



Ministry of Health and Sports

Implementation Research ethics

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Presentation outline

- Introduction to IR
- Ethical considerations in IR
- Ethical issues in planning IR
- Ethical issues in the conduct of IR
- Ethical issues post-IR conduct



Introduction to IR



- Implementation research (IR) is growing in recognition as an important generator of practical knowledge that can be translated into health policy
- The fundamental ethical principles governing clinical research apply equally in IR, but the application of these principles may differ depending on the IR question, context, and the nature of the proposed intervention.
- IR questions cover a broad range of topics that focus on improving health system functioning and improving equitable and just access to effective health care interventions.



Implementation research

- Develop systematic strategies to take a proven intervention and apply it in an real world
- Goal is to improve access to and use of effective interventions in population in needs
- Focus on disease where control tool exists and would significantly reduce burden of disease
- Demand driven



Example: malaria

- Local health problem
 - Delay in diagnosis
 - Inappropriate treatment
- a strategy could improve the rapidity of correct diagnosis and initiation of appropriate anti-malarial therapy,
- but studies would be needed to determine whether the strategy actually improved malaria diagnosis rates, treatment delays and outcomes, and whether it would also improve the appropriateness of referrals for non-malaria associated fever.
- a strategy could be rapidly scaled-up and rolled-out, and could be implemented elsewhere if found to be effective



Operational research

- Find solutions to local operational problems within specific health programs
- Trouble shooting local bottlenecks
- Focus on service delivery component of health system
- Addresses problems under control of program managers
- Research domain
 - Health system research
 - Implementation research
 - Operational research



HSR

- Addresses health system and policy questions
- Not disease specific
- System functioning
- Impacts performance of the whole health system
- Broad scope of questions including health financing, governance, planning, policy. Management, human resources, service delivery and quality of care



Why IR is necessary?

- We know ITNs work
 - How do we increase consistent use by appropriate individuals?
- We know ARV prolong the life in HIV
 - How can we improve the proportion of HIV positive people treated effectively?
- We know MDA reduce incidence of LF
 - How do we engage the community to participate and achieve optimal community protection?



- The important delays in translating knowledge into practice and highlights the need for IR to understand and overcome these delays.



What does IR study?

- Factors which effect implementation (delivery and uptake)
- Process of implementation
- Outcomes of implementation



IR vs Quality improvement or public health practice

- Hand washing to reduce puerperal infection
- Disinfecting water to reduce diarrheal diseases



Focus on strategies in IR

- Acceptability
- Appropriateness
- Feasibility
- Effectiveness
- Cost
- Coverage
- Sustainability



- OR and IR must be conducted in real-life circumstances to gain as accurate and realistic a picture of whether an intervention works under the local conditions,
- what barriers are encountered,
- how the intervention is accepted and
- how the strategy can be improved.
- Such information is crucial prior to scale-up and the widespread roll out of effective interventions.



- Difference between clinical research and implementation research



Domain	Clinical research	Implementation research
Research participant	Individual	Countries, institutions, communities, and individuals
Informed consent	Informed consent by competent individuals, assent by minors and consent by legally authorized representatives	Consent may be difficult to obtain in cluster randomized trial design. There may be a need for a two level consent—consent for randomization from gatekeepers and consent for participation at the individual level. Sometimes individual consent may not be feasible. However, gatekeeper consent does not replace the need for individual consent. Ethical committee should oversee the informed consent requirement and process E



Equipoise	Clinical equipoise	Clinical as well as contextual equipoise (genuine uncertainty that the implementation will work in a new context as well as whether the implementation package will work at all) P
Pre requisite	Understanding of disease pathophysiology Intervention aimed at disease-specific management	Identification of population health needs Understanding relative priority of need for intervention within local context Community engagement to understand community needs, ensure scalability, and sustainability
Research design	Cross-sectional, case-control studies, Cohort studies, randomized clinical trials	Cluster randomized trials Pragmatic, mixed methods, effectiveness implementation hybrid designs, participatory action research, quasiexperimental design, realist review



Research condition	Generally controlled research environment	Real-life or pragmatic research environment
Integration within health system	Often, there is no a priori plan for health system integration. Findings of clinical research go through IR before integration into health system	IR has a strong health system strengthening focus. It creates horizontal integration into the health system. There is an ethical imperative for health system integration
Predominant research disciplines	Physiology, genetics, biochemistry, and other basic sciences, epidemiology, clinical medicine	Anthropology, Economics Epidemiology, Political science, Public health ,Sociology
Control groups	In most epidemiological designs, control groups are required. But some phase 1 clinical trials and observational studies may not require control groups	Having a no intervention control group may not be acceptable. Alternative designs of quasi-experimental studies do not require a control group



Boundary between research and clinical car	This boundary is usually clear, but may be unclear in case of therapeutic misconception especially in cancer trials Is often unclear, because the intervention is of proven efficacy T	This boundary is usually clear, but may be unclear in case of therapeutic misconception especially in cancer trials Is often unclear, because the intervention is of proven efficacy T
Types of research question	Efficacy and safety of a therapeutic strategy in the individual	Operationalization of an intervention in local context Implementation of an intervention in local context prior to scale-up Policy analysis Health system functioning at multiple levels
Anticipated outcomes	Well-defined hypothesis at the beginning of the clinical research. Expected outcomes clearly stated.	Multifaceted holistic impact on health systems functioning with regard to intervention tested. Sometimes outcomes may be unexpected
Risks assumed by:	Mostly, the risks are for the study participants. However, families and communities may also be affected in specific contexts	Usually population level risks. Moreover, the people getting the benefits and people suffering the risks may be different.



Benefits accrued by:	Benefits accrue to the participants, the community. The research finding may be a common good	Individuals, communities, health system, institutions may benefit. The research findings may be common good. The people accruing benefits may be different from those who suffer risks
Generalizability	Generalizability is sometimes possible in multicentric and well sampled studies, however most studies are specific to the target populations.	Generalizability may be limited by contextual factors. However, findings may be generalizable to similar contexts
Social justice implications	Social justice is usually not a primary consideration. However, justice considerations are required in selection of research participants. Research on vulnerable participants is often contentious because of compromised autonomy and other logistics	Social justice considerations are primary. Working with vulnerable groups essential to understand implementation issues in these groups so that the intervention can reach them



Ethical consideration in IR

- key ethical principles of health systems and IR;
- Ethical justification for IR.



Substantive ethical principle

- Maximize benefits to the population
- Minimize harm to the individual and community
- Proportionality
- Respect individual autonomy
- Reciprocity
- Equity
- Efficiency
- Trust
- Solidarity
- Stewardship



Procedural ethical principles

- Transparency
- Relevance
- Inclusivity
- Responsiveness
- Accountability
- Participation
- Sustainability



Potential conflicts between principles

- Autonomy vs benefit/risk
 - Autonomy vs solidarity
 - Equity vs efficiency
 - Autonomy vs stewardship
-
- Importance of procedural principles



The mHealth system is known to improve data collection and timeliness of data collection by community health workers. Will this be feasible in your country? Will it be acceptable?

- Discussion
- Research on data.
- Data protection and confidentiality.
- Data ownership.
- Is consent from participants needed?
- Who are the participants?
- What can the data be used for?



Performance-based incentives for treatment of malaria has been shown to improve health-worker performance. Can this be adopted in your country?

- Discussion
- Can incentives be sustained?
- Will incentives create sustainable change in health workers' practices?
- Will incentives lead to over diagnosis and false diagnosis of malaria?
- What is the most appropriate study design?



Ethical justification for IR

- Understanding the benefits and harm in local context
- Optimizing implementation by contextualization
- Understanding logistics and practical problems to ensure fairness
- Adapting to local needs (responsiveness)
- Improved quality of services (stewardship)
- Sustainability (cost effectiveness)



Planning phase

- Responsiveness to local needs and priorities
- Equipoise
- Study design
- Stakeholder and community engagement
- Balance between risk and benefit

Implementation phase

- Autonomy and informed consent
- Privacy and confidentiality
- Standard of care
- Ancillary care
- Community/health system empowerment

Post research phase

- Dissemination of research findings
- Data ownership
- Translating research findings into public health action
- Scalability and sustainability
- Benefit sharing



Ethical issues in planning IR



Characteristics of IR

- Systematic
- Multidisciplinary
- Contextual
- Complex



Main steps/consideration in planning IR

- responsiveness to a community's needs
- scientific rationale
- study design
- contextual factors
- selection of research participants
- weigh risks and benefits
- community and stakeholder engagement
- iterative process.



Scientific rationale

- Is there equipoise?
- Genuine uncertainty about the effectiveness of an intervention
 - Clinical equipoise often no longer exist in IR
 - E.g vaccination against Rota virus reduce the child mortality
 - Situational/ context equipoise is usually exist in IR
 - E.g In a rural religious community vaccination may not be easily acceptable



- The ethical concept of equipoise (meaning there is genuine uncertainty whether an intervention is beneficial or not) is fundamental to any study otherwise it would be unethical to include a control/untreated group if the treatment were already known to be beneficial.



Study design

- RCT
- Effectiveness-implementation hybrid trial
- Pragmatic trial
- Participatory Action Research
- Mixed methods
- Open label demonstration projects
 - Each may have specific ethical implication



Approaches and study design

- Distinction between IR, quality improvement and public health practice may be blurred
- Any exposure to potential risk, having a control group, need for consent, questions on whether or not the existing standards of care are acceptable, etc., may all be relevant considerations of any quality improvement or IR that should be subject to ethical review.
- Engaging with research ethics committees at an early stage will help researchers to determine if their proposed research is exempt from ethics review.
- When in doubt, the rule is to ask, discuss and deliberate with the ethics committee. Investigators should not make the choice



Ethical issues relating to examples of implementation research designs

IR design	Features	Example	Ethical concerns
Cluster randomized trials (group randomized, place-based, community wide intervention trials)	Random allocation of groups or “clusters” to study arms and outcomes are measured in individual subjects and at community level	Randomization of clusters of obstetrics unit staff to education on hand washing or usual practice, measurement of rates of puerperal sepsis in women delivering at study clinics	<ul style="list-style-type: none"> ▪ Different units of intervention and outcomes measurement ▪ Consent before and after randomization, whom to consent? ▪ Choice of gatekeepers ▪ No opt-out option within cluster ▪ Risk: benefit balance ▪ Ethics of randomization to known intervention, equipoise, ▪ Identification of vulnerable groups



<p>Effectiveness-implementation hybrid trials</p>	<p>-Assess both effectiveness and implementation strategy simultaneously -Identify intervention—implementation interactions</p>	<p>-Evaluate impact of ITN on reduction of malaria and assess robustness of availability and uptake of ITNs in the community</p>	<p>-The trade-off between the scientific rigor required for effectiveness assessment and the realistic contextual considerations required for implementation is an important ethical consideration</p>
<p>Mixed-methods research</p>	<p>-Use of both qualitative and quantitative methods -Understands various perspectives -Rationales: “participant enrichment”, “instrument validity”, implementation validity”, “meaning enhancement”</p>	<p>-Integration of HIV and TB management in single clinics—patient experience (qualitative) and adherence (quantitative)</p>	<p>-The trade-off between the scientific rigor required for quantitative methods and the realistic contextual considerations required for the qualitative component</p>



Participatory action research	-Research question, design, and data collection in a participative manner by the research participants - “Bottom-up” approach	-Peer support groups to improve adherence to ARV in HIV + subjects	-There is a need for community engagement to ensure responsiveness, sustainability, and scalability
Pragmatic trials	-Effects of intervention in routine practice - Maximize variability of settings, practitioners, patients	Introduction of community health workers for home management of malaria	-There may be concerns of standards of care and ancillary care, which in pragmatic conditions may be ethically debatable.



<p>Quasi-experimental study</p>	<p>-Real-life conditions -With or without control group No randomization</p>	<p>-Open label demonstration project of effectiveness of self reported use of pre-exposure prophylaxis for HIV</p>	<p>-There is a concern regarding scientific rigor of the research</p>
<p>Realist view</p>	<p>-Analysis of how and why an intervention works in a context combining theory and empirical evidence.</p>	<p>-Integration of traditional healers into home management of malaria strategies</p>	<p>-Community engagement is of utmost importance to retain cultural and contextual sensitivity</p>



Contextual factor

- cultural sensitivity,
- geographical location/challenges,
- community structure,
- political climate, etc., which will all potentially have an impact on the study's conduct and outcomes.
- Therefore, close monitoring should be in place to ensure a responsive iterative process to adapt the study as and when potentially unidentified barriers/problems arise.



Selection of study participants

- Institution/ location
- Individuals/ groups
- Inclusion of vulnerable groups
- Identify those experiencing risk vs those gaining benefit
 - Justice implication
 - Informed consent implication



Risk assessment in IR

- Individual harm
 - Risks of intervention
 - Control groups or standard of care
 - Ancillary care responsibilities
- Social harm
 - Stigmatization of groups of subjects involved
 - Potential excess burden experienced by marginalized groups, especially if not consulted
- Financial harm
 - Incentives or vouchers may destabilized local economy
- Communal harm
 - Cultural insensitivity of an intervention, distortion of health promotion messages leading to misinformation
- Harm to health system
 - Overworking/overwhelming health care workers, diversion of resources towards research area



Examples of potential harm in vaccine trial

- HIV
 - Selection of high risk participants to test HIV vaccines may lead to stigmatization
- Rota virus
 - Is administering pneumococcal vaccine in a control arm ethical for a Rota virus vaccine trial?



Identifying non obvious risks or benefits in IR

- Requires meaningful engagement with the community
- Non obvious harm
 - Cultural norms
 - Gender roles
 - Belief about blood samples
 - Pregnancy etc
- Consider undue benefits to certain groups



Community engagement

- A process of working collaboratively with and through groups of people affiliated by geographical proximity, special interest or similar situation to address issues affecting the well-being of those people
- Stakeholder / stakeholder engagement



- What constitutes a community?
- Who makes or should make this determination?



The community engagement continuum

- Sharing information : two way
 - Creating awareness and improving understanding about research and local culture and traditions that might have implications for the conduct of research
 - Opportunity for co learning
- Consulting the community on key aspects of research
 - Community as consultants
 - What is locally and culturally relevant and acceptable/permissible
- Community as consultants
 - All aspects of the research : from inception to dissemination



Ethical norms that underpins the notion of community engagement

- Respect for persons
- Beneficence
- Justice
- Accountability
- Solidarity
- Transparency
- Sustainability
- Public justification



Ethical framework for stakeholder and community engagement

- Three core imperatives
 - Identify and manage non obvious risks and benefits
 - Expand respect beyond individual to stakeholder community
 - Build legitimacy for research project



Community engagement challenges

- Identifying relevant community representatives and legitimacy of representation
- Power imbalance between researchers and communities
- Power imbalance between and within communities
- Involving minority groups
- Voluntary consent if community agreed to participation
- Finding appropriate methods of engagement
- Handling community expectation
- Time and resources, where is the budget
- Little empirical evidence to support practice



Components of Community engagement

- When? Timeline? How early?
- Where ? State facility? Town hall? Traditional venues?
- What? Engage about what?
- How? What method? Medium?
 - Poster? Group meetings? Face to face meeting?
- Duration? Before/during/after study?
- With whom
 - No one-size-fits all



Iterative process

- Ongoing monitoring, evaluation and community engagement throughout the research process to detect and understand barriers and potential harms early on
- Channels for communication should remain open in all directions to obtain obstructive feed back
- Protocols may require adjustment or adaptation once the project has become to optimize success and minimize harms while maintaining scientific rigor
- Potential adjustment may require rethinking of ethical consequences and requirements at all stages
- It is important that the research remains responsive to the identified needs



Ethical issues in the conduct of IR

- ethical aspects of upholding participant autonomy in IR •
 - informed consent •
- promoting justice during the conduct of IR
 - standard of care in the IR design
 - ancillary care
- ethical aspects of data collection and management •
 - data ownership, data sharing, data dissemination
 - privacy and confidentiality.



Justice in conduct of IR

- Issues of fairness in selection of participants
- Issues of appropriate standard of care
- Issues of ancillary care



Sources of data in IR

- Primary data
- Secondary data
- Information system and program management information system



Data use in IR

- Contact tracing
- Partner notification
- Quarantine
- Mandatory vaccination
- Mandatory treatment
- Others?



Data sharing, dissemination and disclosure



Ethical issues in post research phase of IR

- ethical obligations of researchers and donors to disseminate the findings from IR;
- role of IR in research capacity building and health system strengthening;
- post-IR access to interventions;
- ethical obligation to translate IR findings into policy and practice.



- ethical obligations of researchers and donors to disseminate the findings from IR
 - The data emerged from the community
 - Justice requirement to give back to the community
 - Empowerment of community with knowledge
- To whom and how?



Post IR access to intervention

- The interventions in IR are usually system wide
- Ensuring post research access to intervention are challenging
- Post research access may involve cost-intensive system wide changes
- The researchers may not by themselves be able to bring about policy change, but should engage with political stakeholders at the beginning or the IR
- There is an ethical obligation to ensure the research participants benefit because of the intervention



Ethical obligation to translate IR findings to policy and practice

- Documented delay in translation of research to practice
- However IR is a special form of research which is done to study the best method of delivering the intervention
- There is an ethical obligation to adopt IR into practice
- Having a policy adoption plan at the beginning of the IR is very important and therefore stakeholder engagement is useful
- There is also an ethical obligation to sustain the intervention



- Does the study address a priority concern of the community?
- Who are the stakeholders in this study?
- How should community or stakeholder engagement occur?
- Who should represent the community in determining participation in the study?
- Should informed consent be obtained? If yes, from whom?
- Who are the research subjects?
- Who will own the data?
- How will privacy and confidentiality of data collected electronically be assured?
- Are there potential harms associated with the intervention? If so, for whom?
- Who stands to benefit from the study?



Questions, Comments & Suggestions

