**Clinical equipoise in health policy and systems research**

**Abstract**

Health policy and systems research refers to the research conducted on how health policies are formulated, what are the consequences of health policies, how health systems organize and function, how to optimize the functioning of health systems and how the health policies and systems work towards achieving health for all. There is emerging scholarship on the ethics of conducting such health policy and systems research. Ethics of health policy and systems research, though similar to ethics of traditional clinical research in many ways, has several important distinctions. In traditional clinical research on human participants, where two treatments or interventions are compared, clinical equipoise is an important ethical consideration. This refers to the genuine uncertainty among professional peers on whether one of the treatments is better than the other. Unless such an equipoise exists, clinical research is said to be unethical from benefit-risk balance and justice considerations. In health policy and systems research such a clinical equipoise position is often not relevant. This article will describe the clinical equipoise condition in health policy and systems research, its applications and challenges.

Key words: clinical equipoise, health policy and systems research

**Introduction**

Health policy and systems research (HPSR) refers to all research that attempts to understand the way the health system functions and methods to strengthen it.[1,2] The important goals of HPSR are to understand the dynamics of functioning of the health system, to study how interventions impact the functions and outputs of the system, to evaluate the influence of policies on health system functions and outcomes and to strengthen the health system through interventions and policies that are grounded in evidence. Therefore, HPSR is a multidisciplinary enterprise involving contributions from health care providers, public health experts, policy makers and people living in the community. HPSR involves research on health financing, governance mechanism, service delivery, human resources for health, information technology, as well as supply of drugs, devices and other utilities for optimal functioning of the health system.[2] It also attempts to understand the norms, values and power dynamics within the health system that lead to its effective functioning. One of the unique characteristics of HPSR is that the research is situated in the real-world context.

For the purpose of this article traditional clinical research will be defined as all research aimed at identifying burden of disease, its distribution, severity, risk factors, clinical features, course of illness, treatment options, preventive interventions, long term outcomes, complications and prognosis. There are several important distinctions between traditional clinical research and HPSR. To explain with an example, a traditional clinical research on efficacy of a vaccine would conduct a vaccine trial in which healthy volunteers are allotted to two groups, one group receiving the new vaccine and the other receiving routine care. The difference in incidence of the infection will be studied to understand its efficacy. However, HPSR will look at issues such as logistics and supply chain of the vaccine to the community, how the acceptance of the vaccine in the community can be increased, what should be its pricing in the market etc. Therefore in the spectrum of health research, there is basic science research which begins in the laboratory, there is research on human participants which happens at the bedside in clinical trials and finally there is HPSR which is research in the real world context.

There is emerging scholarship on the ethics of HPSR.[1] Some of the key ethical considerations in HPSR, as in most forms of research on human participants, include upholding the autonomy of the individuals and communities who participate, establishing a fine balance between benefits and risks to individuals and communities, considerations of justice, responsiveness to the local needs of the community and health system, sustainability, scalability and post-research commitment to the community and health system, and a strong community and stakeholder engagement from the stage of research design.[4,5]

One of the highly debated ethical issues in traditional clinical research has been the issue of clinical equipoise. In this commentary, which is one of the articles in a theme issue on ethics of Biomedical and Health Research, I will attempt to frame the idea of clinical equipoise in the context of HPSR and discuss the challenges of using it as an ethical requirement to conduct research.

**The debate surrounding clinical equipoise in traditional clinical research**

Clinical equipoise in the clinical trial context is a highly debated ethical issue and over the past 40 years, it has evolved from an absolute evidentiary basis for justifying treatments provided in the arms of a CT to a relative notion that there exists a genuine professional disagreement among the community of experts on the best treatment. In early 1970’s Fried defined clinical equipoise as the clinician-researcher’s belief that there is no evidence to support that either of the two (or more) interventions that are studied are superior to the other(s). This is referred to as the absolute evidentiary criterion for clinical equipoise. However, such a stringent criterion of clinical equipoise makes the conduct of any CT extremely challenging because, there always exists some evidence, sometimes from pre-clinical animal experiments that one is better than the other. Moreover, even if there does exist an equipoise at the start of the CT, with the progress of the trial, theoretically the equipoise will increasingly be disturbed, even though the clinician-research does not do an analysis. Freedman, in 1987, came up with a revision of the clinical equipoise criterion, where he proposed that rather than the individual clinician-researcher making the absolute evidentiary decision on the uncertainty of which treatment is superior, the criterion should be a ‘genuine professional disagreement among a community of expert peers’.[6]

The other point of debate in clinical equipoise, is whose equipoise matters? The clinician-researcher in a CT may have justifiable clinical equipoise, but if the patient-participant in the research prefers one treatment to the other because of its less invasive nature or other forms of acceptability, then can equipoise really said to be existing? In the era of patient centred care where patients and communities must be equal partners in health care, health knowledge is understood to be embedded in communities. Judgment of patients and communities counts as support to evidence-based medicine and public health. This concept of equipoise further complicates the debate on the clinical equipoise condition to ethically justify research.[7,8]

The main ethical principles that underpin the clinical equipoise condition are benefit-risk balance and justice. The presence of clinical equipoise ensures that benefits are optimized, risks are minimized and there is fairness in the distribution of benefits and risks between the arms in the CT. If equipoise does not exist, then one of the two arms in the CT will be intentionally subject to an inferior treatment compared to the other arm. This goes against the principle of risk-benefit balance and justice in the CT. However, the idea of clinical equipoise in HPSR requires a different framing.

**Challenges of Clinical Equipoise in HPSR**

The Gadchiroli Home Based Newborn Care (HBNC) study is a very good example of a HPSR and I will describe it and use it to highlight the challenges of using clinical equipoise criterion in HPSR. Abhay and Rani Bang and their team initiated a field trial to study the impact of HBNC on early detection, management of neonatal sepsis and reduction of neonatal mortality. They allotted 39 villages to intervention and 47 to control, where the intervention was to train village level health workers to make home visits and closely monitor all neonates, identify low birth weight, birth asphyxia, hypothermia, breastfeeding problems and sepsis and treat them at the home. The control villages received routine care by the government health system, which involved care of the new born during the post natal visits at home by the government employed health workers who did not receive these training and referral to a hospital if the health worker found any health problems in the new born. Data on births and neonatal deaths were collected to estimate mortality rates. The trial began in 1993 and by 1996, about 93% of all new borns in the intervention cluster received the HBNC. At the end of the study in 1998, the researchers demonstrated a reduction in case fatality rate due to neonatal sepsis from 16.6% to 2.8%. The study also showed a 50% reduction in perinatal and neonatal mortality rate in the intervention clusters.[9] The findings of this study and concerted public health advocacy of the research team has led to adoption of some of the components of the HBNC in the Integrated Management of Neonatal and Childhood Illnesses program (IMNCI) by the Ministry of Health and Family Welfare of the Government of India. It has also led to the state government of Maharashtra to implement the Gadchiroli HBNC model in 5 districts of the state where access to health care is poor.

Critics have raised concerns about the conduct of the HBNC trials. One of the major concerns was the lack of clinical equipoise between the clusters who were provided the HBNC and the control clusters who received ‘routine care’, which often implied no care in the remote tribal district which was grossly underserved with respect to health care. The critique was because there can be no uncertainty that any intervention is better than ‘no intervention’ which was the reality on the field. Rather than leaving the control clusters to routine care, the critics commented, they should have been provided some ‘basic intervention’. The researchers have responded to this critique by describing the realistic situation that prevails in the field and this is a very good example of the challenge of clinical equipoise in HPSR.[10] The researchers are obliged to conduct a HPSR in the real-world situation of the health system prevailing in the area. In Gadchiroli, where this research was conducted, the prevailing reality was ‘no new born care’. A good HPSR can bring out the effectiveness, acceptability, feasibility of the HBNC only if conducted within the realistic context. Only then they can firmly advocate for a policy change as has happened in this case. If they had created an artificial ‘minimum basic intervention’ in the control clusters, it would not have given them a convincing result to strongly advocate for policy change. HPSR that is conducted in low- and middle-income country settings are often faced by this issue of ‘less than optimal intervention’ for the control group who receives routine care. However, the clinical equipoise condition that is applicable to strictly controlled experimental studies cannot be imposed on these research ventures. Moreover, any intervention for the control clusters would have involved much higher costs and efforts that would have prevented the trial in the first place. **Thus, clinical equipoise condition in HPSR is faced by two major challenges – of necessity and of feasibility.**

In some situations, clinical equipoise may be both necessary as well as feasible in HPSR. I will take a more recent example of a study where clinical equipoise condition was attempted in a HPSR cluster randomized controlled trial. A study was designed among 40 community health centres (CHCs) of the states of Haryana and Karnataka, where the CHCs were randomly assigned to intervention, an mobile phone based health application (mHealth) system for electronic data capture, storage and mobile based decision support system for integrated management of hypertension, diabetes, tobacco use, alcohol use and depression, or control which involved training of physicians to clinical management of these 5 conditions, display of treatment algorithms on the clinic walls, training of nurses and provision of a tablet PC for electronic data capture by the nurses.

The study did not find an incremental benefit of the mHealth intervention over enhanced routine care.[11] In this study clinical equipoise can be said to exist because the two arms received interventions which were similar – capacity building of health care providers in delivering care for patients with non-communicable diseases, using two modalities. **While there is no uncertainty that capacity building will have effect, there was genuine uncertainty about which of the two interventions would work out better.** The clinical equipoise was feasible because both interventions involved similar content delivery albeit through different modalities. One could argue that the clinical equipoise condition in this trial was not necessary and it is because of comparison with enhanced usual care that the mHealth intervention did not show incremental benefit. However, the study failed to establish the superiority of mHealth intervention over an enhanced usual care, which may have cost implications for the health system, which may accomplish the goal of effective management of non-communicable diseases at a lower cost by providing capacity building of the physicians rather than investing on mHealth systems.

**Possible solutions to the challenges of clinical equipoise in HPSR**

One of the solutions to the problem of clinical equipoise for HPSR is to understand the concept differently considering the unique characteristics of the research goals. Often in HPSR the research goals are related to how best to adopt a new health policy, or how to optimize the health system to improve health outcomes. In such a context it is understood that basic efficacy, safety, effectiveness studies of the intervention are already completed. In other words, there is no reason to believe that the intervention is ineffective, and the criterion of uncertainty is non-existent. **Therefore, HPSR must he held to a different standard of equipoise, the pragmatic equipoise.** Pragmatic equipoise is a practical (rather than theoretical) consideration. It asks “is there genuine uncertainty about the effectiveness of an intervention when implemented in the real world context?” This question should guide equipoise decisions in HPSR.

The other most important solutions to the clinical equipoise problem in HPSR is **innovative study design**. HPSR is characterised by more pragmatic and realistic evaluations. The study designs are usually flexible and adopt mixed methods. Cross sectional assessments and case studies can provide valuable information and can overcome the challenges inherent to experimental designs. Participatory research methods that emerge from critical social science traditions, provide very useful information about interventions in the health system. In Participatory Action Research (PAR) the emphasis is on collaborative designing, data collection, analysis and action based on the findings. All stakeholders in the research actively engage in the research enterprise. The PAR goes through a process called the PAR spiral with plan-act-observe-reflect-revise-plan-act….going in a spiral fashion. It is an iterative process and the issue of clinical equipoise does not arise as there is no control group. The PAR technique is pragmatic, in the real-world context and immediately action based.[12] Rather than insisting on randomized controlled trials for HPSR, more open ended, flexible, realistic and pragmatic designs must be adopted. Quasi experimental studies without comparison groups, effectiveness-implementation hybrid designs are useful in overcoming the equipoise problem. Stepped-wedge cluster randomized controlled trial helps ensure that all the clusters receive the intervention in a phased manner, thus overcoming the issue of clinical equipoise.[3,13]

**Conclusion**

While conceptualizing clinical equipoise in traditional clinical research, the goal was to ensure benefit-risk balance and ensure justice as described above. However, the goals of HPSR are different and this warrants a careful reframing of the clinical equipoise condition. The original idea of clinical equipoise, which was developed in the context of CT, if applied to HPSR is likely to lead to serious delays, high costs and unresponsiveness to the needs of the health systems and local communities. Many times clinical equipoise condition may not be feasible or necessary in HPSR as seen in the description above. Ethical guidance on HPSR must carefully consider the clinical equipoise criterion and must frame it in a manner that best suits HPSR in various contexts.

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