



Vaccine safety in the next decade: why we need new modes of trust building

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ABSTRACT

Among the realm of highly varied vaccine perceptions and concerns expressed by publics around the world, vaccine safety is the most frequently cited. While many of the safety questions raised have substantial evidence to address the concerns, vaccines do have small risks, and need vigilant and responsive systems to address them. With more and more new vaccines, combinations of vaccines and new technologies to develop and deliver them, new safety concerns will arise that need attention. Adding to this landscape is the dramatic impact which digital communication has had on how fast rumours and vaccine concerns can spread, making the task of the public health and scientific community even more pressing. One of the more recently characterised vaccine safety issues, now named ‘immunisation stress-related-response,’ has gained particularly high visibility given these highly globally connected social media networks. To better anticipate and address these rapidly shared vaccine safety concerns, a number of global efforts and local responses are being made. Co-created social media campaigns engaging parents and adolescents have been effective, while the WHO’s Vaccine Safety Net (VSN) initiative has grown its global network to increase awareness about vaccines and contribute to building confidence in vaccines. The VSN reviews websites around the world to assess their quality and accuracy to ensure and promote access to trustworthy and science-based information on vaccine safety for internet users. These and the efforts of the multiple network partners are more crucial than ever to sustain public confidence in this evolving vaccine safety landscape.



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THE STATE OF CONFIDENCE IN VACCINE SAFETY

In 2016, the Vaccine Confidence Project published a study on the global state of vaccine confidence.¹ One of the core questions in the 67-country study asked whether respondents strongly agreed, tended to agree tended to disagree or strongly disagreed with the statement ‘vaccines are safe’. The study found that confidence in vaccine safety varied considerably across countries but was consistently lower than reported confidence in the importance of vaccines. Other studies, too, have found that fear of vaccine side effects is

Summary box

- ▶ Confidence in vaccine safety varies across countries but public confidence in safety is consistently lower than overall confidence in the importance of vaccines.
- ▶ The rise of internet-mediated communication has had a significant impact on how fast public safety concerns can spread, including travelling transnationally.
- ▶ Typically, emotional contagion has been studied within small face-to-face networks but images, video and even text sent through social media can also provoke the spread of emotional states including psychosomatic reactions to vaccination.
- ▶ The Global Advisory Committee on Vaccine Safety has recognised the importance of the phenomenon they have characterised as an ‘immunisation stress-related response’ (ISRR). This is an interplay of contextual issues with individual psychological vulnerability, knowledge and preparedness for immunisation.
- ▶ Failure to differentiate between the clinical manifestations of ISSR—fainting, anxiety and associated hyperventilation following immunisation—and other conditions such as anaphylaxis which has resulted in mismanagement of cases and avoidable harm.
- ▶ Even when an adverse event following immunisation is assessed as being unrelated to the vaccine, the perception of a causal relationship can persist, and public anxieties need to be addressed.
- ▶ While social media has amplified fears, anxieties and uncertainties, social media can also be successfully used to listen to and engage publics in positive ways.

one of the most frequently reported vaccine concerns.^{2,3}

In 2018, the European Commission requested that the Vaccine Confidence Index used in the 67-country study, be run again in the 28 EU countries to be able to monitor any changes in sentiment. In only 2 years, there were already changes. Some countries became more confident and in others confidence declined, reflecting the volatility of sentiment towards vaccines—and particularly vaccine safety. In the same year, the Wellcome Trust launched their first Global Monitor⁴

Vaccines are	Important?	Safe?	Vaccines are	Important?	Safe?	Vaccines are	Important?	Safe?
Algeria	65%	43%	Ghana	88%	78%	Niger	79%	74%
Benin	79	64	Guinea	81	64	Nigeria	91	83
Botswana	91	75	Ivory Coast	76	57	Rep Congo	84	63
Burkina Faso	83	56	Kenya	89	76	Rwanda	94	82
Burundi	95	82	Liberia	92	87	Senegal	87	61
Cameron	84	58	Madagascar	83	73	Sierra Leone	90	84
Chad	68	57	Malawi	95	89	South Africa	82	68
Comoros	89	79	Mali	82	59	Swaziland	85	58
DR Congo	82	66	Mauritania	81	64	Tanzania	94	85
Ethiopia	96	86	Mauritius	84	45	Togo	72	33
Gabon	73	42	Mozambique	85	76	Uganda	89	75
Gambia	89	82	Namibia	84	71	Zambia	84	69
						Zimbabwe	90	74

Data collected between 2016-2018 using Vaccine Confidence Index™
 Representative sampling by phone, internet or house visit in local language

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Figure 1 Across Africa, confidence in vaccine safety is well below perceived importance.

study asking populations in 144 countries how they felt about science and health. Amidst the many questions related to trust, the Wellcome study included the VCI core questions. Consistent with the 2016 study, reported confidence in the safety of vaccines was consistently lower than confidence in the importance and effectiveness of vaccines. Even in Africa, where vaccine-preventable diseases are still a visible threat, the highest confidence in vaccine safety was reported in Malawi at 89%, compared with the even higher 95% reporting confidence in the importance of vaccines. Togo was the African country where only 33% of those surveyed agreed that vaccines are safe, although a much higher 72% were confident that vaccines are important [figure 1](#). An even more recent analysis published in 2020, investigating global trends in vaccine confidence between 2015 and 2019, shows that some countries have improved in confidence over that time period, while others have declined. Across the domains of confidence in the importance, effectiveness and safety of vaccines, safety again was the least to improve globally and some countries showed declining confidence in vaccine safety over that time period.⁵

SCIENTIFICALLY ASSESSED SAFETY RISKS VS RISK PERCEPTIONS

There is vaccine safety and there are perceptions of safety. There are scientific reports of adverse event following immunisation (AEFI) and there are socially shared reports of adverse events following immunisation. Both matter and both must be considered. Even when an AEFI is investigated and officially deemed to be unrelated to a vaccine or vaccination the perception of a causal relationship between vaccination and a subsequent adverse event can persist and needs to be addressed. As risk expert Paul Slovic characterised it, there is ‘risk as analysis’ as well as ‘risk as feelings’. He particularly points out the ‘complex

interplay between emotion and reason that is essential to rational behaviour.⁶ In short, while reason and emotion are often seen as different, sometimes conflicting, influences on behaviour, Slovic and a growing number of neurologists are stressing the inter-relatedness of emotions and reason on health decisions and outcomes.⁷

While some of the public concerns and anxieties about vaccine safety are driven by rumours and misinformation, some of the seeds of those emotions stem from the reality that vaccines do have their risks, as small as they may seem relative to the public health benefits. And, when trust in government, in the local health system or in international stakeholders is weak, perceptions of even the smallest risks are amplified.⁸

Among the multiple safety concerns raised by different publics, the most recurring ones are about vaccine ingredients (eg, thiomersal, adjuvants), perceptions about the risks of autism and autoimmune conditions resulting from vaccination, anxieties about too-many vaccines overloading the immune system, and non-specific effects of vaccination innovations and new technologies, such as the new COVID-19 vaccines using messenger RNA. In some of these cases, despite the available science assuring the safety of a particular vaccine in question, perceptions and anxieties about safety persist and can strongly affect individual and group vaccination decisions.⁹

Some vaccine safety questions posed by the public do need more scientific investigation. In May 2019, for instance, around 30 vaccine safety experts gathered at the Wellcome Trust to take a hard look at which of the persisting vaccine safety questions have clear scientific answers, but need better communication, and which questions actually need more scientific studies.¹⁰ Continuing efforts to stay on top of new questions as they evolve, while also continuing to be responsive to public concerns will be crucial moving forward.

IMMUNISATION STRESS-RELATED RESPONSE

One of the more recently characterised vaccine safety issues that the Global Advisory Committee on Vaccine Safety (GACVS) has given more attention to is what they have now named as a ‘immunisation stress-related response’ (ISRR). WHO has introduced this new terminology to describe the entire spectrum of manifestations (symptoms and signs) of a stress response. The biopsychosocial model scientifically describes the evolution of ISRR in an individual through an interplay of the social context of immunisation with physiological factors in an individual interplaying with his or her psychological strengths as well as vulnerability, knowledge and preparedness for immunisation.¹¹ Even though stress related events following immunisation have been reported from all over the world in the last three decades,¹² newer modes of digital media have contributed to their increased visibility.¹³ Social media in particular has allowed new levels of emotional contagion around vaccines. The rise of internet-mediated communication has had a significant impact on how fast vaccine rumours and anxieties can spread, now travelling transnationally in and instant.

A recent study in Italy showed that despite there being some positive videos about human papillomavirus (HPV) on YouTube, the ones conveying negative messages are the most engaging, most watched and receive the most “likes.”¹⁴ Additionally, emotionally charged content tending to be shared more often and more quickly compared to neutral ones.¹⁵

Stress-related events following immunisation, particularly those that occur in clusters—affecting from a few to over 800 individuals, have adversely affected immunisation programmes in both developed and low/middle-income countries.²

Doubts and uncertainty about vaccine have led to somatic reactions in different settings. Clusters of immunisation stress-related responses following immunisation have been registered in countries such as Denmark, Japan, Pakistan and Colombia. These clusters of reactions following vaccination, besides being disruptive to immunisation programmes, can impact overall public trust in immunisation and negatively affect vaccine coverage. Typically, emotional contagion has been studied within small face-to-face networks, however, it is argued that physical proximity may not be necessary and that images, video and even text-based communication across social media can provoke the spread of emotional states.¹⁶

In 2013, Colombia had one of the highest HPV immunisation rates in the Americas, at over 90%. In May 2014, after routine HPV immunisation at a school in the rural area of Carmen de Bolívar, a group of 15 girls from the same school were admitted to the hospital presenting symptoms of tachycardia, shortness of breath and numbness of limbs. Following media coverage of the cases and videos uploaded online, symptoms spread to other cities in Colombia affecting over 500 girls. The Colombian Institute of Health conducted an epidemiological investigation of the girls affected, but no organic link was found

between HPV immunisation and reported symptoms. Nonetheless, the events affected public confidence and HPV immunisation coverage in Colombia dropped to as low as 17.5% in 2016.¹⁷

These types of reactions are not unique to HPV vaccination. One single incident in Pakistan during a polio mass immunisation campaign in 2019 caused mass contagion, and hundreds of children were rushed to hospital with complaints of abdominal pain, vomiting and fainting following polio vaccination, triggering angry protesters to burn down a healthcare facility.¹⁸

Such phenomena, also reported in the literature as mass sociogenic illness or mass psychogenic illness, consists of physical symptoms involving otherwise healthy people. Incidents usually start after exposure to a trigger (real or perceived), rumour or observing someone else becoming ill. Symptoms are subjective and vary within individuals and between episodes, but can include headache, dizziness, nausea, motor impairment, syncope and fatigue.^{19 20}

Doctors struggle with the concept of psychogenic nature of symptoms as much as the patients do, at times giving organic diagnosis such as postural orthostatic tachycardia syndrome (POTS), chronic fatigue syndrome (CFS) or myalgic encephalomyelitis. Health providers should be able to recognise anxiety related or psychosomatic symptoms and distinguish those from other conditions to avoid potentially harmful clinical interventions which might exacerbate symptoms.

Events such as complex regional pain syndrome, POTS and CFS have been reported as AEFIs. With some of these conditions, the symptoms and signs remain unexplained even after thorough and appropriate medical investigations and no causal association to the vaccine established.²¹

While the vaccine may be assessed as having no causal link to adverse events, it is now recognised that the experience of vaccination can play a role in triggering stress-related responses following immunisation. These symptoms equally need attention in order to mitigate individual as well as public anxiety, and possible disruptions to immunisation programmes.

PREPAREDNESS AND RESPONSE TO ADDRESS ISRR

With the evolving social, cultural, communications and media landscape, surrounding vaccination it is important to anticipate, prepare for and respond effectively to ISRR. Healthcare providers not only need to have the knowledge and skills to administer vaccines, but also be trained to anticipate and address atypical adverse events such as ISRR. A friendly, confident, relaxed approach with empathy and supportive communication to build trust with the vaccine recipient and caregiver will be key to mitigate the occurrence of ISRR.²²

Before administering a vaccine, individuals with predisposing risk factors such as being in the adolescent age group (10–19 years), having a history of vasovagal

syncope, previous negative experience of immunisation, an expressed fear of injections or needles or pre-existing conditions such as an anxiety disorder or a developmental issue such as autism spectrum disorder should be identified, and their special needs addressed at the time of vaccination. To respond to clusters of ISRR at a programme level, it is important for immunisation programmes and relevant staff have a clear pre-established communications strategy to decide if, when and what needs to be communicated should ISRR occur. When clusters of such events occur, they should be thoroughly investigated, causality assessed and stakeholders—including the media, healthcare providers and public—should be kept informed to mitigate the spread of unfounded rumours. Monitoring public sentiment across social media, if feasible, can be helpful to detect and guide emerging misinformation at the nascent phase before it spreads.²³

At an individual level, the responses to stress due to needles (and vaccination) vary from person to person or may change according to age, time or context. It can manifest with variable severity of symptoms and may range from mild feelings of worry and ‘butterflies’ in the stomach, increased heart rate, palpitations, difficulty in breathing or rapid breathing (hyperventilation), loss of consciousness and/or seizures. Thus, the spectrum of an ISRR can vary from acute stress response including a vasovagal reaction where the onset of symptoms maybe just prior to, during or immediately after vaccination (usually within 5 min) or a dissociative neurological symptom reaction (with or without non-epileptic seizures) that may take hours to days to develop after immunisation. Failure to differentiate between the clinical manifestations of fainting, anxiety and associated hyperventilation and other conditions such as anaphylaxis has resulted in mismanagement of cases and causing additional avoidable harm.²⁴

INNOVATIVE INTERVENTIONS TO BUILD AND SUSTAIN VACCINE CONFIDENCE

While social media has amplified fears, anxieties and uncertainties, social media has also been successfully used to listen to and engage publics. HPV vaccination coverage in Denmark dropped dramatically from 79% to 17% following fears of adverse events due to episodes of ISSR.²⁵ Danish Health authorities, after listening to parents, learnt that Facebook was where many of them were getting their information about the HPV vaccine. Among various social media interventions, they developed collaboratively with teenage girls, was a social media campaign, including a Facebook page to help answer parent’s questions and share stories.²⁶

In addition to direct interventions with the public, another important initiative is the Vaccine Safety Net (VSN) (Coauthor Isabel Sahinovic is the Coordinator of the VSN and has authored this section) which is a worldwide network of websites, verified by WHO, that provide

reliable information on vaccine safety. The initiative has two main goals: to facilitate access to trustworthy and science-based information on vaccine safety for internet users, and the second goal is to collaborate, as a network, with other international initiatives, to increase awareness about vaccines and contribute to building confidence in vaccines. Newly qualified VSN websites are authorised to host a VSN visual identity on their homepage to signal to visitors that they are accessing a safe place for trusted vaccine information that meets the good information practices criteria defined by the GACVS.²⁷

The Network’s greatest asset is the diversity of its websites. Trusted information is generated from different parts of the world and in multiple languages. This allows for culturally sensitive material, tailored to local contexts, that takes into consideration the audience’s interests and health literacy. The Network comprises websites owned by governments, professional associations, academia, information platforms, fact-checking websites but also popular women magazines, community owned websites, from high-income and low-income countries. As at April 2020, 82 websites, from 36 countries were providing information in 26 languages. It is estimated that 2 million new users are accessing information made available by VSN members every month and that last year, some 72 million pages were viewed on VSN websites.

Social media are powerful information and influencing channels, so increasing the VSN Network visibility through social media networks has also been crucial. Among other projects, the VSN Network is exploring the use of artificial intelligence and machine learning to continuously improve the delivery of tailored messaging, including testing new ways of interacting such as through chatbots. VSN members will be involved in the content development of a Vaccine Safety chatbot to address most common concerns the public has around issues related to vaccine safety.

CONCLUSION

Public perceptions and concerns around vaccine safety are unlikely to be redressed in a letter or rebuttal to a scientific Journal, but by understanding what is driving public anxieties and sentiments to better address them. In some cases, these concerns may flag an emerging new safety concern, in others it may be an issue of good science but poor communication, historic distrust in the information provider or an ISRR. Whatever the issue, if not taken seriously and addressed promptly, perceptions of risk will not only persist, but will keep growing—a phenomenon risks specialists call ‘the social amplification of risk’.²⁸

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