REVIEW ARTICLE

One Year of Experience with European Union Approved Public COVID-19 Vaccination in Germany

Hari Hendarto[1], Hans Joachim Freisleben[2], Femmy Nurul Akbar[1], Chris Adhyanto[3]

[1] Department of Internal Medicine Faculty of Medicine, Universitas Islam Negeri Syarif Hidayatullah Jakarta, 15412, Ciputat, Timur, Banten, Indonesia,
[2] Regional Public Covid-19 Vaccination Centre in Eltville am Rhein, 65346, Germany,
[3] Department of Biochemistry Faculty of Medicine, Universitas Islam Negeri Syarif Hidayatullah Jakarta, 15412, Ciputat Timur, Banten, Indonesia

ABSTRACT

Various types of vaccines are being developed and tested for SARS-CoV-2. The SARS-CoV-2 genome encodes spike glycoproteins, plays essential roles in virus attachment and entry into the host cell. The surface location of the spike glycoprotein has been the main target for the development of vaccines against SARS-CoV-2 which have been proven effective in generating neutralizing. This study aim was to summarise base on vaccination activities that have been carried out after one year of Covid-19 cases taking place in Europe, especially in Germany. Many study suggests that vaccinations prevented Covid-19 infections. Study from Germany found a connection between high vaccination rates and comparatively low excess mortality. A series of vaccines based on the spike glycoprotein has been tested with clinical success and has been shown to be efficient enough to protect individuals. Among the Covid-19 vaccines applied in Germany, the two mRNA vaccines appear more effective and safer than the vector vaccines. All vaccines approved in Germany use the spike glycoprotein as the active immunogenic agent.

Keywords: Covid-19 vaccines, SARS-CoV-2, Spike glycoprotein

Corresponding Author:
Hari Hendarto, PhD
Email: hari.hendarto@uinjkt.ac.id
Tel: +62 82261656561

INTRODUCTION

According to the review by Poland et al on Covid-19 immunity, 4 structural SARS-CoV2 proteins, spike glycoprotein, envelope protein, membrane protein, and nucleocapsid protein differently, induce adaptive immune reactions (1). Three of these proteins, spike glycoprotein, membrane protein, and nucleocapsid protein have epitopes targeted by CD4+ and CD8+ T-cells, whereas the spike and nucleocapsid proteins also induce antibodies against them, and only the spike glycoprotein induces neutralizing antibodies. Envelope and membrane proteins may possibly induce antibody formation, too; but this appears still questionable (1).

Spike-proteins are responsible for the entry of viruses into host cells, but these proteins can be recognized by the immune system triggering a protective response. This is also one of the main goals of vaccines. Various types of vaccines are being developed and tested for SARS-CoV-2 based on inactivated or attenuated virus, adenovirus vectors, viral subunits, or mRNA (2). An important issue of concern to the scientific and medical community is how long the vaccine can protect us from SARS-CoV-2 and its variants (3). Table I shows the vaccines that are approved to be used in Europe and Germany. The aim was to summarise base on vaccination activities that have been carried out after one year of Covid-19 cases taking place in Europe, especially in Germany.

Comirnaty BioNTech-Pfizer

The BioNTech-Pfizer Covid-19 vaccine (ComirnatyR) was the first Covid-19 vaccine approved for marketing authorization (conditional approval) in the European Union (EU) and thus in Germany (4). Meanwhile, three distinct forms of this BioNTech-Pfizer vaccine exist, all of them in multidose vials: 1) the original concentrate for individuals 12 years and older, 2) the diluted version for 12 years and older, and 3) the concentrate for children, aged 5 to 11 years (4).

1) Comirnaty contains the concentrate for dispersion of a nucleoside modified mRNA which is indicated to be injected into individuals 12 years of age and older for active immunization to prevent COVID-19. The nanoparticles are composed of ((4-hydroxybutyl) azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate) (ALC-0315); 2-[(polyethylene glycol)-2000]-N,N-ditetradecyl acetamide (ALC-0159); 1,2-di-stearoyl-sn-glycerol-3-phosphocholine (DSPC); cholesterol and the

Table I: Vaccines approved in Europe and Germany

	Comirnaty BioN-Tech-Pfizer	Comirnaty for children	Spikevax Moderna	Vaxzervria Astrazeneca	Janssen Johnson & Johnson	Novavax
Type	mRNA	mRNA	mRNA	DNA/vector	DNA/vector	Protein subunit/ split vaccine
Immunogenically active SARS-CoV-2 component	Proline-modified, prefusion-stabilized viral spike protein	Proline-modified, prefusion-stabilized viral spike protein	Proline-modified, prefusion-stabilized viral spike protein	Spike protein	Spike protein	Recombinant full length viral prefusion spike protein
Vehicle	Liposomal/lipid nanoparticles	Liposomal/ lipid nanoparticles	Liposomal/ lipid nanoparticles	Replication deficient chimpanzee adenovirus	Replication incompetent human adenovirus serotype 26	Nano particles
Storage	9 months -75°C/ 31 days 2-8°C	9 months -75°C/ 31 days 2-8°C	-20°C/ 30 days 2-8°C	6 months 2-8°C	-20°C/3 months 2-8°C	6 months 2-8°C
	2 doses, 21 days apart	2 doses, 21 days apart	2 doses, 28 days apart	2 doses, 9-12 weeks apart	1 dose (see booster)	2 doses 4-12 weeks apart
Booster	With mRNA	With mRNA	With mRNA	With mRNA	2nd dose recommended with mRNA	?
Age	12 and older	5-11 years	30 and older	Over 65	Over 65	
Original efficacy	95% for disease, 87.5% for severe disease	95% for disease, 87.5% for severe disease	94% for disease, 100% for severe disease	64% after 1 dose, 70.4% after 2 doses	72% (USA), 66% (Latin America, 57% (South Africa)	89.7% (UK), 60% (South Africa)
Efficacy towards Omicron	Up to 58% after booster	?	78% after booster	38% after booster	?	?
Efficacy during Delta vs Omicron waves	93% during Delta wave vs 70% during Omicron wave	?	?	?	?	?

buffer system contains potassium chloride / potassium dihydrogen phosphate; sodium chloride / disodium phosphate dihydrate; sodium hydroxide / HCl (for pH adjustment); sucrose; and water for injections. The concentrate is in multidose vials with purple caps and must be diluted before use. After thawing, the concentrate in the multidose vials is diluted with 1.8 mL sterile NaCl 0.9 % with a 21-Gauge under aseptic conditions. One vial with 0.45 mL concentrate will contain 2.25 mL dispersion after dilution, sufficient for 6 doses of 0.3 mL with 30 µg of tozinameran embedded in lipid nanoparticles. Tozinameran is a single-stranded, 5'-capped messenger RNA (mRNA) produced using a cell-free in vitro transcription from the corresponding DNA templates, encoding the viral spike (S) protein of SARS-CoV-2. In order to extract 6 doses of 0.3 mL from a single vial, we use needles and syringes with a low dead-volume of 35 µL, only. Excess volume in the vial is discarded. Excess vaccine from multiple vials should never be pooled.

Long-term storage of BioNTech Comirnaty concentrate up to 9 months must be at -75°C (± 15°C). Within this time unopened vials can be stored and transported at -20°C (± 5°C) for up to 2 weeks and subsequently be stored again at -75°C (± 15°C). Transport is also possible at -75°C (± 15°C) on dry ice. The multidose vials can be thawed in the original package at 2-8°C within 3 hours and can then be stored at 2-8°C for one month. Within this period, up to 12 hours can be used for transport at 2-8°C. Single vials can be thawed at room temperature (up to 30 °C) within 30 minutes and then used within 2 hours. Afterwards, the vial must be discarded and cannot be frozen again. After dilution, physicochemical stability during usage – including transport – is up to 6 hours at 2°C to 30°C. From the microbiological point of view, the product should be used immediately (within one hour), unless the method of dilution prevents the risk of microbial contamination. For that purpose, we use a Laminar Airflow Workstation.

In our hands, we use 2 mL syringes with 21 Gauge needles for the dilution with sodium chloride 0.9% solution for injection. Injecting 1.8 mL solution into the vial increases the pressure in the vial which has to be equalized before removing the needle from the vial stopper by withdrawing 1.8 mL air into the empty diluent syringe. The diluted vaccine is gently inverted 10 times (the vial should not be shaken!) and checked by visual control that the dispersion is off-white and does not contain any particles. Then, 6 times in a row, 1-mL syringes are used for the preparation of the vaccination. Different needles are used to fill the syringes (21 Gauge) and for injection (e.g., 23 Gauge). For each candidate who is going to be vaccinated, needles for injection are adjusted (e.g., longer needles for overweight candidates). Generally, ComirnatyR is administered by intramuscular injection into the deltoid muscle of the upper arm. The amount of 30 µg per dose is officially approved for individuals of 12 years of age and older. A second dose of 30 µg should be administered 3 weeks after the first dose and a third dose at least 3 months after the second dose. Severely immunocompromised individuals may receive a third dose of ComirnatyR earlier, at least 28 days after the second dose. No dose adjustment is required in the elderly of 65 years or older.

2) Comirnaty dispersion contains the dispersion of a nucleoside modified mRNA ready for injection to individuals 12 years of age and older for active immunization to prevent COVID-19 caused by the SARS-CoV-2 virus. The multidose vial of 2.25 mL

dispersion for six doses of 0.3 mL containing 30 µg/dose of tozinameran, a COVID-19 mRNA Vaccine (embedded in lipid nanoparticles). This dispersion in multidose vials with grey caps should not be diluted. The lipid nanoparticles are composed of ((4-hydroxybutyl) azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate) (ALC-0315); 2-[(polyethylene glycol)-2000]-N,N-di-tetradecyl acetamide (ALC-0159); 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC); Cholesterol; and the buffer system contains trometamol / trometamol HCl, sucrose, and water for injections. Unopened frozen vials can be stored for 9 months at -75°C (± 15°C). Thawed unopened vials can be stored and transported for 10 weeks at 2-8°C. If the vaccine is delivered at 2-8°C, it should be stored at this temperature. It cannot be frozen again without damaging the nanoparticles and mRNA. If the multidose vial is stored frozen it must be thawed prior to use.

3) Comirnaty 10 µg/dose concentrate for dispersion a paediatric formulation available for children 5 years to less than 12 years of age. After thawing, the concentrate in the multidose vials (with orange caps) is diluted with 1.3 mL sterile NaCl 0.9 % with a 21-Gauge cannula under aseptic conditions. After dilution the vials contain 10 doses of 0.2 mL, each, with 10 µg of tozinameran, a COVID-19-mRNA-vaccine embedded in lipid nanoparticles. The lipid nanoparticles are composed of ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl) bis(2-hexyldecanoate) (ALC-0315); 2-[(polyethylene glycol)-2000]-N,N-di-tetradecyl acetamide (ALC-0159); 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC); cholesterol and the buffer system contains trometamol / trometamol HCl, sucrose, and water for injections.

Contraindication towards the BioNTech-Pfizer vaccine is the hypersensitivity to the active substance or to any of these components. Unopened frozen vials can be stored for 9 months at -75°C (± 15°C). Within the 9-month shelf-life, thawed vials can be stored and transported at 2 - 8 °C. Expiry dates must be adjusted accordingly. Prior to use, unopened vials can be stored for up to 12 hours at room temperatures between 8 and 30°C. Thawed vials should not be re-frozen.

Spikevax Moderna

A multidose vial of Spikevax dispersion for injection COVID-19 mRNA vaccine contains 10 full-doses of 0.5 mL each or a maximum of 20 half-doses of 0.25 mL each. One full-dose of 0.5 mL contains 100 µg of messenger RNA, one half-dose of 0.25 mL contains 50 µg of mRNA embedded in SM-102 lipid nanoparticles. The single-stranded, 5'-capped mRNA is produced using a cell-free in-vitro transcription from the corresponding DNA templates, encoding the viral spike glycoprotein (S) of SARS-CoV-2 (2). The lipid nanoparticles contain lipid SM-102 (heptadecan-9-yl 8-{(2-hydroxyethyl)[6-oxo-6-(undecyloxy)hexyl]amino}octanoate); cholesterol; 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC); 1,2-Dimyristoyl-rac-glycerol-3-methoxy polyethylene glycol-2000 (PEG2000 DMG) and the buffer system is composed of trometamol / trometamol HCL; acetic acid / sodium acetate trihydrate, sucrose, and water for injections (4).

Spikevax Moderna vaccine can be stored at -20°C (± 5°C) for up to 9 months. Once thawed, unopened vials can be stored at 2-8°C for 30 days or at room temperature of 8-25°C for 24 hours. After the first puncture, physicochemical stability of the vaccine in the vial was shown for 19 hours. Because of the risk of contamination, we generally inject prepared ready-to-use syringes within one hour, intramuscularly. Besides reactions, which are known from other vaccinations (like fever, dizziness or aching at the injection site) rare cases of Bell's palsy and myocarditis or pericarditis (5) have been observed after vaccination in our centre. There was one case of anaphylaxis obviously because of unknown hypersensitivity towards PEG2000 DMG.

Vaxzevria AstraZeneca-Oxford

Replication incompetent adenoviruses are widely used as vaccine vectors (6), a Chimpanzee Adenovirus in the case of the AstraZeneca vaccine. The multidose vials contain 10 or 11 full doses of 0.5 mL vaccine. One dose of 0.5 mL contains "not less than 2.5 Ч 108 infectious units (Inf.U) of the Chimpanzee Adenovirus encoding the SARS-CoV-2 Spike glycoprotein (ChAdOx1-S) produced in the genetically modified human embryonic kidney (HEK) 293 cells and by recombinant DNA technology" (4).

In our hands, Vaxzevria showed more reactions and side effects than the mRNA vaccines. Until June 2021, we applied Vaxzevria routinely, afterward only in single cases for the elderly who asked for this vaccine. Venous thrombotic embolism was reported in rare or very rare cases, cerebral sinus venous thrombosis, and immune thrombo-cytopenia, in some cases with capillary leak syndrome in younger individuals under the age of 60 years (7).

Covid-19 vaccine Janssen – Johnson &Johnson

The multi-dose vials with 5 doses of 0.5 mL Ad26.COV2-S contains human Adenovirus serotype 26 "not less than 8.92 log10 infectious units (Inf.U) encoding the SARS-CoV-2 spike glycoprotein produced in the PER.C6 TetR Cell Line and by recombinant DNA technology" (4). The approval in Europe is still for only one dose; however, we experienced low immunity and it is now recommended to apply a second dose for immunization, preferentially with mRNA vaccine BioNTech or Moderna. Side effects of the Covid-19 vaccine Janssen are similar to those observed with the AstraZeneca vaccine.

Covid-19 vaccine Novavax - NuvaxovidR

The Novavax vaccine is the only protein vaccine containing the recombinant spike glycoprotein of SARS-CoV-2. We do not yet have any experience with this vaccine in Germany, since this vaccine – albeit already approved by EMA – has not yet been delivered to the German market.

The official information about this vaccine says: One dose of 0.5 mL contains 5 µg of the of SARS-CoV-2 spike protein produced by recombinant DNA technology using a Baculovirus expression system in an insect cell line that is derived from Sf9 cells of the Spodoptera frugiperda species. In addition, one dose contains an adjuvant "Matrix-M", 42.5 µg fraction-A and 7.5 µg fraction-C of Quillaja saponaria Molina extract (4).

DISCUSSION

Vaccines reduce the risk of COVID-19, including the risk of severe illness and death among fully vaccinated people. In addition to data from clinical trials, evidence from real-world vaccine effectiveness studies suggested that the COVID-19 vaccine helps protect against COVID-19 infection, with or without symptoms (asymptomatic infection). The effectiveness of the vaccine against hospitalization has remained relatively high over time, although it tends to be slightly lower for older adults and for people with weakened immune systems.

Currently, a vaccine for Covid-19 is underway in order to prevent severe illness, hospitalization, and death. Research on vaccines is still being improved, especially in protection against new variants of Covid-19. The emergence of several highly contagious variants of SARS-CoV-2 is a new challenge for current vaccines. SARS-CoV-2 mutations are common, these mutants are not considered new strains, but simply variants, and they represent concerns regarding the effectiveness of the current vaccine. So far approved vaccines protect us against infection, but questions still remain about the effectiveness of the vaccines currently in use against new variants.

Since glycoprotein S plays an important role in viral entry into host cells, it has been the main target of many vaccines because antibodies to this protein block viral entry, thus inhibiting viral replication. This is the basis for the development of a vaccine against SARS-CoV-2 targeting glycoprotein S, which aims to induce neutralizing antibodies (nAbs). The development of nucleic acid-based vaccines for Spike glycoproteins is one method of using vaccines because they can be produced quickly so that they are a good alternative for rapid response to pandemics. However, nucleic acid-based vaccines require a carrier factor for the vaccine to work properly. On the other hand, the development of whole glycoprotein S-based vaccines has also been developed, with the aim of trying to maintain the original structural characteristics and induce a strong immune response that protects the individual against possible infection from the original virus.

The four vaccines can be put into 3 groups: 1) mRNA vaccines in lipid nanoparticles, 2) vector vaccines containing DNA, and 3) recombinant subunit protein vaccines. The mRNA vaccines use the muscle cells in the vicinity of the injection including dendritic cells to produce the protein encoded by the respective messenger RNA. This process involves the endoplasmic reticulum (ER) and further cytoplasmic, especially ribosomal instrumentation of these cells, but does not involve their nuclei (8).

It is important to point out that the material of the vaccine does not enter the nucleus and thus cannot be incorporated into the cell's gens. Some people in Germany are afraid of genetic manipulation by the mRNA vaccine, but the mode of action clearly rules out the possibility of reverse transcription as it is the case in HIV infection, or via similar mechanisms. The vehicle by which RNA is transported into the cells is on a liposomal basis. The lipid nanoparticles have been developed from liposome technology. A variety of lipids have been used for vaccine delivery systems (9,10). Some of them had been shown to have adjuvant properties (11). Lipids are not typically immunogenic by themselves. However, derivatives as for instance glycolipids may become immunogenic, especially if they have longer the polysaccharide chains.

Polyethylene (PEG) derivatives had been developed for so-called "stealth liposomes", PEGylated lipids (12). Although these lipids are intended to sneak lipid particles through our immune system, there are some individuals who may react allergically to them. Such PEGylated lipid is also used in the lipid nanoparticles that transport mRNA into the muscle cells, for instance PEG-myristoyl-phosphatidylcholine. This may be the reason, why very few people with PEG allergies show allergic reactions towards mRNA vaccines. However, allergic reactions have seldomly been seen in our immunisation campaign. The picture is somewhat different with vector vaccines, Vaxzevria AstraZeneca-Oxford and Janssen-Johnson&Johnson (Janssen J&J). The surface of Adenoviruses is strongly immunogenic. The vehicle itself induces immune reactions which may not necessarily be adjuvant to anti-SARS-CoV-2 immunity.

The immunogenicity of the vector may be the reason why we see stronger reactions and more side effects with these vaccines than with mRNA lipid nanoparticles. On the other hand, the combination of adenoviral vector and DNA is more stable than mRNA in lipid nanoparticles, which makes the storage and handling of the vaccines easier. Because of more specific side effects, the vaccines

have finally been differentiated: for example, because of very rare cerebral thrombotic events especially in younger women vector vaccines (AstraZeneca and Janssen J&J) are not recommended for young women any more. Similarly, slightly more frequent myocarditis and pericarditis events by Spikevax Moderna than by Comirnaty Biontech in younger individuals led to the recommendation of Comirnaty Biontech vaccine for individuals under the age of 30 years (Table II). Hence, in Germany nowadays, only elderly over 60 years of age are injected with vector vaccines and younger individuals under the age of 30 years are only vaccinated with Comirnaty Biontech (Table II).

Vaccination, in general, and of course, in particular against SARS-CoV-2 has several aims, firstly to impede infection, secondly to reduce hospitalization, thirdly to avoid the severe course of the disease with the need for ICU and ECMO, and last but not least to avoid deaths caused by the disease i.e. increased or excess mortality. The Ernst-Abbe-University of Applied Sciences Jena, Germany, conducted a study on the correlation between vaccination rate and excess mortality across all German States as shown in figure 1 (13). The background of this study was a great variation in vaccination rates in the 16 German States (three of which are City-States; Berlin, Hamburg, and Bremen) (13). In our context, it may not be important to understand the details within each of the states, but to see the general picture: whereas the City-State of Bremen had the highest vaccination rate of over 80% and excess mortality of 1.4% during the survey period, there were other States below 65% vaccination rate (Brandenburg, Saxony, Thuringia) with excess mortality around 15%, Thuringia highest with 16.5%. The majority of seven States had vaccination rates between 65% and 70% and a range of excess mortality between 5.4% and 12.2%, whereas States with vaccination rates from 71% to 75.6% (5 States) had excess mortality rates from 4.4% to 5.2%. From these results, a strong correlation between vaccination rates

Table II: Current official vaccination recommendations in German

Age		**Full immunisation/optimizing Janssen J&J**		**Booster**	**Minimum interval to the 2nd dosage**
	1st Imunisation	2nd immunisation	Interval	3rd immunisation	
5-11 years	Comirnaty 10 µg/0.2 mL	Comirnaty 10 µg/0.2 mL	3-6 weeks		**3 Months**
12-29 years	Comirnaty 30 µg/0.3 mL	Comirnaty 30 µg/0.3 mL	3-6 weeks	Comirnaty 30 µg/0.3 mL	
>30-59 years	Comirnaty 30 µg/0.3 mL	Comirnaty 30 µg/0.3 mL	3-6 weeks	Spikevax 0.25 mL or Comirnaty 0.3 mL (<30 years of age)	
	Spikevax 0.5 mL	Spikevax 0.5 mL	Minimum 4 weeks		
>60 years, not recommended <60; only <60, when already started before	Vaxzevria	Vaxzevria	Minimum 4 weeks	Spikevax 0.25 mL or Comirnaty 0.3 mL (<30 years of age)	
	Janssen J&J	Janssen J&J			
	Vaxzervria or Janssen J&J	Spikevax 0.5 mL	Minimum 4 weeks	Spikevax 0.25 mL	
		Comirnaty 0.3 mL	3-6 weeks	Comirnaty 0.3 mL	
Pregnant women from 2nd trimester	Comirnaty 30 µg/0.3 mL	Comirnaty 30 µg/0.3 mL	3-6 weeks	Comirnaty 30 µg/0.3 mL	
5-11 years with severe ID	Comirnaty 10 µg/0.2 mL	Comirnaty 10 µg/0.2 mL	3-6 weeks	Comirnaty 10 µg/0.2 mL	
>12 years with severe ID	Comirnaty 0.3 mL <30 years	Comirnaty 0.3 mL <30 years	3-6 weeks	Comirnaty 0.3 mL (<30 years) or Spikevax 0.25 mL (>30 years)	Minimum 4 weeks
	Spikevax 0.5 mL	Spikevax 0.5 mL	Minimum 4 weeks		
Chemotherapy should start 2 weeks after immunisation					
All individuals who received vaccines which are not approved in EU should obtain new full immunisation with an EU-approved vaccine			Minimum 4 weeks	Spikevax 0.25 mL or Comirnaty 0.3 mL (<30 years)	**3 Months**
Individuals who recovered from COVID-19					
1st event	2nd event	Full immunisation	Interval	Booster >18 years	Minimum interval to the 2nd dosage **3 months**
COVID-19 infection	-/-	Comirnaty 0.3 mL (<30 years) or Spikevax 0.5 mL (>30 years)	Minimum 4 weeks after end of COVID-19 symptoms	Comirnaty 0.3 mL (<30 years) or Spikevax 0.25 mL (>30 years)	
1st immunisation	COVID-19 infection <4 weeks after immunisation				
COVID-19 infection with ID	Comirnaty 0.3 mL	Comirnaty 0.3 mL	3-6 weeks		
	Spikevax 0.5 mL	Spikevax 0.5 mL	Minimum 4 weeks		
One immunisation dose	COVID-19 infection >4 weeks after immunisation	No further basic immunisation recommended			
Full immunisation	COVID-19 infection				
Booster <18 yrs only recommended if ID (not severe) or at high professional exposition				Comirnaty	

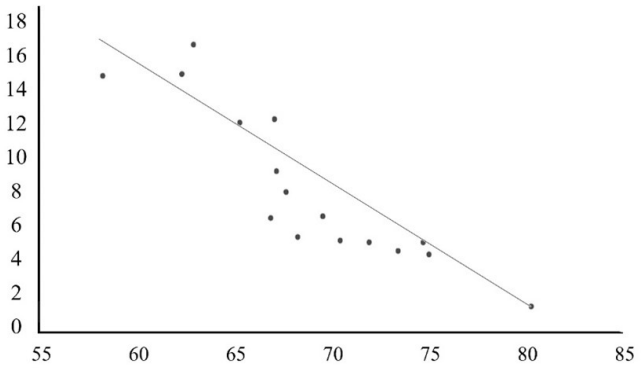

Figure I: Vaccination Rate (VR) vs. Excess Mortality (EM) in the 16 German States

[VR%/EM%]: Saxony 58.7/14.7; Brandenburg 62.8/14.7; Thuringia 63.4/16.5; Saxony-Anhalt 65.8/12.0; Baden-Wuerttemberg 67.4/6.5; Mecklenburg-Vorpommern 67.6/12.2; Bavaria 67.7/9.2; Hesse 68.2/8.0; Rhineland-Palatinate 68.8/5.4; Berlin 70.1/6.6; Lower Saxony 71.0/5.2; North Rhine-Westphalia 72.5/5.1; Schleswig-Holstein 74.0/4.6; Hamburg 75.3/5.1; Saarland 75.6/4.4; Bremen 80.9/1.4. Highly significant negative correlation rate of -0.88 or -0.89, according to the mode of calculation. [Data from Ernst-Abbe University of Applied Sciences Jena published in Deutsches Aerzteblatt/de, 27.09.22. (The presentation used here is translated and modified from the original publication in German).

and excess mortality was claimed: a highly significant negative correlation rate of -0.88 or -0.89, according to the mode of calculation (figure 1).

The new Omicron variant may be more contagious but less pathogenic than former mutants of SARS-CoV-2, especially the Delta variant (14,15). Hospital admission appears reduced up to 65% and ICU admission with severe Covid-19 or even death up to 83%. Boosters with mRNA vaccines appear to have some protection against Omicron (16-18). Furthermore, vaccines adapted versus Omicron are under investigation and expected in the market for spring 2022.

CONCLUSION

In Germany, 74.9% of the population obtained at least one vaccination dose; 72.5% two doses, and 54.2 three doses. Amongst >60 years of age, 88.4% have got one dose; 87.7% two doses, and 68.6% three doses. Children and youngsters <18 years of age 61.6% obtained one dose; 55.9% two doses, and 11.6% three doses. In total, these immunisation rates do not appear sufficient for successful herd immunity in the case of SARS-CoV-2 pandemic. The intended immunisation rate of at least 80% was only reached in the German City-State of Bremen resulting in excess mortality of only 1.4%, whereas lower vaccination rates in the other States showed up to more than 10-fold higher excess mortality. Among the Covid-19 vaccines applied in Germany, the two mRNA vaccines appear more effective and safer than the vector vaccines.

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