

The role of a Prospective Public Health Intervention Study Register in building public health evidence: proposal for content and use

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Abstract

Evidence informed practice is a key component of public health and the focus of much discussion, of which the nature of evidence and how it is best gathered and appraised has formed a large part. Prospective registration of trials is now a key component of rigor and quality in clinical research and has been supported at an international level through the WHO International Clinical Trials Registry Program. This paper discusses the scope and benefits of trial registration in clinical research, including greater transparency and reduced publication bias. It then considers the potential for a Prospective Public Health Intervention Studies Register (PPHISR) specific to the needs of public health and aspects to be included in such a register. It is argued that this initiative has the potential to facilitate increased global cooperation and efficiency in the production of high quality evidence and ultimately in improved health outcomes for populations.

Background

The importance of evidence informed practice in public health practice is well recognised¹⁻³. Much of this discussion has focused on the nature of evidence within public health and on appropriate methods of gathering and appraising such evidence⁴.⁵ Knowledge synthesis, translation and exchange between research, policy and practice is also a growing area in public health, with many now exploring the most appropriate ways of facilitating and supporting these processes^{1,2}. Evidence informed practice helps to identify the potential best buys for health across the broad spectrum of health services from both up stream and down stream perspectives.

Within clinical research a key mechanism for ensuring rigour and quality, and to aid the production of unbiased systematic reviews and meta-analyses, is the prospective registration of clinical trials³. Without prospective registration there is a strong danger that disappointing findings will disappear without trace, thus distorting publicly available research evidence. Additionally, trials may be unnecessarily duplicated or subject to less rigorous ethical and scientific critique³. This paper will explore the scope and benefits of clinical trial registration before then considering the potential for a Prospective Public Health Intervention Studies Register (PPHISR) specific to the needs of public health.

Importance of Registering Clinical Trials

The importance of registering clinical trials is increasingly recognised at an international level with the World Health Organisation approving the International Clinical Trials Registry Program in 2005^{9, 10}. Recognised benefits of clinical trial registration include greater transparency regarding studies in progress which aids communication between researchers and reduces unnecessary replication, reduced publication bias, and improved recruitment as the public is better informed about the conduct and purpose of trials⁴. With these benefits in mind, the WHO program was established to provide leadership in the development of international norms and standards for clinical trial registration and reporting. Its intent is not to develop a WHO administered trial register, but rather to establish a global network of registers that meet internationally acceptable criteria and to define minimum standards for the reporting of trial results⁵. In effect, it will allow interested parties to access a web based portal enabling all registered trials to be searched at a global level⁵. The importance of trial registers within health research is internationally recognised^{3, 6-8}, as demonstrated by a policy implemented by the International Committee of Medical Journal Editors in 2005⁹. From 1 July 2005 a number of prestigious scientific journals now only publish intervention trial results if trials were registered in a publicly accessible register at their commencement⁹.

Within evidence based health research and practice, clinical trials are considered foundational to decision making^{3, 5}. Accordingly, access to information about research is critical to researchers, practitioners and policy makers, as well as health care consumers^{3, 5}. Prospective registration of clinical trials is considered important for a number of key reasons, a number of which are encompassed by the notion of transparency in health research^{11, 12, 15, 16}. According to WHO, transparency in this context refers to 'public knowledge about what research questions have been asked, what has been learned, and what has happened in clinical trials of health interventions in humans' (p.1)¹⁰.

Registration of trials in a publicly accessible register provides full information to researchers, practitioners, decision makers and consumers from the inception of the trial. This ensures a trial is public knowledge well before final results are published in a scientific journal³. A number of benefits result, including subjecting trials to greater scrutiny and review by those outside of the trial and fulfilling ethical responsibilities to participants through the provision of complete information regarding trial conduct, potentially reducing harm from poorly conducted or unethical trials^{5, 11}. This is particularly important with the increasing trend of conducting early clinical trials in developing countries where regulation and monitoring is often poor⁴. Greater

knowledge of ongoing trials also minimises unnecessary duplication of research and assists the identification of gaps in knowledge leading to better use of research funds and sharing of methods and tools^{8, 10, 15, 17}. It also improves the accuracy of research conducted on research processes, and increases the quality of systematic reviews, meta-analyses and other forms of knowledge synthesis, translation and exchange^{8, 11-13}.

Trial registers also increase transparency through reduction of publication bias^{8, 17}, the publication or non-publication of research findings according to the nature of results¹². In their review of types of reporting biases found in medical research Egger *et al.* found that the majority of studies published in medical and social science research report significant results or a beneficial treatment effect, while many studies that find no effect remain unpublished^{12, 14}. They identify a number of papers which found that the delay in publication of trials from the initial time of approval by an ethics committee was much greater for studies with null results than those with positive findings¹². In addition, positive effects of trials were more likely to be published in the English language rather than in the original authors' native language^{11, 12}. Selective publication where only some, usually positive, trial outcomes are reported, and multiple reporting of studies also bias the literature and can be alleviated through greater transparency and universal registration of studies¹¹.

The International Clinical Trials Registry Platform has engaged in extensive consultation with key stakeholders in order to reach agreement on 20 items for minimum trial registration data^{4, 7}. Part of this process has involved discussion regarding the timing of trial registration, and whether this should include early or phase 1 trials, as well as whether trial registration information should be completely disclosed at the time of registration⁴. Despite the clear benefits that prospective trials registers have with regards to improved transparency, debate has centred around concerns that transparency needs to be balanced with the need to protect academic or commercial advantage which may be compromised by early registration^{4, 10}. For example, early publication of new and emerging interventions may increase the possibility of other parties inappropriately benefiting from the original researchers' efforts so reducing potential for commercial or academic gains. The incentive to compete or innovate may be reduced by this early openness. However, Sim *et al.* report that there is no evidence to support this notion, and conversely openness may actually enhance innovation through enhanced communication and collaboration between researchers and other key stakeholders⁴. Additionally, the rights of trial participants are far more important than commercial or career interests^{4, 10}. As a consequence, the two principles identified by WHO as foundational to trial registration are that all intervention trials, including early phase studies, should be registered, and secondly, that at the time of registration all of the 20-item minimum dataset components must be disclosed^{4, 7}.

Aspects of the registration process still need to be defined, including the possibility of broadening the minimum dataset to include further detail⁷. For example, the proposed minimum dataset does not include a number of items proposed by the Ottawa Statement on Principles for Trial Registration, produced by an international group of stakeholders interested in trial registration, including systematic reviewers and representatives from the pharmaceutical industry⁸. Undoubtedly the make-up of the WHO minimum dataset will be an issue for ongoing debate and refinement.

Relevance to Public Health

As evidence is critically important to all areas of public health is well recognised¹⁵, the arguments for the arguments for trials registers also apply to health promotion and public health research. A foundational part of the production and utilisation of evidence is the conduct of high quality primary research and evaluation together with research synthesis activities such as the production of systematic reviews and health technology assessments. As with clinical medical research, the prospective registration of public health intervention studies is a vital part, in fact a key first step, in the conduct of both primary research and research synthesis and hence in the production of rigorous evidence.

Public health randomised controlled trials can be registered within clinical trial registers currently available. However, the nature of research and evidence within public health and health promotion means that often other study designs evaluating complex community interventions which are generally complex and multi-faceted are vital for informing the evidence base¹⁵⁻²¹. The notion of complexity is now recognised within the public health evidence arena as greatly effecting design, measurement, analysis and use of findings from evaluations of community interventions¹⁵. Rigorous randomised controlled trials are often insufficient and can be particularly challenging for evaluating interventions that are more complex and community based rather than simple interventions of single issues or single health promotion objectives^{1, 3}. The importance of utilising multiple methods and data sources, including qualitative and quantitative, experimental and observational research, in developing public health evidence is now well recognised^{17, 18}.

This emphasis on multiple methods in public health evidence reflects the growing awareness of the importance of contextual, including social, political and organisational, factors in which an intervention is conducted, to evaluation design and interpretation of findings^{19, 22}. Consideration of the impact of interventions on health equity, such as differences in outcomes for groups within the intervention population, is also viewed as important when conducting evaluations and systematic reviews in health promotion and public health. This recognition of the need to focus on health inequalities provides added weight to the argument for multiple methods in order to ensure that appropriate data is collected in order to build a comprehensive evidence base²³.

In the light of these arguments, it needs to be asked whether clinical trial registries are appropriate to the unique and complex needs of public health research and evaluation. The public health evaluation literature supports the need not for a public health *trials* registers, but for a *prospective intervention studies* register specific to the requirements of public health research given their relevance and importance to evidence informed practice.

As with clinical research, surely public health would benefit from greater transparency and accountability regarding the research currently being undertaken. Many resources are being directed into current public health 'hot topics' such as child obesity and mental health promotion, and a prospective trial register would assist in the reduction of unnecessary duplication of studies and hence the better use of

research funds. Better dissemination and synthesis of findings through systematic reviews and meta-analyses would also be promoted, as would the identification of gaps in the evidence. Many public health interventions work with vulnerable or disadvantaged groups such as children, those experiencing poverty, unemployment, or other forms of marginalisation. All of these groups would benefit from the increased protection from potential harm caused by poorly conducted intervention studies which would be gained from increased transparency and accountability.

The broader inclusion of design methodology for public health may provide a challenge as to whether a study is appropriate for the registry. For example, a health agency may provide a health promotion initiative to one area and not to another, and in the process undertake a robust evaluation utilising the un-serviced areas of their jurisdiction as the control. The establishment of a registry will require an agreement as to at what point a study emerges in the delivery of a previously unevaluated health intervention. Conceivably a grey area will occur where under-reporting of potentially applicable study designs occurs. Capturing whether or not the study received approval from a human ethics committee will be important in assessing the prospective nature of the design.

More work is needed to identify the particular aspects to be included in a Prospective Public Health Intervention Studies Register. This will need to be developed over time in consultation with key stakeholders including researchers, policy makers, practitioners and consumers. However, ensuring that a public health intervention studies register is consistent with the WHO proposal is important to allow for consistency and international access¹⁰. Table 1 outlines the WHO Trial Registration Data Set, many of which are applicable to public health intervention studies. In addition, a number of items that we argue should also be included in a public health intervention studies register are included. Many of these are informed by the Cochrane Health Promotion and Public Health Guidelines for conducting systematic reviews²³ which have been developed through the process of identifying core information for decision makers integrated with cutting edge developments in high quality intervention development and evaluation design.

We believe that the contribution of this proposed Prospective Public Health Intervention Studies Register to the public health evidence base would be considerable and ensure that public health research is subject to the same checks and balances as clinical research. For example, the public health work program of the UK National Institute of Clinical Excellence (NICE) has been championing the use of public health evidence in population health guidance, and the relationship between commissioning, evaluating and use of evidence would be greatly strengthened by increased awareness of what studies are underway or proposed internationally. This initiative has the potential to facilitate increased global cooperation and efficiency in the production of high quality evidence and ultimately in improved health outcomes for populations.

New Cochrane reviews and protocols from Issue 2, 2007

New Reviews

- Bicycle helmet legislation for the uptake of helmet use and prevention of head injuries
- Contracts between patients and healthcare practitioners for improving patients' adherence to treatment, prevention and health promotion activities.
- Effectiveness of brief alcohol interventions in primary care populations
- Electronic mosquito repellents for preventing mosquito bites and malaria infection
- Methods to increase response rates to postal questionnaires
- Screening for abdominal aortic aneurysm
- Wholegrain cereals for coronary heart disease

New protocols

- Alcohol and drug screening of occupational drivers for preventing injury
- Antenatal breastfeeding education for increasing breastfeeding duration (2006 HPPH Field bursary recipient)
- Educational interventions for the prevention of eye injuries
- Hepatitis B immunization in persons not previously exposed to hepatitis B or with unknown exposure status
- Home-based HIV voluntary counselling and testing in developing countries
- Interactive computer-based interventions for sexual health promotion
- Kinship care for the safety, permanency, and well-being of children removed from the home for maltreatment
- Methods to influence the completeness of response to self-administered questionnaires
- Mono and multifaceted allergen reduction interventions for preventing asthma in children at high risk of developing asthma
- One-to-one dietary interventions undertaken in a dental setting for a change in dietary behaviour and the prevention of dental caries and erosion
- Social and lifestyle interventions for preventing low birthweight in South Asians
- Supplementary feeding with nutritional education for caregivers for promoting growth and development in young children in developing countries

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Table 1 Potential items for a public health intervention studies register

<i>Item</i>	<i>WHO Trial Registration Data Set 10</i>	<i>Potential Adaptations for Public Health</i>
1	Primary register and Trial ID#	Trial ID#
2	Date of registration in Primary Register	Date of registration
3	Secondary ID#s	Secondary ID#s
4	Source(s) of Monetary or Material Support	Source(s) of Monetary or Material Support
5	Primary Sponsor	Primary Sponsor
6	Secondary Sponsor(s)	Secondary Sponsor(s)
7	Contact for Public Queries	Contact for Public Queries
8	Contact for Scientific Queries	Contact for Scientific Queries
9	Public Title	Public Title
10	Scientific Title	Scientific Title
11	Countries of Recruitment	Countries of Recruitment
12	Health Condition(s) or Problem(s) Studied	Expanded to reflect broader scope of public health e.g. population health and social outcomes, improvements in health equity, reduction in inequalities
13	Intervention(s) (e.g.name, dose, duration and control)	Expanded to incorporate wide range of interventions, including those that are complex and multi-faceted
14	Key Inclusion and Exclusion Criteria	Key Inclusion and Exclusion Criteria eg. baseline and outcome health status/environment/behaviour data, health status data, studies which comprise intervention and comparison groups/data
15	Study Type (e.g. single arm, randomized controlled)	Expanded to include a broader range of study designs
16	Date of First Enrolment	Date of First Enrolment
17	Target Sample Size	Target Sample Size
18	Recruitment Status	Recruitment Status
19	Primary Outcome(s)	Primary Outcome(s)
20	Secondary Outcome(s)	Secondary Outcome(s)
21		Program logic or theoretical framework
22		Process evaluation methods
23		Resource use assessment and Economic impact methods
24		Impact on health inequalities
25		Sustainability considerations
26		Contextual issues (individual, school, community, organisational, structural)
27		Approval from a human research ethics committee

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