Conducting research that is both ethical and responsive to the health needs of a developing country

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Abstract: There is no substantial difference in conducting research that is both ethical and responsive to the health needs in developing and developed nations. Differences are in financial constraints, technological expertise in identification and addressing needs, and in the perception of equal partnership of all stakeholders. There will be differences in emphasis of research but this is slowly blurred due to globalisation. Public health emergencies in developing countries need timely and effective global collaborative research to implement control strategies. Research needs should be based on predictive models with learning from past emergencies, technological advances, strategic critical appraisal of local and global health information, and dialogue with all stakeholders. Adequate funding will be challenging and resources from national, international and aid foundations will be needed. Issues associated with such funding include deployment of international rapid response teams, collaborating researchers, transfer of technology, and intellectual property ownership. While all types of research ranging from basic, applied, clinical studies, meta-analysis, and translational research are relevant, the relative importance and specific allocation of resources to these may differ. Is the choice related to responsiveness or based on researchers' perception of their contributions to evidence-based practice and research? Ethical issues relating to vulnerable groups, risk distribution, quality issues, research integrity and oversight are just as important. Internationally funded research including clinical trials must be sensitive to such issues to avoid allegations of exploitation. Thus the potential of utilisation and buy-in of research findings and recommendations must be considered.

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Introduction

Developing countries are in various stages of economic attainment and have differences in health problems and needs. Although we can only generalise about the specific needs, the principles of ethical considerations and responsiveness of research will be similar.

It is perhaps pertinent first to define ethical and responsive research, and then discuss whether there are differences in such research in developing and developed countries.

Responsive research needs the elements of prior identification, prioritisation, adequate funding, participation of all stakeholders, the research process, analysis and application of findings, and evaluation of the quality of outcomes. Full participation of all stakeholders is needed, including patients or those who are involved in the process and subsequent applications of the research findings. Implicit in this will be the necessity for such research. Participation of research means involvement at every stage of the decision making process (including necessity for the study, etc.), conduct, data collection, interpretation, communication and utilisation of the research results. This is clearly not very obvious in some medical and health research, the most obvious examples being randomised controlled trials (RCTs) for drugs, devices, and procedures.

Another not too commonly thought of research is field based research e.g. release of genetically modified insects for the control of diseases or genetically modified crops. Unlike RCTs where patients or subjects have the choice of participation in the study, the community or population affected by the study may not be given the opportunity to make informed decision.

This paper will focus on the necessity for such studies and participation in the various stages of the research process, the potential implications on various stakeholders, and the feasibility of such an approach in developing economies. Responsive research implies

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participation in the decision making on the necessity, and how the research process is implemented.

Prioritisation of identified research, resource allocation, approval processes, oversight and governance, as well as outcomes evaluation are also important issues. An equally important area but often neglected, will be difficulties involved in the approval and conduct of qualitative research.

Responsive Research

Identification and prioritisation of the research needs in a country are important elements in responsive research. The identification of research has traditionally been top down or researcher initiated for most biomedical research. Clinical trials are generally sponsor initiated and/or occasionally investigator initiated. Research identification originating from patients or the community is rare. Prioritisation has normally been influenced by the funders of the studies and to meet health policy needs.

Research Process

For health policy and decision making in health services, studies are often identified from past experiences such as public health emergencies and surveillance systems or based on discussions with all stakeholders and not just sponsors of research. Funding support for these studies will determine to a large extent the prioritisation of studies. In resource poor countries such funds are mainly from:

a. National governmental sources
b. Multinational companies
c. Foundations: Bill and Melinda Gates Foundation
d. International organisations such as UNDP and WHO

Those charged with such research in and for developing countries include some of the following:

a. Local scientists and health professionals
b. Collaborating foreign scientists
c. International agencies
d. International rapid response teams

It is important to ensure buy-in of all stakeholders involved in the research studies. Consultation and a common understanding of why the studies are carried out and the expected potential applications will need to be conveyed to all involved in the research process.

It is accepted that meaningful participation of all stakeholders including patients and those involved in the research process, including those affected by the utilisation or application of the research findings is needed. Patient and public involvement is so important that the UK National Institute for Health Research has established a strategy in 1996 to support active public involvement in NHS, public health and social care research. The strategy adopted is given the acronym INVOLVE (National Institute of Health, UK, 2012).[1]

Ethical issues

Institutional Ethics Review Boards (IRBs) are tasked with addressing issues of vulnerable groups, risk distribution, quality issues, research oversight and management.

Application of research in resource poor countries may engender ethical issues involved (cost issues, accessibility, etc.). In clinical trials, special considerations should be given to:

a. Early phase clinical trials
b. Quality of informed consent
c. Distributive risk
d. Access to costly therapeutic advances
e. Oversight issues
f. Standard of care

In the conduct of clinical trials in developing countries, it is important to note that any decision based on application of contextual analysis cannot justify application of ethical double standard for research.[2]

Research Participation

Concept of Participation

The concept of participation at the individual and community levels needs clearer definition as there is a spectrum of understanding and practice seen among researchers and even IRBs. Participation in RCTs or other human experimentation is usually defined by institutional, national, and international guidelines on research involving human subjects. These guidelines do not completely cover participation at the community level.

As pointed out by Arnstein, citizen participation can be classified into various levels ranging from non-participation to control.[3] The ethical issues governing individual and community participation need to be discussed.

The burning question will be who decides what studies are carried out and their priorities. Is the community or patient sufficiently knowledgeable to empower themselves with these decision making processes? The initiator of the discussion could be research professionals who would be in the position to identify the problems in the initial discussion with volunteers and other stakeholders and thus the decision making involves participation of the patients. There will be challenges but the compliance is expected to be much better.

Participation is more than dialogue with these groups to explain and enlist their consent to be participants. The important principle is that all stakeholders including subject participants (patients, individuals, special groups, community members involved, etc.) need to be consulted and be involved, from the beginning of the full research process.

Patient Participation in RCTs

Responsive research in the health setting would involve equal partnerships of all stakeholders including patients in the research process from the beginning to the end.[4] True patient participation in clinical research can be challenging but involvement of patients as partners in the research process can be beneficial e.g. in patient compliance.

At the individual level, altruism may not be the only reason for participation. In situations where the medical treatment is expensive or not effective, participation may be the only way patients who enrol in the study may avail themselves of best currently available treatment or potentially more effective drugs. It would be expected that in such situations compliance with the requirements of the study is expected to be good.

To deny such patients this avenue would raise ethical issues if the RCT is designed to test the efficacy of the new drug with existing best available therapy. However, in the unlikelihood that a placebo control group is involved, this would also create ethical issues.

Impacting on the concept of the ethics of participation is the current burning issue on the increase of First in Humans (FIH) studies in developing countries where the infrastructure for clinical studies and ethical review and oversight are perceived to be less established than those in developed countries. Such FIH studies for drugs, vaccines and other interventions that are targeted at health problems in such countries are expected to be most needed in these countries but if the required infrastructure needed for this are found wanting, would the potential benefits outweigh the associated ethical dilemmas?

These are cogently discussed by Kapiriri *et al.* and arguments for and against these are eloquently expressed.[5] The presence of these health conditions in such countries, the possible differences in gene mutations of drug metabolising enzymes in unique populations, the improved facilities and associated benefits in capacity building arising from such studies are some of the positive reasons for such studies, if the protection of subjects meet international guidelines.

Community Participation in Health Research

Public health emergencies have their unique challenges and research needs. Lurie *et al.* analysed major emergencies during the last couple of years and stressed that lessons learned from timely and effective research before (anticipated), during and after such emergencies are critical for our future capacity in meeting such challenges.[6] They stressed that experts and the community must be engaged in three vital areas, these being to:

a. Identify special research needs of and community participation in the research
b. Ethical issues that may arise
c. Management of public trust to avoid perception of exploitation

The recent outbreak of H7N9 avian influenza in China and how the Chinese health authorities are dealing with this is a classic situation where responsive research is initiated by governmental response to an outbreak situation. The opportunities for responsive research must be recognised and carried out in a timely fashion, during and after the outbreak so that the findings can help evaluate the appropriate responses for similar outbreaks and prevention of future outbreaks.

Utilisation and application of research findings and recommendations

It is assumed that participant-identified research needs will result in more responsive research but is this translated into more applicable research findings? If it is presumed that the identification of the research topic reflects a real need, will the findings be applicable eventually? Are the perceived research needs aligned with health policy or clinical management needs? If professional researchers are involved in the process, then the alignment can be presumed to be better.

Views on compensation and benefits to participants, institution and community of human drug trials and other human experimentation

There are no generally agreed guidelines between countries and even between institutions within the same country. A generally agreed principle is that the benefits include provision of health care services, capacity building, and others. Monetary payments are very often labelled as compensation for transportation costs, loss of earnings but not for inconvenience and financial benefits.

It is also agreed that the risks-benefit ratio must be acceptable but what the balance is will be expected to differ between countries. What is unacceptable would be when the decision to participate at the individual or community level is influenced by financial and other perceived benefits disproportionate to the potential risks.

It is generally agreed that unfair distribution of benefits is considered exploitative and should not occur. These issues are not unique to developing countries, and recently an in-depth study of these issues was carried out in Kenya.[7]

Institutional Ethics Board (IRB)

There are concerns that IRBs may not be adequately meeting their expected roles.[8] An important concern is the perceived inappropriate application by IRBs of research governance principles based on biomedical concerns on qualitative research. This is especially so when elements of evolving and negotiated micro-ethics are involved and in studies on sensitive topics and hard to reach groups.[9] These are important areas for discussion but will be beyond the scope of the current paper.

Conclusions and recommendations

Responsive research implies the full participation of all stakeholders in every step of the planning and conduct of the research. While the identification of the research area or topic may be by sponsors or funding agencies, it is recommended that all participants in the study must be involved in the whole research process, from planning to final utilisation and evaluation of the

research outcomes. Such an approach is expected to lead to meaningful participation that will ensure that such studies are needed and that the research findings are applicable to the participants and community. These would only be possible if the choice of the study is made based on the full understanding of the requirements, potential risks and benefits, of the research process and application of the findings, and that no party exploits any other. It also presupposes that IRBs are competent and effective in the performance of their expected roles.

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