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Vaccination at a crossroad: science, politics and public trust

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Summary

Vaccine hesitancy threatens to erode one of medicine's greatest achievements. Recent measles outbreaks in Europe and the United States illustrate the consequences of declining confidence. At the centre lies misinformation, amplified through digital networks, from the discredited vaccine–autism claim to the misconception that COVID-19 mRNA vaccines were rushed. Such narratives echo longstanding resistance to vaccination, magnified by political polarisation and compounded by inequities in access. Yet pathogens continue to evolve, requiring sustained innovation in immunology, genomic surveillance, artificial intelligence and mRNA platforms. Science alone, however, cannot overcome mistrust. Transparent communication, broad engagement by healthcare teams and equitable distribution are indispensable. Protecting trust is essential if vaccines are to prevent disease, reduce mortality and prepare society for future infectious threats.

Introduction

Vaccination is among the greatest achievements of modern medicine, reshaping global health and extending human survival. In 17th-century England, life expectancy was only 37–40 years and infant mortality exceeded 250 per 1000 live births. As recently as the 1970s, when fewer than 5% of children in low-income countries received vaccines, infant mortality worldwide remained close to 100 per 1000. Since then, immunisation – together with improved sanitation, antibiotics and nutrition – has reduced infant mortality to fewer than 25 per 1000, transforming one of humanity's greatest vulnerabilities into a public health success. Vaccines also protect adults, preventing severe illness, disability and premature death, and supporting healthy ageing [1, 2].

Yet this progress is fragile. In 2024, the European Union/European Economic Area recorded 35,212 measles cases, almost nine times the number reported in 2023, primarily among unvaccinated individuals [3]. In 2025, northwest Texas experienced a measles outbreak in a region with vaccine coverage of only 40–65%, resulting in 1319 cases, 165 hospitalisations and 3 deaths [4]. These events underscore the dangers of declining vaccine confidence and highlight the urgent need to rebuild public trust.

Here, we examine the drivers of vaccine hesitancy, the risks of politicising science and the potential of vaccine innovation to counter emerging infectious diseases.

Vaccine hesitancy: definition and determinants

The World Health Organization (WHO) Strategic Advisory Group of Experts (SAGE) defines vaccine hesitancy as the "delay in acceptance or refusal of vaccines despite availability of services" [5]. Determinants include lack of trust in institutions, perceived low risk of infection and barriers to access or affordability. Hesitancy has escalated in the past decade, amplified by misinformation circulating through social media.

Resistance is not new. Jenner's smallpox inoculation in the 18th century provoked caricatures of patients sprouting bovine features, and by the 19th century anti-vaccination leagues had spread across England and the United States. In 2019, the WHO listed vaccine hesitancy among the top ten global health threats, reflecting persistent perceptions of vaccines as unsafe despite overwhelming evidence of benefit. Today, these longstanding traditions are magnified by digital platforms, transforming local scepticism into a global challenge [5].

The vaccine-autism myth

In 1998, Andrew Wakefield and colleagues at the Royal Free Hospital in London published a case series of 12 children with gastrointestinal complaints, suggesting an association between the measles-mumps-rubella (MMR) vaccine and autism [6]. Based only on parental recall and lacking epidemiological evidence, the report was later discredited and retracted. Ten of the twelve co-authors withdrew their interpretation, and in 2010 the UK General Medical Council found Wakefield guilty of falsifying data and failing to disclose financial conflicts of interest [7].

Although retracted, the Wakefield paper has been cited nearly 5000 times on Google Scholar and fuelled a global anti-vaccine movement. In its aftermath, MMR coverage fell below herd immunity thresholds in several countries. In contrast, large-scale studies involving hundreds of thousands of children have consistently shown no association between MMR vaccination and autism [8]. Similarly, a Danish cohort of more than 1.2 million children found no increased risk of autoimmune, allergic or neurodevelop-

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mental disorders after early childhood immunisation with aluminium-adsorbed vaccines, including those against pneumococcus, Hib, diphtheria, tetanus, pertussis and poliomyelitis [9].

The Wakefield episode illustrates how a single flawed study, magnified by media and social networks, can undermine public health for decades.

The "rushed" COVID-19 vaccine misconception

The rapid development of COVID-19 vaccines – nine months from the WHO's declaration of a pandemic in March 2020 to the first Pfizer–BioNTech vaccination under emergency use authorisation in December – fuelled the perception that these vaccines were "rushed". In reality, their success rested on more than three decades of sustained research [10].

As early as 2000, Karikó and Weissman showed that mRNA encoding the HIV gag protein could be delivered to dendritic cells, presciently noting that "the ability to deliver mRNA to DC (dendritic cells) in vivo as a vaccine approach is attractive as it can be easily and inexpensively administered to large populations" [11]. In 2005, they reported the critical observation that RNA containing natural nucleoside modifications – such as pseudouridine or 5-methylcytidine – does not activate innate immune receptors, unlike unmodified RNA, which strongly triggers cytokine release [12]. This explained why bacterial and mitochondrial RNAs, poor in modifications, are immunostimulatory, whereas mammalian RNAs, rich in them, are largely silent. Even limited incorporation of modified nucleotides blunted innate sensing, stabilised mRNA and increased protein expression [12].

Equally transformative was the development of lipid nanoparticle (LNP) carriers, which protect mRNA from degradation, facilitate cellular uptake, enable cytoplasmic release and provide critical adjuvant properties. The convergence of nucleoside modification and lipid nanoparticle technology transformed mRNA from a fragile laboratory tool into a robust therapeutic platform [13].

Thus, when the sequence of the SARS-CoV-2 genome was released on 10 January 2020, mRNA vaccine design was completed within days. The first clinical trial (NCT04283461) began in March, and the FDA granted emergency use authorisation in December. In its first year, mRNA vaccination is estimated to have prevented 14.4–19.8 million deaths worldwide [14]. What might have seemed "rushed" was, in fact, the culmination of long-term investment, scientific foresight and unprecedented global collaboration.

Politics, science and biomedicine: lessons from history

Political interference has repeatedly derailed biomedical progress. A pseudoscientific movement led by Trofim Lysenko in the Soviet Union and the Cultural Revolution in China suppressed genetics and molecular biology for decades [15, 16]. Between 1920 and 2000, 82 Americans but no Soviets or Russians won the Nobel Prize in Physiology or Medicine. In Physics, the gap was narrower, with 67 American laureates compared with 8 from the Soviet Union/Russia. The difference in proportions is significant ($p \approx 0{\cdot}002$, Fisher's exact test). It illustrates how political priorities shape scientific trajectories: in the United States, both physics and biomedicine thrived; in the Soviet Union, only physics.

Public mistrust has also been fuelled by ethical breaches. The Tuskegee syphilis study enrolled nearly 400 African American men under the pretext of "free medical care", withholding diagnosis and therapy even after penicillin became the standard of care in 1947. Participants were never informed of their disease, and many died or transmitted infection to family members [17]. More recently, Merck withdrew rofecoxib (Vioxx®) in 2004 after FDA analyses and litigation revealed that early randomised trials had signalled increased risks of myocardial infarction and stroke, yet cardiovascular safety data were incompletely reported. The episode underscored the hazards of selective disclosure, the limits of post-marketing surveillance and the need for rigorous transparency in the evaluation of adverse events [18].

Ideology, unethical research and delayed transparency erode trust in science and compromise patient care. Such failures, though not unique to vaccines, fuel scepticism towards biomedical institutions. The United States – long the world's biomedical leader – recently faced a proposed $18 billion cut to the NIH budget for FY 2026, nearly 40% below the FY 2025 appropriation [19]. Advanced by the administration but rejected by Congress, the proposal underscores that threats to sustained funding will recur. Retrenchment of this scale would jeopardise mRNA research so central to vaccine development, destabilise programmes, drive young scientists from academia and weaken the nation's capacity for vaccine innovation, clinical trials and pandemic preparedness [19].

Sustained, depoliticised investment is essential to safeguard biomedical progress, global health and the public trust on which vaccination depends.

Infection and immunity: coevolution and the future of vaccination

Over the past five decades, the emergence of HIV, SARS and COVID-19, the resurgence of drug-resistant tuberculosis and the deliberate release of anthrax have underscored the persistent challenge of infectious diseases [20]. These episodes exemplify an evolutionary arms race in which pathogens continually adapt to evade host defences while immune genes co-evolve in response. This antagonistic process is often described as the Red Queen Effect, a metaphor from Lewis Carroll's *"*Through the Looking-Glass*"*, in which the Queen remarks that "it takes all the running you can do, to stay in the same place". In biology, it conveys the necessity for constant adaptation simply to maintain equilibrium [21].

Pathogen variability is central to this dynamic. In HIV, high replication rates and error-prone reverse transcription generate frequent escape mutations that undermine neutralising antibodies. Influenza viruses undergo both antigenic drift (gradual mutation) and antigenic shift (genome reassortment), necessitating continual reformulation of seasonal vaccines. Plasmodium falciparum evades recognition by switching *var* expression, while Trypanosoma brucei al-

ternates among variant surface glycoproteins. Even herpesviruses and certain bacteria have evolved immune-modulating strategies, but HIV, influenza and malaria remain the textbook examples [22].

Host capacity to keep pace is variable. Advanced HIV infection depletes $CD4^+$ T cells, haematological malignancies compromise immune surveillance, autoimmune disease diverts responses against self, and iatrogenic immunosuppression constrains adaptability. These conditions weaken both natural and vaccine-induced protection and explain why vaccines against pathogens such as HIV, influenza and malaria remain difficult to design, require regular updating and demand sustained innovation.

Confronting this relentless evolutionary race requires vaccine science to accelerate. Atomic-level structural insights have enabled rational drug discovery – HIV protease inhibitors and imatinib emerged directly from crystallography – but experimental approaches are slow, costly and limited in scope. Artificial intelligence (AI) now permits *in silico* modelling of protein conformations across the proteome within days. Systems such as AlphaFold and RoseTTAFold are transformative, enabling rational drug design, clarifying receptor–ligand interactions and accelerating vaccine development by identifying B- and T-cell epitopes in rapidly evolving pathogens.

With the pathogen's genetic sequence as the starting point, AI can generate three-dimensional models, predict conformational epitopes, and prioritise them for stability and conservation. In parallel, *in silico* paratope design yields high-affinity antibody candidates before any wet-lab testing. Coupled with mRNA platforms, these approaches allow both vaccines and therapeutic antibodies to be designed digitally and generated directly *in vivo,* reducing reliance on large-scale protein manufacture [23–25].

This convergence heralds a new era of vaccine and antibody development – faster, more precise and less constrained by laboratory bottlenecks. Clinically, the capacity to update vaccines or produce antibodies *in silico* and deliver them via mRNA could shorten the interval between pathogen emergence and protection from years to months or weeks. Such acceleration may prove decisive in pandemics, while precision targeting could benefit immunocompromised patients. Yet speed and innovation must be matched by equity: without global access to sequencing, computational infrastructure and distribution networks, these advances risk widening rather than narrowing disparities. The challenge is therefore dual – scientific and societal – and meeting it will determine whether next-generation vaccines fulfil their promise for global health.

Restoring trust, overcoming hesitancy

In 2015, a global survey of 65,819 individuals across 67 countries and all six WHO regions revealed striking regional differences in vaccine attitudes [26]. Respondents were asked whether vaccines are important for children, safe, effective, and compatible with religious beliefs. In Europe, scepticism was most pronounced: 15.8% doubted safety and 7.7% questioned importance, with distrust reaching 41% in France and 36% in Bosnia and Herzegovina. In contrast, South-East Asia showed the lowest scepticism, with only 4.4% questioning safety and 2.3% importance. The Western Pacific region occupied an intermediate position, with 15.0% doubting safety and 6.2% importance, and showing the greatest concern about religious compatibility. Across all regions, perceived importance consistently exceeded perceived safety, suggesting that many accepted vaccines despite persisting doubts. Socioeconomic associations were paradoxical: while higher income generally correlated with greater confidence, higher levels of education and broader health service coverage were linked to increased scepticism [26].

Although conducted before COVID-19, the advent of mRNA vaccines and the transformative influence of social media, the 2015 survey's central lesson remains pertinent: vaccine confidence depends on transparent communication and culturally attuned engagement. This conclusion was echoed in subsequent European assessments [27, 28]. The EU27 Flash Eurobarometer 505, carried out between 7 and 15 February 2022 with 26,658 participants, found that 75.3% of respondents were pro-vaccine, 6.9% hesitant, 10.6% opposed and 7.2% undecided. A complementary inquiry, the "State of Vaccine Confidence in the EU 2022", conducted between March and August, confirmed these trends and highlighted persistent scepticism in certain countries [27].

Healthcare professionals remain the most trusted source of vaccine information. Surveys in Europe confirm this pattern [28, 29], and similar results are likely worldwide. Yet such trust is fragile. It depends on dialogue and continuity, both increasingly constrained as consultation times shrink. Clinicians often lack the opportunity to explain benefits, dispel doubts and strengthen the relationships on which vaccine acceptance depends.

Protecting this trust requires extending communication beyond the physician encounter. Nurses, pharmacists and other frontline professionals can reinforce consistent, evidence-based messages, while digital tools can prepare patients before visits and sustain reassurance afterward. Equitable access is equally vital: shortages, delays or uneven distribution erode confidence quickly and magnify hesitancy. In the end, vaccines protect populations only when health systems protect trust.

Conclusion

Vaccine hesitancy, fuelled by misinformation, inequity and erosion of trust, threatens to undermine one of the greatest achievements of modern medicine. The rapid development of COVID-19 mRNA vaccines – built on decades of research and unprecedented collaboration – saved millions of lives, yet was often dismissed as "rushed". Such mistrust now clouds the promise of vaccines against HIV, tuberculosis, malaria and other high-burden infections.

Scientific advances in immunology, genomic surveillance, artificial intelligence and adaptive trials can accelerate innovation, but science alone cannot secure success. Transparent communication, equitable access and sustained community engagement are essential. Ultimately, only trust will allow vaccines to realise their full potential in improving global health.

Potential competing interests
Both authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts

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