Environmental Innovation and Societal Transitions 48 (2023) 100736

Contents lists available at ScienceDirect

Environmental Innovation and Societal Transitions

journal homepage: www.elsevier.com/locate/eist

Research article

An elephant in the glasshouse? Trade-offs between acceleration and transformation in COVID-19 vaccine innovation policies

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ARTICLE INFO

Keywords:
Innovation missions
Transformative innovation policy
Vaccine innovation
Accelerator missions
Innovation systems
Pandemic preparedness

ABSTRACT

Against the backdrop of a failing vaccine innovation system, innovation policy aimed at creating a COVID-19 vaccine was surprisingly fast and effective. This paper analyzes the influence of the COVID-19 landscape shock and corresponding innovation policy responses on the existing vaccine innovation system. We use document analysis and expert interviews, performed during vaccine development. We find that the sharing of responsibility between public and private actors on various geographical levels, and the focus on accelerating changes in the innovation system were instrumental in achieving fast results. Simultaneously, the acceleration exacerbated existing societal innovation barriers, such as vaccine hesitancy, health inequity, and contested privatization of earnings. Going forward, these innovation barriers may limit the legitimacy of the vaccine innovation system and reduce pandemic preparedness. Next to a focus on acceleration, transformative innovation policies for achieving sustainable pandemic preparedness are still urgently needed. Implications for mission-oriented innovation policy are discussed.

1. Introduction

Immediately after the outbreak of the coronavirus (COVID-19), governments took a central role in fighting the pandemic and formulated innovation policies with the aim to get the virus under control. Measures like lockdowns, social distancing and mask mandates took central stage in the beginning. At the same time, many stakeholders saw the pursuit of a COVID-19 vaccine as central to an ultimate solution for the pandemic (OECD, 2020). Governments turned to science and technology and sought to "beat COVID-19 through innovation" (Azoulay and Jones, 2020). Many regarded the development of COVID-19 vaccines as the most important technology-based solution to be pursued (Reale, 2021) and the "only long-term solution that will allow societies and economies to return to normal life" (OECD, 2020). This technology-led innovation endeavor (Nelson, 1977) was combined with the 'functional procurement' of a viable vaccine (Edquist and Zabala-Iturriagagoitia, 2020) and ultimately delivered a multitude of effective vaccines.

The effective COVID-19 vaccine innovations can be regarded as a success. The publication of the viral SARS-CoV-2 genome on January 11th, 2020 triggered intensive R&D efforts, resulting in the first vaccine quickly entering human clinical trials on March 16 of that year (Le et al., 2020). Next to that, regulatory authorities like the Food and Drug Administration (FDA) and the European Medicines Agency (EMA) assessed (pre)clinical data of COVID-19 vaccines on the basis of specially designed emergency protocols. This

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https://doi.org/10.1016/j.eist.2023.100736
Received 29 May 2022; Received in revised form 6 May 2023; Accepted 14 May 2023
Available online 24 May 2023

has led to the expedited approval of several vaccines based on a revolutionary messenger ribonucleic acid (mRNA) technology, such as Pfizer/BioNTech's Comirnaty and Moderna's mRNA-1273 (Jackson et al., 2020; Tanne, 2020), next to other vaccines that are based on more traditional technology platforms.

The fast creation of a COVID-19 vaccine came as a surprise because at the start of the outbreak the vaccine innovation system was regarded as ill-equipped to quickly develop and adopt novel technologies due to market and systemic failures (Janse et al., 2021), as further outlined in Section 4.1. There was – and still is – an unmet societal need for a vaccine innovation system that is more resilient and prepared for future pandemic outbreaks. The current system requires changes, either through incremental improvements or through more immediate change into a fundamentally different system of production, consumption and innovation (Geels and Schot, 2010; Grin et al., 2010; Moradi and Vagnoni, 2018; Rotmans, 2003). Such transition can be fueled by landscape shocks to the innovation system caused by broader developments (Geels, 2002), and indeed, already early on in the COVID-19 pandemic, commentators saw the development of COVID-19 vaccines as a much-needed boost for the further development of the vaccine innovation system, to ultimately be able to cope with future virus outbreaks (McCarthy, 2020; UK Government, 2020).

The COVID-19 crisis may support an accelerated transition to a new vaccine innovation system, or a reversion to past solutions (Wells et al., 2020). Therefore, it is of interest to study how the changes introduced by the COVID-19 pandemic and the associated socio-technical developments are expected to be integrated into the vaccine innovation system in general, and to what extent legitimacy, engagement and cooperation among different actors is governed (Borrás, 2017; Schot and Steinmueller, 2018). Here, we respond to calls for in-depth empirical inquiry on system-level implications of the COVID-19 period (Wells et al., 2020).

The innovation policy response to the COVID-19 landscape shock built on a focus to deliver a specific, ambitious and time-bound technological objective to fulfill a targeted and urgent unmet need. As we outline below, governments and other organizations have articulated such targets as missions. Yet, in the case of creating a COVID-19 vaccine these missions do not have the same coordinated nature as the ones usually studied in the context of mission-oriented innovation policies. To explore the structure and dynamics of the vaccine innovation systems, we make use of the established functions of technological innovation systems. In addition, we borrow functions related to mission-oriented innovation systems – most notably providing directionality and market destabilization (Wesseling and Meijerhof, 2021) – that enable us to shed light on some of the elements that come into play when setting such specific and ambitious technological objectives. We are especially aware of 1) the various geographical levels at play, e.g. through the influx of new players, including providers of finance, resources and novel intellectual property; and 2) the temporal dimension – and especially the urgency involved in designing those innovation policies. The temporal dimension opens up questions about whether these policies, which were designed under enormous time pressure, can both accelerate innovation efforts on the short run and transform systems on the long run (Wittmann et al., 2020).

The aim of our article is thus to explore the influence of landscape shocks, like the COVID-19 pandemic, and the corresponding innovation policy responses by governments, on existing innovation systems. We investigate this by making a first and tentative structural and functional analysis of the vaccine innovation system geared towards the COVID-19 mission. Our results can form the basis for developing scenarios for transitions that support the engagement of stakeholders in discussions on how to design innovation and transition policies, in line with transition pathways (Moradi and Vagnoni, 2018; Schippl, 2016), specifically for a more effective vaccine innovation system (Koopmans et al., 2019). Vaccine innovation involves a wide variety of actors and institutions that are active on various geographical levels, which resembles other sustainability transition processes like energy and food system transitions. Lessons learnt might therefore be wider applicable.

2. Theoretical background

2.1. Systemic approach to understanding emerging vaccine technologies

To acquire a deeper understanding of the discovery, development and deployment of new vaccine technologies in a wider, socio-technical field, we advance the notion of a vaccine innovation system. As technological advancement is crucial in the context of vaccine innovation, such an innovation system is first and foremost to be characterized as a technological innovation system (TIS). The framework that enables exploring TIS proposes a structural analysis of all actors, institutions and networks that comprise the system. Furthermore, the TIS framework takes a dynamic approach and focuses on driving processes that establish such innovation systems around an emerging technology, so-called 'functions' (Bergek et al., 2008; Hekkert et al., 2007), such as knowledge development, entrepreneurial activity, market formation, and resource mobilization. The functions can be used to diagnose which elements of innovation systems form barriers in the emergence of these systems, and which elements require more attention.

During the COVID-19 pandemic, however, the vaccine innovation system was heavily influenced by policy targets and interventions. Across the world, many governments and international organizations explicitly articulated the objective to fight COVID-19 through creating vaccines (see Section 4.2). The World Health Organization (WHO) took the lead by univocally expressing the need for a COVID-19 vaccine. Soon after that, many national governments, companies, public knowledge institutes and public-private partnerships, like the Coalition for Epidemic Preparedness Innovations (CEPI) and the Global Alliance for Vaccine Initiative (GAVI), reiterated this objective. For understanding the vaccine innovation system under the influence of a landscape shock and resulting policy targets, more is needed.

Setting these ambitious objectives within the vaccine innovation system resulted in innovation policies that were far from straightforward and unambiguous in technologies and governance involved. To this day, policies involve contestation, complexity and uncertainty, as well as institutional questions, such as the legitimization of vaccine distribution (Reale, 2021; Wanzenböck et al., 2020). Also, the various arenas in which the strategy, programming and implementation of mission policy is formed (Janssen et al.,

2021) are not strongly aligned and are geographically distributed, so there is no question of coordinated mission-oriented innovation policy.

Still, we borrow from literature on missions to capture activities in the context of mission-oriented innovation, including most notably providing directionality and market destabilization (Hekkert et al., 2020). The technological innovation system framework is then adjusted and complemented as to be able to assess missions. For the functional analysis of mission-oriented innovation systems, Wesseling and Meijerhof (2021) propose an adjusted set of functions, including the abovementioned TIS functions as well as functions related to providing directionality, market destabilization and withdrawal of legitimacy. They advance a three-step approach. First, in a structural analysis the innovation system under study is demarcated, including the different actors, institutions and networks involved. Here, this includes the WHO, national governments, multinational vaccine incumbents, and innovative biotech companies, and the way they interact with each other. Second, a problem-solution analysis defines the focal societal problems, followed by a demarcation of the different types of solutions that are considered relevant to address those problems. In our case that relates to the problem of the COVID-19 pandemic and the demarcation towards the development of a safe and effective vaccine. And third, in a functional analysis, the extent to which the different functions of innovation systems are fulfilled are analyzed.

Thus, we determine the vaccine innovation system as a technologically-focused field embedded in social dynamics and influenced by missions. Having done so, two important dimensions still need to be defined: the geographical and temporal dimensions.

2.2. Geographical and temporal dimensions of the vaccine innovation system

When exploring the vaccine innovation system that is influenced by landscape shocks and related policies, we need to define its geographical demarcation. On the one hand, the vaccine innovation system has a shared, global vaccine development agenda with distributed sets of institutions, actors and technologies, as also indicated by the WHO R&D Blueprints, acting as global coordination mechanism (Kieny and Salama, 2017). On the other hand, various decisions have a strong footing in national and local settings, e.g. about fair, effective and efficient vaccine distribution. The vaccine innovation system can thus best be characterized as a global innovation system (Binz and Truffer, 2017) (de Haan et al., 2021), emphasizing innovation and valuation activities on various geographical levels, linked through structural couplings. We study the vaccine innovation system by taking into account global and national levels of aggregation.

Also, the temporal dimension sets COVID-19 vaccine innovation policies apart from other innovation policies: COVID-19 innovation policies were formulated and executed under immense time pressure due to the urgency of the pandemic outbreak. The question is how such urgency relates to expanding a sustainable and resilient vaccine innovation system.

To better understand the temporal dimension of urgency with which innovation policies were designed and implemented after the landscape shock provided by COVID-19, we build on the distinction between accelerator and transformer policies proposed by Wittmann et al. (2020). As accelerator policies typically focus on "finding an answer to a challenge with a relatively confined scope […], but do not aim for a comprehensive system change" (Wittmann et al., 2020), they are easier to formulate under immense time pressure. Transformer policies, however, have been proposed to go beyond – and still include interventions for – market and systemic failures, contributing to changes in socio-technical innovation systems (Schot and Steinmueller, 2018). Such policies are not just concerned with providing public investment, but also play a role in coordinating innovation efforts, thereby contributing to changes in socio-technical innovation systems (Hekkert et al., 2020; Schot and Steinmueller, 2018). To do this, a thorough understanding of the complex problems underlying those failures is needed. Moreover, they are increasingly called to address a new type of transformative failures, e.g. related to how to define directionality (Weber and Rohracher, 2012).

Under threat of high mortality figures as well as economic and societal disruption due to e.g. lockdown measures, innovation policies focusing on the development of a COVID-19 vaccine could be seen as policy focused on acceleration: there is a predefined technology (COVID-19 vaccine) for which multiple innovation pathways are open (different technological platforms available) and which involve many stakeholders (scientists, pharmaceutical companies, governments, hospitals) that require strong coordination. At the same time, as put forward in Section 1, the push for developing a COVID-19 vaccine could also be seen as transformational policy as it requires strengthening and re-thinking the vaccine innovation system and improving pandemic preparedness. Or, as the OECD (OECD, 2020) put it: "a more transformational approach to innovation [is urgently needed] that looks not just at innovation in products and processes, but at entire paradigms and ways of doing things". Not only do such policies sort their effect on different time scales, the temporal dimension here refers to the time pressure under which these policies were defined. Given the urgency with which innovation policies were defined and implemented, it is interesting to study to what extent accelerator policies have taken precedence at the expense of transformative policies. The current pressure on the vaccine innovation system is thus an exquisite opportunity to study its intricacies and complexities.

We use the mission-oriented innovation systems perspective as a lens to the transitions of the vaccine innovation system, since we are primarily interested in the influence of innovation policies designed during the COVID-19 pandemic on the innovation system. At the same time, we use the framework against the background of the geographical and temporal characteristics sketched in Section 2.2. The framework should be able to study innovation policy formulation and activities on various geographical levels, which are uncoordinated yet interlinked, and which have both short- and long-term ambitions.

3. Methods

This study builds on a qualitative analysis of the vaccine innovation system for COVID-19 vaccines and combines two sources: documents and interviews. The document analysis informed the structural analysis of the vaccine innovation system, delineating the

key actors that play an important role. Subsequently, it informed the problem-solution alignment and how this compared to other proposed solutions for the vaccine innovation system in the context of pandemic preparedness. To gain insight into the functional dynamics in the innovation system during an unfolding pandemic, we relied on qualitative data collection. Through this approach we collected subjective assessments and opinions from key individuals, which were the best data available at that point in time. Finally, we clustered all findings in a simplified overview based on the multi-actor framework involved in sociotechnical regimes, in Fig. 1.

3.1. Documents

A non-systematic review of documents was used to construct a narrative, including a timeline of major events and an overview of major stakeholders in the vaccine innovation system. We searched for newspaper articles, reports by major organizations like the WHO and CEPI, and press releases by relevant pharmaceutical companies. We performed the search using Google and Google Scholar, using keywords such as COVID-19 vaccine, vaccine development, vaccine trials, etc. The narrative served as a backbone for the interviews and provided information for the structural analysis (Section 4.1) and problem-solution diagnosis (Section 4.2). With the ambition to create a basis for the interviews to build and elaborate on in the functional analysis (Section 4.3), we also built on previous qualitative and quantitative research on innovation barriers in the vaccine innovation system performed in our group (Janse et al., 2021).

3.2. Interviews: sampling

Semi-structured expert interviews with 17 Key Opinion Leaders (KOLs) took place between March and May 2021, the period in which COVID-19 vaccine developments were in their final stages and deployment was commencing. KOLs were defined as influential and knowledgeable individuals within the extensive and rapidly changing field of vaccine development, and part of existing networks on this topic. They therefore not only conveyed insights from their own experience, but also from the broader networks they are a part of. All KOLs were in senior-or-above positions in their respective organizations.

Vaccine innovation consists of a number of distinct but closely interrelated subprocesses that need to align for successful innovation: science, business development, market and society (Van de Burgwal et al., 2018). Typically, different actors are active in each of those subprocesses, and thus identified obstacles can be external or internal to each actor (Schuitmaker, 2012). Data collection therefore draws from actor perspectives across the vaccine innovation cycle, to gain insight into which transitions are related to institutional arrangements, and which are a result of interfering actions of other stakeholders (De Cock Buning et al., 2008; Sondeijker et al., 2006). Purposive sampling aimed to maximize the depth and richness of the data, and therefore interviewees from each of the stakeholder groups were invited, taking into account their availability in light of covid-related responsibilities and willingness to participate.

17 out of 66 invited KOLs (26%) agreed to participate in interviews that took place between April and May 2021. Different areas of expertise were included in the study, as reflected in the background of the interviewees: two CDMOs (12%), two CROs (12%), one VC (6%), one NGO (6%), three pharmaceutical companies (18%), two academics (12%), three governmental representatives (18%), three interest group representatives (18%). The interviewed KOLs and the respective organizations that they are active in are summarized in Table 1. 16 out of 17 KOLs (94%) were based in Europe, while only one KOL (6%) was from the US. While this disbalance might introduce a bias in our research findings, it is important to note that the vaccine innovation system is global, yet highly condensed and key companies and knowledge institutes as well as markets with purchasing power are concentrated in the US and Europe (Possas et al., 2020). As a result, the experts we interviewed represented significant parts of the global vaccine innovation system.

Table 1
Interviewed KOLs and their respective organizations.

Interviewee number	Type of organization that interviewee is active in
R1	Pharmaceutical company
R2	Non-Governmental Organization
R3	Governmental Research Organization
R4	Pharmaceutical Company
R5	Governmental Funding Agency
R6	Interest Group
R7	Academia
R8	Governmental Funding Agency
R9	Academia
R10	Government Representative
R11	Non-Governmental Organization
R12	Pharmaceutical Company
R13	Contract Development Manufacturing Organization
R14	Venture Capital
R15	Contract Research Organization
R16	Contract Development Manufacturing Organization
R17	Contract Development Manufacturing Organization

3.3. Interviews: interview design

The aim of the interviews was to gain insights into the dynamics of the vaccine innovation system. As innovation barriers are an indication of how the system is configured (Geels, 2005), this was seen as a specific means to gain insight into how the different functions of the innovation system performed. The semi-structured interviews were based on a topic list, consisting of the following topics: 1) identification of innovation barriers that may persist after the pandemic, 2) identification of innovation barriers that will arise or did arise during the pandemic, 3) interviewees' experience on the development of possible solutions to these barriers and 4) confirmation of all identified barriers and additional commentary. For each identified barrier, follow-up questions were asked to establish cause and effect relationships. On average, interviews lasted for 30 min (22 – 43 min). To remedy the relatively short duration of the interviews, we presented a previously collected, validated and prioritized list of innovation barriers pre-covid and during covid (Janse et al., 2021) at the start of the interview. In combination with their knowledgeability, the respondents were able to quickly dive into the topic. All interviews ended only after the whole interview design was completed, and none of the interviews were cut short due to time constraints.

3.4. Interviews: data analysis

Interview respondents provided their verbal informed consent at the beginning of the interview. Interviews were recorded and transcribed using Otter.ai software. The important insights from the finalized interview transcripts were analyzed using Atlas.ti software. Text fragments relevant to the study question were highlighted and subsequently analyzed by two independent researchers using the conventional content analysis approach until consensus was reached (Hsieh and Shannon, 2005). The statements were linked to the seven functions of innovation systems as presented in Section 2.3. To improve transparency of data presentation, for each of the perceived innovation barriers and innovation system dynamics, the reference number of the respondent(s) discussing those insights is indicated in the results section, e.g. (R1). The background of the respondents can be cross-checked in Table 1. Finally, the dynamics within the innovation system were broadly mapped to the multi-actor framework involved in sociotechnical regimes (Geels, 2002), indicated between brackets, e.g. [1.3] in the results and Fig. 1 to provide a more visual and comprehensive overview of the findings.

4. Results

4.1. Structural analysis

The existence of market failure for R&D, and specifically for R&D in the context of emerging infectious diseases, has long been acknowledged. Infectious diseases have underdetermined, yet often small market sizes, and therefore a limited return on investment (Darrow et al., 2018). With market values for vaccines dropping (Pronker et al., 2011, 2013; Thakor et al., 2017), many large pharmaceutical companies have abandoned their development programs in the field of infectious diseases (Rex et al., 2019). As a result, the current innovation system consists of a handful of large incumbents (i.e. GSK, Merck, Sanofi, Pfizer, and AstraZeneca) funding and managing their own R&D pipelines (Abi Younes et al., 2020; Possas et al., 2020; Van de Burgwal et al., 2018), next to a few innovative biotech companies financed by philanthropic organizations (Douglas and Samant, 2018).

Academic institutes, national institutes of public health, and philanthropic organizations play a relatively large role in vaccine innovation (MacDonald et al., 2020; Possas et al., 2020). Systemic failures for vaccine innovation are thus rooted in inherently conflicting institutional norms and incentives, as well as legislative restrictions and ambiguities in regulatory frameworks that hamper stakeholders from engaging in an open manner (Flach et al., 2019; Heymann et al., 2016; Ribeiro et al., 2018, 2018). In the past, politicians and the public sector have created a market in order to enable private institutions to function in an efficient market (Possas et al., 2020). However, individual countries themselves have an incentive to 'free ride' on investments made by other countries (Kremer, 2000; Meissner, 2016; Røttingen et al., 2017). As a result, the successes of philanthropic agencies focusing on vaccines (e.g., Bill & Melinda Gates Foundation, CEPI, GAVI), were substantially driven by efficient R&D of private institutions (Gouglas et al., 2019; Possas et al., 2020).

COVID-19 vaccine development brought in an even more diverse set of actors (Dance, 2020). They include public knowledge institutes, small biotech companies, large vaccine incumbents, and technology suppliers (Bok et al., 2021; Patrucco et al., 2022). All actors are embedded in highly accelerating institutional contexts (Castillo et al., 2021). This includes operations in the US, EU, and China supporting dedicated development of vaccines, advanced purchase agreements by governments across the globe, and programs to optimize regulatory environments (Puślecki et al., 2021; Winch et al., 2021).

4.2. Problem-solution diagnosis

The challenge to develop a vaccine against COVID-19 is derived from the broader challenge to deal with the COVID-19 pandemic (Azoulay and Jones, 2020; Reale, 2021). Many countries articulated missions for creating a COVID-19 vaccine. Already in February 2020 the White House Coronavirus Task Force called for a 'Manhattan Project' for vaccines (Gross and Sampat, 2022) and the US later invested heavily in Operation Warp Speed with a clear goal to produce and deliver 300 million doses of vaccines within 6 months. Countries such as the UK, Canada, Korea and China, the European Union and organizations like the WHO and CEPI all announced programs – which they often referred to as missions – to support the creation of a COVID-19 vaccine within a pressing timeframe (for an overview of programs, see Geulette (2020), UK Department for Business (2020) and European Commission (2020)). Despite the sudden

virus outbreak and rapid articulation of missions, the creation of COVID-19 vaccines would build on and mobilize organizations, institutions and resources in the existing vaccine innovation system. Early reports in Spring 2020 on the COVID-19 vaccine mission acknowledge the use of the prevailing structures. A substantial amount of COVID-19-related research was driven by collaborative efforts based on the fundamental principles of open innovation (Patrucco et al., 2022). Innovation policies that support the development of COVID-19 medical countermeasures are in line with efforts previously made in small-scale experiments: engagement of public and private stakeholders (Ho, 2021), large-scale governmental funding (Yamey et al., 2020), calls for equitable access and distributive justice (Abbas, 2020; Bedford et al., 2019; Bollyky et al., 2020) and reciprocity (Jenek et al., 2021).

4.3. Functional analysis

The interviewees provided insight on their perspective on the dynamics within the innovation system for COVID-19 vaccine development.

4.3.1. Knowledge development

Working on the mission for innovative COVID-19 vaccines requires sufficient knowledge of immunology, pathogeneses, and host-pathogen interaction (Respondents R3, R17), and future development of such knowledge may in the future enable rational design of vaccines (R3), see box [1.1] in Fig. 1. While vaccine innovation pre-covid was sparse (R3, R4, R12, R15, R17), the COVID-19 pandemic enabled the influx of "scientific creativity which normally comes from biotech companies" (R14). Many stakeholders, particularly those active in the oncology and immunology therapeutics field, began testing whether the mRNA technology they were working on could be a fit to the COVID-19 problem (R2, R12, R16), see box [2.1] in Fig. 1. KOLs considered it very unlikely that technological innovators would have spent these substantial R&D efforts and budgets solely for the purpose of developing vaccines against infectious diseases (R12, R13, R14).

Multiple KOLs highlighted that this early success strengthens the momentum of mRNA vaccines and is likely to result in radical changes to the current vaccine innovation system, with mRNA technology possibly becoming the new gold standard for vaccines (R2, R6, R9, R11, R13), see box [3.1] in Fig. 1. Stakeholders anticipate that mRNA technology, as an "extremely innovative idea" (…), will definitely be applicable to other vaccine developments" (R16). In addition, they expect new biotech companies to enter the mRNA technology space with innovative applications, and foresee important linkages with e.g. work on eliminating cold chain requirements or addressing scarcity of lipid nanoparticles (R9, R10, R14), and thus fueling further knowledge development in this field, see box [1.2] in Fig. 1.

4.3.2. Entrepreneurial activities

While at the onset of the pandemic, incumbent vaccine companies stuck to further developing existing vector-technologies, the COVID-19 pandemic also proved pivotal for incorporating radical innovation in vaccine development (R16). This disruption of the dominant technology platforms was enabled by academia and biotech companies, including University of Oxford, BioNTech, CureVac and Moderna (R12, R13, R14, R15), see box[2.1] in Fig. 1. The dependence on innovative biotech companies – while omnipresent in the traditional pharmaceutical value chain – is new for the vaccine innovation system (R12, R13, R14). As a result of unattractive, low-profit markets, see box [4.4] in Fig. 1, to date vaccine innovation depended on a handful of large incumbents funding their own R&D pipelines and a few innovative biotech financed by philanthropic organizations: "There was not such a huge number of experienced biotechs in this field. And that obviously leads to a lack of innovation" (R12). The COVID-19 innovation effort thus increasingly relied on the entry of entrepreneurial biotech companies (R12, R13, R14), which brings opportunities for further development of the vaccine industry (R13, R14, R15) and perhaps even non-infectious disease areas (R14), see box [1.2] in Fig. 1.

The production of vaccines in general, and mRNA in particular, is highly complex and it is no wonder that BioNTech and the University of Oxford quickly sought support from large incumbents, see box [2.2] in Fig. 1. These incumbents possessed large production facilities capable of producing biologics and had expertise in vaccine manufacturing: "Innovation is coming from small biotechs, not from large companies. (…) But they were unable to guarantee the deployment without Pfizer or without AstraZeneca." (R16). In this light, it is also of interest that Sanofi and Novartis, vaccine incumbents who to date did not successfully develop their own COVID-19 vaccine, have come to the aid in upscaling production (R6, see also (Irwin, 2021)). "There's patents now that are going to protect the technologies. And there's also proprietary know-how involved in scaling up the manufacturing of these molecules (…) So from the multinationals point of view, how to keep control of what suddenly may become a much more diverse and dynamic, better environment could become a real concern in vaccines" (R11). Collaborating with these emerging, innovative technology frontrunners will potentially enable the big pharma companies to gain access to valuable tacit knowledge on the use of this platform technology, providing them with the means to secure their future after this technological transition, see box [2.3] in Fig. 1. As one interviewee commented: "Again, if you're not one of the big winners in the covid [pandemic], you may not even stick around" (R11).

Overall, interviewees commented positively on the efficiency of private organizations and their speedy reaction to address something that would normally have taken 8 to 10 years to develop (R12, R14, R16). "The work was (…) highly efficiently performed by private institutions, (…) and the same is true for manufacturing [as well as] for the organization of the vaccine campaigns (…). So, whenever the public sector was in charge, it was not as efficient as the private sector"(R12).

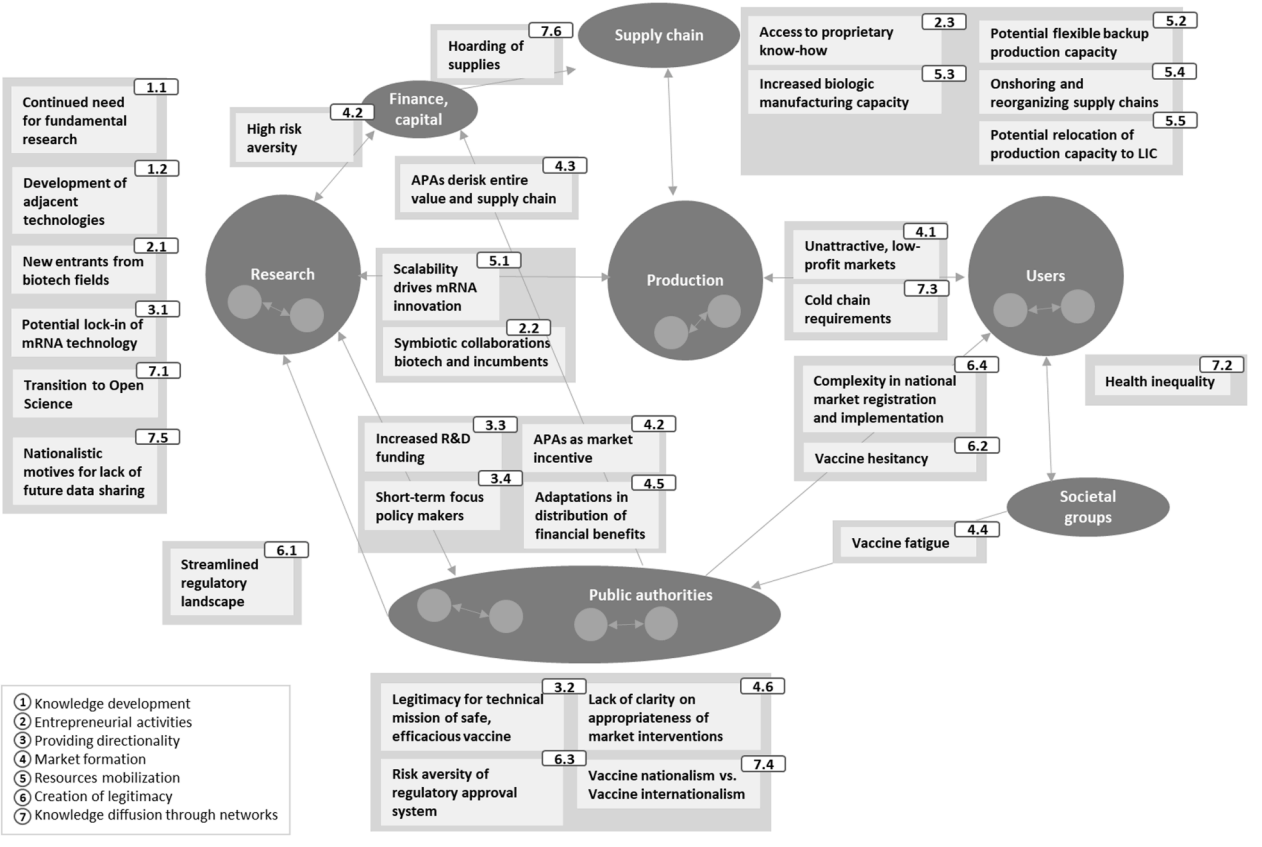

Fig. 1. The COVID-19 pandemic induced dynamics across functions and between actors in the vaccine innovation system, as mapped to the multi-actor framework involved in sociotechnical regimes.

Table 2
Quotes from interviews illustrating function 3 – Providing Directionality.

Quote number (#)	Quote and interviewee
1	"You know, viral vector vaccines were studied in small clinical trials for many applications, and saw limited use clinically for some indications like Ebola. But what's being learned about them now may really have dampened enthusiasm for viral vector vaccines going forward. So there could be a whole area of technology there that falls by the wayside."- Respondent #11 – Non-Governmental Organization
2	"What we already see is that some of the mRNA vaccines are getting so much attention and trust, that it will become difficult for other vaccine platforms to develop their products." – Respondent #9 - Academia
3	"One of the things about nucleic acid vaccines is that it makes it very easy to start projects but finishing them is just as costly and time consuming as it was before. (…)- Respondent #11 – Non-Governmental Organization
4	At the beginning of the pandemic, it was easy to find 20,000 patients for vaccination because we just had to wait a short amount of time and then data came in, this may not be happening that fast anymore. It may be taking much longer until you have the safety data of 5000 or 10,000 patients. So that may then prolong the approval of new drugs or new vaccines." – Respondent #13 – Contract Development and Manufacturing Organization

4.3.3. Providing directionality

None of the interviewees questioned the formulation of the mission for a safe, efficacious vaccine, see box [3.2] in Fig. 1. In contrast, experts commented on the late activation of some national authorities, either in preparedness by developing relevant technologies (R1, R2), surveillance (R9), or reaction to the outbreak with most notably Europe being seen as significantly later and providing significantly fewer funds than the US (R8, R10, R13). The late reaction by Europe was in part seen as a result of the need to coordinate between many different member states (R4, R13).

With the mRNA technology quickly developing into the new gold standard (R2, R6, R9, R11, R13), interviewees fear the future loss of a more diversified knowledge development (R2, R12), see box [3.1] in Fig. 1. They perceived a waning commercial (R11, R13) and political (R6, R9) interest for alternative technologies: "They don't want to talk to us about protein-based or subunit based vaccine. No interest" (R13; see also quotes #1 and #2 in Table 2). Moreover, while widespread circulation of the coronavirus significantly reduced the size and duration of the clinical evaluation, such supportive clinical trial conditions might not be present during future outbreaks nor allow for development of new vaccine technology in between pandemics. Interviewees discussed non-inferiority trials becoming prohibitively expensive due to reduced numbers of naïve people, enormous numbers of patients included in mRNA trials, and lack of circulation of the virus (R3, R7, R9, R10, R13, see also quotes #3 and #4 in Table 2. Importantly, interviewees mentioned notable downsides of this lock-in to mRNA technology with homogeneous innovation limiting preparedness to other infectious diseases (R1, R3, R7, R9), see box [3.4] in Fig. 1. Moreover, unknown long-term effects, were mentioned as important risk factors for depending too much on one technology (R13), next to inherent downsides to mRNA technology such as temperature and logistics requirements (R9).

Many experts also emphasized the need for continued focus on improved preparedness against future pandemics, which should be funded by the public sector (R1, R2, R4, R5, R8, R9, R12, R15, R16) [3.3]. Such directionality should follow from a risk assessment (R2) and should include directionality on which pathogens to prioritize (R9, R17), whether to prioritize the development of vaccines or antivirals (R17), the development of alternative administration methods, e.g. different needles, intranasal, patches (R4, R14, R16, R17), underscoring the need for prevention, either through lifestyle interventions or vaccination (R2, R6, R13), and epidemiological knowledge on the spread and development of zoonotic epidemics (R4). One interviewee even commented on the need for governments to proactively design programs and bring consortia together (R15), while another worried about the lack of knowledge among policy makers (R13). While regionality of certain diseases may lead to higher unmet needs felt by some governments (R4), KOLs found that such directionality should be aligned internationally (R3, R4, R6, R8, R12). Whether such directionality would indeed be provided, however, was doubted, due to the short-term focus of policy makers, see box [3.4], and the 'vaccine fatigue' setting in post-covid, (R7, R11, R12, R13, R15, R16, R17), see box [4.4] in Fig. 1.

4.3.4. Market formation

The advent of new mRNA vaccines and the rapid upscaling of production capacity was critically enabled by the unprecedented support by public authorities (R2, R3, R5, R6, R7, R10, R16, R17). According to KOLs, radical innovations often do not arise in markets with limited profit margins, and KOLs commented on the difficulty for market formation in low-income countries that have a significantly lower purchasing power and are primarily dependent on vaccine donation programs like COVAX (R3, R17), see box [4.1] in Fig. 1. The investments in both R&D funding and advanced purchase agreements (APAs) were seen as pivotal in countering the risk for development and downward price pressures on vaccines, and de-risking the entire supply chain of raw materials and production (R3, R5, R6, R10, R16, R17), see boxes [4.2 and 4.3] in Fig. 1. KOLs argued both push and pull factors should remain in place post-covid to enable further investment in vaccines with poor market opportunities (R3, R6, R10, R12, R15, R16, R17).

Although two KOLs were positive about future investments in market formation by governments (R8, R9), most KOLs were skeptical on the role state-governmental actors would play in supporting vaccine innovation and pandemic preparedness post-covid. Multiple KOLs commented that the general public and politicians may 'forget' about the need for pandemic preparedness post-covid (R17, R15, R16), lose interest (R7, R12) or even exhibit 'vaccine fatigue' following the COVID-19 pandemic (R11, R13), leading to disinvestments from vaccine innovation and preparedness measures, see box[4.4] in Fig. 1. Interestingly, none of the interviewed KOLs indicated that the importance of vaccines in opening up economies would form an argument favoring a post-pandemic influx of public funding. Similarly, while stockpiling is a prominent strategy for personal protective equipment and influenza vaccines (Jennings et al.,

Table 3
Quotes from interviews illustrating function 4 – Market Formation.

Quote number (#)	Quote and interviewee
5	"Europe is currently centrally purchasing these vaccines, but for how long? When will the pandemic end and will a normal, healthy market be re-established? Because Europe is buying billions of vaccines from a few suppliers. (…) Eventually we will be in a totally different, endemic situation with annual vaccinations. But the market is already saturated for the upcoming years. This means that other vaccine developers will not invest in developing new vaccines, because of this unequal competition that is now being established. This will eventually lead to less vaccine innovation." – Respondent #4 – Pharmaceutical Company
6	"We have failed to impose strict requirements to the de-risking of vaccine development. (…) We are already publicly funding the fundamental research, and now also the late-stage development while the pharmaceuticals are taking up all the revenue. This seems strange to me." – Respondent #5 – Governmental Funding Agency

Table 4
Quotes from interviews illustrating function 5 – Resources Mobilization.

Quote number (#)	Quote and interviewee
7	"If you would have asked a year ago, everyone would have said R&D would be the most difficult step, but now it turns out that actually production is" - Respondent 1 – Pharmaceutical Company
8	"the shortage of manufacturing capacity is a barrier that will disappear, because we are already creating new capacities for this pandemic, and they will stay." – Respondent #12 – Pharmaceutical company
9	"The question remains whether we need the increased manufacturing capacity for future pandemics, or that we need to organize a smarter network with strict international agreements and shorter supply chains." – Respondent #8 – Governmental Funding Agency
10	"Biologics companies have taken advantage of the market opportunity to move into vaccines. They have created a lot of capacity very fast. They may be wanting to go back to their more profitable, steadier pursuits once the initial rush is over, but they may not be able to do this because we don't know where covid is going to go. If it really becomes an annual shot that has to be given to everybody on the planet, that's a huge drain of capacity. So, one of the things that may happen, at least in the short run, is that capacity can't grow to enable new products." – Respondent #11 – Non-Governmental Organization
11	"What we have seen in Europe, is that people are now paying attention. We have become highly dependent on China and India for crucial supplies. This was already the case for certain types of antibiotics. Essential antibiotics that were produced in one single factory in China. Looking geopolitically and economically, and such a factory stops, we have a problem. That is risky. For essential medicines or essential vaccines you shouldn't want to be dependent of a single company." – Respondent #1 – Pharmaceutical company
12	"If every country decides to set up their own facilities, shortage of supplies will become more evident. If every country then starts to hoard, upscaling of manufacturing will become even harder. This 'me-first' attitude is a serious threat." – Respondent #10 – Government Representative

2008; Larsen and Disbrow, 2017; Straetemans et al., 2007), only one KOL mentioned this as a mechanism supporting further innovation (R8). In contrast, respondents discussed the persistence of market failure post-pandemic with pricing reimbursement barriers due to low pricing of vaccines (R12, R16), see box [4.1] in Fig. 1. In sum, while the overall public return on investment of vaccines might actually outweigh the investments made by state-governmental actors, KOLs remained modest in their expectations of future support. In addition, many interviewees pointed towards the disbalance in public funding of privately developed innovations, (see box [4.5] in Fig. 1), the complexity of funding mechanisms, the lack of clarity when governmental market interventions are appropriate (box [4.6]) and the disproportionate risk-aversity of biopharmaceutical companies (box [4.2]) as barriers for lasting changes in the role of public authorities in vaccine innovation (R2, R3, R5, R6, R8): "In the future, when spending public money, we need to set clear conditions."(R5). Quotes #5 and #6 in Table 3 illustrate this as well.

4.3.5. Resources mobilization

The scalability of mRNA vaccines in comparison to culture-based vaccines is seen as a major advantage (R13, R15), see box [5.1] in Fig. 1. Still, the majority of KOLs saw the global manufacturing capacity as the main barrier for the effective deployment of vaccines (R1, R5, R8, R17, R10, R11, R12, R13, R14, R16, R17, see also quote #7 in Table 4). Nevertheless, the pandemic and the accompanied advanced purchase agreements de-risked development and paved the way to expand manufacturing facilities, to build up capacity for delivering products that match high quality standards, and to form new partnerships with vaccine manufacturing companies (R6, R11, R12, R14, see quote #8 in Table 4).

Many KOLs raised the question of whether flexible backup manufacturing infrastructure that could be scaled in times of pandemics would be feasible, see box [5.2] in Fig. 1, without providing clear answers. They saw the flexibility being inherently limited due to technological and human capital constraints (R1, R4, R8, R11, R15, R17, see quote #9 in Table 4) as vaccine manufacturing requires highly skilled personnel and the sharing of tacit knowledge among them (R11). Others mentioned financial constraints that would become surmountable when there would be sufficient political will (R3, R16, R17). One KOL emphasized that biopharmaceutical companies producing biologics took advantage of the window of opportunity and shifted their focus towards covid-vaccines, driven by

the publicly funded development of, and soaring global demand for such vaccines (R11). While the COVID-19 pandemic may thus prove a pivotal tipping point for large-scale investments in production capacity, see box [5.3] in Fig. 1, such pharmaceutical companies and contract manufacturing organizations may also switch their focus back to markets with higher profit margins than vaccines, even though their manufacturing capacity might still be required for covid-related countermeasures (see quote #10; Table 4). And finally, one KOL mentioned the limited capacity in clinical trials being a major barrier for pandemic response (R11).

Many KOLs discussed the pressure on international supply chains (R1, R8, R10, R11, R13, R16, R17). They felt risks of being too dependent on offshored supply chains or manufacturing facilities, which might result in onshoring and reorganizing of supply chains (R1, R8, R16, R17; see also quote #11 in Table 4 and box [5.4] in Fig. 1). They cautioned against the dispersion of production among too many actors during pandemic times, as this would lead to an increase in costs, lead times and interdependencies within supply chains (R10, R17, see also quote #12 in Table 4). At the same time much pandemic nationalism was observed during the pandemic, with countries hoarding supplies (R1, R8, R10, R17). Only a few KOLs highlighted the opportunities for low-income countries to take on a greater share of the production, see box [5.5] in Fig. 1, and thus become less dependent on the production and equitable distribution of vaccines by high-income countries, but simultaneously saw patent protection as a hurdle to technology access (R5, R11, R16).

4.3.6. Creation of legitimacy / counteract resistance to change

The highly accelerated development of covid-vaccines was further enabled by a streamlined clinical trial landscape with regulatory pathways that allowed for expedited authorization (R2, R7, R10, R11, R13, R15), see box [6.1] in Fig. 1. Multiple KOLs reflected on the conventional regulatory environment hindering innovation by overemphasizing safety concerns (R5, R7, R11, R13), with one KOL pointing out discrepancies in strict regulatory processes for new medical versus lenient processes for repurposing existing drugs (R5). During COVID-19, however, clinical trials were performed in parallel, in combination with rolling reviews assessing outcomes while trials were still ongoing (R1, R2, R5, R6, R7, R11, R15). Some KOLs also indicated condensed timelines to be the result of the postponement of consistency lot testing as well as amended guidelines for animal studies and the use of GMOs (R5, R7, R11). KOLs did not think the regulations themselves have become less strict (R13, R15), but placed more emphasis on post-market surveillance, or pharmacovigilance, in part enhanced by the natural challenge model that COVID-19 presented (R3, R15). In turn this provides opportunities for more advanced evaluations supported by big data analytics (R3, R14).

At the same time, however, some KOLs mentioned that the speed with which vaccines were developed was an important contributing factor for vaccine hesitancy (R4), see box [6.2] in Fig. 1, with a lot of importance being placed on the communication with the general public, which should be transparent, honest and complete without invoking fear (R2, R4, R5). Multiple KOLs commented on covid denial and vaccine hesitancy, especially with multiple dosages being required (R2, R4, R5, R10, R13).

Some KOLs were hopeful that the newly adapted regulatory guidance would be continued (R5, R7, R10, R13; see quote #13, Table 5), and also reflected on the improved business case for vaccine development (R7, R9). Others anticipated concerns with respect to efficiency, and sensitivity around safety risks would ensure a return to pre-pandemic processes in a post-pandemic setting (R2, R5, R7, R11, R14, R15; see quotes #14 and #15 in Table 5) and that the costly expansion of capacity needed to maintain the amended regulatory guidance would become too expensive (R11), see box [6.3] in Fig. 1. One KOL mentioned a possible exemption for 'platform vaccines', like the mRNA vaccines, where minor changes should not require a full iteration of the clinical process (R9). Furthermore, KOLs reflected on agencies and policy makers in various countries insisting on conducting individual assessments of clinical evidence despite (a) the existence of overarching regulatory agencies, such as the EMA (R10, R11), and (b) the global reach of infectious diseases in today's world: "it is an illusion to think that an American citizen would respond differently to a vaccine than a European citizen" (R10). Finally, KOLs commented on the regulatory complexity of vaccination programs that may hamper future adoption of mRNA vaccines (R4), see box [6.4] in Fig. 1.

Table 5
Quotes from interviews illustrating function 6 – Creation of Legitimacy.

Quote number (#)	Quote and interviewee
13	"The warp speed project in the US skipped over the whole consistency lot and postponed it until later in order to get data quicker. But the normal thing [to do] is to make three consistency lots of scale, or scale or something close to it, and test those in the phase III trial, which was not done in the US this time. And nothing terrible seems to have happened. So, there are some barriers that might be reduced in scope. (…) And it doesn't sound like much, but you're talking about saving like three to four years off a development timeline." – Respondent #11 – NGO
14	"An important barrier is GMO regulation in Europe, while GMOs are safe by design. (…) These regulations were lifted during the pandemic. I hope the public will pressurize this lifting of regulations, because it will not be coming from policy makers." – Respondent #7 – Academia
15	"We have a very neurotically coordinated regulatory approval system, and pharmaceutical companies have followed the increasingly stricter guidelines. Therefore, this system now keeps itself in place in its own complexity. (…) It has become so complicated to perform clinical studies with the vast amount of data that has to be gathered, that the CRO-market has become a market on its own, where incredible amounts of profit are being made. So, companies and regulators keep this system in place, but it remains questionable what the usefulness of this system is." – Respondent #5 – Governmental funding agency

Table 6
Quotes from interviews illustrating function 7 – Knowledge Diffusion Through Networks.

Quote number (#)	Quote and interviewee
16	"I'm impressed by the speed of publishing of scientific results. We have seen results being published within days, giving access to data to people across the world. They might not always have been interpreted and reviewed optimally, but the speed of data sharing is extraordinary." – Respondent #10 – Government representative
17	"Every country wants to vaccinate its own people first. (…) But if we forget to vaccinate, for instance, India, then it's just a matter of time before a new variant arises and we can start vaccinating all over again." – Respondent #13 – Governmental funding agency
18	"The Nagoya protocol is a wish from the developing countries like Brazil and South-Africa to protect themselves. They are willing to share the data so that products can be developed based on those data. However, they want access to resources in return. The health inequality that is point of discussion here could hinder the sharing of crucial data." – Respondent #11 - Academia
19	"Once there is this threat to the Western world, it's horrible to say, but then all of a sudden the problem comes closer to the decision-making people in the boardrooms of those large companies. And then all of a sudden it becomes our problem too instead of [LICs'] problem." – Respondent #4 - VC

4.3.7. Knowledge diffusion through networks

KOLs praised the successful scientific collaboration during the pandemic, not only between academics, but also between academia and industry, with the sharing of the SARS-CoV-2 genomic sequence and the unprecedented fast development of the first generation covid vaccines (R1, R5, R10, R15). Interviewees also marked the abundance of preprints of academic work and simultaneously noted the risks of speeding up peer-review processes (R10, see #16 in Table 6 and box [7.1] in Fig. 1).

At the same time, KOLs found data sharing between high-income and low-income countries, as well as high-income countries hoarding vaccines and supplies for vaccine production troublesome, making health inequality painfully visible (R5, R10, R13, R14, R16), see box [7.2] in Fig. 1. Not only are countries in the Global South challenged by complex logistical challenges (R4, R9, box [6.4] in Fig. 1) and limited purchasing power (R4, R16, box [4.4] in Fig. 1), but also vaccines are not developed to accommodate for cold chain requirements (R9, R12, R15, R16, R17, box [7.3] in Fig. 1). While high-income countries were unwilling to support opening up patent protection by the World Trade Organization (R5, R11, R16), contributions to the COVAX program remain relatively inconsequential to the global demand for vaccines (Lancet, 2021). The KOLs' consensus is that failure to distribute vaccine shots across the globe in a timely manner, and time delays between vaccine shots and exposure, would potentially lead to immunity-escaping mutations, in turn possibly rendering early vaccinations useless (R1, R13, R14), as illustrated by quote #17 (Table 6). KOLs emphasized this increased the risk of escape mutants caused by inequity in vaccine distribution could lead to further exacerbation of the pandemic's impact, see box [7.4] in Fig. 1.

This nationalistic behavior is in stark contrast to the transition related to open science and data sharing. Following the refusal of Indonesia to share virus samples in the wake of the first SARS outbreak in 2011 (Fidler, 2012), it remains to be seen whether or not this vaccine nationalism will have a detrimental effect on the sharing of samples as the pandemic progresses, and – post-covid – if a new one should emerge (box [7.5] in Fig. 1). KOLs identified the hoarding of supplies creates even more supply scarcity and health inequality, leading to R&D nationalism and providing a substantial barrier in the transition towards vaccine internationalism (R1, R8, R10, R17, see quote #17 in Table 6 and box [7.6] in Fig. 1). One KOL indicated that genomic data sharing under the Nagoya protocol has become more troublesome due to discrepancies in interests between high-income and low-income countries (R7). This KOL argued that the lack of data sharing could eventually lead to reduced vaccine innovation and is therefore a barrier for future vaccine innovation, see quote #18 and #19 (Table 6). In conclusion, vaccine nationalism appears to play a significant role in slowing down vaccination programs, contributing to escape mutants, and obstructing effective international collaboration and innovation.

5. Discussion and conclusion

We explored the influence of landscape shocks, like the COVID-19 pandemic, and the corresponding innovation policy responses by governments, on existing innovation systems. Based on an innovation system analysis that borrowed insights from recent mission orientation in innovation policy, we found that the pre-COVID vaccine innovation system suffered from an innovation backlog. The COVID-19 pandemic, however, showed acceleration could take place by linking with a well-functioning life sciences innovation system that is characterized by distributed coordination of responsibility (Cockburn et al., 2011). Various national and pan-national governmental organizations articulated innovation policies to create COVID-19 vaccines in a condensed timeframe. The formulation of the ambitious objective for a COVID-19 vaccine (providing directionality), and the subsequent allocation of grants and advanced market commitments (market formation), enabled biotech companies to engage in vaccine development and large pharmaceutical companies to direct efforts to COVID-19 vaccines (entrepreneurial activities, new entrants). Public coordination here was limited to the selection of promising innovation projects as being eligible for additional funding, and moderation of the regulatory landscape necessary to expedite implementation (creating legitimacy). Within different geographical areas, various technologies were further developed, leading to a global diversity of innovation projects. However, the mission could not be achieved if it did not build upon technologies that were developed earlier in the wider life sciences innovation system (knowledge development) as well as based upon Open Science principles and the Nagoya Protocol specifically developed to foster knowledge diffusion. In a similar vein, market commitments indicated a surge in demand that enabled supply chain stakeholders to prioritize deliveries to vaccine manufacturers, while coordination was not necessary given the limited number of actors being able to produce vaccines (resource mobilization).

In the case of COVID-19 vaccine development, governance responsibility was shared between public and private actors, together fueling development towards a clear ambitious goal, and successfully overcoming scientific and methodological barriers (Torreele, 2020). Interviewees indicated that private actors have proven their worth in being able to address societal challenges, maybe being even more efficient than public institutions. The private actor efforts were supported by condensed and accelerated innovation policies for COVID-19 vaccines, which successfully led to quite extensive vaccination coverage, at least in high-income countries, and a dampening effect on COVID-19 infections and mortality rates. At the same time, innovation policies struggled to address societal anxieties. The large role played by corporate actors is not only seen in the development phase but throughout the subsequent implementation phase as well. Vaccine deployment has been quite compelling – and in some cases even mandatory – in order to reach population immunity as quickly as possible. This forceful deployment created backlash amongst some groups in society, and might even have enforced vaccine hesitancy for other infectious diseases (creation of legitimacy and market formation), as trust in health authorities and vaccines is a major mediating factor to vaccine hesitancy (Truong et al., 2022).

A second issue related to the prevailing industry logics involves the privatization of earnings from the innovative vaccines (Mazzucato, 2011), even in the case of substantial public funding (market formation). Third, high-income countries continued prioritizing the immunization of their own populations, leading to less equity and distribution of vaccine doses to low-income countries (knowledge diffusion). The challenge for equitable access remains broadly framed, with unclear problem legitimacy and responsibility, and limited knowledge on the underlying values and interests that shape the problem (Wanzenböck et al., 2020). While the COVAX vaccine donation program is presented as a solution, there is a low willingness to cooperate, fueled by limited knowledge on the effects and side effects of such social innovation, especially in light of direct consequences for donating countries. These three issues – vaccine hesitancy, privatization of profits, and global inequity – might lead to further questioning of the legitimacy of vaccine innovation systems. The accelerated COVID-19 policy interventions may thus have even disturbed the existing vaccine innovation system in such a way that it might have acted as an 'elephant in the glasshouse'.

The urgency associated with COVID-19 vaccine innovation made it easier to advance policy interventions as part of an acceleration agenda (Wittmann et al., 2020). There is a need for strong (solution) directionality, based on constant articulation of urgency, ambitious targets and milestones (Wesseling and Meijerhof, 2021). The activities conducted in the context of acceleration, however, did not contribute to the wider goal of improving pandemic preparedness by boosting and changing the vaccine innovation system. In other words, the activities were not part of a transformation agenda, with reflexive governance enabling changes of existing institutional arrangements (Wittmann et al., 2020). The inclusion of a wide range of sectors and actors, seen as crucial for transformer missions (Mazzucato, 2018; Soete and Arundel, 1993), had been limited and knowledge remained contained within the pharmaceutical sector. A 'new' mission-oriented project would require a wider discussion that includes perspectives on how to prevent outbreaks of newly emerging infectious diseases (Larsen and Van de Burgwal, 2021) and on how to respond as a society (Moleman et al., 2021), thus leading to system-wide transformation.

Next to the temporal issues regarding the influence of COVID-19 vaccine policies on the vaccine innovation system, we also need to point to the geographical distribution of activities. Whereas vaccine R&D could make use of global knowledge spillovers, in practice many companies and knowledge organizations are distributed across the globe. We saw that the manufacturing, distribution and valuation part of vaccines is directly dependent on geographical boundaries and distinct institutional backgrounds. This led to nuances in formulation of policy objectives and activities across countries. At the same time, our results show linkages between geographical scales as well as countries mimicking each other's policies (Patrucco et al., 2022), which indicate that vaccine innovation takes place in a specific form of a global innovation system (Binz and Truffer, 2017). For mission policy, this means that we studied a case in which directed policy objectives and activities are not coherently organized on one geographical level and/or in which vertical coordination between levels is not straightforward, which makes it different from interventions usually studied in the context of mission-oriented innovation policy (Larrue, 2021).

We add to current literature that for tackling societal challenges related to resilience and preparedness of innovation systems, it is not enough to broaden purely technology-focused and global innovation policies. Innovation policies formulated with considerable urgency, like in the case of COVID-19, harbor the risk of limited deliberation among actors, as well as limited inclusion of a wide variety of actors. Following this, policy makers are urged to draft innovation policy that is able to take into account activities on various, yet linked geographical levels. Taking COVID-19 as an example where urgency was of the essence, and mindful of other crises that may share a similar sense of urgency, policy makers should furthermore aim to balance accelerator and transformer activities, so as to not prematurely destroy parts of the innovation systems that are needed for more long-term, societal transformation.

5.1. Strengths and limitations

The current study provides a clear overview of the main issues in the transitioning landscape of vaccine innovation. Data gathering took place between April and May 2021, a period during which the pandemic had not fully subsided yet, therefore the possibilities for further and other developments influencing the vaccine innovation system were still open. As a direct consequence, identification of possible changes in the innovation system might be imperfect or incomplete. European KOLs are overrepresented in this study, compared to KOLs from other regions, which may question the extent to which we were able to present a full picture of the global vaccine innovation system. Additionally, several crucial types of interviewed KOLs, such as venture capital funds and regulatory agencies, are underrepresented in this study.

Conceptually, the current study starts from an existing vaccine innovation system. Whether that innovation system is best demarcated by a technological definition is ambiguous, as vaccine development is based on a number of different platform technologies (Ramezanpour et al., 2015). Also in terms of geographical demarcation, clear system boundaries are difficult to draw as some

parts of the vaccine innovation system have global reach, such as knowledge development, whereas valuation-focused activities, such as legitimacy creation and market creation, are generally deeply embedded in national-level activities (Yap et al., 2022). As such, our work builds on and adds to literature on global innovation systems (Binz and Truffer, 2017) in which these valuation-focused activities on multiple geographical levels are connected (de Haan et al., 2021).

Finally, we contribute to current work on mission-oriented innovation systems. Although a vaccine innovation system is not formed as a result of a mission, the COVID-19 vaccine challenge did have a lasting impact on the system and conceptually the directionality-related activities contribute to understanding changes following mission articulation. The MIS framework that was previously developed and applied to a national context (Wesseling and Meijerhof, 2021) proved helpful to analyze the dynamics of this technological innovation system. The proposed MIS function of providing directionality, with its distinction into problem directionality, solution directionality and reflexivity enabled us to dissect different aspects of innovation policy that were implemented. The function creation of legitimacy provided a relevant lens to understand how accompanying policies can aid in development and dissemination of solutions.

5.2. Societal implications

Going forward, calls to coordinate outbreak response are getting louder. Vaccine inequity is not only morally unacceptable, but it also leads to prolonged exposure to new virus variants escaping vaccine immunity. Public sectors are called to take leadership in building an end-to-end health innovation system where innovation towards public health demands (e.g. vaccines, therapeutics, diagnostics) is supported in a portfolio approach within a symbiotic public-private partnership (Ramchandani et al., 2021; Reperant et al., 2014; WHO, 2021). Long-term and visionary investments in the innovation system could lead to a virtuous cycle, in which the vaccine sector benefits from innovative technologies, and in turn contributes to innovations in other pharmaceutical subsectors, like the mRNA platform does for oncology (Bonanni et al., 2018). It thus seems imperative that transformative innovation policies address these persistent complex problems in the vaccine innovation system.

Beyond a focus on technological acceleration, whether we will be able to transform to a model that prioritizes social and environmental wellbeing over economic approaches to infectious disease preparedness remains to be seen (de León et al., 2021), but the historic neglect of vaccine innovation and pandemic preparedness does not bode well. A united front by state-governmental, economic, civil society and academic actors, however, could enable a well-managed transition towards a more sustainable regime (Van de Burgwal et al., 2019; Van der Waal et al., 2020; Wells et al., 2020). This transition should thus not neglect transformer activities at the benefit of mere accelerator activities if we are to enable sustainable change.

As the transition towards a global, pandemic-prepared vaccine innovation system involves various actors and institutions on various geographical levels, our findings might even inform sustainability transitions more broadly. Transformations towards prepared innovation systems in volatile, uncertain, complex, ambiguous contexts are not easily defined, and require deliberation, vertical alignment and geographical distribution. COVID-19 innovation efforts show that despite elaborate insight into systemic failures and an expressed and broadly shared need for transformation, innovation policies in times of crisis default towards acceleration measures. Here we show that such policies may even be detrimental towards the initial transitions that were started. We therefore urge scholars and practitioners in other innovation systems to work on transformative innovation policies during ‘peace times’, especially linking global-level with local-level valuation-focused activities, as to enable rapid deployment when needed. We also encourage reflection on and promotion of remedies or mitigation measures for potential downsides of acceleration measures before implementing them.

Declaration of Competing Interest

The authors have no competing interests to declare. Linda van de Burgwal is also a consultant and entrepreneur in life sciences; Tom van der Valk is currently employed at Kempen Investment Banking; Manual Gadau was employed at Raymond James Corporate Finance, an international investment bank, during the majority of the time of data collection and writing; Hannes Kempter is employed at Raymond James Corporate Finance.

Data availability

The data that has been used is confidential.

Funding

This work was supported by the Dutch Research Council (NWO) [grant number VI.Veni.201S.044].

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