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Are public-private partnerships the solution to tackle neglected tropical diseases? A systematic review of the literature

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ABSTRACT

Pharmaceutical companies are reluctant to invest in research and development (R&D) of products for neglected tropical diseases (NTDs) mainly due to the low ability-to-pay of health insurance systems and of potential consumers. The available preventive and curative interventions for NTDs mostly rely on old technologies and products that are often not adequate. Moreover, NTDs mostly affect populations living in remote rural areas and conflict zones, thereby hampering access to healthcare. The challenges posed by NTDs have led to the proliferation of a variety of public-private partnerships (PPPs) in the last decades. We conducted a systematic review to assess the functioning and impact of these partnerships on the development of and access to better technologies for NTDs. Our systematic review revealed a clear lack of empirical assessment of PPPs: we could not find any impact evaluation analyses, while these are crucial to realize the full potential of PPPs and to progress further towards NTDs elimination.

1. Introduction

Neglected tropical diseases (NTDs) are a diverse group of communicable diseases that affect more than one billion people, mainly across the developing world. The World Health Organization (WHO) lists 17 NTDs: Buruli Ulcer, Chagas disease, Dengue, Chikungunya, Dracunculiasis (guinea-worm disease), Echinococcosis, Endemic treponematoses, Yaws, Human African trypanosomiasis (sleeping sickness), Leishmaniasis, Leprosy, Hansen disease, Lymphatic filariasis, Onchorcerciasis (river blindness), Rabies, Schistosomiasis, Soil-transmitted helminthiases, Taeniasis, Cysticercosis, Trachoma [1]. It is common for people infected with NTDs to be hit by multiple pathogens; impairing physical and cognitive development, and leading to an estimated 534,000 death yearly [2]. These diseases were associated with 26.06 million disability adjusted-life years (DALYs) [3]. NTDs have a serious impact on work productivity: the largest of which seems to be due to blindness from onchocerciasis and severe manifestations of schistosomiasis [4]. Overall, these 17 diseases have been estimated to cost billions of dollars to developing economies each year [3].

The development of new treatments and vaccines cannot be incentivized through the usual patent system, for the ensuing reasons. First, the patent system grants monopoly power to pharmaceutical companies, usually for a period of 20 years, to encourage investment in research and development (R&D). The resulting lack of competition enables pharmaceutical companies to recoup R&D investment costs by setting a market price well above the marginal cost of production. Pharmaceutical companies are hence reluctant to invest in R&D for diseases that predominantly affect low and middle-income countries (LMICs) because of the health insurance system and consumers' reduced ability-to-pay. Second, as LMICs are often characterized by poor local infrastructure and sanitation, lack of political commitment and bad governance in the health sector, lack of drug safety harmonization and weak legal frameworks, there can be no guarantee that a developed product will necessarily reach the population in need, thereby discouraging investment in R&D [5–7].

Translating this market failure into real facts, only five new therapeutic products were approved for NTDs between 2000 and 2011, accounting for less than 1% of the total products approved (i.e. 5 products out of 850). A significant share of the newly approved products instead targeted neuropsychiatric disorders (13%) and

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cardiovascular diseases (10%) [8]. This issue was pointed out by Bill Gates who, in 2008, called for "creative capitalism" [9], which include push, pull and mixed (push-pull) schemes. Push schemes reduce upfront costs inherent to R&D activities through various grants and subsidies offered prior to product discoveries – examples include R&D grants and direct funding. Pull schemes, on the contrary, offer a variety of rewards that are contingent on successful product discoveries – examples include advance market commitment (AMC) and priority review voucher (PRV). Push, pull and mixed schemes offer avenues for PPPs to overcome the barriers to the development of products for NTDs.

In 2011, half of the 34 new formulations for NTDs in clinical development – of which 85% were in Phase 2 or 3 – were sponsored through PPPs, charities, foundations and philanthropic institutions [8]. PPPs, so far, have mainly used push schemes, with government (e.g. The United Kingdom Department for International Development) or philanthropic (e.g. Bill and Melinda Gates Foundation) bodies providing upfront financing for clinical trials. The role of PPPs mainly lies in product development (PDPs; e.g. The Drug for Neglected Disease Initiative (DNDi)) and in product delivery and uptake (Access PPPs; e.g. The Onchocerciasis Control Program (OCP)). Other types of PPPs include financing and coordinating partnerships [10]. The different types of partnerships are not mutually exclusive: while it is more common for partnerships to dedicate themselves to one particular role, some use a hybrid model [10].

Tackling NTDs has become a major goal subscribed by the international community: the London Declaration – signed in 2012 – aims to reach the control or elimination of at least 10 NTDs by 2020 [11]. Various PPPs, with differing models, have hence been put in place to achieve this objective [12]. These have expanded over the past 20 years, and for some, the impacts are now measurable. Accordingly, we believe that it is now within researchers' reach to assess the effectiveness and impact of these alliances. We thus conducted this review to respectively: (i) assess the scientific opinion on the adequacy and viability of PPPs; (ii) identify potential best mechanism(s) between push, pull and mixed ones; (iii) map the different partnerships and analyze their role in reaching the globally set goal to control, eliminate or eradicate NTDs.

2. Study data and methods

2.1. Search strategy and selection criteria

A systematic literature search on PPPs for NTDs was performed over three databases: a general (Scopus), a bio-medical (PubMed) and an economic (IDEAS – Research Papers in Economics, REPEC) database. The search was conducted over three different databases to capture the multidisciplinary facets of PPPs. The REPEC database, for instance, enabled us to capture the economic perspective – a crucial feature – of PPPs and hence of the push, pull and hybrid mechanisms. In order to not discard any initiatives (e.g. Onchocerciasis Control Program was launched in 1974), we searched for peer-reviewed articles published between – and as far as – January 1970 and August 2016 in English or French using the following search terms: (public-private partnership* OR public private partnership* OR PPP* OR product-development partnership* OR product development partnership* OR PDP*) AND (neglect* tropical disease* OR neglect* disease* OR each NTD of the WHO list). We first screened the "titles", "abstracts" and "keywords" of all extracted records. We then read the full text articles to evaluate them according to our inclusion criteria. The titles and abstracts of the extracted records were independently reviewed by two investigators (CA&TS). Records were excluded if, PPPs (i) were only mentioned in the conclusion or as a recommendation; (ii) focused on diseases that are not on the World Health Organization (WHO) NTDs list; (iii) considered NTDs of the WHO list but not for human species. Additionally, editorial material such as interviews, forum/symposium and round table discussion, comments and profile articles were excluded. All the remaining records were included in the review. If discordances occurred, they were resolved through discussions with a third investigator (ES); who would retrieve the full text in case of a doubt. The full text papers were then classified into three categories; based on the nature of their content:

- Descriptive studies of PPPs context
- Descriptive studies of PPPs experiences
- Empirical studies

'Descriptive studies of PPPs context' review the weaknesses and strengths of the push, pull and mixed schemes. These were scrutinized tabulating the following features (cf. Table V in appendix): scheme(s) or type(s) of partnership discussed; associated drawback(s); recommended scheme(s) or partnership(s); associated advantage(s); policy recommendation(s); and whether the paper mentions elimination. 'Descriptive studies of PPPs experience' report the existence, main characteristics, achievement and limitations of PPPs. These were analyzed tabulating the following aspects (cf. Table VI in appendix): name of the PPP and year of creation; partners; disease(s); tool(s) used; what is the PPP resolving at; the outcome of the PPP; the limitation(s) of the PPP; and whether the paper mentions elimination. 'Empirical studies' had a concise research purpose that was addressed via data-based analyses (qualitative and/or quantitative). These were examined tabulating the following features (cf. Table VII in the appendix): research question; methodological approach; main finding(s); limitation(s) of the study; and whether the paper mentions elimination.

3. Results

The search resulted in 198 non-duplicate articles, among which 6 could not be accessed. After abstract screening and full-text review, 74 articles were assessed eligible (cf. Fig. 1 for PRISMA diagram).

3.1. Descriptive studies of PPPs context

3.1.1. Push schemes

Push schemes have been heavily criticised in the literature. First, since push schemes subsidize research input and not research output, they may finance unsuccessful R&D activities [13]. Second, they tend to suffer from a moral hazard and adverse selection problem [5,14]. Moral hazard arises due to asymmetric information between grant recipients and donors. Since donors know less than grant recipients about the success probability, cost and evolution of the project, they cannot perfectly monitor the activities of grant recipients. The effectiveness of the program can then be jeopardized if grant recipients have differing incentives from donors. Accordingly, donors are faced with the issue of picking the 'right' grant recipient. Common examples of push schemes are R&D grants, R&D tax credit and patent pools – which are described in Table 1.

So far, push mechanisms have been advocated to decrease the costs of R&D for NTDs: mostly to stimulate investment in early phases (i.e. basic research) providing a basis for later applied research. Nevertheless, some may argue that the cost of R&D per se does not explain the market failure attributed to these diseases. Pharmaceutical companies often make risky and expensive investment in products for which they beleive in having a market [15]. Accordingly, the unviable market attractiveness of NTDs, relative to the cost and risk of R&D investment, is a potentially more credible barrier than the cost of R&D per se [15]. This would suggest that