

Public health psychopharmacology: a new research discipline comes of age?

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(Accepted for publication in Epidemiology and Psychiatric Sciences – section: EPIDEMIOLOGY FOR CLINICAL PSYCHOPHARMACOLOGY. Please keep CONFIDENTIAL)

Financial support: No financial support was received for this paper from any funding agency, commercial or not-for-profit sectors.

Conflict of interest: None.

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Unstructured abstract

Research evidence guiding the identification of pragmatic and effective actions aimed at improving the selection, availability, affordability and rational prescribing of medicines for mental disorders is sparse and inconsistent. In order to boost the development of new research, in this commentary we suggest to organise and classify all the activities in this area under a common theoretical framework and nomenclature, adopting the term “public health psychopharmacology”. Public health psychopharmacology is proposed as a research discipline, based on contributions from the fields of regulatory science, health services research and implementation science. Implementing the term public health psychopharmacology may offer advantages, as the scientific community would be more focused on common goals and objectives, with, likely, an increasing body of research evidence of practical use.

Key-words: selection of medicines, availability, affordability, rational prescribing, psychotropic medicines

Main Manuscript

Appropriate use of medicines for mental disorders is a major challenge worldwide, being based on a complex interaction of different aspects, such as a functioning selection process, a dynamic health infrastructure assuring medicine availability and affordability, and an effective set of policies enhancing rational prescribing (Barbui *et al.*, 2017a). Appropriate use of medicines has been conceptualized as the expectation that individuals receive medicines that are appropriate to their clinical needs, in doses that meet their individual requirements, for an adequate period of time, and at the lowest cost to them and their community (World Health Organization, 2015a).

In order to improve access and appropriate use of medicines for mental disorders, the Gulbenkian Mental Health Platform and the WHO Department of Mental Health and Substance Abuse recently worked on the identification of a set of practical key actions to be implemented by policy makers and clinicians in charge of governing mental health systems (Barbui *et al.*, 2016). One aspect that the document clearly highlighted is the paucity and sparseness of research evidence to guide the identification of pragmatic and effective actions. As a consequence, most actions were recommended more on the basis of common sense and exemplary practice than on research findings.

Lack of an adequate evidence base needs to be properly addressed. One way to give more visibility to the existing research activities in this area, and to boost the development of new multidisciplinary projects and innovation initiatives, is to organise and classify all the research efforts aimed at increasing knowledge on aspects related to access, rational prescribing, and appropriate use of medicines for mental disorders, under a common theoretical framework and nomenclature. Here we suggest the term “public health psychopharmacology” (PHP).

PHP should be considered a research discipline. Regulatory science, health services research and implementation science may represent research areas of interest (Figure 1). For each of these research areas, challenges, aims and examples of research activities relevant to PHP may be identified (Table 1).

Insert Figure 1

Insert Table 1

A first challenge for PHP is to increase knowledge on how psychotropic medicines should be effectively selected. Research evidence is needed to help countries, regions, health districts and non-governmental organizations develop and implement effective rules governing the approval of psychotropic medicines. Examples of research areas that PHP should cover include:

- analyses of the consequences of accepting the use of placebo in conditions where active psychotropic medicines are available (Barbui and Bighelli, 2013a; Ostuzzi *et al.*, 2017), as well as ensuring appropriate doses of comparators, which was a concern with the second generation antipsychotics (Geddes *et al.*, 2000);
- the role of superiority versus non-inferiority versus equivalence designs (Barbui and Bighelli, 2013b; Garattini and Bertele', 2007);
- the potential added value of regulatory meta-analyses as an integral part of the drug approval process (Barbui *et al.*, 2017b), ideally associated with a thorough qualitative appraisal of data (e.g. by employing the GRADE approach). The inclusion of systematic descriptions of the evidence in support or against a new psychotropic medicine in public assessment reports not only would ensure transparency, but could also orientate future research in effectively addressing evidence-to-practice gaps (Barbui *et al.*, 2017b).

These regulatory themes are within the scope of PHP and should require careful research consideration (Garattini and Chalmers, 2009).

A second challenge for PHP is to increase knowledge on strategies to make psychotropic medicines available across mental health systems at affordable prices, especially in lower and middle income countries where an appreciable proportion of medical costs are out-of-pocket and illness can have catastrophic consequences on the family (World Health Organization, 2015b). Research evidence is needed to help countries, regions, health districts and non-governmental organizations develop and implement effective and sustainable policy actions (World Health Organization, 2003). Examples of research areas that PHP should cover include analyses of factors related to the development of sustainable and reliable medicine supply systems, studies on the impact of different regulation systems for psychotropic medicines recognizing that boundaries between certain classes such as first and second generation anti-psychotic medicines are becoming blurred, studies investigating measures to limit the diffusion of counterfeit or substandard or degraded psychotropic medicines, and analyses of different financing systems to ensure economic sustainability at affordable prices for the end-user. This includes making quality generic medicines available at low prices (Woerkom et al., 2012), with typically no difference in outcomes between generics and originators to reduce co-payments as an issue. Furthermore, the area of health services research may be interested in evaluating particular needs of selected settings (for example prisons, emergency or humanitarian settings), where prescriptions may be particularly high in number, used off-label with poor clinical rationale, or not supported by adequate clinical resources (e.g. laboratory tests for monitoring adverse events) (Hassan *et al.*, 2016). This would provide an evidence base for rationally addressing prescribing attitudes in settings where common guidelines do not easily apply. These health services themes are within the scope of PHP and should require careful research consideration.

Selected psychotropic medicines that are available at affordable prices should be rationally prescribed and appropriately used according to the context's features. Examples of irrational use of psychotropic medicines include prescribing or dispensing too many medicines per patient (polypharmacy), prescribing inappropriate dosages, poor adherence to correctly prescribed medications, as well as misuse, underuse or overuse (Jaracz *et al.*, 2014). At a global level, more than 50% of all medicines are prescribed, dispensed or sold inappropriately, and half of all patients fail to take them correctly (Osterberg and Blaschke, 2005). Therefore, a third challenge for PHP is to produce knowledge that may support rational prescribing and appropriate use of medicines building on initiatives such as the Essential Medicines List (World Health Organization, 2015a). A number of research activities and study designs, with the background rationale of filling the gap between the production of evidence and its uptake in practice, may be employed (Table 1) including systematic reviews of randomised or observational evidence, evidence-based guidelines, pharmacoepidemiological studies based on administrative databases, observational or randomised studies with pragmatic designs. PHP should effectively implement these research tools to discover better and more effective strategies to support physicians in optimizing the use of psychotropic medicines. We argue that more than the development of new and more effective psychotropic medicines, the greatest benefit in the next decade will derive from the generation of knowledge on how to provide better care based on current treatments.

Organising research activities on aspects related to access, rational prescribing and appropriate use of medicines for mental disorders under a common nomenclature may offer advantages. The scientific community would be more focused on common goals and objectives, with, likely, an increasing body of research evidence of practical use. International calls for funding may be interested in supporting research in the area of PHP, and scientific societies and journals might be more open to recognise the value of research in this area. Junior scientists and clinicians may

appreciate that research activities in this area, being focused on implementation and quality of care, may effectively complement clinical practice.

Ultimately, the search for a better understanding of how psychotropic medicines should be effectively selected, made available to those in need at affordable prices, and prescribed rationally, is of importance to improving mental health care of individuals with these disorders in all countries. This is the ultimate goal of PHP.

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**Table 1. Description of the main aims and research activities of public health
psychopharmacology**

RESEARCH AREA	CHALLENGE	GENERAL AIM	EXAMPLES OF RESEARCH ACTIVITIES
Regulatory science	Selection of psychotropic medicines	Improving the rules governing the approval process of psychotropic medicines	Analyses of the beneficial and harmful consequences of using placebo in conditions where active psychotropic medicines are available
			Analyses of superiority versus non-inferiority versus equivalence designs
			Analyses of the potential role of regulatory meta-analyses in the approval process for psychotropic medicines
			Analyses of the consequences of using a systematic description of the evidence in support or against a new psychotropic medicine in public assessment reports
Health services research	Availability and affordability of psychotropic medicines	Improving timely obtainability of psychotropic medicines in the mental health system at affordable prices	Analyses of factors related to the development of sustainable and reliable supply systems
			Development of studies on the beneficial and harmful consequences of different regulation systems for psychotropic medicines
			Epidemiological studies on factors associated with counterfeit or substandard or degraded psychotropic medicines
			Analyses of health system factors related to distribution strategies to reach those in need
			Analyses of different financing systems to ensure economic sustainability for the health system
			Epidemiological analyses of different policies for affordable prices for the end-user

Implementation science	Appropriate use of psychotropic medicines	Improving rational prescribing and appropriate use of psychotropic medicines	Production of systematic reviews of randomized and observational studies
			Development of evidence-based guidelines and recommendations
			Analyses of administrative information systems to monitor trends in psychotropic medicine prescribing and to establish associations between medicine exposure and outcome variables
			Development of training and education activities, including audit and feedback initiatives
			Development of epidemiological and pragmatic intervention studies on the beneficial and harmful consequences of psychotropic medicines

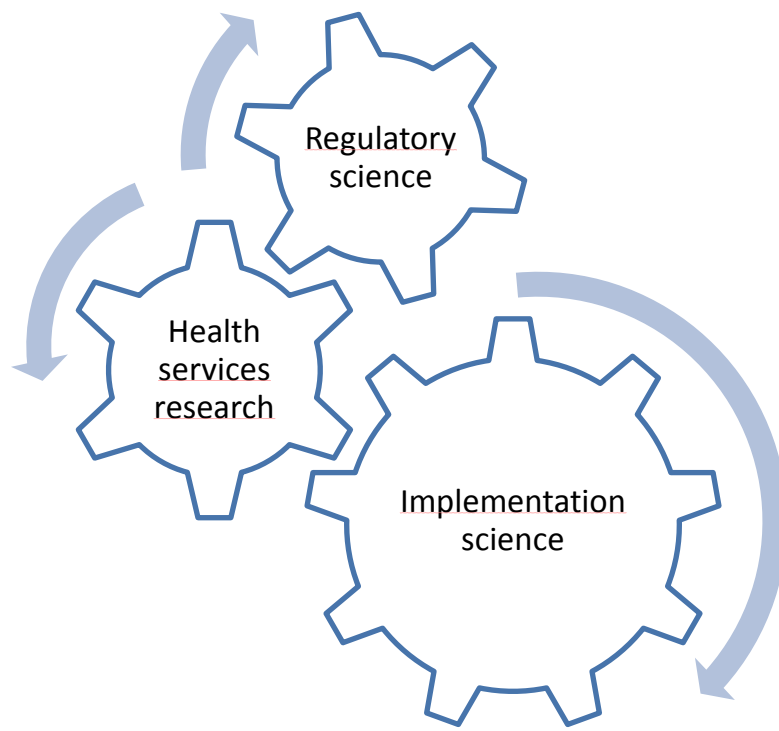


Figure 1. Research areas of interest for public health psychopharmacology