Deconstructing vaccine hesitancy: an interplay of knowledge, trust, and confidence across different populations

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Abstract

Vaccines are one of the most effective tools in preventing contagious, dangerous and deadly diseases, and immunization programs are considered amongst the most important public health achievements worldwide. They have helped in eradicating diseases such as small pox, and contributed to the elimination of diseases such as poliomyelitis, neonatal tetanus, and rubella in many regions of the world, while reducing mortality and hospitalization rates and increasing life expectancy. Vaccines have been around for more than two centuries, evolving with changing times, from live attenuated vaccines to vector vaccines, and to mRNA vaccines. However, the differences in their design and mechanism of action are often not fully understood by the general population and this lack of understanding combined with other factors can heavily influence public mistrust in vaccines and other medical treatments.

This study provides a comparative overview of the major vaccine types and their mechanisms of action. To complement this analysis, a cross-sectional survey was conducted across diverse groups to assess public knowledge, perception, and behaviour regarding vaccine safety. The findings highlight vaccine knowledge, awareness, acceptance, and perceived risks across different demographics. The insights gained aim to support improvements in public health communication strategies.

Vaccines: an overview

Vaccines are among the most significant developments in the healthcare industry. They are crucial for maintaining public health and safety as well as preventing infectious diseases. Vaccines' composition and the way that they stimulate the immune system determine how they are categorised. Because pathogens, such as bacteria and viruses, can differ significantly in their life cycles, structures, and modes of infection, vaccines must be specifically tailored to trigger an effective immune response.

The ability of pathogens to mutate produces variants that can evade the immune responses triggered by particular vaccines. Furthermore, certain bacterial strains produce toxins or have outer structures which are really complex, necessitating the use of distinct approaches to guarantee vaccination efficacy. The creation of different vaccines, hence, allows researchers to address the various characteristics of the pathogen and its variants, commonly categorised into 7 types such as live-attenuated, inactivated, viral vector, mRNA, recombinant, conjugate, and toxoid vaccines. In addition to improving individual health, vaccines also promote herd immunity and make it possible to eradicate fatal diseases worldwide. For instance, smallpox, which was once among the deadliest diseases until the 1980s, was eradicated thanks to the use of live-attenutated technology (1). Vaccines are extremely important for safeguarding global health and eradicating infectious diseases nationwide and worldwide. The risk of the disease spreading from one person to another reduces as the vaccinated person's body produces an immune response against the targeted disease. Therefore, high vaccination rates shield even those who cannot receive vaccinations, such as the immunocompromised population, from the spread of infectious or contagious diseases.

Adding to their life-saving benefits, vaccines are also cost effective. Certain vaccines, such as the HPV vaccine, prevent diseases leading to more severe health complications like cancer (2). This helps improve the quality of life of patients and reduces the long-term healthcare costs associated with treating such fatal infections (3). For all these reasons, vaccines remain a cornerstone of global health initiatives and are widely celebrated in both the medical community and society at large.

Although vaccines possess numerous advantages, not all vaccines are perceived in a positive light by the population. Vaccine hesitancy has historically existed for a number of established vaccines, like the HPV and MMR, and the more recent mRNA vaccines too have been facing public scrutiny. Due to concerns about their novelty, fast-paced development, and questions around long-term safety, mRNA vaccines have been standing out as major drivers of hesitancy in the recent years (4).

Mechanism of vaccine-induced immunity

Vaccinations stimulate the immune system to recognize and fight pathogens without actually causing the disease (5). When a vaccine is administered, antigen presenting cells (APCs) like macrophages and dendritic cells recognize and ingest the vaccine's antigens through pattern recognition receptors (PRRs) such as Toll-like receptors (TLRs) (Fig 1.) (5). These antigens are then processed and presented on the cell surface via Major Histocompatibility Complex (MHC) Class II molecules (Fig 1.). Antigens presented on MHC Class II molecules are recognized by $CD4^+$ helper T cells, which stimulate B lymphocytes and support the activation of cytotoxic T cells/ killer T cells ($CD8^+$) through the secretion of cytokines (signalling molecules) (Fig 1.). $CD8^+$ cells recognize infected cells and destroy them directly, preventing further infection. The targeting and elimination of the pathogen by $CD4^+$ and $CD8^+$ cells is a process referred to as cell-mediated immunity (Table 1) (6). $CD4^+$ helper T cells also stimulate B cells to produce antibodies specific to the antigen. These B cells differentiate into plasma cells, which are the cells responsible for secreting large quantities of antibodies (Fig 1.). This entire process is known as humoral immunity (Table 1). The antibodies bind to the pathogen, marking it for destruction by other immune cells.

Upon re-exposure to the same antigen via a booster dose of the administered vaccine, the immune system initiates a fast secondary immune response. This faster response is due to the presence of memory B cells and memory T cells, which were formed during the primary immune response triggered by the initial vaccination. Memory B cells rapidly differentiate into plasma cells and produce large quantities of specific antibodies. At the same time, memory T cells (including both helper $CD4^+$ and cytotoxic $CD8^+$ subtypes) are quickly reactivated. Memory $CD4^+$ T cells help amplify the immune response by stimulating B cells and other immune cells, while memory $CD8^+$ T cells directly identify and destroy infected cells. This coordinated response enables the body to neutralize the pathogen much more efficiently than during the initial exposure, often preventing illness altogether.

Table 1. Comparison of humoral and cellular immunity.

Features	Humoral Immunity	Cellular Immunity

Mediated By	B lymphocytes	T lymphocytes
Main Function	Production of antibodies	Direct cell death of cancerous/infected cells
Targets	Extracellular pathogens like bacteria	Intracellular pathogens like viruses
Response Time	Rapid	Slow
Memory Formation	Memory B cells	Memory T cells
Type of immune response	Antibody-mediated	Cell-mediated
Mechanism Of Action	Produces antibodies for neutralization, opsonization and complement recruitment	T cells recognise and destroy infected cells

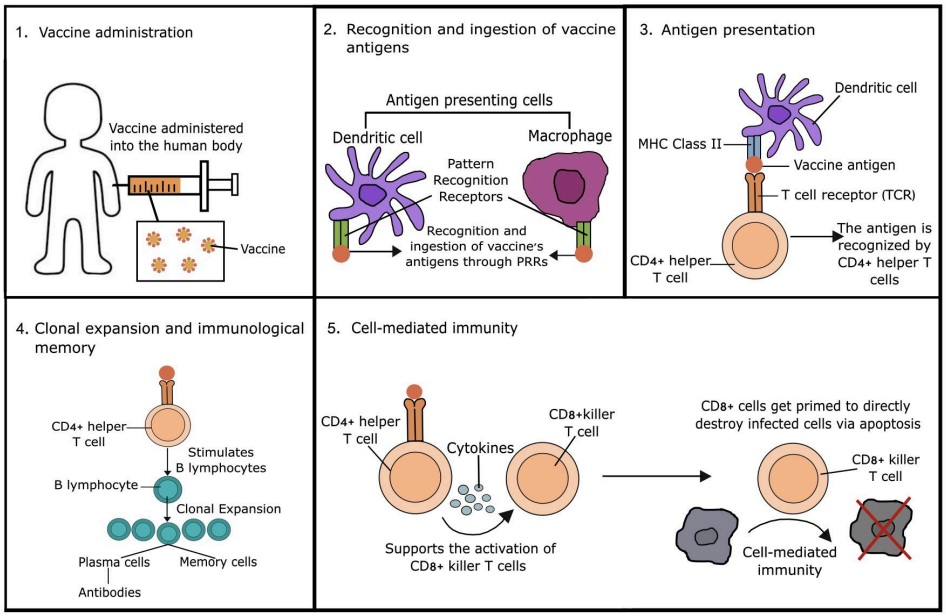

Figure 1. Schematic representation of vaccine administration and immune response. The vaccine is administered to the body. Upon uptake, the vaccine is recognised as foreign and ingested by macrophages and dendritic cells through pattern recognition receptors. The vaccine gets degraded and small peptide/antigens are presented on the cell via Major Histocompatibility Complex (MHC) Class II molecules and recognized by $CD4^+$ helper T cells. CD4+ helper T cells stimulate B lymphocytes and support the activation of cytotoxic T cells/ killer T cells (CD8+) through the secretion of cytokines. Once the body undergoes a real infection, the infected cells get eliminated via the CD8+ killer T cells.

Vaccines types

As described earlier, the immune system neutralizes pathogens through various components of the immune system. Vaccines mimic this natural process by safely introducing antigens that train the immune system to recognize and eliminate threats without causing illness. The following section will explain the major vaccine platforms currently in use, starting with live-attenuated vaccines.

A live-attenuated vaccine is a type of vaccine that contains a weakened form of a pathogen that can still replicate in the body but does not cause disease (Fig. 2A). An example of this is the MMR vaccine. The virus is attenuated by repeatedly culturing it in non-human cells or animal embryos (Fig. 2A). As it adapts to replicate in these foreign hosts, it loses its ability to cause illness in humans (7). In addition to passaging, codon deoptimization, a relatively modern approach, is used to weaken viral replication in human cells while preserving antigen production. Because the weakened virus can replicate and present antigens in a way similar to natural infection, live-attenuated vaccines induce a strong immune response by activating both B cells and T cells, resulting in the production of antibodies and memory cells (Fig. 2A). Therefore, live-attenuated vaccines stimulate both humoral and cell-mediated immunity in the vaccinated individual (Table 1).

Inactivated vaccines use pathogens that have been killed or inactivated through exposure to high temperatures and gamma irradiation or through chemicals like formaldehyde and beta-propiolactone, e.g. Influenza vaccine (8). As a result, the nucleic acids necessary for viral replication denature, and the pathogen present in the vaccine cannot cause disease. Inactivated vaccines stimulate an immune response primarily leading to antibody production (Fig. 2B), but generally require multiple doses to achieve sufficient immunity due to a weaker response compared to live-attenuated vaccines. This reduced immunogenicity is precisely why they are particularly useful for immunocompromised individuals or older adults, as they offer a safer alternative while still providing protective immunity without the risk of causing disease, though the immune response may be weaker compared to live-attenuated vaccines (8).

mRNA vaccines use synthetic messenger RNA that encodes a specific protein from the pathogen. The mRNA strand is encapsulated in lipid nanoparticles to be delivered into human cells (Fig. 2C) and once injected, human cells take up the mRNA and produce the protein on the cell surface. The immune system recognizes this protein as foreign, leading to the production of antibodies and activation of T cells. This results in both humoral and cellular immunity (Fig. 2C). An example of a vaccine that uses this mechanism is the Pfizer-BioNTech COVID-19 vaccine (9).

Recombinant vaccines, on the other hand, involve the insertion of a gene encoding a pathogen-specific antigen into a suitable expression system (e.g. yeast or bacterial cells). The gene is then expressed *in vitro*, leading to the production of the desired protein antigen (Fig. 2D). These antigens are later harvested and purified before being used as the active ingredient in the vaccine. Once the protein is administered into the human body, the recombinant antigens are recognized as foreign by the host's immune system (Fig. 2D). This recognition triggers a humoral response (10). The body recognizes these proteins as foreign, stimulating an immune response without using live pathogens, e.g. Hepatitis B vaccine. This makes recombinant vaccines safer for immunocompromised individuals since there is no risk of infection. They are also highly specific, stable, and easier to produce at scale using biotechnology, though sometimes adjuvants or multiple doses to enhance immunogenicity are required.

Conjugate vaccines, like the pneumococcal vaccine, consist of a weak antigen, often a polysaccharide from the bacterial capsule, covalently linked to a strong antigen, usually a protein carrier. This combination is crucial for eliciting a robust immune response. Polysaccharide antigens from bacterial capsules typically elicit a weak immune response and result in the production of primarily IgM antibodies with limited immunological memory. Normally, polysaccharides alone trigger a weak, short-lived immune response that does not involve T cells and does not generate memory, so to enhance both the strength and duration of protection and stimulate a more effective immune response, the polysaccharide is covalently linked to a strong protein antigen (Fig. 2E), converting the polysaccharide into a T-dependent antigen (11).

Toxoid vaccines contain inactivated toxins produced by bacteria rather than the bacteria themselves (Fig. 2F). These toxoids stimulate an immune response against the toxin rather than the bacteria by being recognized as antigens by the immune system. As a result, if the actual toxin is encountered later, the immune system is already primed to neutralize it before it causes harm. They induce strong antibody production specifically targeting bacterial toxins, and provide effective protection against toxin-mediated diseases. They are used for protection against diseases caused by bacterial toxins rather than direct infection, e.g. tetanus (12).

Lastly, viral vector vaccines like the AstraZeneca COVID-19 vaccine use an adenovirus as a delivery system to introduce genetic material (DNA) for the target pathogen's spike protein into host cells (Fig. 2G). Once it enters the host cell, the gene for the virus spike protein can be read by the cell and copied into mRNA. Following this, the mRNA leaves the nucleus, and the cell's ribosomes begin assembling spike proteins. Some of these spike proteins are processed and broken down into short peptide fragments (usually 8–13 amino acids long), which are presented on the cell surface by MHC class I molecules, allowing cytotoxic T cells to recognize infected cells. Additionally, extracellular spike proteins can be taken up by APCs, processed, and presented on MHC class II molecules, which can be recognized by helper T cells. These helper T cells then activate B cells and cytotoxic T cells, coordinating a broader immune response (Fig. 2G).

Viral vector vaccines are particularly useful because they can elicit strong cellular and humoral immune responses, making them advantageous in situations where T cell-mediated immunity is especially important. Compared to mRNA vaccines, which deliver mRNA directly into the cytoplasm, viral vector vaccines use DNA and require nuclear entry for transcription. This additional step can be seen as a disadvantage due to the potential for slightly delayed expression (ranging from days to weeks, as compared to mRNA vaccines, which only take a few hours to days) or reduced immunogenicity in certain individuals (13). This was a significant reason why mRNA vaccines, like Pfizer BioNTech, for COVID-19 were developed alongside viral vector vaccines, such as the AstraZeneca COVID-19 vaccine (13,14).

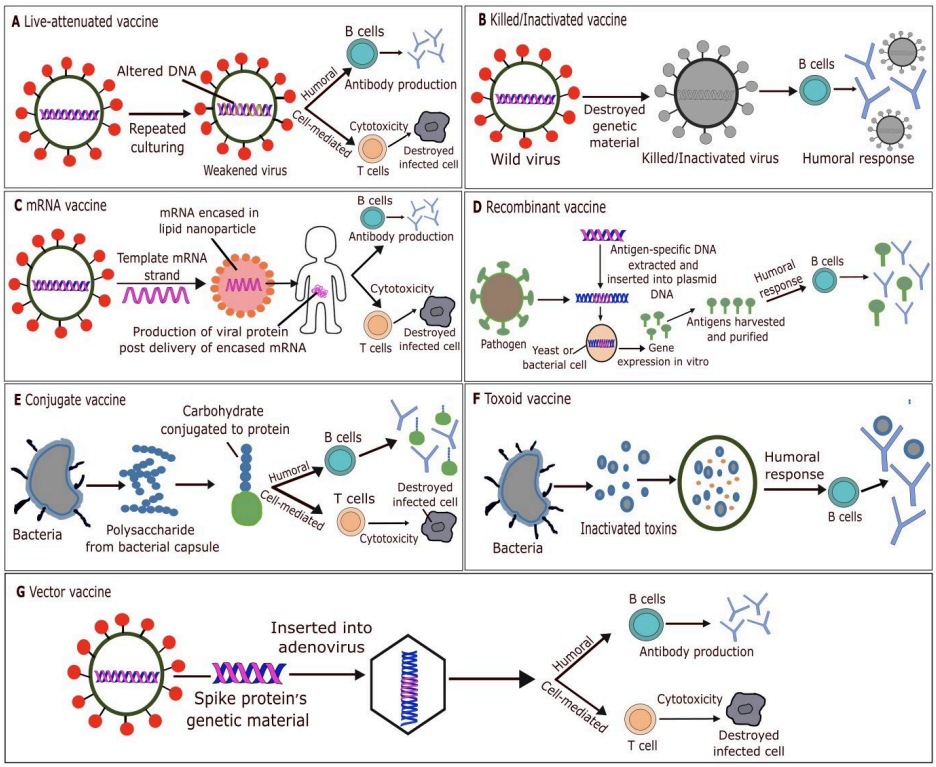

Figure 2. Summary of the different types of vaccines

(A) Live-attenuated vaccine: Altered DNA and repeated culturing produce a weakened virus. Induces both humoral (B cell antibody production) and cell-mediated immunity. (B) Killed/Inactivated vaccine: The wild virus with destroyed genetic material is rendered inactive. Stimulates a humoral response through B cell antibody production. (C) mRNA vaccine: Encased mRNA is delivered into host cells, leading to viral protein production post-administration. Triggers humoral and cell-mediated immune responses. (D) Vector vaccine: Viral genetic material is inserted into an adenovirus vector. Activates both humoral and cell-mediated responses via antibody production and T cell cytotoxicity. (E) Toxoid vaccine: Inactivated bacterial toxins induce a humoral response by stimulating B cell antibody production. (F) Conjugate vaccine: Polysaccharides from bacterial capsules are conjugated to proteins. This produces both humoral and cell-mediated responses. (G) Recombinant vaccine: Pathogen-specific DNA is inserted into plasmids and expressed in yeast or bacterial cells. Harvested antigens are purified to stimulate a humoral response via B cell antibody production.

Why one vaccine does not fit all

Not all vaccines work the same way. Different types of vaccines trigger different immune responses, which can be the key to offering adequate protection against certain pathogens. Some vaccines can be tweaked to go after specific variants, which is really important when dealing with rapidly mutating viruses like influenza or SARS-CoV-2. Moreover, vaccines have to work in a wide demographic setup, including different age groups, ethnicities, and immune system responses. Diversity allows the tailoring of vaccination strategies according to pathogen properties and target populations (15).

Conjugate vaccines, for example, are highly effective in young children whose immune systems do not respond sufficiently to polysaccharide antigens. Polysaccharide antigens stimulate a T-cell independent immune response, which does not lead to class switching to more effective antibody types like IgG. However, conjugate vaccines solve this problem by chemically linking the polysaccharide to a protein carrier, which allows the antigen to be presented to T-helper cells. This activates a T-cell dependent pathway, leading to a stronger immune response that includes class switching and the development of memory lymphocytes even in children with underdeveloped immune systems (16). As for mRNA vaccines (like Pfizer-BioNTech and Moderna), they can be rapidly modified to protect against new, evolving variants, making them ideal for a fast response. Viral vector vaccines (like AstraZeneca) are generally more stable and easier to distribute than mRNA vaccines (17,18). Protein subunit vaccines (like Novavax) offer strong safety but often require adjuvants like Matrix-M and boosters to strengthen the immune response.

Inactivated vaccines (like Sinovac) are easy to manufacture using traditional methods but generally produce weaker immune responses and often require booster doses (8,19). Besides, one type of vaccine cannot protect individuals from every type of pathogen, e.g. inactivated vaccines cannot be used for every type of virus. This is because some viruses, especially non-enveloped ones like adenovirus, are particularly difficult to inactivate reliably using standard inactivation procedures such as treatment with formaldehyde, β-propiolactone (BPL), or heat because of their extremely stable capsids. Poliovirus can be inactivated (as in IPV), but the Cutter Incident showed how even small failures in the process can cause catastrophic outcomes (20). The Cutter Incident 1955 involved an inactivated poliovirus vaccine that contained live poliovirus due to insufficient purification during production, and caused vaccine-associated paralytic poliomyelitis in over 40,000 recipients (20).

Various vaccines have distinct safety profiles and routes of administration that make them suitable for different populations and scenarios. For example, the oral polio vaccine (OPV) is administered orally and is preferred in mass immunization campaigns in low-resource settings because it is easy to administer without medical personnel and induces strong mucosal immunity in the gut, which is the primary site of poliovirus replication (21). However, it carries a small risk of vaccine-derived poliovirus (VDPV), so inactivated polio vaccine (IPV), given via intramuscular injection, is used in countries with low transmission to avoid this risk. Similarly, the BCG vaccine against tuberculosis is administered intradermally to target local immune cells effectively and create a strong localized reaction; improper administration (e.g. subcutaneously) can reduce efficacy or cause abscesses. mRNA vaccines (like Pfizer-BioNTech and Moderna) must be injected intramuscularly to ensure proper cellular uptake and avoid rapid degradation, and they're currently not approved for use in infants younger than 6 months due to limited safety data.

In contrast, live-attenuated vaccines (like MMR) are contraindicated in immunocompromised individuals or pregnant women because the attenuated pathogen, while weakened, still replicates in the body. These differences in safety profiles and administration routes arise from the underlying biology of the vaccine platform: such as whether the antigen is live, inactivated, or subunit, and influences how the immune system is activated, what types of immunity are induced, and how safely the vaccine can be delivered to different groups (15,22). To address global vaccination needs, particularly in pandemics, many different vaccine candidates are developed simultaneously. This strategy maximizes the chances of producing sufficient doses rapidly to cover high-risk populations. During the COVID-19 pandemic, for

instance, around 115 vaccines were developed to ensure that billions of doses could be manufactured and distributed quickly. Among them, mRNA vaccines stood out, not just for their speed of design, but for how easily they could be adapted to target new variants (23).

Table 2. Overview of vaccine types and their characteristics

Vaccine type	Examples	Mode of action	Safety and risk	Type of immune response induced	Efficacy	Storage	Suitability
Live-attenuated vaccines	Measles Mumps Rubella (MMR) Yellow Fever	Live, weakened form of pathogen	Low risk of causing disease, pathogen can still replicate	Humoral and cell-mediated response	Long-lasting protection 1-2 booster doses needed	Cold chain storage (+2 to +8 °C)	Not suitable for immuno-compromised individuals and pregnant women
Inactivated vaccines	Polio (Salik Vaccine), Hepatitis A Influenza	Inactivated/ killed pathogens	Very safe Non-infectious pathogen	Humoral response	Low efficacy Requires multiple doses	Cold chain storage (+2 to +8 °C)	Suitable for all
mRNA vaccines	COVID-19	Synthetic mRNA	Long-term safety unknown Rare allergic reactions	Humoral and cell-mediated response	High efficacy and adaptability	Ultra-cold storage (-70°C)	Most adults, including pregnant women
Viral vector vaccines	Ebola COVID-19	DNA on viral vector backbone	Generally safe Rare risks due to viral vector	Humoral and cell-mediated response	High efficacy	Cold chain storage (+2 to +8 °C)	Less effective in older populations
Re-combinant vaccines	Hepatitis B	Recombinant protein	Very safe No live pathogen used	Humoral response	High efficacy	Cold chain storage (+2 to +8 °C)	Suitable for both children and adults

Conjugate vaccines	HPV Pneumo-coccus	Weak antigen + carrier protein	Very safe	Humoral and cell-mediated response	High efficacy, especially for children	Cold chain storage (+2 to +8 °C)	Suitable for all
Toxoid vaccines	Tetanus	Inactivated bacterial toxins	Very safe	Humoral response	High efficacy,	Cold chain storage (+2 to +8 °C)	Suitable for both children and adults

Shift of focus to mRNA vaccines

Amongst researchers, mRNA technology has started gaining significant attention due to offering several advantages compared to traditional vaccine types, making them a significant advancement in immunization technology. mRNA vaccines can be designed and produced much faster than traditional vaccines (24). They do not require the growth of live pathogens, which can be time-consuming. Instead of relying on living cells to produce antigens, as is done in the cell-based system, synthetic mRNA can be rapidly generated *in vitro* using a cell-free enzymatic reaction, once the genetic sequence of the antigen is known. This mixture is then purified using chromatography and tangential flow filtration, and encapsulated within lipid nanoparticles for delivery (25). This rapid *in vitro* production of synthetic mRNA allows for faster development, scalability, and adaptability in response to emerging variants, enabling large-scale production in a shorter timeframe and also, supporting herd immunity.

Clinical trials have shown mRNA vaccines to have high efficacy rates in preventing severe illness, hospitalization, and death. For example, the Pfizer-BioNTech and Moderna COVID-19 vaccines demonstrated approximately 90% efficacy in preventing symptomatic infection in initial trials, compared to approximately 65.7% to 80.2% for non-mRNA COVID-19 vaccines against symptomatic PCR-confirmed infection (26–28). Moreover, another study demonstrated vaccine effectiveness of mRNA-based COVID vaccines to be from 64% to 90% against SARS-CoV-2 infection, 73% to 84% against symptomatic illness, and 63% to 100% against COVID-19-related hospitalization in vulnerable and immunocompromised populations (29). This level of protection is particularly valuable for these high-risk groups, who are more likely to experience complications from COVID-19.

Furthermore, while many traditional vaccines also stimulate humoral and cellular immunity, mRNA vaccines have been shown to produce strong T-cell responses alongside robust antibody production, enhancing the durability of protection, especially against rapidly mutating viruses like SARS-CoV-2 (30). They do not use live or inactivated pathogens, reducing the risk of causing the disease they aim to prevent. The mRNA does not integrate into the host DNA and is quickly degraded by the body after use. Since they are produced in a cell-free environment, there is a lower risk of contamination with toxic agents or other pathogens compared to traditional vaccine production methods (9). The technology allows for rapid modification of the vaccine to target emerging variants of viruses. This adaptability is crucial for addressing mutating pathogens like influenza or SARS-CoV-2 (1). As technology advances, the cost of producing mRNA vaccines is expected to decrease further. However, mRNA vaccines

also pose slight risks: although rare, there is a small but increased chance of myocarditis, especially in young males, mostly after the second dose, due to sex hormones, such as testosterone, inhibiting anti-inflammatory cells and causing an immune response. Through this, it can be learnt that age and sex are the most important risk factors; specifically, males aged between 12-30 are at the highest risk of developing myocarditis following mRNA COVID vaccination (31,32). Other rare side effects include severe allergic reactions, like anaphylaxis and Bell's palsy (temporary facial paralysis), to vaccine ingredients (33).

mRNA vaccines also face storage problems. For example the Pfizer-BioNTech BNT162b2 vaccine initially required -80°C to -60°C storage conditions for long-term stability. Although later data showed an improvement in storage condition allowing for storage at standard freezer temperatures (-25°C to -15°C) for up to two weeks. However, this improvement has not been significant enough and ultra-cold storage still remains a barrier for broad global access. This not only leads to high operating costs, but also reduces accessibility in low-income countries that face a lack of infrastructure for ultra-cold storage and transport, hence leading to temperature excursions.

Public perception of mRNA vaccines post COVID pandemic

The general public's attitudes toward vaccines are broadly positive, with most people worldwide recognizing the importance, safety, and effectiveness of vaccination (34). However, this does not seem to be the case for mRNA vaccines. A sentiment analysis showed that mRNA vaccines are facing much more negative attitudes, particularly driven by concerns over their safety, efficacy, and unknown long-term effects (35). Another study has also shown that negative attitudes dominate discussions on mRNA vaccines, particularly on social media platforms. The study found that 69.5% of online conversations on Twitter expressed skepticism around mRNA vaccines (35).

In light of this, a cross-sectional survey was conducted to investigate whether the online skepticism surrounding mRNA vaccines reflects broader public opinion. The survey examined several key factors that might influence vaccine attitudes and behaviors. Specifically, the study aimed to explore the relationship between participants' awareness of specific vaccines and their actual uptake, as well as how individuals perceive the safety of different vaccine platforms, including mRNA and traditional types. It also assessed the general public's level of education and vaccine-related knowledge, contrasting self-perceived understanding with actual knowledge-based responses. Furthermore, the survey evaluated the role of information sources such as healthcare providers, social media, and news outlets in shaping individuals' safety perceptions and trust in vaccines. Together, these variables were analyzed to gain insight into the underlying factors contributing to mRNA vaccine hesitancy and to identify potential gaps in vaccine literacy.

A total of 165 individuals participated in this survey, which was conducted both online and in person between January and April 2025, roughly two years after the COVID-19 pandemic. Respondents represented a wide range of nationalities and demographic backgrounds. In terms of age, the largest groups were those aged 30-60 (41.10%) and those under 18 (33.10%). Educationally, 40.50% had completed or were pursuing postgraduate studies, while 35.60% were in or had completed high school.

Unexpected gaps in vaccine knowledge

An essential aim of this study was to evaluate the public's level of education and general knowledge about vaccines. Given that vaccine-related decisions have direct implications for both individual and public health, it is critical to understand whether the general population is sufficiently informed to make evidence-based choices regarding vaccination. The survey sought to explore whether respondents possessed foundational knowledge about how vaccines work and the types of vaccines that exist. This helps determine whether the public is well-equipped to make informed health decisions, or whether knowledge gaps could be contributing to vaccine hesitancy, misinformed refusal, or the spread of misconceptions. In addition, the survey aimed to examine whether vaccine knowledge levels correlate with demographic factors, specifically age and education level. It is commonly hypothesized that individuals with higher levels of formal education and older age groups may possess a stronger foundation in health-related topics, including immunization. This assumption is based on their likely increased exposure to science curricula, public health messaging, and real-world vaccine campaigns over time. By analyzing knowledge accuracy across different age groups and education levels, the survey sought to determine whether such demographic factors significantly influence vaccine literacy and, by extension, whether targeted interventions should focus on younger or less formally educated populations to improve understanding and confidence in vaccination.

To assess the accuracy of participants' actual knowledge, participants were presented with five true-or-false statements specifically focused on mRNA vaccines. These statements were designed to test their understanding by evaluating whether respondents could correctly identify factual information (by selecting "true" for scientifically accurate statements and "false" for inaccurate ones).

In contrast to commonly held assumptions, the survey revealed that knowledge accuracy about mRNA vaccines decreased with age. Among respondents under 18, 48.15% answered all five true/false statements correctly, while this figure dropped to 31.58% for the 18-30 age group and further declined to 23.53% for the 30-60 age group. This inverse relationship suggests that younger individuals may be more familiar with recent scientific advancements, possibly due to updated school curricula or increased online exposure during the COVID-19 pandemic. Similarly, education-level comparisons yielded unexpected results. While one might expect knowledge to increase with academic attainment, the data showed that 46.55% of respondents with a high school education scored all correct, compared to only 23.91% of undergraduates and 28.30% of postgraduates. Notably, the middle school group had the lowest full-score rate (25%). These findings indicate that higher academic degrees did not correspond to higher factual knowledge of mRNA vaccines in this sample, and the high school group outperformed both undergraduate and postgraduate cohorts. These results reflect recency of exposure to vaccine information in school settings, overconfidence in higher-educated groups, and a disconnect between general education and specific public health knowledge. Furthermore, these findings indicate that higher academic qualification does not necessarily translate to higher vaccine-specific knowledge in this sample. In fact, recent exposure to vaccine information might be playing a greater role than level of formal education.

Awareness of vaccines does not support uptake of vaccines

A comparative analysis to examine the relationship between participants' awareness of vaccines (whether they had heard of the vaccine) and their actual uptake was conducted to assess whether being informed about the vaccines directly influenced the decision to get vaccinated (Fig 3).

The findings revealed a consistent trend across all vaccines: while a majority of respondents reported having heard of most vaccines, this awareness did not translate proportionally into vaccine uptake. For example, although 80% of participants were aware of the Hepatitis A vaccine, only 46.67% had received it (Fig. 3). Similarly, while 84.24% were aware of the influenza vaccine, just 52.12% reported uptake (Fig. 3). Even in the case of widely known vaccines like the HPV vaccine, awareness stood at 55.15%, yet uptake was less than half of that at 26.67% (Fig. 3). However, the COVID-19 vaccines showed a significantly narrow gap between awareness and uptake, ie. 98.18% and 91.52% respectively (Fig. 3). This relatively high uptake could, in part, be attributed to the fact that many countries implemented mandatory vaccination policies or strong public health campaigns during the pandemic, which likely influenced individuals' decisions to receive the vaccine regardless of personal hesitancy.

Overall, this suggests that awareness alone is not a sufficient determinant of vaccine uptake. Despite being informed about the existence of a vaccine, many individuals choose not to receive it, pointing to the presence of other influential factors such as perceived safety, access, misinformation, or perceived necessity. This highlights the importance of addressing barriers beyond simple awareness in efforts to improve vaccination coverage. The gap between awareness and uptake highlights that decisions about vaccination are shaped less by knowledge of a vaccine's existence and more by perceptions of its safety and trustworthiness. This distinction is especially relevant when examining attitudes toward newer mRNA vaccines, which are often viewed more skeptically compared to legacy vaccines with a longer history of use.

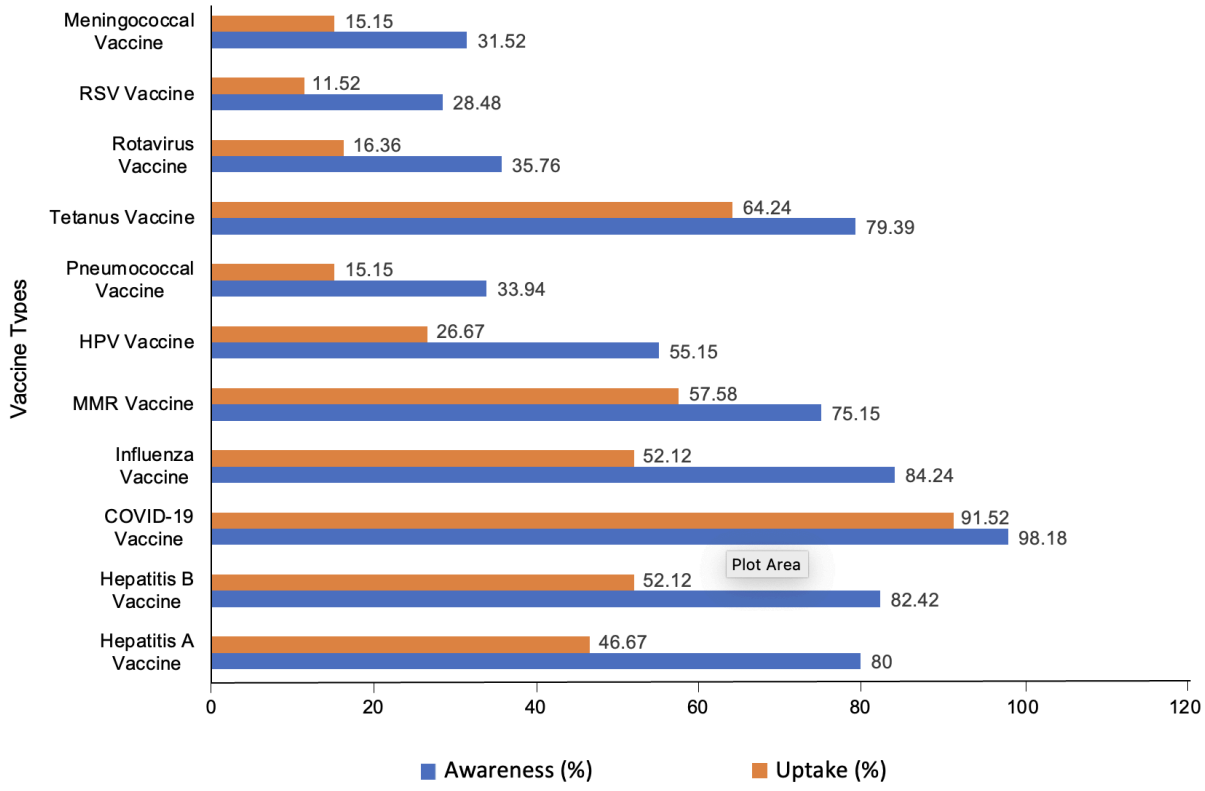

Figure 3. Awareness of vaccine compared to uptake of vaccine (n=165)

The percentage of respondents who reported being aware of the specific vaccine is shown in blue (Awareness) while the percentage of respondents who reported receiving the same vaccine is shown in orange (Uptake).

Legacy vaccines viewed as safer than newer mRNA alternatives

The survey also aimed to compare how participants perceived the safety of different vaccines. Specifically, it aimed to analyze the distribution of safety perceptions across various vaccines to determine whether certain types, such as the COVID-19 mRNA vaccine, were viewed as safer or less safe than others. This comparison helped explore whether mRNA vaccines in particular were perceived as unsafe and to identify the reasons participants provided for their views.

The COVID-19 mRNA vaccine received the highest proportion of safety ratings at level 1, indicating that the largest percentage of respondents perceived it as the least safe (Fig. 4). Conversely, it received the lowest proportion of most safe answers, suggesting that comparatively fewer respondents considered it to be the safest option among the vaccines listed. Among all respondents who identified the COVID-19 mRNA vaccine as the least safe option, their reasoning predominantly clustered around five key themes: perceived lack of long-term research (40%), concerns about side effects (24%), the novelty of mRNA vaccines (20%), and limited knowledge of the vaccine and a general lack of information (16%). These findings were consistent with those reported by Ali et al. (33).

In addition, Polio was rated by 51.20% of respondents as the safest vaccine (Fig. 4), likely due to its long-standing presence and widespread use in public health campaigns (36). Its historical success in nearly eradicating poliomyelitis, especially in countries like India, has contributed to a strong perception of reliability and effectiveness (37). The vaccine's association with large-scale government initiatives, such as National Immunization Days and door-to-door polio drives, may have reinforced public trust (38). Additionally, the relatively low profile of adverse effects and minimal controversy surrounding its use, particularly in comparison to newer vaccine technologies like mRNA, could explain its high safety ratings.

However, despite this strong reputation, the polio vaccine also received a notable number of "least safe" ratings (14.89%) (Fig. 4). This polarised response potentially stems from lingering concerns over the Oral Polio Vaccine (OPV), which, although extremely rare, has been associated with vaccine-derived poliovirus cases and vaccine-associated paralytic poliomyelitis. In some regions, especially those with a history of vaccine hesitancy or mistrust toward health authorities, the OPV has been subject to misinformation and conspiracy theories (39). Some individuals may also lack clarity between the different types of polio vaccines, such as OPV, which contains a live-attenuated virus, and the Inactivated Polio Vaccine (IPV), which uses a killed virus, leading to generalised safety concerns. Furthermore, negative personal or community experiences with past polio campaigns, including issues with cold chain management or expired doses, may have influenced perceptions. These findings suggest that while polio enjoys a legacy of success, regional, informational, and historical factors can still contribute to doubts about its safety (39).

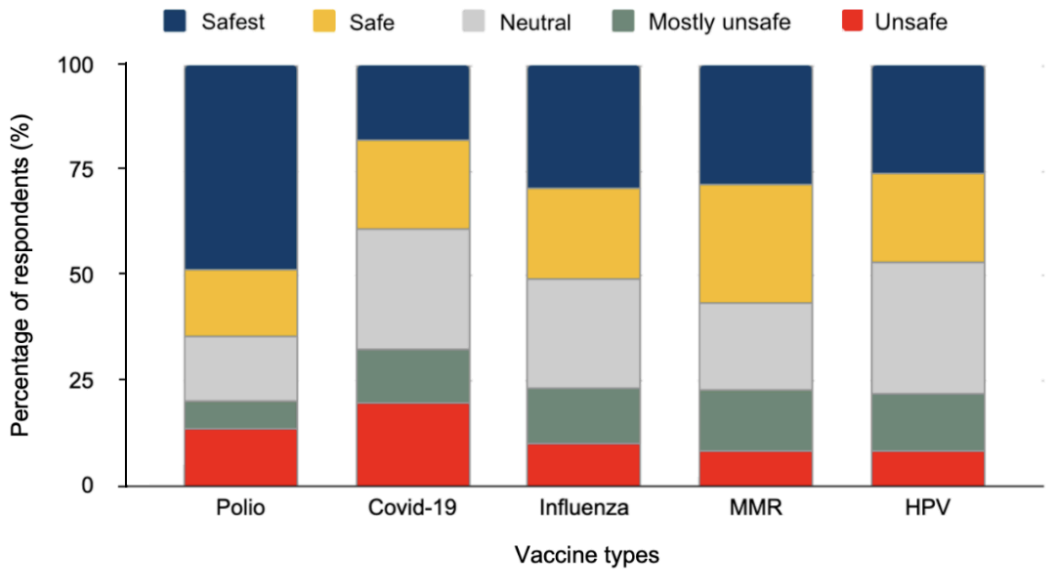

Figure 4. Comparing the distribution of safety perception across different vaccines
Distribution of respondent ratings (1–5) for each vaccine, with 1 indicating 'unsafe' (red) and 5 indicating 'safest' (blue). The y-axis represents the percentage of respondents assigning each rating, while the x-axis lists the vaccines they were asked to evaluate.

Incomplete information leaves individuals feeling underconfident

In addition to assessing perceptions of vaccine safety, the survey also investigated how confident individuals felt in their own understanding of vaccines compared to their actual knowledge. This analysis aimed to explore whether individuals who believe they are well-informed about vaccines truly possess accurate scientific knowledge, or whether a disconnect exists between perceived and actual understanding.

Understanding this kind of discrepancy is important because when people are overconfident in their knowledge of vaccines, particularly when misinformed, it can contribute to the spread of misinformation, lower people's trust in healthcare systems, and even reduce their willingness to follow public health guidance. This issue becomes even more relevant in the context of mRNA vaccines, where the mix of novelty and misinformation has made the gap between what people believe they know, and what they actually know, much wider. Conversely, those who underestimate their knowledge will be less likely to engage in vaccine education or advocacy, despite being reasonably informed. This perception gap could impact vaccine decision-making, willingness to receive new vaccines, and responsiveness to educational interventions. To evaluate the relationship between self-perceived and actual knowledge of vaccines, respondents were asked to self-assess their understanding using a Likert scale ranging from 1 to 5, with 1 indicating "low" understanding and 5 indicating "high" understanding. The question posed was: "How good do you believe your understanding of vaccines to be?". This aided in capturing participants' subjective perception of their vaccine-related knowledge. Subsequently, the survey compared these self-ratings with their actual performance on a set of five true/false statements related specifically to mRNA vaccine mechanisms and properties,

mentioned previously. This helped assess whether higher perceived understanding correlated with better factual accuracy or not.

Respondents who rated their knowledge as low (≤3) had a 33.00% rate of scoring a perfect 5/5, while those who rated their knowledge as high (≥4) had a 33.82% perfect score rate (Table 3). This negligible difference suggests that actual knowledge levels were largely independent of perceived confidence.

Interestingly, this also reveals a confidence gap, whereby individuals often possess greater knowledge than they believe themselves to have. A significant number of respondents underestimated their knowledge, performing well despite reporting lower confidence. This could indicate a broader lack of self-efficacy or trust in one's own scientific literacy, particularly in contexts where vaccine information is perceived as complex or controversial. Alternatively, it reflects the success of public health messaging in shaping accurate knowledge, even if individuals do not perceive themselves as well-informed. This also might suggest that, while individuals may have absorbed correct information incidentally, they have not actively accessed or sought out vaccine knowledge themselves. In other words, their understanding may be accurate but passive, lacking the intentional engagement that builds confidence. This could stem from limited access to detailed, comprehensible scientific information, or from a broader disconnection between public health messaging and individuals' perceived capacity to interpret it. As a result, even those who are well-informed may doubt their own understanding, highlighting the need for accessible, engaging educational efforts that not only provide information but also empower individuals to recognize and trust their knowledge.

To investigate whether the underestimation of self-perceived vaccine knowledge was linked to a lack of informational exposure, respondents were asked whether they believed the sources they typically accessed had explained mRNA vaccines in great detail. The response options were "Yes," "No," or "Not sure."

Even among respondents who answered all questions correctly, most reported that their usual sources had not provided detailed explanations of mRNA vaccines. Specifically, among respondents who scored 5/5 on factual vaccine knowledge but rated their own understanding as 2/5, only 1 individual believed their sources had explained mRNA vaccines well, while 6 respondents explicitly answered "No." Similarly, among those who rated themselves as 3/5, 8 respondents said "Yes," but a significant 17 said "No" or "Not sure". This pattern strongly suggests that many underconfident individuals were not receiving in-depth or satisfying information from their chosen sources. Despite possessing accurate knowledge, they perceived their understanding to be low, likely because they did not actively seek information or felt that what they accessed lacked depth or clarity.

This has broader implications: it highlights shortcomings in public health communication, educational outreach, and media efforts to explain complex vaccine technologies like mRNA, which might be contributing factors to why people feel underconfident in what they know despite being informed.

When individuals are not confident in their understanding, even if correct, they may struggle to trust their own judgments, disengage from vaccine-related decisions, or become more vulnerable to misinformation. It emphasizes the need for clearer, more accessible, and more empowering vaccine education efforts to support not just knowledge acquisition, but confidence in that knowledge as well.

Table 3. Relationship between self-perceived and actual vaccine knowledge

Self-Percieved Understanding	Number Of Respondents (n=165)	Percentage Of Respondents scoring 5/5 (%)
≤3/5	97	33.00
≥4/5	68	33.82

mRNA distrust is linked to non-traditional information sources

To better understand how individuals form their opinions about vaccine safety, particularly in relation to mRNA versus traditional vaccines, respondents were asked to select one or multiple sources they relied on to stay informed about vaccines, ongoing developments, and related news. The survey offered six predefined options: news outlets, social media, healthcare professionals, family or friends, scientific journals or articles, and Google Search, with an additional "Other" option that was not selected by any participant.

For the purpose of the post-survey analysis, these sources were grouped into two broad categories. Trusted sources, defined as evidence-based and scientifically rigorous, included healthcare professionals and scientific journals or articles. In contrast, non-traditional or less-trusted sources included social media, family or friends, and Google Search. These channels are often decentralized, anecdotal, or algorithm-driven, and have been frequently associated with the circulation of misinformation.

This categorization allowed for further analysis on whether the type of information source influenced individuals' safety perceptions of vaccines, particularly whether reliance on trusted versus non-trusted sources affected how safe respondents considered mRNA vaccines compared to traditional ones.

This revealed notable patterns in how different information sources shaped perceptions of vaccine safety, particularly regarding mRNA vaccines versus traditional vaccines. Respondents who primarily relied on healthcare professionals and scientific journals or articles, the most scientifically reliable sources, were substantially more likely to express uncertainty rather than outright distrust. For instance, over 52.2% of those who consulted healthcare professionals and 61.3% of those who referenced scientific journals reported uncertainty about mRNA vaccine safety (Table 4), suggesting a more cautious but not overtly skeptical attitude. This could indicate that while trusted sources are effective in preventing misinformation, they may not be providing information in a sufficiently accessible or confidence-boosting manner for lay audiences.

Conversely, reliance on non-traditional or informal sources was associated with greater polarization in perception. Notably, respondents who used social media, google search, or consulted family and friends exhibited a higher proportion of traditional vaccine preference and greater skepticism toward mRNA vaccines (Table 4). Among those relying on Google Search (n=61), for example, only 23.33% considered mRNA vaccines safe, compared to 30% who favored traditional vaccines, with the rest unsure (Table 4). This aligns with potentially broader concerns regarding search engine algorithms amplifying unverified content, which might be leading to distorted impressions of new vaccine technologies. A study by Xu et al. found that social media has been acting as a vector for amplifying concerns and misinformation surrounding COVID-19 vaccines (35).

Interestingly, individuals who accessed news outlets demonstrated a relatively even distribution across all safety perception categories. This reflects the mixed quality of reporting in mainstream media, which often blends expert input with politicized or emotionally driven narratives.

Overall, these findings suggest that the source of information does have an effect on vaccine safety perception, and particularly attitudes toward newer technologies like mRNA. The comparatively low confidence in mRNA vaccines among those relying on less-trusted sources reinforces the need for targeted public health communication. Campaigns should not only aim to disseminate accurate information but also work to amplify the visibility and accessibility of trusted sources, especially in digital and informal spaces where misinformation thrives. Additionally, healthcare professionals and scientific communicators must adapt their language and engagement strategies to reduce uncertainty without oversimplifying complex science.

At the same time, this pattern also raises concern that misinformation exposure is reinforcing pre-existing biases, particularly among individuals already inclined to distrust newer vaccine technologies. Addressing this requires not just information correction but restoring trust in institutions and promoting scientific literacy through education and transparent communication.

Table 4. Sources of vaccine information

Primary source of vaccine information	Respondents who used primary source (%)	Respondents viewing mRNA vaccines as Safe (%)	Respondents viewing traditional vaccines as Safe (%)	Respondents not sure (%)
Trusted Sources	**57.15**	**67.04**	**69.50**	**163.50**
Healthcare professionals	33.75	24.30	23.53	52.20
Scientific journals or articles	15.40	17.74	20.97	61.30
News outlets	8.00	25.00	25.00	50.00
Non-traditional Sources	**39.10**	**64.53**	**92.64**	**142.82**
Social media	9.70	20.51	33.33	46.15
Family or friends	14.40	20.69	29.31	50.00
Google Search	15.00	23.33	30.00	46.67

Conclusion

The survey revealed several important takeaways about what drives vaccine apprehension, including the root causes of doubt and mistrust. Understanding these factors is crucial for reducing hesitancy, improving confidence in vaccine development, and strengthening trust in healthcare systems, which should ultimately lead to more positive attitudes and increased vaccine uptake.

A key finding was epistemic dissonance, where people held both accurate and inaccurate beliefs. This duality was seen when many who rated their knowledge as high scored poorly on questions testing their theoretical knowledge, while some who answered correctly still felt uninformed. This shows that knowledge alone does not create confidence, especially when language feels inaccessible. Campaigns should therefore prioritize boosting perceived comprehension through simple, relatable explanations that validate the audience's ability to grasp complex concepts.

Younger participants outperformed older and more educated groups, suggesting that familiarity with academic discourse likely leads to an illusion of proficiency and fosters overconfidence, while exposure to simplified science supports better retention. This insight can be leveraged by targeting science communication efforts toward older and more educated populations through frequent exposure to short, clear, and concise formats, which will help maintain attention spans, simplify complex or overwhelming content without lowering accuracy, and reduce the likelihood of information overload, thus preventing triggering resistance or disinterest. This will close the gap between perceived and actual knowledge.

Awareness alone did not translate into uptake; for instance, many who knew about the HPV vaccine had not received it, and this pattern repeated for every vaccine mentioned in the survey. This suggests that campaigns should prioritize addressing emotional and motivational barriers, in addition to informational barriers. This finding also invites a shift from mass public campaigns to context-specific behavioural nudges, such as linking vaccines to personal relevance and social norms.

Moreover, the survey responses underscored the crucial role of information sources in shaping public perceptions of vaccine safety, particularly for newer technologies like mRNA vaccines. Reliable outlets reduced distrust but failed to resolve uncertainty, likely due to a lack of accessible and clear communication. On the other hand, social media, where unverified content has large visibility, amplified skepticism. The association between informal sources and vaccine distrust reflects a broader epistemic vulnerability: misinformation does not operate in isolation, but interacts with existing fears, cognitive biases, and low institutional trust. Addressing this will require systemic efforts to rebuild public confidence through transparency and education. Effective communication must be both accurate and accessible, bridging the gap between scientific rigor and public relatability.

Distrust was largely emotional, often framed as vaccines being "too new" or "not researched." While large-scale clinical trials demonstrate their safety and efficacy, the public also needs reassurance, clarity, and transparency to build trust. Broader skepticism of biotech progress reflects a cultural tendency to equate speed with recklessness. Communicators must reframe innovation as rigorous and humane to counter the psychological aversion triggered by newness.

Despite the survey's small sample size, its cross-country scope makes its insights useful in shaping future policies and informing new strategies aimed at strengthening public trust, which will be crucial in fostering optimism toward vaccines and future medical innovations.

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