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Roundtable: How Can Disclosing Clinical Trial Costs Increase Access to Medical Products?

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Speakers:

- Benjamin J. Smith - Chief Health Counsel, U.S. House of Representatives, Committee on Oversight & Reform
- Professor Glenda Gray - President & CEO, South African Medical Research Council (SAMRC)
- Matheus Falcão – Health Analyst, Brazilian Institute for Consumer Protection (IDEC)
- Rachel Cohen - US Executive Director, Drugs for Neglected Diseases Initiative (DND*i*)

Moderator: Yannis Natsis – Director, European Social Insurance Platform (ESIP)

Background and rationale

High prices for medicines, vaccines and diagnostics are often justified by the pharmaceutical industry with claims that it costs billions in research and development (R&D) to bring them to market. However, companies do not routinely disclose how much they actually spend on R&D in any detail. Clinical trials are widely regarded as the most expensive part of this process, yet the costs of clinical trials are rarely made public even when they are funded by the public sector. Making clinical trial costs public would help determine the true cost of late-stage clinical research, inform evidence-based decision making and policy development, and enable governments and treatment providers to regulate and negotiate prices more effectively.

As we start to learn lessons from the COVID pandemic, there are a number of multilateral initiatives that aim to improve global collaboration and coordination related to the development of and access to lifesaving medical products. One of these is the resolution on clinical trials that was tabled and adopted at the World Health Assembly (WHA) 2022. While this initiative aims to strengthen the coordination of clinical trials, avoid duplication of efforts and encourage timely publication of data, the resolution missed the opportunity to mandate reporting of clinical trial costs, including those funded by the public sector.

The 2019 WHA transparency resolution (WHA 72.8) on "improving the transparency of markets for medicines, vaccines and other health products" urges member states to take steps to enhance dissemination of, and access to, the costs of clinical trials. Legislation is also beginning to emerge in a number of countries with a focus on disclosure of R&D costs, including in the US and Brazil. Work is also being done to define how clinical trial costs can be captured on a practical level, and what data are needed.

To build on these initiatives and highlight the importance of clinical trial cost transparency for access to medical products, the MSF Access Campaign hosted a roundtable on 17 May 2022, in the week leading up to the 2022 WHA. This report summarises the themes of the discussion and provides key recommendations from the roundtable.

Key themes and recommendations

1. Clinical trial costs are largely unknown

All participants noted that the pharmaceutical industry claims that high prices for medical products are justified due to the high costs of R&D, and that clinical trials are the most expensive part of this process.

However, there was also agreement that there is a lack of evidence for these claims, in particular for what clinical trials actually cost.

Benjamin Smith highlighted some of the work done in the US by the House Committee on Oversight & Reform in scrutinising the evidence that is available, which does not support the claims made by industry. "*Over the course of five hearings and eight reports, and based on our review of hundreds of thousands of internal company documents, the committee revealed that the justifications that are frequently offered by the pharmaceutical industry for high prices, which include R&D, manufacturing and other costs, were simply not supported by the data,"* he said.

Matheus Falcão expanded on this, especially in relation to clinical trials being cited as the most expensive part of the R&D process. Falcão stated that cost transparency would reveal the true costs of clinical trials, and would also help determine the level of public funding. "*It would confront companies on this point that they always make that they have to charge this very high price because they invested in innovation, they paid for the clinical trials. We don't know if that is true, we don't know how much a clinical trial really costs, we don't know much the company put forward of its own resources in these clinical trials because there is a lot of public funding,"* he noted.

2. Where public money has funded clinical trials, the costs should be publicly disclosed

All participants stressed that particularly where public money has funded clinical trials, the costs of these trials should be disclosed and publicly available. This was seen as being important for transparency, accountability, and to ensure public return on public investment. Professor Glenda Gray said, *"It is critical for funding information to be publicly available, especially when trials have been funded from government organisations.*"

The role of the US National Institutes of Health (NIH) as the biggest global funder of clinical trials was discussed at length, including the potential impact of attaching conditions to NIH funding to ensure transparency of clinical trial costs and access to successful products. Gray used the case of long-acting cabotegravir (CAB-LA) for pre-exposure prophylaxis (PrEP) for HIV as an example. "*We know the cost of long-acting PrEP will be US$2,400, and that the NIH bankrolled the clinical trial development. So why something that is going to help control HIV at a global level and in particular in low and middle-income countries, is so expensive is hard to understand. It is hard to understand the exit price when federal funding has bankrolled it. So I think it is in the public interest to share this information.*"

Gray specifically acknowledged that collecting data on clinical trial costs is not enough in itself; this information needs to be made public to ensure accountability and inform evidence-based policy discussions for clinical trial funding. *"South African Good Clinical Trials guidelines say that an investigator must disclose costs to the research ethics commitee and the sources, but it does not really talk about public disclosure. This leads to a lack of disclosure and a lack of assimilation of costs."*

In order to achieve more transparency in clinical trial costs, attaching conditions to public funding for clinical trials was raised multiple times, including how this could then affect prices and access to these products. This was cited by Rachel Cohen as a critical step if we are going to "*shift our approach*" and "*learn our lessons… to ensure equitable access globally for all".* Agreeing with Cohen, Gray added "*Particularly when federal or public money is used for clinical trials, there should be some kind of agreement between the public funding (agency) and the pharmaceutical company that protects the cost of goods should the vaccine or the drug be successful."*

3. Learning from clinical trial costs that are made public now

Cohen highlighted that DND*i* publish their own figures of what it has cost them to develop the twelve treatments they have delivered to tackle neglected tropical diseases (NTDs) in recent years. DND*i* consider transparency, including of clinical trial costs, to be an important principle because most of their funding is

from governments or philanthropic organisations. They are transparent about the way they use these funds in order to *"build trust and understand what it means to have a public return on public investment in R&D,*" she said.

"For new formulations or new combinations of existing drugs, it has cost us between EUR4-10 million (raw figure)/EUR4-12 million (with attrition), and for a new chemical entity, it has cost between EUR45-70 million (raw figure)/EUR60-190 million (with attrition)," she noted. While these figures are for the full R&D process, Cohen explained that DND*i* break down their costs by product type, including the costs of developing a new formulation or combination of existing drugs vs a new chemical entity, and also by R&D stage – early discovery, translational research and then late-stage clinical trials (phase 2 and 3 plus registration). They report raw figures and, to the extent possible and with a specific methodology, attrition.

Cohen stressed that while the DND*i* figures cannot be considered an "*apples to apples comparison"* with figures that are often cited by industry because there are many methodological and other technical differences, they do show an *"order of magnitude difference when comparing this real-life costing data with some of the industry estimates that are out there."* They also help identify some of the main cost drivers and areas of potential savings.

R&D costs, including industry estimates, for the development of new drugs range widely, from US$43.4 million to $4.2 billion. Without full transparency of R&D costs from drug developers, it is not possible to determine the true costs of each stage of the R&D process for each drug, the total R&D cost, and which of these costs are related to clinical trials.

4. The impacts of knowing clinical trial costs

Informing policies and evidence-based decision-making

Disclosing true clinical trial costs was discussed as a way to improve policy and decision-making guided by evidence. Specifically, it would provide the evidence and data needed for governments and others to make informed decisions about how much and where to invest in clinical trials. As Cohen said, "*Clinical trial cost transparency is critical because it is the only way to have a better sense of what a realistic range is to help governments make decisions about the level of their financial investments*" as well as to "*maximise these investments*" for impact and access.

Gray talked about how knowing the costs of clinical trials, including the per participant cost in South Africa, helps work towards equity across trial sites, and aims to prevent inflated spending. *"The SAMRC scrutinise the budget, and homogenise the costs of the trials that we fund so we know and work out a reasonable per-participant trial cost and have a band around it. This ensures there is equity at clinical trial sites in South Africa and that there is no competition or people that are loading their budgets,"* she said.

Promoting innovation

A lack of transparency on clinical trial costs may be deterring investments in clinical trials, as they may be seen as being too expensive. Knowing the true costs could therefore incentivise clinical trial investments by governments and other actors. The US House Committee on Oversight and Reform concluded in its review that cost transparency would incentivise innovation, Smith said. "*Requiring drug companies to report overall R&D expenditures as well as disaggregated costs for individual clinical trials…would provide valuable data on companies' investments in pharmaceutical innovation, enable detailed evaluation of pharmaceutical industry claims about R&D expenditures and form future policies to inform meaningful innovation. It would increase and promote transparency while also increasing and promoting innovation in the drug space,*" he added.

Price negotiation

The impact of transparency of clinical trial costs on the ability of governments and other procurers of medical products to negotiate prices was also discussed. Where clinical trial costs are not known, even if there has been public investment partially or fully, it is difficult to challenge high prices. Pharmaceutical companies argue that these high prices are needed to "recoup" investments in R&D, in particular for the costs of clinical trials. There are two key challenges: the overall clinical trial costs are not known, and it is not known how much was invested in the clinical trial by the company vs the public/other investors. On this point, Gray said, *"it is important for us to understand the commitment of government funding because that should influence the cost of goods at the end, because if public funds have bankrolled all the risk there is no reason why these drugs or vaccines are priced at a certain value."*

Falcão argued that price negotiation/regulation was one of the biggest potential impacts of transparency of clinical trial costs. He said, *"With transparency, we would have a clear view and perspective (on clinical trial costs), and this would provide better bargaining power for governments to confront companies on their prices*." He noted that transparency of costs would help address the issue of excessively high prices because these would not be justifiable based on the true costs of development.

Falcão also observed that transparency of clinical trial costs could be impactful for price regulation, particularly where there is a lack of competition. *"When we consider a company with a monopoly, they would say that they have to charge high prices because of the investment in innovation and clinical trials. This is why adding some requirements on transparency of clinical trial costs would give governments better bargaining power,"* he said. This is very relevant to tackle access challenges that we are seeing for new products and technologies, including genetic therapies, monoclonal antibodies or biotechnological drugs, where it can be more challenging to ensure competition. These are areas where it would be "*interesting to explore drug pricing regulation and transparency as mechanisms to reduce prices and increase access."*

Accountability

There was broad acknowledgement that transparency of clinical trial costs is needed for accountability, particularly where public funding is involved. Gray noted that in South Africa, data on clinical trial site costs is collected through the South African Clinical Trial Registry, and is required to *"inform the spending on clinical research in South Africa by the national Department of Health. We can also use these data to understand the budget spending on different types of trials and trends in financing over a period."*

While information related to clinical trial costs is critically important for governments and funders in order to inform decision making, clinical trial costs should also be made publicly available to ensure there is accountability for how public money has been spent, trial outcomes and how this translates into access to the final products if successful.

5. Other mechanisms for achieving transparency of clinical trial costs

There was some discussion about the different mechanisms for mandating transparency of clinical trial costs beyond attaching conditions to public funding for clinical trials. Highlighting the different options that have been explored in Brazil, Falcão suggested three routes to achieve transparency of trial costs.

First, transparency could be made a requirement for the act of registering a medical product. "*In order to get market approval, companies would have to disclose data on a few items, which we call transparency requirements*," he said. He highlighted that there are already some transparency requirements in Brazil, for example, on manufacturing costs, but more transparency is needed on the innovation side, including clinical trial costs and R&D costs more broadly.

Second, he said it is possible to add transparency requirements to the act of procurement, *i.e.*, when the Ministry of Health is procuring medicines, they could require information about clinical trial costs as a condition before procurement.

Finally, Falcão pointed to anti-trust authorities as another mechanism for obtaining information on clinical trial costs. He explained that this is related to the process for filing a complaint about the price of a drug (e.g., sofosbuvir in Brazil for hepatitis C). *"It is possible to ask the anti-trust authority to mandate that the company disclose their R&D costs for this drug because this is the main argument they use to justify the price,"* he said.

In South Africa, some information on clinical trial costs is collected by the South African Clinical Trial Registry but is not currently made public. In the US, the legislation introduced by the House Committee on Oversight & Reform would require pharmaceutical corporations and other drug developers to disclose the costs of future clinical trials in a public, searchable cost data repository linked to the website (ClinicalTrials.gov) where trial results are currently published publicly. If passed, it would also mandate that drug manufacturers report disaggregated clinical trial costs in their annual securities filings.

Recommendations

- Governments should introduce legislation to mandate disclosure of clinical trial costs by pharmaceutical corporations as well as other drug developers. Costs should be published in a publicly available and accessible format.
- Conditions should be attached to public funding of clinical trials to ensure full public disclosure of the costs.
- Other mechanisms should be explored to increase transparency of clinical trial costs, including making it a requirement for market approval, as a condition for procurement, and through anti-trust authorities.
- The WHA clinical trial resolution and the upcoming "Best Practices document" should contain explicit requirements for public disclosure of disaggregated clinical trial costs.
- Clinical trial cost transparency should be included in the Pandemic Treaty currently under negotiation at the WHO, within a broader chapter on transparency as it relates to pandemic response and access to health products.