ELSEVIER

Journal of Clinical Epidemiology ■ (2018) ■

Journal of Clinical Epidemiology

ORIGINAL ARTICLE

A mapping of 115,000 randomized trials revealed a mismatch between research effort and health needs in non−high-income regions

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Accepted 15 January 2018; Published online xxxx

Abstract

Background: Concerns exist as to whether the allocation of resources in clinical research is aligned with public health needs. We evaluated the alignment between the effort of clinical research through the conduct of randomized controlled trials (RCTs) and health needs measured as the burden of diseases for all regions and a broad range of diseases.

Methods: We grouped countries into seven regions and diseases into 27 groups. We mapped all RCTs initiated between 2006 and 2015 that were registered at the WHO International Clinical Trials Registry Platform to regions and diseases. The burden of diseases in 2005 was mapped as disability-adjusted life years (DALYs), based on the 2010 Global Burden of Diseases study. Within regions, we defined a research gap when the proportion of RCTs concerning a disease in the region was less than half the relative burden of the disease.

Results: We mapped 117,180 RCTs planning to enroll 42.6 million patients and 2,220 million DALYs. In high- versus non−high-income countries, 130.9 versus 6.9 RCTs per million DALYs were conducted. We did not identify any research gap in high-income countries. We identified research gaps for all other regions. In particular, for Sub-Saharan Africa, we identified research gaps for common infectious diseases (CID) and neonatal disorders (ND): 5.8% (95% uncertainty interval 4.7−6.9) and 2.0% (0.9−4.5) of RCTs in Sub-Saharan Africa concerned CID and ND, although these diseases represented 22.9% and 11.6% of the burden in the region, respectively. For South Asia, we identified research gaps for the same two groups of diseases.

Conclusions: In non−high-income regions, the conduct of RCTs was misaligned with the distribution of major causes of burden, in particular infectious diseases and neonatal disorders in Sub-Saharan Africa and South Asia.

Keywords: Clinical trials; Burden of diseases; Mapping; Research priorities; Research gaps

1. Introduction

The conduct of clinical trials, in particular randomized controlled trials (RCTs), helps creating evidence on the efficacy and safety of health interventions. Conducting RCTs worldwide might be particularly of interest to increase the external validity of treatment effects or to find local solutions when known solutions are not efficient or applicable in specific settings [1]. Concerns have been raised regarding the alignment of the allocation of clinical research and public health needs [2,3]. Clinical research activities, and in particular the conduct of RCTs, may be driven by specific interests or constraints that may differ from local health priorities [4]. Although not encompassing all types of clinical research effort, a comprehensive mapping of RCTs may be helpful to understand the processes guiding clinical research, and to steer limited resources toward local health priorities, particularly in low-resource settings [2,5].

Several studies have shown that research is lacking in low-income countries [6,7] and that diseases receiving the most research attention are those that are predominant in

Funding: This work did not receive any specific grant.

Conflict of interest: All authors declare no conflict of interests.

Ethical approval: Not applicable for this study. The study only used data concerning the design and settings of clinical trials retrieved from publicly accessible clinical trial registries, and national-level aggregated database of the burden of diseases from publicly accessible databases.

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https://doi.org/10.1016/j.jclinepi.2018.01.006
0895-4356/

What is new?

Key findings

- We showed that in high-income countries, the distribution of the number of randomized controlled trials (RCTs) conducted across diseases was aligned with burden of diseases measured as disability-adjusted life years. In all other regions, we identified local research gaps relatively to the burden.
- For Sub-Saharan Africa, highly prevalent diseases as HIV and malaria were receiving high research effort, but other major causes of burden remain neglected by research effort, in particular common infectious diseases and neonatal disorders.

What this adds to what was known?

- We highlighted research gaps for regions and diseases not stated elsewhere, in particular concerning common infectious diseases and neonatal disorders in South Asia, and cardiovascular and circulatory diseases in Eastern Europe and Central Asia.

What is the implication, what should change now?

- Research gaps may be considered by local funders or health authorities to drive research toward local needs. Further analyses are now needed to identify what research type is more likely to help reducing the largest amount of burden.
- We may know efficient and safe solutions in high-income countries for health conditions such as common infectious diseases and neonatal disorders. Nevertheless, these conditions cause a high burden in low-resource regions such as Sub-Saharan Africa and South Asia and are understudied by local RCTs. There is a need for finding local solutions through the conduct of RCTs.

high-income countries [2,8]. Other studies have suggested that in low-income regions such as Sub-Saharan Africa, the conduct of RCTs is aligned with the burden across diseases [9]. However, previous studies focused on specific regions or specific diseases, and a global-scale analysis may bring novel insights.

We evaluated the alignment between the research effort (measured as the number of RCTs conducted) and the burden of disease across all world regions and a broad range of diseases. Within each region, we estimated the research effort across diseases and identified the diseases for which the research effort was too low as compared with the burden they cause. At a global level, for each disease, we estimated the research effort across non−high-income regions and identified the regions for which the research effort was too low as compared with the regional disease burden.

2. Methods

We compared the effort in clinical research to the health needs across regions and diseases. The number of RCTs was used to measure the research effort, and the burden of diseases to measure health needs. By using clinical trial registries, we mapped the RCTs initiated between 2006 and 2015 to seven regions and 27 groups of diseases. By using the 2010 Global Burden of Diseases (GBD) study [10], we mapped the burden in 2005. For each region, we analyzed the distribution of the research effort across groups of diseases and identified diseases for which the regional effort of research was lacking as compared with the regional burden. For each group of diseases, we analyzed the distribution of the research effort across regions, excluding high-income countries, and identified regions for which the disease-specific effort of research was lacking as compared with the disease burden.

2.1. Mapping the effort of clinical research

We downloaded all records of clinical trials registered in the World Health Organization International Clinical Trials Registry Platform (WHO ICTRP) by January 1, 2016 [11]. We identified RCTs according to the study type and study design fields of the trial records (e.g., by excluding observational and nonrandomized trials, see Supplementary Information on the journal's web site at www.elsevier.com). Because the International Committee of Medical Journal Editors recommended registration before considering interventional trials for publication since September 2005, we restricted our analyses to RCTs enrolling the first patient after January 2006 [12].

Country locations were extracted from the clinical trial records. We categorized countries into seven epidemiological regions defined in the 2010 GBD study: high-income countries, Latin America and Caribbean, Eastern Europe and Central Asia, South Asia, Southeast and East Asia and Oceania, North Africa and Middle East, and Sub-Saharan Africa. Countries not included in the 2010 GBD study were excluded.

We classified RCTs in terms of 27 predefined groups of diseases [13]. RCTs were classified automatically by using a knowledge-based classifier that was validated by comparing automatic and manual classifications for an external test set of 2,763 trials [13]. Trials classified for none of these disease groups may have studied nondisease contributors to morbidity (injuries), health conditions considered not relevant for burden estimation by the 2010 GBD study (e.g., pain management), or residual causes of burden excluded from the 27-class grouping [10].