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Scientific interferences in public awareness and health during the pandemic COVID-19

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Abstract. The pandemic promoted the need to understand evolutionary principles to solve aspects of human behavior that hinder biomedical innovation and the application of public health services, behaviors that denote insecurity, mistrust and reluctance towards vaccines.Estimating the efficacy of the vaccine (VE) against COVID-19 is essential to assess population protection levels and future booster dose needs to cope with the re-emergence of epidemic waves. This minireview aimed to investigate the relationships between the time course of global SARS-CoV-2 infections (as assessed by case rate and mortality rate) and the development of SARS-CoV-2 vaccination campaigns and post-vaccination follow-up, respectively. The World Health Organization convened the Technical Advisory Group on SARS-CoV-2 Virus Evolution to develop guidance on how best to estimate Strategies for the prevention and control of COVID-19. These detailed overviews of the processes followed, the data used and the methods applied were provided from studies found in the scientific literature.

Keywords. COVID-19, vaccine development, strategies, prevention

Introduction

The COVID-19 pandemic was a public health emergency that required massive control, similar to that of the 1918 flu pandemic, the HIV pandemic, and the eradication of smallpox. SARS-CoV-2 variants that were more transmissible or caused more serious consequences than the original variant in Wuhan, China were not detected until the end of 2020. During this period, non-pharmaceutical interventions were adopted worldwide. These measures aimed at reducing the number of effective transmission contacts between susceptible and infectious individuals in the population and, with this, viral transmission [1]. Without a doubt, the development of vaccines was one of those the biggest breakthroughs in the fight to reduce scale and impact the COVID-19 pandemic. Following deployment vaccination programs in late 2020 and early 2021 in many countries relaxation measures could be adopted. Vaccines must be implemented effectively to maximize its public health benefits [2].

Vaccination campaigns have brought hope of minimizing the burden of 2019 coronavirus disease (COVID-19). However, the emergence of new types of coronaviruses implicated in the development of severe acute respiratory syndrome (SARS-CoV-2) and the decrease in neutralizing antibodies a few months after vaccination have raised concerns about the effectiveness of vaccines. Statistics indicate that the COVID-19 vaccination, including booster

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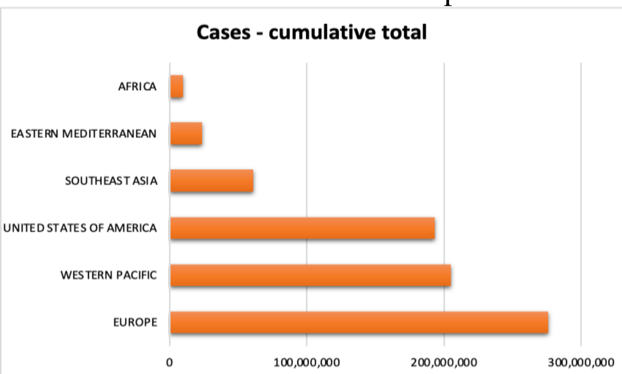
administration, has been beneficial in reducing the extent of health system collapse but new long-term vaccination strategies may be needed to enhance the effectiveness and durability of vaccine-induced protection during possible waves of new SARS-CoV-2 infections [3].

1. Globally evolution over time of SARS-CoV-2 infections

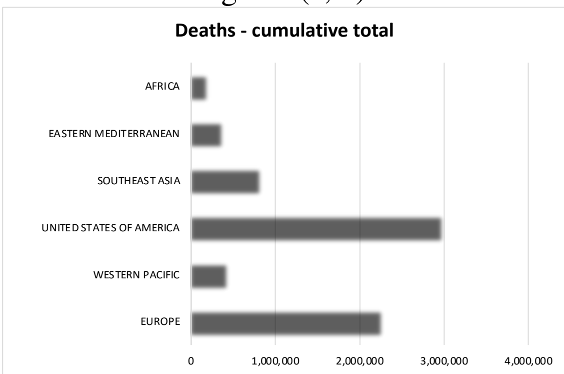
Since its appearance, the SARS-CoV-2 virus has continued to evolve, with several variants existing to date: B.1.1.7 (Alpha), B.1.351 (Beta), P.1 (Gamma) and B.1.617.2 (Delta). In late 2020, new variants appeared namely C.37 (Lambda) and B.1.621 (Mu) [4]. The Alpha variant is estimated to have a 61 % (42–82 %) higher risk of death than pre-existing variants, with higher infectivity and disease severity [5]. P.1, another highly contagious variant, has been circulating in Brazil since mid-2020. This variant has been linked to an outbreak of infections in Manaus, the Amazon region of Brazil. B.1.351 was discovered late last year in South Africa [6], while the Delta variant is known to be notorious for being highly contagious. Within five weeks of its discovery in April–June 2021, the Delta variant became the dominant variant of SARS-CoV-2 in Mesa County, Colorado, and is now the dominant variant in the United States [7]. At the same time, the variant B.1.1.529 (Omicron) was first identified in November 2021 in Botswana and South Africa [1].

Worldwide, on July 12, 2023, 767.972.961 confirmed cases of COVID-19 **(Figure 1 - a),** including 6.950.655 deaths **(Figure 1- b)**, were reported to the World Health Organization. By July 8, 2023, a total of 13.474.185.140 vaccine doses **(Figure 1 – c, d)** have been administered [8].

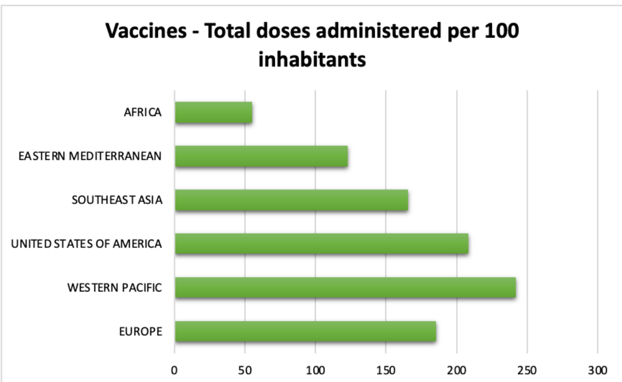
Figure 1. Total SARS -CoV-2 cases per region (a), total death cases per region (b) and vaccine doses used per 100 inhabitants in different regions (c, d)



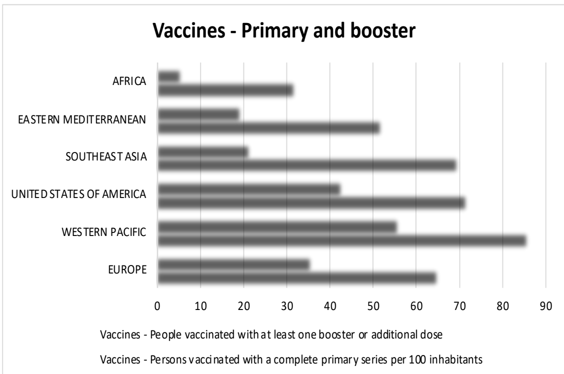
a)



b)



c)



d)

2. Anti SARS-CoV-2 vaccine development

The development of vaccines has been one of the biggest breakthroughs in the fight to reduce the scale and impact of the SARS-CoV-2 pandemic. The United Kingdom was the first country to begin its vaccine rollout campaign, quickly followed by Israel, the U.S. and European nations [9]. Generally, several vaccination groups (eg, staff and residents of long-term care facilities, health care workers, and people with comorbidities) were prioritized for vaccination. After this, the vaccination rollout was carried out on eligible age cohorts, starting with the oldest and ending with the youngest [10], closely following the criteria for risk of hospitalization and death from COVID-19. Such targeted control measures are common in epidemiology. More recently, the vaccination strategy has focused on protecting vulnerable groups such as the elderly, healthcare workers and people with medical risk conditions [11].

2.1. Vaccination campaigns against SARSCoV-2

Vaccination campaigns against SARSCoV-2 in Europe were launched in early 2021 and were met with varying levels of hesitancy [12]. However, by the end of the year, 69 % of the European Economic Area (EEA) population had completed the initial vaccination protocol consisting of two doses of BNT162b2 (BioNTech/Pfizer, mRNA-1273 (Moderna) or AZD1222 (Oxford/AstraZeneca), or a single dose of AD26.COV2.S (Janssen/ Johnson & Johnson)4. Although the use of certain vaccines in the EEA varied, BNT162b2 was the most administered product in the EEA countries [13]. Natural immunity induced by SARSCoV-2 infection also protects against reinfection [14].

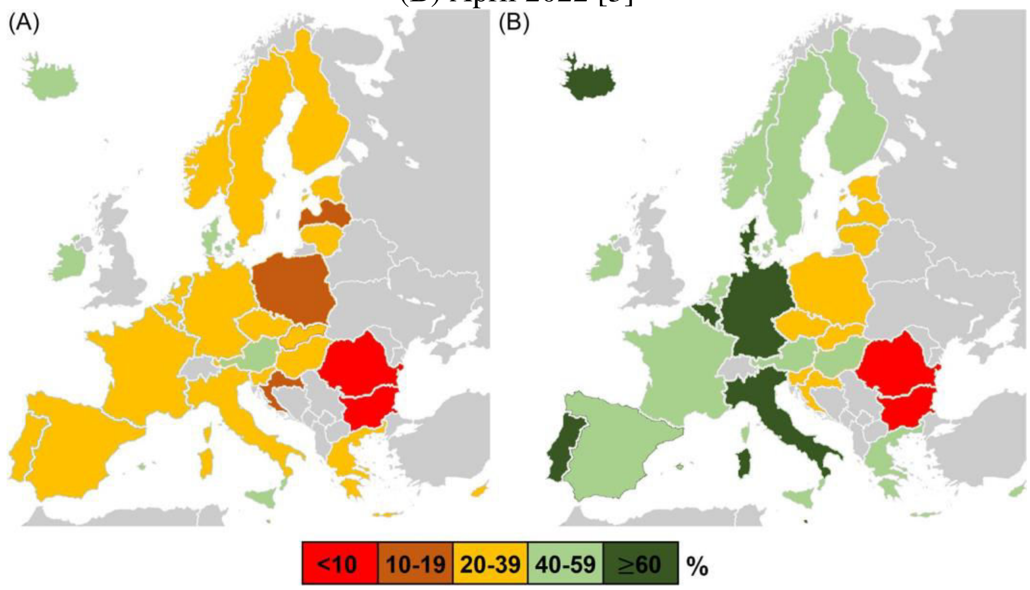
Large observational studies have confirmed significantly reduced risk of subsequent infection by more than 80% for at least 6 – 12 months in individuals with prior infection [15].

Within a study, the evidence published in the specialized literature on the effectiveness of vaccines used in preventing laboratory-confirmed SARS-CoV-2 infection and symptomatic disease was combined to estimate the duration of vaccine-induced protection against the two variants Delta and Omicron. The results were used to quantify the level of protection induced by the vaccine since the last dose.

The performed analysis highlighted the effectiveness of the primary vaccination cycles both against the symptomatic disease and against the infection with the two strains, Omicron and Delta. Vaccination efficacy (VE) against infection with the laboratory-confirmed Omicron strain is initially lower and declines more rapidly compared to the vaccination efficacy observed for the Delta strain. Consistent estimates of VE were obtained for different age segments of the population. Administration of a booster dose was associated with VE levels comparable to those obtained immediately after the primary vaccination cycle. The estimates from this study are consistent with the 125 % increase in VE against Omicron resulting from booster administration [16]. However, it was noted that 9 months after a booster, the mean VE against symptomatic disease and laboratory-confirmed Omicron infection was less than 20 % and 30 %, respectively. Other systematic reviews and meta-analyses have assessed temporal changes in VE, providing evidence of a decline in VE over time against laboratory-confirmed SARS-CoV-2 infection and symptomatic disease [17].

According to the European Center for Disease Prevention and Control (ECDC), 35 % of the EEA population has already received a booster dose of the COVID-19 vaccine by the end of 2021 [13]. However, booster programs have been met with varying reluctance in European countries, especially among young people, the main reasons against accepting booster doses of the COVID-19 vaccine including side effects experienced after previous doses, uncertainties about safety and the view that additional vaccination is not necessary. As a result, variable use of booster doses was observed in the EEA, with the highest rates, which exceeded 60 % in April 2022, observed in Belgium, Germany, Italy and Portugal, while the lowest (< 10 %) were recorded in Bulgaria and Romania **(Figure 2)** [3].

Figure 2. Proportion of people who received a booster dose of SARS-CoV-2 vaccine in different European Economic Area (EEA) countries at the beginning of (A) January 2022 and (B) April 2022 [3]



The maximum vaccination coverage advocated by public health authorities to control the pandemic had important consequences. In the shorter term of a few months, this approach facilitated a decrease in the number of infections, helped to free up hospitals and reduce mortality from COVID-19 [1].

Vaccination is still crucial because it can prevent about 90 % of illness and death from COVID-19 [18].

2.2. Post-vaccination monitoring

Post-vaccination monitoring can be achieved through two pharmacological approaches, namely pharmacovigilance and pharmacoepidemiology. Pharmacovigilance, also known as drug safety surveillance, is primarily concerned with the timely identification of new adverse drug reactions (ADRs) that are distinct in clinical nature, severity, and/or frequency. Pharmacoepidemiology deals with the study of drug administration and its associated risks in large population studies [19,20]. The FDA's Adverse Event Reporting System (FAERS) was created in the United States of America to collect adverse drug reactions from healthcare providers, patients, and pharmaceutical corporations [21]. Additionally, in Indonesia, the Food and Drug Administration (Badan Pengawas Obat dan Makanan/BPOM) monitors the safety, efficacy, and quality of COVID-19 vaccines. To guarantee compliance with the requirements, BPOM continues to supervise the implementation of clinical trials, including the acceleration of the evaluation process for the granting of approval of the clinical trial protocol (Persetujan Protokol Uji Klinik/PPUK) and subsequently the inspections that ensure that the clinical trials are conducted in accordance with the approved clinical trial protocols and the regulations on the implementation of good clinical practices (GCP). Monitoring the safety of clinical trial subjects was established by the Padjadjaran University Health Research Ethics Committee.

BPOM has implemented comprehensive inspections of vaccine production facilities to ensure that manufacturers apply Good Manufacturing Practice (GMP) standards throughout the vaccine production process, consistently starting with the manufacture of vaccine raw materials (upstream) and then vaccine formulation (downstream), to the vial filling process to obtain the final product. The evaluation process is carried out through conferences with the National Committee for Drug Evaluation, experts, and doctors from the Association of Indonesian Doctors (Ikatan Dokter Indoensia/IDI). Specifically for vaccines, conferences were held with the Indonesian Technical Advisory Group on Immunization (ITAGI) [22]. Internationally, the WHO Uppsala Monitoring Center (UMC) maintains a large database of adverse reaction reports known as "VigiBase". VigiBase is the world's unique global WHO database of Individual Case Safety Reports (ICSRs). It is the largest database of its kind in the world, with more than 25 million reports of suspected adverse drug reactions submitted by member countries of the WHO Program for International Drug Monitoring since 1968. It is constantly updated with new reports. In addition, Ontario will analyze the effectiveness of COVID-19 vaccines in relation to a variety of outcomes and subgroups of interest using ICES-linked data (eg, age group and comorbidities) [23].

3. Strategies for the prevention and control of COVID-19

The continued circulation of SARS-CoV-2 and the emergence of variants requires constant vigilance and a global mechanism to track, monitor and evaluate the evolving situation. In June 2020, WHO established an Informal Expert Group on Virus Evolution (VEWG) to specifically assess the evolution, mutations, and variants of SARS-CoV-2. This independent group of experts was formalized as the Technical Advisory Group on SARS-CoV-2 Virus Evolution (TAG-VE) and continues to meet regularly to discuss and analyze the impact of SARS-CoV-2 variants on transmissibility, clinical presentation, disease severity, diagnosis, and therapy and to determine according to WHO definitions, whether a particular variant constitutes a variant of interest (VOI) or a variant of concern (VOC). TAG-VE consists of 30 experts from the fields of genomics, epidemiology, virology, bioinformatics, health and public health policy, laboratory sciences, pharmacology, clinical management, and molecular evolution. Selected from around the world, they come from government agencies, universities, laboratories, and health systems. TAG-VE recommendations are used to inform WHO global, regional and national strategies for the prevention and control of COVID-19 and are used by other WHO advisory groups such as the Expert Advisory Group on COVID-19 Vaccine Composition (TAG-CO-VAC), the Strategic Advisory Group of Experts on Immunization (SAGE) and the Strategic and Technical Advisory Group on Infectious Hazards (STAG-IH).

As an advisory body to WHO, the main functions of TAG-VE are:

- to advise WHO on strengthening the mechanisms for identifying and prioritizing relevant (potential) SARS-CoV-2 mutations, including strengthening the global capacity to assess SARS-CoV-2 variants;
- to develop and apply a framework for analyzing and evaluating SARS-CoV-2 variants and their impact on transmissibility, disease severity, antigenicity and diagnosis or therapeutics;
- to provide periodic and updated recommendations to the WHO regarding the global characterization of VOI and SARS-CoV-2 VOCs and VOC classification;
- alerts WHO to relevant mutations/variants and advises on their potential impact on viral characteristics (eg virulence, transmission) and countermeasures (eg diagnostics, vaccines and therapies);
- WHO recommends specific investigations on the impact of specific mutations (including controlled laboratory *in vitro* and *in vivo* studies of mutants);

- advise WHO on mitigation strategies to reduce the adverse effect of SARS-CoV-2, VOI and VOC mutations that could affect viral behavior or countermeasures; and
- to advise WHO, as appropriate, on other relevant topics related to this field of activity [24,25].

Conclusions

In conclusion, it is suggested that the efficacy of COVID-19 vaccines against infection with different laboratory-confirmed strains of SARS-CoV-2 virus declines rapidly over time after the administration of primary vaccination and booster dose.

SARS-CoV-2 vaccines could reduce the risk of SARS-CoV-2 infections and effectively prevent the most severe infections and the risk of death.

The magnitude of vaccine effectiveness could vary depending on different populations, as suggested by the moderate to high effect of the vaccine.

These results may help in designing appropriate targets and timing for future vaccination programs.

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