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SPOTLIGHT

Pandemic preparedness

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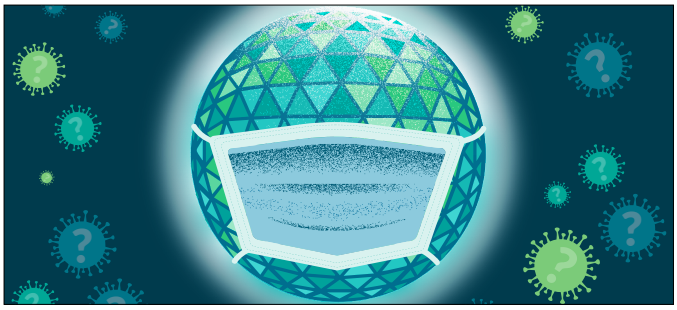
Pandemic preparedness



COMMENTARY

Challenges in outbreak vaccine development in the changing political climate

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Despite significant advances during the COVID-19 pandemic, the vaccine R&D ecosystem faces mounting challenges from geopolitical tensions, declining multilateral cooperation, and volatile funding patterns. Our analysis of historical funding reveals concerning trends, including reactive investment cycles, geographically concentrated funding sources, and excessive dependence on US government agencies that now face potential budget constraints. We identify five interconnected vulnerabilities threatening outbreak preparedness: funding volatility, pipeline bottlenecks especially at later clinical stages, regulatory pathway gaps, manufacturing capacity constraints, and insufficient portfolio diversity. These challenges cannot be addressed in isolation; effective solutions must leverage synergies across diagnostics, therapeutics, and vaccines through coordinated investment approaches, harmonized regulatory frameworks, and shared technological platforms. We propose actionable strategies to strengthen resilience in outbreak vaccine development amid political uncertainty and rising vaccine hesitancy, including diversified funding mechanisms, innovative regulatory pathways, and integrated development models that maximize cross-functional efficiencies between all medical countermeasures. Urgent collective action is needed to maintain recent gains in vaccine preparedness as the political climate continues to evolve, and the threat of emerging infectious diseases intensifies.

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OVERVIEW

Pandemics devastate lives and livelihoods. COVID-19 exemplified this with over 6.9 million deaths and global economic losses exceeding $12.5 trillion, including a 3.5% economic contraction in 2020 [1,2]. Beyond the direct toll, the World Health Organization (WHO) reported nearly 15 million excess deaths attributable to the pandemic's broader impacts on healthcare systems, exacerbated inequalities, and

undermined economic stability [3]. We cannot afford frequent pandemics of this scale, yet data suggests they could become more common. A 2021 study found a 38% lifetime probability of experiencing a COVID-19-scale pandemic, with such events occurring on average every 129 years [4]. The researchers warn this risk could double in coming decades due to increased disease emergence from environmental change. More than ever, pandemic preparedness is crucial for securing global and national health and security.

Vaccines, therapeutics and diagnostics when used in unison are the backbone of any pandemic response effort. One study showed that developing COVID-19 vaccines within 100 days (instead of the approximately 300 days it actually took) could have saved 8 million lives globally [5]. This underpins the origins of the 100 Days Mission (100DM), which aims to ensure that safe, effective, and affordable diagnostics, therapeutics, and vaccines (DTVs) are authorized and ready for scaled production within 100 days of a declared Public Health Emergency of International Concern (PHEIC). The urgency of enhancing vaccine development capacity is highlighted by ongoing threats such as the mpox PHEIC, rising H5N1 influenza transmission, and regional outbreaks of Marburg, dengue, and Oropouche viruses. The distinction between endemic and epidemic diseases is blurring, as pathogens once confined to specific regions more readily evolve into epidemics and could escalate into pandemics due to environmental and behavioral changes. Reflecting this, WHO's updated scientific framework for epidemic and pandemic research preparedness replaces static lists of pathogens with a dynamic, family-based approach which categorizes pathogens as priority, prototype, or 'Pathogen X' [6]. This broader lens includes endemic pathogens with pandemic potential and supports proactive, family-level research and development (R&D).

Vaccines played a critical role in controlling the COVID-19 pandemic, providing valuable lessons that must be built upon to strengthen our preparedness for future pandemic threats [7]. However, while vaccines remain essential, the global preparedness and response framework must focus on the synergistic development and deployment of DTVs. These complementary tools form the foundation of effective pandemic prevention, preparedness and response (PPR), and necessitate targeted R&D investment where significant gaps persist [8]. When developed and distributed equitably, these medical countermeasures (MCMs) not only accelerate response timelines and alleviate pressures on healthcare systems but also strengthen global health security by enabling all regions to effectively detect, contain, and mitigate emerging infectious disease threats [9].

Despite significant advances in vaccine technology during COVID-19, the funding landscape for vaccine R&D targeting emerging infectious diseases remains vulnerable. Progress has become increasingly difficult to sustain amidst a complex polycrisis environment characterized by limited resources, rising global vaccine hesitancy, and competing political priorities—challenges that are likely to intensify as geopolitical landscapes continue to evolve [10]. This paper analyses the current vaccine R&D ecosystem for priority pathogens with pandemic potential, identifies key vulnerabilities in funding mechanisms and development pathways, and proposes actionable solutions to strengthen global preparedness for future pandemic threats.

HISTORICAL CONTEXT: REACTIVE PATTERNS IN VACCINE R&D FUNDING

An examination of vaccine R&D funding across three recent major outbreaks—the 2014–2016 West Africa Ebola epidemic, the 2015–2017 Zika epidemic, and the

2020–2023 COVID-19 pandemic—reveals a consistent yet troubling pattern: sharp increases in funding during outbreak emergencies are followed by rapid declines as public attention and cases wanes.

During the West Africa Ebola epidemic, global vaccine R&D funding rose from less than $50 million in 2013 to over $600 million in 2015, only to decline by more than 40% in subsequent years [11]. Similarly, Zika vaccine funding peaked at approximately $163 million in 2017 before falling to $43 million in 2019; in 2023, only $23 million was reported, while there is still no approved vaccine for Zika [12]. Most dramatically, COVID-19 vaccine funding reached unprecedented levels (exceeding $9 billion globally in 2020–2022), but has since contracted by nearly 50% in 2023 [12].

This reactive funding pattern creates significant challenges for sustained vaccine development and preparedness efforts. Between the 2022 and 2024 mpox PHEICs there were missed opportunities to intervene and address unmet needs between outbreaks. This reactiveness is reflected in the R&D funding space which saw investment decrease by nearly two-thirds in 2023, consistent with the cessation of the WHO PHEIC in May 2023 [13,14]. The intermittent nature of support disrupts progression of promising candidates through the development pipeline, as well as continuity in research programs, leading to loss of institutional knowledge and expertise, and creating inefficiencies as programs repeatedly scale up and down [15]. Furthermore, the concentration of funding during outbreaks often leads to duplicative efforts and suboptimal resource allocation.

Reactive funding is particularly problematic for priority pathogens that have not yet caused large-scale outbreaks but pose a significant pandemic risk. Nipah virus, for example, has received minimal funding despite its high case fatality rate (40–75%) and potential for human-to-human transmission, with annual R&D investment rarely exceeding $10 million until recent increases [16]. This disparity highlights the troubling disconnect between evidence-based prioritization frameworks, such as the WHO's Blueprint list, and actual resource allocation decisions, revealing how reactive funding approaches fundamentally undermine proactive pandemic preparedness efforts [17].

VACCINE R&D FUNDING LANDSCAPE

Looking at vaccine funding in 2023, an 'intrapandemic year', demonstrates both promising developments and concerning trends. The 100 Days Mission Scorecard, developed by the International Pandemic Preparedness Secretariat and Impact Global Health, provides an objective evaluation of global readiness to develop and deploy critical diagnostics, therapeutics, and vaccines within 100 days of an emerging pandemic threat being declared [18]. Impact Global Health's G-FINDER data shows that in 2023, vaccine R&D funding for priority pathogens fell by 42% compared to 2022. An overwhelming majority (88%) of vaccine R&D funding for epidemic diseases remained concentrated on COVID-19 in 2023 [19]. Overall vaccine funding dropped by $1,148 million, with COVID-19 accounting for 99% (down $1,134 million) of this decline [20]. Even excluding COVID-19 figures, vaccine R&D for all other priority pathogens experienced a 7.1% reduction between 2022 and 2023 [21].

Only Chikungunya saw significant increased vaccine investment in 2023. Chikungunya investment surged substantially due to funding from the European Commission to the Coalition of Epidemics Preparedness Innovations (CEPI) [22], though this may represent a concentrated initial investment rather than guaranteed long-term support [23]. Funding for Marburg virus vaccines remained stable,

and all other priority pathogen vaccine R&D saw declining investment.

When examining geographical sources of funding, US government agencies accounted for approximately 63% of all public vaccine R&D investment for priority pathogens between 2014 and 2023—rising to 80% when excluding COVID-19-specific expenditures (Figure 1) [24]. In 2023, significant reductions by two major funders, the US National Institutes of Health (NIH) (a reduction of $654 million, or 45%) and the Biomedical Advanced Research and Development Authority (BARDA) (a reduction of $650 million, or 60%), affected multiple disease and product portfolios [14]. At the pathogen level, we see certain vaccine portfolios at particular risk, like Marburg vaccine development which in 2023 saw 99% of investment contributed from BARDA (60%), US Department of Defense (21%), and NIH (18%) [25]. This disproportionate reliance on one nation's funding priorities introduces profound structural vulnerabilities, as the continuity of global research becomes dictated by national political cycles and economic fluctuations.

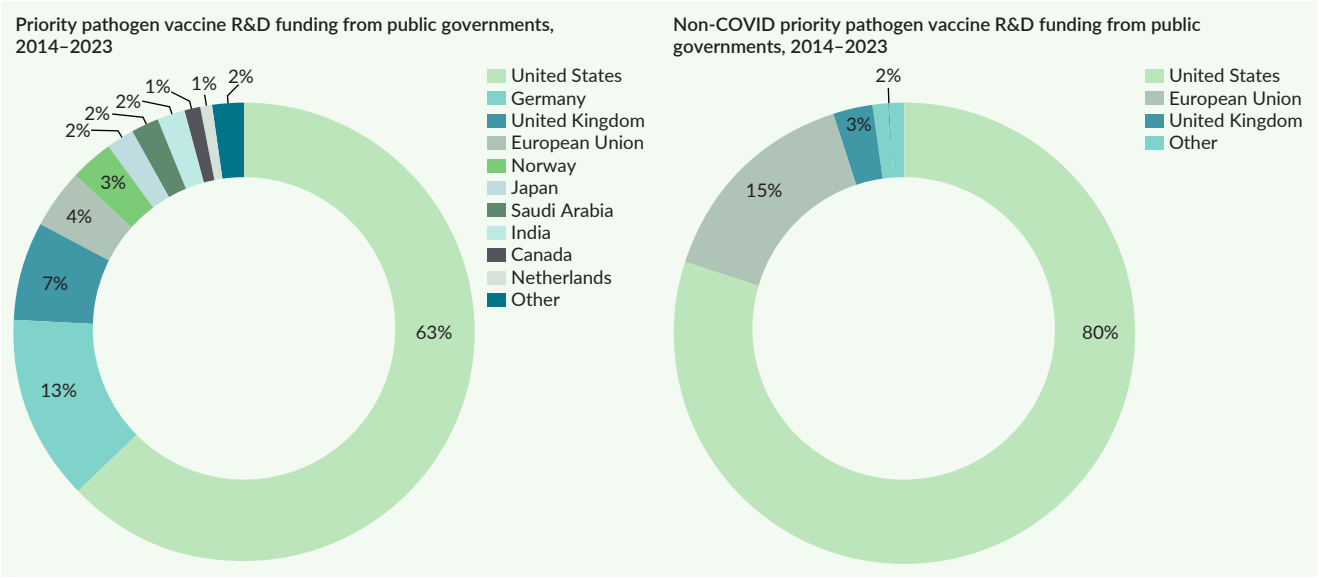
Compounding this challenge is the broader contraction of Official Development Assistance (ODA) for health. The UK, historically a major contributor, has significantly reduced its global health aid by over 30% between 2020 and 2022 [26] and further reductions have been announced in 2025 [27]. Similar reductions have been observed in other donor countries, including Belgium, France, the Netherlands, Sweden, Switzerland, and the USA with many redirecting funds toward domestic priorities or geopolitical imperatives [28]. The announced reductions in ODA so far in 2025 are equivalent to a 15–22% decrease compared to 2023 [28]. These shifts undermine the sustainability of vaccine development efforts for neglected and emerging pathogens, particularly in low- and middle-income countries that rely heavily on international support for research and manufacturing capacity.

VACCINE PIPELINE ANALYSIS

Despite challenges in sustainable funding, the vaccine landscape shows promising diversity in platform technology utilization

FIGURE 1

Global vaccine R&D funding for priority pathogens.



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at a rate greater than is seen in either diagnostics or therapeutics. Platform technologies using adaptable systems like messenger ribonucleic acid (mRNA) or viral vectors are essential for pandemic preparedness because they enable rapid, flexible responses to emerging threats and allow for swift development and scaling of DTVs [29]. The advanced utilization of platform technologies in vaccines demonstrates their potential to accelerate response to novel threats. This pipeline analysis is based on the most recent 100DM Scorecard, correct as of October 2024, and is updated on an annual basis (see reference for methodology) [18].

Clinical vaccine candidates for non-COVID priority pathogens employ seven different platform technologies, with viral vector platforms comprising the majority (60%, 31 candidates) [18]. Within viral vector platforms, significant diversity exists, with chimpanzee adenovirus (11 candidates) and recombinant vesicular stomatitis virus (8 candidates) being the most common [24].

Across pathogens of pandemic potential, vaccine pipeline progression was primarily concentrated at the preclinical-to-Phase 1 transition. Seven vaccine candidates entered Phase 1 clinical development in 2023, including three for Nipah, two for Rift Valley fever, and one each for Marburg and COVID-19. A single pan-filoviral vaccine candidate advanced to Phase 3, potentially offering protection against Ebola and Sudan virus, as well as Marburg virus, the latter two currently lacking approved vaccines [18].

This observed pipeline distribution with numerous candidates in preclinical and Phase 1 stages but few progressing to Phase 2/3 reflects both normal attrition in product development and specific challenges in advancing vaccines for diseases with sporadic incidence. Traditional vaccine development pathways typically require large-scale efficacy trials, which are difficult or impossible to conduct for diseases that are not actively circulating. This creates a structural bottleneck, as promising early-stage candidates cannot easily progress to licensure without outbreaks that enable efficacy testing. Overcoming this requires innovative approaches which we will discuss later in this paper.

KEY VULNERABILITIES IN THE VACCINE DEVELOPMENT LANDSCAPE

As highlighted above, the vaccine space stands out as one of the most well-resourced product areas, having the largest clinical pipelines with the most platform technology diversity [30]. This speaks to the global community's focus on preventative vaccines as a pillar of preparedness and reflects the benefit of strong multilateral leadership and investment [15]. Despite this level of coordination and maturity of vaccine development programs, our analysis of the current vaccine R&D landscape identifies several critical vulnerabilities.

Funding volatility and geopolitics

As discussed, vaccine funding remains reactive, with large outbreak-related spikes followed by rapid declines as public attention shifts. This pattern fails to support the sustained investment needed to build and maintain robust vaccine pipelines and capacities across multiple potential threats. The overreliance on US government sources, which account for more than 60% of global funding for emerging infectious disease vaccine R&D, creates significant vulnerability to shifting political priorities and budgetary constraints—this concerning dependence is evident across investments in vaccine development for both priority pathogens and platform technologies. Furthermore, the strong multilateral leadership and investment from CEPI and Gavi in the vaccine R&D ecosystem is

now at risk due to funding cuts, potentially reversing years of critical progress.

Recent developments starkly illustrate this vulnerability. Following the 2024 US elections, proposed budget cuts to agencies like BARDA and NIH threaten to disrupt numerous vaccine development programs [31,32]. Similarly, reductions in ODA from European nations following economic challenges have further destabilized the funding landscape [28]. This volatility undermines long-term planning and preparedness efforts and threatens continuity in vaccine development programs globally.

For example, multiple NIH-funded grants for next-generation COVID-19 and pan coronavirus vaccines, many of which could be adapted for other high-risk pathogens, were terminated at numerous institutions [33,34]. In the UK, AstraZeneca cancelled plans for a £450 million expansion of its vaccine manufacturing site in Liverpool, citing the government's decision to scale back public funding for pandemic vaccine preparedness [35]. These examples shine a light on how political and economic volatility can undermine long-term planning and continuity in vaccine R&D programs.

Pipeline bottlenecks at later clinical stages

While the transition from preclinical to Phase 1 clinical testing is relatively well-supported, progression through later clinical phases faces significant challenges for diseases that are not actively circulating. Traditional vaccine development requires demonstrating efficacy through randomized controlled trials during disease outbreaks, creating a fundamental mismatch with preparedness goals.

Without clear pathways for advancing candidates through late-stage development in the absence of ongoing outbreaks, promising early-stage candidates languish in development limbo for years. For example, several Nipah vaccine candidates have remained in Phase 1 for over 5 years despite promising immunogenicity data, due to challenges in designing and implementing Phase 2/3 studies for a disease with sporadic, geographically limited outbreaks [36].

For Lassa fever, a disease causing thousands of cases annually in West Africa, only two vaccine candidates have progressed to early clinical stages, and delays in advancing to Phase 2 have been attributed to difficulties in trial site readiness and limited funding for trials in endemic settings [37]. Similarly, a Rift Valley fever vaccine candidate that showed promising results in preclinical animal models has not progressed due to a lack of outbreak-driven trial windows and absence of enabling frameworks [38]. There is a pressing need for enablers to ensure continued momentum through later development phases, which we will discuss later.

Regulatory pathway gaps

Current alternative regulatory pathways for vaccines against emerging infectious diseases remain insufficiently defined, validated, and de-risked to encourage developers to pursue innovative approaches beyond traditional large-scale randomized controlled trials. For example, the US Food and Drug Administration's (FDA) 'Animal Rule', which permits vaccine approval based on efficacy data from animal studies if human trials are deemed unethical or unfeasible, serves as a potential facilitator for alternative pathways for vaccine development [39]. Notably, BioThrax® (Anthrax Vaccine Adsorbed) received approval under this rule for post-exposure prophylaxis against inhalational anthrax, supported by studies in rabbits and non-human primates [40]. Despite this precedent, regulatory approval through the Animal Rule remains limited, as many high-priority pathogens lack validated animal models that accurately reflect

human disease progression and treatment response.

For instance, while African green monkeys have been used to model Nipah virus infection, the variability in disease manifestation across species complicates the establishment of a universally accepted model [41]. In the case of the Marburg virus, even though non-human primates are considered the gold standard for testing MCMs, no vaccine has 'full' regulatory approval to date [42,43]. These examples highlight that the absence of standardized, regulatory-accepted animal models for these diseases impedes the progression of vaccine candidates through the approval pipeline.

During recent outbreaks, national regulatory authorities have demonstrated dynamic approaches through emergency use authorizations. Rwanda approved Sabin's investigational Marburg vaccine during its 2024 outbreak [44] while Nigeria and the Democratic Republic of Congo granted emergency authorization for mpox vaccines [45,46]. While these emergency authorizations demonstrate regulatory adaptability during crises, the lack of harmonized, pre-established alternative pathways for vaccine development continues to impede systematic progress toward licensure during non-outbreak periods.

These regulatory gaps increase the risk for developers, particularly when combined with funding uncertainty. Without clear, validated, de-risked regulatory pathways, commercial vaccine developers will remain reluctant to invest in diseases with limited market potential, leaving critical gaps in preparedness.

Manufacturing capacity constraints and lack of geodiversity

Geographically concentrated manufacturing capabilities limit global access to vaccines during emergencies and create vulnerabilities in the supply chain. During COVID-19, vaccine manufacturing capacity was heavily concentrated in high-income countries, leading to significant inequities in access [47].

In an effort to increase global manufacturing capabilities, the African Vaccine Manufacturing Accelerator (AVMA), founded in 2024, pledged $1.2 billion over 10 years to stimulate vaccine production across Africa [48]. As of mid-2024, 25 projects were active, with several commercial-scale facilities underway [49]. This extended timeframe reflects the inherent complexity of building manufacturing capacity, highlighting that these are long-term investments rather than quick fixes. The full benefits of these initiatives will likely take many years to materialize, creating a gap between current needs and future solutions that requires careful consideration.

Complementing AVMA's efforts, the Regional Vaccine Manufacturing Collaborative (RVMC)—established by CEPI, the US National Academy of Medicine, and the World Economic Forum—has emerged as a global coordination platform. RVMC supports the development of regional manufacturing ecosystems by providing technical advice, fostering alignment across initiatives, and monitoring global progress toward equitable vaccine manufacturing capacity [50].

Furthermore, the WHO/Medicines Patent Pool (MPP) mRNA Technology Transfer Program has established a hub in South Africa including agreements with partners across Southeast Asia and Latin America, to further bolster regional capacity, although Argentina's intention to withdraw from WHO may reverse some of this progress [51,52]. These initiatives aim to reduce dependency on centralized suppliers and create resilient supply chains tailored to regional needs; however, regional capacity continues to be limited outside of high-income countries.

Finally, the economic challenges of maintaining manufacturing capacity

between outbreaks further complicate preparedness. Without sustainable models that blend routine production with the ability to surge during emergencies, manufacturing facilities may become financially unviable, leading to capacity loss during interpandemic periods.

Insufficient portfolio diversity

Vaccine R&D is disproportionately concentrated on a few high-profile pathogens due to funding priorities and scientific and technical barriers. The concentration of investment in high-profile pathogens like influenza and SARS-CoV-2, while understandable given their known impact, leaves significant gaps for other viral families that could cause the next pandemic [53]. Some pathogens such as Nipah and Crimean-Congo hemorrhagic fever (CCHF) viruses, while included in the WHO Blueprint prioritization, have few candidates in clinical stages [18]. This creates fundamental blind spots in preparedness, and leaves populations vulnerable to specific threats. For instance, CCHF has a high case fatality rate and geographical spread yet has no vaccines in Phase 2 clinical trials or above [54]. Others like SARS-CoV-1 do not have any vaccine candidates in clinical development as shown in the 100DM Scorecard [18].

In many of these cases, the limited pipeline reflects not only a lack of investment but also the complexity of the pathogens themselves. Scientific barriers such as incomplete understanding of the pathophysiology, difficulty in identifying conserved immunogenic targets, or lack of reliable animal models complicate the development of viable vaccines. In such instances, vaccines may not be the most appropriate or effective tool. For some pathogens, particularly those with non-human reservoirs or environmentally driven transmission dynamics, diagnostics or therapeutics may offer more feasible or impactful public health interventions. MCM strategies must therefore be aligned with the biological and epidemiological realities of each threat.

Portfolio-based R&D and prototype pathogen approaches remain essential to closing these gaps. These must be pursued with a nuanced understanding that while vaccines are important tools in the MCM arsenal, they are not the only critical first line of defense. Ensuring that the right tools are developed for the right pathogens will maximize impact and reduce wasted effort.

INNOVATIVE SOLUTIONS FOR STRENGTHENING VACCINE PREPAREDNESS

To overcome the systemic vulnerabilities outlined above, and to keep the 100DM within reach, the global vaccine R&D ecosystem requires a shift towards more proactive, collaborative, and context-specific solutions. This includes strengthening and diversifying funding mechanisms, adopting regulatory frameworks that support speed and safety, and ensuring that manufacturing and product development capacities are distributed equitably. Innovation must be designed to deliver speed, safety and sustainability, while remaining grounded in scientific feasibility and public health relevance. The following solutions aim to build a 100DM-ready vaccine ecosystem that is more efficient, resilient, equitable, and strategically aligned with the realities of public health threats that we face.

Diversified funding mechanisms

Amid growing fiscal austerity and a resurgence of inward-looking national strategies, diversified funding mechanisms are more important than ever to stabilize the vaccine R&D ecosystem. Portfolio-based funding, while ideal in theory, faces political headwinds in the current climate. This emphasizes the need for creative approaches to PPR funding such as

adapting its implementation to match today's constraints by leveraging smaller, modular portfolios, aligning incentives through regional cooperation, and anchoring funding in shared global infrastructure.

Research has shown that the COVID-19 pandemic highlighted the value of agile public-private coalitions, with successful examples emerging in infectious disease surveillance systems that require multisectoral collaboration and efficient use of limited resources [55,56]. Innovative financing solutions like public-private partnerships (PPPs), venture capital mechanisms, and pooled regional investments can help bridge the widening funding gap. These mechanisms have enabled more flexible, responsive, and sustained funding environments for priority pathogens.

Public–private partnerships demonstrated value during the COVID-19 response, enabling the rapid mobilization and coordination of resources and expertise across different sectors [57,58]. A notable example is the 2024 expansion of the CEPI Investment Strategy, which formalized long-term strategic partnerships with biotechnology firms and regional manufacturers to accelerate vaccines for priority threats such as Lassa fever and Nipah virus [59]. This represents a shift from reactive to proactive partnership models. Similarly, the WHO's mRNA Technology Transfer Hub, initially established in South Africa, has since attracted PPPs to expand technology access and regulatory alignment across Latin America and Southeast Asia [60].

Beyond traditional global health partnerships, alternative financing approaches have also emerged. Recent years have seen increased engagement of venture capital in pandemic-relevant biotechnology, which has been particularly effective in particularly stimulating innovation in vaccine technologies and delivery platform in middle income countries [61]. Innovative funding vehicles such as PandemicTech illustrate creative approaches to pandemic preparedness, including the use of venture philanthropy and innovation-focused funding mechanisms to support early-stage solutions for emerging infectious disease threats [62]. These new financing models work in tandem with targeted investment funds in the African and Southeast Asian regions to address early-stage capital gaps for emerging infectious disease solutions.

Beyond individual projects, broader pooled mechanisms have gained traction. The African Union-backed African Vaccine Manufacturing Accelerator (AVMA) blends concessional finance and performance-linked subsidies to support vaccine manufacturing at scale. The AVMA model draws inspiration from the Global Fund [48] and aims to leverage multi-donor contributions to reduce market risk and build long-term regional resilience.

With these advances in alternative forms of funding, the role of governance remains critical. As noted in the literature [63], the influence of commercial determinants of health and misaligned incentives in PPPs can undermine public health objectives if not carefully regulated. Ensuring that funding models are transparent, equitable, and accountable to public health goals is therefore paramount.

Beyond these financing mechanisms, strategic approaches can further strengthen the funding ecosystem. Investments in endemic disease research offer one such approach by creating adaptable infrastructure that remains active between outbreaks. By aligning pandemic preparedness with ongoing endemic disease programs, this strategy ensures that facilities, expertise, and supply chains serve both everyday health needs and emergency response. Platform technologies that can pivot between endemic and pandemic products help address a fundamental challenge: keeping research and manufacturing systems operational during 'peacetime' while ensuring they can be quickly mobilized during emergencies.

Cross-funding DTV development represents a strategic model with significant benefits for pandemic preparedness - not only for systems and infrastructure, but ultimately for people. This integrated approach recognizes that these countermeasures are fundamentally interdependent, creating synergistic efficiencies while reducing overall portfolio risk. The COVID-19 pandemic demonstrated these advantages when the UK Vaccine Taskforce and the US Operation Warp Speed simultaneously funded complementary DTVs, enabling diagnostics to accelerate vaccine clinical trials and therapeutics to protect populations while vaccines were still in development [64,65]. This integrated funding approach enabled rapid identification of monoclonal antibody treatments, with insights from antibody discovery helping to guide vaccine design and facilitated the design of diagnostic tests that could differentiate between vaccine-induced immunity and natural infection.

The CEPI and Foundation for Innovative New Diagnostics (FIND) partnership for Lassa fever and Nipah virus demonstrates how coordinated funding across countermeasures can strengthen health systems. This collaboration recognizes that diagnostics are essential frontline tools for outbreak detection and response in their own right, while also acknowledging their critical role in enabling effective vaccine development and evaluation [66].

In summary, a diversified and strategically governed funding ecosystem that blends public and private capital, supports regionally embedded R&D, and fosters cross-sectoral collaboration will be key to advancing vaccine development for high-consequence pathogens and reducing global vulnerability to future pandemics.

Advanced regulatory frameworks

Developing regulatory frameworks that focus on platform technologies rather than individual products could significantly accelerate approval processes. The FDA's draft guidance on platform technology designation offers a potential model, allowing developers to leverage safety and manufacturing data across multiple products using the same platform [67,68]. Similarly, the European Medicines Agency (EMA) launched the PRIME initiative, which provides enhanced regulatory support for priority medicines. The EMA guidance notes that alternative data sources, including platform/pilot scale data, can be considered provided their relevance to the product is established [69]. These platform-focused approaches are complemented by alternative development pathways that can circumvent traditional efficacy trial requirements.

Controlled Human Infection Models (CHIMs) are gaining traction as valuable R&D enablers, offering a way to accelerate efficacy testing and rapidly downselect and de-risk vaccine candidates, while also generating critical insights into immune correlates of protection to inform vaccine design and evaluation [70]. Recognizing this, WHO developed guidance for conducting controlled human infection studies [71]. CHIM data has contributed to the development of key vaccine candidates (e.g., typhoid conjugate and oral cholera vaccines), supporting their WHO pre-qualification and facilitating faster access to vaccines in markets where they are needed most [72]. However, ethical considerations surrounding CHIMs, particularly regarding the safety and welfare of volunteers, are paramount. Researchers emphasize the need for comprehensive ethical frameworks to navigate the challenges of intentionally infecting healthy individuals [73].

As discussed above, for pathogens where human challenge studies are not ethical or feasible, the animal rule pathway offers another alternative. Developing approved animal models for high priority pathogens may serve as a valuable alternative

pathway to licensure. These developments are strengthening regulatory frameworks for vaccines against diseases where traditional efficacy trials remain impractical.

Increased investment in identifying and validating immunological correlates of protection (CoPs) represents another promising avenue for accelerating vaccine licensure [74]. In 2022, Wellcome convened an international multi-stakeholder workshop to discuss the use of CoP to accelerate vaccine development, including developers, manufacturers, regulators, public health officials and policymakers from 17 countries, including seven low- and middle-income countries, leading to a funding call [75,76]. These efforts should be supported and expanded upon and may significantly reduce reliance on clinical disease endpoints for vaccine approval. A critical next step will be working with regulators to develop a shared framework that clearly defines the data needed to support the use of CoP biomarkers in licensure pathways.

The integration of these approaches, alongside innovative trial designs that can adapt to outbreak scenarios, are essential to move promising candidates through the pipeline. Implementing these within modernized regulatory frameworks would create a more flexible ecosystem for outbreak vaccine development. However, challenges remain, particularly around global regulatory harmonization and acceptance of these novel pathways in different jurisdictions. These are not quick fixes but require sustained investment, and early, continuous dialogue between developers, funders and regulators.

Sustainable manufacturing models

Developing economic models that blend routine and emergency vaccine production would help maintain manufacturing capacity between outbreaks. This might include incentives for production facilities capable of rapidly switching between routine vaccines and pandemic countermeasures, or guaranteed procurement mechanisms that ensure minimum production volumes during interpandemic periods [77].

Regional manufacturing initiatives, such as the AVMA, require sustained support beyond initial capital investments. Technical capacity building, stable funding mechanisms, and supportive regulatory environments are essential for these initiatives to succeed over the long term [48]. While these long-term investments are essential, interim solutions are urgently needed to bridge the gap between their initiation and operationalization. These could include coordinated sublicensing and technology transfer agreements with existing manufacturers, capacity reservation contracts that ensure access to doses during emergencies, and strategic stockpiling of essential components. It could also include inter-regional partnerships, shared manufacturing agreements, or investment in modular, scalable platforms that can be activated quickly when needed. Without such interim measures, the manufacturing bottleneck will persist for years despite ongoing long-term investments.

Advanced market commitments, building on successful models like Gavi's pneumococcal vaccine program, could provide market incentives for continued development and manufacturing even in the absence of ongoing outbreaks [78]. These mechanisms guarantee future purchases at predetermined prices, reducing market uncertainty for developers and manufacturers.

Coordinated and adaptable approaches for speed and access

Investments in pathogen agnostic R&D and enabling technologies, such as the prototype pathogen approach, innovations in programmable platform technologies, geo-diversified manufacturing, and standardized clinical trial protocols offer a

strategy to build transferable capabilities across vaccines and thus create efficiencies in innovating vaccine development.

The prototype pathogen approach operates by investing in 'prototype vaccines' for representative pathogens within viral families to create scientific knowledge, manufacturing processes, and regulatory precedents that can be rapidly adapted to related emerging threats. WHO's support for prototype vaccines against pathogen families through its Collaborative Open Research Consortia (CORCs) exemplifies this strategy, aiming to foster viral-family level coordination across a wide range of viral families with pandemic potential [79].

A key element of this broader strategy is advancing vaccine platform innovations that are scalable, affordable, and adaptable to multiple pathogens. Initiatives like CEPI, BARDA's Project NextGen, and Wellcome Leap's R3 program are driving the development of innovative technologies, such as thermostable mRNA vaccines, controlled-release formulations for multiple-dose delivery, alternative administration systems like microarray patches and oral formulations, and modular, geo-diversified manufacturing platforms [80–82]. These innovations are crucial for enabling rapid product pivots, scaling production, reducing costs, and ensuring equitable access.

Master protocols for vaccine trials across multiple pathogens could also create efficiencies in clinical development and regulatory review [83]. By establishing standardized approaches to key elements of trial design, these protocols could reduce startup times during outbreaks and improve comparability of results across studies [84].

Coordinated R&D and technology investments are a strategic approach to create an infrastructure that supports preparedness regardless of which specific pathogen emerges next. The efficiency of this approach contrasts sharply with siloed, pathogen-specific investments that fail to leverage cross-cutting opportunities.

CONCLUSION

The vaccine development landscape for outbreak-prone diseases presents a striking contrast. Vaccines exhibit the most robust pipeline and platform diversity among MCMs, reflecting decades of strategic investment and multilateral coordination by key stakeholders. Yet this progress remains precarious—funding is reactive, pathogen-specific, and heavily dependent on US government sources. Recent political shifts and rising vaccine hesitancy threaten established funding mechanisms, with potential reductions to CEPI and Gavi creating immediate risks to the vaccine ecosystem.

A more sustainable approach requires diversifying funding sources beyond traditional donors. Current funding patterns create structural vulnerabilities, particularly given the disproportionate reliance on US government agencies. There is an opportunity to redistribute decision-making influence through expanded participation from emerging economies and innovative financing solutions like public-private partnerships, venture capital mechanisms, and pooled regional investments. Additionally, leveraging investments in endemic disease research offers practical advantages for maintaining funding continuity while addressing both immediate health needs and pandemic preparedness objectives. Moreover, as COVID-19 demonstrated, diagnostics, therapeutics, and vaccines function as an integrated system: diagnostics are essential not only for early detection but also for enabling targeted public health interventions and facilitating efficient vaccine trials, while therapeutics bridge protection gaps during vaccine development. Shared technological platforms like mRNA have potential to benefit multiple countermeasures, creating efficiency and resilience.

Strengthening outbreak vaccine development to keep the 100DM within reach in the current political climate requires

coordinated action across five areas: diversifying funding sources to reduce vulnerability to political cycles; implementing alternative regulatory pathways such as immunobridging to advance vaccines without outbreak-dependent efficacy trials; building sustainable regional manufacturing capacity; investing in cross-cutting platform technologies; and strengthening coordination mechanisms that integrate vaccine efforts with complementary diagnostics and therapeutics.

These measures would build a more resilient vaccine ecosystem capable of responding to outbreak threats despite geopolitical fluctuations. Such resilience extends beyond pandemic prevention to strengthen routine health systems globally [65]. The scientific advances in vaccine technology must now be complemented by equally innovative financing and governance structures that maintain consistent focus on pandemic preparedness despite changing political landscapes.

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PANDEMIC PREPAREDNESS

SPOTLIGHT

Rethinking the global vaccine funding landscape: where do we go from here?

Rebecca F Grais

VIEWPOINT

"This moment offers a chance to address long-standing imbalances and build a system that is more accountable, locally rooted, and globally inclusive."

On February 17, 2025, **Charlotte Barker**, Editor, *Vaccine Insights*, spoke to **Rebecca Grais**, Executive Director, Pasteur Network, about the power imbalances in the global health network, including the distribution and development of vaccines, and the importance of creating a more sustainable and equitable system. This article has been written based on that interview.

On January 20, 2025, Donald Trump was inaugurated as the 47th President of the USA and signed an executive order to immediately freeze USAID funding. Many programs were later cancelled, and the USA formally withdrew from the World Health Organization (WHO). This abrupt withdrawal has further exposed the fragility of a global health system that has historically leaned heavily on US financial contributions—particularly in the areas of vaccine development and programming. While these funding cuts are harmful in the short term, they also present an opportunity to rethink how the global health system is structured—and to build something more equitable, resilient, and representative of all regions.

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BEYOND DEPENDENCY: RETHINKING GLOBAL HEALTH FINANCING?

For decades, the financial engine of global health has largely come from rich countries, flowing into other countries via bilateral aid and multilateral institutions. Vaccine programs—routine immunization, mass campaigns, and emergency responses—have been no exception. Organizations like Gavi have played a central role, with substantial US backing. But this concentration of financial power among a handful of donors has introduced serious vulnerabilities.

The sudden removal of a major donor exposes the consequences of this imbalance: vaccination campaigns may stall or cease altogether in some countries, and vital research initiatives could be disrupted. Worse still, it may signal to other wealthy countries that retrenchment is acceptable, encouraging them to scale back their own contributions at a time when global needs are growing.

THE COST OF VOLATILITY AND DISTRUST

Inconsistent aid flows don't just affect programs—they erode trust. For many governments and communities, especially those with painful histories of extractive or exploitative global partnerships, such unpredictability can reinforce skepticism. Vaccine hesitancy and misinformation already challenge immunization efforts globally; unreliable support may add to the disillusionment, reducing both uptake and participation in future collaborative research and public health initiatives.

REDEFINING LEADERSHIP AND EXPERTISE

Normative guidance on vaccines can support country decision-making. Entities like WHO's Strategic Advisory Group of Experts (SAGE) have provided essential frameworks for vaccine introduction and policy decisions via vaccine position papers. Yet these global platforms must evolve to reflect a broader, more inclusive spectrum of expertise and leadership.

Strengthening regional scientific institutions, regulatory capacity, and vaccine production capabilities around the world is essential. This isn't just about filling gaps left by departing donors; it's about recalibrating the system so that health solutions are developed *with* and *by* the communities they aim to serve. Ensuring that communities are included in decision-making, and that vaccines are appropriate and wanted by those communities, would be a significant step forward.

PREPAREDNESS THROUGH LOCAL STRENGTH

Epidemic and pandemic preparedness has been another area heavily shaped by US funding in many geographies. But the best preparation for future pandemics comes not from external intervention, but from robust local health systems: strong primary care, reliable supply chains, open data-sharing, and mutual trust between governments, clinicians, scientists, and communities. These elements are best built from the ground up, in every country.

The measles resurgence in the USA illustrates how fragile vaccine confidence can be—even in high-income settings. But globally, the challenges are magnified by power disparities, histories of medical exploitation, and rapidly spreading misinformation. Addressing this means prioritizing trust, agency, and local ownership.

A ROLE FOR GLOBAL NETWORKS

Organizations like the Pasteur Network, which are not state-based, with a presence in 25 countries across all continents, are uniquely placed to foster

cooperation, share scientific knowledge, and provide neutral platforms for coordinated response. These types of distributed networks are essential to detect, prevent, and respond to epidemics—locally and globally.

SEIZING THE MOMENT: TOWARD SUSTAINABILITY AND EQUITY

A truly global health system cannot rely on the priorities of a few. The moment demands a shift toward a system where all regions can contribute meaningfully to research, development, and manufacturing—especially in vaccines. Strengthening regional production capacity and innovation ecosystems is essential not just for autonomy, but for resilience in the face of epidemics, pandemics, supply chain disruptions, and geopolitical shifts.

The current US policy shift should serve as a wake-up call for many. Regardless of whether these changes are temporary or long-lasting, they underscore the danger of an overly centralized model. This moment offers a chance to address long-standing imbalances and build a system that is more accountable, locally rooted, and globally inclusive.

While the outlook may seem uncertain, history has shown that crisis often catalyzes change. The challenge now is to ensure that this change moves us toward a fairer, more collaborative global health future—one where solutions are driven by shared goals, diverse leadership, and mutual respect.

BIOGRAPHY

Rebecca F Grais is the Executive Director of the Pasteur Network. Previously, she served as the Director of Research at Epicentre, an epidemiology and research branch of Médecins Sans Frontières. Her work primarily focuses on the prevention of infectious diseases and emerging infections in low- and middle-income countries, with an emphasis on public health intervention studies and efficacy trials of new vaccines and therapeutics. She also prioritizes professional development, mentoring, and management training for underrepresented populations in scientific research to foster career advancement and healthcare innovation. Dr Grais holds a doctorate, two Master's degrees, and a Bachelor's degree from Johns Hopkins University, Baltimore, MD, USA as well as a 'Habilitation à diriger des Recherches' from the Faculté de Médecine Paris Saclay, France. She has authored over 200 peer-reviewed publications and participates in numerous scientific, funding, and international organization committees and advisory groups, particularly in vaccine development and epidemiologic studies among vulnerable populations. Additionally, she is a member of the Strategic Advisory Group of Experts at the WHO.

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VACCINE INSIGHTS

PANDEMIC PREPAREDNESS

SPOTLIGHT

COMMENTARY

The role of African scientists in pandemic preparedness

Evelyn Gitau, Uzma Alam, Caxton Murira, and Linda Murungi

The Global Health Security (GHS) index, conducted post-COVID-19, revealed sobering facts about countries' unpreparedness to meet future epidemic and pandemic threats. The majority of African countries scored below the global average in core health security pillars including the ability to prevent, detect and respond to biological threats, presenting a massive opportunity for discourse. This article conveys the message that Africa must take the lead in its own pandemic preparedness agenda, leveraging the significant, yet often hindered and overlooked capabilities of its own scientists, so that the continent is not just prepared, but also actively leading the response to future health crisis. It explores the critical current and future role of African scientists in confronting these challenges and leading the shift in Africa's pandemic response. It also delves into how African researchers are generating context specific data to strengthen health systems, pioneering R&D and local manufacturing to reduce reliance on imports, designing data driven preparedness plans, enhancing clinical trial capabilities and building public trust through community engagement.

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African scientists are integral in not only responding to the systematic gaps that continue to plague the health systems by designing tailor-made responses after a health crisis/emergency but in designing research projects that stay ahead of them and bridge the divide through research, innovation, crafting policies, and building up local capacities.

Over the years, African scientists have stepped up during major outbreaks, including COVID-19, Ebola, HIV/AIDS, Marburg, Mpox and various other infectious diseases. They have played a critical role in running clinical trials that have significantly improved how the continent handles health crises and covering a range of initiatives including developing vaccines and diagnostics, researching new therapies, laboratory testing and bolstering research infrastructure.

However, despite African scientists' demonstrated role in pandemic preparedness, the continent continues to face major challenges in this area. The Global Health Security (GHS) index [1] highlights structural issues, economic hurdles, technology

gaps, a complex regulatory landscape, unclear coordination mechanisms, supply chain challenges, and social factors as roadblocks that make it tough to respond effectively to health emergencies like COVID-19 or Ebola, not to mention any new infectious diseases that might pop up.

BARRIERS TO PANDEMIC PREPAREDNESS IN AFRICA

Weak health systems and limited resources

One of the major challenges Africa faces in responding to pandemics is the weak healthcare system and lack of resources to support the agility needed to respond to pandemics. It is difficult to manage big outbreaks when many countries on the continent don't have enough hospital beds, healthcare professionals, ICU units, and medical facilities overall, particularly in rural Africa, where the majority of the population resides. This situation makes it extremely hard to deal with a surge of patients when a pandemic hits [2].

To make matters worse, many trained healthcare workers leave for better-paying jobs in other countries, which is often referred to as 'brain drain'. This migration weakens an already fragile workforce.

Disruption of essential health services

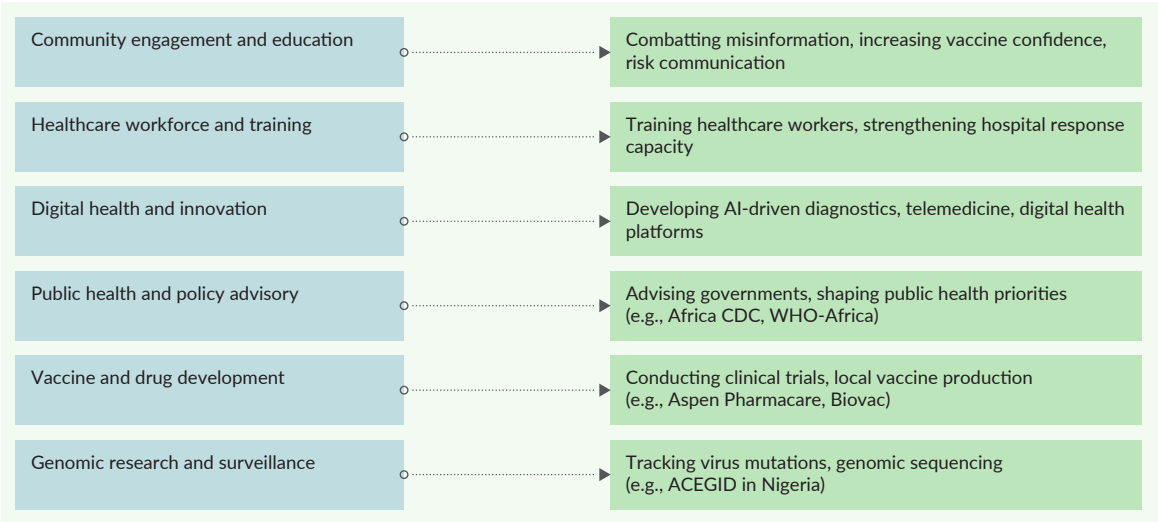
During pandemics, important health services—like maternal care, vaccinations, and treatments for chronic illnesses—often get sidelined. For example, when COVID-19 struck, treatments for HIV/AIDS, malaria, and tuberculosis were thrown into chaos in several African nations [2].

Underuse of modelling and data for decision-making

The use of modelling to allocate resources and predict needs could help address issues related to preparedness and agility during pandemics and epidemics. However, while African researchers have provided good data on the high burden of pre-existing diseases such as HIV/AIDS, tuberculosis, malaria, and malnutrition, which can increase the risk of severe illness and complications from pandemics like COVID-19 [3], many healthcare systems struggle with

FIGURE 1

Role of African researchers in pandemic preparedness.



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managing these diseases while addressing pandemic needs. Modelling could help in designing data driven, community responsive preparedness plans to inform resource allocation, risk communication and resilient strategies, helping systems better navigate the complex challenge of managing multiple health crisis concurrently.

Dependence on imported medical supplies and vaccines

Another major hurdle is Africa's heavy dependence on imported medical supplies, vaccines, and treatments. This reliance makes the continent extremely vulnerable to disruptions in global supply chains during pandemics. Only a handful of countries, like South Africa, Egypt, and Senegal, can produce vaccines themselves. As a result, major delays in receiving vaccines severely slows down response mechanisms [4]. This was clearly demonstrated by the global COVID-19 vaccine distribution which showed that Africa was last in line for vaccine supplies due to reliance on imports. Another example of this is the constant shortage of cholera vaccines to help prevent the numerous epidemics that break out across the continent. Vaccine security for emergency vaccines such as oral cholera vaccine (OCV), requires a mechanism that ensures guaranteed production of vaccines, multi-year vaccine financing, and development of long-term forecasting of vaccine requirements [5].

High cost and inequitable access to pandemic supplies

The heavy reliance on imported goods means that the cost of essential medicines and key pandemic response supplies such as personal protective equipment (PPE) is too high, putting them out of reach for low-income communities and often relying on subsidies from donors. This is further exacerbated by the fact that many African governments struggle to negotiate affordable prices for pandemic-related treatments and supplies [4]. The pandemic led to a significant increase in the demand for medicines, medical equipment, and technologies. This surge made it difficult for individual countries to manage orders effectively, highlighting the need for a collaborative approach to procurement. Beyond existing initiatives such as the Africa Medical Supplies Platform [6] which faced access challenges owing to global supply chain shortages during COVID, African governments could benefit from Joint Procurement Associations (JPAs) to negotiate affordable prices for pandemic treatment supplies, improving access to medical drugs and equipment through pooled purchasing strategies, as demonstrated by the European Union's successful implementation [7].

Fragmented response plans and weak coordination

Tackling a pandemic requires concerted effort from various key players, including governments, policymakers, public health and regulatory agencies, and international organizations. However, many African countries have piecemeal pandemic response plans, which, more often than not, do not rely on solid evidence or input from experts and give relatively little attention to local-level responses, where issues such as continuity of health services, stakeholder participation and resource mapping are critical. Most of these pandemic response plans also fail to align with global and continental plans, thereby creating hurdles in joint response initiatives as well as proper utility of available resources [8]. This has led to mixed messaging when it comes to policies about lockdowns, travel bans, and public health measures [9]. Africa CDC has made advances in trying to enhance coordination among nations. Still, many public health agencies within African countries

are struggling because of a lack of funds and know-how to effectively respond to pandemics.

Underfunded national public health institutes (NPHIs)

The lack of funds in national public health institutes (NPHIs) within African countries is a multifaceted issue influenced by several interrelated factors. These include inadequate government budget allocations, heavy reliance on external funding, and systemic inefficiencies. The financial constraints faced by NPHIs are compounded by broader economic challenges and policy implementation gaps, which hinder the development of robust health systems capable of addressing public health needs [9]. This whole situation tends to limit pandemic responsiveness. Additionally, funds often come with strings attached or get stuck in long, drawn-out approval processes that limit timely intervention. In the current geopolitical climate [10], most African governments will have to rethink and implement sustainable strategies to support its future pandemic preparedness and response efforts.

Limited clinical trial capacity and research infrastructure

The role of adequate clinical trial capacity is pivotal to pandemic preparedness, both for the continent and globally due to its critical function in rapidly developing and validating medical interventions, such as vaccines and therapeutics, during health crises. The COVID-19 pandemic demonstrated the need for rapid development and deployment of vaccines and treatments. Clinical trial networks, such as the COVID-19 Prevention Network (CoVPN) [11] and The Consortium for COVID-19 Vaccine Clinical Trials (CONCVACT) in Africa, were instrumental in quickly operationalizing Phase 3 vaccine trials, leading to the rapid authorization of vaccines within a year of the virus's discovery [12] exemplified the importance of regional collaboration and standardized protocols in enhancing clinical trial during COVID-19 and shoed what is possible with proper coordination. However, lack of sufficient financial resources to support trials in regions with high disease burdens, poor utility of existing well capacitated networks, redundant research efforts and poorly designed trials that fail to produce useful results, hesitance to adopt innovative trial methods, varied and lengthy timelines for trial approvals across different countries, insufficient involvement of diverse populations in trial design and implementation, and exclusion of specific groups such as pregnant women, children, and older people, often leads to non-applicable trial outcomes and greatly impacts timeliness of responses on the continent.

Community mistrust and misinformation

Another barrier to effective responses to pandemics is the common mistrust oof science within communities, which often leads to misinformation and underreporting of cases, as was demonstrated during the COVID-19 pandemic [9] and more recently the Mpox outbreaks in Central Africa [13].

ROLE OF AFRICAN RESEARCHERS IN ADDRESSING BARRIERS TO PANDEMIC PREPAREDNESS IN AFRICA

The Science for Africa Foundation (SFA), has identified ways it can partner and support African researchers to play a pivotal role in transforming Africa's health research and innovation landscape (Figure 1). By investing in locally led science, through programs like DELTAS Africa [14], Grand Challenges Africa [15], and EPSILON Africa [16], SFA foundation is helping to build resilient health systems, reduce reliance on imported goods, and enhance pandemic

BOX 1

Call to action: empowering African scientists for pandemic preparedness

- **Fund African science:** invest in long-term, flexible, African-led research and innovation—especially in AI, genomics, and public health.
- **Empower African researchers:** position African scientists to lead policy, clinical trials, and manufacturing of vaccines, diagnostics, and therapeutics.
- **Align and coordinate:** strengthen national–continental planning alignment with Africa CDC frameworks and integrate local realities.
- **Invest in public trust:** scale community engagement strategies to deepen trust and combat misinformation during health crises.
- **Ensure global representation:** secure African leadership and researcher participation in global health governance and decision-making bodies.

The next pandemic must meet an Africa that is not just prepared—but leading.

preparedness through stronger clinical trials capacity and community engagement.

Key contributions of African researchers include:

Strengthening health systems through research

African researchers generate context-specific data that is critical to health system reform. They help address systemic gaps in disease surveillance, diagnostics, and service delivery, and support evidence-informed policy and integration of innovation into national health strategies. Researchers like Professor Edwine Barasa in Kenya are playing key international roles to provide evidence informed decisions on how to strengthen health systems [17].

Reducing overreliance on imported health technologies

SFA foundation is committed to supporting Africa's journey toward health sovereignty by promoting R&D for region-specific vaccines, diagnostics, and therapeutics, by supporting innovation ecosystems that enable local manufacturing and regulatory science, facilitating partnerships between research institutions, industry, and policymakers. Researchers like Prof Christian Happi, Prof Faith Osier, Prof Shabir Madhi have played a key role in leading conversations on how vaccine development and manufacturing should happen [18–20].

Supporting pandemic preparedness and response plans

African researchers, guided by lived experience and public health expertise, are integral to designing data-driven, community-responsive preparedness plans, informing resource allocation, risk communication, and resilience strategies, and collaborating with regional bodies to align with continental preparedness frameworks [21].

Enhancing clinical trials capacity

SFA foundation invests in platforms and people to advance African-led clinical trials that are ethical, efficient, and impactful by building infrastructure for trial readiness and regional collaboration, strengthening regulatory and ethics systems through harmonization and training and supporting consortia that can activate rapidly during health emergencies [22].

Deepening community engagement and public trust

African researchers, embedded within their communities, lead efforts to co-create

research with communities to ensure relevance and dignity, counter misinformation through trusted messengers and localized communication strategies, and foster long-term public trust in science and healthcare interventions [23].

CONCLUSION

The COVID-19 pandemic, as well as constant epidemics in the African region, have underscored the urgent need for Africa to lead its own preparedness and response agenda, drawing on the expertise and innovation of its scientific community. Box 1 is a call to action for various actors in the ecosystem to support the enterprise of pandemic preparedness. African researchers have already proven their capabilities in shaping resilient health systems, advancing homegrown clinical trials, and building public trust during crises. However, structural and financial constraints continue to hinder their full potential.

To effectively tackle future pandemics, Africa must prioritize and institutionalize pandemic preparedness as a central component of national and continental development strategies. This requires bold investments in science, innovation, regulatory alignment, and health sovereignty—led by African experts and institutions.

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PANDEMIC PREPAREDNESS

SPOTLIGHT

A holistic approach to pandemic preparedness: exploring the importance of integrated advice

Anja Schreijer and Tomris Cesuroglu

VIEWPOINT

"Further developing interdiscplinary advice with an integrated framework and interdiscplinary research readiness is an important part of pandemic preparedness."

On February 25, 2025, **Charlotte Barker**, Editor, *Vaccine Insights*, spoke to the Pandemic and Disaster Preparedness Center's (PDPC) **Anja Schreijer**, Medical Director, and **Tomris Cesuroglu**, Scientific Secretary, about the importance of integrating biomedical, social, and economic advice for effective infectious disease outbreak response. This article has been written based on that interview.

In 2024, the PDPC in Rotterdam, the Netherlands, carried out an avian influenza outbreak simulation to explore integrated advisory approaches in pandemic response. The results revealed that siloed biomedical and socioeconomic advice is often conflicting, which highlights the need for interdisciplinary collaboration. Simulation exercises emphasize critical knowledge gaps and the necessity of integrating biomedical, social, and economic strategies to improve future pandemic response.

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AN INTERDISCIPLINARY APPROACH TO PANDEMIC AND DISASTER PREPAREDNESS

The Pandemic and Disaster Preparedness Centre (PDPC) was launched in 2021, during the COVID-19 pandemic. At PDPC, we take an interdisciplinary approach to pandemics and disasters, which involves examining their mutual causes, such as climate change, and exploring potential solutions. We also work on modelling and forecasting the impact of these emergencies. Additionally, we have a strong research focus on societal and health system impacts.

The COVID-19 pandemic underscored the need for comprehensive, cross-disciplinary advice, with many subsequent evaluations revealed significant knowledge and practical gaps in pandemic preparedness. Nevertheless, pandemic preparedness plans should not be based solely on COVID-19. While it is crucial to incorporate the lessons learned from this pandemic, we must also consider a wide range of potential scenarios that could unfold in the future.

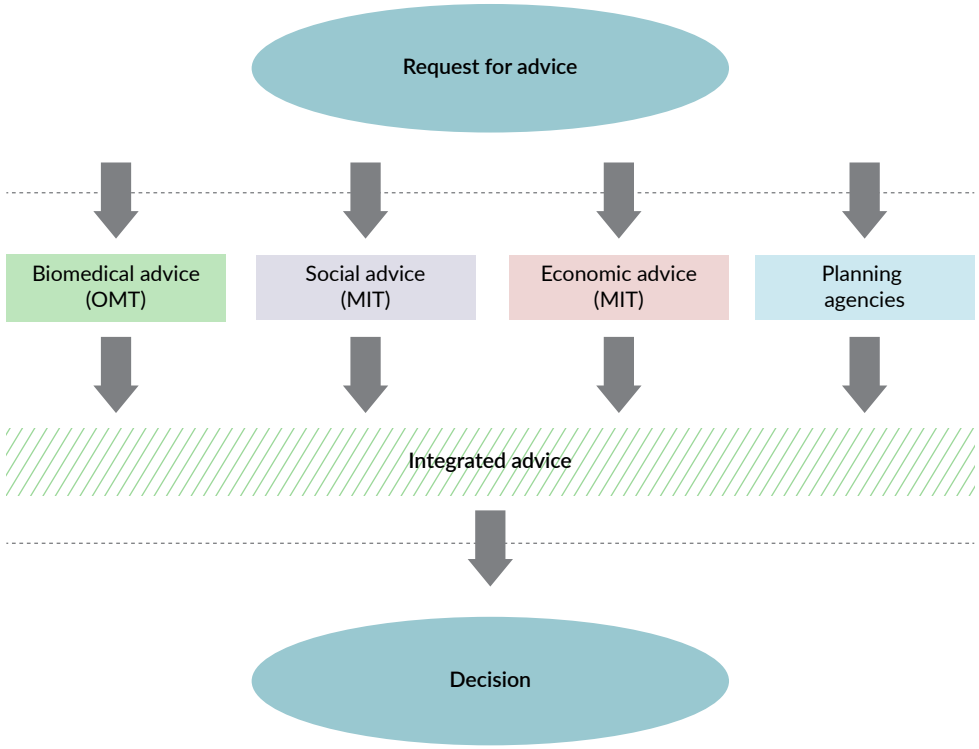
The current highly pathogenic avian influenza (HPAI) outbreak, affecting birds and mammals on five continents, and increasingly infecting humans via livestock, is an important threat.

CASE STUDY: INTEGRATING EXPERT ADVICE FOR BETTER PANDEMIC RESPONSE

In 2024, we embarked on an HPAI outbreak simulation to explore integrated scientific

FIGURE 1

The model of integrated advice for infectious disease outbreak response.



advice for outbreak response. This research is part of a broader line of research on integrated advice for policy at PDPC.

The focus of this study was to determine whether advice from biomedical and socioeconomic experts have distinct characteristics and whether any conflicting advice could be resolved through an integrated approach (Figure 1). Another aim was to identify the biomedical, socioeconomic, and cross-disciplinary knowledge and know-how gaps in HPAI pandemic preparedness.

In the Netherlands and many other countries, experts tend to provide advice within their own silos. For example, during the COVID-19 pandemic, people with biomedical or epidemiological backgrounds were part of the Outbreak Management Team (OMT), while a separate Societal Impact Team (MIT), formed in 2020, provided advice on social and economic consequences. However, this separation may limit the effectiveness of outbreak response.

To explore this hypothesis further, we conducted a multi-method study, which involved a literature review of scientific and grey literature, interviews with more than 30 experts from biomedical, social science, and economic disciplines, as well as two simulation exercises involving 20–23 experts.

We modeled a large-scale avian influenza outbreak simulation, initially affecting poultry and pig farms in the Netherlands, then escalating into widespread human-to-human transmission, primarily affecting individuals under 30.

In our simulation, we followed a two-step approach. In the first round, the experts provided advice from within their own silos, mirroring the current advisory structure for pandemics in the Netherlands. In the second round, we asked them to engage in a more integrated discussion involving different viewpoints. This approach allowed us to explore whether integrated advice could lead to a more comprehensive and effective outbreak response.

BETTER TOGETHER: INTEGRATED ADVICE ADDS VALUE

As you might expect, the key advice from the biomedical team was to contain the virus and prevent a large-scale outbreak by taking prompt action, including school closures, and implementing biomedical guidelines as soon as possible to prevent disruptions in the chain of care (Figure 2A). On the other hand, the socio-economic team was more concerned about preserving social and economic continuity and vitality, and more reluctant to implement school closures as a public health measure. Overall, the teams did not share the same goal and sense of urgency.

One of our key findings from interdisciplinary discussions was that collaboration plays a crucial role in identifying blind spots in risk perception, urgency, and the potential unintended consequences of different recommendations (Figure 2B).

During the study, we also discovered knowledge gaps. For example, biomedical gaps were mostly related to fundamental research and available knowledge that has not yet been incorporated into guidelines. The social sciences gaps were related to the lack of available response guidelines, monitoring structures, and infrastructures in case of a new outbreak. The economic gaps were mostly related to ethical support issues. Finally, we identified interdisciplinary gaps that surfaced during the integrated session and were related to a lack of alignment of response structures or organization.

Overall, interdisciplinary advice added significant value to the decision-making process.

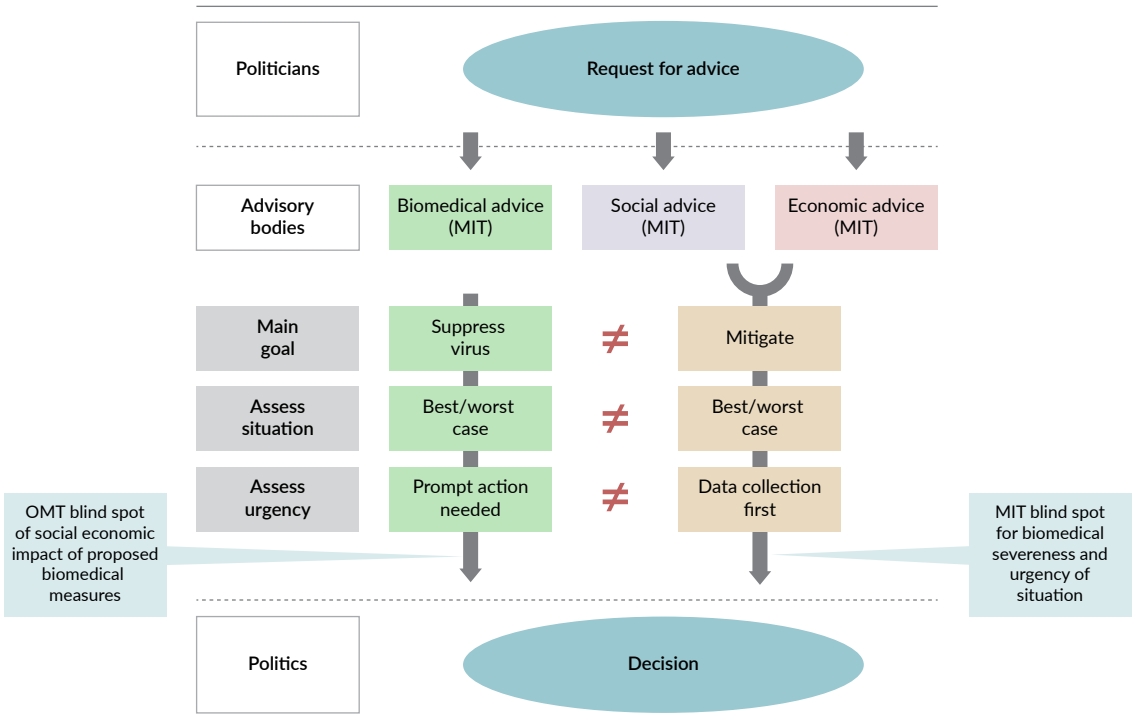
DON'T RELY ON THE STRONGEST MUSCLE: THE NEED FOR A HOLISTIC APPROACH TO PANDEMIC PREPAREDNESS

In the short term, when the next pandemic hits, we will certainly need strong,

FIGURE 2

The comparison between (A) separate advice and (B) integrated advice for infectious disease outbreak response [1].

A Process of separate advice: identifying disciplinary blind spots



Separate advice

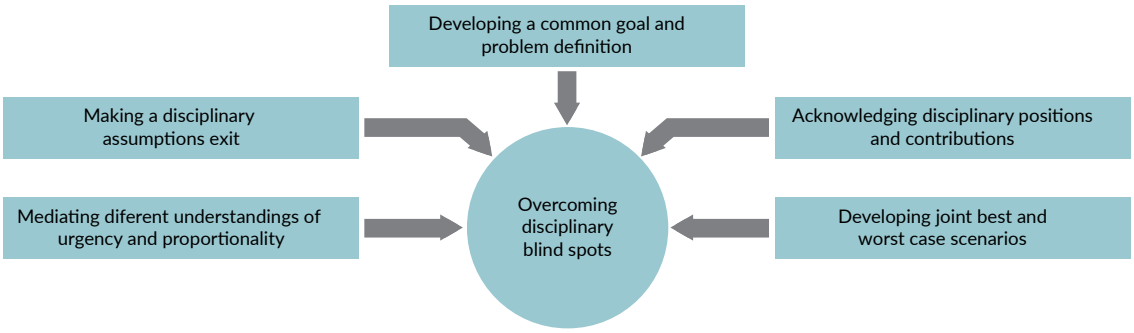
Example of point of conflict in separate advice:

Local lockdown of all children and their families at the schools with children who had tested positive

- OMT: aim for containment of the virus
- MIT: concerned with severe social impact of school closures as learned during COVID

Need for information exchange

B Process of integrated advice: alignment and enrichment of advice



Interdisciplinary advice

Added value of interdisciplinary advice:

- To overcome disciplinary blind spots
- To counter to selective use of scientific evidence
- To support a unified focus and better prepare for coordinated action
- To minimize the unintended consequences of measures through enriched mitigation policies

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evidence-based biomedical advice on how to contain it, especially if containment is still possible in the early stages of an outbreak. However, as the outbreak progresses, we will need advisors to address long-term impacts such as mental health, the economic effects on a country, and how people respond to public health and social measures, as well as pharmaceutical interventions such as vaccinations.

During the COVID-19 pandemic, most countries relied on their strongest capabilities. For example, countries with strong public health systems or primary care leaned on those, whilst countries with good biomedical innovation invested heavily in development of vaccines, and those with robust hospital systems focused on maintaining those, often at the expense of earlier-stage pandemic management.

However, relying on your 'strongest muscle' can only take you so far. While the biomedical community in most European countries is typically well-prepared and can provide quick, effective advice, they can only carry the burden for a limited time. Social, economic, and mental health considerations need to be strengthened before the next pandemic.

Similarly, investing solely in biomedical research for the next vaccine is not enough to be prepared for future pandemics. We also need to invest in the behavioral science behind vaccine uptake. Now is the best time to focus on all of these aspects simultaneously.

CONCLUSION

Simulation exercises provide invaluable opportunities to prepare for national crisis responses, promote understanding across disciplines, and further develop and refine integrated approaches to advice.

The key takeaways from this study emphasize the importance of interdisciplinary advice during a global health emergency. The avian influenza outbreak simulation demonstrated that the interpretations of an emergency can differ, leading to uncoordinated disciplinary advice, while interdisciplinary discussions are crucial to uncovering blind spots in recommendations and overcoming differences in assessment and interpretation.

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BIOGRAPHIES

Anja Schreijer is currently working as Medical Director of the Pandemic and Disaster Preparedness Center, affiliated with the Erasmus Medical Center. She is a medical specialist in infectious disease control who has worked for various national and international governments, WHO, and ECDC. During the COVID-19 pandemic, she chaired the National Consultation on Infectious Disease Control, which was responsible for making scientifically sound agreements about the medical content for nationally uniform control of infectious diseases. In addition, she was a permanent member of the national outbreak management team that advises the Netherlands' government on pandemic control. She has a PhD in

Clinical Epidemiology and she is the co-chair of the Advisory Committee on Public Health Emergencies (ACPHE) that has been recently established by the European Commission.

Anja Schreijer MD PhD MPH, Medical Director, Pandemic and Disaster Preparedness Center, Rotterdam, Netherlands

Tomris Cesuroglu is a Senior Researcher and Scientific Secretary at the Pandemic and Disaster Preparedness Center (PDPC) at Erasmus MC. She works at the intersection of science, policy, and practice, with a focus on knowledge translation, interdisciplinary collaboration, and systems approaches. Trained as a physician, she has over 20 years of experience in health systems, policies, and innovation across academia, consultancy, health tech, and the public sector—including a recent role as senior researcher at the Dutch National Institute for Public Health and the Environment (RIVM), where she led national and international studies on pandemic preparedness.

Tomris Cesuroglu MD PhD, Senior Researcher and Scientific Secretary, Pandemic and Disaster Preparedness Center, Rotterdam, Netherlands

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IMMUNE RESPONSE UPDATE

Outsmarting immune aging: designing vaccines for older adults

INTERVIEW

"It is essential to effectively communicate the benefits of vaccination, especially for the aging population..."

Jokūbas Leikauskas, Editor, BioInsights, speaks to **Birgit Weinberger**, Head of Institute for Biomedical Aging Research, University of Innsbruck, about the impact of aging on immune function, and how this translates to vaccine responses in older adults. They also discuss strategies for improving vaccine efficacy in aging populations, highlighting the significance of both scientific innovation and getting vaccines into arms.

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Q What are you working on right now, and what are the key focus areas at the Institute for Biomedical Aging Research?

BW First and foremost, we study various aspects of biomedical aging research in order to understand the aging process across different levels and biological systems. There are several groups working on topics such as mitochondrial function in different cellular contexts, skin aging, and the differentiation and function of adipocytes derived from adipose progenitor cells.

The second major focus is immunology. One group studies the impact of aging on B cell development, whilst my own group focuses on T cells in the context of aging. We are

currently investigating various T cell populations, primarily regulatory T cells and highly differentiated T cells. Our research also explores how these cells function in the context of aging-related inflammation and senescence.

Another focus area for my group is vaccination. More specifically, we study immune responses to various licensed vaccines in adults across different age groups. We have worked with several licensed vaccines, with our most recent projects focusing on influenza and pneumococcal vaccines. In these studies, we examine both antibody and T cell responses.

Q What are the key hurdles associated with vaccine development for older adults, especially regarding immune response and immunosenescence?

BW The first level of complexity relates to vaccine development itself. In essence, we likely need to elicit different types of immunological responses to protect against various pathogens. In some cases, protection may rely primarily on neutralizing antibodies, while in other scenarios, cytotoxic CD8 T cells may be crucial. For many diseases, we do not even know in advance which type of immune response—or combination of responses—is needed for effective protection.

The second layer of complexity is related to the older population specifically. Age-related changes in the immune system affect all types of immune cells and functions. For example, both B cells and T cells show deficits, and even the innate immune response, such as the initial uptake of antigen, can be impaired. These immunological changes do not occur in isolation: the immune response is the result of a complex interaction between many different cell types and mechanisms, all of which are influenced by aging in various ways. When every player in a complex network is modified, the overall output can be significantly affected.

The third level of complexity is that the older population is not homogeneous. Older adults differ significantly in their health status, and underlying comorbidities can have a major impact on immune responses. We already see this in younger individuals with chronic conditions, where certain immunological responses are altered. In older adults, you have both the effects of age and a range of comorbidities interacting in different ways. The result is a very heterogeneous population, which will likely respond differently to various immunological approaches.

Q What approaches are you taking to improve vaccines for older adults?

BW Firstly, we have seen that increasing the vaccine dose can be effective. For example, the high-dose formulation of influenza vaccines was shown to be more efficient in older adults.

Secondly, we have seen that adjuvants can be very successful in enhancing both the immunogenicity and the efficacy of vaccines, including in older populations. For instance, the adjuvanted herpes zoster vaccine has demonstrated very high efficacy and

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"Very few vaccine antigens administered to older adults represent a real first contact."

effectiveness even in the oldest age groups. This vaccine has now been in use for at least 10 years and provides a relatively long duration of protection.

However, these approaches are not universal solutions. A successful vaccine largely depends on what kind of immune response is required for protection and how well the antigen and adjuvant components work together. You cannot simply mix any antigen with a successful adjuvant and expect a good outcome—it must be a well-matched combination.

Additionally, one area that should receive more attention is implementation. That includes aspects such as booster intervals, the exact timing of vaccinations, and alternative routes of administration. For example, there is a lot of ongoing work on mucosal vaccination.

Another particularly important development over the past few years is the increasing trend of developing vaccines specifically for older adults by including them earlier in clinical trials. This earlier inclusion makes it possible to identify optimal strategies for the target population right from the start. However, there is still a lot of trial and error involved.

Q How can vaccines be better tailored to aging immune systems—do you see promise in personalized or stratified vaccine approaches?

BW Personalized or stratified vaccines sound like a sophisticated, high-tech solution, but unfortunately, we are not there yet.

Firstly, every person has an individual immune response to a specific vaccine and may have pre-existing immunity. Very few vaccine antigens administered to older adults represent a real first contact. For many pathogens, such as influenza, pneumococcus, or RSV, which circulate around us all the time, there is pre-existing immunity even in first-time vaccine recipients, which plays a big role in shaping vaccine response. And even though SARS-CoV-2 was a new pandemic, we still do not fully understand how prior exposure to other coronaviruses may have shaped the immune response.

One could ask whether there is such a thing as a general 'non-responder', who consistently fails to respond well to any vaccine. Personally, I am not convinced that such individuals truly exist—I think it is more likely that every person elicits different immune responses. For example, one person may have robust B cell responses but impaired CD8 T cell responses, or vice versa. And as mentioned above, pre-existing immunity plays an important role here.

Furthermore, there is a question of implementation. We know from experience that more straightforward vaccination recommendations result in higher uptake. For example, focusing on general age groups instead of specific comorbidities or individual risk profiles usually works far better.

In essence, while the idea of personalized vaccination is attractive from a scientific perspective, it is less clear whether people would trust it or want to take it. It is crucial to think about both the science behind a vaccine and its acceptability to patients and healthcare providers. Even the best vaccine in the world is useless if it is not administered. Hence, we need to always keep implementation at the center of our thinking, alongside the scientific and immunological considerations.

"...we have learned that if the infrastructure, opportunity, and sense of urgency are there, the older population responds remarkably well in terms of uptake."

We must also be sure which personalized vaccine strategies people need. If testing and analysis take 3 weeks, and consultations with physicians are required, many people may decide not to do it.

Q What lessons have we learned from the COVID-19 pandemic in terms of vaccine efficacy and deployment in older populations?

BW The key takeaway was that mRNA vaccines worked remarkably well, even in older adults. Even now, in older adults, the vaccines remain highly effective at preventing severe disease.

Additionally, the first wave of vaccination was extremely successful clinically, including in the oldest age groups. In my view, the communication worked well—highlighting that COVID-19 posed a significant danger to this group and that vaccination was crucial. In essence, we have learned that if the infrastructure, opportunity, and sense of urgency are there, the older population responds remarkably well in terms of uptake. Unfortunately, this positive attitude was lost to a certain degree later in the pandemic, and vaccine uptake is now much lower.

We also observed that alternative strategies for delivering vaccines can be effective, even in older populations. For example, vaccination centers were widely used, and campaigns in nursing homes were highly successful. Unfortunately, that is something we have not utilized as effectively for other vaccines, but I think there is a lot to learn there, especially regarding the implementation of that last crucial step: bringing the vaccine into people's arms.

From a scientific standpoint, we have never had access to so much data in such a short period of time. So many studies became possible in the pandemic context because large portions of the population were vaccinated at the same time in a coordinated way, which allowed researchers to study real-world outcomes more easily.

Hopefully, we have learned a lot—both in terms of how to deal with the next pandemic threat and how to improve general vaccination strategies. I hope we can carry over some of what we learned—and some of the infrastructure we built during the pandemic—into other vaccination programs.

Q What are your goals and priorities over the next 1–2 years, both for yourself and for the Institute for Biomedical Aging Research as a whole?

BW The field of biomedical aging research is becoming increasingly important, especially with ongoing demographic shifts. But alongside the research itself, there is another aspect that is becoming ever more crucial—public outreach.

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Research institutions must engage with the community to make it clear that we do not conduct research for our own benefit, but for society as a whole. In the current global climate, it is especially important to invest in building public trust and confidence in science.

This should start early, ideally with children, by making the scientific process more accessible and understandable. We need to re-establish and strengthen public trust in research and independent research institutions such as universities.

Unfortunately, public trust in science sometimes seems to be moving in the wrong direction, and it is something we must actively address. It is essential to effectively communicate the benefits of vaccination, especially for the aging population, and engage all stakeholders in these discussions.

BIOGRAPHY

Birgit Weinberger is a Full Professor of Immunology and the head of the internationally renowned Institute for Biomedical Aging Research at the Universität Innsbruck, where aging processes are studied at the cellular and molecular level. Dr Weinberger leads the Immunosenescence and Vaccination group. Her research focuses on immunosenescence, particularly within the T cell compartment. Besides these basic research topics, the question how vaccinations can be optimized for the elderly is a central interest addressed in research projects analyzing immune responses to vaccination in older adults. Professional and public outreach to promote life-long vaccination concepts is an important part of her work and she is a member of the Adult Immunization Board. In addition, she is teaching immunology and aging-related topics at the Universität Innsbruck and is the Dean of Studies for Biology. Dr Weinberger studied Biology in Regensburg, Germany and Boulder, CO, USA. She holds a PhD from the Institute for Medical Microbiology and Hygiene of the University of Regensburg.

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AUTHORSHIP & CONFLICT OF INTEREST

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