Vaccination in adult patients with chronic lung diseases

Maria Boesing[1, 2], Werner Albrich[3], Pierre-Olivier Bridevaux[4, 5], Florian Charbonnier[6], Christian Clarenbach[7], Jean-Marc Fellrath[8], Pietro Gianella[9], Lukas Kern[10], Tsogyal Latshang[11], Nikolay Pavlov[12], Michael Osthoff[13], Claudia Steurer-Stey[14], Christophe von Garnier[15], Jörg D. Leuppi[1, 2]

[1] Medicine & University Affairs, Cantonal Hospital Baselland, Liestal, Switzerland
[2] Medical Faculty, University of Basel, Basel, Switzerland
[3] Division of Infectious Diseases, Infection Prevention and Travel Medicine, Cantonal Hospital St. Gallen, St. Gallen, Switzerland
[4] Service de pneumologie, Centre Hospitalier du Valais Romand, Hôpital du Valais, Sion, Switzerland
[5] Faculté de médecine, Université de Genève
[6] Service de pneumologie, Hôpitaux universitaires de Genève, Genève, Switzerland
[7] Department of Pneumology, University Hospital Zurich, Zurich, Switzerland
[8] Réseau hospitalier neuchâtelois, Neuchâtel, Switzerland
[9] Ente Ospedaliero Cantonale, Lugano, Switzerland
[10] Department of Pneumology, Cantonal Hospital St. Gallen, St. Gallen, Switzerland
[11] Division of Pneumology, Cantonal Hospital Graubünden, Chur, Switzerland
[12] Department of Pneumology, University Hospital Bern, Bern, Switzerland
[13] Department of Internal Medicine, Cantonal Hospital Winterthur, Winterthur, Switzerland
[14] University of Zurich, Zurich, Switzerland
[15] Lausanne University Hospital, (CHUV) and University of Lausanne, Lausanne, Switzerland

Abstract: In Switzerland, additional vaccinations against influenza, COVID-19, Streptococcus pneumoniae and varicella zoster virus (VZV), are recommended for patients with chronic lung diseases such as COPD, asthma or interstitial lung disease, since infectious diseases often lead to exacerbation of lung diseases resulting in increased disease burden and mortality. In this review we give an overview on recommended vaccinations for patients with chronic lung diseases, also including vaccinations against pertussis and RSV, which are recommended in international guidelines. While continuous development of vaccines against S. pneumoniae has given rise to high-valency vaccines covering up to 68% of S. pneumoniae variants in individuals aged ≥65 years, vaccination rates in this age group remain low in Switzerland (<10% in 2020). Vaccination rates are higher for influenza, and particularly high-dose vaccines account for high vaccination efficacy in years of low strain matching in individuals at risk. Although mortality of COVID-19 decreased since the emergence of the first SARS-CoV-2 variant, patients with chronic lung disease are still at increased risk for exacerbation, unless vaccinated with variant-adjusted vaccines. VZV and Bordetella pertussis vaccination has also significantly countered reactivation and infection rates, respectively, and subunit vaccines against VZV show long duration. However, pertussis vaccination is still limited by its fast waning. A glimpse into the future presumes the introduction of new higher-valence vaccinations against S. pneumoniae, and several types of RSV vaccines are expected to enter the Swiss market soon.

Key words: Vaccine efficacy, chronic lung diseases, viral infections, exacerbation prevention

Impfung von erwachsenen Patienten mit chronischen Lungenerkrankungen

Zusammenfassung: In der Schweiz werden Patienten mit chronischen Lungenerkrankungen wie COPD, Asthma oder interstitieller Lungenerkrankung zusätzliche Impfungen gegen Influenza, COVID-19, Streptococcus pneumoniae und Varizella-Zoster-Virus (VZV) empfohlen, da Infektionskrankheiten häufig zu einer Verschlimmerung von Lungenerkrankungen führen, was eine erhöhte Krankheitslast und Mortalität zur Folge hat. In dieser Übersicht geben wir einen Überblick über die empfohlenen Impfungen für Patienten mit chronischen Lungenerkrankungen, einschließlich der Impfungen gegen Keuchhusten und RSV, die in internationalen Richtlinien empfohlen werden. Obwohl die kontinuierliche Entwicklung von Impfstoffen gegen S. pneumoniae zu hochwirksamen Impfstoffen geführt hat, die bis zu 68 % der S. pneumoniae-Varianten bei Personen im Alter von ≥65 Jahren abdecken, bleiben die Impfraten in dieser Altersgruppe in der Schweiz niedrig (<10 % im Jahr 2020). Bei der Influenza sind die Impfraten höher, und insbesondere hochdosierte Impfstoffe sorgen für eine hohe Impfeffizienz in Jahren mit geringer Stammabstimmung bei Risikopersonen. Obwohl die Sterblichkeit bei COVID-19 seit dem Auftreten der ersten SARS-CoV-2-Variante zurückgegangen ist, besteht für Patienten mit chronischen Lungenerkrankungen nach wie vor ein erhöhtes Risiko einer Exazerbation, sofern sie nicht mit variantenangepassten Impfstoffen geimpft werden. Die Impfung gegen VZV und Bordetella pertussis hat die Reaktivierungs- und Infektionsraten ebenfalls deutlich gesenkt, und die Subunit-Impfstoffe gegen VZV haben eine lange Wirkungsdauer. Die Pertussis-Impfung ist jedoch nach wie vor durch ihr schnelles Abklingen begrenzt. Ein Blick in die Zukunft lässt vermuten, dass neue Impfungen gegen S. pneumoniae mit höherer Wirksamkeit eingeführt werden, und es wird erwartet, dass in der Schweiz bald mehrere Arten von RSV-Impfstoffen auf den Markt kommen werden.

Schlüsselwörter: Impfstoffwirksamkeit, chronische Lungenerkrankungen, Virusinfektionen, Prävention von Exazerbationen

Introduction

Chronic lung diseases present a significant health and economic burden worldwide (1). Exacerbations of chronic lung diseases particularly pose a risk for patients with pulmonary disorders, as they can lead to functional impairment, severe pneumonia, hospitalization, and death (2). For chronic obstructive pulmonary disease (COPD), repeated acute exacerbations may lead to an accelerated decline in lung function, impaired quality of life, disease progression,

and higher mortality. Thus, COPD exacerbations account for 50% to 75% of COPD-associated health care costs (3). Patients with immunosuppression and/or lung transplantation, asthma, COPD or interstitial lung disease (ILD) are at increased risk of complicated infections (2, 3). Indeed, a majority of acute exacerbations of chronic lung diseases are caused by infections, particularly viral ones (4, 5). Viral detection rates range from 22-64%, and rhinoviruses are reported to be the most commonly detected viral triggers (up to 60%), followed by influenza (up to 36%) and respiratory syncytial virus (RSV; up to 28%) with other viral infections reported less frequently (parainfluenza, human metapneumovirus [HMPV], coronaviruses, adenoviruses) (3). Bacterial co-infections, which occur in about 6-27% of cases, may prolong hospitalization even further, and lead to more severe impairments of lung function (3, 6). Thus, prevention of infections through vaccination is a key management concept to reduce acute infection-driven exacerbations and associated worsening of chronic lung disease (7). Since influenza and Streptococcus pneumoniae lead to increased hospitalization rates and mortality in patients with chronic lung diseases, current international guidelines, as well as the Swiss vaccination plan, recommend influenza and pneumococcus vaccinations in this patient group (7, 8, 9). Similarly, a vaccination against the Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2) is recommended for individuals at risk in Switzerland (8, 9). Reflecting the fact that other viral infections such as RSV may also contribute to exacerbations, and show similar or even higher mortality rates than influenza, the Global Initiative for Chronic Obstructive Lung Disease (GOLD) recommends a vaccination with existing RSV vaccines in all patients with COPD (9, 10, 11). Correspondingly, the Federal Office of Public Health (FOPH) has most recently released a recommendation for the RSV vaccination in individuals ≥ 75 years of age and for individuals at high risk of complications, including those with chronic lung disease, above the age of 60 years (12).

This article aims to summarize data on vaccine efficacy (VE) for populations with chronic lung diseases and provides a glimpse into future vaccination options for individuals at risk.

Chronic pulmonary diseases

Chronic obstructive pulmonary disease (COPD)

COPD is the third leading cause of death worldwide, accounting for 3.23 million deaths in 2019 (7, 13). In Switzerland, around 400 000 individuals are affected by COPD (14). It is the 4th most prevalent cause of death in Switzerland, and its incidence is rising (15, 16). COPD affects smokers in particular. However, it can also develop in non-smokers and is characterized by chronic inflammation of lung tissue and loss of lung function, often caused by exacerbations (2). COPD puts a high burden on patients and healthcare systems, with exacerbations causing a decreased quality of life and a negative impact on survival prognosis. In the context of the high burden of COPD, prevention of exacerbation frequently triggered by viral infections is paramount to improve the prognosis of the disease (3).

Asthma

Asthma is a heterogeneous pulmonary inflammation characterized by fluctuating bronchial hyper-responsiveness and variable airflow obstruction. Globally, about 300 million individuals of all ages are affected. This amounts to every 14th person in Switzerland, and incidences are increasing (2, 17). According to the hygiene hypothesis, the increasing prevalence of asthma may be due to a low-er incidence of infections and thus less challenges for the immune system (18). However, other theories claim that RSV or rhinovirus infection early in life may also be associated with a higher risk of developing asthma later in life (19, 20).

Interstitial lung disease (ILD)

The term ILD encompasses a wide range of fibrotic and inflammatory lung diseases, the prevalence of which is difficult to estimate due to the lack of standardized definitions (21). Thus, less evidence exists regarding the role of viral infections in the acute exacerbation of fibrotic lung disease (2). However, one report recorded a 30-day inpatient mortality of 20.6% after a viral infection in selected patients with ILD emphasizing the importance of early infection prevention also in this patient population (22). Mortality rates may however vary between different forms of ILD: for example, acute exacerbation of idiopathic pulmonary disease is associated with very high in-hospital mortality (>50%), as opposed to desquamative interstitial pneumonia, which generally comes with a better prognosis (23, 24).

Swiss Vaccination plan for the general population and specific groups

In Switzerland, there are currently 11 recommended basic vaccinations starting in childhood: tetanus, diphtheria, pertussis, poliomyelitis, Haemophilus influenzae type B, hepatitis B, S. pneumoniae, varicella zoster virus (VZV) and the trivalent vaccine against measles, mumps, and rubella. Vaccination against human papilloma virus follows in adolescence. Additional vaccinations in adulthood are recommended against herpes zoster, influenza, and pneumococcus and it is highly encouraged to stay up to date with all vaccinations according to the Swiss vaccination schedule – see link at the end of the article (8).

For at risk groups (incl. elderly and patients with cardiovascular, respiratory or other comorbidities), the Swiss vaccination plan recommends a yearly vaccination against influenza and coronavirus disease 19 (COVID-19) as well as a single dose vaccination against S. pneumoniae and a two-dose vaccination against herpes zoster for individuals aged ≥50 years depending on the classification of the lung disease (8). Indeed, COPD and asthma may be independent risk factors for herpes zoster. Since November 2024, the RSV vaccination is explicitly recommended for individuals aged ≥75 and individuals at high risk aged ≥60, in particular those with chronic lung disease (12).

International guidelines on vaccinations in COPD

The GOLD guidelines, which focus on individuals with COPD, have similar recommendations. However, they do not only emphasize the need for vaccination against in-

fluenza, COVID-19, S. pneumoniae, and herpes zoster (in individuals aged ≥50 years), but also RSV vaccination for individuals aged ≥60 years and pertussis vaccination in individuals with chronic lung diseases (9).
In the following chapter, incidences of several important infections in patients with chronic lung diseases as well as evidence for vaccination recommendations in this population will be summarized. Our review is limited to adults.

Pneumococcus vaccination

Streptococcus pneumoniae can cause parenchymal infections in many organs, particularly in the lower respiratory tract, and is a major cause of community-acquired pneumonia (CAP) (25). Exacerbations of COPD in combination with CAP are associated with reduced survival rates and an increased likelihood of subsequent exacerbations (26). Particularly, adults >65 years are affected by invasive pneumococcal disease (IPD) with highly increased incidence in those adults with at risk conditions such as asthma, COPD, and cardiovascular comorbidities. Indeed, two-thirds of pneumococcal disease cases are found in 25% of the population with high-risk and at-risk conditions (25, 27). The reported odds ratios from different cohorts to develop IPD in patients with chronic respiratory diseases range between 1.3 and 4.7 compared to healthy individuals (28). These numbers are concerning, since exacerbations of chronic lung disease with concomitant pneumonia are associated with worse outcomes compared to exacerbations without pneumonia. The length of hospital stay is prolonged (7 vs. 4 days), admission rates to intensive care unit (ICU) are higher (12.5% vs. 7.7%; hazard ratio [HR]: 1.63), there is a higher need for mechanical/non-invasive ventilation (6.9%/9.7% vs. 3.3%/6.7%; HR: 2.10/1.45), and both 30-day mortality in first-time cases (12.1% vs. 8.3%; HR: 1.20) as well as mortality at second exacerbation (15% vs. 10.2.0%; HR: 1.14) are increased (29).
A study from 2005 estimated the incidences for pneumococcal infection at 8.8/100,000 in healthy adults and 62.9/100,000 in adults with chronic lung disease (30). How-ever, more recent data from England reported declining incidences probably due to the introduction of new vaccines in the previous decade (25). In Switzerland, pneumococcal conjugate vaccines (PCVs) are the only pneumococcal vaccines recommended since 2014. They are more effective than the previously used 23-valent pneumococcal polysaccharide vaccine (since 2014, PPV23 [Pneumovax®-23] is not recommended in Switzerland) due to many advantages (31, 32). PCVs elicit a T-cell dependent immune response, are effective also in children under the age of 2 years, generate immune memory, a booster effect, and herd immunity. In addition, they have a higher efficacy in risk-groups compared to the former PPV23 (32, 33). The efficacy of PCV13 vaccination (Prevenar 13®) was tested in the CAPiTA study (details see Table 1A) and suggests a number needed to vaccinate (NNV) of 1031 to prevent one case of CAP and a NNV of 2041 to prevent one case of IPD (33, 34). Since 2023, pneumococcal vaccination with a PCV is recommended for all individuals ≥ 65 years (in addition to children and adults with risk factors) by the FOPH, the Federal commission for Vaccinations, and also by international guidelines (8, 9, 35). Beyond PCV13 (33), the newer higher valency vaccines PCV15 (Vaxneuvance®) (36) and PCV20 (Prevenar 20®) (37) have been recently introduced in Switzerland and approved for use in individuals ≥65 years (35). High valency PCVs are important due to serotype replacement in recent years towards non-vaccine serotypes causing an increasing proportion and incidence of pneumococcal disease (38). In Switzerland, there is a considerable difference in the percentage of covered serotypes between the available vaccines in 2023 - 31% (PCV13), 40% (PCV15), and 68% (PCV20) respectively (39). Even though risk for pneumonia, exacerbation, and death are highly elevated in individuals with chronic lung diseases, the awareness for pneumococcal infections and the requirement for PCV vaccination is still rather low in Switzerland. The vaccination rate among individuals with asthma or chronic pulmonary disease was estimated at about 14.8% in 2020, and even lower at 9.6% in those aged 65 to 85 years, leaving many patients at risk unprotected (40).

Influenza vaccination

The influenza virus infects about 10-20% of the global population each year, causing 3-5 million hospitalizations annually. It is a leading cause for mortality, particularly in individuals at risk (41). Influenza also causes a high economical and individual burden in Switzerland, leading to a seasonal average of 4944 (standard error: ± 785) influenza-caused hospitalizations and direct medical costs of up to 77.3 million euros per season (42). A less appreciated danger of the virus lies in complications affecting the cardiovascular system (myocarditis, heart failure), the central nervous system (stroke, encephalitis) or other organs such as the kidneys and liver (acute kidney/liver injury). For example, it is estimated that up to 13% of hospitalized adult patients with influenza develop myocarditis (41). Another study reported acute cardiac injury within the first 3 days of influenza infection in 24% of high-risk patients (43, 44). Several meta-analyses and reviews have summarized evidence that a vaccination against influenza attenuates the severity of an influenza infection in individuals at risk and can prevent such complications. Evidence supporting flu vaccination is mostly based on case-control studies and cohort studies. Indeed, a meta-analysis identified only four randomized controlled trials (RCTs) including patients with COPD. Vaccination against influenza showed long-term benefits for patients with COPD regarding influenza-related respiratory infections, number of exacerbations, hospitalization rates, all-cause mortality, and respiratory mortality (45). Further, it was shown in a meta-analysis of RCTs (vaccination versus placebo) that influenza vaccination was able to decrease the rate of severe adverse cardiovascular events (RR: 0.64; 95% CI: 0.48-0.86) particularly in high-risk patients, giving a favorable NNV of 58 (46). Moreover, vaccination leads to a decrease in stroke occurrence (odds ratio [OR]: 0.81; 95% CI: 0.77-0.86), a reduction of mortality among stroke patients (OR: 0.50; 95% CI: 0.37-0.68) and a decrease of stroke occurrence in COPD (OR: 0.70; 95% CI: 0.61-0.81) (47). Additionally, all-cause mortality was reduced by 4.6% and hospitalization rates for pneumonia and influenza were reduced by 8.5% in individuals ≥65 years, and by 12.4% in individuals aged 50-64 years

Tab. 1 **Vaccination efficacy reported in selected studies**

Study	Study design	Main inclusion criteria	Vaccine group	Control group	Main outcomes	Incidence of outcome in vaccine group
A) PNEUMOCOCCUS VACCINATION						
Bonten et al, NEJM 2015	RCT	≥65 years old without prior pneumococcal vaccination	N=42240 received PCV13	N=42256 received PBO	First episode of confirmed vaccine-type CAP	49 of 42240 1.16/1000
					Invasive pneumococcal disease	7 of 42240 0.17/1000
B) INFLUENZA VACCINATION						
Ghamande et al, CID 2022	prospective test-negative case-control study	adults ≥18 years hospitalized for ARI	N=3679 received influenza-vaccine (NS)	N=1164 not vaccinated	Influenza-positive ARI pneumonia	179 of 3679 48.7/1000
Lewis et al, CID 2024	prospective test-negative case-control study	age ≥18 years with ARI and hospital admission	N=1700 received influenza-vaccine (NS)	N=2007 not vaccinated	Influenza-associated hospitalization	235 of 1700 138.2/1000
Tippett et al, CID 2024	prospective test-negative case-control study	adults ≥50 years AND ≥18 years with CHF or COPD hospitalized with ARI	N=701 received influenza-vaccine (NS)	N=814 not vaccinated	Influenza-related hospitalization	37 of 701 52.78/1000
					Influenza-related hospitalizations for ARI or exacerbation	Data not published
Johansen et al, NEJM Evid. 2023	RCT	Danish citizens 65–79 years	N=6245 received HD QIV	N=6232 received SD QIV	Influenza-associated hospitalization or pneumonia	10 of 6245 1.6/1000
					Hospitalization for respiratory disease	24 of 6245 3.84/1000
					all-cause death	21 of 6245 3.36/1000
C) SARS-CoV2 VACCINATION						
Lin et al, NEJM 2024	retrospective database analyses	COVID-19 test results from NEDSS and vaccination data from NESIIS	N=64462 vaccinated with XBB.1.5 vaccine (<9 months ago)	N=1765626 not vaccinated with XBB.1.5 vaccine, or vaccinated ≥9 months ago	SARS-CoV-2 infection	1008 of 64462 15.64/1000
					SARS-CoV-2-associated hospitalization	65 of 64462 1.01/1000
					SARS-CoV-2-related death	10 of 64462 0.16/1000
D) VZV VACCINATION						
Cunningham et al, NEJM 2016	RCT	≥70 years old (ZOE-70)	N=6950 received 2 doses of RZV	N=6950 received PBO	Herpes zoster infection	23 of 6950 0.9/1000 PY
		≥50 years old (ZOE-50) and ≥70 years old (ZOE-70) (pooled)	N=8250 received 2 doses of RZV	N=8346 received PBO	Herpes zoster infection	25 of 8250 0.8/1000 PY
Boutry et al, CID 2022	RCT	≥50 years old (ZOE-50) and ≥70 years old (ZOE-70) (pooled)	N=7277 received 2 doses of RZV	N=7277 received PBO	Herpes zoster infection	27 of 7277 1.4/1000 PY

Incidence of outcome in control group	IRR with 95 % CI	Risk difference with 95 % CI	NNV with 95 % CI	VE with 95 % CI	Comments
90 of 42256 2.13/1000	0.544 (0.384–0.771)	0.00097 (0.00021–0.00173)	1031 (577 - 4862)	45.6 % (21.8–62.5), P < 0.001	Asthma prevalence: 4.8% (PCV13) and 5.0% (PBO) Lung disease prevalence: 10.1% (PCV13) and 10.3% (PBO)
28 of 42256 0.66/1000	0.250 (0.109–0.573)	0.00050 (0.00013–0.00087)	2012 (1156 - 7764)	75 % (41.4–90.8), P < 0.001	
87 of 1164 74.7/1000	NC#	NC#	NC#	38 % (17–53)	Lung conditions present in 71.8 % of cases (74.5 % of test-negative controls)
479 of 2007 238.7/1000	NC#	NC#	NC#	37 % (27–46)	Chronic respiratory conditions reported in 43 % of all pts, and in 42 % of influenza-positive cases
78 of 814 95.82/1000	NC#	NC#	NC#	63.1 % (43.8–75.8)	In overall study population across two seasons
Data not published	NC#	NC#	NC#	68.2 % (44.8–81.7)	In individuals with CHF/COPD across two seasons
28 of 6232 4.49/1000	0.356 (0.173–0.734)	0.0029 (0.00024–0.00554)	346 (180 - 4174)	64.4 % (26.7–82.7)	Chronic lung disease in 435 pts (7 %) receiving HD and 415 pts (6.7 %) receiving SD vaccine
40 of 6232 6.42/1000	0.599 (0.361–0.993)	0.0026 (–0.00094–0.00609)	388 (NE) §	40.1 % (21.8–65.5)	
41 of 6232 6.58/1000	0.511 (0.302 - 0.865)	0.0032 (-0.00023 - 0.00666)	310 (NE) §	48.9 % (11.5–71.3)	
20980 of 1765626 11.88/1000	NC#	NC#	NC#	30 % (22.5–36.7)	VE estimated at 15 weeks after vaccination for pts vaccinated between Sep 11 and Oct 25, 2023
1299 of 1765626 0.74/1000	NC#	NC#	NC#	40.9 % (–23.8–71.8)	
227 of 1765626 0.13/1000	NC#	NC#	NC#	52.6 % (0.9–77.3)	
223 of 6950 9.2/1000 PY	0.10 (0.067–0.158)	0.0288 (0.0233–0.0343)	35 (29 – 43)	89.8 % (84.2–93.7) P < 0.001	
284 of 8346 9.3/1000 PY	0.089 (0.059–0.134)	0.031 (0.0259–0.0361)	32 (28 – 39)	91.3 % (86.8–94.5) P < 0.001	
169 of 7277 8.6/1000 PY	0.16 (0.106–0.240)	0.0195 (0.0147–0.0244)	51 (41 – 68)	84 % (75.9–89.8)	

Study	Study design	Main inclusion criteria	Vaccine group	Control group	Main outcomes	Incidence of outcome in vaccine group
E) RSV VACCINATION						
Papi et al, NEJM 2023	RCT	≥60 years old	N = 12467 received RSVPreF3 OA	N = 12499 received PBO	RSV-related LRTD as confirmed by RT-PCR	7 of 12466 1/1000 PY
					LRTD restricted to severe disease*	1 of 12466 0.1/1000 PY
Walsh et al, NEJM 2023	RCT	≥60 years old	N = 17215 received one dose of RSVpreF	N = 17069 received PBO	RSV-associated LRTD with ≥ 2 signs/symptoms	11 of 17215 1.2/1000 PY
					RSV-associated ARI	22 of 17215 2.4/1000 PY
Wilson et al, NEJM 2023	RCT	≥60 years old	N = 17572 received one dose of mRNA-1345	N = 17516 received PBO	RSV-associated LRTD with ≥ 2 signs/symptoms	9 of 17572 1.44/1000 PY
					RSV-associated ARI	26 of 17572 4.15/1000 PY

* Based on clinical signs or investigator assessment or on the basis of receipt of supportive therapy.

(48, 49). Besides reducing direct health risks in a vulnerable population, influenza vaccination may also decrease antibiotic use due to prevention of CAP: Seasonal influenza vaccination averts about 1014.7 (95% CI: 803.3-1219.7) million defined daily doses of antibiotics (50).

Recent studies on the efficacy of different available influenza vaccines are summarized in table 1B. Notably, the US HAIVEN study reported an adjusted VE of 38% (95% CI: 17-53) against hospitalization for influenza-associated pneumonia, varying between strains (51). A multicenter study from the US showed a similar VE of 37% (95% CI: 27–46) against hospitalization, also reporting variations depending on strain and age (52). Different results were reported in another prospective study from the US, which found that the adjusted VE against influenza-related hospitalizations was 63.1% (95% CI: 43.8-75.8) in the pooled study population, and 68.2% (95% CI: 44.8-81.7) against hospitalization for exacerbation or acute respiratory infection (ARI) among those with congestive heart failure (CHF) or COPD (53). However, VE is estimated to have varied annually from 19% - 60% in the last 15 years, mainly due to differences in matching of vaccine strains with circulating strains (54). High-dose (HD) vaccines improve VE, particularly in seasons of low matching between the vaccine and the circulating virus strains and in older individuals or those at risk (55). Current Swiss recommendations emphasize the importance of influenza vaccination in individuals at risk, including those with chronic lung diseases (56). In Switzerland, the quadrivalent inactivated vaccines Fluarix Tetra® (57) and Vaxigrip Tetra® (approved from the age of 6 months) (58) are available and reimbursed for individuals ≥65 years and for all individuals with at least one risk factor (56). Recently, the HD quadrivalent influenza vaccine showed a relative VE of 64.4% regarding the prevention of hospitalizations due to influenza or pneumonia and of 48.9% regarding all-cause death, corresponding to a NNV of 346 and 311 respectively (see Table 1B for details) (59). Accordingly, the HD Efluelda® vaccine (60) is available in Switzerland for individuals ≥65 years and reimbursed in all individuals ≥75 years or ≥65 with at least one risk factor (56). Compared to the aforementioned pneumococcal vaccination, the rate of influenza vaccination among people with chronic lung diseases is higher in Switzerland, reaching 21.6% (95% CI: 18.68-24.85) in all age groups and 49.85% (95% CI: 41.61-58.09) in those aged ≥65 (61). For the coming influenza season 2024/2025, the US has decided on a transition back to the trivalent vaccine, as the B/Yamagata strain (included in the quadrivalent vaccines) is no longer circulating (62).

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccination

Despite the decreasing media interest in SARS-CoV-2, the rates of the circulating virus are still high in 2024 (63). With the emergence of new variants, the mortality of a SARS-CoV-2 infection decreased, but is still 35% higher compared to an influenza infection (HR: 1.35; 95% CI: 1.10-1.66) (64). During earlier waves, the rate of severe COVID-19 was significantly higher in individuals who had a lung transplantation (OR: 4.62; 95% CI: 2.71-7.89) or chronic lung disease (OR: 2.11; 95% CI: 1.36-3.30) compared to the general population (65). Although severe COVID-19 cases have decreased in the Omicron era, individuals with asthma and COPD still had a significantly higher risk for developing severe COVID-19 (HR: 1.31; 95% CI: 1.10-1.55 and HR: 1.36; 95% CI: 1.12-1.66, respectively), but booster vaccinations reduced this risk (66). Administration of ≥3 doses of vaccination conferred a significantly reduced risk for a severe infection (OR: 0.35; 95% CI: 0.21-0.60) (65).

A study on the VE of SARS-CoV-2 vaccines is summarized in table 1C. In general, XBB.1.5 vaccines against omicron subvariants showed limited duration against preventing infection, with a VE of 52.2% (95% CI: 44.6-58.7) after 4

Incidence of outcome in control group	IRR with 95 % CI	Risk difference with 95 % CI	NNV with 95 % CI	VE with 95 % CI	Comments
40 of 12 494 5.8/1000 PY	0.175 (0.079–0.391)	0.00264 (0.00123–0.00405)	379 (247 - 811)	82.6 % (57.9–94.1)	Cardio-respiratory conditions reported in 20 %
17 of 12 494 2.5/1000 PY	0.059 (0.0008–0.443)	0.00128 (0.00048–0.00201)	781 (498 - 2097)	94.1 % (62.4–99.9)	
33 of 17 069 3.6/1000 PY	0.33 (0.17–0.65)	0.00129 (0.00026–0.00233)	773 (429 - 3878)	66.7 % (28.8–85.8)	In total, 3996 pts with lung disease (11.7 %)
58 of 17 069 6.3/1000 PY	0.38 (0.23–0.61)	0.00212 (0.00071–0.00353)	472 (284 - 1402)	62.1 % (37.1–77.9)	
55 of 17 516 8.8/1000 PY	0.16 (0.08–0.33)	0.00263 (0.00146–0.00379)	381 (264 - 683)	83.7 % (66–92.2)	COPD was reported in 1938 pts (5.5 %)
82 of 17 516 13.12/1000 PY	0.32 (0.20–0.49)	0.00320 (0.00162–0.00478)	312 (209 - 616)	68.4 % (50.9–79.7)	

Calculations were only performed on RCT studies. **§** includes 0

weeks, and 32.6% (95% CI: 28.1-36.8) after 10 weeks. However, VE against hospitalization and death was sustained over a longer period (67). Thus, protection against SARS-CoV-2 infection itself is only modest, but protection against severe COVID-19 leading to hospitalization remains high after vaccination. Accordingly, the FOPH currently recommends a SARS-CoV-2 vaccination for all individuals at risk, ideally with variant-adjusted vaccines (8). Similarly, also the GOLD-guidelines recommend a yearly COVID-19 vaccination for patients with COPD (9). Currently, the mRNA vaccines Comirnaty® (68) and Spikevax® (69) are available and approved for use in Switzerland. In general, the FOPH recommends the use of an mRNA vaccine targeting the current SARS-CoV-2 variants, regardless of previously administered vaccinations (70).

Varicella-zoster virus (VZV) vaccination

VZV causes varicella (chickenpox) and herpes zoster (shingles). Varicella typically manifests in childhood, characterized by a highly contagious vesicular rash and mild fever. Herpes zoster occurs due to reactivation of latent VZV, usually in older adults or immunocompromised individuals causing a painful, localized rash and severe nerve pain (postherpetic neuralgia) (71, 72). Worldwide, almost 84 million people are affected annually, leading to around 14,500 deaths per year. Although death rates appear to be rather low, the disease burden in affected people is high (72). The risk for developing herpes zoster is 24% higher in patients with asthma, and 41% higher in patients with COPD. This risk is further increased by the use of corticosteroid medication. Moreover, an exacerbation of COPD seems to be coupled with herpes zoster appearance and there is a higher risk for herpes zoster complications (postherpetic neuralgia, zoster ophthalmicus) in patients with asthma and COPD (73). Even though incidences are rising due to increased aging of the population, disease burden and death rates have decreased during the last decades. This is mostly attributable to vaccination, in particular with subunit vaccines (Shingrix®) (72, 74). Table 1D provides a summary on the VE of this recombinant VZV vaccination from two randomized controlled trials (RCTs). One study suggests a NNV of 35 (95% CI: 29-43) to prevent herpes zoster infection in ≥70-year-old patients, and a NNV of 32 (95% CI: 28-39) in ≥50-year-old patients (75). A 7-year follow-up on the cohort of patients ≥50 years reported a NNV of 51 (95% CI: 41-68) (76). In contrast, the protection of the live, attenuated vaccine waned over this time period (77). In Switzerland, vaccination with the recombinant subunit vaccine Shingrix® (78) is recommended for individuals aged ≥ 65 years, for individuals aged ≥ 50 years with severe asthma, COPD or immunodeficiency, and for individuals aged ≥ 18 years with severe immunosuppression (8).

Pertussis vaccination

Pertussis, or whooping cough, is a highly contagious disease characterized by severe coughing. It is caused by the bacterium Bordetella pertussis and affects about 50 million people worldwide every year, causing 300,000 deaths annually (79). Incidence in healthy people amounts to 0.5 per 100,000 and is significantly increased among patients with COPD (2.47 per 100,000; incidence rate ratio [IRR]: 4.94; 95% CI: 4.0-6.1;). Pertussis incidence in asthma patients is even higher with 3.35 per 100,000 (IRR: 6.70; 95% CI: 5.7-7.9) (79). Thus, specifically in patients with chronic lung disease, pertussis events cause a significant increase in health care resource utilization and direct medical costs (80). With the introduction of vaccines, mortality was significantly reduced, but there are still surges of the disease, which may be countered with up-to-date booster vaccinations (81). The surges may be attributable to the rather fast waning of protection from acellular vaccine as reported by a study on the Tdap-vaccines (tetanus, diphtheria, acellular pertussis) Boostrix® (82) and Adacel® (83). While

VE was 75.3% (95% CI: 55.2-86.5) within 1 year, it decreased to 11.9% (95% CI: -11.1-30.1) within 4-5 years (84).
The FOPH currently recommends a basic pertussis vaccination in infants and boosters in childhood and adolescence. Moreover, a booster vaccination with either Boostrix® (82) or Adacel® (83) is recommended in adults who are in contact with infants and pregnant women. However, patients with COPD and asthma are not particularly mentioned (8). Also GOLD recommends a pertussis booster only in COPD patients who were not vaccinated in adolescence (9).

Future perspectives in Switzerland

In this section, we aim to provide a view of the future vaccination landscape in Switzerland, with a focus on new pneumococcus vaccines with higher serotype coverage and the first RSV vaccines already and soon to be available in Switzerland.

New pneumococcus vaccines

Currently, PCV15 and PCV20 are recommended for use in Switzerland (35). The US Federal Drug Administration (FDA) recently approved PCV21 for people aged ≥65 years, which represents a new concept of PCVs as it targets the majority of serotypes which currently affect adults. PCV21 does not include all pediatric serotypes, but it currently covers up to 85% of serotypes in those aged ≥65 years (85, 86). The U.S. Advisory Committee on Immunization Practices has already recommended this PCV21 as an option for adults. This recommendation also applies to individuals who had already received PCV13 in the past (86). Due to the coverage of 11 different serotypes, it is expected to bring benefits in terms of quality of life for the older population and a potential benefit for patients at risk for IPD (87). This approval is based on a recent study on the PCV21 vaccine in adults, which had proven a good tolerability and safety profile, while showing a non-inferior response to all included serotypes in comparison to previous PCV vaccinations covering fewer serotypes (88). Additionally, there are ongoing studies on a novel 24-valent PCV, which aims to increase even further serotype coverage (89).

Respiratory syncytial virus (RSV) vaccines

RSV is an RNA-virus, with its infections peaking in the winter months, causing a range of respiratory tract symptoms, and sometimes even pneumonia. Severe cases affect mostly infants, young children, and the elderly, leading to higher mortality in those age groups (90, 91). There are already two approved protein-based RSV vaccines available in Switzerland (92), and a third mRNA-based vaccine is currently in the approval process. Vaccination recommendations for older individuals and patients at high risk for complications, including those with chronic lung disease, have recently been published by the FOPH (93). Similarly, the GOLD guidelines recommend RSV vaccination for patients with COPD (9). This recommendation is based on the fact, that RSV is associated with more severe disease outcomes in comparison to influenza or SARS-CoV-2, even though less people are hospitalized with RSV (94). However, chronic lung diseases are among the major predictors for hospitalization of patients, infected with RSV (95). A recent modeling study reported a 2- to 4-fold increased risk of hospitalization for adults with COPD and RSV infection and a 1.5- to 3-fold increased risk for adults with asthma and RSV infection (96). Moreover, hospitalization due to RSV infection is associated with acute cardiac events, particularly in patients at risk (97).
In recent years, many RSV-vaccinations were studied in clinical trials, aiming to elicit an immune response against the RSV fusion protein F in its prefusion conformation (preF) (98). Besides the adjuvant RSVPreF3-antigen vaccination mentioned above (99), there is also a bivalent vaccine including the preF from both RSV A and B (100) as well as an mRNA vaccine (101) already available in some markets, albeit not approved in Switzerland yet. Several RCTs testing those different vaccines are summarized in table 1E. For the AS01E-adjuvanted RSV preF based candidate vaccine (RSVPreF3 OA) a NNV of 379 (95% CI: 247-811) was reported regarding the prevention of RSV-related lower respiratory tract disease (LRTD) (99). For the bivalent RSV preF based vaccine (bivalent RSVpreF) a NNV of 773 (95% CI: 429-3878) for RSV-associated LRTD with ≥2 signs/symptoms, and a NNV of 472 (95% CI: 284-1402) for RSV-associated ARI was reported (100). Lastly, the mRNA vaccine mRNA-1345 show-ed a NNV of 381 (95% CI: 264-683) against RSV-associated LRTD with ≥2 signs/symptoms and a NNV of 312 (95% CI: 209-616) for RSV-associated ARI (101). The immunization against preF was able to maintain a high VE against LRTD over a period of at least two to three seasons (102, 103). While the VE regarding severe RSV and LRTD is well studied in current RSV vaccines, data on VE regarding the prevention of hospitalizations is still limited. In the US, three RSV vaccines (one adjuvant RSVPreF3, one bivalent RSVpreF, and the mRNA vaccine) are already approved for adults ≥60 years, and the first safety data were recently presented (104). So far, injection site and systemic reactions were more frequently reported among patients receiving the adjuvant RSVPreF3 vaccine compared to the available bivalent RSVpreF. How-ever, the estimated rates for Guillain-Barré syndrome (GBS), which had been raised as a safety concern, were higher in people vaccinated with the bivalent vaccine (4.4 per 1 million administered doses) compared to the adjuvant one (1.8 per 1 million doses administered) (104). Even though GBS rates were more commonly reported than initially expected, the high efficacy in reducing severe RSV cases and exacerbations of chronic lung disease still suggests the importance of those RSV vaccines in at-risk patients.

Discussion

In summary, the Swiss vaccination plan provides specific recommendations for the vaccination of individuals at risk, including patients with chronic lung diseases (8). Still, the vaccination rate among patients with chronic lung diseases, particular for S. pneumoniae, remains low in Switzerland, highlighting the need for more awareness in clinics and among general practitioners (40). Moreover, due to serotype replacement in pneumococcal disease observed in recent years, recommendation for newer PCVs covering

more serotypes, especially for individuals at risk, should be made (38). This may include the PCV21 in the near future, as it has recently been approved by the FDA (86). While the GOLD guidelines have already recommended RSV and pertussis vaccinations for patients with COPD, the recommendations regarding RSV were only recently anchored in the Swiss recommendations (8, 9, 12). This recent update reflects the potential severity of an RSV infection for patients with chronic lung diseases (94). Indeed, the FDA has already approved three RSV vaccines in the last years (104). Also, Switzerland has recently introduced two vaccines on the market for adults aged ≥60 years (93). Several impor-tant questions remain regarding RSV vaccination, such as the efficacy of repeated vaccination, duration of response and most importantly the effectiveness in populations with comorbidities (105). Moreover, safety and immunogenicity of coadministration with for example influenza vaccines are still under investigation. Current studies suggest that coadministration is probably acceptable, even though a slight reduction in RSV antibody responses was observed (106). In general, even though RSV vaccinations are associated with certain risks such as GBS, those are outweighed by the successful prevention of exacerbations and cardiovascular events in individuals at risk (107). This goes in line with the protective properties of for example influenza and S. pneumoniae vaccines, which have shown to reduce the risk for myocardial infarction and cardiovascular additionally to pulmonary exacerbations (107).

Our review has several limitations. It is not a systematic review and meta-analysis, as we incorporated only selected studies evaluating the NNV and VE of various vaccin-es recommended for patients with chronic lung diseases. Furthermore, most of those vaccination studies were not explicitly performed in patients with chronic lung diseases. While some of the mentioned studies assessed the percentage of patients with chronic lung diseases, COPD and asthma in particular, there was almost no record of ILD. In general, a lot of the recommendations for vaccination in patients with chronic lung diseases focus on COPD (9). Although there are some studies on the role of infection-driven exacerbations in asthma, data on the impact of res-piratory infections on the exacerbation of ILD are scarce (21).

In conclusion, aiming for a higher vaccination rate among individuals with chronic pulmonary diseases is crucial in preventing exacerbations and thus morbidity and mortality in this vulnerable population. The introduction of new and more effective vaccines, such as updated PCVs and RSV vaccines in Switzerland as well as the constant variant-adjustment of influenza and SARS-CoV2 vaccines will be pivotal in ensuring protection in comorbid patients in the future. Strategies to improve vaccination rates may include the identification of drivers of and barriers to vaccinations to make informed decisions, as well as patient education and training for healthcare providers and national authorities (108).

Link to the FOPH vaccination recommendations

Prof. Dr. med. Jörg Leuppi
Chief Medical Officer
Medicine & University Affairs
Cantonal Hospital Baselland
Rheinstrasse 26, CH-4410 Liestal
joerg.leuppi@ksbl.ch

Conflict of interest

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Abbreviations

ARI	acute respiratory illness
CAP	community acquired pneumonia
CI	confidence interval
CHF	congestive heart failure
COPD	chronic obstructive pulmonary disease
COVID-19	coronavirus disease 19
FEV1	Forced Expiratory Volume in one second
FOPH	Swiss federal office of public health
GOLD	Global initiative for chronic obstructive lung disease
HD	high dose
HMPV	human metapneumovirus
HR	hazard ratio
ILD	interstitial lung disease
IPD	invasive pneumococcal disease
IRR	incidence rate ratio
LRTD	lower respiratory tract disease
mRNA-1345	mRNA-based RSV vaccine encoding the stabilized RSV prefusion F glycoprotein
NC	not calculable
NE	not estimable
NEDSS	Nebraska Electronic Disease Surveillance System
NESIIS	Nebraska State Immunization Information System
NS	not specified
NNV	number needed to vaccinate (rounded to unit)
OR	odds ratio
PBO	placebo»
PCV	pneumococcal conjugate vaccine
PPV	pneumococcal polysaccharide vaccine
PY	person years
QIV	quadrivalent influenza vaccine
RCT	randomized controlled trial
RR	risk ratio
RSV	respiratory syncytial virus
RSVpreF	bivalent RSV prefusion F protein-based vaccine
RSVPreF3 OA	AS01E-adjuvanted RSV prefusion F protein–based vaccine
RZV	glycoprotein E (gE)-based adjuvanted recombinant zoster vaccine
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
SD	standard dose
VE	vaccine efficacy
VZV	varicella zoster virus

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