
:: What are the relevant analyses of harm-benefit "ratios"?
:: What mitigating strategies and associated costs (planned and potential) have been defined and projected?

Cluster B: - Protocol Design: Scientific Validity/Feasibility; Research Focus: Relative Priority; Team Strength: Competence/Collaborative Structure; Declared Interests

:: What is the relative importance/priority that this protocol should enjoy in the larger context of evidence-building for humanitarian response?

:: Why are the institutions and individuals involved in the proposed team – including local (in-country) researchers and supporting staff – uniquely qualified to conduct this research? What are the weaknesses or "holes" in the team structure that might be strengthened before the research is implemented?

:: How are the declared interests of all investigators and institutions involved in the research relevant to its conduct? Do any these interests represent "conflicts" that might compromise the integrity of the research, the team or the evidence sought?

Cluster C: Independent Ethical Review/Oversight; Safeguards/Security/Exits

What ethical review processes and review entities (REBs/IRBs: institutional/internal, independent, contracted, local/in-country) will be involved in approving this protocol?

:: What are the known and anticipated strengths and weakness of these review bodies, including their capacity to provide initial, continuing and summary oversight of the protocol?

:: Are there any mitigating strategies around weaknesses and are there costs associated in addressing them?

:: What safeguards, security, exit strategies, and associated costs have been developed with regard to research subjects (both those involved in the intervention and those in "control" groups) and the research team itself over the proposed duration of the project?

Cluster D: Community Engagement; Cultural Context/Norms/Values

:: What community engagement strategies have been undertaken to date, and what engagement actions are planned?

:: How does the protocol address the unique cultural context(s), norms and values of the population(s) involved?

Cluster E: Community/Individual Benefit; Confidentiality/Data Security

:: How will the research directly benefit – with reasonable immediacy – the community and individuals involved? If it will not, who will benefit and when? By what process were benefits presented to and affirmed by the research subjects and their community?

:: How does the protocol address data confidentiality and security? What are the anticipated risks and mitigation strategies/costs?

Cluster F: Informed Consent

:: What informed consent strategies and processes are proposed for subjects of the research as well as the research staff involved?

:: Are these strategies credible, and is adequate documentation planned?

6.0 R2HC Ethical Framework: Discussion Supporting Framework Questions

We present below a discussion of the ethical framework questions to provide a fuller consideration of our thinking. These questions track the summary presented above.

Cluster A: Emergency Context Requirement/Benefits-Harms-Risks

:: Why must this research must be conducted in a humanitarian crisis or emergency context, and why the expected evidence and benefit cannot be gained from implementation of the protocol in more stable (non-emergency) settings?
:: What are the known and potential harms and risks to individuals and the subject population overall by involvement in the proposed research? :: What are the relevant analysis of harm-benefit "ratios"?
:: What mitigating strategies and associated costs (planned and potential) have been defined and projected?

Discussion

While it is clear that the evidence base informing humanitarian response needs to be strengthened, it is critically important that research undertaken to build that evidence base be conducted in appropriate settings – with no presumption that the appropriate research setting be a humanitarian crisis or emergency setting per se.

The authors assert that the special vulnerabilities of individuals and populations in humanitarian crises/complex emergencies must be respected, and that research interventions should proceed only if there is a clear justification as to why they must proceed in an emergency/crisis context.

Conversely, it must be clear that the research cannot be successfully conducted in a context *other* than a humanitarian crisis or emergency. Further, we believe that the evidence and benefits to be gained from conducting the research in such a setting must clearly outweigh the risks and potential harms to subjects of the research in any setting but particularly in crisis/emergency settings.

For example, the implementation of a clinical drug or vaccine trial in a refugee camp for reasons of convenience – subjects easy to find, no loss-to-follow-up, etc. – is clearly unacceptable because the same research could be done in situations where participants have much greater agency. On the other hand, studies of the impact of a new treatment for severe acute malnutrition may have to be conducted in humanitarian settings, because these are the only settings in which sufficient numbers of subjects can be identified.

Further, if a protocol specifies a specific context such as an ongoing crisis, a specific site, or geography, it should also address why this is a specific requirement to the research protocol's design and evidence benefits. Also, where a protocol does not include an intervention on the ground but does involve data/tissue samples, etc. already collected and controlled from emergency settings, it should clearly address why this data is of unique relevance to the research questions involved.

The authors assert that the evidence and benefits to be gained from conducting the research in a crisis/emergency setting must clearly outweigh the risks and potential harms to subjects of the research. We believe that protocols should include a full discussion of benefits and risks, along with any relevant analysis of harm-benefit "ratios", and a full discussion of mitigating strategies and associated costs (planned and potential).

Cluster B: - Protocol Design: Scientific Validity/Feasibility; Research Focus: Relative Priority; Team Strength: Competence/Collaborative Structure; Declared Interests

:: What is the relative importance/priority that this protocol should enjoy in the larger context of evidence-building for humanitarian response?

:: Why are the institutions and individuals involved in the proposed team – including local (in-country) researchers and supporting staff –uniquely qualified to conduct this research? What are the weaknesses or "holes" in the team structure that might be strengthened before the research is implemented?

:: How are the declared interests of all investigators and institutions involved in the research relevant to its conduct? Do any these interests represent "conflicts" that might compromise the integrity of the research, the team or the evidence sought?

Discussion

The R2HC programme's intent is to fund research that makes a substantive contribution to the evidence base informing humanitarian health practice. The authors assert that protocols should present a perspective on how the evidence and benefit expected to accrue from the proposed research moves the field forward and why it should enjoy priority for funding.

A concern for the vulnerable populations involved in such research argues that the research teams involved be of the highest competence and demonstrate collaborative strategies involving research institutions, practicing NGO organizations, and others. We believe the research team's unique strengths for doing the work, and doing it in humanitarian crisis/emergency settings, are a critical dimension for ethical, as well as technical review.

Equally, we believe that a frank discussion in the protocol of team weaknesses or "holes" in team structure and how they will be strengthened before the research is implemented is an important component.

Finally, we believe that careful and complete disclosure of interests by all principal researchers and staff associated with the protocol, as well the institutions, organizations and commercial entities they may have ties with, is critical. We are careful to urge researchers/teams and their institutions to recognize that "interests" in this sense are not limited to those the researchers may judge to be "conflicts of interest". The reviewing body should have a full capture of interests to identify where such conflicts may exist and what the implications of such conflicts might be.

Cluster C: Independent Ethical Review/Oversight; Safeguards/Security/Exits

:: What ethical review processes and review entities (REBs/IRBs: institutional/internal, independent, contracted, local/in-country) will be involved in approving this protocol?

:: What are the known and anticipated strengths and weakness of these review bodies, including their capacity to provide initial, continuing and summary oversight of the protocol?

:: Are there any mitigating strategies around weaknesses and are there costs associated in addressing them?

:: What safeguards, security, exit strategies, and associated costs have been developed with regard to research subjects (both those involved in the intervention and those in "control" groups) and the research team itself over the proposed duration of the project?

Discussion

We assert that independent peer review of research protocols is a key element for conducting ethically viable research overall, especially where that research may be conducted in humanitarian or emergency settings. Independent assessment of the research protocol's stated risks, harms and benefits are very important to this ethical peer review, and may not be deemed to be acceptable when the subjects are already being exposed to great risk.

Our frank concern here is preventing exploitation – intended or inadvertent – by parties on the ground where research activity may be active. In addition, humanitarian crises and emergencies may compromise the ability of subjects to give informed consent or of researchers to obtain it.

It is thus critically important that adequate review by REBs/IRBs/research ethics committees be conducted to help protect highly vulnerable subjects. This means:
(a) Engaging relevant IRBs/REBs in the sponsor's country which are familiar with research involving vulnerable subjects and, if possible, research in emergency, catastrophic or humanitarian crises situations,
(b) Ensuring that investigators and project personnel are all familiar with existing research ethics requirements governing vulnerable subjects,
(c) Ensuring that engagement has occurred with appropriate review bodies in the countries where the proposed research is to be conducted and that local subject interests are adequately reflected in the local review process,
(d) Provision has been made for ongoing oversight of the research by an IRB/REB and/or, when appropriate, a data safety and monitoring board, and
(e) Provisions have been made in the review process to insure the timely and full disclosure of all research findings to both the appropriate persons in the study locations and in publicly-accessible forums, publications and electronic environments.

During the course of any research project it is possible that participants may suffer harm from known, or newly encountered, side effects (adverse events) of a preventive or curative intervention such as a vaccine, a medicine or a medical procedure. The nature, risk and response to such adverse events/side effects should be explained in full to the potential participants regardless of what informed consent process is adopted and implemented.

Depending on the nature of the research, it is also possible that more serious adverse effects might occur. A monitoring system must be in place to record all such events and these must be reported to all those overseeing the research – including the relevant REBs/IRBs that gave approval for the project to proceed and that are monitoring the project, the R2HC Funding Committee and others as specified in the final grant.

In humanitarian settings, it should be assumed that all research participants have undergone and/or continue to suffer from substantial psychological stress and may require more frequent contact with members of the research team than in other settings.

For these reasons, we assert that all research protocols for these settings include discussion about the planned inter-personal contact between the research team and the population affected by the emergency/disaster – including all surveys and other relevant non-invasive research activities. The protocols should also include a full explanation of how monitoring for side effects and adverse reactions, both anticipated and non-anticipated, will be established, conducted and evaluated.

Protocols should also indicate under what circumstances project activities, including site monitoring, might be delayed or suspended. In addition, proposals should include a description of what recourse research participants in both intervention and control groups will have for adverse events, and for what duration, as well as for suspensions or withdrawal of the research project. Budgetary

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implications of establishing such a monitoring system and of providing treatment for real or perceived physical or mental harm should also be discussed.

Further to the discussion above, we assert that protocols should specifically address:
- what measures are proposed to protect both research subjects and researchers from physical harm or undue mental stress directly attributable to the research,
- what effective and timely recourse to assistance is planned for any harm, health-related or otherwise, which they perceive might occur (or does occur) to either group as a result of their participation in the research,
- what circumstances might arise that would lead to the suspension or termination of the proposed research at an earlier date than proposed, and,
- what impact on the anticipated evidence and/or benefits of the research would such an event or events have?

Cluster D: Community Engagement; Cultural Context/Norms/Values
:: What community engagement strategies have been undertaken to date, and what engagement actions are planned?
:: How does the protocol address the unique cultural context(s), norms and values of the population(s) involved?

Discussion
We see it as an imperative to involve the relevant communities where research is proposed to be conducted along a project full life course – as the protocol is conceived (where possible), refined, approved and implemented. Depending on the protocol and the specific context it proposes for the research, this engagement can take varied forms. We believe protocols should address how community engagement was approached/will be approached, what scenarios have been considered in terms of continuing community engagement, as well as how the research team is prepared to adapt to factors from continuing engagement over the protocol life-cycle.

Such engagement can be successful only if there is appreciation for, understanding of, and provision made in protocols for the cultural context(s), norms and valued of the research subjects and their communities. Protocols should discuss how these contextual factors informed the research design and its implementation, and how these factors will be evaluated and by whom during the project.

Cluster E: Community/Individual Benefit; Confidentiality/Data Security
:: How will the research directly benefit the community and individuals involved? By what process were those benefits presented and affirmed by the research subjects and their community?
:: How does the protocol address data confidentiality and security? What are the anticipated risks and mitigation strategies/costs?

Discussion
The authors assert that those who will participate in the research (and give their voluntary informed consent to do so) should benefit as directly, substantially and immediately as possible from that research.

Such benefit includes being informed of research results and other work products of the project, as well as sharing downstream benefits from the research. Downstream benefits may range from the invention of new medical procedures or intervention strategies, to intellectual property (IP), to new or improved commercial products or processes.

Protocols should discuss how the communities and individuals participated in defining appropriate benefits, and what processes were employed to gain approval of commitments made in this regard. If the proposed benefits of the research are not expected to immediately impact the research participants and their community, the protocol should discuss who is likely to benefit and when, and how these deferred benefits justify the research given the absence of immediate benefit for those directly involved. Further, the affirmation of deferred benefit by the subject populations is an important transaction to be addressed and documented.

In principle, strategies and safeguards around the collection, identification and use of data are of very high practical and ethical importance for human subjects research of any kind. But humanitarian crises and complex emergencies – especially where they may involve conflict or post-conflict dynamics – often compound these risks to critical levels.

Protocols should address the strategies that will be employed to assure data confidentiality and security from a process, technology and researcher perspective. They should outline the specific risks, mitigation strategies and associated costs, and what training will be employed for staff involved. Finally, protocols should discuss how data will be properly anonymized and how it will be maintained and protected along the entire collection/aggregation/transfer/storage/utilization chain.

Cluster F: Informed Consent
:: What informed consent strategies and processes are proposed for subjects of the research as well as the research staff involved?
:: Are these strategies credible, and is adequate documentation planned?

Discussion
Voluntary informed consent is the anchor ethical imperative associated with any research involving human subjects. This imperative can be met insofar as:
- culturally appropriate and effective strategies are employed,
- conclusive informed consent transactions are achieved and documented before research begins, and
- it is re-engaged as often as the research context – and its associated risks, harms and benefits – changes sufficiently to warrant additional action.

The authors recognize that achieving credible informed consent as above is likely to be difficult, and perhaps not even realistic, in some crisis and emergency contexts. This is, in part, why informed consent considerations come as a final stage in this ethical framework, building on earlier review steps.

Protocols should discuss the thresholds above, and address any special challenges to this informed consent standard that are inherent in the research design, the context where it will be implemented, or other relevant factors. Equally, the protocol should provide a full discussion of the strategies and processes they will employ, and the quality of informed consent transaction they believe can be achieved.

Further, protocols that are implemented in humanitarian crises/emergency contexts will likely require research staff to be on the ground. Those research staff persons may face security, health and other risks and should be addressed as part of a voluntary informed consent process covering all staff involved. Any variance from this standard should be described in full.

7.0 Summary

An ethical framework is proposed to both guide development of research designs and protocols intended for implementation in humanitarian and emergency contexts to help assure their ethical viability, and to support ethical review of such protocols by independent ethical reviews bodies (REBs, IRBs), funders, and other organizations of interest. The framework intends to be used as a practical tool for these purposes. The authors appreciate that use of the framework against actual protocols submitted under the R2HC programme will be a key strategy to help refine and strengthen it and to assure it broad utility. We anticipate that such refinement will occur as the R2HC programme unfolds over the next 18 months.

ANNEX A

R2HC Ethical Framework Project

Project Bibliography
Derived from search strategies as presented plus recommendations from
informants and continuing investigation

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R2HC Evidence Review Team - Dr Karl Blanchett and Dr Bayard Roberts, London School of Hygiene and Tropical Medicine. Available: http://www.elrha.org/uploads/LSHTM%20Evidence%20Review%205%20June.pdf

ANNEX B

Name	Title	Organisation
R2HC Funding Committee		
Alastair Ager	Program on Forced Migration and Health	Columbia University
Gilbert Burnham	Co-Director, Center for Refugee and Disaster Response	Johns Hopkins University
Rebecca Grais	Director	Epicentre
Paul Spiegel	Deputy Director, Division of Programme Support and Management	UNHCR
Michelle Gayer	Coordinator, Surge and Crisis Support, ERM	WHO
Robin Nandy	Chief, Child Survival & Development Cluster	UNICEF
Francesco Checchi	Senior Humanitarian Health Advisor	Save the Children
Myriam Henkens	International Medical Coordinator	MSF
Name	Title	Organisation
Susan Davis	CEO	BRAC-USA
Elizabeth Ferris	Co-Director, Brookings-LSE Project on Internal Displacement, Senior Fel	Brookings Institute
Mike Toole	Deputy Director (International Program Strategy	Burnet Institute
Jerome Amir Singh	Research in South Africa (CAPRISA), Durban, South Africa.	CAPRISA
Jeanette J Rainey	Global Immunization Division,	CDC
Phil Nieburg	HIV/AIDS Task Force	Center for Strategic and International Studies
Stacey White	Senior Advisor, Policies and Programs	DARA
Bryan Schaaf	Policy Analyst, Bureau of Population, Refugees and Migration	Department of State, BPRM
Jorge Castilla-Echenique	Health Sector Global Advisor	ECHO-European Comission for Humanitarian Aid
Carol Molenski	CEO, USA	ECPAT
Ruth Macklin	Professor, Department of Epidemiology & Population Health Dr. Shoshanah Trachtenberg Frackman Faculty Scholar in Biomedical	Albert Einstein College of Medicine
Margie Ferris-Morris (hard C	Food Security, Nutrition Health Monitoring and Evaluation	FMA, Inc.
Rebecca Katz	Professor of Health Policy and Emergency Medicine	George Washington University
Jim Tielsch	Chair of the Department on Global Health	George Washington University
Susan Forbes Martin	Director of Refugee Program	Georgetown University
Melissa Goldstein	Ethics	GWU
Jennifer Leaning	Professor for the Practice of Health and Human Rights	Harvard University
Riennzi Kern	Director, M&E	Heifer
Francis Stevenson	Director, M&E	HelpAge
Ruth Faden	Ethics	Hopkins
Nancy Kass	Ethics	Hopkins
Jeremy Sugermann	Ethics	Hopkins
Nan Buzard	Executive Director	International Council of Voluntary Agencies
Dr. Emmanuel d'Harcourt	Senior Health Director	International Rescue Committee
Joost Martins	Senior Health Director	IRCT
Lisa Schwartz	Associate Professor, Department of Clinical Epidemiology & Biostatisti	MacMaster University
Matthew Hunt	Humanitarian health	McGill University
Edward J Mills	Associate Professor and Canada Research Chair, Faculty of Health	McMaster University
Rony Zachariah	Operational Research Director	MSF
Nathan Ford		MSF
Rony Brauman	Research Director	MSF Crash Foundation
Nathan Ford	Infectious Disease Epidemiology and Research	MSF/University of Cape Town
Allen S Keller, M.D.	[Bellevue/NYU Program for Survivors of Torture (PSO	NYU
Sarah Haacke	Director of Ops, PSOT	NYU
Beth Charpentier	Program Officer, Forced Migration and Health	Columbia University, Mailman
David Townes	Public Health Advisor	OFDA/USAID
Erin Steiber	VP, Programs	OP Smile
David Kaslow	VP Programs/Technology	PATH
Steven Hansch,	Chairman of the Finance & Operations Committee	Relief International
Ben Ciglasi	Director, M&E	Tostan
Angus Dawson	History (MESH)	University of Birmingham
Doris Schopper	Medical Faculty, Education and Research in Humanitarian Medicine	University of Geneva
Ross Upshur	Lana School of Public Health Joint Centre for Bioethics	University of Toronto
John Pringle	PHD Candidate	University of Toronto
John Pringle	Epidemiologist	University of Toronto/MSF
Stephen Martin	OCV Stockpile	WHO
BRENNAN, Richard John		WHO
VAN OMMEREN, Mark Humphrey		WHO
THOMAS, Lisa Jane		WHO
REIS, Andreas Alois		WHO
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David Forster JD, MA, CIP	Chief Compliance Officer	WIRB-Copernicus Group
Stuart Horowitz	COO	WIRB-Copernicus Group
Iulianna Lindsey, VP of Prog	VP of Programs	Women for Women Int

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ANNEX C
SEARCH STRATEGY SUMMARIES

Literature Review: Search Strategies/Overview

We employed various strategies to pull as broad a cross-section of literature as might be relevant to the ethical framework for Health interventions I humanitarian crises. Specific strategies employed are summarized on the following pages.

Where a search strategy identified viable papers, we examined each to determine what contribution they might make to our overall thinking, and whether they might be appropriate to include in the "milestone" review of key literature presented in the project paper [posted here: http://hiltonlaureatesarchive.wordpress.com/joint-projects/r2hc-project/ [password: r2hcethicalframework].

Through the project like cycle we have continued to aggregate literature that was relevant into a bibliography posted on a public page here: http://hiltonlaureatesarchive.wordpress.com/joint-projects/r2hc-ethics-framework-project-work-products-public-access/

Reflecting the overall findings of the evidence review underway by the LSHTM-Harvard-ODI team (June presentations) we anticipated that insofar as the literature on health interventions research was very limited in volume and evidence quality, we would see a very modest literature base discussing the *ethics* of conducting this research.

Our literature research confirmed this expectation.

Further, we came to realize that peer-reviewed papers that do address ethical issues surrounding such research in humanitarian contexts almost exclusively present *inventories* of ethical principles arranged in different formulations, rather than *frameworks* which describe a review *process* or have a usable structure.

This result meant we did not have a set of alternative active frameworks which we could compare for utility, efficiency or effectiveness. Even the MSF ethical framework – intended to address a wide array of research protocols arising from MSF field operations – was more a set of thematic areas than a defined process.

As discussed in the earlier white project paper, our team developed – iteratively – trial clusters of ethical principles, ordered to define a process and tested the framework as expert informant interviews and interactions unfolded during the latter stages of the project.

Annex 1: Details for systematic review on publications that cite three key articles, identified by Mr. David Curry and Dr. Arthur Caplan, as relevant to this project. This preliminary search was conducted to find preexisting publications that address topics relevant to this project.

Sources:
Published literature: ISI Web of Science/Web of Knowledge [v.5.12] (using the "Cited Reference Search" function to capture results)

(1) Title: Ethics of conducting research in conflict settings.
Authors: Ford, Nathan; Mills, Edward J; Zachariah, Rony; et al.

Search terms used: "Ethics of conducting research in conflict settings" (cited title)
Sources: Web of Knowledge, Medline, Science Citation Index Expanded (Sci-Expanded), Social Science Citation Index (SSCI), Arts and Humanities Citation Index (A&HCI)
Languages searched: All
Document types searched: All

Screening Process:

Results: 11 total results
7 peer-reviewed articles
3 review articles
1 letter

Stage 1: Peer reviewed literature: electronic database search (N=7)

Stage 2a: Peer reviewed literature: title/abstract review (N=7)

5 excluded (non topic)

Stage 3: peer reviewed literature (N=2)
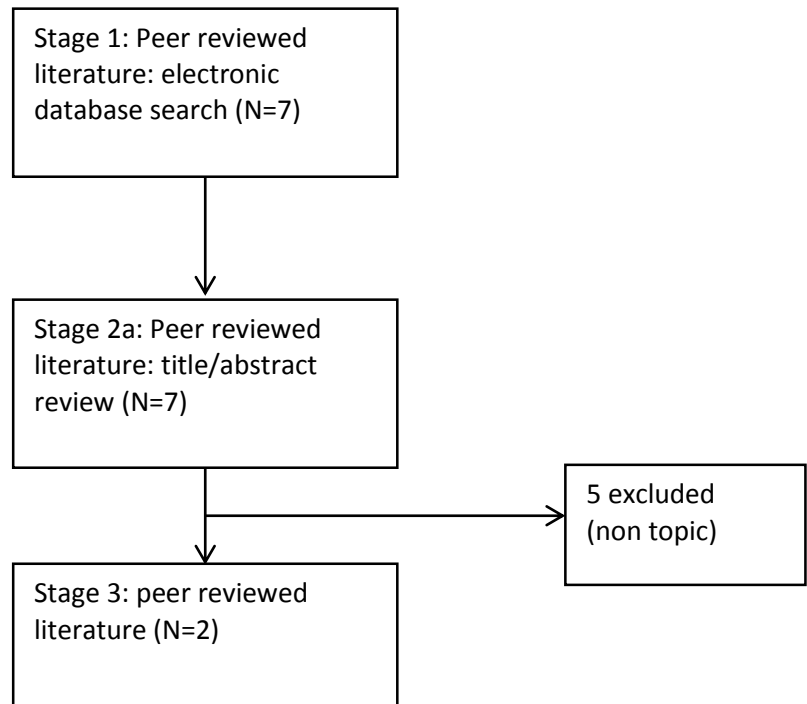
Results
1. Sheather J, Shah T (2011) Ethical dilemmas in medical humanitarian practice: cases for reflection from medicins sans frontiers. Journal of Medical Ethics

2. Tansey C, Jerridge M, Heslegrave R, et. al. (2010) A framework for research ethics review during public emergencies. Canadian medical association journal

(2) Title: Ethics of Research in Refugee Populations
Authors: Leaning, Jennifer

Search terms used: "Ethics of Research in Refugee Populations" (cited title)
Sources: Web of Knowledge, Medline, Science Citation Index Expanded (Sci-Expanded), Social Science Citation Index (SSCI), Arts and Humanities Citation Index (A&HCI)
Languages searched: All
Document types searched: All

Screening process:

Results: 39 total results
28 peer-reviewed articles
4 review articles
3 editorial material
2 letters
2 proceedings papers

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┌─────────────────────────┐
│ Stage 1: Peer reviewed  │
│ literature: electronic  │─────────────────────┐
│ database search (N=28)  │                     ▼
│                         │              ┌──────────────┐
└─────────────────────────┘              │ 1 duplicate  │
             │                           └──────────────┘
             ▼
┌─────────────────────────┐
│ Stage 2a: Peer reviewed │
│ literature: title/abstract │──────────────────┐
│ review (N=27)           │                     ▼
│                         │              ┌──────────────┐
└─────────────────────────┘              │ 25 excluded  │
             │                           │ (non topic)  │
             ▼                           └──────────────┘
┌─────────────────────────┐
│ Stage 3: peer reviewed  │
│ literature (N=2)        │
│                         │
└─────────────────────────┘
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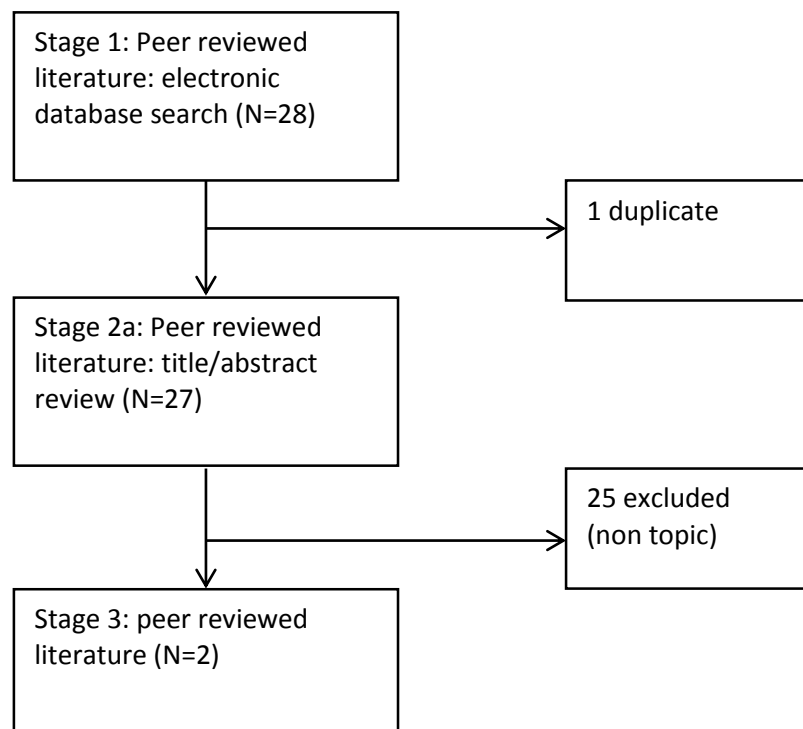
Results
1. Chung B, Jones L, Larry X (2008)   National recommendations for enhancing the conduct of ethical health research.
   Ethnicity and Disease
2. Mackenzie C, McDowell C, PIttaway E (2007) 'Do no harm': the challenge of constructing ethical relationships in refugee research.
   Journal of Refugee Studies

(3) Title: Research Ethics Review in Humanitarian Contexts: The Experience of the Independent Ethics Review Board of Medecins Sans Frontieres
Authors: Schopper, Doris; Upshur, Ross; Matthys, Francine; et al

Search terms used: "Research Ethics Review in Humanitarian Contexts: The Experience of the Independent Ethics Review Board of Medecins Sans Frontieres" (cited title)
Sources: Web of Knowledge, Medline, Science Citation Index Expanded (Sci-Expanded), Social Science Citation Index (SSCI), Arts and Humanities Citation Index (A&HCI)
Languages searched: All
Document types searched: All
Screening process:

Results: 10 total results
7 peer-reviewed articles
2 review articles
1 editorial material

Stage 1: Peer reviewed literature: electronic database search (N=7)

2 duplicates

Stage 2a: Peer reviewed literature: title/abstract review (N=5)

5 excluded (non topic)

Stage 3: peer reviewed literature (N=0)
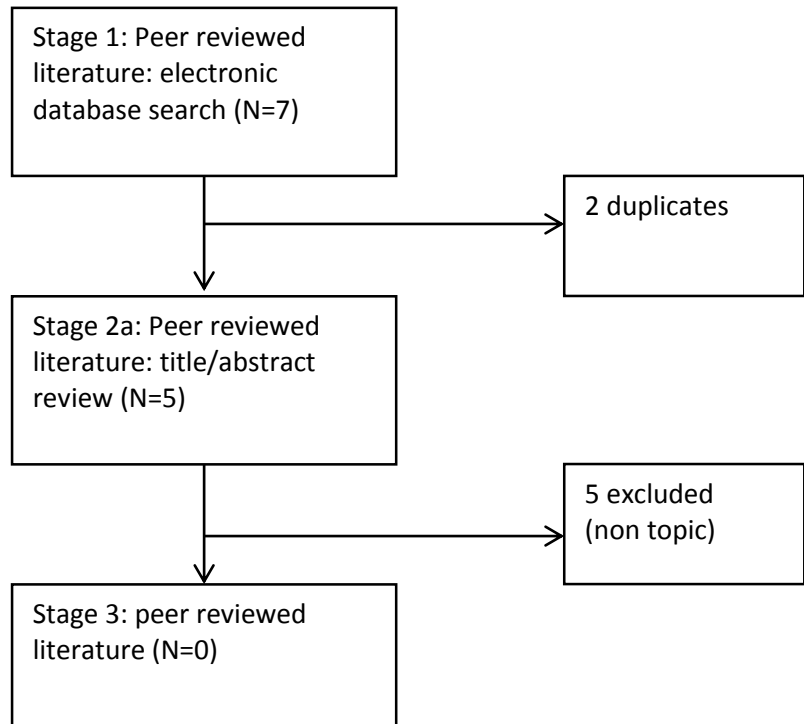
Annex 2: Literature searches
Sources:
Published literature: PubMed, Ovid
Search terms used: "ethical framework" and "humanitarian"
Sources: PubMed, Ovid
Languages searched: All
Document types searched: All
Years Searched: 2003-2013

Screening process:

Results: 8 total results

Stage 1: Peer reviewed literature: electronic database search (N=8)

Stage 2a: Peer reviewed literature: title/abstract review (N=8)

8 excluded (non topic)

Stage 3: peer reviewed literature (N=0)

Sources:
Published literature: PubMed, Ovid

Search terms used: "ethics" and "humanitarian"
Sources: PubMed, Ovid
Languages searched: All
Document types searched: All
Years Searched: 2003-2013

Screening process:

Results: 142 total results

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┌─────────────────────────┐
│ Stage 1: Peer reviewed  │
│ literature: electronic  │
│ database search (N=142) │
└─────────────────────────┘
             │                        ┌──────────────────────────┐
             │───────────────────────▶│ 44 excluded              │
             │                        │ (years searched modified │
             ▼                        │ to 2008-2013)            │
┌─────────────────────────┐          └──────────────────────────┘
│ Stage 2a: Peer reviewed │
│ literature: title/abstract│
│ review (N=98)           │
│                         │            ┌──────────────────────────┐
│                         │───────────▶│ 96 excluded              │
│                         │            │ (non topic or duplicate) │
│                         ▼            └──────────────────────────┘
┌─────────────────────────┐
│ Stage 3: peer reviewed  │
│ literature (N=2)        │
└─────────────────────────┘
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Results

1. Hunt M, Schwartz L, Sinding C, Elit L (2012) The ethics of engaged practice: a framework for health professionals in humanitarian assistance and development work. Developing World Bioethics
2. Lee I (2012)   The humanitarian responses and their ethical implications.   Asia Pacific Journal of Public Health

Sources:
Published literature: PubMed, Ovid

Search terms used: "ethics" and "humanitarian" and "health"
Sources: PubMed, Ovid
Languages searched: All
Document types searched: All
Years Searched: 2003-2013

Screening process:

Results: 91 total results

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┌─────────────────────────┐
│ Stage 1: Peer reviewed  │
│ literature: electronic  │
│ database search (N=91)  │
└─────────────────────────┘
            │              ┌──────────────────────────────┐
            │─────────────▶│ 42 excluded                  │
            │              │ (years searched modified to  │
            ▼              │ 2008-2013)                   │
┌─────────────────────────┐└──────────────────────────────┘
│ Stage 2a: Peer reviewed │
│ literature: title/abstract│
│ review (N=49)           │
└─────────────────────────┘
            │              ┌──────────────────────────────┐
            │─────────────▶│ 48 excluded                  │
            │              │ (non topic or duplicate)     │
            ▼              └──────────────────────────────┘
┌─────────────────────────┐
│ Stage 3: peer reviewed  │
│ literature (N=1)        │
└─────────────────────────┘
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Results

1. Hunt M, Schwartz L, Fraser V (2013) "How far do you go and where are the issues surrounding that?" Dilemmas at the boundaries of clinical competency in humanitarian health work. Developing World Bioethics

Sources:
Published literature: PubMed, Ovid
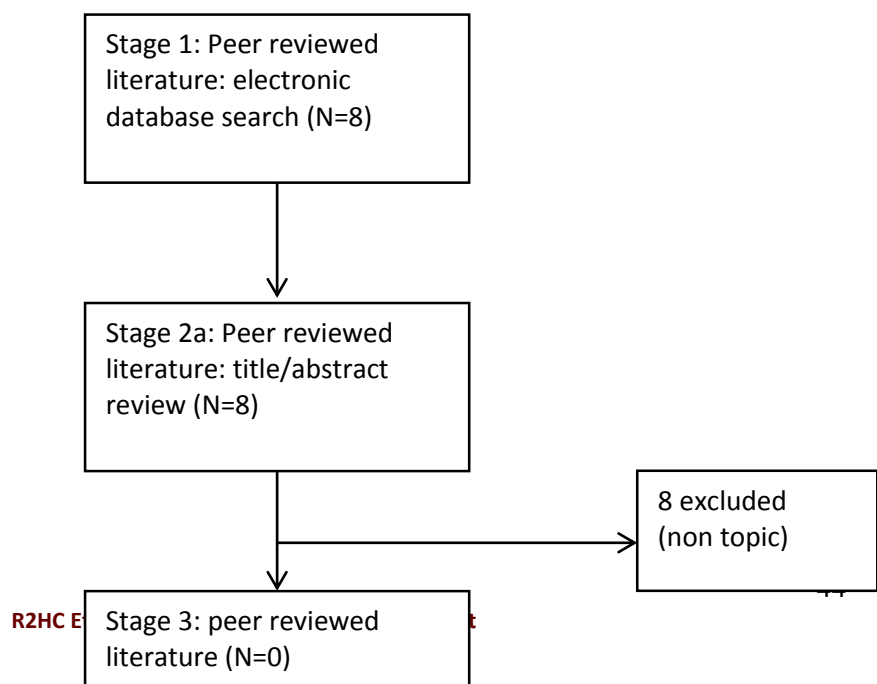
Search terms used: "ethics" and "framework" and "crisis"
Sources: PubMed, Ovid
Languages searched: All
Document types searched: All
Years Searched: 2003-2013

Screening process:

Results: 17 total results

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┌─────────────────────────┐
│ Stage 1: Peer reviewed  │
│ literature: electronic  │
│ database search (N=17)  │
└─────────────────────────┘
             │
             ▼
┌─────────────────────────┐
│ Stage 2a: Peer reviewed │
│ literature: title/abstract│
│ review (N=17)           │
└─────────────────────────┘
             │                    ┌──────────────────────┐
             │────────────────────▶│ 15 excluded          │
             ▼                    │ (non topic or duplicate)│
┌─────────────────────────┐       └──────────────────────┘
│ Stage 3: peer reviewed  │
│ literature (N=2)        │
└─────────────────────────┘
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Results
1. Barnett DJ, Taylor HA, Hodge JG, Links JM (2009) Resource Allocation on the frontlines of public health preparedness and response: report of a summit on legal and ethical issues. Public Health Reports
2. Thompson AK, Faith J, Gibson JL, Upshur RE (2006) Pandemic influenza preparedness: an ethical framework to guide decision-making. BMC Medical Ethics

Sources:
Published literature: PubMed, Ovid
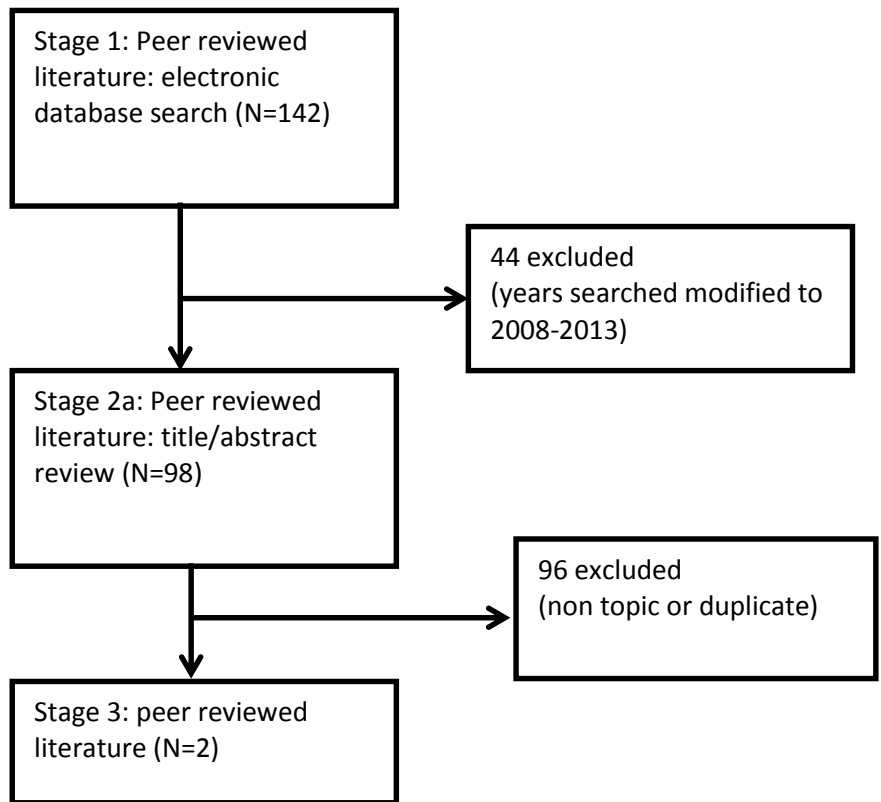
Search terms used: "informed consent" "humanitarian"
Sources: PubMed, Ovid
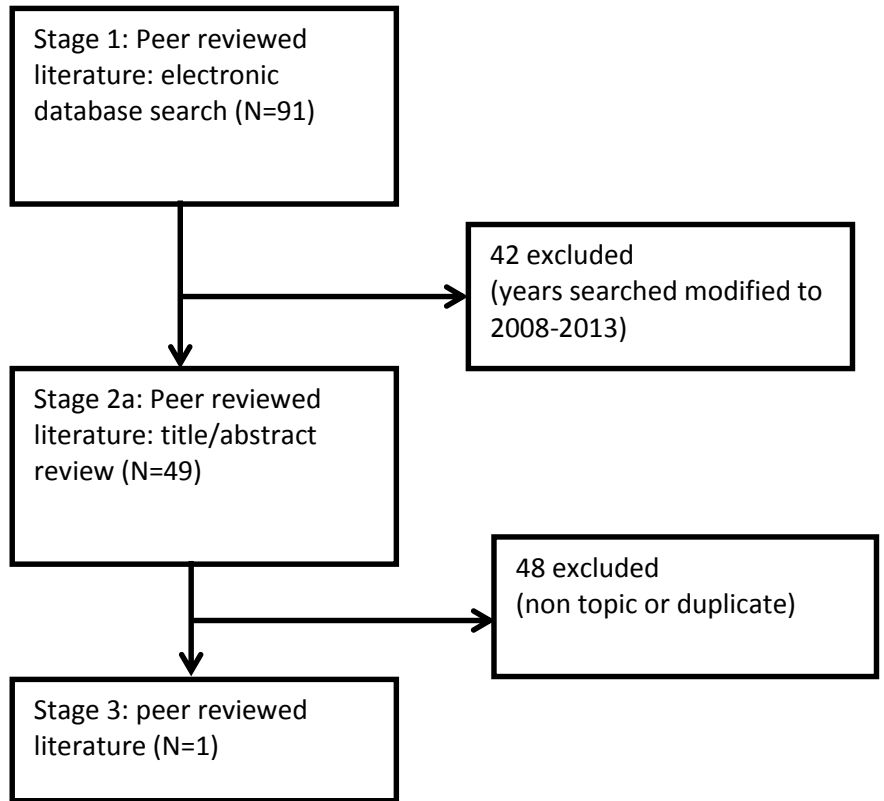Languages searched: All
Document types searched: All
Years Searched: 2003-2013

Screening process:

Results: 18 total results

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┌─────────────────────────┐
│ Stage 1: Peer reviewed  │
│ literature: electronic  │
│ database search (N=18)  │
└─────────────────────────┘
             │
             ▼
┌─────────────────────────┐
│ Stage 2a: Peer reviewed │            ┌─────────────────────────┐
│ literature: title/      │  ────────▶ │ 16 excluded             │
│ abstract review (N=18)  │            │ (non topic or duplicate)│
└─────────────────────────┘            └─────────────────────────┘
             │
             ▼
┌─────────────────────────┐
│ Stage 3: peer reviewed  │
│ literature (N=2)        │
└─────────────────────────┘
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Results

1. Holt GR (2012)   Ethical conduct of humanitarian medical missions: I. informed consent.
   JAMA Facial Plastic Surgery
2. Mfutso-Bengo J, Masiye F, Muula A (2008) Ethical challenges in conducting research in humanitarian crisis situations.
   Malawi Medical Journal.

Sources:
Published literature: PubMed, Ovid

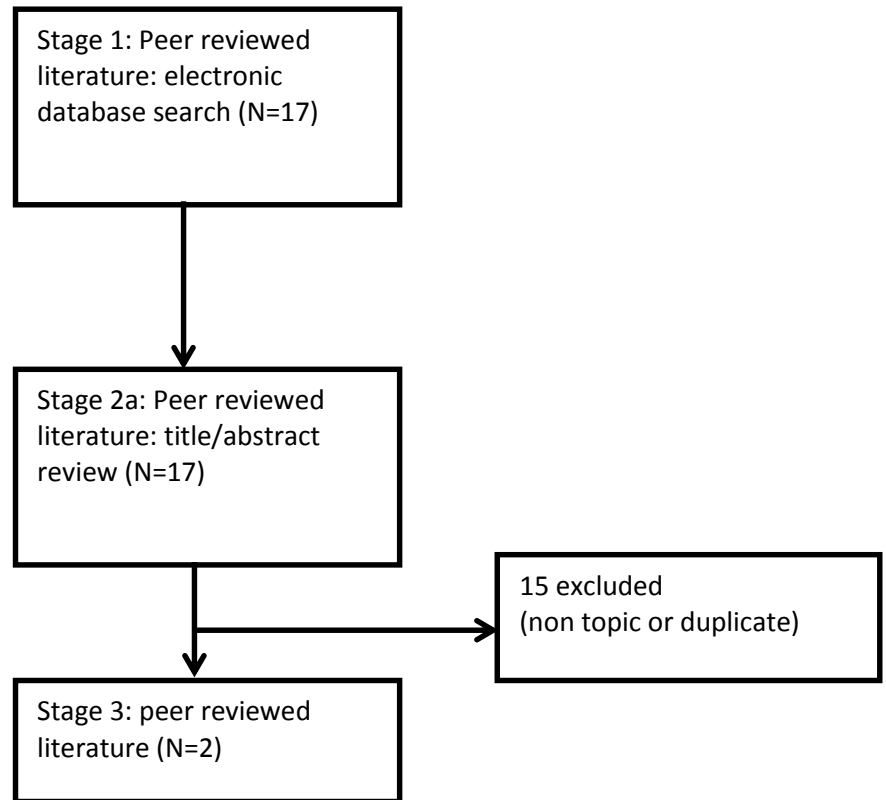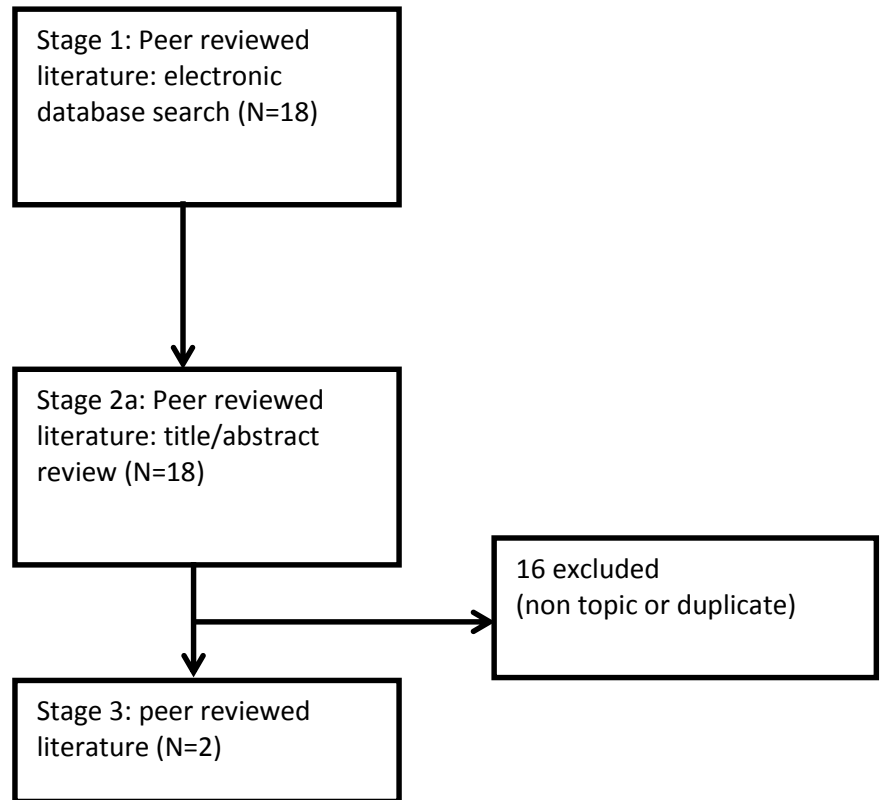Search terms used: "qualitative research" and" humanitarian"
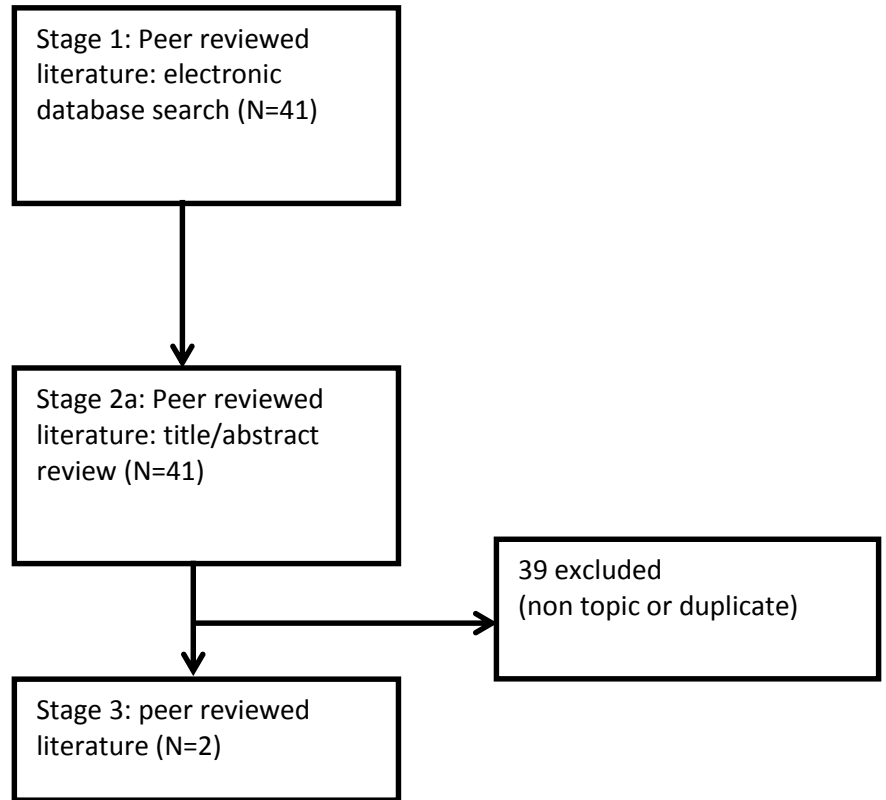Sources: PubMed, Ovid
Languages searched: All
Document types searched: All
Years Searched: 2008-2013

Screening process:

Results: 41 total results

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┌─────────────────────────┐
│ Stage 1: Peer reviewed  │
│ literature: electronic  │
│ database search (N=41)  │
└─────────────────────────┘
            │
            ▼
┌─────────────────────────┐              ┌─────────────────────────┐
│ Stage 2a: Peer reviewed │              │ 39 excluded             │
│ literature: title/abstract│───────────▶│ (non topic or duplicate)│
│ review (N=41)           │              └─────────────────────────┘
└─────────────────────────┘
            │
            ▼
┌─────────────────────────┐
│ Stage 3: peer reviewed  │
│ literature (N=2)        │
└─────────────────────────┘
```

Results

1. Hunt MR (2009) **Strengths and challenges in the use of interpretive description: reflections arising from a study of the moral experience of health professionals in humanitarian work.** Qualitative Health Research

2. **Familiar I, Sharma S, Ndayisaba H, Munyentwari N, Sibomana S, Bass JK (2013)** Community perceptions of mental distress in a post-conflict setting: A qualitative study in Burundi. Global Public Health

Sources:
Published literature: PubMed, Ovid

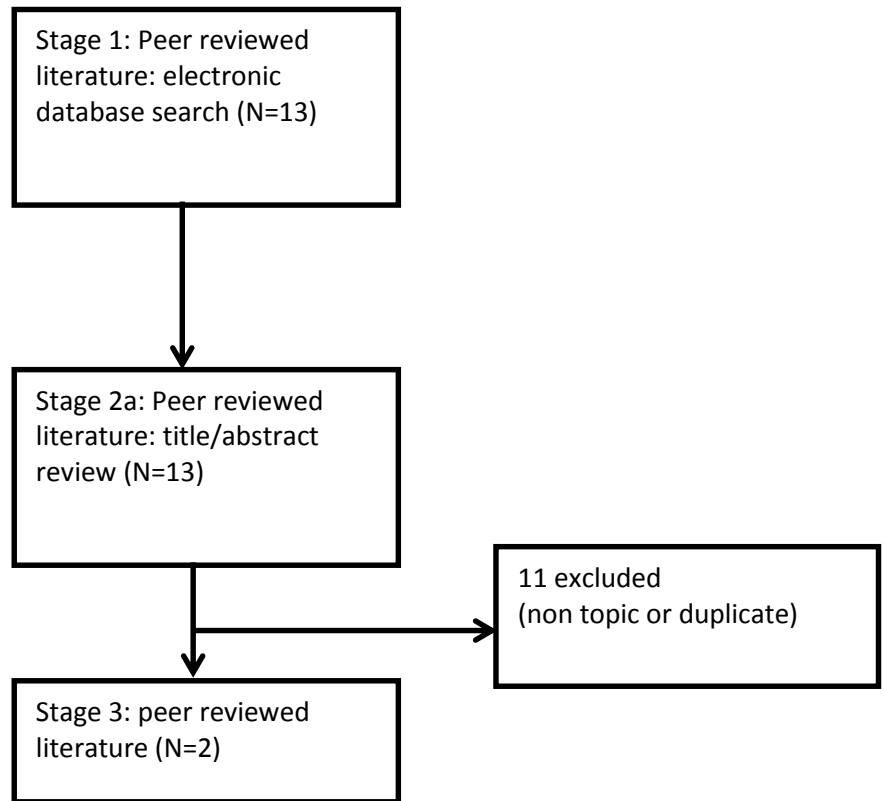Search terms used: "adverse events" and "humanitarian"
Sources: PubMed, Ovid
Languages searched: All
Document types searched: All
Years Searched: 2003-2013

Screening process:

Results: 13 total results

Stage 1: Peer reviewed literature: electronic database search (N=13)

↓

Stage 2a: Peer reviewed literature: title/abstract review (N=13)

→ 11 excluded (non topic or duplicate)

↓

Stage 3: peer reviewed literature (N=2)

Results
1. Alirol E, Schrumpf D, Heradi JA, Riedel A, de Patoul C, Quere M, Chappuis F (2013) **Nifurtimox-Eflornithine Combination Therapy for Second-Stage Gambiense Human African Trypanosomiasis: Médecins Sans Frontières Experience in the Democratic Republic of the Congo.** Clinical Infectious Disease
2. **Plurad D, Blaschke G, Pfeiffer J (2008)** A case of malignant hyperthermia in a child encountered during a humanitarian assistance mission to the Philippines. Military Medicine

<u>Sources</u>:
Published literature: PubMed, Ovid, Google Scholar

<u>Search terms used</u>: "humanitarian research" "therapeutic misconception"
<u>Sources</u>: PubMed, Ovid, Google scholar
<u>Languages searched</u>: All
<u>Document types searched</u>: All
<u>Years Searched</u>: all years
<u>Results</u>: 0

<u>Sources</u>:
Published literature: PubMed, Ovid

<u>Search terms used</u>: "humanitarian research" and "devices"
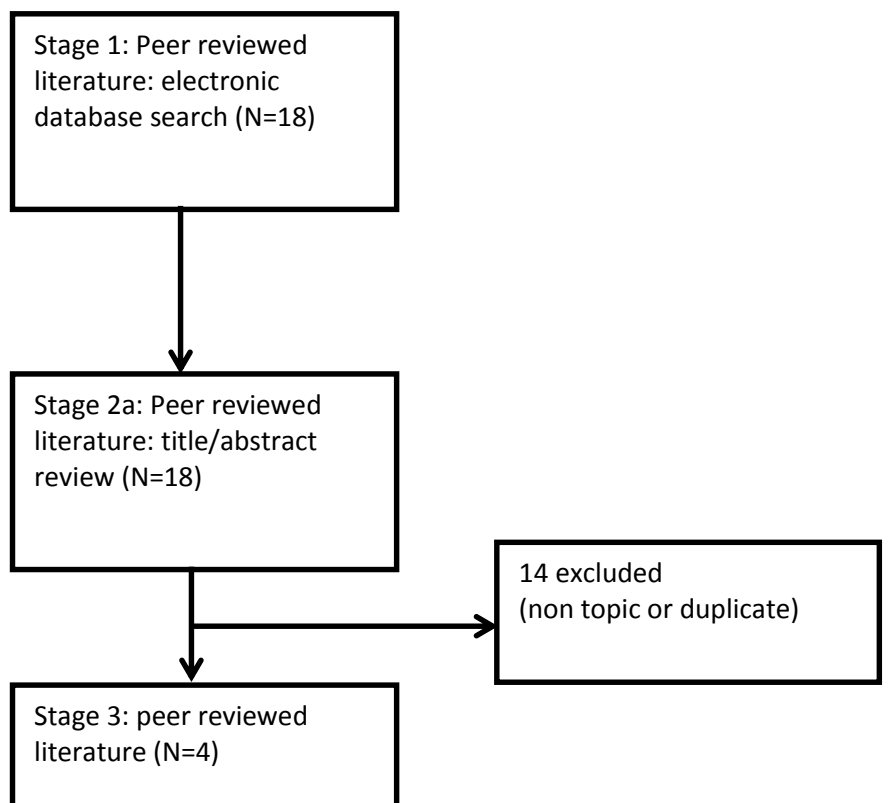<u>Sources</u>: PubMed, Ovid
<u>Languages searched</u>: All
<u>Document types searched</u>: All
<u>Years Searched</u>: 2008-2013

Screening process:

<u>Results</u>: 18 total results

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┌──────────────────────────┐
│ Stage 1: Peer reviewed   │
│ literature: electronic   │
│ database search (N=18)   │
└──────────────────────────┘
             │
             ▼
┌──────────────────────────┐
│ Stage 2a: Peer reviewed  │
│ literature: title/abstract│        ┌──────────────────────┐
│ review (N=18)            │──────▶  │ 14 excluded          │
└──────────────────────────┘        │ (non topic or duplicate)│
             │                       └──────────────────────┘
             ▼
┌──────────────────────────┐
│ Stage 3: peer reviewed   │
│ literature (N=4)         │
└──────────────────────────┘
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<u>Results</u>
1. Saunders J, Barrs D (2011) Cochlear implantation in developing countries as humanitarian service: physician attitudes and recommendations for best practice. Otolaryngology-Head and Neck Surgery
2. Fins JJ, Mayberg HS, Nuttin B, Kubu CS, Galert T, Sturm V, Stoppenbrink K, Merkel R, Schlaepfer TE (2011). A case of malignant hyperthermia in a child encountered during a humanitarian assistance mission to the Philippines. Health Affairs
3. Gordon EJ, Philpott S (2008) The convergence of research and clinical practice: institutional review board review of humanitarian use device applications. Journal of Empirical Research on Human Research Ethics.
4. Bernard DM (2009)   Humanitarian Use Device and Humanitarian Device Exemption regularly programs: pros and cons. Expert Review of Medical Devices.

Annex D

Osaka Declaration on Disaster Medicine

PREAMBLE
Gathered in Osaka, Japan, from 24 to 26 November 1988, as the Asian-Pacific Conference on Disaster Medicine, under the sponsorship of the Japanese Association for Acute Medicine and the Japan International Cooperation Agency, and having exchanged our views, knowledge and experiences in the health and medical sciences related to large-scale disaster management;

CONSIDERING
that the Asian-Pacific region is marked by frequent disasters, including earth quakes, volcanic eruptions, typhoons, cyclones, floods and simultaneously a great number of refugees;

NOTING
that the regions also has many countries where the socio-economic infrastructure has not fully developed, with the result that when a major disaster occurs, the stricken community and its authorities are not able to cope fully with medical and disaster relief measures, thus causing many victims;

CONVINCED
that to strengthen medical relief in order to minimize the amount of suffering and the number of victims, it is important to promote international cooperation both at ordinary times with preventative systems, and at actual disaster times with concerted relief actions;

WE REPRESENTATIVES
of twenty nations and major international relief organizations herewith make the following

DECLARATION
1. We shall continue our efforts to develop and fortify emergency medical systems for large scale disasters worldwide by recognizing the problems associated with such disasters and discovering effective countermeasures.
2. We shall make effort to improve in particular the Asian and Pacific countries' capability of disaster medicine by developing channels of information exchange among such countries of the region regarding disaster countermeasures.
3. We shall internationally promote studies related to disaster prevention in collaboration with specialists in non-medical fields and related sectors of science and technology, so that results can be properly reflected in the administrative policies and multidisciplinary measures of each country.
4. We shall deepen our understanding of the importance of regional and international cooperation at the time of disaster, in order to develop smooth cooperation mechanisms and to formulate study programs for disaster relief medicine.
5. In particular, we shall fully collaborate with the United Nations to make the International Decade for Natural Disaster Reduction more fruitful and meaningful.

6. With the development of the mass media, we propose that concerned countries and organizations recognize the need for and establish an international integrated centre for information exchange, research and training in disaster medicine, and take positive measures to establish such a regional centre as early as possible.

7. The Asian-Pacific Conference on Disaster Medicine was the first region-wide comprehensive attempt at opinion exchange by people involved in disaster prevention, emergency medicine and refugee health problems. We resolve to meet in Japan again so that this forum provides a continuing opportunity for the Asian and Pacific countries to further deepen their mutual understanding regarding the importance of international medical cooperation in total disaster management.

It is our earnest wish that this medical conference, in collaboration with other disciplines further stimulates interest in disaster prevention and response and that it contributes to developing the world's medical and other facilities against disaster.

Made on 26th November, 1988, in Osaka, Japan, at the Asian-Pacific Conference on Disaster Medicine

Annex E

MSF ERB Research Ethics Framework Template and Guidance Documents, v1 Nov 2013

[accessed 29 December 2013]
Guidance:
http://fieldresearch.msf.org/msf/bitstream/10144/305288/5/MSF%20Research%20Ethics%20Framework_Guidance%20document%20%28Dec2013%29.pdf
Template:
http://fieldresearch.msf.org/msf/bitstream/10144/305302/1/MSF%20Research%20Ethics%20Template%20%28Nov2013%29.docx

Excerpt from Guidance Document

The Ethics Framework

   The proposed framework is based on accepted ethical principles for research involving humans and builds upon the most influential international guidelines. It attempts to capture the diversity of research carried out by MSF.

   The framework consists of twelve questions, structured into three broad sections following a temporal logic. Section 1 addresses issues to be considered in defining the research and developing the methodology. Section 2 asks questions related to the implementation phase of the research. Finally, section 3 is concerned with what will occur once research has been completed or stopped.

1. Research Question and Methodology

(1.1) What is the research question? Why is it important?
The research question should be the central element in any protocol. Where there is more than one question they should be presented in a logical order.

a. Why is the research question(s) scientifically important? What knowledge gap will it fill?

b. Why is the research question(s) important to the community affected?

c. If other alternative research questions are possible, why was the particular question selected?

d. What potential harms might arise if the research is not conducted?

(1.2) How is the methodology and proposed analysis appropriate given the research question(s)?
It is important that the proposed method and analysis will not only allow the researchers to answer the question that they have set, but that it is the best way to do so.

a. How will the research design and analysis provide the best means of answering the proposed question (e.g. sample size and method, selection of study population etc.)?

b. What scientific/methodology review has been obtained prior to submission for ethical review?

c. How have ethical considerations shaped the proposed methodology? For example, what justification exists for any standard of care in the proposed research?

(1.3) What is the context in which the research will be conducted? How has this influenced the research design? The protocol must include details about existing and planned community engagement and collaborative partnerships and how they have influenced or shaped the proposed research[2].

*2 The **concept of 'community'** can be used in a number of different ways. Most commonly, it is used in a descriptive sense to pick out a particular geographic, linguistic, functional or socio-cultural entity with characteristics such as shared interests and experiences, values, common fate or cultural affinity. Sometimes a community will have a pre-existing structure, such as a village committee, that may be used as a means of engagement. However, care needs to be taken to avoid assuming that such structures represent all relevant interests in the community; otherwise there is a danger of reflecting prior repressive or coercive structures, potentially interfering with the voluntariness of decisions about participation. In some*

conflict-ridden environments where MSF works, the social structure has been damaged or destroyed. In such contexts it is especially important to consider carefully who would best represent the interests of the relevant population.

a. How have the community's views about their needs and research priorities been taken into account? What is the researchers' strategy to engage the community as part of the research process?

b. What collaborative research partnerships or agreements exist in relation to this project? What engagement has occurred with local or national health authorities?

c. To what extent can partnerships be structured in a fair and equitable manner?

e. Has research ethics review been obtained by all appropriate ethics review boards at the local/regional/national level?

(1.4) Are there any other parties involved in the research? What potential interests of these parties might conflict with MSF's mission and values?
a. Who may benefit directly and indirectly from the research?

b. Where other parties (e.g. companies) benefit from the research, how will the interests of participants, community and MSF be protected?

c. What are the potential benefits relating to spin-off interests or intellectual property etc? How will they be apportioned?

(1.5) Are all relevant resources for the research secured?
a. What is the budget for the research? Is it secured?

b. What additional infrastructure is required? Is it secured?

c. What possible changes might occur in the field? What plans are in place to respond to such alterations?

d. Is there an operational commitment for the expected time of the study?

(1.6) Have the research staff the relevant training and protections?
a. Have the research staff the required expertise to carry out the research?

b. What training has been conducted with the research staff, or how will this be provided?

c. What risks of harm might researchers be exposed to? How can this be minimised?

d. Have any of the research staff double allegiances (being both carer and researcher)? How will potential conflicts of interest be avoided?

2. Respecting and Protecting Research Participants and Communities
(2.1) What are the anticipated harms and benefits?
Considering all relevant harms and benefits is an essential part of assessing whether a proposed piece of research is ethical. As MSF works mostly with populations at risk, there are multiple opportunities for considerable harm.
a. Given the best available evidence and any relevant experience what are the anticipated harms and benefits of the research? How likely and how significant are any harms and benefits to research participants?

b. What are the potential wider social harms and benefits to communities?

c. What protections will be put in place to avoid or mitigate anticipated harms?

d. Benefits and burdens of research may be unequally distributed between sub-groups. How are harms and benefits distributed between participants and communities? Have researchers ensured that any proposed inclusion/exclusion criteria are fair?

e. What is the process to monitor unknown harms/new information arising in the study? Will a data and safety monitoring committee be needed?

(2.2) What are your plans for obtaining consent?

A requirement to inform participants is often seen as being an important way to show respect and promote patient autonomy and welfare.

a. What information ought to be provided? This will usually include the following elements: the reasons for doing research, details about who is doing the research, why the potential participant is being asked to be involved, details about what any intervention might involve and any on-going commitments of participation, details about anticipated risks and benefits, the fact that participants are free to refuse or withdraw, that any findings will be communicated back to the participants etc. The information given should be proportionate to any risks, but this does not mean that the higher the risk, the more information ought to be provided. Sometimes, calling attention clearly to a common or significant particular risk is more important than listing every possible remote risk.

b. Providing information does not guarantee it has been understood. How can information be provided at an appropriate linguistic level, without jargon or technical terms, and appropriate to the local language and culture?

c. Should information be provided in oral and/or written form?

d. How will the consent process be conducted? You may want to consider issues such as: who will consent, where they will do so (is the place appropriate to allow a confidential discussion), will a witness to the consent be required, how much time will be offered to consider whether to be involved? Prior engagement with communities can be a useful way to ensure that the consent process meets local expectations and sensitivities. How will the act of consent be recorded (e.g. signed and witnessed document, thumb print etc.)?

e. Alternative or additional consent procedures may need to be developed where potential participants are minors, minor parents, or suffering from short or long-term incapacities etc.

f. It should not be assumed that a long and complicated information sheet is always necessary and in exceptional cases it may be justifiable not to seek informed consent. Where researchers believe that this is appropriate, they should be careful to provide reasons for this in the protocol.

(2.3) How do you plan to protect confidentiality?

Data will include all information (medical and non-medical) about or derived from participants.

a. What data security policies are in place?

b. Where will data be gathered and stored? Who will have access to it? Where will it go?

c. Will it be anonymised or coded? Will it be linked, or could it be linked, to other data sets? If so, are adequate protections in place?

d. Will data be placed in the public domain (in line with the MSF data sharing policy)? How will confidentiality be protected?

(2.4) How do you plan to access, store and distribute any collected biological material?

a. Will biological material be collected, retained, stored, exported or destroyed? If so, how will this be done? If collected for one purpose, could it be used for other purposes?

b. Is the relevant consent obtained?

c. Where transfer of material is planned what national or international regulations are relevant? Have the necessary authorisations been sought? Is there a material transfer agreement in place? If so, what does this say?

3. Implications and Implementation of the Research Findings

(3.1) What will happen when the research is either stopped or is complete?

Good planning for a project will consider how it will end.

a. Under what conditions would you consider stopping the project earlier than planned?

b. What will happen to investments in infrastructure, human and other resources, when the research is complete or ends early?

(3.2) How will the findings be disseminated?

a. How will the results be disseminated? Through publication? Where? Will they be available through open access or on the MSF web site?

b. How will MSF communicate the results of the research directly to the community/participants involved?

c. What is the plan for dissemination if the research findings are negative?

(3.3) How will the findings be implemented?

It will not be possible, before results are known, to establish all the details about implementation. However, it is often possible to think about such issues in advance.

a. What is MSF's obligation to the research participants?

b. What is MSF's obligation to others in the immediate programme or community where the research occurred?

c. What is MSF's obligation to others in the same situation elsewhere?

d. How will MSF fulfil any post-research obligations entailed by the results of the research?

e. Is there an (advocacy) plan in place to assure access to benefits of the study results if applicable? This is particularly important where individuals and communities are unable to access an intervention for some reasons (e.g. it is too expensive).

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