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Playing vaccine roulette: Why the current strategy of staking everything on Covid-19 vaccines is a high-stakes wager

Keywords: Covid-19; vaccine; health policy

Highlights:

- The global community has disproportionately invested in vaccines to fight Covid-19
- This is at the expense of alternative strategies and health system strengthening
- Social determinants and co-morbidities should be factored as part of any response strategy
- Risk-benefit analysis and the precaution principle should guide vaccination policy
- A more diversified response to Covid-19 and future diseases should be adopted

Introduction

Many high-income countries and international institutions have bet the proverbial farm on the quick development of a vaccine to respond to the Covid-19 pandemic, implementing measures such as lockdowns and personal restrictions as delaying options while waiting for the vaccine -with enormous collateral damage in terms of increased poverty, intra-familial violence, mental health, undiagnosed health conditions, poor follow-up or lack of treatment [1]. By early July 2021, it was estimated that US$12.445 billion had already been awarded for vaccine development, a large part from public resources [2]. International Covid-19 funding was overwhelmingly dedicated to vaccines, at the expense of other strategies. Take the example of the Access to Covid-19 Tools (ACT) Accelerator, a 'global collaboration of the world's top international health organisations working together to accelerate the development, production, and equitable delivery of Covid-19 tests, treatments, and vaccines'. The overall aim of ACT-A is 'to speed up an end to the pandemic by supporting the development and equitable distribution of the tests, treatments and vaccines the world needs'. As of 9 July 2021, public and private donors had already pledged over US$12.2 billion to COVAX (the vaccines pillar of the (ACT) Accelerator) [3]. By contrast, very little has been invested in the search for treatment, or for health system strengthening, or system readiness, especially in terms of enhancing primary care, human resources, and training.

Table 1 shows the estimated needs (targets) and pledges to the ACT Accelerator along its four pillars as of 9 July 2021. The vaccine pillar received 84% of confirmed financing, leaving the pillar with a gap of 7% of estimated needs. This contrasts with the three other pillars, which face a funding gap of 82% (therapeutics), 89% (diagnostics) and 91% (health system) of needs, respectively. What this suggests is that the Covid-19 response policy remains fixated on vaccines, where all other bets are off.

Table 1 : Estimated needs and commitments to the four arms of the ACT Accelerator as of 19 February 2021

Billion US$	Diagnostics Pillar	Therapeutics Pillar	Health Systems Connector	Vaccine Pillar
Revised Budget, 12 March 2021 (*% of total)*	9.7 (*29%)*	3.9 *(12%)*	7.9 *(24%)*	11.7 *(35%)*
Confirmed (% of total)	1 *(7%)*	0.8 *(6%)*	0.6 *(4%)*	12.2 *(84%)*
Gap (% of budget)	89%	82%	91%	7%

Source : Authors, based on ACT-Accelerator Commitment Tracker [3]

Here, we do not question the principle of immunisation, particularly immunisation that prevents disease transmission and infection, which has led to undisputable successes in many areas and is, overall, 'one of the best health investments money can buy' [4]. Moreover, it would be churlish to dismiss the unprecedented feat and pace of development of anti-Covid-19 vaccines. The vaccines approved to date have proven to be safe and very effective – at least in the short run [5–10]. This gives the world hope that the pandemic can ultimately be controlled.

Yet, at this point, we do not readily accept the majority narrative that we've hit the jackpot through vaccines. Here, we argue that the current strategy of staking everything on vaccines, without sufficient hindsight on its risk-benefit ratio, and at the expense of complementary strategies (treatment, health system strengthening, non-pharmaceutical prevention, promotion of safe conditions that prevent transmission, and healthy lifestyles), was – and may still remain – insufficient, reactive, short-sighted, and an unnecessary high-stakes wager that is tempting fortune. Below, we highlight a number of limitations of the "vaccine-focused" strategy, and

discuss the lack of complementary strategies. We conclude by proposing avenues for designing a more balanced and risk-adverse Covid-19 response policy.

Remaining uncertainties about the vaccine gamble

First, many unknowns remain as for the medium-term performance, including sustainability, of the Covid-19 vaccine strategy. The efficacy of candidate vaccines has been determined through randomised controlled clinical trials (RCTs), coined the gold standard in clinical designs for their high internal validity. Yet, context is essential when interpreting the results of any randomised trial [11] because no intervention acts on two persons in an identical fashion, and results are influenced by individual risk factors [12]. Moreover, the criteria used by clinical trials to evaluate Covid-19 vaccine efficacy were not fully relevant for managing the pandemic [13,14]. Considering the extremely diverse patterns of SARS-CoV-2 epidemiology, it is feasible that RCTs are limited in their capacity to comprehend the complexity of the interaction between each patient, their immune system, and the vaccine. As a result, policy that bets heavily on post-facto pandemic vaccine discovery, RCTs, and expedited approval processes, risk to be too standardised to accommodate for various subgroups' specificities, like pregnant women or ethnic minorities [15,16], and therefore risks being suboptimal. As one example, problems have emerged for people with serious allergies, who were vaccinated with severe side-effects, but who were later discovered to be excluded from the Pfizer clinical trials, leaving clinicians in the UK unprepared [17].

We contend that the precautionary principle should be applied since the balance between the risks and benefits of SARS-CoV-2 infection vs. new vaccines is not only largely unknown over the medium term, but also extremely variable, in the short term. For example, variability from one age decadal to another, from one individual to another (with differential expected risks from Covid-19 – thus, expected vaccine benefits – sometimes bigger than 10,000 to 1) – and even from one vaccine to another [18]. Most infected people do not develop symptoms and,

although we do not yet know the long term implications of infection, it is estimated that Covid-19 infection fatality rates in people under 70 years of age turns around 0.05% [19]. Immunisation is generally justified on the grounds of preventing transmission to a significant share of susceptible groups and as a means to ensure herd immunity. Even if preliminary data from several countries are quite encouraging [20–22], it is still unclear whether the Covid-19 vaccines will deliver the outcomes that really matter, namely, long-lasting protection, reduction in mortality and the occurrence of transmission (for herd immunity) [13,23]. In the case of Pfizer and Moderna, the vaccine trials were unable to determine the exact duration of immunity to severe disease beyond six months nor the potential frequency of additional booster doses (Pfizer has already started to suggest that boosters are needed just eight months since mass vaccinations began), representing a further gamble within a process where there are concerns about protocol adherence, data quality, proper reporting and overall effectiveness [15]. There are already indications that current vaccines are less effective against some SARS-CoV-2 variants [24,25], that countries with high vaccination coverage may still experience surges in SARS-CoV-2 infections [26], and that herd immunity may not be reached [27]. This is of particular concern for vaccines that could entail short-term risks and long-term adverse impacts [28], especially due to the fact that gene therapy vaccines are new platforms, not yet tested through mass vaccination campaigns.

We also contend that given the unknowns about the potential of Covid-19 vaccines to be effective against variant strains, to reduce mortality, and to prevent transmission – whereas long-term adverse effects of these vaccines of are also unknown – there are arguments to pursue an immunisation policy that is targeted on high-risk populations (e.g. old people, people with comorbidities and healthcare workers), rather than mass vaccination campaigns. This also means avoiding copy-paste vaccination policies from other countries, rather adapting policy to each context in terms of population structure, vaccine acceptance, system capacities and epidemic timing [29].

Given the complexities in sense-making, it is curious to observe how immediate claims in vaccine safety have been made – with assertions as strong as “there is no question that the current vaccines are effective and safe” [30] – while vaccine hesitation is high worldwide [31], while some rare scientists warn against potential negative side-effects [28,32] and while, by definition, with such a short observation period, no one actually has any idea of medium- and long-term effects of Covid-19 vaccines. This threatens to escalate knock-on risks associated with public vaccine hesitancy – which is already present with Covid-19 vaccines [33,34], but which could also spill over to undermine trust in other well-proven, effective and efficient vaccines.

Need of complementary strategies

Beyond the questions about efficacy, a particularly worrying gamble relates to real-life vaccine effectiveness and equity. This is because it is one thing to create a vaccine and quite another to manufacture, distribute and effectively administer the vaccine at scale, especially in a way that is equitable. Our over reliant bet on vaccine discovery has now revealed serious concerns about Covid-19 vaccine access, manufacturing, cold-chain storage, distribution, system readiness, vaccine nationalism, and acceptability. In many ways it is reasonable to envision that vaccine distribution and logistics, human resource capacities, the governance of programs, and conditions of access, will become the biggest global health governance challenge for the foreseeable future, overshadowing more balanced and holistic approaches to public health (as witnessed at the last Government of Seven G7 Summit). Yet, as illustrated above with ACT-A, insufficient funding has been dedicated at the global level to sustain health systems.

Moreover, in many countries the Covid-19 response was elaborated without properly evaluating the real threat of the pandemic on different populations (age groups, etc.), without appropriately targeting vulnerable populations, without taking sufficient account of the harms

of restrictions imposed while waiting for vaccines to be delivered [35–37], and without taking account of long-proven public health and health promotion experience [38]. In particular, Covid-19 response has focused on virus control, paying insufficient attention to other factors such as social determinants, age, co-morbidities, and previous exposure to a certain range of infections [39], which play a determining role in explaining the 'transition' from SARS-CoV-2 infection to severe forms of Covid-19 [40]. In terms of hedging one's bet, overextending a single wager within a complex problem like Covid-19 undermines efficiency [41]. In terms of a preparedness strategy, reliance on this paradigm becomes increasingly high-stakes as the risks from emerging epidemics and syndemics are estimated to intensify with increased habitat encroachment, intensifying social inequality, degradation of living, social environments and ecologies, urban density, and climate change [42,43].

Conclusion: Hedging one's bets

We have argued that the current strategy of staking everything on the vaccine, however successful it looks today, was a risky and insufficient strategy. Instead of gambling everything on vaccine strategies, we call for adopting a more holistic and diversified response to both the current Covid-19 pandemic and future disease preparedness. One that hedges its bet on a continuum of strategies including health promotion and healthy lifestyles [38], targeted prevention of other determinants of health (e.g., nutritional deficiencies [44]), adequate primary care and early treatment (especially now that we have a more evidence of effective or promising treatments [45–47]), health system strengthening [48], and sufficient national, regional and global system policy preparedness for emerging epidemics, enabling to build "pandemic proof health systems" [49]. In particular, vaccination strategies need to be more nuanced and targeted, and new Covid-19 vaccines need to be configured within an overall public health strategy that will differ in profile for different countries. Strategies should also consider the already acquired natural immunity amongst those that have been infected [50,51]. An optimal mix of policies should be chosen according to a careful risk-benefit assessment,

adopting the precautionary principle to new vaccines, and ensuring public health policy coherence. At the global level, such an approach also includes appropriate financing of the other ACT pillars in the short-term. None of this precludes publicly pooled and coordinated investments in vaccine development and use, since effective vaccines when embedded within the aforementioned health continuum will have far better odds of hitting a health jackpot. Nevertheless, it does preclude continuance of the current policy and the mess we find ourselves in, which is to wait for acute health emergencies, to implement delay tactics, while staking everything on a spin of the vaccine roulette.

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