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Increasing Influenza Vaccination Coverage in Healthcare Workers

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List of Abbreviations

COVID-19	Coronavirus Disease 2019
CDC	Centers for Disease Control and Prevention
CVS	Central vaccination site
ECDC	European Centre for Disease Prevention and Control
EMA	European Medicines Agency
EU	European Union
FDA	Food and Drug Administration
GISRS	Global Influenza Surveillance and Response System
HA	Hemagglutinin
HCW	Healthcare workers
MVE	Mass vaccination event
MVT	Mobile vaccination team
min	Minutes
mRNA	Messenger ribonucleic acid
NA	Neuraminidase
OH	Occupational health department
OKaPII	Online-Befragung von Krankenhaus-Personal zur Influenza-Impfung
OSV	On-site vaccination
PCR	Polymerase chain reaction
PEI	Paul-Ehrlich-Institute
PDSA	Plan-do-study-act
RKI	Robert Koch Institute
RNA	Ribonucleic acid
RT-PCR	Reverse transcriptase-polymerase chain reaction
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
UK	United Kingdom
US	United States

USA	United States of America
WHO	World Health Organization

1. Zusammenfassung

Influenza wird durch Influenzaviren verursacht und präsentiert sich als akute Atemwegsinfektion. Insbesondere Kinder, ältere Menschen, Personen mit chronischen Grunderkrankungen einschließlich Immunsuppression und Schwangere können einen komplizierten Verlauf, häufig gekennzeichnet durch eine Lungenentzündung, einer Influenza-Erkrankung erleiden. Für diese Risikogruppen wird eine jährliche Influenza-Impfung empfohlen. Darüber hinaus ist die Influenza-Impfung für medizinisches Personal indiziert, da sie einem erhöhten Infektionsrisiko ausgesetzt sind, was zu nosokomialer Infektionsübertragung auf Patienten sowie Fehlzeiten am Arbeitsplatz führen kann. Trotz dieser Empfehlung liegt die Influenza-Impfquote bei medizinischem Personal in vielen europäischen Ländern weiterhin unter dem von der Europäischen Union und der Weltgesundheitsorganisation festgelegten Gesamtimpfziel von 75%.

Während der ersten Influenzasaison 2020/21, die mit der Coronavirus-Krankheit 2019 (COVID - 19) zusammenfiel, bestand das Risiko einer zu hohen Belastung des Gesundheitssystems durch Atemwegserkrankungen. Diese Situation unterstrich die Notwendigkeit, die Influenza-Impfquoten von Gesundheitspersonal zu erhöhen. Das Ziel unseres Forschungsprojekts war es, auf Grundlage unserer Literaturrecherche die intensivierte Influenzaimpfkampagne 2020/21 für medizinisches Personal der Universitätsklinik Köln bezüglich erreichter Influenza-Impfquote im Vergleich zu Vorjahren zu analysieren.

Unser Review-Artikel zu Strategien für Influenza-Impfkampagnen für Beschäftigte im Gesundheitswesen zeigte, dass mögliche Strategien eine Informations-/Werbekampagne, eine verbesserte Organisation, Anreize zur Impfung oder Vorschriften umfassen. Durch Informations-/Werbekampagnen und organisatorische Strategien, wie etwa die Impfung direkt am Arbeitsplatz, konnten relative Erhöhungen der Impfquoten beobachtet werden, die jedoch selten zu einer Gesamtimpfquote von über 40% führten. Hingegen führten Vorschriften wie „Impfen-oder-Maske-tragen“, die obligatorische schriftliche Ablehnung der Impfung, oder Impfmandate zu einer Gesamtimpfquote von über 75% (oft >90%), die über mehrere Jahre aufrechterhalten werden konnten. Wenn Vorschriften nicht umsetzbar sind, sollten Kampagnen daher die übrigen Strategien kombinieren und insbesondere organisatorische Maßnahmen ausgeschöpft werden.

In Anlehnung an diese Erkenntnisse umfasste die Influenzaimpfkampagne 2020/21 an der Universitätsklinik Köln eine Informations-/Werbekampagne und konzentrierte sich auf organisatorische Strategien. Es wurde ein Mobiles Impfteam gebildet, das Impfungen vor Ort auf Stationen und in Instituten anbot, Impfungen ohne Terminvereinbarung an einem zentralen Ort ermöglichte und zusätzliche Impfaktionen durchführte. Zusätzlich bestand weiterhin die

Möglichkeit die Influenza-Impfung bei dem Betriebsärztlichen Dienst zu erhalten. Die Werbekampagne umfasste ein einheitliches Kampagnendesign, Intranet-Präsenz, E-Mails, Aufklärungsvideos, eine Flashmob-Aktion mit der Verteilung von Fahrradsattelbezügen mit Kampagnenlogo und die Veröffentlichung von Fotos geimpfter Personen in der Pose des Kampagnenlogos. Im Anschluss an die Kampagne wurde eine Umfrage durchgeführt, in der unter anderem die Auswirkung der COVID-19-Pandemie auf die Influenza-Impfmotivation analysiert wurde.

Die Influenzaimpfkampagne 2020/21 startete im September, sobald der Impfstoff zur Verfügung stand und dauerte bis Ende Dezember an. Zwischen Mitte Oktober und Mitte November kam es zu Influenza-Impfstoff-Lieferengpässen, was eine Reduktion des Impfangebots an der zentralen Impfstelle nötig machte.

Die Influenzaimpfkampagne 2020/21 führte zu einem signifikanten ($p < 0.001$) Anstieg der Gesamtimpfquote um das 2,4-fache von 17% (2465/14 505) in 2019/20 auf 40% (6048/15 290) in 2020/21. Ein signifikanter Anstieg der Impfquoten war in allen Berufsgruppen zu beobachten. Die höchste Gesamtimpfquote wurde bei ärztlichem Personal erzielt (81%, 1215/1505, Verdopplung). Der höchste relative Anstieg (7,7-fach) wurde bei Wissenschaftlichen Personal gezeigt (69% Impfquote, 675/981). Bei Pflegekräften, einer vorab festgelegten Zielgruppe mit üblicherweise niedrigen Influenza-Impfquoten, stieg die Quote um das 2,7-fache auf 48% (1060/2215). In der Berufsgruppe Verwaltung wurde eine Impfquote von 62% (542/872, 1,3-fache Erhöhung), im Funktionsdienst (definiert als Labortechnisches Personal, Medizintechnisches Personal, Patientenservice) 35% (1080/3072, 2,3-fache Erhöhung), unter Studierenden/Auszubildenden/Praktikanten 22% (1023/4717, 4,4-fache Erhöhung) und in Tochterfirmen 16% (295/1897, 3,2-fache Erhöhung) erreicht.

Das Mobile Impfteam führte 67% (4071/6048) aller Impfungen durch. Bezüglich der möglichen Impfoptionen wurden 33% beim Betriebsärztlichen Dienst, 31% am Arbeitsplatz vor Ort und 30% in der zentralen Impfstelle durchgeführt, was darauf hindeutet, dass die Vielfalt der Angebote vorteilhaft war. In der letzten Phase der Kampagne wurden vier Impfaktionen für Medizinstudierende veranstaltet, was zu 6% aller durchgeführten Impfungen führte. Eine weitere Analyse der Zielgruppe Pflegepersonal zeigte eine Präferenz für Impfungen an festen Standorten (34% zentrale Impfstelle, 31% Betriebsärztlicher Dienst), im Gegensatz zu Impfungen vor Ort auf den Stationen (24%) oder extern (10%, z. B. in der hausärztlichen Praxis).

Die Umfrage ergab eine selbstberichtete Impfquote von 73% (2413/3327), von denen 13% (318/2413) angaben, die Impfung extern erhalten zu haben. Fast ein Drittel (29%) der Geimpften gab an, dass die Influenza-Impfung 2020/21 ihre erste Influenza-Impfung überhaupt oder die erste seit langer Zeit (d.h. seit über zehn Jahren) war. Die höchste Rate an Erstgeimpften wurde bei Forschungspersonal und Mitarbeitenden der Tochterfirmen festgestellt (38%, bzw. 37%), während die niedrigste Rate beim ärztlichen Personal zu verzeichnen war (11%). Von allen Erstimpflingen gaben 72% an, dass die COVID-19-Pandemie die Impfbereitschaft erhöht habe und 60%, dass die Kampagne ihre Bereitschaft zur Impfung positiv beeinflusst habe. Insbesondere unter erstmalig Geimpften im Pflegepersonal gab die Mehrheit (78%) an, dass die COVID-19-Pandemie ihre Impfmotivation erhöht habe. Unter allen bereits zuvor Geimpften bestätigten 30%, die COVID-19-Pandemie habe ihre Impfentscheidung positiv beeinflusst, während 40% angaben, die Kampagne habe ihre Impfbereitschaft erhöht. Diese Ergebnisse deuten darauf hin, dass die COVID-19-Pandemie die Influenza-Impfbereitschaft insbesondere bei Erstimpflingen positiv beeinflusst hat.

Die Analyse der Influenzasaisons vor der COVID-19-Pandemie ergab insgesamt geringe Impfquoten (2017/18: 11%, 1514/14 272; 2018/19: 16%, 2289/14 224; 2019/20: 17%, 2465/14 505). Vor 2020/21 wurde die höchste Impfquote in der Verwaltung (2017/18: 22%, 2018/19: 52%, 2019/20: 46%) und bei ärztlichem Personal (2017/18: 38%, 2018/19: 52%, 2019/20: 41%) beobachtet. Mit Ausnahme von Pflegepersonal in 2018/19 (21% Impfquote), erreichten die übrigen Berufsgruppen zwischen 2017/18 und 2019/20 keine Impfquoten von mehr als 20%.

Obwohl das Ziel der Impfquote von 75% in der Influenzaimpfkampagne 2020/21 nicht erreicht wurde, hat unsere Untersuchung gezeigt, dass durch die Umsetzung organisatorischer Strategien aufbauend auf einer Informations-/Werbekampagne eine signifikante Steigerung der Influenza-Impfquote in allen Berufsgruppe des medizinischen Personals erreicht werden konnte. Darüber hinaus zeigt unsere Studie mögliche Strategien, wie eine große Anzahl von Gesundheitspersonal in einer Pandemie geimpft werden kann.

Summary

Influenza disease is caused by influenza viruses and presents as an acute respiratory infection. Especially in children, the elderly, persons with underlying chronic disease including immunosuppression and during pregnancy influenza disease can be severe due to complications, often characterized by pneumonia. Annual influenza vaccination is recommended for these populations at risk. Furthermore, influenza vaccination is indicated for healthcare workers due to the higher risk of infection leading to possible nosocomial infection transmission to patients as well as work absenteeism. Despite this recommendation influenza vaccination coverage in healthcare workers remains off the 75% overall vaccination coverage target set by the European Union in alignment with the World Health Organization in many European countries.

In 2020/21 the concern of the first influenza season coinciding with the Coronavirus Disease 2019 (COVID-19) pandemic possibly leading to high respiratory disease burden emphasized the need to increase influenza vaccination coverage in healthcare workers. The aim of our research project was to analyze the intensified influenza vaccination campaign for healthcare workers at the University Hospital of Cologne in 2020/21 based on findings of our literature review in comparison to prior seasons.

Our review on influenza vaccination campaign strategies for healthcare workers showed that possible strategies include education/promotion, organization, incentives and mandates. If campaigns comprise education/promotion and organizational strategies such as on-site vaccination a substantial relative increase in vaccination coverage can be observed but rarely exceeds 40% overall coverage. In contrast, policies such as vaccinate-or-wear-a-mask, mandatory declination or vaccine mandates lead to exceeding 75% (often >90%) overall vaccination coverage which can be sustained over multiple years. If policies are infeasible, campaigns must therefore combine remaining strategies and exhaust organizational measures.

Building on these findings, the influenza vaccination campaign 2020/21 at the University Hospital of Cologne comprised educational and promotional elements and focused on organizational measures. Neither incentives nor mandates were used. A mobile vaccination team conducting vaccinations on-site at wards and institutions, walk-in vaccinations at an easily accessible central vaccination site as well as four mass vaccination events was formed. Additionally, the preexisting option to receive influenza vaccination at the occupational health department was possible. Promotion and education included a concurrent campaign design, intranet presence, e-mails to staff, educational videos, a flash-mob distribution of bicycle saddle covers depicting the campaign logo and vaccinated personnel were portrayed in poses

replicating the campaign logo on. Following the campaign a survey was performed analyzing, among others, the impact of the COVID-19 pandemic on influenza vaccination motivation.

The influenza vaccination campaign 2020/21 led to a significant 2.4-fold increase ($p < 0.001$) in overall vaccination coverage from 17% (2465/14 505) in 2019/20 to 40% (6048/15 290) in 2020/21. A significant increase in vaccination coverage was observed across all professional fields. Highest overall vaccination coverage (81%) was yielded in physicians (1215/1505, twofold increase). Highest relative increase (7.7-fold) was observed in research personnel (69% overall vaccination coverage, 675/981). Among nurses, a predetermined target group due to commonly low vaccination rates, coverage increased 2.7-fold, resulting in 48% (1060/2215).

The mobile vaccination team performed 67% (4071/6048) of all vaccinations. Regarding vaccination site distribution, 33% of vaccinations were conducted at the occupational health department, 31% on-site and 30% at the central vaccination site, suggesting that the variety of options was advantageous. During the last phase of the campaign four mass vaccination events directed at medical students led to 6% of all vaccinations, emphasizing their efficiency. Further analysis of the target group nursing staff suggested preference for vaccination at fixed sites (34% central vaccination site, 31% occupational health department) versus on-site at wards (24%) and even less so externally (10%, as in at their general health practitioner).

Almost a third (29%) of vaccinees reported the 2020/21 influenza vaccination being their first ever or in a long time (as defined by over ten years) influenza vaccination. Highest rate of first time vaccinees was found in research personnel and subsidiary company employees (38% and 37%, respectively), compared to lowest rate in physicians (11%). Out of all first time vaccinees, 72% affirmed the COVID-19 pandemic and 60% affirmed the conduct of our campaign positively influenced vaccination decision. Especially among first time influenza vaccinees in nursing staff, a majority (78%) reported a positive impact of the COVID-19 pandemic on vaccination decision.

Analysis of pre-COVID-19-pandemic influenza seasons showed low vaccination coverage overall (2017/18: 11%, 1514/14 272; 2018/19: 16%, 2289/14 224; 2019/20: 17%, 2465/14 505). Prior to 2020/21, highest overall vaccination rate was observed in administration staff (2017/18: 22%, 2018/19: 52%, 2019/20: 46%) and physicians (2017/18: 38%, 2018/19: 52%, 2019/20: 41%). The remaining professional fields did not exceed and maintain 20% vaccination coverage between 2017/18 and 2019/20.

Although the 75% vaccination coverage target was not met in the 2020/21 campaign, our research demonstrated a significant increase in influenza vaccination coverage across all healthcare worker professional fields can be attained by implementing intensified organizational strategies building on education and promotion. Furthermore, our study outlines a strategy on how to vaccinate large numbers of healthcare workers in a pandemic setting.

2. Introduction

2.1. Influenza

The origin of the word “influenza” is thought to stem from Italian “influenza di freddo”, meaning the influence of the cold. This term was likely first used in 1743.[1] Other authors suggest that the term may be older and date back to a time when illnesses were believed to arise due to the influence of planetary alignments, as in “the influence of the stars”.[2] Though the origin of the term “influenza” may be unknown, the name remains appropriate as influenza still has a great influence on the world to this day.

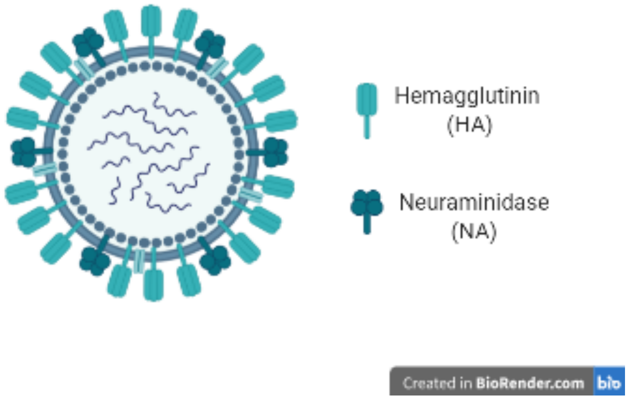
2.1.1. Influenza virus

The influenza virus is a ribonucleic acid (RNA) virus belonging to the family of Orthomyxoviridae. Influenza viruses are categorized into four types: A, B, C and D. Out of these four types, influenza type A and B are the most relevant for humans. Influenza type C is less common and usually causes only mild influenza disease in humans. Influenza type D concerns cattle and is not known to infect humans.[3,4] Influenza virus type A can further be classified regarding the surface proteins hemagglutinin (HA) and neuraminidase (NA) (Figure 1). Concerning HA, 18 types are known, while 9 NA types are known. New influenza A strains can emerge through antigen drift and antigen shift.[4] Antigen drift entails point mutations in the viral genome which lead to minor changes in viral epitopes. Mutations occur regularly due to lacking proofreading mechanisms during the viral replication cycle. These epitope-altering mutations can impact the glycoproteins of HA and NA.[5] Antigen shift, on the other hand, can alter and completely change HA and NA. Since the influenza virus genome is segmented, these segments can be exchanged when two different influenza viruses infect one host cell. This causes reassortment and antigen shift which can then lead to new influenza viruses emerging.[6] Due to the lack of immunity towards new influenza strains, the severity and transmission rate increases, possibly causing new epidemics or even pandemics.[5] Influenza virus type B is not further classified regarding surface proteins, but rather in lineages. Two genetically different lineages circulated worldwide: B/Yamagata and B/Victoria. Since 2020 only influenza viruses type B of Victoria lineage have been detected, therefore B/Yamagata is considered to be extinct.[4]

Influenza is further classified regarding the timing and extent. Seasonal influenza occurs annually. When new influenza strains emerge, pandemic influenza can occur.[3]

For seasonal influenza the hosts are humans. Regarding zoonotic influenza such as avian or swine influenza, humans are not the natural hosts. However, zoonotic influenza can infect humans. In South East Asia, avian influenza A(H5N1) emerged in 2003 and continues, among other avian influenza viruses, to be of threat to humans.[7,8]

Figure 1. Influenza virus with surface proteins hemagglutinin and neuraminidase



2.1.2. Influenza disease

Influenza is a highly contagious disease commonly transmitted through droplets and smear. Droplets (particles larger than 5µm) from coughing and sneezing of infected individuals can come into contact with mucous membranes, thereby transmitting the disease. Transmission is also possible through touching of surfaces or handshaking and subsequent touching of mucous membranes such as mouth and nose or the eyes.[4] Influenza can further be transmitted via aerosols (particles smaller than 5µm).[9]

Incubation time is short, ranging from one to two days. During this period transmission of influenza is already possible.[4]

Influenza disease is characterized by a sudden onset of cough, fever, headache, muscle ache and sore throat. Further symptoms are general malaise, rhinorrhea, sweating or, less commonly, diarrhea, nausea and vomiting. Typically, these symptoms last up to seven days. Of note, the severity of symptoms varies greatly between individuals. Mild symptoms to severe illness and even death is possible.[3] Pauci- and asymptomatic influenza cases are possible as well.[10]

Complications can prolong the disease. Populations at risk for complicated influenza include: children under the age of five, the elderly, individuals with certain underlying medical conditions, immunosuppressed individuals and pregnant women. Severe cases are often characterized by pneumonia. Pneumonia can develop due to two reasons: the influenza virus itself can cause viral pneumonia or through bacterial superinfection with Streptococcus pneumoniae, Staphylococcus aureus or Hemophilus influenzae. Also, underlying lung diseases such as chronic obstructive lung disease can exacerbate through influenza infection. Further complications include, among others, encephalitis, myositis and rhabdomyolysis as well as myocarditis.[4]

Influenza is often clinically diagnosed via anamnesis and physical exam. However, the differential diagnosis of influenza-like-illness caused by other pathogens cannot be excluded clinically. Influenza-like-illness can be caused by, among others, adenoviruses, rhinoviruses or parainfluenza viruses. Only through laboratory testing can influenza be differentiated from influenza-like-illness. Through naso-/pharyngeal swabs, tracheal aspirates or washings, material for testing can be collected. Laboratory confirmation can be conducted through detection of influenza RNA via reverse transcriptase-polymerase chain reaction (RT-PCR). Furthermore, direct antigen testing (rapid influenza diagnostic tests) or viral isolation is used.[3]

Patients with uncomplicated influenza disease are merely treated symptomatically. If risk factors for complications are present, antiviral medications can be considered. In case of severe disease or complications, antiviral medications are indicated. Among the possible medications, NA inhibitors are most commonly used. Oseltamivir or Zanamivir inhibit the NA, subsequently inhibiting further virus release. If signs suggesting a bacterial superinfection are present, antibiotics can be indicated.[4]

Of great importance is the inhibition of further spreading and transmission of the disease. Therefore, infected outpatients with uncomplicated influenza disease, must be educated to reduce the risk of transmission. Social distancing and hygiene are of outmost importance to protect others.[3] For inpatients, isolation should be implemented.[4] Transmission through pauci- and asymptomatic individuals is also possible.[10]

2.1.3. Epidemiology

Seasonal influenza occurs annually worldwide. In the northern and southern hemisphere (World Health Organization (WHO) definition) influenza shows seasonality.[3] In these parts of the world influenza occurs in the respective winter months annually.[4] Regarding the tropics, a seasonality is not given. Influenza spreads throughout the year showing no clear singular peak.[11]

In Germany the peak for influenza infections has been January and February in recent years. It is estimated that around 5% to 20% of the population in Germany are infected with influenza annually. This number varies between different seasons. The German Robert Koch Institute (RKI) estimates one to seven million influenza related patient-doctor contacts in Germany annually.[4]

Globally, influenza-associated respiratory excess mortality rates range from 0.1 to 6.4 per 100 000 individuals in the age group <65 years, 2.9 to 44 per 100 000 individuals for people 65 to 74 years of age and 17.9 to 223.5 per 100 000 in the population >75 years of age. Globally, 291 243 to 645 832 (4.0 to 8.8 per 100 000) influenza-associated respiratory deaths are estimated to occur annually.[12]

2.1.4. History of influenza epidemics and pandemics

Epidemics are defined as a geographically limited increased activity of an infectious disease. In regard to influenza, an influenza epidemic is defined as seasonal influenza activity exceeding expected activity.[13] In contrast, pandemics are not geographically limited and can affect the entire world. Influenza pandemics can occur when new influenza strains emerge. So far, only influenza type A has caused influenza pandemics.[4]

Although there is evidence of possible influenza pandemics from before the 15th century, the first influenza pandemic is considered to have occurred in 1580.[14] The first well documented pandemic, however, was the “Russian” pandemic caused by Influenza A(H2N2) at the end of the 19th century.[15] From 1889 to 1892, the “Russian” pandemic, sometimes referred to as “La Grippe” spread across the globe.[16] It remains unclear, whether the pandemic originated in Russia. However, spreading of the disease from Asia to the west is considered likely.[15] Although, the total number of deaths is unknown, case fatality rate during the “Russian” pandemic is estimated 0.1% to 0.28%.[16]

The “Spanish” Pandemic of 1918 was caused by influenza A(H1N1) and occurred in three waves (spring and autumn 1918, as well as winter 1918-19).[17] Although “Spanish” is colloquially used, it is unlikely that the pandemic originated in Spain. “Spanish” originated rather because during the time, Spain did not censor press and regularly reported on the pandemic. Other countries appear to have not reported on the pandemic as much, most likely to avoid lowering the morale of troops and society during World War I.[18,19] The geographic origin of the pandemic is considered the Midwest of the United States of America (USA). Most likely, influenza spread via troop transport from USA to France, from where it spread over Europe and the entire world.[18] Possibly however, the pandemic strain was already circulating before 1918.[20] It remains unclear what caused the pandemic to emerge in the first place.[21] Pandemic influenza infected over one third of the global population resulting in 50 million deaths.[18,19] Case fatality rate is estimated >2.5%.[18,19] Especially, healthy young adults were affected.[18,22] Therefore, the mortality curve was W-shaped showing peaks in infants, young adults and the elderly. In comparison, the mortality curve of influenza regarding age groups is usually U-shaped.[17] The high death rates in young adults were linked to a dysregulated pro-inflammatory response, a “cytokine storm”.[18] Comparably, the mortality among the elderly was lower than expected. Prior exposure to the virus, possibly from 1847 may have resulted in protective immunity.[23] Not until 1933 was influenza associated with the 1918/19 pandemic.[18,24] In the late 1990s the influenza virus was isolated successfully for the first time from preserved lung tissue from patients who died in 1918.[18]

In 1957, influenza A(H2N2) emerged causing the so-called “Asian” pandemic with subsequent recurring outbreaks over the next three years. The pandemic strain is considered to have emerged through reassortment of an avian and a human strain.[25] Between 1957 and 1959 global excess mortality due to respiratory disease is estimated to have been 4.0 deaths per 10 000 individuals which corresponds to 1.1. million excess deaths. The mortality burden due to the pandemic varied greatly between countries with highest burden in South America, especially in Chile.[26] The phenomenon of primary influenza virus pneumonia was highlighted during this pandemic in comparison to the presumed dominance of bacterial superinfections during the "Spanish" pandemic.[27]

Influenza A(H3N2) caused the "Hong Kong" pandemic in the seasons 1968/69 and 1969/70 which resulted in approximately 1 million deaths.[28] The novel virus subtype emerged after a shift in hemagglutinin, replacing A(H2N2) which was circulating since 1957.[29] As in 1957, this shift originated in reassortment between an avian and a human strain.[25] The severity of the two years differed between regions. While excess mortality was highest in the first year in North America and Canada, two-thirds of influenza related deaths occurred in the second pandemic season in Europe and Asia. Due to this reason the pandemic is sometimes referred to as "smoldering".[29] Influenza A(H3N2) has since been circulating, causing seasonal influenza.[4]

The last influenza pandemic to date occurred between 2009 and 2010. Influenza A(H1N1pdm09) emerged causing pandemic "swine flu". This novel influenza strain of swine origin had not been identified in humans or swine before.[30] The first laboratory confirmed cases were found in USA and Mexico in April 2009.[31] The virus spread rapidly across the globe and by May 5th 2009, cases were reported from 21 countries worldwide.[32] In April 2009 the first pandemic influenza virus cases occurred in Germany.[13] By September 2009, four monovalent vaccines were approved by the Food and Drug Administration (FDA). However, not until late November 2009, a sufficient quantity of vaccines was produced.[33] WHO reported 18 449 laboratory confirmed deaths due to pandemic influenza.[34] The Centers for Disease Control and Prevention (CDC) estimated 201 200 respiratory deaths and 83 300 cardiovascular deaths due to the pandemic strain.[35] Similarly, a different study applied multivariate linear regression to estimate the number of respiratory deaths. This study estimated 189 000 respiratory deaths globally. In comparison, the authors estimated 148 000 to 249 000 respiratory deaths due to seasonal influenza annually. The difference being the distribution in age group: while 62% of the respiratory deaths due to the pandemic strain are estimated to have occurred in individuals younger than 65 years of age, only 19% of respiratory deaths occur in this age group due to seasonal influenza.[36] This shift in age group is observed and described regarding earlier pandemics and is considered a characteristic of influenza pandemics.[29,37] As observed in other pandemics as well, mortality rates differed greatly between geographic regions.[36] In August 2010, WHO announced the end of the A(H1N1) pandemic.[38] Influenza A(H1N1pdm09) is still circulating, causing seasonal influenza worldwide.[4]

2.1.5. Influenza surveillance in Germany between 2009/10 and 2019/20

Annually, RKI analyzes influenza samples and provides updates on the surveillance of influenza in Germany. Between 2009/10 and 2019/20, influenza A(H1N1)pdm09 and A(H3N2), as well as influenza B/Yamagata and B/Victoria were circulating.[4] Milder influenza seasons occurred in 2010/11, 2013/14, 2015/16 with no observed excess mortality attributable to influenza. In comparison, the influenza seasons 2012/13, 2014/15, 2016/17 and 2017/18 resulted in estimated excess mortality exceeding 20 000.[39]

During the pandemic season 2009/10, 258 laboratory-confirmed influenza deaths were reported to RKI. No excess mortality was observed in the pandemic year. In 2009/10, only influenza A(H1N1pdm09) was isolated by RKIs' influenza surveillance team. The influenza season 2010/11 was comparably mild with no excess mortality and 165 laboratory-confirmed influenza deaths. Influenza A(H1N1pdm09) was still the dominant strain (62%), while B/Victoria was isolated in 37% of cases. In the season of 2011/12 excess mortality reached 2400, with the dominant strain being A(H3N2) in 75% of isolated cases. During 2012/13 excess mortality surged (20 700) equally by both circulating A strains and B/Yamagata. After a mild influenza season in 2013/14, excess mortality reached 21 300 in the season of 2014/15 with the dominant strain being A(H3N2). This same pattern repeated in the following two seasons. No excess mortality was observed in 2015/16, while excess mortality almost reached 23 000 in 2016/17. The season 2017/18 stood out with 1674 laboratory-confirmed influenza related deaths and excess mortality of 25 100.[39] During this season, privately insured citizens regularly received tetravalent influenza vaccines, while most public insurances only covered vaccination with trivalent vaccines. The trivalent vaccine did not include influenza B/Yamagata, which turned out to be the dominant strain. This contributed to high excess mortality and number of laboratory-confirmed influenza related deaths.[40] Consequently, RKI recommended the usage of tetravalent influenza vaccines[41] and public health insurances covered quadrivalent vaccination in following seasons.[42] In the season of 2018/19, 182 000 laboratory-confirmed influenza cases were reported to RKI. Out of these, 40 000 (22%) were hospitalized and 954 laboratory-confirmed influenza-related deaths were reported. During this season, both influenza A strains were dominant (A(H1N1)pdm09 51%, A(H3N2) 49%), while influenza B was not detected in sentinel samples.[39] With a span of only eleven weeks, the influenza season 2019/20 was shorter in comparison to the previous five seasons (average 13-15 weeks).[43] Similarly to the previous season, both influenza A strains were detected predominantly, while influenza B/Victoria was detected in 14% of analyzed sentinel samples.[44] Excess medical consultations were estimated 4.9 million and 542 laboratory-confirmed influenza associated deaths were reported.[45]

An overview on influenza from 2009/10 to 2019/20 in Germany regarding season, distribution of influenza strains, laboratory-confirmed influenza cases, laboratory-confirmed influenza-associated deaths and estimated excess mortality can be found in Table 1.

Table 1. Influenza seasons in Germany between 2009/10 and 2019/20

Season	**Distribution of influenza strains [%]***			**Laboratory-confirmed influenza cases****	**Laboratory-confirmed influenza-associated deaths***	**Estimated excess mortality***
	A(H1N1) pdm09	A(H3N2)	B°			
2009/10	100	0	0	225 729	258	0
2010/11	62	1	37	41 000	165	0
2011/12	1	75	24	9 500	14	2 400
2012/13	34	31	35	66 000	196	20 700
2013/14	30	61	9	6 200	23	0
2014/15	15	62	23	70 000	274	21 300
2015/16	43	2	55	71 000	237	0
2016/17	1	93	6	114 200	722	22 900
2017/18	28	4	69	334 000	1 674	25 100
2018/19	51	49	0	182 000	954	n.a.
2019/20	41***	45***	14***	188 119***	547***	n.a.

°Both B/Yamagata and B/Victoria. *Adapted from RKI seasonal influenza report 2018/19 Table 3 (p.47)[39] except 2019/20. **Data extracted from respective RKI seasonal report[13,39,40,46-52] except 2019/20. ***Data extracted from RKI Season 2019/20 monthly report 2020-39.[53]

2.1.6. Economic impact of influenza disease

When considering the economic impact of influenza, both severe cases and death as well as mild influenza disease must be regarded. Especially, mild to moderate cases have a high impact on work absenteeism and production days lost.[54]

A United States (US) study estimated that annually their economic burden of influenza disease reaches $11.2 billion. This number can be further divided into direct medical costs ($3.2 billion) and indirect medical costs ($8.0 billion). The annual days of productivity lost were estimated 20.1 million.[55]

During the severe influenza season 2017/18 in Germany, excess medical consultations were estimated to have been 9 million. Excess work absenteeism, including providing for sick relatives was estimated 5.3 million days. Excess hospitalizations reached 45 000.[40] In comparison, in the relatively mild influenza season of 2018/19, the medical consultations due to possible influenza infections were an estimated 3.8 million. The influenza associated production days lost, were considered at 2.3 million.[39]

2.2. Influenza vaccine

2.2.1. Influenza prevention and immunity

Influenza is a preventable disease. Among the possible preventive measures, influenza vaccination is most effective.[3] A study in the US showed that in the season of 2017/18 the vaccine prevented more than 100 000 hospital administrations and 8000 deaths.[56] A different US study estimated 9.6 million to 37.2 million averted influenza infections nationwide due to vaccination. The authors concluded, 20.8% to 47.5% of potential influenza infections can be avoided through vaccination, depending on the influenza season. Comparably, only 1% of infections were avoided through vaccination during the pandemic 2009/10, since vaccination was only available in a late stage of the pandemic.[57] Although evidence is limited, vaccination also likely contributes to herd immunity.[58]

Furthermore, antiviral medication can be used as pre-exposure or post-exposure prophylaxis.[3] Pre-exposure antiviral prophylaxis can be used if vaccine efficacy is expected to be low, as might be the case in severely immunocompromised individuals. Post-exposure prophylaxis using antiviral medication can be implemented when influenza outbreaks, for example, in residential or nursing homes occur.[4] Additionally, face masks and hand hygiene support the inhibition of influenza transmission.[59,60] WHO recommends the following additional protective measures: avoiding personal contact with ill persons, regular hand hygiene, respiratory hygiene, reduced touching of one's face and self-isolation when symptoms of influenza are present.[3]

2.2.2. Influenza vaccine types

Regarding the production process, three technologies exist: 1) egg-based, 2) cell-based, and 3) recombinant influenza vaccines. Out of the three, egg-based influenza vaccines are predominantly (80%) manufactured.[61] Candidate vaccine viruses are introduced into fertilized hen's eggs and incubated until virus replication is sufficient.[62] The harvested viruses are then killed, usually via exposure to formaldehyde or β-propiolactone, to create inactivated influenza vaccines.[63] For live attenuated influenza vaccines, the viruses are merely weakened. This procedure requires a large amount of chicken eggs and a longer period of production time. Cell-based influenza vaccines are manufactured by candidate vaccine viruses being injected into and incubated in mammalian cells. Currently, only one cell-based vaccine is approved by the FDA and European Medicines Agency (EMA).[62,64] This process does not require chicken eggs and is potentially quicker concerning production time. Recombinant influenza vaccines do not depend upon candidate vaccine viruses. This type of vaccine is created synthetically incorporating recombinant technology.[62]

Influenza vaccines can further be categorized regarding the number of surface antigen strains included into trivalent and tetravalent vaccines. In recent years, trivalent influenza vaccines included A(H3N2), A(H1N1pdm09) and either B/Yamagata or B/Victoria. In comparison, tetravalent influenza vaccines contained both influenza B types.[41] Because B/Yamagata has not been detected since 2020, WHO recommended excluding this virus in influenza vaccines as off September 2023.[4,61] Furthermore, influenza vaccines can be differentiated into attenuated/live and inactivated vaccines. Apart from the egg-based live-attenuated influenza nasal spray vaccine, all current influenza vaccines are inactivated.[62] Depending on the type of vaccine, influenza vaccines use nasal, intramuscular or subcutaneous administration.[65] Concerning the enhancement of influenza vaccines, high-dose or adjuvanted vaccines can be used.[66] Adjuvanted vaccines include MF59, an oil-in-water-emulsion derived from squalene oil. Adjuvants can improve the immune response to the vaccination.[67]

For the season 2020/21 in Germany, ten vaccines were approved by the Paul-Ehrlich-Institute (PEI), including seven egg-based inactivated, one cell-based inactivated, one live attenuated influenza vaccine and one adjuvanted influenza vaccine (approved for >65 years). Only tetravalent vaccines were approved.[65]

2.2.3. Recommendations on the composition of seasonal influenza vaccines

The composition of influenza vaccines is based on the recommendation of WHO. Biannually, WHO consults experts and uses data from the Global Influenza Surveillance and Response System (GISRS) to develop recommendations. GISRS consists of 160 institutions, including National Influenza Centers and laboratories worldwide. The respective recommendation is based on surveillance data from GISRS, antigenic and genetic characterization of isolated viruses, human serology studies with influenza vaccines, information from modelling systems forecasting the season, test results on antiviral resistance, tests on vaccine efficacy and the availability of candidate vaccine viruses. The vaccines are then produced in accordance with the recommendations. In February, the recommendations for the following influenza season in the northern hemisphere is given. For the southern hemisphere, the recommendations are usually published in September. This early date is due to the six to eight months necessary for vaccine production.[68]

In comparison to the prior season, the recommendation for 2020/21 differed regarding three of the four components. The recommendation for the northern hemisphere for egg-based tetravalent vaccines included: A/Guangdong-Maonan/SWL1536/2019 (H1N1)pdm09-like virus; A/Hong Kong/2671/2019 (H3N2)-like virus; B/Washington/02/2019 (B/Victoria lineage)-like virus; and B/Phuket/3073/2013 (B/Yamagata lineage)-like virus. The recommendation for cell-based tetravalent vaccines was only different regarding the phylogenetic origin of A(H1N1pdm09). Here, the usage of A/Hawaii/70/2019 (H1N1)pdm09-like virus was recommended.[69] This difference was due to the feasibility regarding the different production techniques.[70] The recommendation on the composition of trivalent vaccines did not include B/Phuket/3073/2013 (B/Yamagata lineage)-like virus.[69] Whether trivalent or tetravalent vaccines were used, was decided by the respective national institutions.[41]

2.2.4. Efficacy of influenza vaccines

The efficacy of influenza vaccines varies and depends on the following factors: the individual receiving the vaccine, the influenza season and the vaccine itself.

Regarding the individual receiving the vaccine, following factors influence vaccine efficacy: age, status of the immune system including usage of immunosuppressive drugs and underlying conditions.[11] Immunosenescence refers to the gradual age-associated decrease in the capabilities of the immune system.[71] This on top of the gradual increase in comorbidities with age, negatively impacts vaccine efficacy.[11,72] Certain comorbidities such as chronic kidney disease,[73] obesity[74] and any form of immunosuppression[75,76] impair the immune response to vaccines and therefore decrease vaccine efficacy.[11]

Of great importance is the match between vaccine and the circulating influenza viruses. During the production time of the vaccines (six to eight months), circulating virus strains may change due to antigen drift, possibly reducing the match between vaccine and circulating viruses.[77,78] Furthermore, efficacy may vary depending on the type of vaccine administered. Some authors suggest that cell-based vaccines may have higher efficacy in comparison to egg-based vaccines.[77-80] Research on nucleic acid influenza vaccines with a broader spectrum is being conducted to increase vaccine efficacy.[81]

A systematic review and meta-analysis on vaccine efficacy found, a pooled overall efficacy of 33% for A(H3N2), 54% for influenza B strains and 61% for A(H1N1)pdm09. Among the elderly (>60 years), pooled vaccine efficacy was 24% for A(H3N2), 63% for influenza type B and 62% for A(H1N1)pdm09.[82] The comparably low immune response in the elderly to A(H3N2) vaccines is also described elsewhere.[83-85] The analysis of vaccine efficacy in 2017/18 in Germany shows, efficacy can be as low as 1% if vaccine and virus do not match. In 2017/18 cross-reactivity of trivalent vaccines with B/Victoria was insufficient regarding the dominantly circulating strain of B/Yamagata, resulting in vaccine efficacy of 1% for trivalent vaccines against influenza B. Between 2009/10 and 2019/20 in Germany, pooled vaccine efficacy was highest for A(H1N1)pdm09 with 58% in 2012/13.[40]

Among discussed methods to increase vaccine efficacy are: optimized timing of vaccination including biannual vaccination, usage of an adjuvanted vaccine, cell-based vaccine, high dose vaccine and intradermal application.[11] Recruiting dermal populations of dendritic cells on top of efficient migration to lymph nodes by way of the dermal vascular network, is the underlying hypothesis of increased vaccine efficacy through intradermal application.[86] A meta-analysis reviewing strategies to enhance vaccine efficacy in the elderly, found 82% higher postvaccination titers to A(H3N2) after application of high-dose vaccines compared to standard vaccine, 52% higher postvaccination titers after MF-59-adjuvanted vaccines compared to standard vaccine and 32% higher postvaccination titers after intradermal application versus standard vaccine.[87]

2.2.5. The search for a universal influenza vaccine

As the efficacy of the vaccine varies substantially, especially in patients who are at high risk of complicated influenza course, the search for a “universal” influenza vaccine is considered necessary.[88,89] The optimal influenza vaccine would require only one administration and provide prolonged protection against all influenza strains, regardless of antigenic drift or even shift.[11,78]

Approaches towards more “universal” influenza vaccines include: targeting of conserved structures[90] and gene-based approaches including messenger RNA (mRNA).[91] Conserved structures such as the stem of HA are considered to be more evolutionary constrained and thus may be possible vaccine targets.[92] A phase 1[93] and a phase 1/2 clinical trial[94] on mRNA vaccines targeting HA showed no safety concerns, supporting this vaccine platform approach.[81] Other highly conserved proteins are nucleoprotein and matrix, both of which may also be potential vaccine targets.[90]

As such universal influenza vaccines are not approved to date, currently available vaccines remain the most effective form of influenza prevention.[3]

2.2.6. Indications for influenza vaccines

WHO recommends annual influenza vaccination for the following individuals: children (six months to five years old), chronically ill individuals, elderly (>65 years), healthcare workers and pregnant women at any stage of pregnancy. Excluding healthcare workers, all of these groups have an increased risk of a complicated influenza course in common.[3] Further individuals for whom the influenza vaccination is recommended are: homeless people, nursing home residents and long-term care residents.[11] Also, ethnic groups such as Native Americans are possible target groups, since influenza-associated mortality rates are considered higher in these populations.[95] Furthermore, vaccination is recommended for individuals who care for the beforementioned risk groups.[4]

Annually, estimated 9 243 to 105 690 influenza-associated respiratory deaths occur in children under five years of age.[12] Vaccination of children may also reduce influenza burden in communities.[11,96-99] Because of these reasons, WHO recommends annual influenza vaccination in children six months to five years of age.[3]

Among the chronic illnesses considered as indications for receiving influenza vaccines are: chronic heart, kidney, liver, neurologic, metabolic and respiratory disease. Furthermore, endocrine disorders such as diabetes type II and morbid obesity (body mass index ≥40 kg/m²) are indications. Another important target group are patients with primary or secondary immunodeficiencies. Among the secondary immunodeficiencies, cancer, human immunodeficiency virus disease and taking immunosuppressive drugs are common relevant indications.[11]

Out of the 291 243 – 645 843 individuals who die of influenza-associated respiratory deaths annually, 41% are in the age group >75 years.[11,12] A Canadian survey with 5 014 elderly participants reported that 39.3% of influenza infected elderly took longer than two weeks to fully recover, 13.9% reported hospital admission and 3.1% did not fully recover at all.[11,100] Thus, influenza vaccination is highly recommended for the elderly.

In 2012, WHO singled out pregnant women as the highest priority group to receive influenza vaccination.[101] Influenza vaccination is recommended for pregnant women due to four equally important reasons.[11] First, due to the cardiovascular and respiratory physiological changes during pregnancy, pregnant women have an increased risk for complicated influenza disease.[102] Second, especially during pandemic years, such as 1918, 1957 or 2009/10, the increased influenza associated mortality during pregnancy is evident. Although pregnant women only accounted for 1% of the population at risk, they accounted for 5% of influenza related deaths in the USA during the 2009/10 pandemic.[103] Third, influenza infections during pregnancy have a negative effect on the fetus itself, showing an increased risk for preterm-delivery, low birth weight or still-birth.[103] Fourth, through maternal immunization antibodies are transferred through the placenta to the fetus leading to the protection of the newborn. This is of relevance because infants have an increased risk of complicated influenza course and vaccination is not feasible until the age of six months.[104]

There are a few differences regarding influenza vaccination recommendations from the WHO and RKI. Firstly, RKI to date does not recommend influenza vaccination for children without underlying disease. Secondly, the cutoff age for elderly is lower with 60 years of age in the RKI recommendations in comparison to 65 years regarding WHO. Thirdly, RKI recommends the vaccination for healthy pregnant women as of the second trimester. Pregnant women with the beforementioned underlying conditions are recommended to receive the vaccine regardless of pregnancy stage. As inactivated influenza vaccines are considered safe to use during pregnancy, WHO recommends the vaccination regardless of pregnancy stage.[3,4] The reason behind the recommendation of RKI is of psychological nature. Since miscarriages are common in the first trimester, RKI wants to prevent pregnant women from linking a miscarriage to receiving vaccines during pregnancy.[105]

In addition, influenza vaccination is explicitly recommended for healthcare workers by the WHO and national public health institutions worldwide. Personal safety and the prevention of nosocomial infections are among the reasons the vaccination is recommended for healthcare workers.[3,4]

2.2.7. Contraindications to receiving influenza vaccines

In general, there are no contraindications to receiving influenza vaccines. However, the type of vaccine and the timing of vaccination should be selected in an individualized context.

Since commonly used influenza vaccines are harvested using hen's eggs, severe egg-allergy can be seen as a contraindication to receiving egg-based influenza vaccines. In this case, egg-free vaccines such as cell-based or recombinant based vaccines can be used.[106] Of note, guidelines regarding the administration of egg-based influenza vaccines in individuals with egg-allergy have been softened. Children who have only developed hives in the past, can be vaccinated, if they are observed for at least 30 minutes (min) after vaccination. Other allergies regarding vaccine components such as gelatin or latex should be considered as well. During the administration of vaccines, the attending physician should be able to recognize and treat anaphylaxis appropriately.[106,107]

The association between influenza vaccination and Guillain-Barré-Syndrome is still discussed. In 1976, in Fort Dix, New Jersey USA, a cluster of swine influenza cases emerged, which led to the initiation of a US national immunization program.[27] This program had to be stopped due to increased Guillain-Barré-Syndrome cases occurring among the vaccinated. Other than this event, no clustering of Guillain-Barré-Syndrome after influenza vaccination has been observed.[108] Influenza infection, on the other hand, has been associated to the development of Guillain-Barré-Syndrome.[108,109] A self-controlled risk interval study demonstrated a higher attributable risk of Guillain-Barré-Syndrome after influenza infection than after influenza vaccination.[110] If a history of Guillain-Barré-Syndrome is known, it may be advisable to consult neurologists prior to vaccination.[108]

2.2.8. Timing of influenza vaccination

The optimal timing of influenza vaccination is still unknown and subject of discussion. It is, similarly to the efficacy of influenza vaccines, dependent on multiple factors: the climate and region, the individual receiving the vaccine, the respective influenza season and the vaccine itself.[11] The timing of vaccination is of concern, since studies have suggested the efficacy of influenza vaccination wanes over the course of one influenza season.[111-118]

Commonly, influenza vaccination is conducted in the northern hemisphere between October and November with influenza peaks usually in January and February.[3,119] Comparably, in Australia influenza peaks in August and influenza vaccination is typically administered between March and April.[120] Regarding countries without seasonal influenza peaks, WHO suggests the adaption of the timing in accordance to regional influenza surveillance with subsequent vaccination before expected regional peaks.[11]

A study in Spain measured the risk of influenza infection and hospital admission between early and late vaccination, concluding that the elderly may profit from later vaccination.[113] However, the delay of vaccination may result in missed or forgotten vaccination, which in turn decreases uptake rates.[119,120] Also, the unpredictability of influenza seasons regarding onset, duration, dominant influenza strains and severity further complicates the question of optimal timing.[119] Furthermore, the time necessary to mount sufficient antibody titers also must be considered. This time span is on average fourteen days.[66] The CDC therefore suggests influenza vaccination between September and October for the northern hemisphere, while stating vaccination may also still be beneficial in December or even later.[121]

2.3. Influenza vaccination campaigns for healthcare workers

2.3.1. Influenza vaccination coverage in healthcare workers

Although influenza vaccination is recommended for healthcare workers by many national public health institutions, influenza vaccination coverage remains unsatisfactory in many countries. In European countries influenza vaccination coverage in healthcare workers ranged from 15.6% to 63.2% between 2015 and 2018 [122]. In the season 2017/18, CDC conducted a survey among 2 265 US healthcare workers, reporting that overall, 78.4% received influenza vaccination. Vaccination coverage was highest when vaccination was mandatory (94.8%) and lowest (47.6%) if vaccination was neither promoted, mandatory nor offered on-site.[123] In a survey from 2014/15 conducted in Germany among 677 healthcare workers, self-reported vaccination rate was 55%, differing between physicians (72%) and nursing staff (45%).[124] Lower vaccination rates in nursing staff in comparison to physicians is reported in several publications worldwide.[125-130]

2.3.2. Factors influencing influenza vaccination coverage in healthcare workers

The German study *„Online-Befragung von Krankenhaus-Personal zur Influenza-Impfung"* (*OKaPII*) surveys influenza vaccination coverage and motivation at German hospitals. The questionnaire regarding motivations and hesitancy towards the vaccine is derived from the "4C model". The four "Cs" are *confidence*, *convenience*, *complacency* and *calculation*. *Confidence* entails believing in the safety and efficacy of the vaccine. *Convenience* regards the facilitation of vaccination regarding financial, geographical and timing aspects. *Complacency* means the risk perception regarding the severity and infectivity of the disease. *Calculation* comprises the risk-benefit-assessment of vaccination. In the survey the most common argument pro vaccination in all regarded professional fields was self-protection, followed by patient safety and safety of family and friends. The most common argument against influenza vaccination in doctors were organizational aspects, whereas nurses reported a lacking risk-benefit-analysis and low confidence in the efficacy of the vaccine. Overall, nurses reported lacking *confidence*, whereas doctors were influenced by *convenience.*[131] This model was expanded to include *collective responsibility*, meaning the willingness to protect others, and is known as the "5C model". Furthermore, this model replaced *convenience* with its negative counterpart *constraints*.[132]

A survey conducted in Belgium among 5 141 healthcare workers reported on motivation and beliefs regarding influenza vaccination in 2015. Up to 90% of all healthcare workers remarked it was of concern to them not to infect their patients. However, only 20% of non-vaccinated healthcare workers considered influenza vaccination necessary to prevent nosocomial influenza infection in their patients. Up to 40% of unvaccinated staff believed they could be infected with influenza via vaccination and that their immune system was weakened by immunization. Furthermore, only 20% of unvaccinated staff believed they were at risk of contracting influenza. Reasons given by unvaccinated staff to receive vaccination in the future were self-protection and protection of their families.[133]

2.3.3. Impact and consequences of influenza vaccination coverage in healthcare workers

When regarding the impact and consequences of influenza vaccination coverage among healthcare workers the following determinants can be considered: the risk of healthcare workers contracting influenza, the rate of nosocomial influenza infections in patients and work absenteeism regarding influenza infections in healthcare workers.

During one influenza season up to 23% of healthcare workers may contract influenza. Out of these, 28% to 59% may show subclinical, yet potentially transmissible, disease.[134-136] At a Chinese hospital the cross-transmission of pandemic influenza A/H1N1 in 2009 was analyzed. The infection rate in healthcare workers was 2.1% in comparison to 1%-1.5% in a comparable community group.[137] In Mexico during a retrospective study over two influenza seasons the relation between healthcare workers' vaccination coverage to influenza infection in healthcare workers was analyzed. While vaccination coverage increased from 21.3% to 42.7%, the number of influenza-like-illness and influenza cases was reduced by 67.4% despite the second season being more severe than the first.[138] In the season of 2016/17, five French hospitals were analyzed regarding influenza incidence in healthcare workers. Positive influenza polymerase chain reaction (PCR) in nasal swabs and/or detection of virus-specific seroconversion in blood samples were considered as influenza positive. Out of the 278 healthcare workers included in the analysis, 62 showed evidence of influenza infection of whom 46.8% reported asymptomatic and 41.9% pauci-symptomatic influenza. Only 11.3% were symptomatic.[139]

During two subsequent nosocomial influenza outbreaks at a Japanese hospital, eleven patients and thirteen healthcare workers contracted influenza, involving two different genotypes of influenza A/H3N2. The two highly homologous viruses spread rapidly resulting in a nosocomial outbreak. The index case was considered to have been a healthcare worker. The authors reported one of the infected healthcare workers working for an entire day in the hospital although symptoms were present.[140] During the 2011/12 influenza season, a nosocomial influenza outbreak at a geriatric ward in a French Hospital occurred. Sequence analysis of the transmission chain showed three influenza clusters, out of which two were attributable to a healthcare worker being the source of infection.[141] A retrospective cross-sectional study at a 550-bed tertiary care hospital in the USA analyzed the effect of influenza vaccination coverage in healthcare workers regarding nosocomial influenza infections. Although vaccination coverage in healthcare workers increased from 47% to 90% over the course of five influenza seasons, the rate in nosocomial influenza infections did not significantly decrease. The authors concluded that vaccination coverage of over 50% may not significantly decrease nosocomial influenza. The authors also noted that this may be due to a possible ceiling effect in vaccination coverage. Other precautions like patient hygiene, healthcare workers' hand hygiene and patient isolation could possibly have had an effect as well.[142]

In a retrospective observational cohort study from the USA, influenza vaccination in healthcare workers was significantly associated to a decrease in work absenteeism time.[143] At an Italian pediatric hospital an excess of 0.38 to 0.46 day work absenteeism in unvaccinated vs. vaccinated healthcare workers was found. The hospital employed approximately 2 100 healthcare workers. The authors estimated a total amount of 690.1 to 795.3 production days lost during one season. Furthermore, the incurred costs due to work absenteeism and production days lost was estimated 117 176€ to 134 885€ per influenza season.[144] In a United Kingdom (UK) analysis higher vaccination coverage in healthcare personnel was associated with reduced work absenteeism. The authors concluded a 10% increase in vaccination rate would be associated with a 10% decrease in work absenteeism.[134] An Australian systematic review also concluded that influenza vaccination shortened the work absenteeism period in healthcare workers.[145]

2.3.4. Influenza campaign strategies for healthcare workers worldwide

As part of our research project, we performed a review analysis of influenza campaign strategies for healthcare workers worldwide (Publication 2). The key interventions education/promotion, incentives, organizational strategies, regulatory measures and combinations of the beforementioned strategies can be differentiated.[146]

Educational and promotional aspects are at the basis of influenza vaccination campaigns. Among others, educational pamphlets, posters, stickers and videos can be used to overcome misconceived notions about the vaccine.[146] Representation of hospital or department heads also plays a crucial role.[147,148] Promotional materials with a concurrent design can increase visibility and therefore increase discussion among colleagues. One study from Spain reported sharing humorous pictures of vaccinated staff on the intranet which in turn increased discussions on influenza vaccination.[149]

Incentives are often part of multifaceted campaigns.[146] Employee-bonus programs can also be implemented.[150,151] Prizes given away among vaccinated personnel can be used as incentives.[149] Also, prizes for wards which reach satisfactory vaccination coverage can be implemented.[147] One campaign in the USA included a 25 US Dollar gift card for each employee if vaccination coverage at the hospital exceeded 95%.[152]

Organizational strategies include decentralized vaccine supply, mass vaccination events, on-site vaccination through mobile vaccination teams and vaccination stands.[146] Especially, on-site vaccination is of relevance for healthcare workers since it may not be feasible for physicians or nurses to leave their wards. Mobile vaccination teams visiting wards especially during shift changes can therefore be beneficial.[129] A decentralized vaccine supply entailing the distribution of prepared influenza vaccine kits among wards for peer-to-peer vaccination can also be implemented.[153,154] Mass vaccination events can be successful as well.[150] Influenza vaccination stands at hospital entrances can also be used.[147]

Regulatory measures comprise declination forms, mandatory vaccination policies or vaccinate-or-wear-a-mask policies. Especially in the USA and in Asia, mandatory vaccination policies are employed.[146] In these cases, refusal to receive vaccination can lead to end of employment. Medical and religious exemptions are occasionally allowed.[155-159] Declination forms entail the actively written refusal to receive the vaccine.[152,160,161] Declination forms can include a statement acknowledging the imposed risk on others.[152] A vaccinate-or-wear-a-mask approach is beneficial due to two reasons: it can be seen as an incentive to receive vaccination and can reduce the risk of influenza transmission through unvaccinated staff.[162] Any regulatory measures can, however, be met by litigation, possibly decreasing feasibility especially in European countries.[146]

Combined interventions of the beforementioned strategies can also be employed. One campaign from the USA employed annual plan-do-study-act (PDSA) cycles on top of educational/promotional aspects and on-site vaccination. During the PDSA cycles “fear of needles” was identified as a barrier. Therefore, nasal vaccination was provided to reduce this obstacle. During another PDSA cycle, on-site vaccination targeting employees who exclusively work night shifts was introduced.[163] A different campaign from the USA comprised a declination form and having to wear a badge saying, “I’m vaccinated because I care”. Regardless of vaccination status, employees were required to wear a mask, if the badge was not worn. Additionally, noncompliance was included in performance evaluations.[150]

Concerning overall vaccination coverage, highest vaccination rates can be reached via implementation of regulatory measures, especially if noncompliance has consequences. However, possible litigations must be considered. Although education/promotion and organizational aspects do not regularly exceed vaccination rates of 40% when employed on their own, they should still be implemented whenever possible. Incentives can be used as part of multifaceted campaigns while considering ethical as well as moral aspects. Maintaining a high influenza vaccination rate in healthcare workers over several years is possible through the implementation of mandatory measures or thorough multifaceted campaigns.[146]

2.3.5. Influenza campaign strategies for healthcare workers in Germany

Few reports on influenza vaccination campaigns in Germany prior to the season 2020/21 have been published. In 2019, in a German Hospital, a “Be a flu fighter” influenza vaccination campaign for healthcare workers was initiated. The campaign included promotional and educational aspects, a mobile vaccination team and prize drawings as incentives among vaccinated healthcare workers. Vaccination coverage reached 72% in physicians and 50% in nurses. Baseline values were not provided by the authors.[164]

2.4. COVID-19 pandemic

2.4.1. COVID-19

Coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). In December 2019, a cluster of atypical pneumonia cases of unknown origin occurred in Wuhan, China. On January 9th, 2020, the pathogen was identified as a novel coronavirus. On January 13th the first COVID-19 case outside of China was diagnosed in Thailand with subsequent first cases in the USA on January 21st and in Europe on January 24th. By the beginning of March, the number of COVID-19 cases surpassed 100 000 worldwide. On March 11th, COVID-19 was declared a pandemic by WHO.[165]

COVID-19 is transmitted from human to human via aerosols, droplets and smear. Typically, COVID-19 presents with cough, fatigue, fever and loss of smell or taste. Severity of the disease varies, ranging from asymptomatic to critical illness and death.[166] In late 2020, out of the potential therapeutics investigated, remdesivir and dexamethasone were proven effective.[167,168] Over the course of 2020, multiple vaccine candidates were studied. The first COVID-19 vaccine was approved for emergency use in the USA on December 11th and in Europe on December 21st 2020.[169] By December 2020, over 80 million COVID-19 cases had occurred, corresponding to over 1.7 million deaths worldwide.[170] An unprecedented worldwide vaccine roll-out targeting COVID-19 followed. By the end of 2023, over 13 billion COVID-19 vaccinations were administered worldwide.[166] Due to the decreasing trend of COVID-19 related hospitalizations and deaths and increased levels of population immunity to the virus, WHO announced the end of the emergency phase of the COVID-19 pandemic in May 2023.[171] As of July 2025, WHO reported more than 700 million COVID-19 cases and 7 million confirmed deaths attributed to COVID-19 worldwide.[166]

2.4.2. Influenza season 2020/21 during the COVID-19 pandemic

The influenza season 2020/21 must be seen in context of the COVID-19 pandemic. COVID-19 and influenza share certain similarities: both are respiratory viruses with similar routes of transmission and symptoms.[172] In regard to the route of transmission, strategies such as social distancing, wearing masks and increased hand-hygiene were already suspected to have a positive impact on the transmission of influenza.[173] However, co-infections of influenza and COVID-19 had already been observed at the time.[174] To alleviate the overall burden of respiratory disease, efforts were being taken to increase influenza vaccination coverage in the season 2020/21.[173] In Australia, Chile, Netherlands, New Zealand, Norway and the UK strategies like drive-through vaccination stands or vaccination free of charge were employed to increase influenza vaccination coverage in respective communities. In some countries, influenza vaccination was declared mandatory for healthcare workers in 2020/21.[175]

In context of the COVID-19 pandemic, CDC recommended, in accordance with the Advisory Committee on Immunization Practices, influenza vaccination for all individuals aged six months or older, provided no contraindications were present. CDC emphasized on the importance of influenza vaccination in 2020/21 to alleviate the burden on healthcare structures during the COVID-19 pandemic. Furthermore, the importance of influenza vaccination of healthcare workers during this season was emphasized. Regarding the timing of influenza vaccination, CDC stated that vaccination can be conducted earlier (i.e. July, August), if this facilitated vaccination in the context of social distancing, isolation, quarantine or people working from home.[119]

RKI published recommendations on influenza vaccination during the COVID-19 pandemic in summer 2020. The groups at risk for severe disease course are similar regarding COVID-19 and influenza. Therefore, RKI highlighted the necessity of high vaccination coverage in these high priority groups. As only a limited amount of influenza vaccine was available for the upcoming season 2020/21, RKI recommended that individuals at risk of severe influenza disease course should be prioritized to receive influenza vaccination. In their statement, RKI also highlighted the importance of vaccination of healthcare workers.[176]

2.5. Influenza vaccination campaign 2020/21 at the University Hospital of Cologne

2.5.1. Influenza vaccination coverage in healthcare workers of the University Hospital Cologne

The annually conducted survey *OKaPII* in selected German hospitals revealed an influenza vaccination coverage of 44.7% in healthcare workers of the University Hospital of Cologne. This rate is below the average of other German hospitals. Especially, vaccination coverage in nursing staff was unsatisfactory (37.2%). The most common reason against vaccination given by survey participants was “organizational barriers”. As this data stems from surveys, i.e. self-reported vaccination coverage, a selection bias cannot be excluded and responding participants may not be representative. However, it is unlikely that the true vaccination coverage exceeds the rate surveyed (unpublished data). Therefore, the goal was to analyze influenza vaccination coverage in prior seasons and ultimately, to increase influenza vaccination coverage in healthcare workers of the University Hospital of Cologne in 2020/21. Especially, with the ongoing COVID-19 pandemic, an increase in vaccination coverage was of particular concern.

2.5.2. Concept of the vaccination campaign 2020/21 at the University Hospital of Cologne

Building on the findings of our review on influenza campaign strategies for healthcare workers,[146] an intensified campaign was conducted in the season 2020/21 to increase influenza vaccination coverage in healthcare workers at the University Hospital of Cologne. The key element of the campaign was a mobile vaccination team providing on-site vaccination as well as recurring walk-in vaccinations at an easily accessible central vaccination site. Furthermore, the campaign included educational and promotional action. Additionally, four mass vaccination events for students were conducted. As before, employees could receive vaccination during the opening hours at the occupational health department. With the ongoing COVID-19 pandemic, all elements of the campaign were conducted in accordance with safety measures required by RKI and the hospital board. A tetravalent egg based vaccine was used for most of the campaign. Following the vaccine shortage a tetravalent cell based vaccine was available.

2.6. Research questions and aim of thesis

Amidst the COVID-19 pandemic an intensified influenza vaccination campaign was conducted at the University Hospital of Cologne to relieve overall respiratory burden in 2020/21.

The intensified influenza vaccination campaign of 2020/21 was analyzed in the context of the COVID-19 pandemic to evaluate the effect of the used strategies on vaccination coverage. To identify possible target groups with remaining unsatisfactory vaccination rates, prior influenza seasons were analyzed and compared. Furthermore, an outlook on future vaccination campaigns was given. In this context, the following research questions were answered.

2.6.1. Influenza vaccination campaign 2020/21 at the University Hospital Cologne

a. What vaccination coverage in healthcare workers of the University Hospital of Cologne did the campaign 2020/21 yield?
b. How did the vaccination coverage differ between professional fields?
c. Which option (*mobile vaccination team, occupational health department, recurring central vaccination site, mass vaccination event*) was preferred among different professional fields in the season of 2020/21?
d. Does the availability of on-site vaccination increase vaccination coverage in the predetermined target group nursing staff?
e. How did the vaccination rate per week vary over the course of the campaign 2020/21 and which determinants (*reminders per e-mail, vaccine shortage etc.)* coincided with such variation?
f. What percentage of vaccinated employees was motivated to receive the vaccine this year for the first time or for the first time in a long time (>10 years) due to the COVID-19 pandemic?
g. How did efficiency regarding time invested differ between the vaccination sites offered by the mobile vaccination team?

2.6.2. Comparison between the campaign 2020/21 to the three prior influenza seasons at the University Hospital of Cologne

a. What vaccination coverage was achieved during prior influenza seasons (2017/18 - 20219/20) and what campaign strategies were employed during this time?
b. Does the influenza vaccination campaign of 2020/21 increase vaccination rates in employees in comparison to prior years (2017/18 - 20219/20) at the University Hospital of Cologne?
c. How does the vaccination rate differ between professional fields in comparison to prior years (2017/18 - 20219/20)?

2.6.3. Outlook on future vaccination campaigns

a. Which strategies can be recommended for future influenza vaccination campaigns?
b. Can this campaign be a model for future vaccination campaigns?

3. Publications

Publication 1: Increasing influenza vaccination coverage in healthcare workers: analysis of an intensified on-site vaccination campaign during the COVID-19 pandemic

Publication 1: Supplementary material

Publication 2: Increasing influenza vaccination coverage in healthcare workers: a review on campaign strategies and their effect

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RESEARCH

Increasing influenza vaccination coverage in healthcare workers: analysis of an intensified on-site vaccination campaign during the COVID-19 pandemic

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Abstract

Purpose Influenza infections have substantial impact on healthcare institutions. While vaccination is the most effective preventive measure against influenza infection, vaccination coverage in healthcare workers is low. The study investigates the impact of an intensified influenza vaccination campaign in a maximum-care hospital on influenza vaccination coverage in healthcare workers during the COVID-19 pandemic in 2020/21.

Methods Building on findings from our previously published review Schumacher et al. (Infection 49(3): 387, 2021), an intensified influenza vaccination campaign comprising a mobile vaccination team providing on-site vaccination and vaccination at a recurring central vaccination site in addition to promotional measures was performed and analysed regarding vaccination coverage. A survey querying vaccination motivation was performed. Campaign strategies and vaccination coverage of influenza seasons between 2017/18 and 2019/20 were analysed.

Results The influenza vaccination campaign 2020/21 led to a significant 2.4-fold increase yielding an overall vaccination coverage of 40% among healthcare workers. A significant increase in vaccination coverage was observed across all professional fields; especially among nurses, a 2.7-fold increase, reaching a vaccination coverage of 48%, was observed. The COVID-19 pandemic positively influenced vaccination decision in 72% of first time ever or first time in over ten years influenza vaccinees. Vaccination coverage during prior vaccination campaigns focusing on educational measures did not exceed 17%.

Conclusion A mobile vaccination team providing on-site vaccination and vaccinations at a central vaccination site in addition to promotional measures can be implemented to increase influenza vaccination coverage in healthcare workers. Our concept can inform influenza and other vaccination campaigns for healthcare workers.

Keywords Influenza · Vaccination · Healthcare workers · Vaccination campaign · COVID-19 · Vaccination coverage

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Introduction

Influenza is caused by seasonal viruses which increase mortality rates worldwide. Annually, 291,243 to 645,832 influenza-associated respiratory deaths are estimated to occur globally [1]. Influenza vaccination is the most effective form of prevention against infection [2]. Although influenza vaccination is recommended for healthcare workers (HCW) by most public health institutions, vaccination coverage (VC) is disconcerting across Europe [3]. Especially, VC in nursing staff is unsatisfactory and has repeatedly been reported to be lower than in physicians [4–9].

Regarding the impact of influenza in hospital settings, the risk of HCW contracting influenza at the workplace [10–12], the risk of nosocomial influenza infections in patients transmitted by HCW [13, 14] and work absenteeism of HCW due to influenza infection must be considered [15].

To increase influenza vaccination coverage in HCW, education and promotion, incentives, organisational strategies, regulatory measures and combinations of the before-mentioned strategies can be implemented [16]. Influenza vaccination policies such as declination forms, "vaccinate-or-mask" policies or mandatory vaccination are associated with highest overall VC [16]. Despite being the most effective strategy, regulatory measures regarding influenza vaccination are infeasible in many countries to date, especially in Europe. Therefore, influenza vaccination is recommended yet not mandatory for healthcare workers in most European countries [17]. In these countries, education and promotion, incentives and especially organisational measures need to be developed and strengthened [16].

Among pre-COVID-19 influenza seasons in Germany, the season 2017/18 was considered severe with 1674 laboratory-confirmed influenza-related deaths and excess mortality of 25,100 reported to the German public health institute *Robert Koch Institute* (RKI). During 2018/19, 182,000 laboratory-confirmed influenza cases were reported. Out of these, 40,000 (22%) were hospitalised and 954 laboratory-confirmed influenza-related deaths were recorded [18]. Spanning only eleven weeks, the influenza season 2019/20 was shorter in comparison with the previous seasons [19].

With the ongoing COVID-19 pandemic, the world continuously faces an unprecedented challenge. To alleviate the overall burden of respiratory disease, efforts needed to be taken to increase influenza vaccination coverage in the season 2020/21. Thus, an intensified influenza vaccination campaign for HCW of the University Hospital of Cologne (UHC), Germany, was conducted. The key component constituted a mobile vaccination team (MVT) providing on-site vaccination (OSV). Here, we present the implemented strategy and respective resulting VC. Additionally, the prior influenza campaigns during the seasons of 2017/18 and 2019/20 at UHC were analysed.

Materials and methods

Study setting

UHC is a maximum-care university hospital with 1,540 beds. The number of HCW decreased from 14,272 in 2017/18 to 14,224 in 2018/19 and increased to 14,505 in 2019/20. During the season 2020/21, 15,290 HCW were employed at UHC. Reference date is 31st of December during each season.

Baseline concept

The concept of the three seasons prior to 2020/21 is considered the baseline concept. During the seasons 2017/18 and 2018/19, the campaigns included educational, promotional and organisational measures. Vaccination was provided by the occupational health department (OH) during opening hours at OH facilities. Walk-in vaccination days were provided two and three times, respectively, per season at a central vaccination site (CVS). Furthermore, strategies included announcement of the campaign via e-mail to all employees, intranet presence, an interview promoting influenza vaccination in the hospital newspaper and promotional materials such as posters, pens, stickers and buttons. A few, mostly off-campus, institutes received on-site vaccination (OSV). During 2019/20, two new concepts were included on top of the before mentioned strategies. Firstly, a single mass vaccination event (MVE) for medical students was established. Secondly, educational measures were increased by distributing postal cards which addressed common misconceptions about influenza vaccination (Supp. 1).

Intervention

Concept of the intensified influenza vaccination campaign 2020/21

An intensified influenza vaccination campaign was conducted between beginning of September and end of December 2020. The concept of the intensified influenza vaccination campaign consisted of organisational as well as educational and promotional elements, the focus being an MVT providing OSV as well as vaccination at a CVS. In addition to these interventions, employees could receive vaccination during the opening hours at the OH as before.

The campaign was announced by the hospital board to all employees via e-mail. As a reminder, monthly e-mails were sent to employees providing news of the campaign. Considering the COVID-19 pandemic, all elements of the campaign were conducted in accordance with safety measures required by national public health authorities as well as the UHC hospital board.

An MVT was set up comprising a physician and nurse; both were employed for the conduct of the campaign. OSV was provided on a flexible time schedule often during shift changes or at the beginning or end of recurring team meetings to reach as many employees as possible at the same time. Team members could arrange an appointment for their team via a central email account or phone to receive influenza vaccination on-site at wards or institutions. The MVT reached out via email and phone to all remaining departments inquiring on the need for on-site appointment. Additionally, the MVT was stationed at the CVS twice a week during lunch time, where HCW could drop in to receive vaccination without having to schedule an appointment. The CVS was in the centre of the hospital campus, next to the cafeteria and easily accessible for every employee. All employees were informed that vaccination was taking place whenever a flag depicting the campaign logo was set up outside the CVS. This allowed for the MVT to set up additional CVS vaccination slots spontaneously. At the end of the campaign, three mass vaccination events (MVE) for medical students were organised in cooperation with the student body faculty.

Furthermore, a promotional campaign was developed. The logo (Fig. 1) showed a vaccinated woman in an empowering pose displaying the vaccinated arm with band aid. This logo was used consistently throughout the campaign. The MVT handed out small packages of hygienic swipes showing the campaign logo as well as stickers and buttons stating "Vaccines save lives" during vaccination appointments. Additionally, two educational videos were prepared. Firstly, an infectious diseases specialist (OAC) employed at UHC addressed concerns of influenza vaccination, such as low efficacy of the vaccine or fear of side effects. Secondly, the department head of nursing appealed to the nursing staff to receive flu vaccination to protect HCW, patients and relatives as well as friends. These videos were circulated via e-mail and shared in the UHC intranet (Supp. 2.). An article about the campaign was included in the autumn issue of the internal hospital magazine at the beginning of the campaign. Furthermore, during the campaign, pictures of vaccinated HCW were taken in the same empowering pose showing their vaccinated arm with band aid. These pictures were available online in the UHC intranet. During the last third of the campaign, a flash mob action of covering bicycle saddles on campus with saddle covers depicting the campaign logo took place.

Fig. 1 Campaign logo of the intensified influenza vaccination campaign 2020/21. Figure shows the campaign logo of the intensified influenza vaccination campaign in 2020/21 stating "Together against the flu" in the speech bubble and "Get vaccinated now! Dates and additional information can be found on the intranet" in the left bottom corner in German

Analysis

Evaluation of prior influenza seasons 2017/18 to 2019/20

The number of employees receiving vaccination per season with respective age, professional field and sex distribution among vaccinees was provided by the OH department. The information on concepts of the prior seasons as well as the promotional materials was provided by the corporate communications department and infectious diseases division.

Data collection during the campaign 2020/21

Due to data protection reasons, the dataset of the season 2020/21 is only complete for HCW vaccinated by the MVT. The age group, sex and professional field of each person vaccinated by the MVT were documented anonymously during vaccination. This information was not documented by those vaccinated at the OH. The complete data set including age, sex and professional field was only available for those vaccinated by the MVT and only the overall number of vaccinated HCW was available for the OH dataset. To estimate the distribution of those vaccinated by the OH per professional field, we performed a web-based anonymised survey (see *Survey on vaccination campaign 2020/21)*. The survey dataset was filtered for the distribution of professional fields among those stating having received vaccination by the OH. The respective distribution of professional fields identified in this survey was extrapolated to the total number of vaccinations performed by the OH. Estimated numbers of those vaccinated by the OH were combined with the data collected by the MVT, resulting in an approximate of the overall VC per professional field for the season 2020/21.

Survey on vaccination campaign 2020/21

Following the end of the campaign 2020/21, an anonymous survey was developed to receive feedback on the conduct of the campaign and to complete the unavailable information on vaccinees as mentioned above. The survey was compiled using the EFS Summer 2021 software (TIVIAN, Cologne, Germany). The conduct of the survey was approved by the hospital board, staff committee, data protection officer and equal opportunity commissioner. The survey was e-mailed to all 15,290 HCW once and remained available for three weeks during February and March 2021. The survey queried vaccination status and professional field. If the participating person stated receipt of vaccination, additional questions regarding the motivation to receive vaccination were queried. Also, individuals could give free-text feedback. A translated version of the survey can be found in the Supp. 3.

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics (version 27.0, IBM SPSS Inc, Chicago, IL, USA). Categorical variables such as VC were provided in frequencies, and percentages and proportions were compared using the Chi-squared test. Continues variables were provided by calculating median and interquartile range.

Data security

The data collected for analysis during vaccinations by the MVT were collected anonymously. The adherence to data protection guidelines of the data provided by the OH department for the seasons 2017/18 to 2019/20 including the overall number of vaccinations in 2020/21 was confirmed by the UHC data protection officer. Additionally, the UHC data protection office ensured adherence to data protection guidelines of the conducted survey on the season 2020/21.

Ethics statement

According to §§ 17 and 40 of the Data Protection Act of North Rhine-Westphalia (Cologne), retrospective analysis and anonymised reporting of patient data without informed consent are appropriate. Further ethical approval is waived.

Definitions

HCW in this context refers to any personnel of the hospital and includes UHC employees, medical students of the Medical Faculty of the University of Cologne and subsidiary company employees. Vaccination coverage is defined as the percentage of HCW vaccinated in relation to all HCW. Professional fields were determined beforehand to group vaccinated HCW into a respective category during vaccination by the MVT. These categories included administration staff, functional services, nursing staff, physicians, research personnel, students/trainees/interns and subsidiary company employees.

Results

Analysis of past vaccination campaigns

Following the season 2017/18, a significant increase ($p < 0.001$) in overall VC was observed in the season of 2018/19, yielding a VC of 16% (2289/14,224) in comparison with a VC of 11% (1514/14,272) in the prior season, which corresponds to a 1.5-fold increase. Concerning professional fields, a significant increase in VC occurred in all categories except for subsidiary company employees. Highest relative increase was observed in administration staff (22% (182/819) to 52% (420/809), 2.4-fold increase, $p < 0.001$), followed by functional staff (8% (260/3257) to 15% (472/3187), 1.9-fold increase, $p < 0.001$) and nurses (13% (225/1696) to 21% (354/1668), 1.6-fold increase, $p < 0.001$). Among different professional fields, VC was highest in physicians in the season of 2017/18, further increasing from 38% (538/1422) to 52% (714/1383) in 2018/19 (1.4-fold increase, $p < 0.001$). In the season 2018/19, both physicians and administration staff yielded highest VC reaching 52% (Fig. 2, Table 1).

Between the seasons of 2018/19 and 2019/20 a significant increase ($p = 0.040$), albeit only corresponding to a 1.1-fold increase, in VC occurred as well. The overall VC of 16% (2289/14,224) in 2018/19 increased to 17% (2465/14,505) in the season of 2019/20. Keeping in mind that documentation of professional field of vaccinees was not available for 4% in 2018/19 and for 11% in 2019/20, a decrease in VC per professional field was observed across all fields. Notably, in 2019/20, VC per professional field was highest in administration staff, closely followed by physicians. VC did

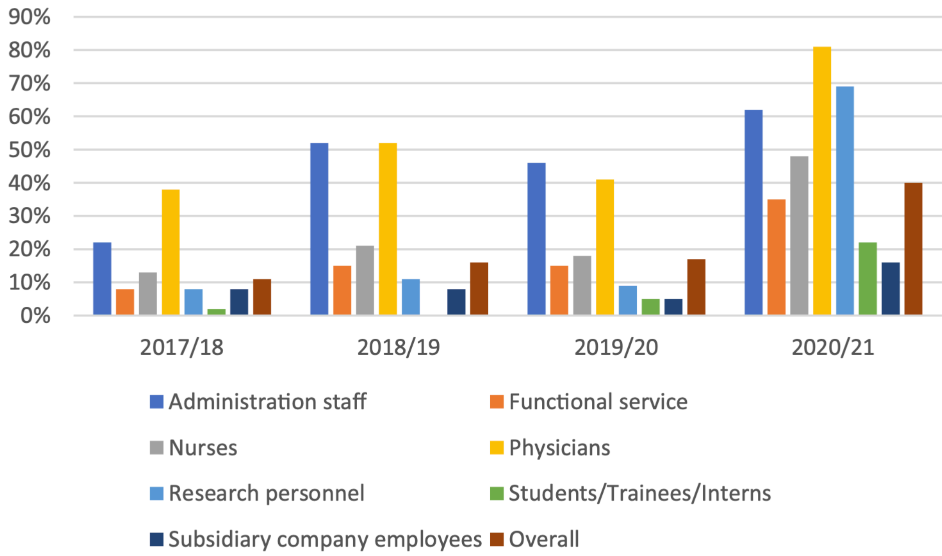

Fig. 2 Vaccination coverage overall and per professional field in the seasons 2017/18 to 2020/21. Bar graph shows the vaccination coverage (VC) per professional field as well as the overall VC in healthcare workers per season over the course of 2017/18 to 2020/21. No data were available on the professional field category students/trainees/interns in 2018/19

not exceed 18% in nurses, 15% in functional staff and was lowest in subsidiary company employees (Fig. 2, Table 1).

Demographics of HCW vaccinated over the course of the three seasons between 2017/18 and 2019/20 are shown in Table 2.

Analysis of the 2020/21 campaign

The intensified influenza vaccination campaign 2020/21 led to a significant increase in overall VC from 17% (2465/14,505) in the previous season to 40% (6048/15,290) (2.4-fold increase; $p<0.001$) in 2020/21 (Fig. 2). Excluding medical students, the overall VC increased from 22% (2230/10,084) in 2019/20 to 48% (5025/10,573) in 2020/21 (2.2-fold increase; $p < 0.001$).

The increase in VC within each professional field was significant across all professional fields (Table 1). Yielded VC was highest in physicians with 81% (1215/1505, twofold increase; $p < 0.001$), followed by research personnel with 69% (675/981, 7.7-fold increase; $p < 0.001$), administration staff with 62% (542/872, 1.3-fold increase; $p < 0.001$), nurses with 48% (1060/2215, 2.7-fold increase; $p < 0.001$), functional staff with 35% (1080/3072, 2.3-fold increase; $p < 0.001$), medical students/trainees/interns with 22% (1023/4717, 4.4-fold increase; $p < 0.001$) and subsidiary company employees with 16% (295/1897, 3.2-fold increase; $p < 0.001$) (Fig. 2, Table 1).

Out of all vaccinees, 4071 (67%) were vaccinated by the appointed MVT (OSV, CVS and MVE) while 1977 (33%) HCW received the flu vaccine by the OH. Concerning vaccination sites, 33% received vaccination at the OH, 31% were vaccinated on-site, 30% were vaccinated at the CVS and 6% during MVE (Fig. 3). Out of the 4071 HCW vaccinated by the MVT, 2598 (64%) were female and 1473 (36%) were male, in comparison with the overall sex distribution of 69% female and 31% male employees at UHC. Further demographic information on HCW vaccinated is presented in Table 2.

The demographic data of MVT vaccinees were further analysed regarding the three vaccination sites provided by the MVT. Among those vaccinated by the MVT, the age distribution between OSV and CVS was similar with a median age of 38 (IQR: 29 – 51) at the CVS in comparison with the median age of 37 (IQR: 29 – 49) of OSV vaccinees. Those vaccinated during MVE (almost exclusively medical students) were generally younger (median: 22, IQR: 21 – 24). Regarding sex, 46% of female vaccinees were vaccinated at the CVS, 45% on-site and 9% at the MVE, whereas male vaccinees mainly received vaccination on-site (48%), followed by vaccination at the CVS (42%) and MVE (10%). Physicians and nursing staff both predominantly received vaccination at the CVS (59% and 57%, respectively) in comparison to OSV (41% and 43%, respectively), while research personnel and administration staff predominantly chose OSV (89% and 57%, respectively) compared to vaccination at the CVS (12% and 43%, respectively) (Table 3).

The campaign of 2020/21 kicked-off on September 7th, as soon as the vaccine shipment arrived. During the first few days, the MVT was at the CVS daily during lunchtime and HCW could drop in spontaneously. The campaign was officially announced via e-mail to all HCW by the hospital board on September 10th; simultaneously promotional material (posters, pamphlets) was spread across the hospital campus. Almost 3,000 HCW were vaccinated by the MVT by the time a vaccine shortage hit on October 13th which lasted for almost a month. During this time, the opening hours at the CVS were shortened. To inform on the arrival of new vaccine supplies, a second e-mail to all

Table 1 Vaccination coverage per professional field between 2017/18 and 2020/21

	2017/18	2018/19			2019/20			2020/21		
	VC in % (Vacc./ employees)	VC in % (Vacc./ employees)	*p* value (2017/18 vs 2018/19)	Relative change (2017/18 vs. 2018/19)	VC in % (Vacc./ employees)	*p* value (2017/18 vs 2018/19)	Relative change (2018/19 vs. 2019/20)	VC in % (Vacc./ employees)	*p* value (2017/18 vs 2018/19)	Relative change (2019/20 vs. 2020/21)
Administration staff	22 (182/819)	52 (420/809)	< 0.001	+ 134%	46 (387/836)	0.023	− 11%	62 (542/872)	< 0.001	+ 34%
Functional service	8 (260/3257)	15 (472/3187)	< 0.001	+ 86%	15 (463/3152)	0.892	− 1%	35 (1080/3072)	< 0.001	+ 139%
Nursing staff	13 (225/1696)	21 (354/1668)	< 0.001	+ 60%	18 (340/1920)	0.008	− 17%	48 (1060/2215)	< 0.001	+ 170%
Physicians	38 (538/1422)	52 (714/1383)	< 0.001	+ 36%	41 (599/1457)	< 0.001	− 20%	81 (1215/1505)	< 0.001	+ 96%
Research personnel	8 (76/914)	11 (101/911)	0.045	+ 33%	9 (82/915)	0.131	− 19%	69 (675/981)	< 0.001	+ 668%
Students/trainees/interns	2 (76 /4468)	n.a	–	n.a	5 (235/4421)	–	n.a	22 (1023/4717)	< 0.001	+ 308%
Subsidiary company emp	8 (139/1696)	8 (133/1759)	0.489	− 8%	5 (94/1804)	0.004	− 31%	16 (295/1897)	< 0.001	+ 198%
Other	15	n.a	–	–	n.a	–	–	158	–	–
n. a	3	95	–	–	265	–	–	–	–	–

Table shows the VC per professional field of the seasons 2017/18 to 2020/21 including *p* value of change in VC per professional field between prior and the respective following season calculated using Chi-squared test

VC vaccination coverage, *Vacc.* Vaccinations, *n.a.* not available

Table 2 Demographic data of vaccinees during the seasons 2017/18 – 2020/21

	Category	2017/18	%	2018/19	%	*p* value (2017/18 vs 2018/19)	2019/20	%	*p* value (2018/19 vs 2019/20)	2020/21	%	*p* value (2019/20 vs. 2020/21)
Vaccinated/Employees	–	**1514**/14272	11%	**2289**/14224	16%	< 0.001	**2465**/14505	17%	0.040	**6048**/15290	40%	< 0.001
Age (years) distribution among vaccinated	< 20	14	1%	38	2%	0.056	41	2%	0.993	55	1%	0.003
	20–29	376	25%	656	29%	0.009	777	32%	0.032	1236	20%	< 0.001
	30–39	436	29%	580	25%	0.018	643	26%	0.556	1129	19%	< 0.001
	40–49	293	19%	429	19%	0.638	421	17%	0.135	687	11%	< 0.001
	50–59	295	19%	420	18%	0.380	390	16%	0.021	701	12%	< 0.001
	≥ 60	100	7%	165	7%	0.474	193	8%	0.417	263	4%	< 0.001
	n. a	0	–	1	0%	–	0	–		1977	33%	< 0.001
Sex distribution among vaccinated	Female	904	60%	1380	60%	0.721	1501	61%	0.670	2598	43%	< 0.001
	Male	605	40%	906	40%	0.815	963	39%	0.717	1473	24%	< 0.001
	n. a	5	0%	3	0%	–	1	0%	–	1977	33%	< 0.001
Professional field distribution among vaccinated	Administration staff	182	12%	420	18%	< 0.001	387	16%	0.015	542	9%	< 0.001
	Functional service	260	17%	472	21%	0.008	463	19%	0.111	1080	18%	0.315
	Nursing staff	225	15%	354	15%	0.612	340	14%	0.103	1060	18%	< 0.001
	Physicians	538	36%	714	31%	0.005	599	24%	< 0.001	1215	20%	< 0.001
	Research personnel	76	5%	101	4%	0.384	82	3%	0.052	675	11%	< 0.001
	Students/Trainees/Interns	76	5%	n. a	n. a	–	235	10%	–	1023	17%	< 0.001
	Subsidiary company employees	139	9%	133	6%	< 0.001	94	4%	0.001	295	5%	0.033
	Other	15	1%	n. a	n. a	–	n. a	n. a	–	158	3%	–
	n. a	3	0%	95	4%	–	265	11%	–	–	–	–

Bold indicates the number of vaccinated healthcare workers per season

n.a. not available

Table shows the demographic data of vaccinees during the seasons of 2017/18–2019/20. The p-value for the change in distribution among vaccinees in different categories (age, sex and professional field) between the previous and the following season was evaluated using the Chi-squared test. The category "other" applied whenever the professional field was known but did not fit into the given categories

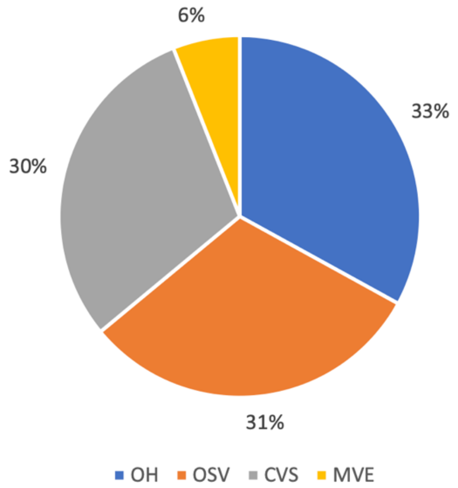

Fig. 3 Distribution of vaccinations per provided vaccination site in season 2020/21. *OSV* on-site vaccination, *OH* occupational health department, *CVS* central vaccination site, *MVE* mass vaccination event. Pie chart showing the distribution of vaccinations per available vaccination site or event during the season of 2020/21. Vaccinations at OSV, CVS and during MVE were performed by the mobile vaccination team

HCW was sent out on November 11th. In the same week, a promotional flash mob of distributing saddle bike covers depicting the campaign logo on bicycles across campus took place. During end of November and beginning of December, four MVE for medical students were conducted by the MVT. Two weeks before the end of the intensified campaign, a third "last call" reminder e-mail was sent out to all HCW. Of note, when comparing Tuesdays (main weekly CVS day) before and after, all three e-mails to HCW by the hospital board led to an increase in vaccinations per day. The milestone of 4,000 vaccinations by the MVT was reached on December 10th. Following the end of the intensified campaign on December 18th, HCW could still receive influenza vaccination at the OH during opening hours in the following weeks (Fig. 4).

Analysis of the survey following the campaign 2020/21

A response rate of 22% (3327/15,290) was observed in the 2020/21 influenza vaccination campaign survey, which was conducted from February 17th to March 3rd, 2021. Out of all participants, 73% (2413/3327) reported having received influenza vaccination during the 2020/21 season. Out of the reportedly vaccinated employees, 13% (318/2413) stated having received the vaccination externally (e.g. at their primary care physician). Out of all vaccinated respondents, the COVID-19 pandemic contributed to a positive vaccination decision for 30% (720/2413) of those vaccinated. For 40% (968/2413) of

Table 3 Demographic data of mobile vaccination team vaccinees of the 2020/21 campaign by vaccination site

VS	Age	Sex		Professional fields							
	Median (IQR)	Female (% per site)	Male (% per site)	Administration staff (% per site)	Functional service (% per site)	Nursing staff (% per site)	Physicians (% per site)	Research personnel (% per site)	Students/trainees/interns (% per site)	Subsidiary company emp. (% per site)	Other (% per site)
CVS	38 (29 – 51)	1203 (46%)	625 (42%)	115 (43%)	473 (52%)	367 (57%)	511 (59%)	53 (12%)	207 (30%)	81 (40%)	19 (95%)
OSV	37 (29 – 49)	1166 (45%)	706 (48%)	154 (57%)	434 (48%)	272 (43%)	362 (41%)	408 (89%)	119 (17%)	122 (60%)	1 (5%)
MVE	22 (21 – 24)	229 (9%)	142 (10%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	371 (53%)	0 (0%)	0 (0%)

Table shows the demographic data of MVT vaccinees including age, sex and professional field per vaccination site

VS vaccination site, *CVS* central vaccination site, *OSV* on-site vaccination, *MVE* mass vaccination event

Fig. 4 Timeline of the 2020/21 campaign depicting vaccinations per day (conducted by MVT) and corresponding events. *MVT* mobile vaccination team, *OSV* on-site vaccination, *CVS* central vaccination site, *MVE* mass vaccination event. Line graph depicts the number of vaccinations per day conducted by the MVT and corresponding events during the intensified influenza vaccination campaign 2020/21. As the number of vaccinations per day conducted by the occupational health department was not available, only MVT vaccinations per day are shown

those reportedly vaccinated, the intensified 2020/2021 vaccination campaign increased vaccination readiness. For 29% (706/2413), the 2020/21 season's vaccination was their first influenza vaccination ever or their first influenza vaccination in over 10 years. Out of these first timers, 60% (421/706) stated the intensified campaign had a positive impact on their decision to receive vaccination. Additionally, 72% (510/706) of first timers stated the COVID-19 pandemic positively influenced their decision to receive vaccination. Concerning the response per professional field, for 31% (116/379) of vaccinated nursing staff, the 2020/21 influenza vaccination was reportedly their first flu vaccination ever (or in over 10 years). Out of these first timers among nursing staff, 78% (90/116) stated the COVID-19 pandemic and 53% (61/116) stated the intensified campaign positively influenced their decision to receive flu vaccination. For 43% (50/116), both the COVID-19 pandemic and the intensified campaign contributed positively to their vaccination decision (Table 4).

The optionally written feedback in the survey repeatedly highlighted the options to receive vaccination spontaneously at the CVS on the way to or from lunch as well as the option to receive OSV. A few comments pointed towards misconceptions, such as not wanting to receive vaccination due to pregnancy and not wanting to receive a live vaccine. Furthermore, reasons for declining vaccination were expressed, such as wanting to be ready for the COVID-19 vaccination at any given moment or believing flu vaccination to be unnecessary due to COVID-19 policies.

Discussion

The intensified influenza vaccination campaign 2020/21 comprising OSV and vaccination at a recurring CVS led to a significant 2.4-fold increase during the COVID-19 pandemic, yielding a VC of 40% among HCW. Increase in VC was significant across all professional fields. Especially among nurses, a professional field with historically low VC [4–9, 20], we observed a 2.7-fold increase reaching a VC of 48%. Highest overall VC was found for physicians with 81%, while highest relative increase in VC was found for research personnel (7.7-fold). The analysis of pre-COVID-19

Table 4 Survey results following the 2020/21 campaign by profession

	Overall $N=3327$ (100%)		Admin. staff $N=581$ (17%)		Functional services $N=300$ (9%)		Physicians N 412 = (12%)		Research personnel $N=449$ (14%)		Students/ trainees/ interns $N=588$ (18%)		Subsidiary company employees $N=190$ (6%)		Other $N=211$ (6%)	
	N	[%]	*N*	[%]	*N*	[%]	*N*	[%]	*N*	[%]	*N*	[%]	*N*	[%]	*N*	[%]
Vaccinated	2413	73	395	68	214	71	382	93	336	75	430	73	134	71	143	68
Vaccination site																
OSV	729	30	138	35	84	39	107	28	175	52	36	8	53	40	47	33
CVS	682	28	136	34	60	28	144	38	75	22	57	13	42	31	38	27
OH	558	23	77	19	49	23	96	26	60	18	92	21	26	19	39	27
Ex	318	13	44	11	21	10	34	9	26	8	122	28	13	10	19	13
MVE	126	5	0	0	0	0	1	0	0	0	123	29	0	0	0	0
First timers[1] overall	706	29	124	31	68	32	41	11	126	38	134	31	49	37	48	34
COVID-19[2] overall	720	30	139	35	82	38	61	16	121	36	104	24	46	34	42	29
COVID-19[2] among first timers[1]	510	72	98	79	60	88	25	61	91	72	75	56	35	71	36	75
Campaign[3] overall	968	40	166	42	71	33	126	33	147	44	202	47	62	46	60	42
Campaign[3] among first timers[1]	421	60	76	61	36	53	24	59	83	66	82	61	30	61	29	60

Table shows the results of the conducted survey on the intensified influenza vaccination campaign 2020/21. The number and percentage of vaccinations as reported are shown for each professional field. Furthermore, the vaccination site per professional field, whether this year's vaccination was their reportedly first (or first time in over 10 years) vaccination, whether the COVID-19 pandemic positively influenced their decision to receive the vaccine and whether the intensified campaign increased their vaccination readiness in the season of 2020/21 per professional field are outlined

N number, *MVT* mobile vaccination team, *OSV* on-site vaccination, *CVS* central vaccination site, *OH* occupational health, *Ex* externally (e.g. primary physician's office), *MVE* mass vaccination event

[1]First time influenza vaccination ever or in over 10 years

[2]COVID-19 positively influenced vaccination decision

[3]Intensified vaccination campaign positively influenced vaccination decision

influenza vaccination campaigns had underlined the limitations of influenza vaccination campaigns which focus on educational measures instead of exhausting organisational measures, yielding a maximum VC of only 17% [16].

As 67% of all vaccinees were vaccinated by the specifically arranged vaccination team, the appointment of a dedicated team can be considered successful. This corresponds to the findings of an influenza vaccination campaign conducted at another German hospital in 2019 highlighting the importance of a committed team [21]. When comparing the distribution of vaccinees between the three major vaccination sites (OSV, CVS and OH) at our hospital, all three options were equally used. However, keeping in mind that the organisational and logistical time effort is considerably higher for OSV, offering walk-in vaccinations at central sites seems to be more efficient and just as high in demand. Interestingly, nurses and physicians preferably received vaccination at the CVS in comparison to OSV at wards. Furthermore, monthly reminder e-mails increased VC when comparing specific weekdays before and after the notification. The overall VC in the season of 2020/21 may be even higher, as 13% of vaccinated survey participants reported having received vaccination externally. This could be associated with the temporary vaccine shortage during our campaign. Of note, the conduct of the campaign was not compromised during high COVID-19 activity most likely due to strict adherence to COVID-19 safety measures [22].

The survey underlined the impact of the COVID-19 pandemic on the majority of vaccinees, especially among first time (or first time in over ten years) influenza vaccinees. This may point to a change in perception and awareness of vaccinations overall [23–25]. The survey, however, also highlighted the significance of the intensified campaign itself. Interestingly, for first time vaccinated nurses the COVID-19 pandemic seems to have played a major role, positively influencing vaccination decision in 78% in comparison to the intensified campaign itself (53%). Even though educational strategies implemented on their own are not proven to reach sufficient VC [16], misconceptions mentioned during the survey still point to a lack of knowledge even among HCW. Notably, the survey did not query the impact of public German mass media coverage, which during that time strongly highlighted the need for influenza vaccination as well [22].

One other influenza vaccination campaign for HCW during the same period has been published so far [26]. The campaign conducted at an Italian research and teaching hospital comprised educational, promotional and organisational (OSV, CVS) strategies and is comparable to our campaign except for an incentive strategy: a competition ranking VC between hospital departments. Of note, most data were analysed regarding different hospital departments in comparison with professional fields in our analysis. An increase in overall VC from 22% in the previous season to 43% in 2020/21 is comparable to our results. Furthermore, physicians also reached highest overall VC, while highest relative increase was found for administrative staff in comparison to research personnel in our study. While physicians showed a preference for vaccination at CVS in our study, a trend towards OSV was evident at the Italian hospital. While our survey suggests COVID-19 to be a strong motivation to receive vaccination, analysis of a questionnaire on vaccination motivation during the Italian campaign could not show the same trend [26]. However, findings of the 2021/22 campaign at the same Italian hospital underlined the crucial role of COVID-19 on vaccination decision [27].

The analysis of past influenza vaccination campaigns showed a significant increase between all seasons, higher relative change being observed from 2017/18 to 2018/19. This change could be due to the severity of the 2017/18 influenza season in Germany [18]. Even though efforts were taken to increase VC further through educational measures, overall VC did not exceed 17% during 2019/20. This moderate increase in VC is comparable to other campaigns focusing on educational measures [5, 28].

Limitations include the incomplete data set of OH vaccinees due to data protection reasons. Since the professional field of HCW vaccinated by the MVT was categorised subjectively and the distribution of professional fields among OH vaccinees was extrapolated using the survey data, a bias is possible. Furthermore, data collected during campaign and survey were anonymised, precluding a cross-analysis between both data sets.

Despite our endeavours, the WHO-recommended HCW vaccine rate of 75% was not reached [29]. This finding is in line with other pre-COVID-19 influenza vaccination campaigns focusing on educational, promotional and organisational campaign strategies without implementation of vaccine policies [5, 8, 16, 30, 31]. Comparably, VC exceeding 75% among HCW was reached by non-European influenza vaccination campaigns which include policies such as mandatory declination forms, a "vaccinate-or-mask" policy or mandatory vaccination for HCW [16, 32–36]. Other vaccinations, such as measles-mumps-rubella, are mandatory for HCW in some European countries, and the need for such mandates is debatable [17]. In the context of COVID-19, vaccination mandates have gained traction and were realised for HCW in France and Germany [37, 38]. Comparably, COVID-19 VC at our hospital UHC surpassed 90%. An analysis following the implementation of a COVID-19 vaccination mandate for HCW in Italy suggests an increase in vaccine uptake lowering COVID-19 infection rates among HCW [39]. Potentially, COVID-19 vaccine mandates across Europe could pave the way for future influenza vaccine mandates for HCW such as possible influenza "vaccinate-or-mask" policies [36, 40, 41].

Concerning future influenza vaccination campaigns for HCW, a dedicated vaccination team, OSV and recurring vaccination options at a CVS should be integrated [16]. Potentially, a live calendar showing the location of the MVT during OSV in the hospital intranet could help inform on vaccination opportunities and decrease the communication work of the MVT itself. An online tool for appointment scheduling may further streamline the organisation. Furthermore, a decentralised vaccination supply including the distribution of "flu-kits" and "peer-to-peer" vaccination could be implemented [33, 35]. Also, an efficient "blitz" campaign focusing on a shorter time span with a larger vaccination team could be explored [34].

In conclusion, an intensified campaign comprising a dedicated team providing OSV and vaccinations at a CVS in combination with intensified promotional strategies showed a substantial increase in VC in a university hospital setting across all professional fields. The presented concept has potential to be successfully used for upcoming influenza as well as other, including COVID-19, vaccination campaigns for HCW.

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Author contributions SS conducted the influenza vaccination campaign 2020/21, collected the data, conceived the survey, performed the statistical analysis and drafted the manuscript. JSG advised on statistical analysis and reviewed the manuscript. AL organised vaccinations at the central vaccination site during the campaign 2020/21, aided in data collection and reviewed the manuscript. MR assisted during the influenza vaccination campaign 2020/21, collected data and reviewed the manuscript. DS conceived the survey and reviewed the manuscript. SCM conceived the study idea, advised on the conduct of the influenza vaccination campaign 2020/21 and revised the manuscript. OC conceived the study idea, advised on the conduct of the influenza vaccination campaign 2020/21 and revised the manuscript.

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Availability of data and materials Data and materials are available upon reasonable request in accordance with General Data Protection Regulation.

Declarations

Conflict of interest SS declares that she has no conflict of interest. JSG reports speaker honoraria from Gilead and Pfizer. AL declares that she has no conflict of interest. MR declares that she has no conflict of interest. DS reports grants and speaker honoraria from Pfizer Pharma. SCM reports grants from University of Cologne (KoelnFortune), grants from Dr Manfred Plempel Stipend, grants from DZIF Clinical Leave, personal fees from Octapharma, outside the submitted work. OAC reports grants or contracts from Amplyx, Basilea, BMBF, Cidara, DZIF, EU-DG RTD (101037867), F2G, Gilead, Matinas, MedPace, MSD, Mundipharma, Octapharma, Pfizer, Scynexis; Consulting fees from Abbvie, Amplyx, Biocon, Biosys, Cidara, Da Volterra, Gilead, Matinas, MedPace, Menarini, Molecular Partners, MSG-ERC, Noxxon, Octapharma, Pardes, PSI, Scynexis, Seres; Honoraria for lectures from Abbott, Al-Jazeera Pharmaceuticals, Astellas, Grupo Biotoscana/United Medical/Knight, Hikma, MedScape, MedUpdate, Merck/MSD, Mylan, Pfizer; Payment for expert testimony from Cidara; Participation on a Data Safety Monitoring Board or Advisory Board from Actelion, Allecra, Cidara, Entasis, IQVIA, Janssen, MedPace, Paratek, PSI, Pulmocide, Shionogi; A patent at the German Patent and Trade Mark Office (DE 10 2021 113 007.7).

Ethical approval According to §§ 17 and 40 of the Data Protection Act of North Rhine-Westphalia (Cologne), retrospective analysis and anonymised reporting of patient data without informed consent are appropriate. Further ethical approval is waived.

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Supplement 1. Educational postcards addressing misconceptions distributed during the season of 2019/20

A

B

C

A. Postcard stating “Flu vaccination: I do not have any patient contact! The influenza virus is transmitted via droplets and smear. Transmission is possible without direct contact.”

B. Postcard stating “Flu vaccination: Unsatisfactory risk-/benefit ratio? Influenza vaccination provides protection for yourself, your patients, and others around you.”

C. Postcard stating “Flu vaccination: Can cause influenza! No! The implemented vaccine is not a live vaccine and therefore cannot cause nor transmit influenza. However: Elevated body temperature and malaise is possible following vaccination. This is due to the unspecific activation of the immune system.”

Supplement 2. Links to educational videos distributed during the intensified influenza vaccination campaign 2020/21

https://www.youtube.com/watch?v=Y1Ozg8v16QM&t=13s
https://www.youtube.com/watch?v=vBzXNM_8TFs&t=3s

Supplement 3. Survey on campaign 2020/21 (translated from German)

“Introductory text to survey:

Welcome to the survey on the “influenza vaccination campaign 2020/21”

Your participation will support the evaluation of this year's influenza vaccination campaign and help optimize future vaccination campaigns.

Survey:

1. Have you been vaccinated against influenza („the flu“) in the season of 2020/21?
    a. Yes
    b. No

2. Which professional group do you belong to?
    a. Physicians
    b. Nursing staff
    c. Research staff
    d. Administration staff
    e. Functional service
    f. Students/Trainees/Interns
    g. Subsidiary company employees
    h. Other

If yes to 1:

3. Where did you receive the influenza vaccination?
    a. On-site through the mobile vaccination team of UHC
    b. At the central vaccination site
    c. At the occupational health department
    d. I received the flu vaccine externally (e.g., primary health physician) or in a different not here mentioned way

If yes to 1:

4. Did you get vaccinated against influenza for the first time this year or was your last vaccination more than 10 years ago?
    a. Yes
    b. No

If yes to 1:

5. Was the COVID-19 pandemic a decisive factor in your decision to get vaccinated against influenza this year?
    a. Yes
    b. No

If yes to 1:

6. Has the intensified 2020/21 flu vaccination campaign increased your willingness to get the flu shot?
    a. Yes
    b. No

Your comments on the 2020/21 influenza vaccination campaign:

(Text field)

Thanks for the participation:

Thank you very much for participating in our survey

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REVIEW

Increasing influenza vaccination coverage in healthcare workers: a review on campaign strategies and their effect

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Abstract
Purpose Increasing influenza vaccination coverage in healthcare workers is a challenge. Especially during the ongoing COVID-19 pandemic, high vaccination coverage should be attained. This review analyzed strategies to increase influenza vaccination coverage in healthcare workers.
Methods A literature search using PubMed was conducted and 32 publications on influenza vaccination campaigns for healthcare workers were reviewed for key interventions and resulting vaccination coverage.
Results Among key interventions analyzed, mandatory vaccination policies or multifaceted campaigns including a vaccinate-or-wear-a-mask policy as well as mandatory declination reached vaccination coverage in healthcare workers of over 90%. Although campaigns solely based on education and promotion or on-site-vaccination did not regularly exceed an absolute vaccination coverage of 40%, a substantial relative increase in vaccination coverage was reached by implementation of these strategies.
Conclusion Mandatory vaccination policies are effective measures to achieve high overall vaccination coverage. In clinics where policies are infeasible, multifaceted campaigns comprising on-site vaccination, vaccination stands and educational and promotional campaigns as well as incentives should be implemented. Lessons learned from influenza campaigns could be implemented in future SARS-CoV-2 vaccination campaigns.

Keywords Healthcare personnel · Seasonal influenza · Influenza virus · Immunization · Vaccine uptake rate · Immunization programs

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Introduction

Influenza is a highly contagious disease, causing 4.0–8.8 respiratory deaths per 100 000 individuals annually worldwide [1]. Vaccination is the most effective form of influenza prevention. Children under 5 years of age, chronically ill and immunocompromised patients, the elderly (> 65 years) and pregnant women are at high risk of complicated influenza courses. The World Health Organization (WHO) recommends annual influenza vaccination for these vulnerable populations as well as healthcare workers (HCW) [2]. HCW may transmit influenza to vulnerable patients, thereby compromising patient safety [3].

Despite this recommendation, vaccination rates among HCW are low ranging from 15.6 to 63.2% (median 30.2%) in Europe [4]. Other than allergies against vaccine compounds, there are no medical contraindications for influenza vaccination. If allergy to egg protein is known, a cell- or recombinant-based vaccine can be used [5]. The challenge is addressing personal reasons among unvaccinated staff against influenza vaccination. In the German OKaPII study, doctors stated mainly organizational aspects, whereas nurses declared lacking confidence in efficacy and safety of vaccines [6]. Organizational and educational issues can be approached and overcome. It should, therefore, be possible to increase influenza vaccination rates.

Most university hospitals in Germany treat high numbers of vulnerable patients. As immunocompromised patients may have an impaired immune response to vaccines, herd immunity is even more important [7]. To protect these patients, high influenza vaccination rates in HCW have to be achieved [8]. At the University Hospital of Cologne, we are planning an intensified influenza vaccination campaign for the upcoming season 2020/2021. Therefore, we analyzed the current literature on influenza vaccination campaigns for HCW.

In context of the ongoing coronavirus disease 2019 (COVID-19) pandemic, public health implications of the influenza season 2020/2021 must be considered. Coinfections of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and influenza virus have been described [9]. Sick leaves of HCW due to influenza or coinfections with SARS-CoV-2 could impact workforce availability. This, in combination with high infection rates in patients, could overburden our healthcare systems. Thus, high influenza vaccination rates among HCW should be attained [10].

Methods

To identify influenza vaccination campaign strategies, we performed a literature search using the PubMed® database. The following query was defined: ((“health personnel/analysis” [MeSH Terms] OR “health personnel/statistics and numerical data” [MeSH Terms]) AND “influenza, human/prevention and control” [MeSH Terms]) NOT (review [Publication Type]). Articles published from January 2010 to August 2020 were included. No language restrictions were applied. Publications were selected by screening title and abstract. Studies implementing interventions to increase seasonal influenza vaccination rates among HCW were included. Studies focusing on pandemic influenza in 2009–2010 were excluded. The interventions needed to be clearly defined. Also, the selected studies had to include an evaluation of effect in comparison to a control group or in comparison to at least one previous season. Studies which conducted surveys in a number of institutions comparing different campaign strategies among each other were excluded. If the studies differentiated between nursing homes and acute care hospitals, we focused on acute care hospitals. Additionally, references of relevant publications were examined to identify further suitable studies (Fig. 1).

Each publication was reviewed for key interventions and resulting vaccination coverage (VC). VC was defined as the proportion of the vaccinated population in relation to the entire study population. The interventions of interest were education and promotion, incentives, organization, and policies. Education and promotion included providing material and spreading awareness. Incentives included free vaccine or giving away prizes among the vaccinated. Organizational interventions contained on-site vaccination, peer-to-peer vaccination, mass vaccination events and assignment of dedicated staff. Mandatory vaccination, vaccinate-or-wear-a-mask policies and declination forms to be submitted by unvaccinated HCW were grouped under policies. Moreover, combinations of these interventions were examined. The effect of the implemented strategy was evaluated by comparing VC before and after intervention. The relative increase in percent between initial and resulting VC was considered to evaluate the potential increase in VC regarding the key interventions.

Results

Literature search

Our initial search yielded 231 publications. After screening titles and abstracts, 41 publications remained. These full-text articles were assessed and subsequently 23 studies were included. Additionally, 9 publications found through references of relevant literature were added. In total, 32 articles were reviewed (Fig. 1).

Of the selected studies, 14 were conducted in the USA, 5 in Italy, 3 in Australia, and 1 each in Canada, France, Germany, Israel, Japan, Korea, Qatar, Spain, Switzerland, and Turkey. Most ($n = 28$) studies compared VC before and after a specific vaccination campaign conducted at individual or clustered institutions. Other studies ($n = 4$) compared vaccination rates between an intervention group and a control group. The majority ($n = 30$) of the studies were performed in hospitals, while two studies only analyzed nursing homes. In the following sections, the outcome per key interventions is described. Further details such as number of subjects described in each study can be found in Table 1. One study is listed under two key interventions [11].

Key intervention: education and promotion

Among the selected studies, six built their campaign mainly upon educational and promotional aspects [12–17]. Overall, the key intervention education and promotion increased VC relatively by 65.9% (standard deviation (SD): ± 55.8%, range: 14.5–162.5%) (Table1).

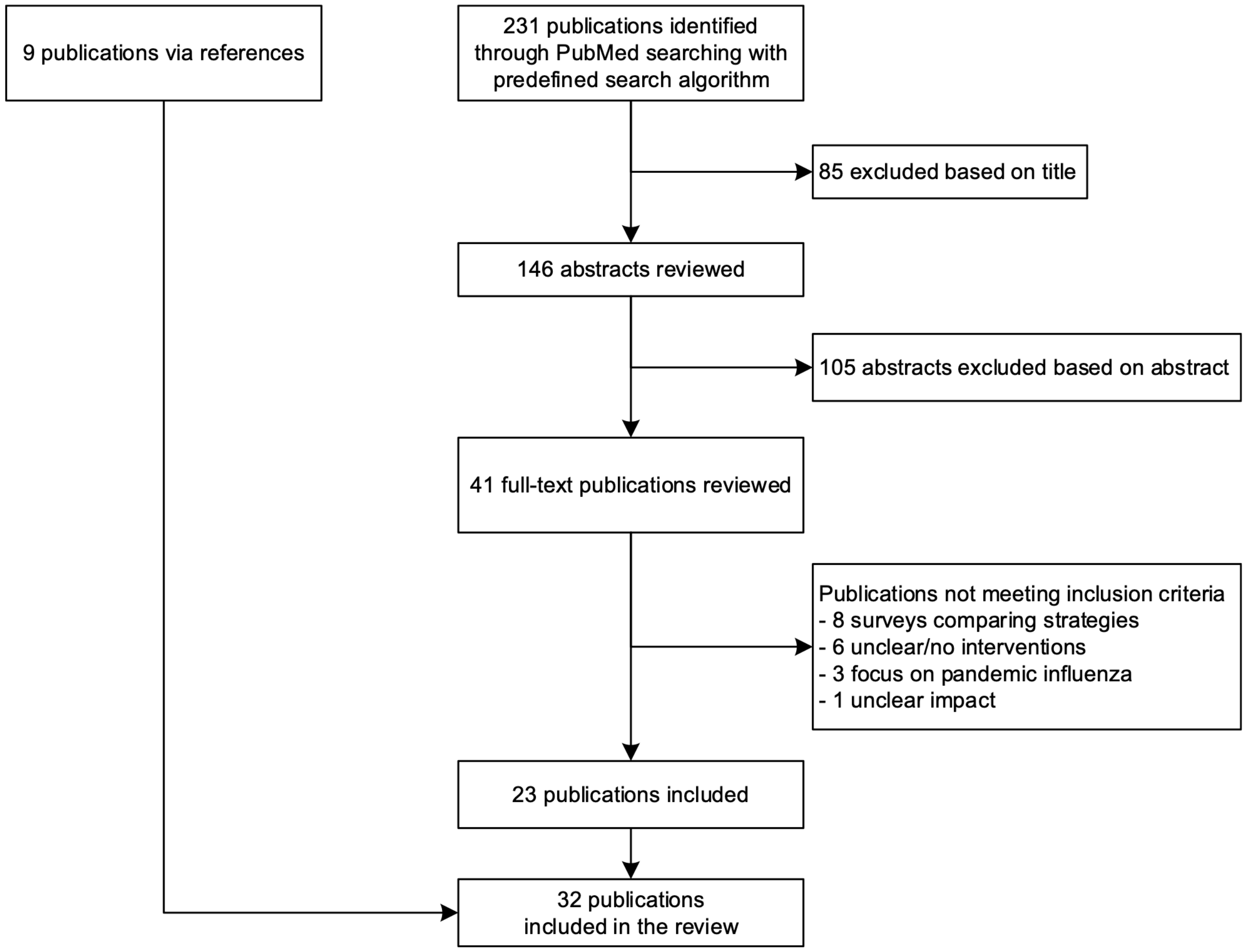

Fig. 1 Study selection flow. Flowchart showing the study selection after searching with the following predefined search algorithm on PubMed®: [("health personnel/analysis" (MeSH Terms) OR "health personnel/statistics and numerical data" (MeSH Terms)] AND "influenza, human/prevention and control" (MeSH Terms)] NOT [review (Publication Type)]. Additionally, nine publications were found through references of relevant publications

In one randomized trial from Israel, the intervention group ($n = 163$) received a lecture session, recurring emails containing literature as well as reminders and an appointed key figure from each department personally talked to each participant of the intervention group. Compared to the initial VC of 27%, the final VC was 53% in the intervention group. The VC in the control group increased from 20 to 27% [12]. A cluster-randomized controlled trial conducted in French nursing homes included slideshows and posters regarding prejudices against and reasons for influenza vaccination. VC increased from 28 to 34% in the intervention group. VC decreased from 24 to 23% in the control group [13]. A 1-h training course for all participants concerning influenza vaccination guidelines, vaccine types and administration was used as an intervention in an Italian study. Subsequently, the initial VC of 16% increased to a final VC of 42% in the intervention group. In comparison, VC increased from 13 to 31% in the control group [14]. A different Italian hospital appealed on personal as well as patient safety. It comprised posters in frequented areas, distribution of factsheets and intranet presence. Most survey participants (66%) agreed that the information was useful. Following the implementation of the toolkit, vaccination coverage was 14% which corresponded to earlier VC of 10% [15]. During a Korean campaign, unvaccinated HCW were contacted via phone for a ten-minute educational presentation. As this had no effect, unvaccinated medical doctors then received one-on-one educational counseling with on-site vaccination (OSV). VC increased from 83 to 93% [16]. In a Spanish before-and-after-trial, the key intervention consisted of a "I've already been vaccinated" webpage showing humorous pictures of all heads of departments as well as a vaccinated pregnant woman promoting vaccination also during pregnancy. The

Table 1 Summary of interventions, study population, season (year) and vaccination coverage

Publication	Country	Season	*N*	% VC			Relative increase		Key intervention	Key elements
				Before	After	Average ± SD [Range]	[%]	Average ± SD [Range] [%]		
Abramson et al. [12]*	Israel	2007–08	163	27	53	From 31.2 ± 26.3 [10–83] VC before, to 45.8 ± 27.3 [14–95] VC after	96.3	65.9 ± 55.8 [14.5–162.5]	Education/ Promotion	Lecture, reminders, literature via e-mail, personal interaction
Borgey et al. [13]*	France	2014–15	496	28	34		21.4			Slide shows and posters
Costantino et al. [14]*	Italy	2016–17	38	16	42		162.5			Training course
Cozza et al. [15]	Italy	2012–13	1813	10	14		40.0			Posters, fact sheets, online presence
Jung et al. [16]	Korea	2015–16	1433	83	95		14.5			Education, one-on-one counselling, on site vaccination
Llupia et al. [17]	Spain	2008–09	4500	23	37		60.9			Education, humorous pictures of vaccinated staff
Podczervisnki et al. [11]	United States	2011–12	1586	85	92	From 85 VC before, to 92 VC after	8.2	8.2	Incentive	Incentive
Barbara et al. [23]	Italy	2016–17	1013	10	18	From 11.0 ± 1.4 [10–13] VC Before, to 23.3 ± 11.2 [17–40] VC after	80.0	113.6 ± 102.7 [30.8–263.6]	Organization	On site vaccination
Gilardi et al. [27]	Italy	2017–18	2131	13	17		30.8			On site vaccination
Oguz et al. [25]	Turkey	2017–18	572	11	40		263.6			On site vaccination
Vimercati et al. [26]*	Italy	2017–18	700	10	18		80.0			On site vaccination
Awali et al. [31]	United States	2011–12	3054	80	93	From 74.0 ± 19.0 [40–99] VC before, to 87.8 ± 12.7 [58–99] VC after	16.3	25.0 ± 31.3 [31.1–97.9]	Policy	Mandatory vaccination
Babcock et al. [32]	United States	2008–09	25,980	71	98		38.0			Mandatory vaccination
Batabyal et al. [28]	United States	2008–09	29,000	48	66		37.5			Declination form
Batabyal et al. [28]	United States	2009–10	29,000	66	90	From 74.0 ± 19.0 [40–99] VC before, to 87.8 ± 12.7 [58–99] VC after	36.4	25.0 ± 31.3 [31.1–97.9]	Policy	Mandatory vaccination
Batabyal et al. [28]	United States	2010–11	29,000	90	62		− 31.1			Declination form
Batabyal et al. [28]	United States	2011–12	29,000	62	62		0.0			Declination form
Batabyal et al. [28]	United States	2012–13	29,000	62	86		38.7			Declination form
Batabyal et al. [28]	United States	2013–14	29,000	86	92		7.0			Declination form, vaccinate-or-mask
Batabyal et al. [28]	United States	2014–15	29,000	92	92		0.0			Declination form, vaccinate-or-mask
Batabyal et al. [28]	United States	2015–16	29,000	92	96		4.3			Declination form, vaccinate-or-mask
Esolen et al. [24]	United States	2009–10	12,363	47	90		91.5			Vaccinate-or-mask
Esolen et al. [24]	United States	2010–11	n.a	90	92		2.2			Vaccinate-or-mask
Esolen et al. [24]	United States	2011–12	n.a	92	95		3.3			Vaccinate-or-mask
Esolen et al. [24]	United States	2012–-13	19,985	95	97		2.1			Vaccinate-or-mask
Honda et al. [38]	Japan	2012–13	1616	87	97		11.5			Declination form

Table 1 (continued)

Publication	Country	Season	N	% VC			Relative increase		Key intervention	Key elements
				Before	After	Average ± SD [Range]	[%]	Average ± SD [Range] [%]		
Huynh et al. [29]	United States	2010–11	5300	68	96		41.2			Mandatory vaccination
Kim et al. [34]	United States	2012–13	n.a	74	89		20.3			Declination form, vaccinate-or-mask
Ksienski [35]	Canada	2012–13	48,818	40	74		85.0			Vaccinate-or-mask
LaVela et al. [39]	United States	2013–14	173	54	77		42.6			Declination form
Modak et al. [36]	United States	2011–12	2723	61	85		39.3			Declination form, vaccinate-or-mask
Podczervisnki et al. [11]	United States	2012–13	1641	92	96	From 74.0 ± 19.0 [40–99] VC before, to 87.8 ± 12.7 [58–99] VC after	4.3	25.0 ± 31.3 [31.1–97.9]	Policy	Declination form
Quan et al. [22]	United States	2007–08	6414	44	63		43.2			Declination form, decentralized distribution, flu mobile
Quan et al. [22]	United States	2008–09	6734	63	58		− 7.9			Declination form, decentralized distribution, flu mobile
Quan et al. [22]	United States	2009–10	6568	58	87		50.0			Declination form, vaccinate-or-mask
Quan et al. [22]	United States	2010–11	6582	87	92		5.7			Declination form, vaccinate-or-mask, incentive
Rakita et al. [30]	United States	2005–06	5000	54	98		81.5			Mandatory vaccination
Rakita et al. [30]	United States	2006-–07	5000	98	99		1.0			Mandatory vaccination
Rakita et al. [30]	United States	2007–08	5000	99	99		0.0			Mandatory vaccination
Rakita et al. [30]	United States	2008–09	5000	99	99		0.0			Mandatory vaccination
Rakita et al. [30]	United States	2009–10	5000	99	99		0.0			Mandatory vaccination
Smith et al. [33]	United States	2011–12	30,000	71	97		36.6			Mandatory vaccination
Stuart et al. [37]	Australia	2013	208	47	93		97.9			Vaccinate-or-mask
Drees et al. [18]	United States	2011–12	10,286	66	92	From 67.0 ± 21.1 [17–94] VC before, to 71.4 ± 28.0 [17–94] VC after	39.4	14.4 ± 28.2 [-20–88.1]	Combined intervention	Declination form, vaccinate-or-mask, incentive, penalties, promotion, vaccination stations

Table 1 (continued)

Publication	Country	Season	*N*	% VC			Relative increase		Key intervention	Key elements
				Before	After	Average ± SD [Range]	[%]	Average ± SD [Range] [%]		
Drees et al. [18]	United States	2012–13	10,388	92	94	From 67.0 ± 21.1 [17–94] VC before, to 71.4 ± 28.0 [17–94] VC after	2.2	14.4 ± 28.2 [− 20 to 88.1]	Combined intervention	Declination form, vaccinate-or-mask, incentive, penalties, promotion, vaccination stations
Drees et al. [18]	United States	2013–14	11,046	94	93		− 1.1			Declination form, vaccinate-or-mask, incentive, penalties, promotion, vaccination stations
Drees et al. [18]	United States	2014–15	10,883	93	93		0.0			Declination form, vaccinate-or-mask, incentive, penalties, promotion, vaccination stations
Friedl et al. [41]	Switzerland	2003–04	1322	n.a	20		n.a			Lectures, educational material, incentive
Friedl et al. [41]	Switzerland	2004–05	1163	20	17		− 15.0			Lectures, educational material, incentive
Friedl et al. [41]	Switzerland	2005–06	1236	17	30		76.5			Educational material, promotional material
Friedl et al. [41]	Switzerland	2006–07	1290	30	24		− 20.0			On site vaccination, lectures, educational material
Friedl et al. [41]	Switzerland	2007–08	1415	24	27		12.5			On site vaccination, educational material, incentive
Frisina et al. [42]	United States	2014–15	93	70	85		21.4			On site vaccination, educational material, Plan-do-study-act
Frisina et al. [42]	United States	2015–16	90	85	91		7.1			On site vaccination, educational material, Plan-do-study-act
Frisina et al. [42]	United States	2016–17	104	91	90	From 67.0 ± 21.1 [17–94] VC before, to 71.4 ± 28.0 [17–94] VC after	− 1.1	14.4 ± 28.2 [-20–88.1]	Combined intervention	On site vaccination, educational material, Plan-do-study-act
Frisina et al. [42]	United States	2017–18	102	90	90		0.0			On site vaccination, educational material, Plan-do-study-act
Gilardi et al. [27]	Qatar	2014–15	n.a	71	93		31.0			On site vaccination, mobile cart, education emails, group meetings, declination form
Heinrich-Morrison et al. [40]	Australia	2014	7480	56	80		42.9			Declination form, incentive, promotion, mass vaccination events
Horst-Schaper et al. [20]	Germany	2018–19	4000	n.a	n.a		n.a			Promotion, education, on site vaccination, incentive
Marshall et al. [21]	Australia	2013	8000	42	79		88.1			Declination form, incentive, "flu stop shop", education

Table 1 (continued)

Publication	Country	Season	*N*	% VC			Relative increase		Key intervention	Key elements
				Before	After	Average ± SD [Range]	[%]	Average ± SD [Range] [%]		
Marshall et al. [21]	Australia	2014	8000	79	80		1.3			Declination form, incentive, "flu stop shop", education
Marshall et al. [21]	Australia	2015	8000	80	79		− 1.3			Declination form, incentive, "flu stop shop", education
Marshall et al. [21]	Australia	2016	8000	79	80		1.3			Declination form, incentive, "flu stop shop", education
Marshall et al. [21]	Australia	2017	8000	80	81		1.3			Declination form, incentive, "flu stop shop", education
Marshall et al. [21]	Australia	2018	8000	81	82		1.2			Declination form, incentive, "flu stop shop", education

Table of each reviewed publication with corresponding country, season, study population, VC before and after intervention and key intervention. The vaccination campaigns were evaluated regarding key elements and subsequently grouped under key interventions: education/promotion, combined interventions, incentive, policy, and organization. The average initial and resulting VC ± SD and range in regard to the key interventions is given. Additionally, the relative increase in percent between initial and resulting VC for each season is given. Also, the relative increase (with ± SD and range) in percent for each key intervention overall is given. Out of the 32 studies included, 4 studies were controlled interventional studies (indicated with *). For these studies, only the intervention arm was considered when comparing the VC.

N study population, *VC* vaccination coverage, n.a. not available, *SD* standard deviation

authors concluded that the campaign encouraged the discourse on vaccination increasing VC from 23 to 37% [17].

Key intervention: incentives

Incentives were emphasized as a key intervention in one study. In six other studies, incentives were used as part of multifaceted campaigns [11, 17–22].

The above-mentioned study provided a 25 US Dollar gift card for every employee, if the overall VC reached 95%. This approach increased the VC from 87 to 92% [11]. The key intervention incentive increased VC relatively by 8.2% (Table1).

An employee-bonus program was implemented in two studies [18, 19]. A prize draw among vaccinated staff was part of two campaigns [17, 20]. In one multifaceted campaign, prizes where given to wards if the target VC was achieved [21]. One study took a different approach creating a disincentive for department leaders. Departments could lose budget allocations if vaccination rates were unsatisfactory. This increased vaccination rates from 87 to 92% [22].

The vaccine was offered free of charge in the respective prior season and during all included campaigns. Therefore, no aspect in this regard can be reported.

Key intervention: organizational strategies

Organizational aspects which facilitated access to the vaccine were implemented in eight studies [18, 21–27]; however, OSV was highlighted as a main intervention in only four campaigns [23, 25–27]. OSV as implemented key intervention increased VC overall by 113.6% (SD: ± 102.7%, range 30.8%–263.6%) (Table1). An Italian teaching hospital introduced OSV observing an increase in vaccination rates in medical residents from 10 to 18% [23]. In a different Italian study, the VC increased from 10 to 18% in the intervention group after offering OSV. Of note, out of the vaccinated HCW, 80% received vaccination on-site. In comparison, VC increased by 1.5% in the control group (without offered OSV). Initial and resulting overall VC was not provided by the authors for the control arm [26]. At another Italian hospital, a promotional campaign as well as OSV had already been in place in previous seasons with VC of 13%. Increased availability of the vaccine through extended OSV as well as longer timeslots at vaccination stations and at the occupational health department were added increasing VC to 17% [27]. After offering OSV, the VC increased from 11 to 40% in a Turkish children's Hospital [25].

The following studies used special organizational strategies as part of their campaigns and are discussed under their respective subheading. An approach using peer-to-peer vaccination was taken by two hospitals [22, 24]. A flu kit including the vaccine, consent forms and stickers was handed out to appointed team leaders of individual departments [24]. In the second clinic nurse managers could receive vaccines from the Occupational Health Department to distribute among their personnel [22]. A "flu-stop-shop" in a main area was organized in one Australian study. During the campaign, HCW could receive vaccination at the "flu-stop-shop" at all times without appointment [21]. In another study, a "blitz" campaign was conducted during the first 2 weeks of October. Vaccination stations were set up at all entrances of the hospital. Consequently, about 70% of all employees were vaccinated in the first 2 weeks [18].

Key intervention: policies

Among the selected studies, 15 included policies as key interventions. Overall, policies increased VC relatively by 25.0% (SD: ±31.3%, range 31.1%–97.9%) (Table1). One study conducted in the USA analyzed the effect of several different policies from 2008 to 2016. During seasons, in which policies included a signed declination option, the VC varied from 62 to 66%. Upon addition of educational aspects, VC increased to 86%. After a state-wide mandate in 2013, requiring unvaccinated staff to wear a mask, a maintained VC of 92–96% over the course of three seasons was reached [28].

In five studies, influenza vaccination was mandatory for HCW [29–33]. These publications were exclusively from the USA. Before implementation of the mandate, multifaceted vaccination campaigns had already been in place in all five studies with VC ranging from 54 to 80%. After influenza vaccination was made an employment requirement VC was 93–98%. In every study, "mandatory" implied that contracts with unvaccinated staff without exemptions were to be terminated. Overall, none to 0.14% of staff contracts were terminated due to the mandate. All five campaigns granted medical or religious exemptions. Egg allergy, history of Guillain–Barré syndrome and previously reported severe vaccine reaction were among the regarded exemptions. Exemptions due to medical reasons were acknowledged to 0.7–1.9% of staff and religious exemptions to 0.13–0.3%. One study declared that exemption requests reflected misinformation regarding the vaccine. These exemption requests included immunosuppression or pregnancy as reasons, although vaccination is recommended for both of these conditions [32]. Except for one hospital [29], the exempted unvaccinated staff had to wear a mask during influenza season.

A vaccinate-or-wear-a-mask approach was a key intervention in six publications [22, 24, 34–37]. A deadline for vaccination was set, after which unvaccinated staff had to wear a mask for the duration of the influenza season [34–36]. Vaccinated staff partially had markings on identification badges [22, 35, 36]. Supervisors were informed of their employees' vaccination status and were held accountable in three campaigns [22, 24, 36]. One study implemented a 100 US Dollar fine for noncompliant staff [34]. Another study initially implemented contract termination as consequence of noncompliance, but was forced to retract due to litigation [35]. A sustained VC of 90–97% over 4 years, was achieved through a vaccinate-or-wear-a-mask policy in combination with a decentralized vaccine supply (complete vaccine kits for appointed team captains of different departments) in one study [24]. An Australian pilot study applied a vaccinate-or-wear-a-mask mandate in the nephrology department increasing VC from 47 to 93% ($n=208$) [37]. Amid the six studies, three also included a declination form [22, 34, 36]. Overall, remarkable increases up to 97% in VC were observed after mask mandate [22, 24, 34–37].

Declination forms as a key intervention were used in three of the reviewed studies performed in Japan and the USA [11, 38, 39]. HCW refusing vaccination had to complete a declination form stating their reasons in all three studies. In a Japanese study noncompliant HCW, who neither received vaccine nor handed in declination forms, were interviewed by the hospital vice president. After implementing the mandatory declination form in this study, VC increased from 87 to 97% [38]. A pilot study conducted in a US Veterans Affairs facility included a signed statement acknowledging the personal risks and risks to others in their declination form. This study reported VC increasing from 54 to 77% [39]. Another study evaluated the impact of declination forms. Here, HCW refusing vaccination had to complete a 30-min educational module, receive one-on-one counseling and sign an attestation statement in presence of an occupational health or infection prevention staff. In cases of noncompliance, HCW were required to meet with their managers and a disciplinary letter was included in their employee file. This penalty-based approach increased VC from 92 to 96% [11]. Declination forms also played an important role in four multifaceted campaigns, which are discussed under the subheading "Combined interventions" [18, 19, 21, 40].

Combined interventions

The following studies are campaigns which did not focus on one key intervention but rather implemented three or more interventions as multifaceted strategies (education/promotion, incentive, organization, and policies) [18–21, 40–42]. Overall, combined interventions increased VC relatively by 14.4% (SD: ±28.2%; range: − 20 to 88.1%) (Table1).

For one campaign a task force led by the Infection Prevention Department incorporating Employee Health, Pharmacy, and Nursing departments among others was created. A new policy was implemented which required employees to fill out either a consent, declination or exemption form. This included attestation of vaccination elsewhere. Vaccinated employees were asked to wear a badge saying "I'm vaccinated because I care". If the badge wasn't worn, employees had to wear a mask, regardless of vaccination status. Noncompliance was considered in performance evaluations hindering possible promotions or raises. As a financial incentive, an employee bonus program was implemented. This multifaceted campaign increased VC from 57 to 72% (in the 3 years prior to the campaign) to 92–93% sustaining for four years [18].

Similarly, an Australian campaign consisted of multiple key interventions. For 6 months each year, a full-time influenza vaccination coordinator was employed. Appointed nurses conducted the vaccinations in aforementioned "flu-stop-shop". An intranet page with educational and promotional input was created. Promotions were spread via intranet, stickers and posters across the hospital. The chief executive officer sent emails and held presentations promoting the campaign. If wards achieved target rates, they received prizes. A mandatory declination form was implemented. Managers had access to the vaccination status of their employees via a database and were expected to hold their employees accountable. During the 6 active years of this campaign, VC was 79% to 82% compared to a VC ranging from 42 to 48% before [21].

One hospital implemented a new multifaceted strategy on top of OSV, a mobile cart, educational input and recurring e-mails. They added educational group meetings and a mandatory declination form. Also, progress reports on VC were sent to managers and heads of departments informing them of unvaccinated staff, yet without consequences for noncompliance. This increased VC from 71 to 93% [19].

Another Australian study introduced a database to track vaccination status of all HCW, identification of unvaccinated staff on ID badges, a declination form and awards for VC margins reached in wards (coffee machines in case of more than 80% VC). Following this campaign, VC increased from 56 to 80% [40].

A German hospital initiated the "Be a flu fighter" campaign, thereby managing to increase their VC by 4.5-fold. Key interventions included promotion and education, mobile vaccination teams and prize drawings as incentives among the vaccinated staff. Through the implementation of the campaign, VC reached 72% in physicians and 50% in nurses. Baseline values were not reported [20].

One hospital in Switzerland reported their influenza vaccination campaign being unsuccessful. The campaign included: vaccination daily during lunchtime in the cafeteria for 2 weeks, individualized mobile vaccination appointments at wards or during meetings, a "health week", incentives such as free lottery ticket or a free lunch, educational and promotional flyers and posters, influenza vaccine logo, intranet presence including "frequently asked questions", involvement of the head nurse, personal letters to employees and recurring lectures. According to the authors, the multitude of interventions, however, did not significantly increase VC (increase from 20 to 27% over 5 years). Among nurses the VC even decreased due to fear of potential short- or long-term side effects and doubts of efficacy of the vaccine [41].

As part of a quality improvement study, several plan–do–study–act (PDSA) cycles over the course of four seasons were implemented in one US study. The campaign consisted of educational aspects such as the distribution of a fact sheet and personal discussions on vaccination with HCW. Second, vaccine availability was increased in general and specifically for night shift staff and staff in remote clinics. Also, communicational aspects were enforced by sending out monthly emails showing current influenza epidemiology with a reminder of the availability of vaccination. Because "fear of needles" was identified as a barrier during a PDSA cycle, nasal vaccination was provided reducing this obstacle. Overall, VC increased from 70% to over 90% [42].

Descriptive comparison of key interventions

As shown in Fig. 2, key interventions such as education or promotion ($n=6$) and organization ($n=4$) were used as interventions in campaigns with initially low VC (range 15–25%). Policies ($n=15$) combined interventions ($n=7$) and incentives ($n=1$) were applied in studies with initially high VC (> 70%). In studies with low initial VC, the key intervention led to an increase of the VC ranging from 11 to 18% for organizational interventions and 25–40% for education/promotion. In studies with high initial VC, the key intervention led to an increase of the VC from 79 to 92% for policies and from 85 to 92% for incentives. No change was observed for combined interventions. In the overall group ($n=32$, all studies), VC increased from 71 to 87%.

Discussion

The analysis shows that vaccination campaigns are generally based on multifaceted vaccination strategies. Furthermore, vaccination strategies are implemented on different levels of initial vaccination rate. Most of the published vaccination strategies resulted in an increase in vaccination rates independent of the initial vaccination rate.

When taking into consideration, the overall success based on absolute VC, the most effective campaigns were those that comprised regulatory measures. Implementation of a mandatory vaccination policy generated the highest overall VC. Other policies like vaccinate-or-wear-a-mask or mandatory declination forms represented successful alternatives to mandatory vaccination. A VC of over 90% could be attained, especially if noncompliance with policies had a consequence [11]. Multifaceted campaigns which included

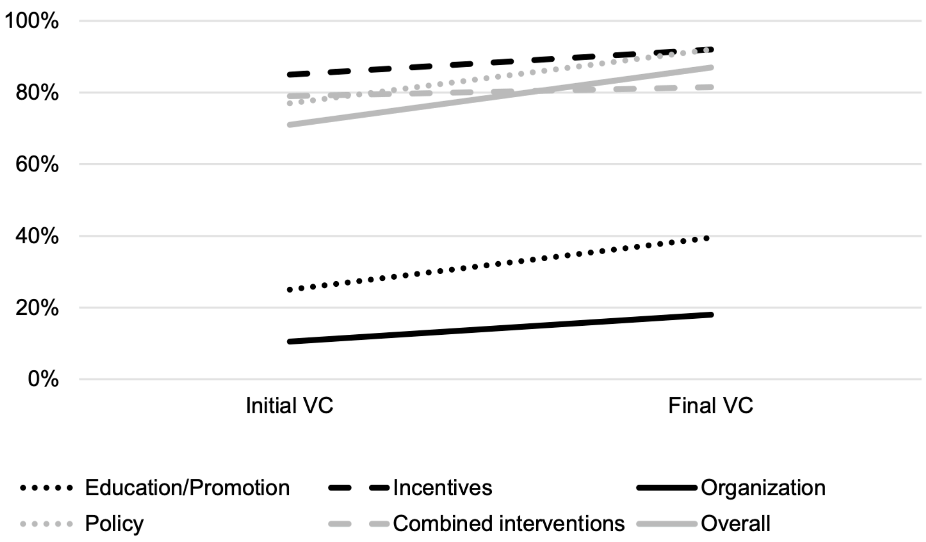

Fig. 2 Median variation of vaccination rates after the application of different policies and overall. VC, vaccination coverage. Line graph of the initial and final VC in regard to implemented key interventions and overall. Education/promotion ($n=6$) included providing material and spreading awareness. Incentives ($n=1$) included prize draws. Organization ($n=4$) included on-site vaccination. Policies ($n=15$) included mandatory vaccination, declination form and vaccinate-or-wear-a-mask approaches. Combined interventions ($n=7$) included combinations of the aforementioned interventions. Concerning the four controlled interventional studies, only the intervention arm was considered when comparing the VC in regard to the key intervention

a vaccinate-or-wear-a-mask approach as well as declination forms were generally more successful than those without policies. Policies were commonly used in Asia, Australia, and the USA.

Concerning the relative increase in VC regardless of initial and achieved VC, the most effective strategies were OSV (relative average increase 113.6%, SD: ±102.7%, range 30.8–263.6%) and education/promotion (relative average increase 65.9%, SD: ±55.8%, range 14.5–162.5%). However, regarding OSV, one outlier has to be considered: after implementation of OSV in a Turkish hospital, VC increased from 11 to 40% [25]. When comparing the potential relative increase between key interventions, the heterogeneity of the studies as well as the unbalanced number of studies in regard to key interventions has to be considered. Also, the studies with the key interventions OSV as well as education/promotion did not compare longitudinal data and mostly only focused on one season. In comparison, studies which employed polices (relative average increase 25.0%, SD: ±31.3%, range 31.1–97.9%) and combined interventions (relative average increase 14.4%, SD: ±28.2%; range – 20 to 88.1%) showed an initial high increase in VC and a maintained high VC over the course of following seasons [18, 21, 24, 30, 42]. Furthermore, before the implementation of policies, multifaceted campaigns comprising educational and promotional aspects as well as OSV had already been in place in the respective studies. This shows that education and promotion as well as OSV are valuable tools to increase VC and should be implemented whenever possible. However, in regard to absolute VC achieved, the key interventions education/promotion and OSV did not regularly exceed a VC of 40%.

Campaigns without regulatory measures focused on organizational, educational and promotional aspects. OSV was identified as an important tool to increase VC [25]. Mass vaccination events were successful [18]. A decentralized vaccine supply using peer-to-peer vaccination was also used [22, 24]. Regarding further organizational aspects, the importance of strong leadership and representation of clinic directors and heads of departments was stressed [21, 40]. Also, the importance of a dedicated team was highlighted in almost all studies. One study explicitly recommended hiring a physician solely dedicated to the influenza campaign over the course of the season [20]. Educational and promotional aspects were used as the basis of all campaigns, but when implemented as the sole key intervention absolute VC did not exceed 40% [17]. Incentives alone were rarely used as a key intervention, but did play an important role in multifaceted campaigns. Among the studies without policies, two studies stood out regarding overall VC achieved. One attained a VC of > 90% by implementing one-on-one counseling in combination with OSV [16]. The other study conducted several PDSA cycles analyzing and addressing barriers [42]. Of note, both studies were conducted in settings with high baseline VC in Korea and the USA (Table 1). These findings are in line with other studies [43–45].

Mandatory vaccination policies are confronted with opposition and even litigations. Any form of policy implies tracking the vaccination status of employees. This alone is a highly controversial topic considering data protection and staff autonomy. In most European countries, mandatory vaccination policies would be hard to implement. Possibly, a vaccinate-or-wear-a-mask policy could be installed in the future considering the current COVID-19 mask policy. HCW are now sensitized on the importance of wearing a mask. A mask not only acts as an incentive to receive vaccination but also reduces influenza transmission [37]. Surprisingly, in a Swiss study, HCW partially preferred wearing a mask over receiving the vaccine [46]. Of note, a vaccinate-or-wear-a-mask approach might not be feasible as an incentive to receive the vaccine in the season 2020/2021 due to already established mask mandates in the context of the COVID-19 pandemic. Ethical implications regarding incentives like prize draws for vaccinated staff should be considered. Alternatively, incentives in an educational context like quizzes could be a way to encourage discourse on the topic. Besides these ethical considerations, monetary and human resources need to be regarded. Further research on the economic impact of HCW influenza vaccination on work absenteeism as well as nosocomial influenza transmission is needed. Conclusive studies could help to integrate and justify policies regarding influenza vaccination for HCW.

With the possibility of a SARS-CoV-2 vaccine, similar issues and barriers regarding HCW vaccination could arise. Lessons learned from influenza campaigns could help to implement successful SARS-CoV-2 vaccination campaigns in the future.

This review has limitations. First, we only searched the PubMed® database. Second, due to the heterogeneity of the studies, we had to subjectively match campaigns to key interventions. Many interventions were part of multifaceted campaigns and not studied as an individual intervention. Therefore, it is difficult to finally assess the individual impact and contribution of the key interventions. Third, we did not perform statistical analysis, but rather focused on describing the strategies and the VC individual campaigns yielded. Fourth, the used key interventions were not balanced with regards to initial VC.

In conclusion, an influenza VC of over 90% in HCW can be reached by mandatory vaccination policies and through multifaceted campaigns which include a vaccinate-or-wear-a-mask-approach as well as mandatory declination policies. Policies, however, are often met by great opposition. In clinics where policies are infeasible, multifaceted campaigns comprised of extensive and individualized OSV and vaccination stands, a thorough educational and promotional campaign as well as incentives should be implemented to aim for an improved VC.

Overall, HCW influenza VC in Europe is far from satisfactory [4]. Although increasing the influenza VC in HCW remains a challenge, it is of utmost importance to protect our staff and our patients.

Author contributions SS designed the study, conceptualized and performed literature search, analyzed and interpreted the data, created the manuscript, created tables and figures, revised and approved the final manuscript. JSG created figures, revised and approved the final manuscript. OAC conceived the idea of the study and revised and approved the manuscript. SCM revised and approved the manuscript.

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Compliance with ethical standards

Conflict of interest SS and JSG declare that they have no conflicts of interest. OAC is supported by the German Federal Ministry of Research and Education, is funded by the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) under Germany's Excellence Strategy—CECAD, EXC 2030–390661388 and has received research grants from Actelion, Amplyx, Astellas, Basilea, Cidara, Da Volterra, F2G, Gilead, Janssen, Medicines Company, Melinta, Merck/MSD, Octapharma, Pfizer, Scynexis, is a consultant to Actelion, Allecra, Amplyx, Astellas, Basilea, Biosys, Cidara, Da Volterra, Entasis, F2G, Gilead, Matinas, MedPace, Menarini, Merck/MSD, Mylan, Nabriva, Noxxon, Octapharma, Paratek, Pfizer, PSI, Roche Diagnostics, Scynexis, and Shionogi, and received lecture honoraria from Al-Jazeera Pharmaceuticals, Astellas, Basilea, Gilead, Grupo Biotoscana, Merck/MSD and Pfizer. SCM was a consultant to Octapharma. She has been receiving research grants from the University Hospital of Cologne (KoelnFortune), from the German center for infection research (DZIF; Clinical Leave Stipend), and from the German Mycological Society (Dr. Manfred Plempel Stipend).

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4. Discussion

The purpose of our research project was to increase influenza vaccination coverage in healthcare workers during the first influenza season coinciding with the COVID-19 pandemic to relieve overall respiratory burden. Therefore, an intensified influenza vaccination campaign for healthcare workers at the University Hospital of Cologne was conducted during 2020/21. Prior to the campaign a literature search on best strategies to increase influenza vaccination coverage in healthcare workers was performed.[146] Building on the findings of this review, the intensified influenza vaccination campaign 2020/21 consisted of organizational, educational, and promotional measures.

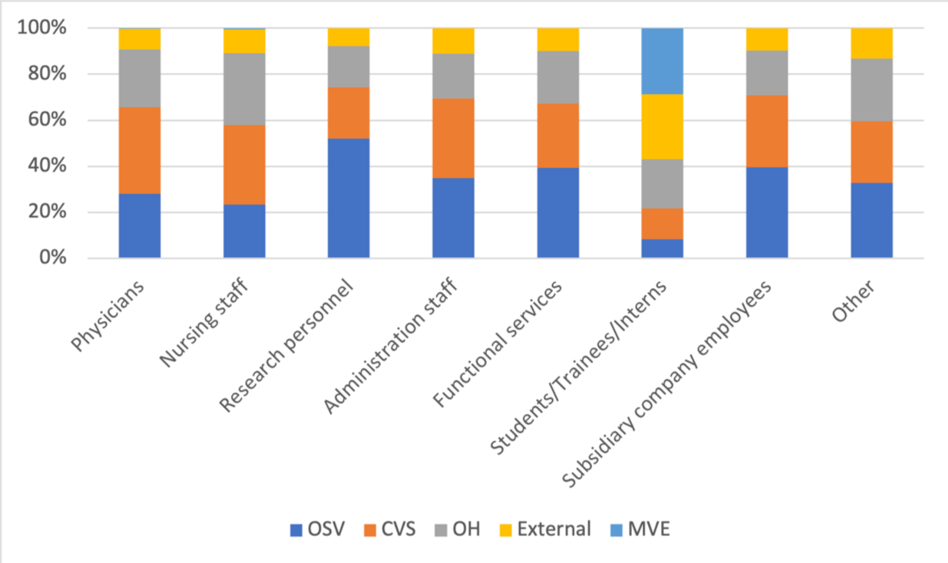
4.1. Campaign strategies and vaccination coverage outcome

Our research demonstrated that the implementation of on-site vaccination, walk-in vaccinations at a recurring central vaccination site and mass vaccination events building on educational and promotional elements led to a significant increase in influenza vaccination coverage in healthcare workers in 2020/21. Following the campaign vaccination coverage increased significantly from 17% in 2019/20 to 40%, which corresponds to a 2.4-fold increase and a tally of 6048 vaccinees in 2020/21. Considering the conducted survey following the campaign, overall vaccine uptake might have been higher, since 73% of survey participants confirmed receiving the influenza vaccine. This could be possible, since 13% of vaccinated survey participants reported receiving vaccination externally at, for example, their general practitioner. However, a selection bias must be considered in the survey.

A few research papers reporting influenza vaccination coverage in healthcare workers during the 2020/21 season have been published.[177-191] Most of these publications did not include interventions but rather focused on surveys.[177,179,180,183,186,187,189-191] One campaign at an Italian research and teaching hospital analyzed by Perrone et. al comprised promotional and educational elements, “ad hoc vaccine delivery”, on-site vaccination and a gaming strategy as an incentive. The “ad hoc vaccine delivery” was comparable to our central vaccination site except for the necessity of having an appointment in the Italian campaign. Overall vaccination coverage increased from 22% in 2019/20 to 43% in 2020/21.[182] Scardina et. al analyzed the impact of an influenza vaccination campaign at another Italian university hospital between 2018/19 and 2020/21. Their 2020/21 campaign consisted of an appointed task force, promotion, on-site vaccination and two fixed vaccinations sites with on-demand vaccine delivery, comparable to our central vaccination site. Before the campaign, a survey was performed in September querying the impact of the COVID-19 pandemic and suggestions regarding the upcoming 2020/21 campaign. Overall vaccination rate increased from 14% in 2019/20 to 40% in 2020/21.[184] At another Italian hospital, Ogliastro and colleagues performed a non-interventional retrospective analysis of influenza vaccine uptake in healthcare workers over three seasons between 2019/20 to 2021/22. Strategies included on-site vaccination, distribution of vaccines to wards for self-administration and publication of ministerial recommendations regarding influenza vaccination on the intranet. Vaccination coverage increased from 12.8% in 2019/20 to 40.9% in 2020/21 and dropped to 23% in the following season.[181]

Notably, these studies are in line with our finding of a significant increase in vaccination coverage, yielding around 40% influenza vaccination coverage in healthcare workers in the first influenza season that coincided with the COVID-19 pandemic. Also, a low baseline vaccination rate, between 12.8 – 22%, in pre-COVID-19 seasons is noticeable. All studies implemented organizational measures building on educational and promotional elements. Concerning the competition between departments as an incentive in one study, the authors later reported that despite the accessibility of the intranet many healthcare workers did not know the competition was taking place, perhaps limiting the informative value of this element.[182,192] A key feature in all campaigns was the distribution of vaccinees across different vaccination sites implementing both fixed sites and mobile on-site vaccination. Closer analysis of vaccinations per vaccination site is lacking in the mentioned studies.[181,182,184] However, in one case an increase in on-site vaccinations in 2020/21 compared to the previous season was noted.[182] Interestingly, the majority of vaccinees (33%) in our campaign preferred the preexisting option of receiving the influenza vaccination through the occupational health department at the respective department, which is not located centrally on campus. On the other hand, this also means that the set-up of the intensified campaign managed by the mobile vaccination team, comprising on-site vaccination and the central vaccination site, led to two thirds of all vaccinations. This shows that the visibility of the campaign worked, since promotional elements focused on the mobile vaccination team. Additionally, all three e-mails led to an increase in vaccinations per day before and after. Furthermore, it implies that the appointment of a dedicated team can have a great impact, as observed in other influenza campaigns.[146,164,182,184] Also, although tendencies regarding vaccination site preference in different professional fields were observed in our campaign (Figure 2), the analysis underlines that all options were used, suggesting that the variety of options contributed to the success of the campaign.

Figure 2. Clustered bar graph of survey data of vaccination site distribution among professional fields



OSV = on-site vaccination, CVS = central vaccination site, OH = occupational health department, External = self-reported external vaccination, MVE = mass vaccination event. Clustered bar graph showing the distribution of vaccination sites among professional fields as self-reported by HCW in survey following the 2020/21 campaign.

Interestingly, reaching an overall vaccination coverage of approximately 40% in healthcare workers when implementing educational, promotional and organizational elements is in line with the findings of our review, despite it analyzing campaigns before the COVID-19 pandemic.[146] Looking at target group vaccination rates in the German public, as reported by RKI, influenza vaccination coverage reached 47.3% in those 60 years of age and older, 39.3% in adults with underlying health conditions and only 23.2% in pregnant women in Germany in 2020/21. Looking at Germany as a whole, vaccine uptake varied regionally favoring eastern versus western federal states in that year.[193] The annual survey *OKaPII* on influenza vaccination among healthcare workers in Germany conducted by RKI was paused in the seasons of 2020/21 and 2021/22 in favor of analysis of COVID-19 vaccination limiting comparison to our results.[194]

The literature suggests that even if educational, promotional and organizational campaign strategies are exhausted, the target vaccination coverage of 75% set by the European Union (EU) in alignment with the WHO and the European Centre for Disease Prevention and Control (ECDC) is not reached in European countries.[195] Conversely, the annual analysis of influenza vaccination rate in healthcare workers in the USA by the CDC showed a high coverage (95.9%) in healthcare settings that mandated influenza vaccination compared to a moderately high coverage (76.2%) when influenza vaccination was only recommended by the employer versus 46% coverage when vaccination was neither required nor recommended in 2020/21. As this analysis was performed through an opt-in internet panel survey a selection bias must be considered.[196]

4.2. COVID-19 pandemic and first time influenza vaccinees

Overall, for almost a third (29%) of vaccinees the 2020/21 influenza vaccination was the first ever (or the first in over ten years) in our campaign. A majority (72%) of these vaccinees affirmed the COVID-19 pandemic positively influencing influenza vaccination decision. Comparingly, our survey showed that the conduct of the intensified campaign also had a high impact; 60% of first time vaccinees affirmed a positive contribution to vaccination decision. Further analysis showed the highest proportion of first timers per professional field in research personnel and subsidiary company employees (38% and 37%, respectively). Approximately a third of administration staff, functional services, nursing staff and students/trainees/interns vaccinees reported being first timers, in comparison to only 11% of physicians. This finding corresponds to highest preexisting vaccination coverage in physicians in our hospital. Most of the here mentioned studies did not perform sub analysis of first time vaccinees in 2020/21.[177-181,183-185] Perrone et al. found highest prevalence ratio for first time vaccinees among males, residents, and personnel in the newborn area and intensive care unit in 2020/21.[182] For healthcare workers who are vaccinated regularly a brief reminder can be sufficient to lead to vaccination.[180,197] Therefore, it seems relevant to analyze first timers and those partly and always hesitant towards vaccination and tailor campaigns specifically to them.[180]

COVID-19 must be considered as an important factor increasing awareness of the relevance of influenza vaccinations.[187,189,190,192,198-201] Although Wang et. al found no overall significant difference in knowledge of medical students on influenza in 2019 versus 2021, the authors did find a significant increase in awareness of topics such as the utility of wearing a mask.[202] Interestingly, pandemic protective measures such as wearing a mask or hand washing did not reduce intention to receive influenza vaccination.[180] Di Pumpo et al. performed a linear regression model predicting influenza vaccine uptake in healthcare workers in 2020/21 using data from the seasons of 2016/17 to 2019/20. Following a steady and slow increase in vaccination coverage in these prior seasons, a statistically significant difference in predicted vaccination coverage and actual reported coverage in 2020/21 was found. The authors concluded that the COVID-19 pandemic was the reason for this discrepancy.[178] A meta-analysis showed a significant impact of the COVID-19 pandemic on influenza vaccination coverage in healthcare workers in 2020/21.[203] Influenza and COVID-19 sharing similar symptoms was highlighted as a determinant for vaccination in 2020/21.[204] Furthermore, considering influenza vaccination useful to differentiate likelihood of influenza versus COVID-19 infection was emphasized as a reason to receive the influenza vaccination in that season.[186] Also, fear of contracting both diseases at the same time was highlighted as a vaccination motivation, especially for first time vaccinees.[187] In contrast, in one survey conducted in late 2020, 45.2% of respondents answered that the pandemic did not influence their plan to receive influenza vaccination in that season.[199]

Interestingly, in reverse, a cross-sectional survey addressing vaccine acceptance in nursing staff amidst the COVID-19 pandemic found having been vaccinated against influenza in the prior season to correlate positively with the intention to receive COVID-19 vaccination.[205] This points to openness for one type of vaccination possibly correlating with a general openness and trust in vaccination.[186,206] The opposite seems to be true as well, negative past vaccination experiences may reduce openness to new vaccinations.[207]

A phenomenon described in the literature is being vaccinated against influenza in the past correlating significantly with higher influenza vaccine acceptance in the present and future.[177,180,183,184] Likewise, 71% of vaccinees in our campaign 2020/21 stated being vaccinated in previous seasons against influenza. These findings beg the question, whether convincing healthcare workers to receive vaccination once is sufficient to have a lasting impact on positive vaccination decision. If this were true, the effect of the pandemic on positive influenza vaccination decision in first timers should be fully utilized. However, a general population-based study in Beijing, China showed increased influenza vaccination rates during the 2009/10 influenza pandemic followed by vaccination rates dropping back to their baseline the following season corresponding to a vaccination coverage of pre-pandemic seasons.[205,208] On the contrary, while keeping in mind that the COVID-19 pandemic was still ongoing, Lecce et al. showed a further increase in influenza vaccine uptake in 2021/22.[192] Others observed a decrease in influenza vaccination coverage in 2021/22.[181,185,203,209] Perhaps the co-administration of COVID-19 and influenza vaccination contributed to the success of the campaign conducted by Lecce et. al.[192] Our research underlines the impact of the COVID-19 pandemic on influenza vaccination acceptance especially for first timers. Future studies are necessary to analyze this influence over time.

4.3. Nursing staff as a critical target group

Using a “susceptible-exposed-infectious-removed model” Gustin et al. found nursing staff presented a higher influenza transmission rate to patients in comparison to medical doctors in 2023.[210] However, nursing staff has reportedly low influenza vaccination coverage in comparison to other healthcare workers.[125,126,128-130,185,191,211,212] This underlines the necessity of continuously viewing nursing staff as a critical target group. Notably, vaccination coverage in nurses, a predetermined target group, increased 2.7-fold yielding a vaccination coverage of 48% in our campaign. Similarly, one Italian hospital reported a 1.8-fold increase yielding 52% vaccination coverage in nurses. However, nursing staff in this study only consisted of 57 persons compared to 1060 vaccinated nurses in our study.[188]

Leaning on the "5C model",[132] a survey during the early stages of the COVID-19 pandemic found intention to receive influenza vaccination among nurses in 2019/20 to correlate with more *confidence* (trust in effectiveness/safety), more *collective responsibility* (protecting others), and less *complacency* (disease perceived as low risk), *constraints* (availability/accessibility perceived as low) and *calculation* (perceived risk/benefit).[213] Furthermore, pre-pandemic data collected through *OKaPII* surveys showed nurses emphasizing a lack of vaccine confidence as reason for being unvaccinated in comparison to organizational barriers highlighted by physicians.[131,214] Also, a cause of unsatisfactory influenza vaccination rate in nurses can be lack of vaccination culture.[185] Misinformation such as the influenza vaccine causing influenza disease has been described as deterrents to vaccination in nurses.[191,215] These studies highlight the necessity of educational and promotional elements of vaccine campaigns to reach nursing staff specifically. To address these issues, our campaign included a video by the head of nursing staff outlining reasons to be vaccinated directed at her nursing staff (Publication 1, Supplement 2) and the set-up of vaccination at the University Hospital of Cologne nursing training academy.

Some data suggest that the possibility of on-site vaccination increases vaccination coverage in nursing staff.[130,185] Interestingly, our survey showed most (65%) nursing staff to prefer influenza vaccination at fixed vaccination sites (34% central vaccination site, 31% occupational health department), in comparison to on-site (24%), and even less so externally (10%) and at mass vaccination events (1%). The analysis of our mobile vaccination team data showed the same trend; 57% of nurses were vaccinated at the central vaccination site versus 43% on-site. Comparingly, a retrospective analysis in Turkey found a third of vaccinations in nursing staff conducted on-site through mobile teams in 2018/19 and 2019/20.[185] One could have expected nursing staff to prefer on-site vaccination because leaving wards during shifts can be infeasible due to workload.[215,216] Potentially there is simply no time to receive the vaccine during the shift. Perhaps nurses prefer receiving the vaccine in non-working hours at fixed sites. Another option could be, that nurses were indeed able to leave their wards to receive vaccination at fixed sites. More research is necessary to shed light on organizational barriers and facilitators for nurses. Still, it is noticeable that a relevant number of nurses used on-site vaccination. Therefore, it is reasonable to keep offering this option going forward.[185] Overall, our results highlight the importance of central vaccination site for nursing staff. Furthermore, our findings underline the need for diverse vaccination site options for nursing staff.

As mentioned above, there is evidence that the COVID-19 pandemic led to a significant increase in influenza vaccine uptake in healthcare workers.[178] Our survey addressed the question whether this was true for nursing staff and for first timers among nursing staff specifically. Out of reportedly vaccinated nurses, 31% were first time (or first time in over ten years) influenza vaccinees. Interestingly, these first time vaccinee nurses reported the COVID-

19 pandemic having a greater impact (78%) on positive vaccination decision than the intensified campaign (53%) itself. Comparingly, 35% of all previously vaccinated nurses affirmed the campaign led to increased vaccination motivation and only a third (33%) of all previously vaccinated nurses affirmed the COVID-19 pandemic positively impacted vaccination decision. This highlights the impact of COVID-19 pandemic on first time vaccinees among nursing staff.

Although the increase in nursing staff vaccination coverage was significant, it was still off the 75% vaccination coverage target.[195] A quality improvement analysis conducted at a Turkish hospital found a lack of continuity of vaccine supply to be a cause of low vaccination rate in nursing staff.[185] Perhaps the vaccine shortage in our campaign was especially detrimental for nurses. Further research is necessary to increase influenza vaccination coverage in this critical target group.[217] Keeping the effect of the COVID-19 pandemic in mind, our multifaceted approach including fixed and mobile vaccination sites and educational elements led to a significant increase in vaccination coverage in nursing staff and should therefore be considered groundwork to build upon.

4.4. Campaign timeline and feasibility in a pandemic setting

Finding an optimal vaccination campaign timeline including when to start and efficient duration is challenging. Our campaign commenced with the arrival of the vaccine in early September (Table 2). This brought up the concern of waning immunity, although immunity against influenza following vaccination is dependent on multiple factors.[11] As mentioned in the introduction, the CDC proposed conducting influenza vaccinations earlier to facilitate compliance with COVID-19 regulations at the time.[119] In one Italian campaign, the hospital board also decided to begin their campaign earlier with the rational of preventing possible co-infections of influenza and COVID-19, to facilitate differential diagnosis between both infections and reduce work absenteeism in their healthcare workers.[218]

Table 2. Timeline of the 2020/21 campaign at the University Hospital of Cologne

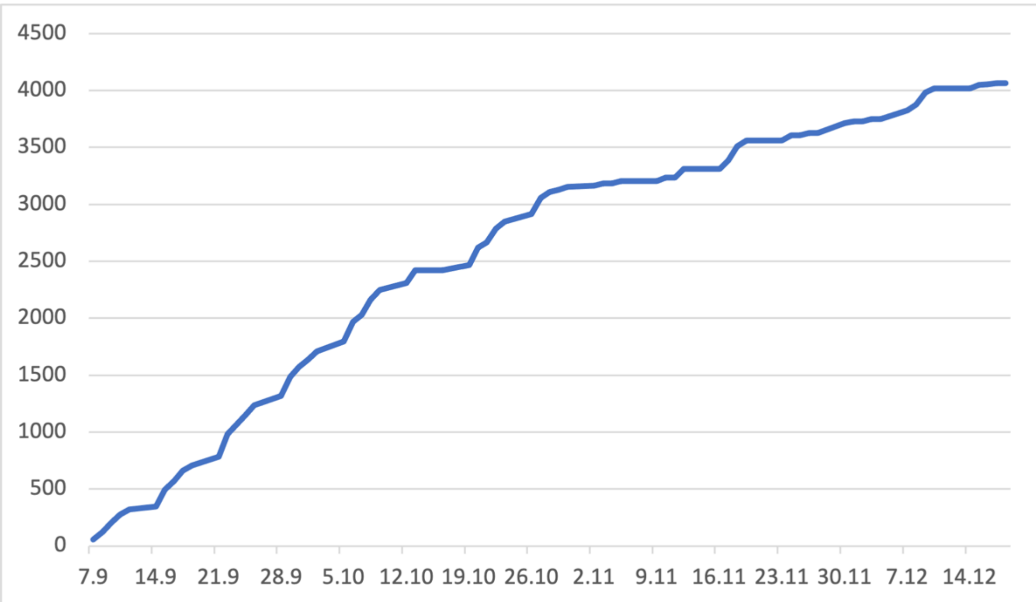
Campaign week	Date	Event	Cumulative Number of MVT vaccinations
1	07.09.2020	Start of the campaign	55
1	10.09.2020	E-mail: Announcement of the campaign	277
3	23.09.2020	Milestone: 1000 vaccinations	1070
5	07.10.2020	Milestone: 2000 vaccinations	2027
6	12.10.2020	MVT was informed about vaccine shortage	2310
6	13.10.2020	Vaccines used up	2419
7	19.10.2020	Arrival of limited number of vaccines	2465
7 - 10	19.10.2020 – 10.11.2020	Limited number of vaccines	
8	27.10.2020	Milestone: 3000 vaccinations	3055
8	29.10.2020	"Red" "Corona-Warn-App"	3128
10	11.11.2020	Arrival of new vaccines E-mail announcing "2nd round" and the arrival of new influenza vaccines	3237
11	16.11.2020	Flash mob distribution of saddle bike covers	3311
11	18.11.2020	1st MVE for medical students	3508
13	30.11.2020	2nd MVE for medical students	3714
14	07.12.2020	E-mail: Last call influenza vaccination: 14 more days 3rd MVE event for medical students	3826
14	09.12.2020	4th MVE event for medical students	3982
14	10.12.2020	Milestone: 4000 vaccinations	4018
15	18.12.2020	End of campaign 2020/21	4071

MVT = mobile vaccination team, MVE = mass vaccination event

The heterogenous timelines of the campaigns point to the impact of hospital size and personnel campaign resources. Scardina et. al focused on a short period of 15 days beginning in mid-October. Perhaps this was only possible due to the large number of vaccinating personnel. Per campaign day eight nurses and eight physicians performed vaccination, reaching a tally of

2505 vaccinations.[184] In contrast, the campaign by Perrone et. al commenced in late November and lasted till the end of December. Notably, promotion of the campaign and education on influenza vaccination already began in September. The authors reported a vaccine shortage disrupting the campaign, similarly to Scardina et. al and our campaign, shortening possible central vaccination site vaccination days. Overall, 2103 vaccinations were performed by multiple teams.[182] A similar tally of vaccinees (N=2536) was reached in another Italian campaign.[181] Comparingly, our campaign lasted for a longer period until the end of December (Table 2). Our tally of vaccinees was higher surpassing 6000, 4071 of which the mobile vaccination team performed across 69 vaccination days. Keeping in mind that our mobile vaccination team constituted just two persons per day, the longer campaign period was necessary to reach this amount of vaccinees. A study from the US showed that on average 50% of all vaccinations took place within the first 14 days of their campaigns. Such timing trends can inform the conduct of campaigns.[152,185] Comparingly, in our campaign the 50% mark of vaccinations conducted by the mobile vaccination team was reached after one month (Figure 3). Perhaps this justifies employing a larger team at the beginning of a campaign that can be reduced after a certain vaccination coverage threshold is reached.

Figure 3. Number of total vaccinations performed by the mobile vaccination team during the 2020/21 campaign



MVT = mobile vaccination team. Line graph showing the total number of vaccinations performed by the MVT over the course of the influenza vaccination campaign at the University Hospital of Cologne in 2020/21.

In our study vaccination at the central vaccination site was performed on 36 days yielding 30% of all vaccinations. On-site vaccination was implemented on 41 days (on some days the mobile vaccination team conducted vaccinations at both the central vaccination site and on-site) reaching 31% of all vaccinations. Time per vaccination was longest during on-site vaccination

3.4 min (total time circa 105 hours). Time per vaccination was comparable during central vaccination site taking 3.2 min (total central vaccination site time circa 96 hours). These numbers however do not exclude waiting time in between vaccinations as well as time needed for documentation and therefore do not equate to actual vaccination time. The set-up of mass vaccination events was very efficient, vaccination taking 1.6 min (total mass vaccination event time circa 10 hours, unpublished data). This efficiency during mass vaccination events was only achievable through a second person vaccinating, doubling the performed vaccinations per time unit, which underlines the impact of available staff. Of note, this data disregards aspects of efficiency. Once established, the recurring site set-up at the central vaccination site was quick and efficient. Also, the spontaneous posting of the campaign flag outside the central vaccination site calling for walk-in vaccinations took no time. On the other hand, on-site vaccination was time-consuming in two regards. Firstly, the communication to arrange appointments by telephone and e-mail was resource intensive. In the first half of the campaign communication was time-consuming due to high demand. In the second half of the campaign the mobile vaccination team reached out to the departments themselves. The mobile vaccination team had circa 100 contact persons to organize respective on-site appointments (unpublished data). Secondly, traveling between on-site vaccination sites on a very large campus such as the University Hospital of Cologne takes time. To that point, the mobile vaccination team approved almost every appointment and did not regard the logistics of the campus sufficiently. But the work of on-site set-up was alleviated using a pre-packed rucksack holding all necessary items, allowing taking the bicycle as sustainable transportation. The mass vaccination events were organized in cooperation with the student body council, which proved highly efficient. Keeping in mind that mass vaccination events were only implemented on four days, a substantial 6% of all vaccinations on these days is of note.

During the influenza season 2020/21 COVID-19 infections were exceptionally high and COVID-19 vaccines were not yet available.[219] The variety of vaccination sites as well as the preplanned on-site timeslots led to distribution of vaccinees over location and time, thereby reducing contact time between waiting vaccinees (for example waiting in line) to receive vaccination and subsequently making keeping in line with COVID-19 policies feasible. Suffice it to say, the sheer number of vaccinations on a large campus by a small team was only possible due to the variety of options regarding vaccination site and the length of the campaign. In this regard, our work represents a feasibility test for vaccinating large numbers of healthcare workers in a pandemic setting with limited personnel resources.

4.5. Vaccination coverage in pre-pandemic seasons

Analysis of prior influenza seasons at the University Hospital of Cologne starting 2017/18 showed unsatisfactory influenza vaccination rates. Highest relative increase in vaccination coverage in these prior seasons was observed between 2017/18 and 2018/19. This could be due to the severity of the influenza season 2017/18 in Germany.[39] Prior to 2020/21, highest vaccination rate was observed in administration staff (22% in 2017/18, 52% in 2018/19, 46% in 2019/20) and physicians (38% in 2017/18, 52% in 2018/19, 41% in 2019/20) in our hospital. Apart from nursing staff yielding 21% vaccination coverage in 2018/19, neither functional staff, nursing staff in the remaining seasons, research personnel, students/trainees/interns nor subsidiary company employees exceeded influenza vaccination coverage of 20% between 2017/18 and 2019/20, partially scoring as low as under 10%. The comparably higher self-reported vaccine uptake in the *OKaPII* survey annually conducted at our and other selected German hospitals (unpublished data) underlines a possible selection bias using surveys analyzing vaccination coverage. These pre-pandemic baseline vaccination rates are comparable to other European hospitals in that time frame.[128,130,181,184,189,220]

Our review analyzing campaigns prior to the COVID-19 pandemic showed that campaigns focusing on educational and promotional as well as organizational strategies lead to a relative increase in vaccination coverage but seldom exceed 40% overall coverage.[146] A further increase is only rarely observed without vaccine policies.[163,221] If policies such as mandatory vaccination, vaccinate-or-wear-a-mask or declination forms are included the 75% vaccination coverage target can be met and sustained.[147,150,153,154,156,222] If, however, mandates are infeasible, the approach must be to exhaust organizational measures building on education and promotion as groundwork as demonstrated in our campaign.[146] Which other options this could include is outlined below in section "4.8 Outlook on future campaigns".

4.6. Challenges of the campaign

The campaign 2020/21 at the University Hospital of Cologne had its challenges. A major test was the month-long vaccine shortage between October and November as reported by other campaigns.[182,184] Interestingly, no official critical vaccine shortage situation was declared because this would have implied vaccine import and reallocation and this was deemed inappropriate at the time because it would have endangered vaccine supply in other countries.[223] For a week, no vaccines were available and then only gradually given out, possibly leading to a loss of momentum. On the other hand, the vaccine shortage potentially led to an increase in vaccination coverage once the vaccine was available again mid-November in the sense of scarcity driving demand as known in economics.[224,225] However, overall, vaccinations per day were lower following the shortage (Figure 3) and further increase in vaccination rate was thereafter driven by mass vaccination events conducted for medical students.

In the pandemic setting and especially during the vaccine shortage, discussions around prioritizing of influenza vaccination in relation to healthcare workers' patient contact came up.

Comparingly, following an influenza vaccine shortage in 2004, the CDC did recommend prioritizing vaccination of healthcare workers who provide direct patient care for the season of 2005/06.[226,227] Although there are models simulating a reduction in influenza transmission if vaccination coverage is high in healthcare workers with high patient contact,[228] current official recommendations by WHO and RKI do not differentiate between different types of healthcare workers and recommend vaccination for all.[3,89,229] In accordance with these official recommendations, we did not prioritize within healthcare workers. It is possible that this discussion and corresponding scarcity mindset reduced overall vaccination coverage.

Not only the vaccine was hit by shortage but also the needles necessary to vaccinate. This made pivoting to a different type of needle necessary in close communications with the head of the pharmacy department. Fortunately, this shortage did not lead to cancellation of appointments.

As the mobile vaccination team was in close contact with over 4000 vaccinees, it was quite remarkable that the team did not contract COVID-19 during the campaign which points to a high compliance with regulations by all parties at the time. Although it was necessary for the mobile vaccination team to remind a few healthcare workers to wear masks during the vaccination appointment, no confrontations resulted. As part of infection control the “Corona-Warn-App” for contact tracing was issued by the German government.[230] At one point, the mobile vaccination team had a “red” status indicating high likelihood of contact to COVID-19 infected persons which led to cancellation of a few vaccine appointments. Following this incident the mobile vaccination team performed regular self-testing for COVID-19 (Table 2).

As previously alluded to, efficiency of the campaign could have been higher. Travel time by bicycle across campus and one-on-one communications via e-mail or phone was time-consuming. Also, no minimum number of vaccinations per on-site vaccination slot was necessary to receive an appointment in the respective ward, which in one case led to only one vaccination, which proved inefficient. On the other hand, this approach reduced work for wards (i.e. collecting number of people who want to be vaccinated) and made it possible for healthcare workers who were uncertain of the vaccine to ask questions without having to agree to vaccination in advance. Although we did not perform analysis of this aspect, verbal feedback to the mobile vaccination team was positive in this regard.

A miscommunication observed was some healthcare workers believing the provided influenza vaccine to be the COVID-19 vaccine, which wasn’t yet available at the time.[219] This misconception was clarified and to our knowledge no healthcare worker was vaccinated believing they were receiving the COVID-19 vaccine instead of the influenza vaccine. Also, in a singular event, one healthcare worker wanted to receive influenza vaccination twice due to fear of waning immunity, which was not approved. Furthermore, during vaccinations many discussions with healthcare workers regarding fear of the vaccines, potential adverse effects and misconceptions such as vaccination potentially causing the disease, took place.

Prior to the campaign the mobile vaccination team physician performed a prophylactic anaphylaxis skill training to be ready for the rare case of anaphylaxis to the influenza vaccine. As part of this strategy the team always carried an epinephrin autoinjector. In two cases an unexpectedly strong localized skin reaction was observed and hence reported to PEI. No anaphylaxis occurred and the use of the epinephrin autoinjector was not necessary.

4.7. Limitations

Our research has limitations. Firstly, the missing data of the occupational health department partly due to data protection reasons and partly due to modest documentation in the past limited a possible analysis. Therefore, the professional field categorization of the occupational health department vaccinees was extrapolated using our survey data resulting in a possible selection bias. Also, the occupational health department dataset of 2020/21 did not include gender, age or date of vaccination further limiting analysis.

Our analysis does not answer the question which of the campaign strategies was most pivotal in yielding a 2.4-fold vaccination coverage increase. Contributing to this limitation is the fact that vaccinations at a central vaccination site, albeit a lot less frequently, and vaccinations on-site, albeit only in locations far of campus, were already established in prior seasons. Educational and promotional elements existed prior to 2020/21 as well. Although we queried the impact of COVID-19 in our conducted survey, the COVID-19 pandemic can still be considered a confounder regarding vaccination rate. Other possible confounders we did not analyze include the impact of media encouraging vaccination and the month-long vaccine shortage.

Our survey only queried those that were vaccinated in detail while those who stated not having been vaccinated had a shorter survey. We did not query why reportedly unvaccinated healthcare workers declined vaccination but rather focused on those vaccinated. The higher self-reported vaccination coverage in the survey in comparison to measured coverage in our campaign could point to a selection bias.

Furthermore, the professional field categorization in the mobile vaccination team data set was subjectively performed by the mobile vaccination team. The categorization into the here defined groups was based on the categories as outlined by the occupational health department in previous years to allow for comparison. Therefore, a mismatch between professional field category assigned by the mobile vaccination team and self-reported profession in the survey was possible. The discrepancy between vaccination rate in functional service in our survey and our documented rate in this group could point to an inadequate classification in this heterogenous professional field. Potentially this category needs to be divided into more clearer subcategories such as physical therapy, kitchen, or sanitary staff etc. to be surveyed. On the other hand, the benefit of a more nuanced categorization is unclear. Perhaps a division of functional services with patient contact versus no patient contact is interesting. To further complicate the matter, many physicians, and nurses, specifically study nurses, could also be considered research personnel since these groups are often formally employed as research personnel at our hospital.

Furthermore, no cross-analysis between mobile vaccination team data and survey data was possible due to anonymity of both data sets. Our research only focuses on one hospital rather than including several.

Regarding our review, limitations include only performing descriptive statistics and not a systematic review.

4.8. Outlook on future campaigns

4.8.1. Strategy: Education & promotion

The older “Health-Belief-Model”[231] and the more recent “5C model”[132] are two approaches used to address vaccine acceptance and hesitancy. The “Health-Belief-Model” describes that engaging in healthy behavior is more likely if perceived susceptibility, severity and benefits are high and perceived barriers are low.[231-233] As outlined above, the “5C model” describes five antecedents of vaccination: *calculation, collective responsibility, complacency*, *confidence*, and *constraints*. Vaccine acceptance is higher if *confidence* and *collective responsibility* are high and *complacency*, *constraints* and *calculation* are low.[132] Leaning on this concept educational and promotional aspects of campaigns therefore target: *confidence*, *calculation* and *collective responsibility*.

Understanding vaccine hesitancy is complex and differs regarding time, population and different vaccines.[132,234] A promotional strategy outlined by Lecce et al. included querying reasons to get vaccinated among healthcare workers and then including these reasons as messages in future campaigns. For example, the authors observed an increase in altruistic motivation to receive the influenza vaccine, perhaps due to the COVID-19 pandemic, compared to an “older trend” of protecting oneself.[192] Perhaps this approach as part of a PDSA cycle could account for regional differences in motivation.[235] This could be even further developed regarding target groups. For example, posters addressing common reasons to be vaccinated provided by nursing staff could be distributed at ward stations commonly frequented by nursing staff.

As an educational and promotional strategy our campaign included addressing common fears and misconceptions per flyers, and per video (Publication 1, Supplements 1 and 2). However, misconceptions such as refusing vaccination due to pregnancy or not wanting to receive a live vaccine mentioned in the free text feedback in our survey highlighted a still relevant necessity for education. Similarly, in other campaigns, 46.6% of healthcare workers did not believe they were at risk of contracting influenza in 2020/21,[180] 14.5% of unvaccinated healthcare workers did not believe they were part of a risk category[184] and only 19% of healthcare workers considered themselves to be at higher risk of contracting influenza in comparison to general populations.[182] Although prior campaigns included “myth debunking”[182] the same trend was visible in 2021/22, colleagues reported healthcare workers believing the coadministration of vaccines to be unsafe.[192] This underlines the need for continuous education. Although a few studies have shown effects of one-on-one counseling on influenza vaccination,[221,236] this approach is time and cost intensive. However, keeping in mind that being vaccinated before correlates with being vaccinated again,[177,180,183,184] this perhaps justifies educational courses combined with the opportunity to receive vaccination at training academies such as nursing schools or other medical schools.

As mentioned above, all e-mails led to an increase in vaccination coverage in our campaign. A study from Poland comparing an educational intervention in person or per e-mail followed by either a reminder per text message or no reminder at all, found highest relative increase in vaccination coverage in nursing staff when an educational intervention was performed in person followed by a text message reminding of influenza vaccination. The reminder per text message only had a significant impact on vaccine uptake if the educational intervention was performed in person.[232] Using the “Health-Belief-Model”,[231] a significant change in attitude towards perceived susceptibility, severity, benefits, and barriers of influenza vaccination was observed in this group. The authors did conclude that the reminder could be interpreted as a “cue to action”.[232] Of note, the sending of text messages requires consent and adherence to data protection laws and education in person is time and therefore cost intensive. If, however, education in person were decentralized and each ward had an “influenza vaccination advocate” who performed education and sent the reminder per text message, cost and time could be decentralized and hence potentially reduced.[237] This could even potentially be integrated in to a “buddy” vaccination program (see below 4.8.2 Strategy: Organization).[154] If this is deemed infeasible, reminder e-mails, as shown in our campaign, are an effective tool.

The impact of different information sources on influenza vaccine uptake must be considered. As mass media underlined the necessity to receive influenza vaccination in Germany and abroad during the season of 2020/21, its impact could be substantial.[182] On the other hand, a survey conducted in the Italian public during 2020/21 showed that the credibility of information was considered high from personal physicians, healthcare institutions and personal pharmacists and lower from friends, daily newspapers, TV or social networks. This could point to a lower impact of media on vaccine acceptance.[238]

Our marketing team developed a catchy campaign logo (Figure 4) leaning on the well-known image “We Can Do It!” by J. Howard Miller in 1943 developed as an American World War II wartime poster. Creative solutions in our campaign included vaccinated healthcare workers posing in the same position as this logo and these photos being published on intranet. Other campaigns have also reported a positive impact of humorous pictures of vaccinated staff, especially if these included head of departments acting as role models.[149]

Figure 4. Campaign logo of the influenza vaccination campaign 2020/21

Picture depicting the campaign logo of the influenza vaccination campaign at the University Hospital of Cologne in 2020/21 as published in “Paper 1". Speech bubble stating “Together against the flu” and in the left lower corner “Get vaccinated now! Dates and additional information can be found on the intranet” in German.

Since the reason behind influenza vaccinations and respective vaccination campaigns is to reduce number of infections, campaigns could also include alternative strategies to reduce infections and transmissions such as informing on hand hygiene including reducing handshaking, cough etiquette or wearing masks. Furthermore, they could include underlining the potential severity of the disease highlighting the fact that coming to work sick could endanger patients and colleagues. A more radical approach shifting more towards mandates could be communicating a “no-entry-policy-if-symptomatic”.[239]

Overall, education and corresponding promotion must still be seen as the backbone of influenza campaigns for healthcare workers.

4.8.2. Strategy: Organization

Leaning on the “5C model”,[132] organizational strategies target *complacency* and physical *constraints*. Reflecting on the set-up of our different vaccination sites, our fixed central vaccination site and mobile on-site vaccinations demonstrated convenience and spontaneity, whereas the occupational health department corresponded to a traditional option. Especially on-site vaccination can be seen as a means of increasing accessibility and thereby reducing barriers. To that point, when asked to give suggestions on further increase in vaccination coverage, healthcare workers most frequently reported an increase in on-site vaccination opportunities in a survey at an Irish Hospital in 2020/21[190] and a survey in nurses underlined the need for on-site vaccination.[185] As mentioned above, however, all sites in our campaign were successful, therefore we propose all sites should be implemented in the future.

The set-up of our mass vaccination events for medical students yielded high numbers of vaccination even at the end of the campaign. Time per vaccination was very efficient, especially due to two people vaccinating simultaneously. Perhaps this concept can be further developed. As outlined by Perrone et al, if the vaccination team is large, the campaign can be compressed into a month. In that campaign, three vaccinators were present at their central vaccination site and teams of two to three vaccinators performed on-site vaccinations to cover two work shifts at each department.[182] Similarly, in a rapid rollout, vaccination stations were set up at all entrances of a US hospital for two weeks yielding 70% of all performed vaccinations in that campaign.[150] Therefore, future campaigns could include an intense phase with more and a maintenance phase with less personnel. According to Section 20c of the German Infection Protection Act (IfSG), pharmacists may administer certain vaccinations such as influenza under specific conditions, meaning prior medical training and suitable facilities.[240] Furthermore, vaccinations can be delegated from doctors to nursing staff if a physician is present.[241] Therefore, these two professional groups could be part of the campaign. Especially because our central vaccination site was stationed at the hospital staff pharmacy, including pharmacists could be an option. If more personnel are involved strategies could even include door-to-door active recruitment, although the cost-benefit analysis of such strategies is unclear.[220] Overall, because the crowd at the mass vaccination events was very large, two points regarding large vaccination events must be considered: Firstly, a crowd can be a problem infection-wise in a pandemic setting and secondly, the medical students waited for their turn, implying they had time to do so.

Although it is conceivable to have only spontaneous walk-ins at all sites (on-site, central vaccination site, mass vaccination events, occupational health department), the set-up of appointments for on-site vaccinations was beneficial in our campaign regarding the approximate number of vaccines needed. As the scheduling of appointments per phone and e-mail was very time-consuming, bookable vaccination slots through the intranet could be an option going forward.[182] Also, a live tracking on the intranet showing the location of the mobile vaccination team allowing for healthcare workers to come to the team could be beneficial in the future. If this is not feasible due to data protection laws, open access to the calendar of the mobile vaccination team could be explored.

Interesting could be the set-up of “influenza vaccination advocates” to create a decentralized “buddy” system leveraging peer support.[237] Decentralized distribution of vaccines to wards for peer-to-peer vaccination has been described.[153,154,237] Of course, this approach should not be conducted without consideration: Personnel able to vaccinate should be on-site, safety measures such as an unbroken cold chain need to be met and documentation of vaccination must be given.[241] The respective influenza advocates could be responsible. Also, this could potentially lead to vaccine waste. On the other hand, this approach could reduce campaign team size. Such a system could even be used for educational and promotional strategies. Possibly an educational event for all advocates addressing common fears and misconceptions could be conducted at the beginning of the campaign. These “influenza vaccination advocates” could be publicly known on the intranet so that reluctant healthcare workers could approach them (see above 4.8.1 Strategy: Education & Promotion).[237]

With the roll-out of COVID-19 vaccines, another organizational strategy emerged: the coadministration of vaccines.[242] Lecce et al. observed a high uptake of influenza vaccination by offering COVID-19 coadministration in 2021/22.[192] Perhaps pneumococcal vaccination could be offered if applicable.[243] Or simply checking the vaccination record for necessary booster vaccinations regarding all vaccinations could be offered. This approach could be considered an incentive.

4.8.3. Strategy: Incentives

Our campaign neither included incentives nor disincentives.

Competitions such as a daily updated ranking of vaccination coverage in departments including public recognition of the winning department[182] or prizes given to wards if the vaccination coverage target is reached have been described.[147,152] Possibly a nation-wide competition between hospitals regarding influenza vaccination rates and best campaign could be conducted in Germany.

Financial incentives can be considered coercive. Interestingly, a Dutch cross-sectional study found that reward based “nudges”, such as receiving a trophy or cake for highest yielded vaccination coverage, were perceived as condescending and least acceptable by healthcare workers, undermining altruistic motives.[197]

Overall, the impact of incentives is rarely evaluated as a sole measure to increase influenza vaccination coverage in healthcare workers.[146] A strategy often overlooked because of its wide implementation is offering the vaccine free of charge. At a tertiary care hospital in the Czech Republic additionally to a promotional campaign, influenza vaccination was offered free of charge for the first time in 2020/21. Out of the vaccinated healthcare workers in 2020/21 only 15.9% reported having received prior influenza vaccination (baseline and resulting vaccination coverage was not reported).[187] In some countries offering the vaccine free of charge is not common practice, therefore this incentive strategy still has an impact.[187,232]

4.8.4. Strategy: Mandates

Our campaign did not include mandates. Yielding 40% influenza vaccination coverage in our campaign is still off the 75% target.[195] Even Lecce and colleagues implementing central vaccination site, on-site vaccination, education and promotion and the possibility of receiving the COVID-19 vaccine simultaneously only reached 52% vaccination coverage.[192] Our review showed mandatory vaccination and policies such as vaccinate-or-wear-a-mask or mandatory declination yielding vaccination coverage on and above target.[146] Interestingly, one study found using mandatory declination to have a high impact even without consequences of noncompliance.[151] Of note, vaccinate-or-wear-a-mask is both a motivation and it offers an alternative to curb infection for hesitant healthcare workers.[244] Furthermore, due to the mask mandates during the COVID-19 pandemic, wearing masks is perhaps normalized.[219] Mandates require transparent access to vaccination status thereby possibly compromising patient data confidentiality. To that point, a vaccinate-or-wear-a-mask mandate overtly indicates vaccination status to the public which could be controversial. One US campaign had vaccinated personnel carry badges, and if they weren't worn, a mask was required.[150]

Finland paved the way as the first European country to implement a nation-wide influenza policy for healthcare workers with close patient contact requiring healthcare institutions to only employ vaccinated personnel. Incompliance meant transferal of the employee to a different unit without patient contact. More nurses reported finding this law to be coercive (41.5%) than doctors (12.7%). Still, this increased vaccination coverage from 59.5 to 99.6% among healthcare workers with close patient contact.[245] Nevertheless, whether influenza vaccination should be mandatory in European countries is still controversial. A German study analyzed influenza vaccine acceptance in emergency departments. Unvaccinated survey respondents were significantly more likely to quit their jobs if vaccination were to be mandatory and affirmed not showing up to work during an influenza pandemic being ethical because work attendance should be entrusted to the employees. Whereas vaccinated employees were inclined towards a mandatory vaccination policy and inclined towards lay-off of employees with poor work attendance during an influenza pandemic. Interestingly, both vaccinated and unvaccinated emergency department personnel agreed to influenza representing a major burden on their resources.[183] In an Italian study, 80% of survey respondents affirmed influenza vaccination should be mandatory for healthcare workers. A selection bias must be considered because this survey took place at a vaccination unit.[177] Similarly, the same question was addressed in a population in which 94% affirmed their intention to receive the influenza vaccine yielding 56% agreement to a vaccine mandate.[190] These studies suggest that a mandate might have a low effect because those in favor are already keen on being vaccinated. On the contrary, a different survey found only a third of healthcare workers agreeing to a influenza vaccination mandate for healthcare workers in 2020/21.[186] An older survey suggests that healthcare workers opposed to a influenza vaccine mandate can be grouped into two types: Firstly, those who lack knowledge on the subject and secondly those who believe vaccination should be an individual decision. While the first group could be targeted with education, the latter is more complex.[245,246] A behavioral experiment showed that if selected vaccinations are compulsory an increase in negative vaccination attitude and a decrease in uptake of other voluntary vaccinations, especially among reluctant vaccinees can be observed.[247]

The acceptance of vaccine mandates or policies varies depending on region. Influenza vaccine mandates for healthcare workers have been in place in multiple hospitals in the United States[155-159,222] and significantly increased in US Veterans Affairs hospitals in light of the COVID-19 pandemic.[248] Comparingly, even COVID-19 vaccination mandates exceeding the pandemic were declined in the “Bundestag” (German federal parliament) in 2022.[249] On the other hand, as the legislature on measles vaccination demonstrated, vaccine mandates can be implemented in Germany.[250] Of note, measles vaccination does not require regular boosters making checking compliance to regulations more feasible.[251,252] Perhaps results from future research will lead to influenza vaccine mandates in European countries.

4.8.5. Strategy: Data collection and plan-do-study-act analysis

Following the axiom “What Gets Measured Gets Managed”,[253,254] only what is measured can be improved. Such a strategy is a PDSA cycle.[235,255]

PDSA cycles in the setting of evaluating campaigns to increase influenza vaccination coverage in healthcare workers are only possible if data is accordingly documented to be analyzed. This underlines the need for predetermined structures to document vaccinations even in a pandemic, i.e. improvised, setting. The mobile vaccination team data we anonymously collected showed the feasibility of such a documentation, if performed with discipline. Many of the difficulties and limitations we encountered in our own analysis were due to poor and insufficient documentation in the past and not only due to limited access to information due to data protection laws. Furthermore, a prerequisite for improvement is evaluation and feedback, i.e. performing surveys.

Some hospitals have performed thorough analysis across multiple years noting an increase in influenza vaccination coverage.[182,192,220] In PDSA cycles barriers can be identified and addressed. In one US study the authors identified an outlier department with low vaccination coverage which significantly reduced overall coverage. Because the barrier identified was lack of education, the campaign team met specifically with this department. In this way PDSA cycles could lead to recognizing target groups and respective highest impact. The authors elaborated addressing specific barriers, such as fear of needles with the option of receiving a nasal live attenuated influenza vaccine or adopting strategies to provide vaccines to night shift workers contributed to reaching the vaccination coverage target. Of note, once the vaccination coverage target of 90% was reached PDSA cycles were no longer necessary, the team did however perform quality control with a shortened survey.[163] On the other hand, PDSA cycles could also identify positive feedback, meaning what worked and should be repeated. This could be especially beneficial for multifaceted campaigns that are cost and time consuming. In our campaign for example, the flashmob action of distributing saddle bike covers depicting the campaign logo (Figure 5) was highlighted multiple times in the free-text feedback of our survey, indicating this or similar strategy should be implemented in the future.

Figure 5. Promotional material of the influenza vaccination campaign 2020/21

Fotos depicting a bicycle saddle cover and disinfection wipes showing the campaign logo 2020/21, as well as stickers stating “Vaccination saves lives” in German. All were distributed among healthcare workers of the University Hospital of Cologne as part of the promotional action.

To compare data longitudinally and between studies defining parameters is essential. Some studies focus on the professional field distribution or the department distribution among those vaccinated[181] rather than vaccination coverage within a professional field or department. This limits comparison because number of healthcare workers per professional field varies across hospitals. Studying the vaccination coverage in a professional field or department ensures focus on the end goal: High vaccination coverage overall and within each professional field and department. As shown in our analysis, the professional field “functional services” is highly heterogenous. To analyze and compare seasons within one hospital and at best with other hospitals adopting defined professional field categories leaning on definitions by official institutions such as the WHO would be beneficial. Since the “International Standard Classification of Occupations” is very detailed,[256] a shorter categorization should be developed.

4.8.6. Future research

Future research could address vaccine hesitancy and acceptance as well as data supporting the implementation of national influenza vaccination policies.[89]

Overall, research underpinning the need for influenza vaccination in healthcare workers varies greatly in data quality and respective results.[89,257] Although data show a significant increase in risk of influenza infection for healthcare workers compared to the public,[137,258] attribution of this increase to higher rate of asymptomatic infections in healthcare workers has been described.[259] Of note, two reviews analyzing vaccine efficacy against laboratory-confirmed influenza in healthcare workers included the same three randomized controlled trials but came to contradictory conclusions.[257,260,261] Burls et al. recommended influenza vaccination as a priority for healthcare workers,[260] while Ng et al. stated results being inconclusive.[261] Furthermore, a review found that healthcare workers' number needed to vaccinate for patient benefit ranges from 3 to 36 000 underlining the heterogeneity of studies on the topic.[262] This points to a need of high quality randomized controlled trials. Optimal would be an analysis on the impact of healthcare workers' influenza vaccination coverage on morbidity and mortality in patients due to transmission and subsequent nosocomial infection and corresponding economic impact, for example patient hospital stay duration.

Furthermore, the economic impact of healthcare workers' absenteeism due to influenza illness can still be elaborated.[262] Although there are studies pointing to a reduction in work absenteeism due to influenza vaccination among healthcare workers,[134,145,263] there are also studies showing inconclusive data.[261] A Dutch randomized controlled trial even found an increase in work absenteeism among vaccinated healthcare workers. The authors did highlight however, that this might be due to more frequent influenza testing in this intervention group.[262,264] Additionally, only a protective effect and no significant association between healthcare worker vaccination coverage and nosocomial influenza incidence was observed in a hospital in Singapore, albeit a country with limited predictive value of influenza seasons, between 2013 and 2018.[265]

In summary, data on the reduction of both morbidity and mortality as well as economic impact through vaccination would be informative. Interesting would be whether the 75% vaccination coverage target[195] would be in line with these findings. A statistical model evaluating all persons for whom influenza vaccination is recommended found a reduction in influenza related events such as hospitalization and death as well as influenza-related costs if the 75% vaccination coverage was reached. The benefit for healthcare workers in comparison to the elderly and chronically ill was however, comparingly low. Furthermore, healthcare workers were partially analyzed together with pregnant women in a "healthy adults" category in that study which limits informative value on healthcare workers.[266]

The question who among healthcare workers drives nosocomial infection in hospitals could be interesting as well. This could inform, whether priority groups among healthcare workers in case of vaccine shortage are justifiable. Also, identifying the most critical group (i.e. highest risk of transmission) with lowest vaccination coverage could lead to new target groups. Building on models as outlined by Polgreen et al. could be beneficial.[228]

Influenza vaccine efficacy varies.[267] Low vaccine efficacy is reported by some hesitant healthcare workers as a barrier to vaccination.[214] An approach to increase vaccine efficacy is better surveillance data to predict virus strains and consequently faster vaccine development to be on time with the right strains. Nucleic acid-based (deoxyribonucleic acid and mRNA) and viral vectored vaccine technologies are being researched.[81,89,93,94] The development of a universal vaccine with broader, as in protecting against more influenza strains, and more durable efficacy would address concerns of vaccine efficacy in healthcare workers.[89] Perhaps this would even lead to longer vaccination intervals and reduce the necessity for annual vaccination and respective campaigns. Regarding vaccine efficacy, establishing an easily and at low-cost measurable correlate of protection would be beneficial. This could improve understanding waning of immunity, thereby informing on optimal timing of vaccination which would influence vaccination campaign timelines. This could be especially beneficial for tropical regions without predictable influenza seasons.[89] One can speculate that if vaccine efficacy is higher, impact on morbidity and mortality in patients as well as economic impact could be higher. Perhaps such data would convince hesitant employees without the need for vaccine mandates and lead to meeting the influenza vaccination coverage target in healthcare workers.

4.9. Conclusion

To this day influenza still has a great influence on respiratory related morbidity and mortality. Our research demonstrated a significant increase in influenza vaccination coverage of healthcare workers across all professional fields by implementing an educational and promotional campaign and organizational strategies including on-site vaccination, as well as vaccination at a fixed central and a traditional site and at mass vaccination events during the first influenza season coinciding with the COVID-19 pandemic. Moreover, our study represents a feasibility test on how to vaccinate large numbers of healthcare workers in a pandemic setting. Still, the 75% influenza vaccination coverage target set by the WHO and EU was not met. Robust data on the impact of healthcare workers' influenza vaccination coverage regarding influenza infection in healthcare workers, transmission to patients and subsequent economic impact is needed.

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6. Appendix

6.1. List of Figures

6.2. List of Tables