

# An overview of the etiology of vaccine hesitancy and refusal

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## ABSTRACT

Vaccination is among the most cost-effective interventions for protecting populations against infectious diseases. Individuals exhibiting vaccine hesitancy may eventually accept some or all vaccines, may delay them, or may reject specific ones. In contrast, vaccine refusal denotes the complete voluntary rejection of all vaccines in the current immunization program. Vaccine refusal represents a significant public health concern, threatening both individual and community health. Opposition to vaccines has existed since their inception and continues to grow, particularly with the influence of the internet and social media. Some of the reasons for vaccine refusal include concerns about the vaccine components, distrust in vaccines, religious beliefs, reservations about the pharmaceutical industry, and fear of adverse effects. This review aims to explore the etiology of vaccine refusal based on current literature.

**Keywords:** Child, Etiology, Vaccine Hesitancy, Vaccine Refusal

## INTRODUCTION

Vaccines are biological products that confer protection against targeted diseases and are derived from attenuated microorganisms, their toxins, or surface antigens (1). Immunization programs rank among the most cost-effective public health strategies, significantly decreasing morbidity and mortality, preventing and eradicating infectious diseases, and promoting public health (2). According to the World Health Organization (WHO), vaccine hesitancy is the delay in acceptance or refusal of vaccines despite the availability of vaccination services. It is a complex and context-specific issue influenced by factors such as complacency, convenience, and confidence. Individuals exhibiting vaccine hesitancy may eventually accept some or all vaccines, may delay them, or may reject specific ones. In contrast, vaccine refusal denotes the complete voluntary rejection of all vaccines in the current immunization program. Figure 1 shows vaccine hesitancy process (3).

### 1- History of anti-vaccination movements

To understand the origins of vaccine refusal and hesitancy, it is essential to consider the historical background.

### Early anti-vaccination movements

Resistance to vaccination emerged in 18<sup>th</sup>-century England, where religious leaders argued that disease was a divine punishment and that preventing it was a defiance of God's will. Between 1840 and 1853, mandatory smallpox vaccination led to the establishment of the anti-vaccination league in London, which opposed compulsory immunization on grounds of personal liberty (4). Sanctions, including imprisonment, against those who refused vaccination generated public outrage (2). In 1867, the vaccination mandate was extended to children up to 14 years old, prompting the formation of the anti-compulsory vaccination league (5). Anti-vaccine publications in the 1870s and 1880s reduced vaccine uptake across Europe and the United States of America (USA), resulting in outbreaks such as the 1874 smallpox epidemic in Stockholm, which claimed over 4.000 lives (4,6). In 1898, under growing pressure, the British Parliament introduced the concept of the "conscientious objector," allowing parents to exempt their children from vaccination (7).

### Anti-vaccination movements in USA

The first American anti-vaccine conference was held in 1907, led by J. Pitcairn, who later founded the Anti-vaccination league of

America in Philadelphia. A parallel movement in Brazil, led by O. Cruz, also resisted vaccination (8). Despite these oppositions, the 1950s and 1960s are regarded as the golden era of vaccine acceptance, marked by successful immunization campaigns against polio, measles, and rubella (9).

### ***Polio vaccine: the cutter incident***

In 1955, a polio vaccine produced by Cutter Laboratories was found to contain live poliovirus, resulting in approximately 70.000 mild infections, 200 cases of paralysis, and 10 deaths. This incident significantly eroded public trust in vaccine safety (10).

### ***The diphtheria, tetanus, and pertussis (DTP) vaccine controversy***

Concerns about the DTP vaccine arose in 1974 following a report linking it to neurological complications in children (11). In 1982, the documentary "DTP Vaccine Roulette" and the book "Shots in the Dark" further fueled fears, alleging that the vaccine caused seizures and permanent brain damage. These claims led to a substantial decline in vaccination coverage and a pertussis outbreak in the England (10).

### ***Swine flu vaccine and Guillain-Barré Syndrome (GBS)***

In 1976, the USA launched a nationwide vaccination campaign against swine flu. Shortly thereafter, reports emerged of an increased incidence of GBS. Although subsequent studies found that the risk was minimal, public anxiety persisted (12,13). Similar allegations surfaced in France in the 1990s, where hepatitis B vaccination was erroneously linked to multiple sclerosis. Later research disproved this association (12,14).

### ***The measles, mumps, and rubella (MMR) vaccine controversy***

In 1998, Andrew Wakefield published a now-retracted study in The Lancet that falsely claimed a link between the MMR

vaccine and autism in children. The article received extensive media coverage and significantly contributed to vaccine refusal worldwide, despite being discredited (15).

### ***Vaccine and infertility***

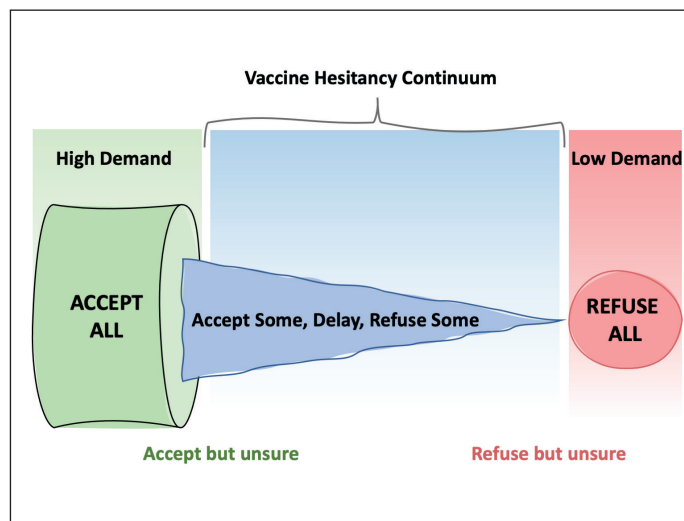
In 2003–2004, Muslim leaders and politicians in Northern Nigeria alleged that oral polio vaccines were part of a Western plot to induce infertility and spread HIV. This resulted in widespread vaccine refusal and a resurgence of polio cases (11,16).

### ***Vaccine hesitancy/refusal in the modern era***

Since the 2000s, the rise of the internet and social media has facilitated the rapid spread of anti-vaccine rhetoric. Public figures expressing anti-vaccine views have further legitimized these beliefs. Online communities and blogs dedicated to vaccine skepticism have emerged, influencing public opinion and reinforcing vaccine hesitancy (17). Figure 2 shows the timeline of vaccine refusal (10).

## **2- Etiology of vaccine hesitancy/refusal**

The introduction of vaccination has consistently been accompanied by opposition. The earliest documented resistance emerged in 18<sup>th</sup>-century England, driven by religious objections (4). Over time, the underlying causes of vaccine hesitancy/refusal have diversified and are now categorized into three main domains: contextual influences, individual and group influences, and vaccine- or vaccination-specific issues (Table I) (3).



**Figure 1:** Vaccine hesitancy process

1798	<ul style="list-style-type: none"> <li>• <b>Smallpox Vaccine</b></li> <li>• Edward Jenner Public opposition, violation of God's will, "cow-mania"</li> </ul>
1853	<ul style="list-style-type: none"> <li>• <b>1st Vaccine Mandate-UK</b></li> <li>• Mandating vaccine for infants during their first 3 months</li> </ul>
1870	<ul style="list-style-type: none"> <li>• <b>Anti-VAXX Movement-EU</b></li> <li>• Anti-vaccination movements started to appear across Europe</li> </ul>
1879	<ul style="list-style-type: none"> <li>• <b>Anti-VAXX Movement-ES</b></li> <li>• Anti-vaccination sentiments in the US towards the end of the 19th century</li> </ul>
1902	<ul style="list-style-type: none"> <li>• <b>Smallpox Epidemic-US</b></li> <li>• Epidemic in Massachusetts-mandatory vaccination of all adults</li> </ul>
1955	<ul style="list-style-type: none"> <li>• <b>Polio Vaccine</b></li> <li>• The Cutter Incident-Several vaccine batches contained live active polio virus</li> </ul>
1974	<ul style="list-style-type: none"> <li>• <b>DTP Vaccine</b></li> <li>• DTP Vaccine Roulette documentary</li> </ul>
1998	<ul style="list-style-type: none"> <li>• <b>MMR Vaccine</b></li> <li>• Andrew Wakefield falsely linked MMR vaccine to autism</li> </ul>
2001	<ul style="list-style-type: none"> <li>• <b>Thiomersal Misconception</b></li> <li>• Removed from childhood vaccines by 2001 (except multi-dose flu vaccine)</li> </ul>

**Figure 2:** Vaccine hesitancy/refusal timeline

### Vaccine and mercury

Contrary to widespread misconceptions, the form of mercury used in vaccines is thiomersal, an ethylmercury compound. The toxic effects associated with mercury arise from methylmercury, which is not present in vaccines. Scientific studies have shown no evidence of neurotoxicity or chronic accumulation of thiomersal. Due to the financial and logistical burdens of producing thiomersal-free single-dose vials, the WHO supports the continued use of multi-dose thiomersal-containing vaccines (18).

### Vaccine and autism

A primary argument of anti-vaccine groups is the alleged link between vaccines and autism spectrum disorder (ASD), often based on methodologically flawed studies. Although rising ASD prevalence is frequently blamed on vaccines, it is more accurately attributed to expanded diagnostic criteria, improved detection methods, and increased awareness among families and professionals. A large-scale meta-analysis encompassing over 1.2 million children found no correlation between ASD and either thiomersal exposure or MMR vaccination (19,20,21).

### Vaccines, pharmaceutical industry and conflict of interest

Public skepticism toward the pharmaceutical industry is frequently cited in vaccine refusal (22). Reports indicate

that drug promotion expenditures totaled \$28 billion in the USA, \$20 billion across several European nations, and over \$26 billion in Japan as of 2012 (23). Despite the industry's contributions to medical advancement, mistrust arises due to perceived commercial motives and inadequate physician awareness regarding drug pricing (24). In Türkiye, all vaccines are imported and undergo regulatory testing; however, public concerns about pharmaceutical companies' influence persist, contributing to vaccine hesitancy/refusal (22).

### The role of social media

In the digital era, social media platforms have become a primary source of health-related information. Parents often seek vaccine-related advice on platforms such as facebook and instagram, where misinformation from non-expert individuals is prevalent. The amplification of biased content, often promoted by celebrities and influencers, undermines public trust in vaccination (25,26). A 2023 report from the Turkish Statistical Institute highlighted whatsapp, youtube, and instagram as the most commonly used platforms (27). Unlike traditional media, social media allows rapid dissemination of unverified content, exacerbating information pollution (26). Enhancing digital health literacy and actively monitoring social media are vital to combating misinformation.

### Vaccine hesitancy/refusal and religion

Religious concerns, particularly in Muslim communities, have centered around the origin of gelatin used in vaccines. Gelatin, employed to stabilize vaccine components, can be sourced from cattle, poultry, or pigs. Due to religious sensitivities, vaccines administered in Türkiye use only bovine-derived gelatin (28). Furthermore, in 1995, the World Islamic Health Federation stated that gelatin, even when derived from pigs, undergoes transformation processes that render it religiously permissible (29). Another religious objection to vaccination stems from the belief that it interferes with divine will (30). However, no religious texts explicitly forbid vaccination, and immunization is mandated for participation in Hajj and Umrah pilgrimages.

### Perceived unnecessary and ineffectiveness of vaccines

Some individuals argue that vaccines are unnecessary, citing natural immunity, the low prevalence of diseases, or reliance on traditional therapies such as herbal medicine or cupping. Others believe that vaccine-induced immunity is passive and short-lived, requiring repeated booster doses (31). Parents who experienced illnesses such as measles or mumps without complications may prefer natural infection for their children, believing it confers lifelong benefits (32). Mistrust in public health data and skepticism toward reported efficacy rates also contribute to vaccine refusal (33). However, data from the Centers for Disease Control and Prevention (CDC) demonstrate substantial reductions in disease incidence post-vaccination, with declines of 96% to 100% for several vaccine-preventable diseases (Table II) (34).

**Table I: Factors affecting vaccine hesitancy/refusal**

Contextual Influences
<ul style="list-style-type: none"> <li>• Communication and media environment</li> <li>• Influential leaders, immunization program gatekeepers and anti or pro-vaccination lobbies.</li> <li>• Historical influences</li> <li>• Religion/culture/ gender/socio-economic</li> <li>• Politics/policies</li> <li>• Geographic barriers</li> <li>• Perception of the pharmaceutical industry</li> </ul>
Individual and group influences
<ul style="list-style-type: none"> <li>• Personal, family and/or community members' experience with vaccination, including pain</li> <li>• Beliefs, attitudes about health and prevention</li> <li>• Knowledge/awareness</li> <li>• Health system and providers-trust and personal experience.</li> <li>• Risk/benefit (perceived, heuristic)</li> <li>• Immunisation as a social norm etc. not needed/ harmful</li> </ul>
Vaccine/vaccination spesific issues
<ul style="list-style-type: none"> <li>• Risk/ benefit (epidemiological and scientific evidence)</li> <li>• Introduction of a new vaccine or new formulation or a new recommendation for an existing vaccine</li> <li>• Mode of administration</li> <li>• Design of vaccination program/mode of delivery (e.g., routine program or mass vaccination campaign)</li> <li>• Reliability and/or source of supply of vaccine and/or vaccination equipment</li> <li>• Vaccination schedule</li> <li>• Costs</li> <li>• The strength of the recommendation and/or knowledge base and/or attitude of healthcare professionals</li> </ul>

**Table II: Morbidity before and after vaccination**

Disease	Pre vaccine era estimated annual morbidity	After vaccine estimates u.s.a cases	Percent decrease (%)
Polio (paralytic)	16.316	0 <sup>2</sup>	100
Diphtheria	21.053	2 <sup>2</sup>	>99
H. influenzae serotype B (invasive, <5 years of age)	20.000	18 <sup>2</sup>	>99
Hepatitis A	117.333	37.700 <sup>3</sup>	68
Measles	530.217	1.275 <sup>2</sup>	>99
Meningococcal disease (all serotypes)	2.886 <sup>4</sup>	371 <sup>2</sup>	87
Pertussis	200.752	18,617 <sup>2</sup>	91
Pneumococcal disease (invasive, <5 years of age)	16.069	1.700 <sup>5</sup>	89
Rotavirus (hospitalizations, <3 years of age)	62.500 <sup>6</sup>	30.625 <sup>7</sup>	51
Rubella	47.745	6 <sup>2</sup>	>99
Smallpox	29.005	0 <sup>2</sup>	100
Varicella	4.085.210	8.297 <sup>8</sup>	>99
Tetanus	580	26 <sup>2</sup>	96

### ***Vaccine hesitancy/refusal and complementary/alternative medicine***

The popularity of complementary and alternative medicine has increased significantly, driven by media coverage and cultural preferences. These approaches are perceived as natural, low-risk, and free from corporate influence (35). Many individuals believe such treatments contain fewer synthetic chemicals and are safer than conventional pharmaceuticals. Parents may choose alternative therapies due to concerns about vaccine ingredients, side effects, or doubts regarding vaccine efficacy (35,36).

### ***Vaccine hesitancy/refusal and population reduction policy***

In certain low-income and minority communities, conspiracy theories suggest that vaccines are used by Western countries as tools of population control, particularly to reduce fertility (37). A study in Pakistan found that vaccine refusal was attributed to fears of infertility (3.3%), perceived ineffectiveness (21.6%), and general distrust (40.2%) (38).

### ***Vaccine hesitancy/refusal in in Türkiye***

Although vaccination is mandatory in Türkiye, immunization rates were 75% before 2007 but rose to 95% thereafter due to improved access. Since 2010, however, vaccine refusal has gained attention. A pivotal event occurred in 2015, when a court ruled in favor of a prosecutor who refused vaccination for his twins, citing individual rights and consent. The media portrayed this as a legal victory, fueling public debate and

encouraging vaccine refusal (2,39). Consequently, the number of families refusing vaccines increased from 183 in 2011 to 23.600 by 2018 (40).

## **CONCLUSION**

In conclusion, addressing vaccine hesitancy and refusal requires a multifaceted, evidence-based approach that integrates transparent risk communication, trust-building with healthcare professionals, and proactive countering of misinformation particularly on digital platforms (41,42). Ensuring equitable vaccine access, especially for underserved populations, remains essential for promoting uptake (43). Educational interventions tailored to cultural and social contexts, along with the integration of vaccine literacy into broader health education, have also shown promise in fostering informed decision-making (43,44). A coordinated strategy involving health authorities, educators, and local communities is vital to restoring public confidence and maintaining high vaccination coverage (41,42).

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### **Conflict of interest**

The authors declare that there is no conflict of interest.

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