Diploma thesis

Vaccination coverage against influenza, pneumococcal infection and pertussis among hospitalized cardiological and pneumological patients at the University Hospital Graz

A Follow-up Study

by

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under supervision of

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Graz, am 06.05.2020 *Charlotte Komarek eh*

Acknowledgement

I would like to express my very great appreciation to Dr. med. univ. Elisabeth Smolle, Dr. med. Holger Flick and Prof. Horst Olschewski for their guidance and helpful advice for this project. Also, I would also like to thank Tanja Röblreiter for her research work, creating the conditions for this.

Finally, I wish to thank my family for their support during my time at university as much as my friends who were always there for me.

Zusammenfassung

Hintergründe.

Ziel dieser Studie war es, Impfprävalenzdaten bezüglich Influenza, Pneumokokken und Pertussis von kardiopulmonalen Patientinnen und Patienten der Universitätsklinik Graz zu erhalten. Somit konnten die vorläufigen Daten, die im vorherigen Jahr durch dieselben Methoden erhoben wurden, erweitert und vervollständigt werden. Risikogruppen, wie Personen mit chronischen kardiopulmonalen Grunderkrankungen, sowie Menschen ab einem Alter von 65 Jahren wird die Influenza Impfung generell empfohlen. Gründe dafür sind unter anderem die Reduktion der Anzahl an Krankenhausaufenthalten und Komplikationen als auch der Mortalität durch Influenza. Auch die Impfungen gegen Pneumokokken und Pertussis werden Personen mit kardiopulmonalen Grunderkrankungen in gleicher Weise empfohlen.

Methoden.

Im Zeitraum zwischen 1. April und 31. Mai 2018 wurden 222 Patientinnen und Patienten auf den klinischen Abteilungen für Pulmonologie und Kardiologie der Universitätsklinik Graz mittels eines Interviews mit Fragebogen befragt. Ziel war es einen Überblick über die Durchimpfungsrate von Influenza, Pneumokokken und Pertussis in unserer Patientenstichprobe zu bekommen und Gründe für fehlende Impfungen zu eruieren. Die Daten, die bereits 2017 mit denselben Methoden erhoben wurden, konnten somit erweitert und mit den nun vorliegenden Daten von 2018 verglichen werden. Außerdem wurden die Ergebnisse im Vergleich zu anderen Ländern diskutiert, um sinnvolle Anpassungsmöglichkeiten im österreichischen Impfprogramm aufzuzeigen.

Resultate.

Es konnte gezeigt werden, dass 22% der befragten Patientinnen und Patienten eine aktuelle Impfung gegen Influenza, 23% gegen Pneumokokken und rund 4% gegen Pertussis aufweisen. Die meisten gaben als Begründung einer fehlenden Grippeimpfung an, nicht vom Nutzen der Impfung überzeugt zu sein. Bei fehlender Impfung gegen Pneumokokken und Pertussis, wurde in den meisten Fällen eine fehlende ärztliche Empfehlung für diese Impfungen angegeben.

Zusammenfassung.

Insgesamt wurden relativ niedrige Impfraten gegen Influenza, Pneumokokken und Pertussis festgestellt. Diese haben sich im Vergleich zum Vorjahr nicht wesentlich verändert. Somit bestätigt die hier vorgelegte Analyse die Daten aus dem Vorjahr. Die österreichische Impfstrategie sollte mit Hinblick auf die hier untersuchten Impfungen dringlich überprüft und verbessert werden.

Abstract

Background.

This study aimed at providing accurate data on vaccine coverage rates of influenza, pneumococcal infection and pertussis vaccination in cardiopulmonary patients at the University Clinic Graz.

Vaccination against influenza is an effective way of preventing influenza and its complications, such as pneumonia, and reduces hospitalizations as well as exacerbations of underlying diseases. Therefore, individuals with underlying cardiopulmonary diseases or those above 65 years are at risk for developing complications, and particularly benefit from influenza vaccination. In Austria, vaccination against pneumococcal infection and pertussis is recommended for elderly patients with chronic cardiopulmonary conditions as well, however, data on how effective general practitioners endorse those vaccinations in patients when indicated, is still lacking.

Methods.

Between the 1st of April and 31st of May 2018, 222 patients were interviewed about their current vaccination status against influenza, pneumococcal infection and pertussis at the cardiological and pneumological department at the University Hospital Graz. In this explorative follow-up-study vaccination coverage rates of influenza-, pneumococcal- and pertussis vaccination, and the patients' reasons for not being vaccinated were investigated, enlarging data from the previous winter season and allowing an overview of the vaccination situation in this target group. Furthermore, recent data on influenza vaccination were discussed in comparison to other vaccination programs in Europe in order to find possible ways of improving Austria's vaccination program.

Results.

Out of all patients interviewed, 22% were vaccinated against influenza during the last winter season, 23% were vaccinated against pneumococcal infection and 4% against pertussis. In most cases, those not vaccinated against influenza claimed not to be convinced of the benefits of this vaccination. Most of those not vaccinated against pneumococcal infection and pertussis declared to have not been recommended this vaccination.

Conclusion.

Overall, vaccination coverages in this cohort of persons at risk are rather low and have not changed much since the previous season, indicating the need of major adjustments in Austria's vaccination program with more emphasis on the effectiveness and importance of vaccination.

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List of abbreviations

ACO = asthma-COPD-Overlap

ARI = acute respiratory infection

COPD = chronic obstructive pulmonary disease

ILI = influenza like illness

TIV = trivalent inactivated vaccine

QIV = quadrivalent inactivated vaccine

LAIV = live attenuated influenza vaccine

ÖVIH = Österreichischer Verband der Impfstoffhersteller

ACIP = Advisory Committee on Immunization Practices

OECD = Organisation for Economic Co-operation and Development

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1 Introduction

1.1 Benefit and objectives of vaccinating against influenza

During the past decades Austrians have shown a large hesitance and refusal towards influenza vaccination, although it is generously recommended in its vaccination program. (Kunze, Böhm and Groman, 2013). But the awareness of this hesitance is slowly growing in Austrian's medical system, as can be seen in the implemented health interviews on influenza coverage by Statistics Austria in 2014 (Klimont and Baldaszti, 2014) and the Austrian Association of Vaccine Manufacturers (ÖVIH) in 2018. Latter questionnaire published in March 2018 focused on influenza vaccination coverage in 1000 persons above 14 years (Österreichischer Verband der Impfstoffhersteller, 2018).
An assessment of the vaccination coverage against influenza in cardiopulmonary patients has not been done under these conditions yet.

Influenza vaccination is the best way of preventing the morbidity and mortality caused by the influenza virus during periods of high infection risk (Armstrong *et al.*, 2004; World Health Organization, 2012b).
It has been shown that influenza vaccination reduces the number of hospital stays and deaths after respiratory diseases as well as after myocardial infarction (Gurfinkel and de la Fuente, 2004; Mangtani *et al.*, 2004). Influenza vaccination minimizes the risk of severe complications such as pneumonia and acute exacerbation of underlying diseases such as chronic heart and lung diseases, which may be caused by influenza (Nichol, Wuorenma and von Sternberg, 1998). People with such underlying diseases are among the group of persons at risk. Besides people with a high chance of developing complications, persons particularly exposed to the influenza virus are also at risk (World Health Organization, 2012b; D'Angiolella *et al.*, 2018).

Not only seniors with cardiopulmonary conditions benefit from influenza vaccination but it has been shown that all individuals above the age of 65 do (Nichol, Wuorenma and von Sternberg, 1998). The Advisory Committee on Immunization Practices suggests that trivalent or quadrivalent, unadjuvanted or adjuvanted inactive influenza vaccination or recombinant influenza vaccines can be used but no matter which vaccine is chosen a delay in vaccination should not occur (Grohskopf *et al.*, 2017).

Furthermore, pregnant women are also recommended the vaccination because they are more vulnerable to suffer from complications and severe illness due to influenza. Inactivated influenza vaccines are the safest, and especially indicated for this group (Grohskopf *et al.*, 2017).

The aim of vaccinating children is to protect themselves and persons at risk by reducing community transmission. Children are recommended vaccination from the age of 6 months onwards, and usually respond better to the vaccine than elderly. The newly licensed live-attenuated influenza vaccine LAIV has to be applied nasally and is therefore better adapted for children (Halloran and Longini, 2006). Currently the inactivated tetravalent vaccine is used for children in Austria. From the age of 6 months to 9 years, two doses with an interval of 4 weeks have to be administered for the first season of vaccination, afterwards one is sufficient (Arrouas and Tiefengraber, 2018).

1.1.1 Cost-effectiveness of influenza vaccination

Evaluating the cost-effectiveness goes along with some considerations about vaccine effectiveness. Vaccine effectiveness refers to clinical benefits in real circumstances, efficiency is measured in ideally controlled conditions in healthy individuals. Effectiveness can be measured in different ways: number of serologically confirmed influenza, complications, hospitalization or deaths due to influenza and varies according to the type of vaccine (TIV, QIV, LAIV), the viruses covered by the vaccination and the age-dependent or risk group-dependent response to the vaccine. Due to the fact that the influenza viruses change, vaccine effectiveness has to be constantly monitored and improved (Centers for Disease Control and Prevention, 2016; Public Health England, 2017).

Under the age of 65 years vaccine effectiveness is at 48,0%, whereas in individuals over 65 years showed it to be at 39,3% (Nichols *et al.*, 2018). The World Health Organization evaluated the effectiveness to be more effective in adults under 65 years than in the elderly of 65 and older but since vaccination is the best method of protection against influenza, this population remains a target group for this vaccination (WHO, 2012b).

Costs involve direct costs, e.g. for hospitalizations, medications and consultations and indirect costs as due to loss of work hours. The different perspectives on cost-effectiveness between the health payer and society have to be distinguished as well (De Waure *et al.*, 2012; D'Angiolella *et al.*, 2018). Several cost-effectiveness evaluations have been published and

reviewed (De Waure *et al.*, 2012; Ting, Sander and Ungar, 2017; D'Angiolella *et al.*, 2018) but the varying methods make an objective comparison difficult.

D'Angiolella et al. (2018) have come to the conclusion that most cost-effectiveness analysis have found it to be cost-saving to vaccinate children and high risk patients as well as elderly people. De Waure et al. (2012) and Ting et al. (2017) have also found influenza vaccination to be cost-effective in elderly and groups at high risk.
In Austria Stoppacher (2008) has shown that a vaccination of all people over the age of 65 years would be cost-saving for the healthcare payer.

Hellenbrand et al (2012) has found the pH1N1 vaccination to prevent pH1N1-hospitalization effectively. PH1N1 is the virus strain responsible for the influenza pandemic in 2009 and is since then part of every vaccine.

1.1.2 Introduction of different influenza vaccination programs

In December 2009 the European Council has set the goal of reaching an influenza vaccination coverage of at least 75% until 2014/15 in persons at risk following WHO recommendations (The Council of European Union, 2009; Mereckiene *et al.*, 2014). The study by P. Jorgensen et al from December 2017 collected data on recent seasonal influenza vaccination from the WHO European Region and showed that only Scotland reached the WHO and European Council goal in 2014/15. England, Northern Ireland and the Netherlands have had vaccination coverages above 65%. Austrian data is missing for this study (Jorgensen *et al.*, 2017).

The Austrian vaccination program recommends the influenza vaccination for elderly people (>50 years), persons with chronic illnesses such as chronic heart failure or chronic lung diseases, as well as pregnant women and infants. Furthermore, people with a suppressed immune system or a close and frequent contact to other people at their workplace, for example health care workers are recommended the vaccination. The influenza vaccination is, however not part of the free vaccination program (Arrouas and Tiefengraber, 2018).

In the UK the National Health Service offers a free flu vaccination every year for eligible persons at risk. This group includes pregnant women and patients with one or more long-

term conditions such as heart, liver and kidney diseases as well as diabetes, lowered immunity and morbid obesity. The general practitioner is able to consider patients with other underlying diseases in order to protect them from influenza and its complications (Public Health England, 2018).
Some community pharmacies in the UK also provide the flu vaccination (National Health Service, 2018b). The vaccine itself is not only available in pharmacies but also in some supermarkets (National Health Service, 2018a).

The Netherlands reached a vaccination coverage for influenza of 49,9% in the entire target group and 69,6% in people older than 65 years in 2017. Since 1997 the Dutch National Influenza Prevention Program enables persons at risk for influenza, such as people older than 60 years and those with certain chronic diseases a vaccination free of charge by the general practitioner (*Flu jab | RIVM*, 2015; Heins, Hooiveld and Korevaar, 2017). In autumn most general practitioners send a letter or notification card to their patients to invite and remind them of vaccination. Some place an announcement in the local paper instead. Together with personal invitations, public information folders on influenza are distributed in family practices and posters put up in hospitals and nursing homes (*Process | RIVM*, 2015).
According to the National Institute for Public Health and the Environment influenza and invasive pneumococcal disease had the highest annual burden from a population perspective in 2013 (Bijkerk *et al.*, 2014).

1.2 Benefit and objectives of vaccinating against pneumococcal infection

The main goal of the pneumococcal vaccine is to reduce the incidence of non-invasive and invasive pneumococcal infection (IPD), which causes a worldwide burden.
For adults, especially for elderly people, the high mortality rate is induced by pneumococcal pneumonia, often transmitted by children carrying *S. pneumoniae* in the nasopharynx (Herold G., 2017).
After introducing pneumococcal vaccination (first PCV7, then PCV13) of children, carriage of *S. pneumoniae* has decreased in all age groups, vaccinated and unvaccinated individuals, showing a reduction in transmission and herd immunity (Jan Van Hoek *et al.*, 2014).

Persons at risk is defined as persons with an increased risk for pneumococcal infection or a severe course of disease (Robert Koch-Institut, 2018).
Pneumococcal pneumonia can be source for IPD, a severe pneumococcal infection with bacteraemia, most frequently affecting infants of 2 years and younger as well as people at the age of 65 years (Drijkoningen and Rohde, 2014). The case fatality rate for IPD is of 30-40% in elderly living in industrialized countries. Aside from an age above 50, other risk factors for pneumococcal infection are chronic heart and lung disease, chronic kidney failure diabetes, cochlear implants, liquor fistula, asplenia and other immune suppressing conditions. Also abusing alcohol and smoking increase the risk of falling ill of pneumococcal disease. (World Health Organization, 2012a; Arrouas and Tiefengraber, 2018)

Currently, two types of pneumococcal vaccines are available: the unconjugated polysaccharide and the conjugated vaccines. In the conjugated vaccines (e.g. PCV10 or PCV13) polysaccharides from the bacterial capsule are joined with a carrier protein in order to stimulate the immune system more effectively (World Health Organization, 2012a; University of Oxford, 2018). People above 50 years should receive PCV13 for their first vaccination followed by the 23-valent polysaccharide vaccine after a year to ensure a better booster impact and an expansion to additional 11 pneumococcal serotypes. Currently, revaccination is necessary if the first vaccination was administered before the age of 65, and if immunosuppressive diseases, chronic renal failure or nephritic syndrome are present. Protection lasts for a minimum of four years and effectiveness varies according to epidemiological data on serotypes (Greenberg *et al.*, 2014; Arrouas and Tiefengraber, 2018).

Another effect of vaccinating against pneumococcal infection results from the smaller need of antibiotics, which allows a reduction of circulating drug-resistant strains (Kyaw *et al.*, 2006; World Health Organization, 2012a).

Patients suffering from chronic respiratory diseases such as COPD and asthma especially benefit from the pneumococcal vaccination, since their lung defence is impaired and pulmonary infections frequently lead to exacerbations and hospitalizations (Froes, Roche and Blasi, 2017). In addition, Divo et al. (2012) showed that patients with COPD often suffer from other underlying diseases, like coronary artery disease, and additional risk factors for pneumonia. In fact, having COPD increases the risk of falling ill of IPD by a factor of five, asthma by a factor of two (Inghammar *et al.*, 2014). According to a review by Walters et al. (2017) it was investigated whether pneumococcal vaccination prevented pneumonia in patients with COPD, and found it to be an effective protection against CAP. Thus, pneumococcal vaccination is recommended to patients with COPD.

1.3 Benefit and objectives of vaccinating against pertussis

In order to prevent severe courses of pertussis and reduce mortality, it is necessary to start the vaccination program early, ideally within the third month of life. The incidence of pertussis is highest amongst non-immune infants, but if vaccine boosts and vaccination programs are not followed correctly, pertussis can occur in adulthood as well. The incidence of pertussis in adults has increased in recent years, though the actual incidence is very difficult to determine. US studies on the estimation of the number of pertussis cases in adults show a far higher incidence rate than documented. This leads to potential transmission to young infants particularly vulnerable to pertussis. Basic immunization or natural infection do not protect over the course of the whole lifespan, because the antibodies decay within a few years (Masseria and Krishnarajah, 2011; World Health Organization, 2015; Chen *et al.*, 2016; Arrouas and Tiefengraber, 2018).

There are two types of pertussis vaccines: the whole cell vaccine and the acellular vaccine. In Austria, as well as in most of industrialized countries the acellular vaccine has replaced the whole-cell vaccine because of lower reactogenicity.

After basic immunization consisting of three doses, a vaccination booster between 1-6 years is recommended by the World Health Organization (World Health Organization, 2015). Afterwards, pertussis vaccination should be renewed every 10 years until the age of 60 and then every 5 years (Arrouas and Tiefengraber, 2018).

1.4 Introduction of diseases discussed in this manuscript

The following table shows the frequently used terms in context with influenza.

Since the terms ARI, ILI and "common cold" are not well described and conflicting in literature, we have tried to summarize them.

Term	Definition	Clinical symptoms - considerations in the context with influenza	Treatment
ARI = Acute respiratory infection	Umbrella term for all respiratory tract infections with a sudden onset, divisible into upper and lower tract infections	Range from mild symptoms to severe life-threatening conditions	Symptomatic or/and antibiotics depending on cause
ILI = Influenza like illness	Clinical diagnosis of an acute febrile respiratory infection caused by a variety of viruses (e.g. rhinovirus, adenovirus, influenza, parainfluenza or others).	"Measured fever of ≥ 38 C° and cough with onset within the last 10 days" (World Health Organization, 2013)	Symptomatic (analgesics, decongestants)
Common cold	Clinical diagnosis of an acute upper respiratory tract infection with rhinopharyngitis	Sneezing, nasal discharge, cough, sore throat, headache, no or only low-grade fever (fever of < 38.5 C°)	Symptomatic (analgesics, decongestants)
Influenza	Laboratory confirmed infection caused by *influenza A* or *B*	Estimated: 1/3 asymptomatic 1/3 mild course of disease as in common cold 1/3 severe course with fever and occurrence of complications	Symptomatic (e.g. analgesics) but neuraminidase inhibitors in selected cases
Pneumococcal infection	Infection by *Streptococcus pneumoniae*, primarily dangerous for elderly by causing severe pneumonia	Cough, expectorations, shortness of breath, fever; in elderly often associated with high mortality rates; a current pneumococcal pneumonia can be predisposing to an influenza pneumonia, due to bacterial proteases, which enable the virus to invade the host cell; bacterial pneumonia can be a complication of an infection with influenza.	General measures, antibiotics according to risk factors (S3-guideline) and national antibiotic resistance data (in Austria 1st choice penicillin or aminopenicillin)

Term	Definition	Clinical symptoms - considerations in the context with influenza	Treatment
Pertussis	Respiratory infection caused by *Bordetella pertussis*	Catarrhal symptoms and whooping cough sometimes followed by vomiting; frequently, persistent cough as only symptom in adolescents and adults	Symptomatic, macrolide antibiotics (during incubation time and the catarrhal stage have a positive effect on the course of the disease, in later time reduce contagiousness)
COPD	Chronic bronchial inflammation characterized by a chronic airflow obstruction, which is not fully reversible	Shortness of breath, sputum, chronic cough, exercise-induced dyspnoea; influenza and pneumococcal infection contribute to exacerbations	Non-pharmacological treatment, pharmacological treatment depending on the GOLD recommendations
Bronchial asthma	Chronic bronchial inflammation with hyper-responsiveness and variable airflow obstruction	Sudden attack of breathlessness in the form of expiratory stridor; respiratory infections can trigger nonallergic asthma	Causal therapy, patient training, pharmacological step-by-step therapy (controller and reliever) depending on the GINA recommendations

Table 1: Overview of diseases discussed in this manuscript

(Arroll, 2011; Bekkat-Berkani *et al.*, 2017; Esposito and Principi, 2016; Herold, 2017; Kothe et al., 2008; Robert Koch Institut-Ratgeber, 2018; World Health Organization, 2007, 2012a, 2013, 2015;)

2 Materials and methods

2.1 Study objectives and design

Main objectives of this study were to evaluate the percentages of vaccinated people at risk and reasons for not being vaccinated. Since in the previous season data was gained with the same study design, an enlargement of sample size and comparison of data were the main goals of this survey.

The aim was not to define a primary endpoint but to perform exploratory research by gathering objectifiable data with a structured questionnaire and therefore providing further insight into this topic. This information was used to describe different relevant aspects, to better understand the current situation at the LKH Graz and to find possible improvements for Austrian's vaccination program consequently.

2.2 Data collection

Between 1st of April and 31st of May 2018 we interviewed 222 patients about their vaccination status against influenza, pertussis and pneumococcal infection at the LKH Graz. In accordance with last year's data where approximately 200 patients were enrolled, we aimed at enrolling a similar number this year. As this is an exploratory survey, a power analysis is not necessary.

The unselected patients at the cardiologic and pneumological department were asked to participate at the study. Dementia or very poor general state of health were reasons for exclusion from the study.

A consent form was discussed and signed before starting the interview. Then, patients were questioned with a questionnaire in paper format (see below). Patients suffering from COPD, asthma or ACO were asked additional questions. If the exact underlying lung disease (COPD, asthma or ACO) was not known, the same additional questions were asked.

After documenting the answers of the interview, data was directly tabulated and analysed. While reviewing this data, different relationships in subgroups were recognized and further analysed. This exploratory analysis consisted in a comparison of binary data of vaccinated and unvaccinated groups, as in a table of 2x2 cells. Thus, the Chi^2-Test was appropriate to use for statistical testing. This test determines, whether expected and observed frequencies differ significantly. Chi^2-test was coupled with Cramer's V test to determine the strength of association. The significance level was set to 5%.

Results were rounded to whole numbers for better overview.

3 Results

The following table shows the absolute number of obtained demographic data.

Department	Cardiology	Pneumology	Total
Number of patients	139	83	222
Median Age	73	68	70.5
Women	46	45	91
Men	93	38	131
Smoker	9	10	19
Non-smoker (i.e. never-smoker)	68	19	87
Ex-smoker	62	54	116
COPD	7	21	28
Asthma	9	3	12

Table 2: Overview of demographic data and relevant results

3.1 Influenza vaccination

The survey showed that 48 patients (22%) were vaccinated and 174 (78%) were not vaccinated against influenza.

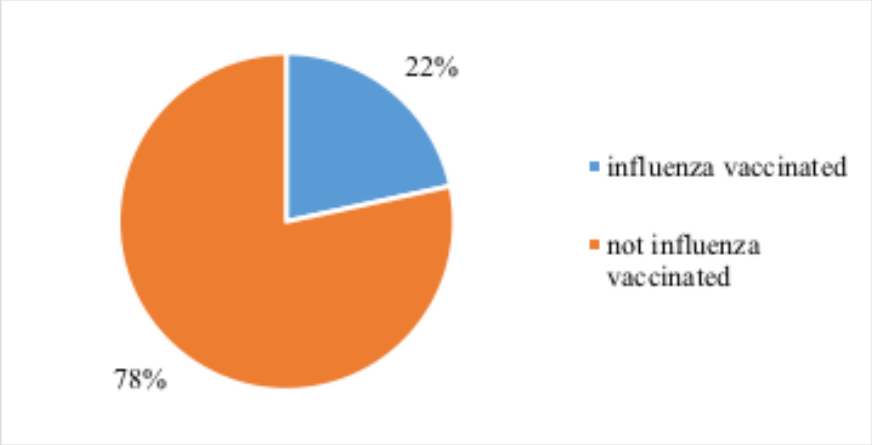

Figure 1: Influenza vaccination coverage

Nearly half (80 patients; 46%) of those not vaccinated against influenza gave as the main reason the answer “I am not convinced of the benefits”. 26 patients (15%) chose the answer: “I have experienced adverse effects.” and 23 (13%) stated that “It was not recommended for me”. 10% said to be scared of adverse effects, 8% forgot about it, while 4 % were advised against it and 3% did not have the time.

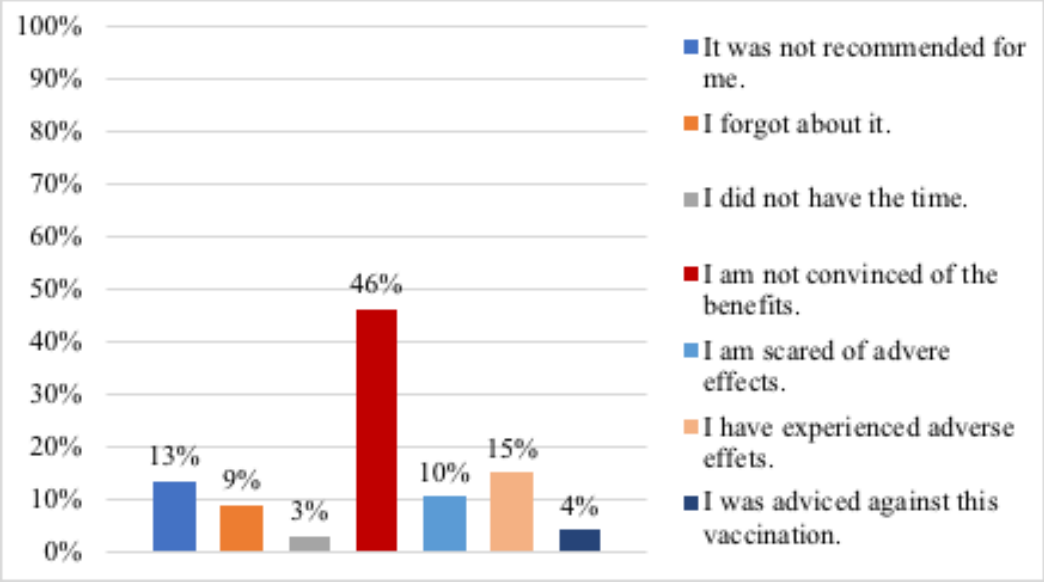

Figure 2: Reasons for not being vaccinated against influenza. Percentages in relation to all unvaccinated patients

3.1.1 Influenza vaccination coverage in different age groups

Under the age of 40 years no one was vaccinated against influenza. Between the age of 40-60 years 4 patients (9% in this age group) were vaccinated and between 60-80 years 33 patients (26% in this age group). Above the age of 80 years 11 patients (28% in this age group) were vaccinated.

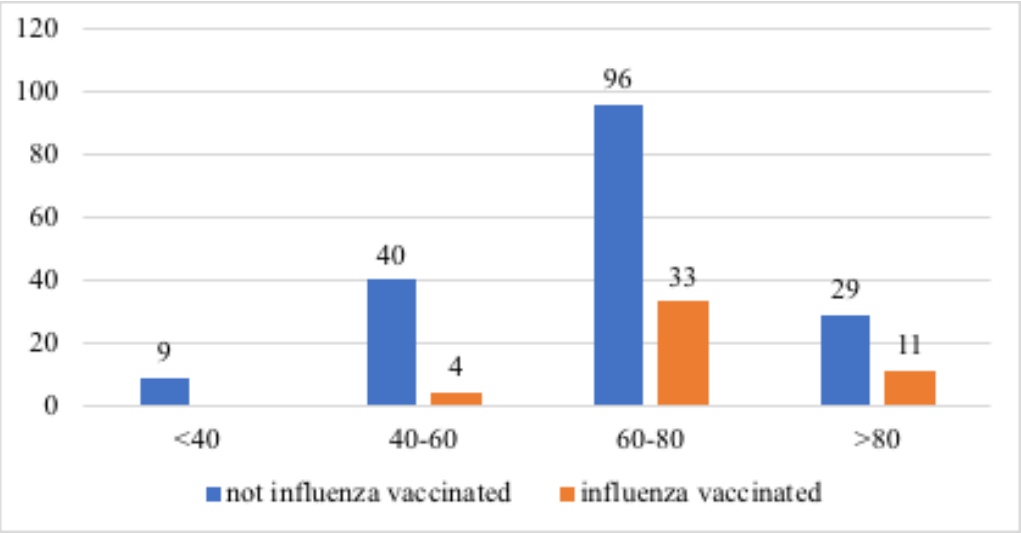

Figure 3: Vaccination coverage within age groups in years

In the age group of 60-80-year-olds 33 were vaccinated patients, which were 69% of all vaccinated patients. Also, this age group held 96 (55%) of all unvaccinated patients. 23% of all vaccinated patients were older than 80 years and the remaining 8% were aged between 40 and 60 years.

3.1.2 Influenza vaccination coverage in relation to consultation of a doctor needed between 01.12.17-31.03.18

The following table shows the distribution of cardiological and pneumological patients in type of consultation and incidence of acute respiratory infection or viral rhinopharyngitis.

	Cardiology	Pneumatology	Total
Type of consultation in previous winter season			
no consultation	29	15	44
hospitalization	36	18	54
ambulatory consultation	46	30	76
hospital stay as well as ambulatory consultation	28	20	48
Development of acute respiratory infection and viral rhinopharyngitis			
neither acute respiratory infection nor viral rhinopharyngitis	74	43	117
acute respiratory infection	31	16	47
viral rhinopharyngitis	19	13	32
both acute respiratory infection and viral rhinopharyngitis	15	11	26

Table 3: Absolute number of patients categorised in type of consultation and development of ARI und viral rhinopharyngitis

Out of all 44 patients, which were not in consultation at all, 3 patients (7% in this group of consultation type) were vaccinated against influenza, 41 (93% in this group of consultation type) were not. 14 patients (26% in this group of consultation type) of all 54 hospitalized patients got vaccinated, 40 (74% in this group of consultation type) did not. 76 patients were in consultation at a doctor's private practice or went to a clinic. 16 (21% in this group of consultation type) of them got a vaccination against influenza, 60 (79% in this group of consultation type) did not. The group of patients that was both hospitalized and in consultation or went to a clinic included 48 patients. 15 (31% in this group of consultation type) of them were vaccinated against influenza, 33 (69% in this group of consultation type) were not.

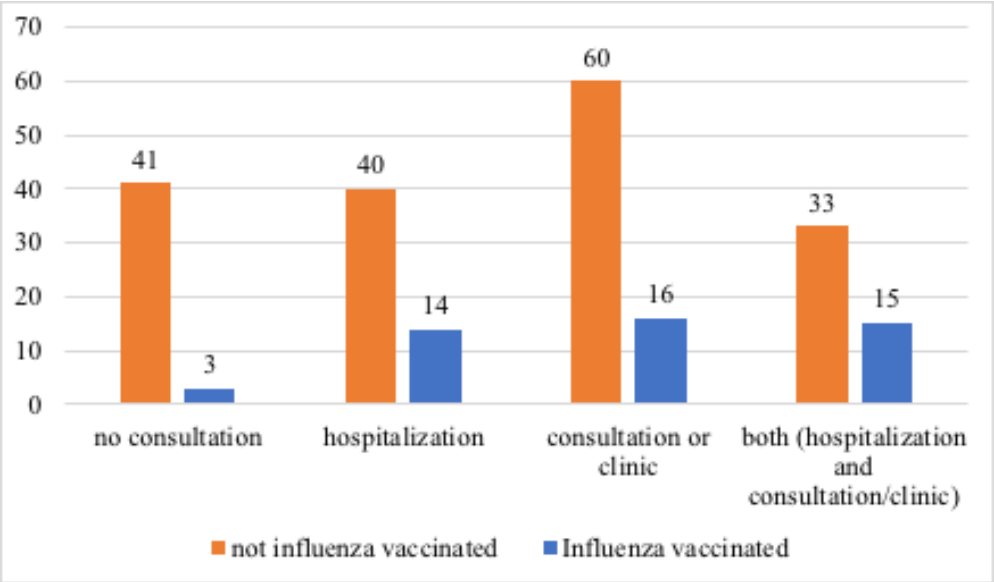

Figure 4: Influenza vaccination coverage relating to consultation form

3.1.3 Influenza vaccination and incidence of acute respiratory illness and viral rhinopharyngitis during 01.12.17-31.03.18

Out of all 48 influenza vaccinated patients 29 (60%) had neither an ARI, nor a viral rhinopharyngitis, 8 (17%) diseased of an ARI and 6 (13%) had a viral rhinopharyngitis. Both conditions occurred in 5 cases (10%). Out of all 174 unvaccinated patients though, 88 (51%) had neither an ARI nor a viral rhinopharyngitis. 39 patients (22%) had an ARI and 26 (15%) suffered from a viral rhinopharyngitis. In 21 cases (12%) both conditions occurred.

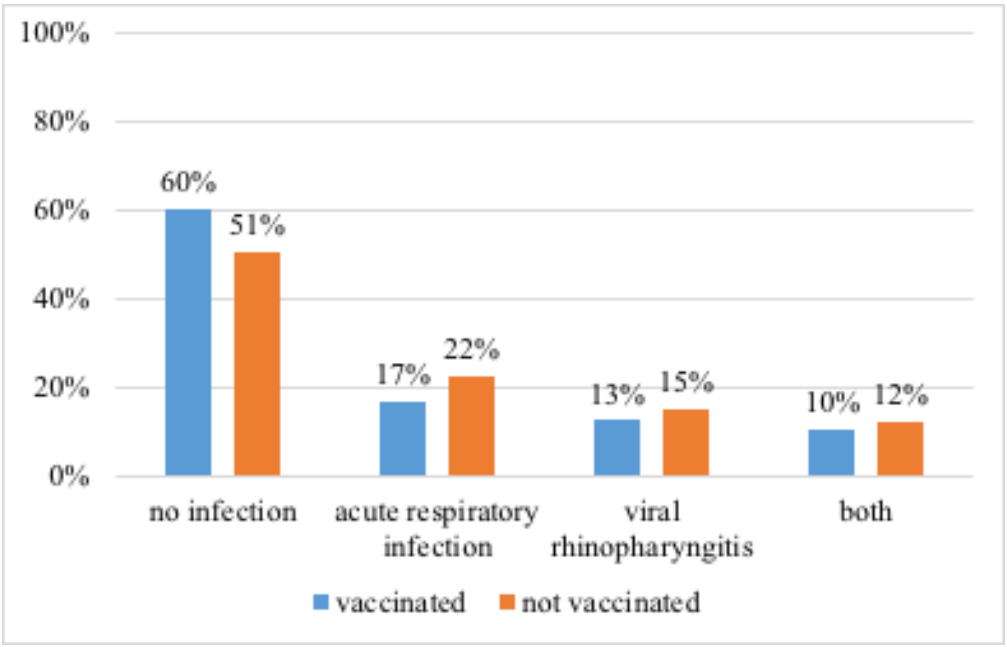

Figure 5: Percentages of infections appearing in vaccinated and unvaccinated patients

The appearances of acute respiratory infection, viral rhinopharyngitis and both infections were grouped together as "event" and contrasted to the appearance of none of these infections. The following table shows the absolute number of patients with and without such event, those vaccinated and not vaccinated against influenza, respectively. Chi^2-test did not show any significant association between influenza vaccination and development of an event like ARI or viral rhinopharyngitis (p=0.227).

	not influenza vaccinated	influenza vaccinated	total
no event	88 (51%)	29 (60%)	117 (53%)
event	86 (49%)	19 (40%)	105 (47%)
total	174 (100%)	48 (100%)	222 (100%)

Table 4: Appearing of an event depending on administration of influenza vaccination

3.2 Vaccination against pneumococcal infection

Within the 222 patients asked, 51 (23%) claimed to be vaccinated against pneumococcal infection and 169 (76%) were not. On average the last vaccination was 2 years and 10 months ago.

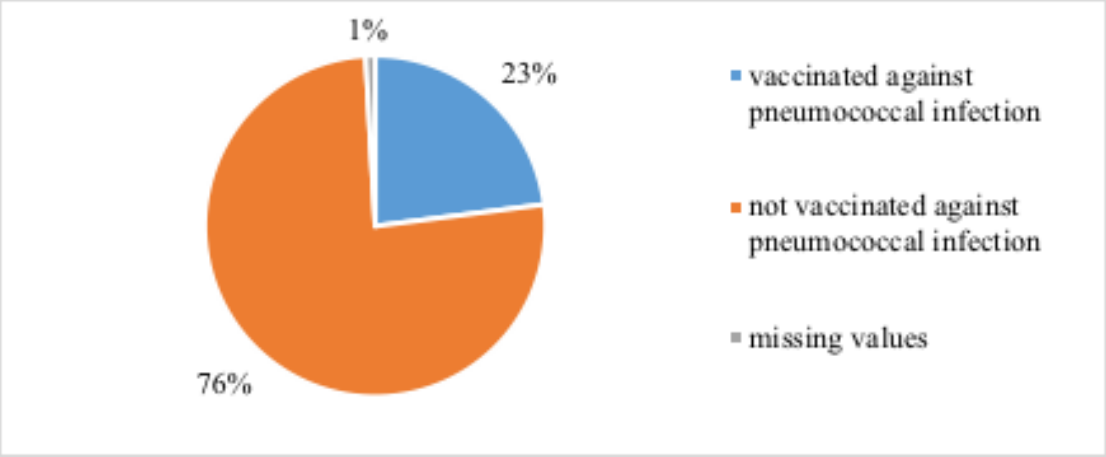

Figure 6: Coverage of vaccination against pneumococcal infection; indicated percentages relating to all questioned patients

Most patients (90 patients; 53%) chose the answer: “It was not recommended for me” as a reason for not being vaccinated against pneumococcal infection. 53 patients (31%) said they were not convinced of the benefits and 14 (8%) were scared of adverse effects.

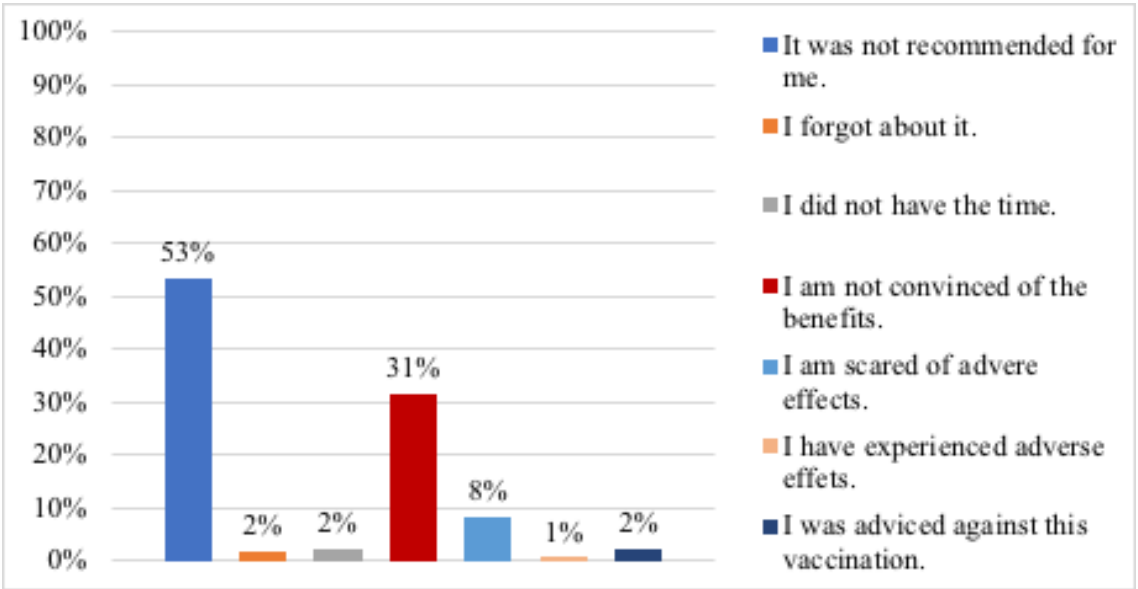

Figure 7: Reasons for not being vaccinated against pneumococcal infection; indicated percentages relating to all unvaccinated patients

3.2.1 Coverages of pneumococcal and influenza vaccination compared

Within all influenza vaccinated patients 35% were not vaccinated against pneumococcal infection but 65% were. Most patients (88%), who were not vaccinated against influenza were not vaccinated against pneumococcal infection either. Chi^2-Test by Pearson showed a significant association between the vaccination coverages against influenza and pneumococcal infection ($p \leq 0.01$). Cramer's V test showed a strength of correlation of 0.518 ($p \leq 0.01$).

	not influenza vaccinated	influenza vaccinated	total
not vaccinated against pneumococcal infection	152 (88%)	17 (35%)	169 (77%)
vaccinated against pneumococcal infection	20 (12%)	31 (65%)	51 (23%)
total	172 (100%)	48 (100%)	220 (100%)

Table 5: Comparison of influenza vaccination and pneumococcal vaccination

3.3 Pertussis vaccination

Out of all questioned patients 82 (37%) were vaccinated against pertussis and 122 (55%) were not.

Of the vaccinated patients 74 (33%) said they had been vaccinated the last time during childhood. The 8 remaining patients (4%) had renewed their pertussis vaccination less than 10 years ago. Of those patients, who were not vaccinated (122; 55%), 17 fell ill with pertussis once in their life.

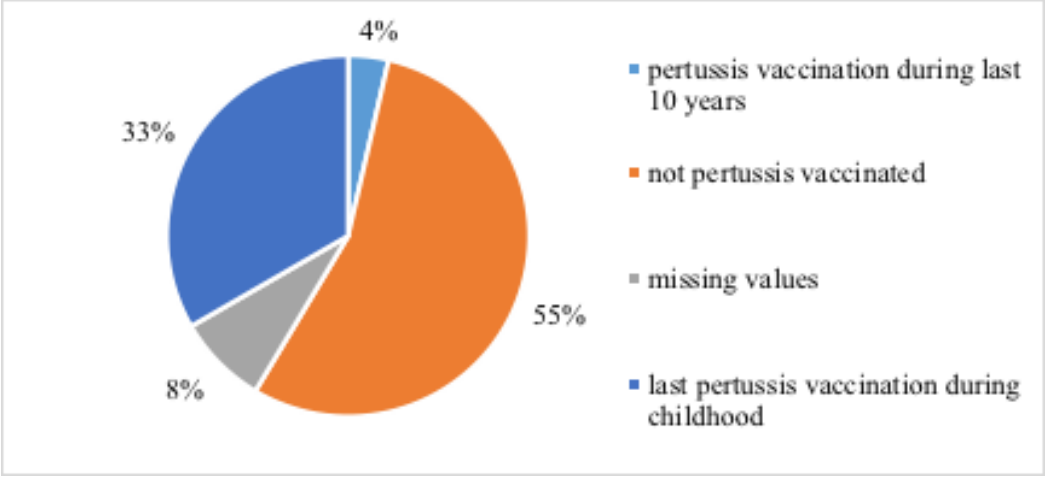

Figure 8: Pertussis vaccination coverage

The main reason for patients (78 patients; 64%) not being vaccinated against pertussis was: “It was not recommended for me”. 18 patients (15%) were not convinced of the benefits and 17 (14%) fell ill with pertussis once. “I am scared of adverse effects.” was true according to 5 (4%) patients.

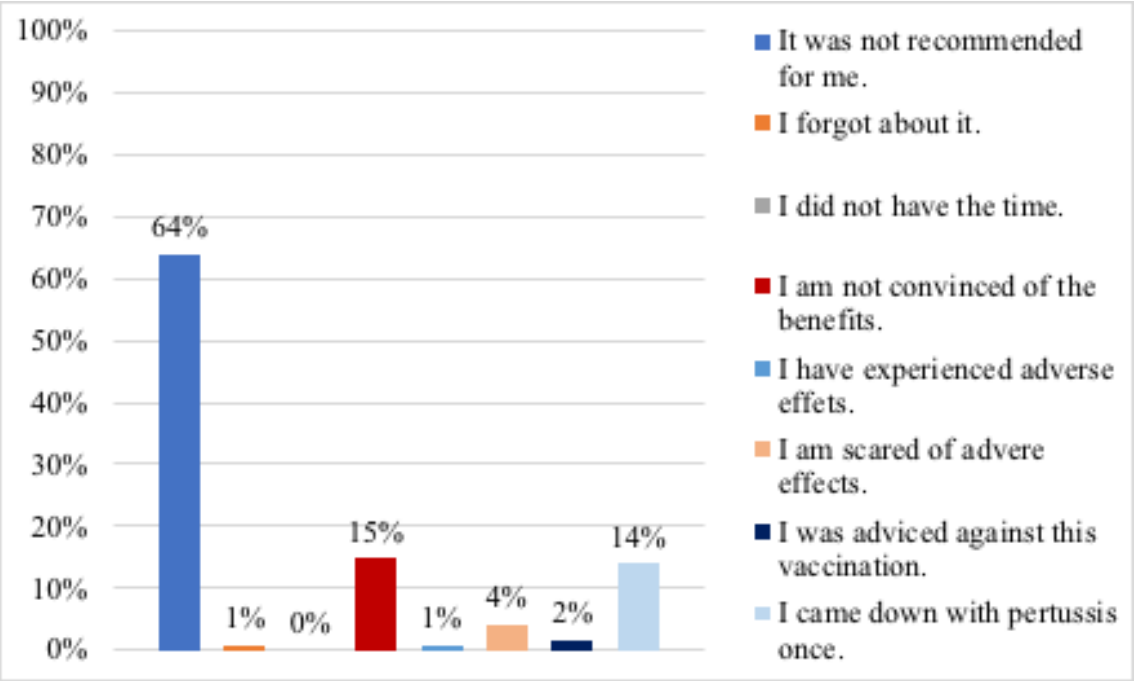

Figure 9: Reasons for not being vaccinated against pertussis

3.4 Comparison to data from the previous winter season (2016/17 vs. 2017/18)

The following figure shows the results in comparison with the previous season 2016/17. As can be seen, no relevant change in the vaccination coverage of influenza and pneumococcal infection is visible compared to the previous season.

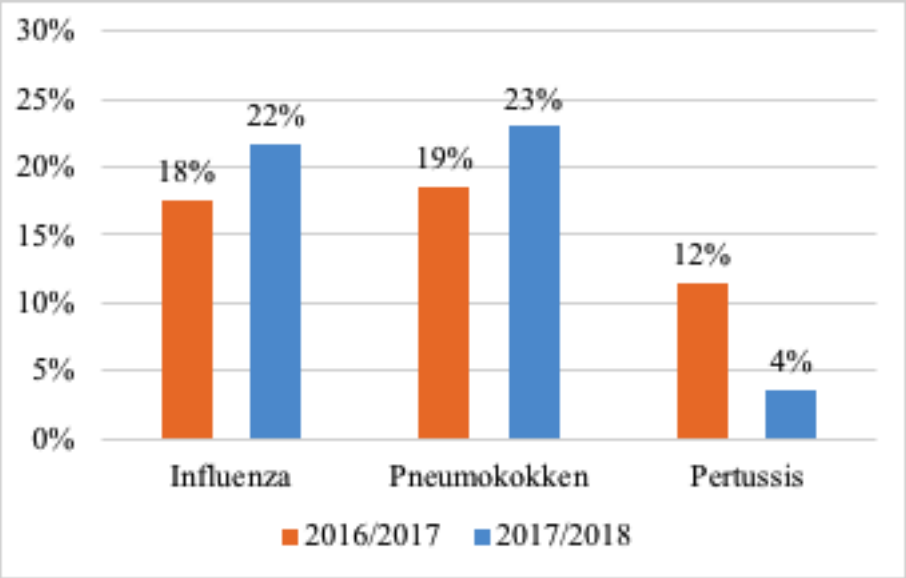

Figure 10: Percentages regarding the number of questioned patients in that year

3.5 Cases of COPD and asthma

Among all 222 questioned patients 28 (13%) suffered from COPD, 12 (5%) from asthma and 2 from ACO. In 5 cases the exact underlying lung disease was not identified.

Of the patients with COPD 32% were vaccinated against influenza and within asthma-patients 33%. Patients without COPD or asthma showed a vaccination coverage of 19%.

Out of 28 patients suffering from COPD 15 (53% of COPD-patients) were vaccinated against pneumococcal infection, whereas in the group of patients without COPD or asthma around 17% were vaccinated against pneumococcal vaccination. Out of all 12 patients with asthma 3 were vaccinated, meaning 25%. Immunization against pertussis was present in 12% of patients with COPD and 25% in patients with asthma.

vaccination against	no COPD, asthma	COPD	asthma	ACO	total
influenza	33	9	4	1	48
pneumococcal infection	31	15	3	1	51
pertussis	5	2	1	0	8

Table 6: Vaccination coverage among patients with COPD or asthma

4 Discussion

4.1 Summary of main results

These results showed a vaccination coverage for influenza of 22% among persons at risk, which is by far not reaching near the 75% goal determined by the World Health Organization in 2017 (Jorgensen *et al.*, 2017). This data confirms and enlarges the data collected with the same methods in the previous season, with a result of 18% of influenza vaccination coverage in a similar population of patients, collected also at the University Clinic of Graz.
To further substantiate this low coverage, data from Statistics Austria from 2014 (Klimont and Baldaszti, 2014) can be adducted, where a prevalence of 17,8% was shown in people at the age of 60 or more.

Most patients in this survey chose the answer "I am not convinced of the benefits." over the answer "It was not recommended to me.", which can lead to the conclusion that physicians are not explaining the necessity of vaccination well enough. Nevertheless, other reasons have to be considered in order to understand this poor coverage and improve it.

To further understand this data, different age groups in this survey were compared to the coverage rates in relation to types of consultations.
People under the age of 40 years were not vaccinated at all, between 40 and 60 years only 9% were vaccinated, between 60 and 80 years around 26%, and above the age of 80 years nearly 28%. So, the age group of over 80-year-olds had the greatest percentage of vaccinated people. When considering the distribution of all influenza vaccinated, the age group of 60 to 80-year-olds contains with nearly 70% the most vaccinated people. These results are consistent with the indications for the vaccination concerning the age but do not allow any interpretation about coverage of patients with other risk factors.
A tendency of higher coverages can be noticed among people in contact with physicians.

Section 3.1.3 investigated the relation between influenza vaccination and the development of one of these events: ARI or viral rhinopharyngitis and did not show any significant correlation. The Chi^2 -test shows, that the null hypotheses ("There is no relationship between influenza vaccination and the development of such an event") cannot be rejected. We can

therefore not claim that influenza vaccination protects against the occurrence of such an event. Further analyses with greater power are necessary to investigate this phenomenon. Moreover, the fact that patients could have been easily influenced through the line of questioning has to be acknowledged and makes conclusions less reliable.

Concerning the prevalence of vaccination against pneumococcal infection we found a coverage of 23%. Compared to a coverage of 19% in previous season it has not changed much. Last vaccination was on average 2 years and 10 months ago. There is no certainty that the reported vaccination is still providing protection. It depends if a booster vaccination was applied or not. Thus, the presumed coverage of pneumococcal infection is probably lower.

About half of all patients, who did not get pneumococcal vaccination, claimed that this vaccination was not recommended for them and thus show an insufficient knowledge within the interviewed patients concerning this matter.
The Chi ^{2}-test showed, that the null hypothesis ("There is no relationship between the vaccination coverage rates of influenza and pneumococcal infection") can be rejected and the alternative hypotheses ("There is a relationship between the vaccination coverage rates of influenza and pneumococcal infection") can be accepted. This means if patients were vaccinated against influenza there was a high chance of them being vaccinated against pneumococcal infection too. Likewise, in case of no influenza vaccination, patients were in most cases not vaccinated against pneumococcal infection either. It is rather unlikely that this result was accidental. Cramer's V result of 0.518 can be interpreted differently according to the source. Possible reasons for this association could be present awareness of vaccinations and their benefits in patients or physicians recommending different vaccinations to their patients at risk. The facts that most patients interviewed did not get vaccinated against influenza or pneumococcal infection at all and these two vaccinations are only partially dependent on one another, encourage to interpret the strength of association only with precaution.

The question about receiving pertussis vaccination presented itself to be the most difficult to answer for patients, as many did not remember this particular vaccination. Just eight people (4%) were certain about having had a pertussis vaccination in the past ten years. This result is rather different to the previous season but cannot be interpreted as such due to the difficult collection of data.

Most patients vaccinated against pertussis did not remember having renewed their immunization since childhood, consequently a protection cannot be assumed, as vaccination does not insure lifelong immunity (World Health Organization, 2010).
Nearly two thirds of the non-vaccinated claimed, that the pertussis vaccination was not recommended for them. Moreover, 17 patients said to have fallen ill of pertussis in the past and therefore would not need any vaccination. Having undergone pertussis once is not a guarantee for natural protection. A reinfection is possible (World Health Organization, 2010).

Although there was just a small population of patients with COPD and asthma (13% COPD and 5% asthma) we can see a slight tendency for a better vaccination coverage against influenza in this risk group. The same applies for immunization rates for pertussis.
Looking at the vaccination coverage of pneumococcal infection in patients with COPD more than half (54%) were vaccinated compared to 18% in patients without COPD or asthma. Despite a low prevalence of COPD, we can see a better immunization in this risk group.

Overall, these results suggest for all three vaccination coverage rates the need for a better monitoring of vaccination certificates and for better informing the elderly and persons at risk. Future studies are needed to explore the main barriers of tailoring Austria's vaccination program. Moreover, vaccination coverage rates against influenza, pneumococcal infection and pertussis have to be further observed in Austria's population.

4.2 Considerations on tailoring Austria's vaccination program

One of the improvements to draw attention to is the out-of-pocket payment for the influenza vaccination, which is still involved in Austria's vaccination program. In terms of program design, this is one differentiating factor between Austria and countries like the United Kingdom or the Netherlands. The OECD ranking showed coverage rates above 60% in people older than 65 years in these two countries (OECD, 2017).
Not only patients benefit from influenza vaccination, but as many cost-effectiveness evaluations have shown, it is economically viable to vaccinate persons at risk and people above the age of 65 years as well.

Austria's vaccination program for influenza can also be improved by starting vaccination campaigns in nursing homes, establishing and promoting vaccination in pharmacies and enforcing vaccination among all health-care workers. Moreover, during winter season electively hospitalized patients could be given an influenza vaccination in the weeks before hospitalization (in case of planned interventions) or when leaving the hospital if they have not been vaccinated yet.
Another strategy to encourage vaccination in family practices could be to send personal invitations to persons at risk and having a lead staff member to organize influenza vaccination campaigns (Dexter *et al.*, 2012; De Lusignan *et al.*, 2016).

The World Health Organization published a guide called "Tailoring Immunization Programmes" (TIP) to help countries with sub-optimal vaccination coverages to make changes in their vaccination programs (World Health Organization and Regional Office for Europe, 2013). Another one has been adapted especially to improve influenza vaccination uptake in health care workers (World Health Organization and Regional Office for Europe, 2015).

4.3 Limitations and strengths

The interviewed patients at the University Clinic of Graz were a representative group to whom the influenza vaccination and a high influenza vaccination coverage of the population are particularly beneficial. The median age was 70.5 years and underlying cardiopulmonary diseases can be assumed. Moreover, the University Clinic of Graz is the central hospital of Styria with a catchment area for 1.6 million people (Steiermärkische Krankenanstaltengesellschaft m.b.h., 2010). However, the interviewed subjects were an unselected group of patients, so young people without underlying disease could be among them, to whom vaccination is not highly recommended.

Although interviews can be rather difficult to objectify, the questions required mostly answers of "yes" or "no", which enabled a solid acquisition of data. This way, it was also possible to compare this data with the one gained during the previous season by another person. According to the fact, that the results from previous season were known, a bias towards the patients' answers has to be acknowledged. We had to rely on the patients' knowledge about their vaccination status, which may not be current. This concerns in particular the pertussis vaccination.

Regarding exploratory analysis, associations and p-values were noticed but need to be interpreted with precaution. Replication of findings is encouraged.

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Annex – Questionnaire

Landeskrankenhaus - Universitätsklinikum Graz

Im Einklang zur Spitze
Medizinische Universität Graz

Fragebogen zur Impfprävalenz

Angaben zur Person:

*Alter (in Jahren)*_____

*Station*_____

Ich bin **MÄNNLICH** ☐ **WEIBLICH** ☐

Ich bin **RAUCHER** ☐ **NICHTRAUCHER** ☐ **EX-RAUCHER** ☐

Ich leide an chronischer obstruktiver Lungenkrankheit (COPD) oder Asthma. **JA** ☐ **NEIN** ☐

Wurden Sie im Zeitraum von September 2017 bis März 2018 gegen Influenza (Grippe) geimpft? **JA** ☐ **NEIN** ☐

Wenn Sie nicht geimpft sind: Weshalb erfolgte die Impfung nicht?

□wurde mir nicht empfohlen
□habe ich vergessen
□habe keine Zeit gehabt
□bin nicht überzeugt vom Nutzen der Impfung
□habe Angst vor Nebenwirkungen
□habe bei Impfungen in der Vergangenheit Nebenwirkungen gehabt

□mir wurde davon abgeraten

wenn ja: von wem wurde Ihnen abgeraten?

FAMILIE ☐ **BEKANNTE/FREUNDE** ☐ **ÄRZTE** ☐ **KRANKENSCHWESTER/-PFLEGER BZW. MEDIZINISCHES FACHPERSONAL** ☐

Sind Sie gegen Pneumokokken (Lungenentzündung) geimpft? **JA** ☐ **NEIN** ☐

Wenn ja, wann erfolgte diese Impfung zuletzt? _____

Was für ein Impfstoff (Pneumovax, Prevenar 13) wurde verwendet? _____

Wenn Sie nicht geimpft sind: Weshalb erfolgte die Impfung nicht?

□wurde mir nicht empfohlen
□habe ich vergessen
□habe keine Zeit gehabt
□bin nicht überzeugt vom Nutzen der Impfung
□habe Angst vor Nebenwirkungen
□habe bei Impfungen in der Vergangenheit Nebenwirkungen gehabt

□mir wurde davon abgeraten

wenn ja: von wem wurde Ihnen abgeraten?

FAMILIE	BEKANNTE/FREUNDE	ÄRZTE	KRANKENSCHWESTER/-PFLEGER BZW. MEDIZINISCHES FACHPERSONAL
☐	☐	☐	☐

	JA	NEIN
Sind Sie gegen Pertussis (Keuchhusten) geimpft?	☐	☐

Wenn ja, wann erfolgte diese Impfung zuletzt? _____

Wenn Sie nicht geimpft sind: Weshalb erfolgte die Impfung nicht?

□wurde mir nicht empfohlen
□habe ich vergessen
□habe keine Zeit gehabt
□bin nicht überzeugt vom Nutzen der Impfung
□habe Angst vor Nebenwirkungen
□habe bei Impfungen in der Vergangenheit Nebenwirkungen gehabt

□mir wurde davon abgeraten

wenn ja: von wem wurde Ihnen abgeraten?

FAMILIE	BEKANNTE/FREUNDE	ÄRZTE	KRANKENSCHWESTER/-PFLEGER BZW. MEDIZINISCHES FACHPERSONAL
☐	☐	☐	☐

In der Zeit von 01. Dezember 2017 bis 31. März 2018 hatte ich

□einen Atemwegsinfekt (Husten)
□einen grippalen Infekt

In der Zeit von 01. Dezember 2017 bis 31. März 2018

□war ich stationär im Krankenhaus

□hatte ich eine ambulante Behandlung / musste einen Arzt aufsuchen

Zusatzfragen für Patienten, die an COPD oder Asthma leiden:

In der Zeit von 01. Dezember 2017 bis 31. März 2018 hatte ich folgende Beschwerden:

☐ zunehmende Atemnot

☐häufigerer und stärkerer Husten

☐vermehrte zähe Schleimbildung in den Bronchien

☐gelb-grünliche Verfärbung des Schleims (Eiterbildung)

☐ein pfeifendes Atemgeräusch

☐zunehmende Schwellung der Beine / Wassereinlagerungen

	JA	NEIN
Aufgrund dieser Beschwerden war ein Krankenhausaufenthalt notwendig.	☐	☐