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REVIEW

Vaccine hesitancy, misinformation in the era of Covid-19: Lessons from the past

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Summary

Background. — As the world has challenged/argued with the Covid-19 pandemic over the last two years, there has been an increase in vaccine misinformation. Although immunity against Covid-19 infection is limited to 4–6 months and requires at least three doses of vaccine to be maximally effective, the current vaccination campaign in industrialized countries shows that vaccinated citizens experience greater immunological protection against severe forms of the disease than unvaccinated citizens.

Methodology. — A perusal of the literature was performed in order to reconstruct the communication methods applied in the managing of the Covid-19 pandemic; the management of the current pandemic was compared with the management of another scourge of the past: polio-myalitis.

Results/Discussion. — In order to raise public awareness on public health issues, it is essential that governments and institutions communicate scientific data to all sections of the population in an unambiguous way. In this sense, it is essential to apply "prebunking", which is a layered defense system available to society that prevents misinformation before it is spread. This is to avoid the subsequent debunking of false information, which generates insecurity and fuels fears. Belief in medical misinformation represents a meaningful problem for public health efforts to fight Covid-19 through vaccination.

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Africa was officially declared polio-free on 25th August 2020 [1]. This epidemiologically relevant achievement was obtained thanks to mass vaccination campaigns. However, the news had little impact on citizen awareness in industrialized countries, which had already been WHO polio-free regions for a long time. Apart from Pakistan and Afghanistan, where the poliovirus is still endemic, the disease caused by the wild-type form of the virus (WPV) has been eradicated from all other developed countries. Therefore, the perception risk has been perceived as nonexistent.

The last case of poliomyelitis in the United States was reported in 1979. In 1994, the World Health Organization (WHO) certified the eradication of poliomyelitis from the Americas and in 2000 from 36 countries in the Western Pacific, including China and Australia. In 2002, Europe was declared polio-free and, in 2014, it was India’s turn. Conversely, the current pandemic caused by the SARS-CoV-2 virus has changed the world population’s perception; each individual is aware of the existence of an invisible and potentially lethal enemy [2]. In less than 1 year, several types of vaccines, mRNA and viral vector, have been developed and the worldwide vaccination campaign against SARS-CoV-2 has been an overall success. However, vaccine hesitancy still persists (https://www.ecdc.europa.eu/en/immunisation-vaccines/vaccine-hesitancy). Following the European Centre of Disease Prevention Control (ECDC), vaccine hesitancy consists in the delay in acceptance or refusal of vaccines despite availability of vaccination services; vaccine hesitancy is complex and context specific, varying across time, place and vaccines. It includes factors such as complacency, convenience and confidence (https://www.ecdc.europa.eu/en/immunisation-vaccines/vaccine-hesitancy).

A significant number of people have come out against the SARS-CoV-2 vaccine for different reasons.

"Many experts have warned against a worldwide decline in public trust in immunisation and the rise of vaccine hesitancy during the past decade, especially in whole Europe” [3].

"Today, we are in the paradoxical situation of having highly effective vaccines but doubting publics. While the majority of the population still believes in vaccines, many of those who are questioning them reject the label of being called ‘anti-vaxers’. There is a growing swell of dissent. People are asking whether we really need so many vaccines. Are they safe? What are the real motives behind vaccination? Political gain? Economic gain by governments and the pharmaceutical companies? Who is the state to impose mandates on our freedom of choice and impose on our religious or other beliefs?” [4].

Vaccine hesitancy, a phenomenon that comes from the past

Although mass vaccinations campaigns in the past led to the containment of many epidemic diseases, including the eradication of human smallpox, vaccine hesitancy and the anti-vax movement have always existed; lively debates on the method of variolation or smallpox inoculation of human smallpox occurred when first introduced [5–7]. "The first anti-vaccine league was founded in the mid-1850s when emotions raged in the United Kingdom against a law-making smallpox vaccination compulsory” [4].

In the early 19th century, Italian rulers and physicians adopted the above strategy to explain the benefits of mass vaccination campaigns to the citizens. Ante litteram communication campaigns were carried out, among others, by Luigi Sacco (1769–1836) in the northern Italian Napoleonic Cisalpine Republic, by Giacomo Barzelliotti (1768-1839) in Siena and in Siena and in the neighborhood, by Michele Troja (1747–1828) and Antonio Miglietta (1767–1826) in the Kingdoms of Naples and Sicily [8]. An equally significant example was the emergency management of the poliomyelitis epidemics in the first half of the 20th century. Poliomyelitis was first described in 1789 by the English physician Michael Underwood (1736–1820). It is a serious infectious disease caused by the Poliovirus which predominantly affects the motor neurons of the spinal cord. Since the beginning of the 20th century, numerous epidemic waves of poliomyelitis were recorded; a peak was registered in 1952 in the United States with more than 21,000 cases and 3,100 deaths [9,10]; this figure was compounded by the large number of individuals who became paralyzed, deformed and unable to breathe outside an iron lung, a machine specially designed to support ventilation impaired by weakness of respiratory muscles [11]. Although the fatal form of the disease claimed few lives, millions of polio-survivors bore the signs of the disease, a reality whose traces can even be found in ancient artworks [12,13]. Due to the ever-increasing number of cases in the first half of the 20th century, virologists
worked hard on the development of an effective an anti-polio vaccine. In the late 1940s, the research group led by John Franklin Enders (1897–1985) succeeded in culturing the polio virus in large quantities in the laboratory. The foundation for the development of vaccines in the following years was laid [14]. In 1954, John Franklin Enders, Thomas Huckle Weller (1915–2008) and Frederick Chapman Robbins (1916–2003) were awarded the Nobel Prize in Physiology and Medicine for their ‘discovery of the ability of the polio virus to grow in cultures of various tissue types [15]. In the early 1950s, based on the findings of Enders and his group, Jonas Salk (1914–1995), a researcher at the University of Pittsburgh, developed the Inactivated Polio Vaccine (IPV). Starting with a formaldehyde inactivated virus injected intramuscularly, the vaccine promoted an immunizing antibody response. In 1952, Salk inoculated 43 boys with the vaccine. An immunization campaign involving one million young people in the United States followed.

On the 12th of April 1955, it was announced to the world that, thanks to the development of the Salk vaccine, the fight against polio was potentially won. However, confidence quickly waned as a result of the “Cutter Incident”, which involved Cutter Laboratories, a pharmaceutical company in the United States.

Two batches of the vaccine contained residues of live poliovirus. As a result, 192 cases of paralytic polio occurred among vaccinated children and their families and community contacts, and 11 people died. This led to the suspension of the vaccination program and a review of federal requirements for vaccine production. The result was a deep public distrust of the vaccination plan and a halt to studies on the development of new vaccines [16–18].

Meanwhile, at the University of Cincinnati, Albert Sabin (1906–1993) developed an oral vaccine made from a live attenuated virus, the Oral poliovirus vaccine (OPV), which became the predominant and most effective vaccine used in the fight to eradicate polio.

In Italy, anti-polio vaccination did not become compulsory until 1966. "From 3–4,000 cases per year in 1959–63, polio dropped to 841 in 1964. Then, the annual cases continued their decline: 254 in 1965, 148 in 1966, 107 in 1967, 90 in 1968. In 1972, there were ten. A great victory for medicine. But, for Italian health, remorse and a lesson to be learned: no more delays or postponements” [19,20]. The delay in starting vaccination with the Sabin vaccine cost Italy almost 10,000 cases of poliomyelitis, with 1,000 deaths and more than 8,000 cases of paralysis [21].

Prevent misinformation through proper communication

Today, the world population is facing the need for mass vaccination against SARS-CoV-2. The lesson from our recent past is that correct information on vaccines, their efficacy and possible health consequences is fundamental.

Even more so given the ease with which news of all kinds, often uncontrolled by specialists of those disciplines, can spread with great speed thanks to the technologies available today. The practice of "prebunking", a layered defense system available to society that prevents misinformation, provides the population with good psychological resistance against fake news on a large scale [22,23]. To put prebunking into practice, it is necessary to know the behavior of the crowd, its emotional reactions to the disease and the possibility of being able to prevent it with a vaccine. "Understanding the contagion of not just viruses but also sentiments and beliefs is crucial to the future of vaccines”. As Lancet Infectious Diseases editor John McConnell wrote in the introduction to a special issue on Mass Gathering and Health: "To minimize health hazards and mass gatherings, it is essential to understand the behavior of crowds” [4].

At the same time, it is crucial to know how social media works and the power it can have. “Understanding crowd behavior includes understanding the web of social networks that converge and connect individuals from larger networks beyond an immediate gathering of bodies, beliefs, and behaviors” [4].

"Recently, the use of social networks such as Facebook, Twitter, and Sina Weibo has become an inseparable part of our daily lives. It is considered as a convenient platform for users to share personal messages, pictures, and videos. However, while people enjoy social networks, many deceptive activities such as fake news or rumors can mislead users into believing misinformation” [24]. "The outbreak of the SARS-CoV-2 novel coronavirus (Covid-19) has been accompanied by a large amount of misleading and false information about the virus, especially on social media” [20].

"A good prebunk addresses people’s concerns, speaks to their lived experience and compels them to share that knowledge. Prebunks are empowering: The whole point is about building trust with your audience instead of simply correcting facts” [25].

This defense system avoids subsequent 'debunking' that is the denial of false information, which generates insecurity in people increasing fears. It is mandatory that information is clear, accessible, provided in an impartial manner, and exclusively based on scientific data [26–29].

"It remains critical that policies to mitigate and recover from the pandemic define a clear, timely, and accurate communication strategy early on, and include a sufficient degree of democratic involvement and coordination involving all stakeholders. Aside from the democratic imperative to do so, the effectiveness of rules and recommendations largely depends on the willingness and ability of populations to adhere to them” [28].

Concerning the communication techniques, the World Health Organization (WHO) has identified six key points for good communication, stating that it should be: 'accessible, actionable, credible and reliable, relevant, timely, understandable'. Furthermore, "WHO strives at all times to ensure that these principles are at the core of its communication activities and are reflected in the full range of materials and activities: social media posts; web-based fact sheets, articles, commentaries, infographics; questions and answers; intranet content for WHO staff; press conferences, press releases and media advisories; videos; visibility and awareness-raising activities [30]."
Supporting citizens’ trust in science

A significant factor in the acceptance of a vaccination practice is the perception of risk factors, safety and tolerability of a drug. “It is necessary—therefore—that information is clear, transparent, based on science and not on politics” [3,31]. In order to overcome vaccine hesitancy [32–34], there is a need for an integrated approach among governments, scientists, doctors, universities, research centers, political parties, trade unions, professional organizations and science journalists.

The establishment of a mutual trust among institutions and citizenship is fundamental. To this end, institutions must provide clear and consistent messaging in order to gain credibility; reassured citizens will turn to appropriate centers for information where they will be informed on various aspects of vaccination and its immediate and long-term benefits.

“...the importance of clear communication strategies that include scientific evidence and openly acknowledge uncertainties, are key to public trust” [28]. This is why it is essential—as Heidi J. Larson, founder of the Vaccine Confidence Project, writes—that “Vaccine acceptance is about a relationship, about putting trust in scientists who design and develop vaccines, industries that produce them, health professionals who deliver them, and the institutions that govern them. That trust chain is a far more important level of acceptance that any piece of information. Without these layers of confidence, even the more scientifically proven and well-communicated information may not be trusted” [4].

At the same time, it is essential to keep in mind that with new technologies, which citizens have used in a particular way during the lockdown, citizens themselves have begun to trust what is found on the net and which is often shared through social networks. In this way many have built their knowledge about the pandemic and vaccines based on information and data that are absolutely unreliable and unverified. And above all, they interrupted the relationship with their trusted doctor. The proactive citizen involvement in health choices, sometimes evoking a “we know better” sentiment, disrupted the age-old trust relationship between doctor and patient, health authority and citizen, and has become particularly acute in the case of vaccines [4,35].

Communication actions by the Italian Government to promote campaign on vaccines against SARS-CoV-2

Today, as in the 1960s, there is an extensive information campaign on vaccines against SARS-CoV-2. With regard to the current pandemic, correct and timely information has accompanied the actions of the Italian Government from the outset. The first intervention dates back to the 13th of February 2020, when the Minister Roberto Speranza speaking to the Council of Health Ministers of the European Union underlined the importance of ‘giving a strong and coordinated response (It is a very important result that all the Health Ministers of the European Union, on the proposal of Italy, today are together to build an adequate response to the Coronavirus’)’ [36].

Since then, daily messages and videos informing about the SARS-CoV-2 pandemic were broadcast on radio and television and published on the Ministry of Health and Government websites. The first press conference concerning the Coronavirus emergency was held by Angelo Borrelli, Head of the Civil Protection Department, and dates back to the 24 of February 2020. A new institutional communication pathway with a day-by-day national update was initiated.

At the same time, the communication campaign started:
- on the 25th February of 2020, the video “Di amoci una mano” (“Let’s help each other”) was shown; a series of daily hygienic practices was presented in order to reduce the risk of being infected with Coronavirus and, in turn, the risk of infecting other people.
- On the 27th December 2020, after the European Medicines Agency’s approval, a mass vaccination campaign was launched in Italy and in Europe.

In 2021, many interventions to encourage vaccination against Covid-19 infections were set up such as such as the campaign “Riprendiamoci il gusto del futuro” (Let’s take back the taste of the future) and “Facciamolo per noi” (Let’s do it for us). Both were produced by the Department for Information and Publishing of the Presidency of the Council of Ministers. These campaigns were aimed at:
- highlighting the importance of the booster dose (third reinforcing dose);
- discussing with pediatricians the advisability of vaccination for children aged between 5 and 11 years [37].

In addition, politicians have repeatedly stressed the need to proceed with vaccinations. The Italian Prime Minister Mario Draghi at the UN General Assembly stated that: “More than a year and a half after the start of the health crisis, we can look to the future with greater optimism. The vaccination campaign has restored our confidence in our ability to achieve a new normality”. The current President of the Italian Republic, Sergio Mattarella, during his end-of-year speech, stressed how “vaccines have been, and are, a valuable tool, not because they guarantee invulnerability but because they represent the defense that allows you to decisively reduce damage and risk, for themselves and for others. Research and science have given us this opportunity much earlier than we could have hoped. Wasting it is also an insult to those who did not have it and to those who are unable to get it today”.

The above statements were fully corroborated by the data provided by the Istituto Superiore di Sanità (ISS), the main center for research, control and technical-scientific consultancy in the field of public health in Italy. In the last few days of 2021, the number of patients admitted to intensive care per 105 inhabitants were as shown in Table 1.

| Date       | Number of Patients Admitted to Intensive Care |
|------------|---------------------------------------------|
| 31st December 2021 | 89% of the population over 12 years of age had already received, at least, one dose of vaccine; 85.84% had completed the vaccination cycle, and a steadily increasing number of citizens were administered their third dose. In addition, vaccinations for the 5–11 age group began in mid-December 2021 [38].

Almost 5 months later, as of May 22, 2022, 48,625,128 people have completed the primary vaccination cycle, equal
to 90.06% of the population over 12 years of age. There are 39,513,373, equal to 82.83% of the population potentially subject to additional dose or booster, those who have completed the vaccination cycle for at least 4 months.

Although in Italy there has been a good response to vaccination, the campaign for administering the 2nd booster dose is struggling to take off. The administration of the second booster or fourth dose is recommended, after four months from the administration of the first booster dose, for people aged 80 and over, guests of residential facilities for the elderly, people aged 60 and over with high frailty motivated by concomitant/pre-existing pathologies. Also as of May 22, 2022, only 0.77% of the immunosuppressed received the second booster in the 60–69 age group, a percentage that rises to 1.34% in the 70–79 age group. Over the age of 80, they are 12.28% [39].

It is necessary to insist on this path because “the administration of the booster will likely improve the quality of life of Covid-19 high-risk groups who otherwise may experience higher stress levels during the autumn—winter waves of Covid-19 cases, hospitalizations, and deaths, all of which are further exaggerated by extensive media coverage and hype surrounding the danger of more transmissible SARS-CoV-2 variants” [40].

Furthermore, “given that developed countries are facing a growing challenge of convincing unvaccinated individuals to receive a Covid-19 vaccine, offering boosters to vaccinated people represents a strategy for a more effective and local control of the pandemic. This strategy may be financially advantageous, particularly considering that, in the temperate zone, SARS-CoV-2 has revealed a strong seasonal pattern, with infections rising in the autumn—winter season. Offering the booster may also contribute to keeping schools open, which is a boon for children’s education, as well as their mental and physical well-being. Vaccine boosters offered to healthcare personnel, who were the first group to receive initial Covid-19 vaccine doses, will decrease the risk of SARS-CoV-2 transmission to patients, including vulnerable groups, and mitigate the disruption of the general healthcare system caused by the quarantine of SARS-CoV-2-positive healthcare workers” [40].

## Conclusions

Independent of the measures adopted by the various governments, the need for a worldwide vaccination program has become obvious. According to Amref Health Africa (May 19, 2022), 58.04% of the world’s population has been fully vaccinated. In Europe 70.2%; in the USA 65.6%; in Italy 84.3%; in Africa 15.8% [41].

SARS-CoV-2 variants have become a major virologic, epidemiological and clinical problem. Viral mutations usually occur in countries where the number of vaccinated people is still extremely low and, then, rapidly spread around the world. However, some surveys suggest that vaccine hesitancy is actually higher in developed countries than in developing ones. Therefore, it is just as likely that the virus will evolve into new forms also in wealthier countries [42].

The difficulty to carry out vaccination campaigns and the lack of fruitful vaccination strategies can threaten the overall success of vaccines e.g. the recent cases of SARS-CoV-2 and infant poliomyelitis registered in the Ukraine population before the current war [43] or the outbreak of poliomyelitis occurred in Malawi in February 2022, where a child developed the disease following infection by a wild-type variant of the virus [44].

Research from psychology has given us important information to better fight misinformation. The studies conducted until now, however, have some limitations, in particular, preventive actions ("prebunking") and retroactive actions ("debunking") have been examined at the same time; hence, it is not clear which is the best approach.

Prebunking and debunking are two important means of reducing the dependence on disinformation. Anyway, we would like to remember that there is a good expression that says: "prevention is better than cure". "Recent research has explored the possibility of building attitudinal resistance against online misinformation through psychological inoculation. The inoculation metaphor relies on a medical analogy: by pre-emptively exposing people to weakened doses of misinformation cognitive immunity can be conferred" [45].

Referring, for example, to "Bad News game, an online fake news game in which players learn about six common misinformation techniques", despite "the lack of a control group, a relatively small number of items to measure effectiveness, and the absence of attitudinal certainty measurements", the authors pointed out that, "compared to a control group, the generalized inoculation intervention not only successfully conferred resistance to online manipulation, but also boosted confidence in the ability to resist fake news and misinformation" [45].

Another practical application of inoculation theory as part of Covid-19 disinformation is the new online game online called Go Viral! It is "a new game developed by Cambridge psychologists in partnership with the UK Government. It builds on research from Cambridge psychologists that found by giving people a taste of the techniques used to spread fake news on social media, it increases their ability to identify and disregard misinformation in the future" [46].

Faced with such a complex broadcast picture, both the History of Medicine and Science can contribute in informing citizens on how, over the centuries, they have helped people to confront and, in some cases, defeat epidemic diseases [47–49]. Therefore, the example of how past epidemics were dealt with can represent a "weapon of knowledge‘ to deal with the current pandemic and future epidemics.

### Table 1

| Vaccination status | Admissions to Intensive Care/10^5inhabitants | Deaths/10^5inhabitants |
|-------------------|-------------------------------------------|------------------------|
| Unvaccinated      | 15.07                                     | 14.45                  |
| Vaccinated        | 1.2                                       | 2.77                   |
| Individuals with a third dose (booster) | 0.58                                     | 1.09                   |
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Disclosure of interest

The authors declare that they have no competing interest.

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