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ORIGINAL ARTICLE

A risk science perspective on vaccines

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Abstract

Vaccines can be seen as one of the greatest successes in modern medicine. Good examples are the vaccines against smallpox, polio, and measles. Unfortunately, vaccines can have side effects, but the risks are considered by the health authorities and experts to be small compared to their benefits. Nevertheless, there are many who are skeptical of vaccination, something which has been very clearly demonstrated in relation to the COVID-19 disease. Risk is the key concept when evaluating a vaccine, in relation to both its ability to protect against the disease and its side effects. However, risk is a challenging concept to measure, which makes communication about vaccines' performance and side effects difficult. The present article aims at providing new insights into vaccine risks—the understanding, perception, communication, and handling of them—by adopting what is here referred to as a contemporary risk science perspective. This perspective clarifies the relationships between the risk concept and terms like uncertainty, knowledge, and probability. The skepticism toward vaccines is multifaceted, and influenced by concerns that extend beyond the effectiveness and safety of the vaccines. However, by clarifying the relationships between key concepts of risk, particularly how uncertainty affects risk and its characterization, we can improve our understanding of this issue.

KEYWORDS
decision-making, risk characterization, risk communication, vaccination risk, vaccine risk

1 | INTRODUCTION

This article discusses risk and risk science issues in relation to vaccines and vaccination. A vaccine is here understood as "a preparation that is used to stimulate the body's immune response against diseases" (Centers for Disease Control and Prevention [CDC], 2021) and vaccination, "the act of introducing a vaccine into the body to produce protection from a specific disease" (CDC, 2021). Vaccination is widely considered one of the greatest medical achievements of modern civilization (CDC, 1999, 2011) and represents a key public health measure to tackle infectious diseases and prevent and contain infectious disease epidemics. However, there is considerable public skepticism toward vaccines, as we have seen recently in relation to the COVID-19 disease. The reasons for this skepticism are many and complex, as thoroughly discussed in the literature (e.g., Browne, 2018; Johnson et al., 2020; Larson et al., 2011). Trust (lack of trust) in persons and institutions is a key factor, which is closely related to perceptions of knowledge and expertise, openness, and honesty. Another major concern is vaccine safety, which relates to judgments about the risks associated with potential side effects of the vaccines. Although health experts and agencies argue that the vaccines are safe and that the benefits of the vaccines clearly outweigh the possible side effects, many people remain hesitant as they consider the risk imposed by the vaccine larger than the risk related to the disease.

The present article aims at providing new insights into these issues by carefully looking into the way risks in relation to vaccines are—and should be—understood, assessed, characterized, communicated, and handled. In our analysis, we distinguish between two categories of vaccination risk: (i) the risk related to contracting the disease, with and without the vaccine and (ii) the risk related to side effects of the vaccine.

The article is based on the conviction that current thinking and practice concerning vaccination risks (i) and (ii) is not sufficiently clear on some of the risk science fundamentals. For example, we claim that most people, including many health experts and agencies, struggle to explain what the concept of risk really means in the context of vaccines, what characterizes a scientifically sound way of describing the risks, and what is the main difference between professional judgments of risk and people's risk perception. A main challenge is the relationship among risk, uncertainty, and knowledge. Current thinking and practice to a large extent relate risks to historical observations which means that important aspects of risks and uncertainties could be downplayed or camouflaged. People's risk perception may respond to these risk and uncertainty aspects, yet, they are to a limited extent captured and incorporated in the risk frameworks of the health experts. Furthermore, the dimension of time plays an essential role in the understanding of risks related to vaccines. Although the importance of considering the temporal aspects of risk, uncertainty, and knowledge is triggered by several factors, including the potential for long-term consequences of vaccination and changes in vaccine effectiveness due to emerging variants, current discussions on vaccine risk often lack a clear conceptual framework for incorporating reflections on the influence of time.

To explain and justify the above claims, we will apply what we will refer to as a contemporary risk science perspective. Following this risk perspective, uncertainty is considered a key component of risk, in contrast to other risk perspectives, for which uncertainty is associated with the estimation of the risk. The difference seems to be minor and technical, but it is important—it has wide-ranging implications for how we understand, assess, communicate, and handle risks, as will be thoroughly discussed in the article. By using a contemporary risk perspective as our basis, we highlight and discuss some key challenges and issues related to vaccine risk and show how current principles, approaches, and methods from risk science can contribute to improving our understanding and handling of these challenges. The article highlights principles and approaches from risk science that are applicable to a wide range of risk problems, and the conceptual framework outlined in this article can be extended to other relevant contexts beyond vaccine risks.

When referring to contemporary risk science and risk science knowledge in the following, a main reference is documents produced by the Society for Risk Analysis (SRA) (2015, 2018) and related supporting material (see, e.g., Aven, 2016; Aven & Thekdi, 2021; Logan et al., 2021). The SRA articles have been developed by a strong group of senior risk scientists—with different academic and practical backgrounds and competencies—and with input from members of the society. Risk science, according to this body of literature, can be defined as the practice that provides us with the most justified beliefs that can be produced at the time being on the subject matter covered by the risk field, covering concepts, principles, approaches, methods, and models for understanding, assessing, characterizing, communicating, and managing risk.

The article is organized as follows. First, in Section 2, we provide an overview of some key events and cases related to vaccines and vaccination risks throughout history, the aim being to point to what we consider important foundational issues in relation to risk understanding, assessment, perception, communication, and handling. In Section 3, we conceptualize risks related to vaccine and vaccination using a contemporary risk perspective. Section 4 provides a discussion of foundational issues from the historical review in light of the conceptual framework presented in Section 3, particularly focusing on issues related to COVID-19. Finally, Section 5 provides some final remarks and conclusions.

2 | A REVIEW OF KEY EVENTS IN THE HISTORY OF VACCINATION

The aim of this section is to provide an overview of pivotal events and incidents in the history of vaccination that serve as illustrative examples of some of the main issues highlighted in the present article. The cases have been purposefully selected to underscore key aspects in the understanding, perception, communication, and handling of risk according to contemporary risk science knowledge.

The history of vaccines dates back to the late 18th century, when the British surgeon, Edward Jenner, discovered that protection against the deadly smallpox disease could be obtained by transferring matter from lesions caused by the much less severe cowpox disease ("variolae vaccinae") to healthy individuals through the use of small scratches or cuts made on the surface of their skin (Conti, 2021). Deliberately exposing healthy people to matter from infected patients was not a novel idea; the procedure (often referred to as variolation) is known to have been used in China in the early 17th century, and variolation using material from patients suffering from a mild to moderate form of smallpox was considered common practice in England and North America in the 1720s (Bazin, 2003). However, the practice was not uncontroversial, and several critical voices had been raised, particularly in religious circles, against what was considered to be "meddling with divine will" (Rothstein, 2015, p. 7). Furthermore, people undergoing this form of variolation were at considerable risk of becoming severely ill and were also prone to infect others in their surroundings; thus, the procedure did not succeed in restricting smallpox outbreaks (Helfert, 2015). By using matter from the less virulent cowpox disease, the risks were significantly reduced; the procedure was shown to be very effective, and Jenner's discovery became an important milestone in the history of immunization and vaccine development.

Today, there is a wide range of vaccines available to protect against more than 20 life-threatening diseases, and the World Health Organization (WHO) estimates that immunization currently prevents 3.5–5 million deaths every year from diseases like diphtheria, tetanus, pertussis, influenza, and

measles (WHO, 2022). The elimination of poliomyelitis in the Americas and the worldwide eradication of smallpox can be credited to successful vaccination programs (Dubé et al., 2013). In some cases, this success has created an environment for vaccine hesitancy, as the effectiveness of the vaccines in diminishing the threat of the disease has led the public to focus more attention on the risks of potential side effects than on the disease itself (Colgrove & Bayer, 2005; Larson et al., 2011). An example is the whole-cell pertussis vaccine, introduced in the United Kingdom and United States in the 1940s against whooping cough. The high mortality rate of the disease led to a situation where, although there had been several reports of potential side effects of the vaccine, including encephalopathy and neurological symptoms, "the vaccine's safety was little discussed until whooping cough became less common" (Helfert, 2015, p. 7). The pertussis immunization program led to a reduction in the number of whooping cough incidences and, as "awareness of the severity of this disease faded, public concern emerged regarding potential adverse reactions to the vaccine" (Wilson & Marcuse, 2001, p. 161). Although a link between the pertussis vaccine and permanent neurological damage remained unproven after reviewing the medical literature, the increased public concern led uptake rates to plummet in several countries, causing a resurgence of the pertussis disease in the ensuing years (Helfert, 2015).

A similar pattern was seen in relation to the measles, mumps, rubella (MMR) vaccine, where a now-retracted report published by Wakefield et al. in the medical journal the *Lancet* in 1998 suggested a link between the MMR vaccine and autism. The claim received "widespread media attention in the United Kingdom and Ireland and was followed by substantial public concern and decreased use of MMR in some regions" (Wilson & Marcuse, 2001, p. 162). Although later studies showed no causal relationship between the MMR vaccine and autism, the doubts that had been put forward in the report lingered for years, causing a decrease in vaccination uptake rates. Consequently, an increase in the incidence of measles infections and measles-related deaths followed, as well as distrust in medical establishments and other vaccines (Larson et al., 2022). It was not until 2004 that public opinion began to turn, as 10 of the collaborators in Wakefield's study formally retracted their support for the autism hypothesis, and media coverage and attention shifted away from the autism controversy and toward the increasing number of measles outbreaks (Colgrove & Bayer, 2005). Although both the pertussis vaccine and the MMR vaccine faced public concern regarding their safety, the MMR vaccine controversy struck a societal nerve as it coincided with an ongoing public debate about the potential causes of autism among children, fueled by a substantial group of parents seeking an explanation for their children's condition. At the same time, the anti-vaccination movement became more organized. As a result, the MMR vaccine controversy led to organized anti-vaccination activity that was significantly more persistent than what was seen in the case of the pertussis vaccine.

There are, however, also examples of vaccine safety incidents where public concern has been justified. In 1955, US health authorities initiated a mass immunization program against polio, using a newly developed inactivated poliovirus vaccine. The vaccine had undergone clinical testing and was proven to be safe and effective. Yet, shortly after the immunization campaign had begun, cases of polio were reported among the recipients. The incidents were found to be linked to batches originating from the Cutter Laboratories, and the Cutter vaccine was recalled immediately (Helfert, 2015). Further investigation revealed that the company had failed to sufficiently inactivate the poliovirus, causing a total of 40,000 cases of mild polio, 200 cases resulting in permanent paralysis and 10 deaths (DeStefano et al., 2019).

In 1976, an influenza outbreak at an army base in New Jersey triggered a mass influenza vaccination campaign across the United States. The influenza vaccine had been judged to be safe, based on pre-licensure trials; yet, shortly after the immunization program was initiated on October 1, 1976, several case reports of the paralytic Guillain–Barré syndrome were made. A number of cases were judged to be significantly higher than the normal population incidence, causing the immunization program to be terminated in December 1976, "with severe consequences, including diminished public confidence in vaccines and the public health care system" (Knipe et al., 2020, p. 1275).

As the number of new vaccines being developed is growing, vaccine safety studies are being conducted at an increasing rate, not only in response to specific concerns but also for proactive and surveillance purposes. Although responding to issues raised concerning vaccination risks is a major part of ensuring the safety and efficacy of vaccines, the increasing number of safety-oriented studies could, in itself, contribute to increasing public concern (Francois et al., 2005). Expressing sensitivity to alleged adverse events following immunization sometimes prompts public health authorities to opt for precautionary measures, suspending vaccination until the concerns have been further investigated through scientific studies. However, there have been cases where regulators and authorities have "failed to reappraise the precautionary measure after the crisis, even when reassuring evidence has been available" (Bouder, 2015).

An example of this was seen in France in the mid-1990s, when the ambitious immunization program against Hepatitis B was put on hold, as case reports began to emerge suggesting a possible link between the Hepatitis B vaccine and autoimmune diseases, including multiple sclerosis and lupus (Bouder, 2015). The decision to suspend the vaccine was based on a judgment of current scientific evidence as inconclusive, and further investigations of the concerns were deemed necessary. Expert consensus panels organized by the French authorities later failed to confirm an increased risk (Cauchi et al., 2022). However, "French regulators did not revise their judgments when reassuring evidence was published and never resumed their large-scale immunization efforts" (Bouder, 2015, p. 10). The incident caused severe damage to public confidence, resulting in "a legacy of distrust and low vaccination rates" (Cauchi et al., 2022, p. 498).

Another example is the controversy that arose in the United States in the late 1990s regarding the use of the preservative, thimerosal, in vaccines, after concerns had been raised about a possible connection between thimerosal and neurodevelopmental disorders, including autism (Wilson & Marcuse, 2001). As a precautionary measure, the American Academy of Pediatrics (AAP) and the US Centers for Disease Control and Prevention (CDC) published a joint statement, in which vaccine makers were asked to remove thimerosal from childhood vaccines as soon as practical (Larson et al., 2022). Although the statement was "issued to show caution and assure the safety of vaccines" (Larson et al., 2011, p. 529), it remained unsupported by scientific evidence, as no link between thimerosal and neurodevelopmental disorders had been confirmed. Thus, the action led to confusion regarding the safety of thimerosal: "While government agencies asserted that thimerosal was completely safe in the amounts found in vaccines, the decision to remove the preservative sent mixed messages as to whether the vaccine actually was safe" (Sutherland, 2013, p. 2). Notably, the recommendation to remove thimerosal, despite any evidence of harmful effects, was "seized upon by anti-vaccination movements as a proof that 'there was something wrong' with vaccines and that public health authorities were 'hiding the truth about the vaccines'" (Dubé et al., 2013, p. 1767).

Furthermore, in both the Hepatitis B case and the thimerosal controversy, the decision to suspend immunization went against the recommendation made by the WHO, indicating a disagreement among expert authorities that further challenged public trust (Larson et al., 2011).

At the beginning of 2009, a new type of influenza emerged, caused by an A (H1N1) type of virus. The influenza, popularly referred to as "swine flu," was declared a pandemic by WHO in June 2009. Although the severity of the H1N1 influenza was assessed to be similar to that of seasonal flu, there were uncertainties concerning morbidity rates varying across social groups and regions, as well as the potential for the virus to mutate into more virulent variants. Thus, national health authorities were encouraged to act quickly, and new vaccines were developed and authorized under considerable time pressure (Carlsen & Glenton, 2016). The rapid vaccine development process left little time to assess the effectiveness and safety of the vaccines, and "assumptions about vaccine effectiveness and safety were largely based on efficacy and safety data from the seasonal flu vaccines and from testing of mock-up vaccines using another strain of flu virus" (Carlsen & Glenton, 2016, p. 2). Despite the fact that the lack of proper testing of the safety and efficacy of the vaccine meant that there were considerable uncertainties present, mass vaccination programs were initiated across the world, based on the rationale that the disease itself would cause more severe consequences than the potential side effects associated with the vaccine (Aven, 2015). Some countries implemented large public relations campaigns, driven by so-called "moral persuasion" and the principle of solidarity (Glover-Thomas, 2019). The pressure to respond quickly and reach the stated vaccination targets led authorities to be less inclined to highlight uncertainties or to practice transparent decision-making, in the fear that this would slow down or prevent vaccine uptake (Carlsen & Glenton, 2016). However, although the influenza turned out to be far milder than predicted, several reports emerged in the years following the mass immunization programs concerning a possible link between the vaccine and cases of narcolepsy among children and adolescents. The link was later confirmed in several scientific studies (Doshi, 2018). The situation challenged public trust in experts and policy, as issues arose concerning both the authorities' inaccurate judgments of the disease risk and the subsequent recommendation to vaccinate, despite the potential for unknown side effects related to the vaccines.

In relation to the current COVID-19 pandemic, vaccines have been highlighted as a key tool for confronting the disease. However, the massive immunization campaigns initiated by authorities and governments worldwide have brought issues regarding vaccination risk to the forefront of both public and scientific discourse. The need for an urgent response triggered efforts to accelerate the process of developing new vaccines, and vaccine manufacturers were "under pressure to develop a vaccine within few months as compared to the conventional process of 10–15 years" (Kashte et al., 2021, p. 726). As a result, the first COVID-19 vaccines were administered in December 2020, less than a year after the pandemic had been declared. The rapid development process was made possible partly by employing innovative technology platforms for vaccine development, including nucleic acid, in which genetic material (RNA or DNA) from a disease-causing virus is used to produce immunity against it (Khuroo et al., 2020). However, the unprecedented speed at which vaccines were developed and authorized triggered concerns among the public as to whether the safety and efficacy of the vaccines were compromised by the accelerated timeline (Dror et al., 2020; Machado et al., 2022; Morrison et al., 2020; Piltch-Loeb et al., 2021). Furthermore, the use of the novel technology "raised concerns about the ability of vaccines to alter the DNA or genetic make-up of humans, and thus contributed to uncertainty around the immediate and long-term adverse reactions or effects of these vaccines" (Larson et al., 2022, p. 1416).

During the initial stages of the vaccine development and distribution, there were a number of non-pharmaceutical interventions in place, including social distancing, facemasks, and travel restrictions. However, at this point in time, there was limited evidence concerning the effectiveness of these measures, making the assessment and communication of the risks and benefits of the vaccines challenging. Although vaccines were hailed as the solution to the pandemic, their effect on controlling the spread of the virus when used in combination with non-pharmaceutical measures was to a large extent unknown (Ge et al., 2022).

When the mass vaccination roll-out began in early 2021, the public were reassured by governments and authorities that the authorized vaccines had been tested and judged to be safe and effective after undergoing pre-licensure testing. However, as illustrated by previous events in the history of

vaccination, the limitations in sample size and duration of pre-licensure trials restrict their ability to detect side effects that are very rare or much more likely among populations not included in the clinical trials. Consequently, "potential safety problems may be identified only after widespread use" (Hampton et al., 2021, p. 1478). These limitations caused significant uncertainties at the vaccination program's initial stages, as there was a lack of knowledge concerning the potential side effects that could emerge when the vaccines were introduced to larger and more diverse populations and, as mass vaccination programs have progressed, reports of adverse events have emerged. After receiving signals of an increased risk of side effects such as myocarditis and pericarditis after vaccination with Moderna, several countries, including Norway, Sweden, and Finland, suspended the use of the vaccine in young people, as a precautionary measure (Paterlini, 2021). Concerns related to the possible association between immunization with the AstraZeneca vaccine and cases of blood clots led to the suspension of AstraZeneca in three Nordic countries, a decision that was subsequently followed by other European countries, including Germany, France, and Italy (Petersen et al., 2022). In both cases, further investigations confirmed a causal link, and the conditions have been included as potential side effects in the product safety information for these vaccines (European Medicines Agency [EMA], 2021; Paterlini, 2021). Another example of an adverse event that was not captured by pre-licensure safety assessments but has since been confirmed to be linked to vaccination is the increased risk of anaphylaxis, which is found to be associated with the Pfizer vaccine, particularly among individuals with a prior history of severe allergic reactions (Hampton et al., 2021; Kayser & Ramzan, 2021). Over the past few months, several studies have surfaced indicating a potential link between COVID-19 vaccines and an increase in cases of Guillain–Barré syndrome (Abolmaali et al., 2022; Yu et al., 2023). According to Fraiman et al. (2022), mRNA COVID-19 vaccines are found to be associated with an excess risk of serious adverse events, raising "concerns that mRNA vaccines are associated with more harm than initially estimated at the time of emergency authorization" (p. 5802). Another significant issue highlighted by Fraiman et al. (2022) and echoed by various authors (see e.g., Doshi et al., 2022; Tanveer et al., 2022), is the lack of accessibility of data from clinical trials, making it challenging to conduct comprehensive studies of vaccine safety and efficacy.

In the early stages of the immunization efforts, the concept of "herd immunity" was frequently referred to. Herd immunity is understood as "the indirect protection from an infectious disease that happens when a population is immune either through vaccination or immunity developed through previous infection" (WHO, 2020). When the mass vaccination campaigns were initiated, achieving herd immunity was put forward as a key objective. The objective was supported by the WHO, who stated that "[h]erd immunity against COVID-19 should be achieved by protecting people through vaccination, not by exposing them to the pathogen that causes the disease" (WHO, 2020). Promoting solidarity and emphasizing the collective benefits of herd immunity provided a strong incentive for encouraging individuals to get vaccinated and became "similar to a mantra in mass vaccination strategies, repeated by governments and researchers" (Atlani-Duault et al., 2021, p. 199).

A major concern related to the COVID-19 pandemic has been the continuous emergence of new variants, leading to uncertainty regarding the long-term efficacy of current vaccines. The unpredictability of the situation has led "both vaccinated and unvaccinated individuals to question the effectiveness of vaccination, creating a communication challenge for decision makers, the media, experts and front-line health professionals" (Karafillakis et al., 2022, p. 700). Increasing evidence of waning immunity and so-called "breakthrough infections" (cases of infection occurring despite vaccination) have led to calls for booster doses (Larson et al., 2022). However, this strategy has "fostered discussions related to the efficacy, safety, and the role of vaccines developed at the beginning of the pandemic" (Machado et al., 2022, p. 2). Moreover, the ongoing emergence of new variants, as well as the waning immunity of current vaccines, has made it "increasingly evident that COVID-19 vaccines are not going to halt the pandemic" (Lai et al., 2022, p. 196), and that "controlling COVID-19 by increasing herd immunity may be an elusive goal" (Morens et al., 2022, p. 195). This, along with the growing acknowledgment that "COVID-19 is likely to be with us, even if at a very low level of endemic community spread and with lower severity, for the foreseeable future" has altered many of the initial assumptions made about the effectiveness of the vaccines and their role in managing the pandemic.

In many countries across Europe and the United States, public sentiment concerning the COVID-19 vaccines has been characterized by an eroding trust in pharmaceutical industries, governments, policymakers, and science (Caron & Dorsey, 2022; Karafillakis et al., 2022). Public mistrust in these institutions has led to concerns that authorities and vaccine manufacturers were motivated by financial gain rather than the health of people (Cascini et al., 2021), and that the severity of COVID-19 has been exaggerated for political purposes (Caron & Dorsey, 2022). When it comes to scientific research and knowledge, public confidence has been challenged by the partial, rapidly evolving, and sometimes contradictory information conveyed by experts and scientists, particularly in the early stages of the pandemic (Bendau et al., 2021; Verger & Dubé, 2020). Furthermore, in an attempt to "hasten the vaccine rollout and potentially vaccine hesitant/refusing individuals to take up vaccines despite misgivings, many governments have considered or implemented vaccine mandates" (Peters, 2022). Thus, COVID-19 vaccines became "the subject of political debates over the benefits of government-mandated vaccinations, concerns over 'immunization cards' that people might be required to carry, and a loss of individual rights by allowing government to make personal health decisions" (Bolsen & Palm, 2022, p. 86).

The above review highlights a selection of significant events and discussions throughout the history of vaccines, the

main aim being to point to what we consider to be some of the key challenges and issues faced in relation to the understanding, assessment, characterization, communication, and handling of vaccine risk. A fundamental theme in several of the cases referred to in this section is the dimension of time, and how it affects the understanding and assessment of the consequences and uncertainties associated with vaccination. Another important aspect is the role of trust in issues concerning vaccine risk understanding and communication. Furthermore, the review points to several instances where governments and public health authorities had to balance the promotion of vaccine uptake with clear and honest descriptions of the risks and uncertainties involved. This delicate balance, along with the herd immunity concept, which requires individuals to weight the risk to themselves against community benefits, exemplifies the differences in perspectives between individuals and the society when it comes to making decisions concerning vaccine risks. These aspects will be further discussed in Section 4.

3 | RISKS RELATED TO VACCINES AND VACCINATION USING THE CONTEMPORARY RISK PERSPECTIVE

In this section, we conceptualize risk related to vaccines and vaccination according to the contemporary risk perspective. From this risk perspective, the risk related to an activity has two main components: the future consequences C of the activity and uncertainties U related to C. For short, we refer to the risk as (C,U). When considering risk related to vaccines and vaccination, the activity is life in the area considered (societal perspective) or the life of a particular person (individual perspective). The activity is observed in a period of time, say $[0,T]$.

There are a number of relevant aspects take into account when addressing vaccination risks. For example, vaccination could have an effect on political risks, as in the case of enforcing vaccine mandates, which may be met by political resistance and public backlash (Bardosh et al., 2022; Ward et al., 2017). Additionally, the development and distribution of vaccines could introduce ethical and social risks, as seen in the tradeoff between speed and rigor in approaches to accelerate vaccine development (Grady et al., 2020), or in discussions concerning vaccine accessibility for vulnerable populations and low-income countries (Sawal et al., 2021). The performance and uptake of vaccines also have an impact on the financial risks associated with vaccination, as low vaccination rates could lead to increased health care costs and economic losses (Ozawa et al., 2016). In the present analysis, we distinguish between risks that result from the direct consequences of vaccines or vaccination, and those that emerge as indirect consequences related to vaccine development, distribution, and uptake, as well as policies and strategies concerning vaccination. The financial, political, ethical, and social risks mentioned above represent the latter type of consequences. Although these aspects are important to consider, they are not directly related to the vaccination activity per se, but rather to the broader social, political, and economic context in which vaccination occurs. The indirect consequences that arise as a result of vaccines and vaccination are complex and may be influenced by a variety of factors outside the scope of the vaccination activity, making a systematic and comprehensive analysis of these aspects a challenging task. The main aim of the present article is to provide an analysis and discussion of vaccine risks that targets fundamental issues concerning their understanding, assessment, characterization, communication, and handling. For this purpose, we consider it sufficient to restrict our considerations here to the direct risks associated with vaccines and vaccination, hereunder (i) the risk related to contracting the disease, with and without the vaccine and (ii) the risk related to side effects of the vaccines. The risk in (i) concerns the efficacy or effectiveness of the vaccine, and we first look into these concepts.

Vaccine efficacy or effectiveness refers to the proportionate reduction in cases among vaccinated persons (CDC, 2012). Vaccine efficacy is measured in controlled clinical trials, whereas vaccine efficiency is measured in terms of how well the vaccine works in the real world (WHO, 2021). Informally, vaccine efficacy or efficiency is defined as (CDC, 2012)

$$(\text{risk amongunvaccinated group} - \text{risk among vaccinated group}) \,/\, \text{risk among unvaccinated group}.$$

The numerator is sometimes referred to as the risk difference or excess risk. Risk is here understood as a fraction, more specifically, the fraction of cases in a population. More formally, let x_n be the number of cases in a sample of n vaccinated persons drawn from the population studied, and let y_m be the number of cases in a sample of m unvaccinated persons drawn from the same population. A case here refers to a person contracting the disease. Risk is then often defined as $p_n = x_n/n$ in the vaccinated group and $q_m = y_m/m$ in the unvaccinated group, and the vaccine efficacy or efficiency—depending on whether a clinical trial or real-life population is considered—is then given by $v_{mn} = (q_m - p_n)/q_m$.

Here, the consequences are restricted to fractions of cases in a defined population. However, when the defined population is small, the fraction becomes less informative. For example, from an individual perspective ($n = 1$ or $m = 1$), this fraction (p_n or q_m) would yield either 0 or 1, which provides no information beyond the fact that the person either has got the disease or not (is an intensive care unit [ICU] patient/has died or not). Thus, to make the fraction a meaningful metric to describe the consequences, the population needs to be large; we have a societal health application.

From the contemporary risk perspective, however, p_n and q_m are not risks but observed historical occurrence rates in a specific population. According to the contemporary risk perspective, risk relates to the future, including unknown fractions and associated uncertainties. Let X_N and Y_M denote the number of cases in the vaccinated and

unvaccinated groups, respectively, in a specific population, comprising N vaccinated and M unvaccinated persons, to be observed in a time period $[0,T]$. Then, we can define $P_N = X_N/N$ and $Q_M = Y_M/M$ as unknown fractions of cases in the population of size N and M, respectively, in this time interval. The vaccine efficiency will then be given by $V_{MN} = (Q_M - P_N)/Q_M$.

That is, C equals P_N and Q_M, and risk is given by (C,U). Thus, risk is not given by these fractions but by these fractions together with associated uncertainties. As a limiting theoretical case, when N or M or both are large, the frequentist probabilities p and q, arising as limits when N and M tend to infinity, are viewed as the consequences C. With this understanding of risk, individual risk is also well defined, as the risk relates to whether the person contracts the disease or not—uncertainty being a key element of the risk concept. In the case of individual risk, knowledge specific to the individual, such as gender, age, or other relevant characteristics, will have an important influence on the uncertainty.

Vaccine efficacy and effectiveness relates to disease cases, that is, to the event of contracting the disease or not. Other events and effects are also relevant when considering the risk related to vaccines and vaccination. The main unwanted potential effects related to a vaccine and vaccination are, if taking the vaccine, the possible unwanted side effects of the vaccine and, if not taking the vaccine, or if the vaccine does not fully protect against the disease, possible complications of the disease and possible side effects of its treatment (WHO, 2015). Common consequence categories include a person being an ICU patient and mortality. The consequence dimension of risk is thus not fully given by the fractions (X_N/N, Y_M/M) or (p,q) but by a greater set of consequences. However, by considering the fractions where the cases are restricted to specific consequences (like deaths), all relevant consequence aspects can be included.

The term "future consequences" when referring to C has so far been used in a wide sense and may then include risk sources RS, events A, and resulting effects/consequences in a narrow sense C. Two key risk sources in relation to vaccine and vaccination risk are the disease agent (virus, bacteria, etc.) and the vaccine. The disease agent, say a virus, may give rise to the event of contracting a particular disease, from which different effects/consequences may result. The consequences given an event or a risk source and associated uncertainty are referred to as vulnerability, and the risk concept $(C,U) = (A,C,U)$ can be decomposed as follows:

$$(C,U) = (A,U) + (C,U|A) = \text{“eventrisk"+“vulnerability"},$$

which, in the context of risk related to contracting a disease, can be relabeled

$$(A,U) + (C,U|A) = \text{“caserisk"} + \text{“vulnerability"}.$$

For an individual contemplating whether or not to take a vaccine, there are two alternative risks to consider: the risk related to taking the vaccine, $(C,U)_{\text{vaccine}}$ and the risk related to not taking the vaccine, $(C,U)_{\text{no vaccine}}$. In the former case, C refers to the consequences of the activity when taking the vaccine, which may include side effects of the vaccine, contracting or not contracting the disease, and effects of the disease if contracted, which may include complications of the disease and side effects of its treatment if the vaccine does not protect against the disease. As illustrated by the historical review in Section 2, the side effects of vaccines could arise from errors made during the production process, as seen in the Cutter vaccine incident, or from adverse effects that were not detected during clinical trials, such as the cases of the 1976 and 2009 influenza outbreaks.

When it comes to the latter type of risk, $(C,U)_{\text{no vaccine}}$, there will be no side effects of the vaccine, but the consequences C will include contracting or not contracting the disease, and effects of the disease if contracted, which may include complications of the disease and side effects of its treatment.

The (C,U) representation explains the concept of risk and forms the basis for risk assessments and characterizations, expressing the magnitude of the risk. A common approach in a societal health application is to estimate C, for example, using observed fractions p_n and q_m to estimate X_N/N and Y_M/M, respectively. In general, we also need to address the uncertainties about C. If we consider the individual case, the uncertainties about X and Y are the key issue. Probability—precise and imprecise—is the dominant tool for expressing these uncertainties, but other methods also exist (Flage et al., 2014). In general, we refer to a measure Q (measure interpreted in a wide sense), leading to a general risk characterization or description (C',Q,K), or (A',C',Q,K), where C' are the consequences specified in the risk assessment, A' the events specified in the risk assessment, and K the knowledge that the assessment (A',C',Q) is based on. Note the difference between the actual events A and consequences C occurring, and the events A' and consequences C' specified in the risk assessment. When considering the future, assessors may overlook some potential events or consequences, as they lack the relevant knowledge. For example, the type of side effects of a vaccine could come as a surprise to the assessors. However, by restricting the events and consequences to fractions X_N/N and Y_M/M, such surprises would be reflected not in differences between (A,C) and (A',C') but in the uncertainty characterizations. Thus, these characterizations are critical. How to best characterize uncertainties is an important research topic in risk science. As the present authors read contemporary risk science knowledge on this topic, it is prudent, for this purpose, to use probability—precise and imprecise—to express the uncertainties, together with judgments of the strength of the knowledge supporting the probability. This knowledge includes data such as observed fractions of the type p_n and q_m, assumptions, models, and other types of evidence. Consider the individual risk case. Then, risk is, for example, expressed by the probability of the person contracting the disease, together with a judgment of the strength of the knowledge supporting this

probability assignment. For the societal level, an uncertainty (prediction) interval $[a,b]$ could be specified for the relevant unknown quantity, for example, X_N/N and Y_M/M, expressing that the interval includes the unknown quantity with a probability of at least 90% (say).

Different types of approaches are used to assess the strength of knowledge (SoK); see the Intergovernmental Panel on Climate Change (IPCC) (2010) and the use of evidence and agreements among experts and the so-called NUSAP system (NUSAP: numeral, unit, spread, assessment, and pedigree) (Berner & Flage, 2016; Funtowicz & Ravetz, 1990; van der Sluijs et al., 2005) and the score systems of Flage and Aven (2009) (see also Aven & Flage, 2018), which are based on judgments of factors such as

- the reasonability of the assumptions made
- the amount and relevancy of data/information
- the degree of agreement among experts
- the degree to which the phenomena involved are understood and accurate models exist
- the degree to which the knowledge K has been thoroughly examined (e.g., with respect to unknown knowns, i.e., others, but not the analysis group, have the knowledge).

By using probability (P) and SoK judgments as an expression of the uncertainty measure Q, the risk characterizations take the general form (A',C',P,SoK,K). If we want to specify the risk sources leading up to the identified events and consequences, we can write $(\text{RS}',A',C'P,\text{SoK},K)$. The expanded formalism allows us to make explicit the various components of the risk description. To demonstrate the practical use of this formalism, Table 1 provides examples of the different elements at general and specific levels of detail, using COVID-19 as an illustrative case.

4 | DISCUSSION

In the following, we will point to and discuss some main issues in relation to vaccination risk, building on the illustrative examples from Section 2, as well as the general framework for conceptualizing and describing vaccination risk presented in Section 3.

The purpose of the present section is not to provide an exhaustive overview and discussion of all relevant aspects of risk in relation to vaccines. Rather, we point to some key challenges and issues faced, the aim being to highlight how the understanding, assessment, characterization, communication, and handling of these risks can be improved by drawing on contemporary risk science literature. In line with the scope of the present article, the discussion focuses on issues related to the direct risks associated with vaccines. However, the discussion can provide useful insights into potential sources of indirect risks, contributing to a better understanding of the broader economic, social, ethical, and political factors that influence vaccine risk.

4.1 | Individual versus societal decision-making

In early 2021, when the first COVID-19 vaccines were offered to the public, achieving herd immunity was touted as a crucial goal of the vaccination efforts (refer to Section 2). The concept of herd immunity is based on the idea that individuals who have not been vaccinated or previously infected with the disease can benefit from the immunity conferred by those who have. For the whole community to benefit, a significant proportion of the population needs to be vaccinated or immune to the disease. From a societal point of view, herd immunity is essential for protecting vulnerable populations and reducing the overall spread of the disease. However, both vaccination and contracting the disease carries risks for the individual, and thus, achieving herd immunity requires balancing a tradeoff between individual risks and community benefits.

In many countries, the individual decides whether to take the COVID-19 vaccine or not. It is up to the individual to weigh up and balance the various considerations and risks. In Norway, for example, the Institute of Public Health (FHI) writes on its website:

> We will inform about the effect of the approved vaccines and their side effects, so that everyone can make an informed choice. The goal is that everyone who is recommended vaccination chooses to take advantage of the offer.

This policy builds on several prerequisites that may be more or less valid. First, it assumes that the authorities are able to make "rational" recommendations applicable for large population groups. However, what can be considered a "rational" or right recommendation is not straightforward, as these judgments are influenced by the underlying goals, values, and intentions of the assessor. These values, goals, and perspectives often remain undisclosed, making it challenging to discern the underlying motivations behind the recommendations, and whether the recommendations are tailored to suit the interests of the individual or the society. Furthermore, it requires that the risks related to the virus and the vaccines are described in a way that allows people to be adequately informed. However, we will argue that such descriptions have not been produced—it has been and remains very difficult for people to obtain easily understandable overviews of such risks (Glette-Iversen et al., 2023). What are produced are numbers of cases and deaths, but, as discussed in Section 3, that is not risk but historical figures, more or less relevant for one particular person.

Upon the public release of the vaccines in the beginning of 2021, historical data were available, providing death rates from 2020 as a function of age and sex (e.g., Bauer et al., 2021). An exponential increase in mortality was observed for above 40 years of age, for which nearly all COVID-19 deaths occur. Males show higher death rates than females.

TABLE 1 Examples of risk description elements based on the extended formalism (RS′,A',C',P,SoK,K) in the context of COVID-19 vaccination.

Risk description element		General/Specific vaccine examples (non-exhaustive)	
Specified consequences (C')	Risk sources (RS′)	Virus	Coronavirus
		Vaccine	COVID-19 vaccine
		Treatment	Ventilator treatment
	Events (A')	Contract disease	Contract COVID-19
		Disease complications	Post-COVID conditions
		Vaccine side effects	Myocarditis, pericarditis, blood clots, etc. (refer to Section 2)
		Treatment complications	Ventilator-associated pneumonia, sepsis, etc.
	Effects/Consequence metrics (C')	Event incidence metric	Fraction of population contracting the disease with and without the vaccine, P_N and Q_M
		Effect/Consequence severity metric	Fraction of population, for example, in ICU without vaccine (refer to C_1/n in Section 4.3)
		Treatment efficacy/Efficiency metric	Vaccine efficacy/efficiency, V_{NM}
Uncertainty measure (Q)	Probability (P)	Prediction interval	$[a,b]$ such that $P(a \le Z \le b\|K) \ge 0.90$ for a defined unknown quantity Z
	Strength-of-knowledge assessment (SoK)	Quality of evidence classifications	Very strong—strong, Strong—moderate, Moderate—weak, Weak
Background knowledge (K)	Justified beliefs	Assumptions	Assumptions about vaccine effectiveness and safety based on efficacy and safety data from vaccines using another strain of flu virus (refer to Section 2)
	Evidence	Data	Sampled case numbers in (un)vaccinated populations
		Information	Observed side effects
		Modeling	Probability models
		Testing	Pre-licensure trials, clinical trials, etc. (refer to Section 2)

Abbreviation: ICU, intensive care unit.

Considerable variation was observed between countries. Typical yearly death rates (also referred to as crude mortality rates) for persons in the age group 60–70, from Europe and USA, as reported by Bauer et al. (2021), were in the range 10^{-4}–10^{-3}. For Norway, the numbers were marginally below 10^{-4}. For persons under 40, the death rates were minuscule.

These data are observations and reflect that measures have been implemented to reduce the risks. To make predictions for the future and to assess risk, the data from 2020 provided valuable background knowledge. The emergence of new variants with altered characteristics in terms of virulence and severity, such as Delta and Omicron, complicates the risk judgments—the risk is increased. However, vaccination is considered to have the opposite effect, by providing protection also against the new variants and thereby reducing risk.

A senior person, say over 65, is motivated by the relatively high death rates to be vaccinated. For a young person, this type of motivation is not as strong, as experts conclude that this person is exposed to a rather low risk due to COVID-19, although the Delta variant also raises some concerns for younger age groups (Aven, 2021).

The vaccine efficacy/effectiveness and the risks related to side effects are consequently critical for the decision of whether to get vaccinated or not. The official approval of the vaccines means that they scored satisfactorily on efficacy and safety (side effects risks). Typical efficacy numbers that were reported from the controlled tests were about 90% for the Pfizer vaccine and somewhat lower for Moderna. The side effect risks were not broadly reported, the message being that tests had shown that the vaccines are safe. There are, however, no objective, clear criteria for what is safe enough. We saw this clearly demonstrated in connection with the AstraZeneca vaccine, which was taken out of the vaccination program in Norway because of the side effect risks but was still approved and used in many other countries; refer to the discussion in Section 2. A review of the side effect cases by the EMA could not say definitively whether the reported cases were linked to the AstraZeneca vaccine and concluded that the benefits of the vaccine outweigh any risk (Remmel, 2021). The issue of what is acceptable risk and safe enough is a relevant aspect to address in relation to vaccination risks. Considerable scientific work has been conducted to discuss this issue in general, and specifically with respect to vaccines (e.g. Fischhoff et al., 1981; Schwartz, 2012). Although the issue is of great importance for both societal and individual risk evaluations and decision-making, a further discussion of this topic is outside the scope of the present article.

As discussed by Remmel (2021), it is challenging to prove that a medical problem was caused by the vaccine itself.

There are uncertainties. These uncertainties contribute to risk but are difficult to assess. Health officials and governments aiming at getting people vaccinated have limited motivation to reveal and focus on these uncertainties and risks. They strike a "delicate balance" when communicating the risk of the side effects alongside the risk of COVID-19 (Remmel, 2021). They are concerned that the uncertainties can fuel anti-vaccine movements. At the same time, they would like to support openness and honesty about the actual risks involved.

Furthermore, from a societal perspective, determining what is the best strategy to achieve and maintain a high level of immunity for the population is not straightforward. For example, there are studies suggesting that infection provides stronger immunity and protection against severe disease than vaccination alone (Gazit et al., 2022; Scully, 2022). As a result, countries with strong vaccination rates may actually have lower community immunity than others (Charumilind et al., 2022).

Health officials and governments also face a different decision problem than that of the individual. Officials and governments operate on a population level; to them, the consequences are mainly characterized by P_N, Q_M, and V_{MN} for large M and N. To the individual, on the other hand, the relevant quantities are $P_1 = X_1$ and $Q_1 = Y_1$. Both rely on historical data and information such as p_n, q_m, and v_{mn} when making the decision of whether to recommend or take the vaccine, respectively, but while such observations may be considered representative on a population level, an individual who is, say, young and healthy may choose to put less weight on these observations. Of course, the individual may face a moral dilemma if they do not want to take the vaccine due to concerns about its side effects and/or because they consider themselves to have a sufficiently robust immune system to handle the illness quite well, as they know that by taking the vaccine they may contribute to reducing the risk for those who cannot take the vaccine for medical reasons or who are vaccinated but still vulnerable to even a less severe course of illness.

There is, thus, a difference in the consequences (quantities) of interest in the professional risk judgments made by the public health authorities and other institutions, versus those in individual risk judgments. Moreover, variations could exist also among the public agencies and institutions, as they may have different priorities, values, and objectives. For example, the primary focus of public health officials could be to minimize the spread of the disease, while government agencies may prioritize economic considerations or maintaining civil liberties. This could result in conflicting recommendations and policies from different expert authorities, as seen in the cases of the Hepatitis B vaccine and the thimerosal controversy (refer to Section 2).

The individual risk judgments may to a greater or lesser extent be affected by perceptional factors, such as fear and dread, but, to the extent that the judgments made are conscious judgments, these are also carried out on different levels, with different risk metrics and with a different knowledge base than that of the population-level risk assessments. The individual may consider population-level historical data more or less relevant, depending on how representative the population is judged to be in relation to the specific individual. A young and healthy individual may, on the one hand, consider historical data for the whole population less relevant to themselves, but, on the other hand, this individual also needs to account for the potential surprises. An individual may have—but be unaware of—some genes that make them more susceptible to the disease, despite being young and healthy. For example, today (September 2022), a study was published (Ostendorf et al., 2022) that links common variants of the apolipoprotein E gene to COVID-19 outcome (mortality) in mice. Early on, very little was known about COVID-19, and even today we still do not understand the causal mechanisms behind the COVID-19 disease: why some people get (very) sick and others do not. The potential for surprises is considerable, and so an individual risk judgment cannot simply rely on comparisons and relevance judgments with respect to historical data.

In the context of vaccination, the tension between individual and societal decision-making could give rise to so-called "tragedy of the commons"-scenarios, in which individuals act in their own self-interest at the expense of the collective good. For example, in the early stages of an outbreak, when exposure is unlikely, individuals may consider it a prudent strategy to wait before getting vaccinated and instead rely on the protection of those who choose to take the vaccine. However, if too many individuals adopt this strategy, it can lead to a situation where too few people are vaccinated to achieve the benefits of herd immunity, causing the disease to spread in the population. A similar scenario could arise at a later stage; once a vaccination program has succeeded in terms of reducing the spread of the disease, the perceived risk of contracting the disease may be low, in which case individuals may find the risks of potential side effects of the vaccine more salient. This could lead to a decline in vaccination rates and a resurgence of the disease, as seen in the case of the whole-cell pertussis vaccine (refer to Section 2). The scenarios outlined above serve as an illustration of how a focus on individual risks and benefits may lead to suboptimal outcomes from a societal perspective. Furthermore, they demonstrate how judgments concerning the risks of vaccination can change over time, highlighting the significance of time as a factor in the understanding of vaccine risks.

4.2 | The time dimension of risk

Using the risk conceptualization and framework (A,C,U)—(A',C',P,SoK,K) presented in Section 3, the critical issue is that the knowledge K is rather weak (early 2021) concerning the side effects of the vaccine, particularly when it comes to the rare and long-term consequences. The sample sizes n and m used to establish p_n and q_m may be too low, and/or the observation time of the individuals in the sample may be too short. Furthermore, the knowledge base could consist of a number of assumptions concerning, for example, exposure,

disease incidence, vaccination rates, vaccine effectiveness, and the effect of other risk-reducing measures. As illustrated in the historical review, for example, in relation to the whole-cell pertussis vaccine, these factors are subject to continuous changes. The time dimension of risk is thus important here. Let τ denote the duration of the activity considered—and thus the length of time during which the occurrence of events A is considered—and η the length of time over which the consequences C of any such events are considered. Then, we can extend the conceptualization of risk to $(A,C,U)_{\tau,\eta}$ and, analogously, the risk description to $(A',C',P,\text{SoK},K)_{\tau,\eta}$ (Logan et al., 2021), which provides the required concepts to address the time dimension of risk with the required sharpness. In relation to a vaccine, the problem is that the observation time for the vaccine trials may be too short to reveal (i) all types of side effects A that the vaccine can lead to and (ii) all types of consequences C that side effects A can lead to. One step to addressing the long-term effects of a vaccine is to be explicit about τ and η, when both assessing and communicating the risk. The risk description could then distinguish between small τ and η, for which the knowledge could be strong, as long as the sample size m is sufficiently large, and large τ and η, for which the knowledge is weaker and for which the description may have to rely on less specific and thus less relevant data and information.

Part of this argument also holds for the COVID-19 disease itself. Let A denote the event that a person contracts COVID-19 and C the consequence of A. When the first vaccines were distributed (December 2020), there was still a lack of knowledge about the long-term consequences of the COVID-19 disease, that is, there was a lack of knowledge about C for larger η, for both unvaccinated and vaccinated persons. Reports around the same time indicated general long-term symptoms such as fatigue but also "specific organ dysfunction […] involving primarily the heart, lungs, and brain" (del Rio et al., 2020, p. 1723), concluding that "[g]ranted that no long-term data of substantial numbers of patients with various presenting symptoms exist and with comparison groups, and that it is still early in the COVID-19 pandemic, it is possible that large numbers of patients will experience long-term sequelae" (del Rio et al., 2020, p. 1724). Decision-making about vaccination was thus a risk-risk trade-off, not only focused on uncertainty about a set of given consequences but also regarding the types of consequences that may occur whether taking the vaccine or not.

Lack of specific knowledge about a risk source tends to lead to heavier reliance on more general knowledge. For example, if there is a lack of data on the activity of interest, it is common to extend the population and rely on data from similar activities. In the case of the COVID-19 vaccine, arguments were provided by both health officials and vaccine skeptics not only about the specific vaccines but also about the type of vaccine technology being used in these. Two of the most prominent COVID-19 vaccines, the Pfizer and Moderna vaccines, are based on mRNA technology. This technology has only recently been made available to the public but has been studied for decades (CDC, 2022b). The lack of previous use of this technology in vaccines was used as an argument for skepticism, and the long-lasting previous research on the type of technology was used as an argument for it being safe.

Over time, as the Coronavirus mutated into other variants, the vaccine turned out to have less effect on case risk, that is, on the risk of being infected, but still reduced the vulnerability to serious illness and death (Mallapaty, 2022). Health institutions reported informative statistics on this vulnerability, by showing the proportions of ICU patients who had been vaccinated compared to those unvaccinated (CDC, 2022a). However, with studies suggesting that the new variants cause less severe illness than previous variants, also among unvaccinated persons (Davies et al., 2022), the trade-off that individuals face when making the decision to get vaccinated or not may change: The risk of contracting the disease may not be assessed as large enough for the individual to willingly accept the risks associated with taking the vaccine.

The emergence of new variants, and the limited ability of vaccines to protect against transmission, has challenged the idea of achieving "herd immunity," a strategy that served as a key premise for recommending and implementing mass immunization campaigns in the initial phases of the vaccination program (refer to Section 2). With herd immunity no longer a main purpose of the vaccination efforts (Morens et al., 2022), the incentive for otherwise healthy individuals to get vaccinated in order to protect others would be significantly reduced. Furthermore, current strategies have shifted toward treating COVID-19 as an endemic, meaning that the disease will be consistently present, but the number of cases is maintained at a baseline level (Mura et al., 2022). With the rapid waning of current vaccines, this would require individuals to receive yearly boosters to maintain immunity against the virus, extending the time frame under which individuals are subject to risks and uncertainties related to the virus and the vaccines (Barouch, 2022).

Several of the examples in Section 2 illustrate the importance of considering how changes in knowledge over time can affect judgments of risk associated with vaccination. The issue is also relevant in relation to updating policies as new knowledge becomes available. Precautionary measures, which are sometimes employed when safety concerns arise, are based on the precautionary principle, which states that, in the case of potential severe consequences and scientific uncertainties, precautionary measures should be implemented, or the activity should not be carried out (SRA, 2015). Although the principle can provide valuable guidance for decision-making in the face of large uncertainties, there have been cases where decision-makers have failed to reappraise the precautionary measure, even when reassuring evidence has become available. The suspension of the Hepatitis B vaccine in France and the recommendation to remove thimerosal from vaccines in the United States are examples of this. Failing to reevaluate precautionary measures in light of changes in knowledge can result in the suspension of vaccines that later scientific evidence suggests are safe, leading to a loss of public trust and low vaccination rates. The issue demonstrates the importance of taking the aspect of time and

the dynamic development of knowledge into account in the handling of vaccine risks, ensuring that decisions are revisited when new knowledge emerges.

4.3 | Characterizing risk and vulnerability

Building on the expression of vulnerability from Section 3 as $(C',Q,K|A')$, an ideal characterization showing the vulnerabilities could take a form like this:

Let A' denote the event that an unvaccinated person contracts the disease. Among a random population of n future ICU patients, say during the next month in an area, let C_1 denote the number unvaccinated. Then, the ratio C_1/n expresses the fraction of these patients who are not vaccinated, and $1 - C_1/n$ is the fraction vaccinated. The consequences (C') are represented by these fractions, and can be estimated using historic numbers. The uncertainties can be represented (Q) for example by deriving a minimum 90% prediction interval $[a,b]$ for C_1/n, such that $P(a \leq C_1/n \leq b|K) \geq 0.90$, where K is the knowledge supporting this probability judgment. As a specific example, think about an estimate of 0.20 and a related interval [0.10, 0.30], where the supporting knowledge is considered relatively weak. The judgments are made by the analysts of the study. The interval reflects variation observed in different populations of this size n. The relatively weak knowledge is a result of the new variants being observed, which could make the historical data more or less relevant to future observations.

Alternatively, we could have conducted a traditional statistical analysis, introduced a frequentist probability expressing the theoretical fraction of the ICU patients not being vaccinated, and estimated this using the historical data. Uncertainties would then be reflected by a confidence interval for the unknown frequentist probability, assuming no trend compared to historical data.

In addition, the risk and vulnerability characterizations should be supported by SoK assessments and characterizations. Frameworks for assessing the quality or strength of medical evidence have existed for a long time. For example, Porter and Matel (1998) classified the strength of evidence of different types of medical evidence, with meta-analysis, well-controlled, randomized and interventional, and cohort studies among the types in the highest category of evidence strength, and anecdotal evidence as an example in the lowest category. Different variants of so-called hierarchies of evidence have been proposed (e.g., Canadian Task Force on the Periodic Health Examination, 1979; Guyatt et al., 1995). In these, randomized control trials and, in later years, systematic reviews are typically listed as providing the strongest form of evidence (Evans, 2003).

The case above provides an example of how the framework for vulnerability characterization outlined in Section 3 can be used to describe vulnerability for an unvaccinated person. However, it is important to note that the framework is not limited to this particular scenario—the framework is general and can be applied also to other events or risk sources. Similarly, the assessment of consequences and uncertainties, as well as the knowledge used to support the judgments, can be tailored to different contexts and levels of specificity. For example, in the case of COVID-19, the framework could be used to characterize vulnerability separately for different age groups, ethnicities, or individuals with underlying health conditions.

4.4 | The role of trust

When the choice is the individual's, the person needs to be informed by the authorities on the risks involved. Currently, we consider this to be difficult, as the risks are not described or communicated in a way that makes it easy to read and understand the risks one faces. We have looked into some of the ways the characterizations can be improved, and in the conclusion section we will summarize these. However, this issue is also about having trust in the authorities. In some countries, for example, the Nordic countries, this trust is strong; in others, it is weak, as in the USA. This relatively high degree of openness and transparency in the Nordic countries can explain much of the trust people have in the authorities. Vaccination is voluntary, but the vast majority would like to be vaccinated. The logic and argumentation is that, through vaccination, the chance of becoming seriously ill is strongly reduced, while, at the same time, one is making a contribution to fighting the disease in society as a whole. Most people in these countries see the positive aspects of vaccination as much larger than the negative ones.

The authorities must make difficult decisions in situations of an epidemic/pandemic because of the time pressure; they have to balance judgments concerning the development of the disease, the efficiency of the vaccination, safety, and risk issues. To confront the epidemic/pandemic, a main instrument is vaccination, and this policy could challenge full openness and transparency in the risk communication and decision-making. The result is often a loss of trust in the authorities. Furthermore, judgments concerning disease severity and vaccine effectiveness could be based on incomplete or inaccurate knowledge, leading to a loss of trust and credibility in the recommendations provided by the authority. As discussed in Section 2, during the Swine flu in 2009, many people did not get vaccinated, although the authorities recommended this. The severity of the disease was not considered large enough to justify a vaccine that had not been fully tested. The authorities initiated moral persuasion campaigns to get people vaccinated, but many people were skeptical of the vaccines. The disease did not turn out to be that serious, but the side effects of the vaccine were quite significant (Ulvestad & Slørdal, 2019). Nevertheless, the authorities need to shape policies and recommendations about vaccination under conditions of uncertainty, and not recommending a vaccine when it is available could damage public trust if the vaccine turns out to be effective, or if the disease turns out to be more severe than anticipated.

A loss of trust in authorities and public health institutions could have serious implications for societal and democratic

TABLE 2 Overview of key issues and contributions of the article.

Highlighted issues in relation to vaccination risks	Contributions
Lack of clarity concerning how risk and its components should be understood and expressed	By conceptualizing vaccination risk using a general risk framework, the article provides clarity on the key components of risk and their interrelationships We outline a general risk description for characterizing vaccination risk, and provide Illustrative examples of how each of the components can be suitably characterized
Incorporating the time dimension	The article highlights the importance of considering the aspect of time in discussions concerning vaccination risks and demonstrates how the conceptualization and description of vaccination risk can be extended to include the temporal dimension Using this framework as a basis allows for a clear and structured delineation of the various aspects of vaccination risk for which time could have an influence
Understanding and addressing various perspectives (individual vs. societal) and judgments (lay people vs. professionals) of risk	The article emphasizes the difference between the individual and societal/professional perspective when it comes to the characterization and perception of vaccination risks. Such a distinction underscores the importance of acknowledging that the specification of events, consequences, and the assessment of associated uncertainties is contingent on the assessor's values, beliefs, and subjective perceptions of risk
The role of trust in relation to the understanding, perception, and handling of risk	The article provides insights into the intricate interplay among trust, risk perception, and risk communication in the context of vaccination. Drawing on contemporary risk science literature, the article underscores the role of trust and skepticism in shaping public understanding and responses to risk, also extending beyond the context of vaccines and vaccination

functions in the country, but fortunately this is not a black and white dilemma; there are nuances. A blind reliance on the truth being presented by the authorities or other information sources is not the ideal; what is required is a type of critical trust, balancing reliance, and some degree of skepticism (Fjaeran & Aven, 2021; Poortinga & Pidgeon, 2003). Too much skepticism is of course also problematic, as important findings and guidance could be ignored.

There is a rich body of risk science literature addressing the concept of trust, its relation to risk perception and risk communication, and the interaction between these. An example is the social amplification of risk framework, which emphasizes the role of trust as a key influence on risk perception, and provides insights into how trust in the source of the risk communication may influence public response and action (Kasperson et al., 1988).

Trust and skepticism are considered core concepts in contemporary risk science literature and play an important role in shaping people's understanding, perception, and response to various types of risks, not only those related to vaccines. As a risk science community, we should stress the importance of finding the balance between reliance and skepticism, in line with fundamental ideas of scientific discourse.

5 | FINAL REMARKS AND CONCLUSIONS

In December 2021, the White House in the USA communicated that "…For the unvaccinated, you're looking at a winter of severe illness and death for yourselves, your families and the hospitals you may soon overwhelm" (The White House, 2021). Clearly, this statement does not inform people about risk, as it is deterministic: uncertainties and likelihood judgments are ignored. The statement was probably motivated by a policy to frighten people to take the vaccine—the goal of the communication was to get people vaccinated, and that was seen as more important than communicating risk in a neutral and balanced way. People were not risk-informed by this message. In our view, it is not prudent risk science—the result is that people quickly lose trust in the authorities (if not already lost), as the message is considered biased and to represent misinformation. Risk science and risk communication promote characterizations of risk that should aim at improving people's risk understanding. Then, deterministic messages like this should be avoided.

Are people not able to understand messages that involve statements about risk, uncertainties, likelihood, and knowledge? We will argue that they are, but the messages need to be delivered in a professional way, building on risk science knowledge. Risk-related information should be provided in a way that is sensitive to the concerns of the target audience, including the level of skepticism among these. People may have different concerns about vaccination that go beyond the safety and effectiveness of the vaccines. Addressing these concerns, and understanding how they affect trust and skepticism, is important in order to ensure that information concerning risk is effectively communicated and understood. Furthermore, the communication needs to be faithful in its representation of the relevant risks, avoiding messages that express misrepresentations of information in order to achieve an objective, even if the objective is well-intentioned.

There exists a rich body of risk communication literature providing guidance on how the content and presentation of risk-related information can be tailored to meet these needs. By drawing on insights from this literature as well as the expertise of risk communication professionals, messages can be developed and presented in a way that ensures scientif-

ically sound representations of risk, while also taking into account the concerns, values, and perspectives of the public and relevant stakeholders.

In the following, we present some characterizations which we consider to be prudent risk science and risk communication. The examples are not tailored to a particular communication situation but are intended to serve as suggestions for how risk-related information should be presented, reflecting the ideas and discussions in previous sections.

Consider first a case like that of the Swine flu in 2009. Instead of ignoring the risk related to side effects, a message from the health officials like this would be more informative:

> The vaccine could have unknown side effects. Some of them are known and we can control them, others are not and we do what we can to investigate and monitor them. We think it is unlikely that severe side effects will occur, but the knowledge base is rather weak and we cannot exclude the possibility (Aven, 2015).

To this, it can be commented that this type of message would make people unsure what to do, probably leading to many people not taking the vaccine. The message opens up the potential for scenarios with severe side effects. Our response is that an honest and fair characterization of the risk cannot exclude such outcomes. In a free and democratic society, a fundamental principle is the individuals' right to be informed and to influence governmental decision-making that may have a significant impact on their lives. Although it is acknowledged that there are cases where decisions affecting individuals are made without fully disclosing the underlying rationale (e.g., due to national security concerns), this raises a pivotal question about the balance between societal interests and individual rights. Thus, even in such cases, where the greater good is prioritized over individual interests, there is value in making these underlying prioritizations and value judgments explicit, as this constitutes the basis for ensuring transparency and accountability in the decision-making process. Similarly, if the authorities adopt a type of mandatory policy, the rationale and argumentation for the policy needs to be presented and justified, and that includes expressing the risks in a faithful way.

Consider now the risks related to COVID-19 and the side effects. Here is a suggestion for how health agencies and authorities can present the risk—it is stressed that this is just an example, an illustration of a way of thinking (some of the statements and assumptions are today contested):

> The probability of getting COVID-19 is large, whether you are vaccinated or not, but the consequences are normally mild. However, some become seriously ill. The disease is likely to be much less severe in the case of you being vaccinated. The knowledge supporting this conclusion is strong, meaning that there are large amounts of relevant, historical data supporting the conclusion, and the assumptions supporting the assessment can be considered reasonable. Even if you are vaccinated, you can become seriously ill because of COVID-19, but the number of people doing so is small. The fraction of people who get seriously ill because of COVID-19 when vaccinated is assessed to be considerably lower than the fraction of people who get seriously ill when not vaccinated. The support for this conclusion is strong.
>
> The vaccine has been thoroughly tested using approved statistical methods, showing that the risk related to side effects is very small. This means that the probability of experiencing severe side effects is small, and there is strong knowledge supporting this conclusion. Even if you are vaccinated, you could experience serious side effects of the vaccine, but the number of people experiencing such effects is assessed to be small. The risk related to the disease is judged to be considerably larger than the risk related to side effects.
>
> If you consider a big group of people, say x persons, all vaccinated, it is likely that one or two of these persons will become seriously ill because of the disease or will experience serious side effects. For a similar group of unvaccinated people, it is likely that more than y become seriously ill because of the disease. The knowledge supporting these judgments is moderately strong. There are some uncertainties related to potential side effects that need further investigations. The controlled test has not been able to check for all potential rare and long-term effects.

Vaccination is a great success in modern medicine, but its implementation is not always straightforward, as we have seen in relation to COVID-19. A main issue is the fact that there are risks associated with both the disease and the vaccine, and that means uncertainties about what will be the consequences of different health and vaccination policies. The present article has aimed at clarifying what these risks are, as seen from a risk science perspective. It is argued that there is a strong need for improvements in the way these risks are characterized and communicated. Some guidance for how to do this has been outlined.

Table 2 provides an overview of the key issues raised in relation to vaccination risks and outlines the main contributions of the article in addressing these issues. The contributions build on principles and approaches from contemporary risk science knowledge.

The main goal of the risk characterization and communication should be to provide people with a fair and honest

representation of the relevant risks, also respecting differences in points of views among experts as well as between professional judgments of risk, and lay people's perceptions of risk.

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