




RESEARCH PAPER



Vaccination coverage of recommended vaccines and determinants of vaccination in at-risk groups

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ABSTRACT

Upon exposure to vaccine-preventable diseases, certain individuals are at increased risk for complications due to preexisting diseases, age or immunosuppressive treatment. Vaccination against influenza, pneumococcal disease and hepatitis B (for some groups) is advised in addition to standard vaccination against diphtheria, tetanus and pertussis. We estimated the vaccination coverage and determinants of recommended vaccinations in patients with diabetes mellitus type 1 (n = 173) and type 2 (n = 177), chronic kidney disease (CKD) (n = 138), heart failure (n = 200), chronic obstructive pulmonary disease (COPD) (n = 187), HIV (n = 201) or solid organ transplantation (SOT) (n = 201) in a monocentric study. Vaccination data were retrieved from documents provided by patients and general practitioners, and from the Flemish vaccination register. Less than 10% had received all recommended vaccines. Overall, 29% of subjects were vaccinated against diphtheria-tetanus, 10% against pertussis, 44% against influenza, 32% against pneumococcal disease and 24% of HIV patients and 31% of CKD patients against hepatitis B. Age was positively associated with vaccination against influenza (OR:2.0, $p < .01$) and pneumococcal disease (OR:2.6, $p < .001$). Patients with COPD, HIV and SOT were more likely to be vaccinated against influenza (OR:2.8, $p < .001$, OR:1.8, $p < .05$; OR:2.0, $p < .001$, respectively) and pneumococcal disease (OR:2.9, $p < .001$, OR:25.0, $p < .001$; OR:2.6, $p < .001$, respectively) than patients with heart failure. Reason for non-vaccination were concerns about effectiveness, necessity and side effects of influenza vaccines, and not being aware of the recommendation for pneumococcal disease. Initiatives to monitor the vaccination status of vulnerable patients are needed, which is why we advocate systematic vaccination registration and frequent communication about vaccination.

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Introduction

The number of people with immunosuppressive conditions and chronic diseases is growing.^{1,2} Due to the nature of their condition, immunosuppressive treatment or their age, these individuals are at increased risk of developing complications upon exposure to infectious pathogens, including those against which they can be vaccinated. For example, patients with diabetes mellitus (DM) are up to 25 times more likely to develop pneumonia and 6 times more likely to be hospitalized upon influenza infection compared to the general population.³ Additionally, they have a higher risk of acquiring nosocomial infection as they frequently visit hospitals for disease follow-up. In patients with a chronic disease, infection can also lead to a deterioration of their condition. For example, in patients with chronic obstructive pulmonary disease (COPD), certain infectious agents such as influenza, *Bordetella pertussis* and *Streptococcus pneumoniae* cause

respiratory disease, which may lead to COPD exacerbation.⁴ In DM patients, infection with influenza may cause metabolic dysregulation and increase blood glucose to precariously high levels.⁵ Vaccination is the best available measure to prevent infection and to decrease morbidity and mortality. For example, influenza vaccination reduces all-cause hospitalization and hospitalization due to influenza or pneumonia in diabetes patients, and all-cause mortality and cardiovascular mortality in patients with heart failure.^{6,7} Hence, it is highly recommended that at-risk patients follow the standard vaccination schedule, with some additions or minor adaptations specific for their condition. It is recommended for all adults to receive a ten-yearly booster of a tetanus and diphtheria vaccine after a primary schedule of at least 3 doses.⁸ In line with the recommendations of the Advisory Committee on Immunization practices (ACIP) in the United States, the Belgian National Immunization Technical Advisory Groups (NITAG) advises to use for this at least once a tetanus,

diphtheria and acellular pertussis (Tdap) vaccine.^{9,10} For seasonal influenza, the NITAG only recommends annual vaccination for people aged 65 years and older, and for all patients with chronic diseases.^{10,11} This is in line with recommendations in other countries, like the United Kingdom, but narrower than the ACIP recommendation of annual vaccination for all adults.^{9,10} Pneumococcal vaccination is also recommended for this target group by most public health authorities.^{9,10,12} The Belgian NITAG recommends using the 13-valent conjugate pneumococcal vaccine (PCV13), followed by a dose of the 23-valent polysaccharide pneumococcal vaccine (PPSV23) with an interval of at least 8 weeks, and subsequently a PPSV23 booster every five years in immunocompromised patients since 2013.¹⁰ Additionally, some vaccines are recommended for particular risk groups. In accordance with the World Health Organization (WHO) and ACIP, Belgian recommendations also include vaccination against hepatitis B for people with an increased risk of exposure to infected blood, such as patients with HIV, DM, CKD and solid organ transplantation (SOT) candidates.^{9,10,13} Furthermore, the Belgian NITAG recommends vaccination with live attenuated vaccines against measles, and mumps, rubella and varicella, but only for nonimmune HIV patients with a CD4-count of at least 200 cells/ μ l and SOT candidates. Live vaccines are, however, contra-indicated in immunocompromised patients. Finally, meningococcal vaccination is recommended for immunocompromised patients with an increased personal or epidemiological risk, and human papilloma virus vaccination has been recommended for adult immunocompromised patients since 2017.¹⁰

Despite these recommendations, few countries monitor or report vaccination coverage in risk groups.⁸ The European Center for Disease Control and Prevention (ECDC) reported that less than 25% of the member states records influenza vaccination coverage in such target groups, and existing data generally indicate low uptake.^{14–19} During a vaccination coverage survey in the general population of children and adolescents in Flanders, illness was frequently given as reason for non-vaccination.²⁰ In 2013, self-reported vaccination coverage was 50% for influenza in the past year and 8% for pneumococcal disease in the past 5 years.²¹ However, studies on documented uptake of recommended vaccines in pediatric or adult risk groups have not yet been performed. We assessed vaccination coverage and determinants of Tdap, seasonal influenza, PPSV23 and hepatitis B vaccinations in adult patients with DM, CKD, COPD, heart failure, HIV and SOT.

Materials and methods

Study procedure and population

This is a monocentric cross-sectional survey in adult at-risk patients at the university hospitals of Leuven, which is the largest tertiary hospital in Belgium. It counts almost 10 000 employees, has 1764 beds and accounts for more than 700 000 outpatient visits annually.²² Patients were approached in the outpatient clinics during consecutive six month periods (one per patient group) between September 2014 and

December 2018. All subjects lived in the Flemish region of Belgium, were at least 18 years of age and had either diabetes mellitus (DM) type 1, DM type 2, heart failure, COPD, CKD, HIV or a history of solid organ (heart or lung) transplantation. The questionnaire was based on a list of questions used in several vaccination coverage studies in children and adolescents between 2005 and 2012, but adapted to the current adult patient population.²³ The questionnaire was tested for clarity and feasibility before the start of data collection. As an example, an English translation of the questionnaire aimed at patients with SOT is available as supplementary data. The survey was taken as a structured interview based on the questionnaire and contained questions on vaccination status, reasons for non-vaccination, socio-economic and socio-demographic characteristics and disease characteristics. Reasons for non-vaccination were only surveyed in patients who had documented vaccination data (e.g. vaccination booklet) available at the time of the survey and/or who were aware of not being vaccinated for at least one recommended vaccine ($n = 367$). Disease severity was determined with the Global Initiative for Chronic Obstructive Lung Disease (GOLD) for COPD, Kidney Disease Improving Global Outcomes (KDIGO) for CKD, and the New York Heart Classification (NYHA) for heart failure.^{24–26} Vaccination records were required for vaccination rate calculation. They were retrieved from documents provided by patients, from the general practitioner's medical records, and from Vaccinnet, the Flemish vaccination register. Vaccination data for hepatitis B were collected for patients with HIV and CKD only. Hepatitis B vaccination data were not collected from patients with DM because the vaccine is not systematically offered in our hospitals, since the risk of infection due to the exchange of needles from blood glucose measurement devices is considered limited. Signed informed consent was obtained from all participants and the study was approved by the Ethics Committee Research UZ/KU Leuven of Leuven, Belgium (S56765).

Definitions of correct vaccination

Correct vaccination against diphtheria and tetanus was defined as a complete course of primary vaccination with 3 doses of a diphtheria and tetanus containing vaccine, and subsequent booster vaccinations every 10 years. In the present study we estimated the coverage of booster vaccination only (i.e. vaccination in the previous 10 years), assuming the basic schedule is complete. Correct vaccination for seasonal influenza implied having been vaccinated during the last vaccination campaign before the survey. Pneumococcal vaccination was surveyed for the 5 years preceding the survey and required having been vaccinated at least once. Correct hepatitis B vaccination equaled i) 4 doses or ii) 3 doses with an interval of at least four weeks between dose 1 and 2, eight weeks between dose 2 and 3 and 16 weeks between dose 1 and 3. Doses were considered invalid if the vaccines were administered more than 5 days before these recommended intervals. Pertussis vaccination was considered correct if the patient had received at least one dose of a pertussis-containing vaccine. Since adult pertussis vaccination has

only been recommended in Belgium since 2013, no time restriction for correct vaccination was needed in the present analysis.

Statistical analysis

We calculated a sample size of 250 patients per disease group to estimate an expected vaccination coverage of 70% with a confidence interval of approximately $\pm 6\%$.²¹ This sample size also allowed to detect differences between disease groups of approximately 10% with a power of 80%. Vaccination coverage rates of recommended vaccines are shown with binomial 95% confidence intervals. Multivariate logistic regression with backwards selection was used to analyze determinants of vaccination coverage for each vaccine independently. A test probability of 5% was considered statistically significant. All data were analyzed with R, version 3.0.2 (R Foundation for Statistical Computing, Vienna, Austria, 2013).

Results

Patient characteristics

The response rate was about 90% in all patient groups, except for COPD (49%), because other studies were running simultaneously, and patients preferred to participate in one study at a time. Other reasons for refusal were lack of interest and time, or not feeling well. In total 1331 patients were included, with either DM type 1 ($n = 173$), DM type 2 ($n = 177$), CKD ($n = 138$), COPD ($n = 187$) heart failure ($n = 200$), HIV ($n = 201$) or SOT ($n = 255$). Table 1 shows patient characteristics. The majority of participants were male (62.7%) and above the age of 40 (86.7%). All CKD patients had a severe disease status (KDIGO classification ≥ 4). In total, 57.8% of the COPD patients and 41.0% of the heart failure patients had a severe disease state (GOLD stage C or D and NYHC class 3 or 4, respectively). In the SOT group, 128 were lung transplant patients and 127 heart transplant patients. Of the HIV patients, 46.9% were men who have sex with men (MSM) and 98% had a CD4+ count of ≥ 200 cells/mm².

Vaccination coverage in adults with chronic diseases

About 10% of the patients had a vaccination document available at the time of the survey and an additional 3% mailed a copy afterward. The general practitioner's response rate varied from 50 to 75%, depending on the disease group. Documented proof of at least one of the studied vaccines could only be found for 68.7% of the patients. In total, only 9.8% of the patients was correctly vaccinated with the recommended vaccines (excluding pertussis and hepatitis B). In all groups, coverage rates were relatively low for all recommended vaccines (Table 2). About 30% were vaccinated against diphtheria-tetanus, 10% against pertussis, 44% against influenza and 32% against pneumococcal disease. In total, 25% of HIV patients and 30% of CKD patients were vaccinated against hepatitis B. Another 8% of CKD patients and 3% of HIV patients were possibly still on a hepatitis B vaccination trajectory as the last vaccine of their incomplete

schedule was administered less than one year before the survey. Among the different groups, COPD patients had the highest coverage rates for diphtheria/tetanus and influenza; and HIV patients for pneumococcal disease. The self-reported vaccination coverage rate was 45.2% for diphtheria/tetanus, 35.6% for pneumococcus and 81.2% for influenza.

Determinants of vaccination coverage in adults with chronic diseases

Factors associated with immunization are shown in Table 3. For diphtheria-tetanus vaccination, no significant determinant was found. Against pertussis, patients with DM type 2 (OR: 2.3 $p < .01$) were proportionally better vaccinated than patients with heart failure. Moreover, those who were occasionally physically active (≤ 2 times/week) were less likely to be vaccinated than those who were never physically active (OR: 0.5, $p < .05$). The influenza vaccination coverage was higher in patients with DM type 2 (OR: 1.6, $p < .05$), COPD (OR: 2.8, $p < .001$), HIV (OR: 1.8, $p < .001$) and SOT (OR: 2.0, $p < .001$) compared to heart failure patients. In addition, a significant increase in influenza vaccination was observed in the age groups 40–64 years (OR: 1.6, $p < .05$) and ≥ 65 years (OR: 2.0, $p < .01$) compared to the younger age groups. Lastly, patients who were frequently physically active (≥ 3 times/week) were more likely to be vaccinated than those who were never physically active (OR: 1.4, $p < .05$). Anti-pneumococcal vaccination rates were higher in COPD (OR: 2.9, $p < .001$), SOT (OR: 25.0, $p < .001$) and HIV patients (OR: 2.6, $p < .001$), but lower in CKD patients (OR: 0.3, $p < .001$) compared to heart failure patients. Patients in older age groups were better vaccinated (OR: 2.6, $p < .001$), and ex-smokers as well (OR: 1.5 vs. nonsmokers, $p < .05$). Against hepatitis B, patients with HIV were less well vaccinated than those with CKD (OR: 0.5, $p < .05$).

In addition to these demographic factors, univariate analysis showed that patients who received information on specific vaccines were better vaccinated against pneumococcus (OR: 4.8, $p < .001$).

Reasons for non-vaccination and information provided about vaccination

Table 4 lists the reasons for non-vaccination with a particular vaccine. For diphtheria-tetanus, the most frequently given reasons were not being informed about the recommendation (38%) and having forgotten it (29%). For influenza, 41% stated that they planned to receive the vaccine. Other reasons were concerns about the vaccine's safety (13%), necessity (6%) and effectiveness (6%), or opposition against influenza vaccination (9%). For pneumococcal vaccination, 89% was not aware of the recommendation.

For influenza, 71% of the patients stated that they had received information concerning vaccination against the disease. Of those patients, 60% received the information from their general practitioner and 30% from a specialist. For pneumococcal vaccination, 29% of the patients received information about the vaccine. Of those patients, 48% was informed by their general practitioner and 47% by a specialist. Other sources of

Table 1. Patient characteristics.

Personal data	All patients (n = 1331) %	DM type 1 (N = 173) %	DM type 2 (N = 177) %	CKD (N = 138) %	COPD ^b (N = 187) %	Heart failure ^c (N = 200) %	HIV (n = 201) %	SOT (n = 255) %
Median age, years (range)	62 (18–94)	44 (18–83)	67 (31–91)	73 (21–91)	65 (29–94)	71.5 (32–91)	46(18–75)	60 (19–87)
Age								
< 40 years	13.3	38.7	1.7	3.6	0.5	1.0	30.9	14.5
40–64 years	43.8	46.8	40.1	19.6	45.5	27.5	64.2	52.9
≥ 65 years	42.9	14.5	58.2	76.8	54.0	71.5	5.0	32.6
Female gender	33.7	46.8	35.6	34.8	32.6	30.5	26.4	32.2
Origin								
Belgian	85.5	86.7	91.5	96.4	91.4	92.5	58.2	86.3
European	8.1	8.1	6.2	3.6	7.5	4.5	10.0	13.7
Non-European	6.4	5.2	2.3	0.0	1.1	3.0	31.8	0.0
Educational degree ^e (years of study)								
Lower education (<12 years)	36.7	11.6	52.5	50.7	42.8	50.0	22.4	31.4
Secondary education (12 years)	33.6	42.8	25.4	29.7	35.3	28.0	38.3	34.5
Higher education (>12 years)	28.8	45.7	22.0	18.1	21.9	19.5	38.3	32.5
Unknown education	1.0	0.0	0.0	1.4	0.0	2.5	1.0	1.6
Employed (full + part time)	67.8	80.9	75.7	69.6	66.3	65.0	70.6	53.3
Net monthly family income								
<1500 euro	23.1	13.3	22.6	23.2	27.4	30.0	26.4	18.8
1500–3000 euro	46.8	49.7	59.9	42.8	46.2	44.0	36.3	49.0
>3000 euro	19.3	36.4	13.0	10.9	8.1	14.0	32.3	18.8
Unknown income	10.8	0.6	4.5	23.2	18.3	12.0	5.0	13.3
Civil status: married/cohabitation	69.0	71.7	71.2	70.3	70.6	66.5	57.2	74.9
Physical activity								
Never	22.5	25.4	32.8	42.0	13.4	28.5	16.9	9.4
Occasionally (≤2 times/week)	15.6	30.6	24.9	18.8	2.1	8.0	16.4	12.2
Frequently (>3 times/week)	62.0	43.9	42.4	39.1	84.5	63.5	66.7	78.4
Smoking								
No smoking	38.7	55.5	40.7	44.2	4.3	35.5	48.8	42.7
Smoker	15.0	17.3	17.5	12.3	17.1	9.5	28.4	5.1
Ex-smoker	46.4	27.2	41.8	43.5	78.6	55.0	22.9	52.2
Alcohol use								
No	50.7	48.6	59.9	58.0	57.8	45.5	33.8	54.1
Occasionally (1–7 glasses/week)	37.0	35.8	27.7	31.2	22.5	45.0	51.2	40.4
Frequently (>7 glasses/week)	12.3	15.6	12.4	10.9	19.8	9.5	14.9	5.5
Disease data								
Comorbidity	44.9	9.2	47.5	64.5	73.3	47.0	31.3	44.7
Years since diagnosis/transplantation (median (range))	8 (0–64)	17.5 (0–59)	11 (0–64)	4.5 (1–57)	6 (0–39)	6 (0–60)	8 (0–46)	7 (1–29)

^aEducational degree: Lower Education = no secondary school diploma, Secondary education = secondary school diploma achieved, Higher education = university of university college diploma achieved.
^bPatients were classified in categories of disease severity according to Global Initiative for Chronic Obstructive Lung Disease (GOLD) GOLD stages: 19.3% had GOLD stage A, 23.0% GOLD stage B, 10.2% GOLD stage C and 47.6% GOLD stage D. The severity of symptoms is measured with the Modified Medical Research Council Dyspnea Scale (mMRC) and the COPD Assessment Test (CAT). Patients with GOLD A and B are at low risk (0–1 exacerbation per year, not requiring hospitalization), GOLD C and D are high risk patients (≥2 exacerbations per year, or one or more requiring hospitalization). GOLD A and C have few symptoms (mMRC 0–1 or CAT <10), GOLD B and D have more symptoms (mMRC ≥ 2 or CAT ≥ 10).²³
^cPatients were classified in categories of disease severity according to New York Heart Classification (NYHA): 25.5% had class I (no limitation in ordinary physical activity), 33.0% class II (Mild symptoms and slight limitation during ordinary activity and comfortable at rest), 36.0% had class III (Marked limitation in activity due to symptoms, even during less-than-ordinary activity and comfortable only at rest) and 5.0% had class IV (severe limitations and experiences symptoms even while at rest).²⁴
 COPD: chronic obstructive pulmonary disease, CKD: chronic kidney disease, DM: Diabetes mellitus, SOT: Solid organ transplantation.

Table 2. Documented vaccination coverage in adult risk patients.

n = 1331	Diphtheria-Tetanus		Pertussis		Influenza		Pneumococcus		Hepatitis B	
	n	% (95%CI)	n	% (95%CI)	n	% (95%CI)	n	% (95%CI)	n	% (95%CI)
All patients (n = 1331)	387	29.1 (26.7–31.6)	136	10.2 (8.7–12.0)	584	43.9 (41.2–46.6)	429	32.2 (29.7–34.8)		NA
DM type 1 (n = 173)	45	26.0 (19.8–33.3)	22	12.7 (8.3–18.8)	39	22.5 (16.7–29.6)	7	4.0 (1.8–8.5)		NA
DM type 2 (n = 177)	54	30.5 (23.9–37.9)	29	16.4 (11.4–22.9)	85	48.0 (40.5–55.6)	43	24.3 (18.3–31.4)		NA
CKD (n = 138)	33	23.9 (17.2–32.1)	7	5.1 (2.2–10.6)	39	28.3 (21.1–36.7)	32	23.2 (16.6–31.3)	43	31.2 (23.7–39.7)
COPD (n = 187)	65	34.8 (28.1–42.1)	23	12.3 (8.1–18.1)	121	64.7 (57.4–71.4)	75	40.1 (33.1–47.5)		NA
Heart failure (n = 200)	58	29.0 (22.9–35.9)	17	8.5 (5.2–13.5)	77	38.5 (31.8–45.7)	40	20.0 (14.8–26.4)		NA
HIV (n = 201)	61	30.3 (24.2–37.3)	7	3.5 (1.5–7.3)	88	43.8 (36.9–50.9)	146	72.6 (65.8–78.6)	49	24.4 (18.7–31.0)
SOT (n = 255)	71	27.7 (22.5–33.8)	31	12.2 (8.5–17.0)	135	52.9 (46.6–59.2)	86	33.7 (28.0–39.9)		NA

NA: not available, CI: confidence interval, CKD: chronic kidney disease, COPD: chronic obstructive pulmonary disease, DM: Diabetes mellitus, SOT: solid organ transplantation.

Table 3. Determinants of recommended vaccinations in adult patient groups: multivariate logistic regression.

n = 1331	Diphtheria-Tetanus	Pertussis	Influenza	Pneumococcus	Hepatitis B
	OR (95%CI)	OR (95%CI)	OR (95%CI)	OR (95%CI)	OR (95%CI)
Age					
< 40 years			Reference	Reference	
40–64 years			1.6 (1.1–2.4)*	1.6 (1.0–2.7) ^o	
≥ 65 years			2.0 (1.3–3.2)**	2.6 (1.5–4.6)***	
Female gender				1.3 (1.0–1.8)	0.6 (0.3–1.1)
Disease group					
DM type 1		1.8 (0.9–3.6) ^o	0.7 (0.4–1.1) ^o	0.3 (0.1–0.6)**	NA
DM type 2		2.3 (1.2–4.5)**	1.6 (1.1–2.5)*	1.4 (0.8–2.3)	NA
CKD		0.6 (0.2–1.5)	0.7 (0.4–1.1)	1.3 (0.8–2.2)	Reference
COPD		1.5 (0.8–2.9)	2.8 (1.8–4.3)***	2.9 (1.8–4.7)***	NA
Heart failure		Reference	Reference	Reference	NA
HIV		0.4 (0.2–1.0) ^o	1.8 (1.1–2.8)*	25.0 (13.9–46.3)***	0.5 (0.3–0.9)*
SOT		1.5 (0.8–2.9)	2.0 (1.3–3.0)***	2.6 (1.6–4.1)***	NA
Origin				Reference	
Belgian				0.7 (0.4–1.2)	
European				0.6 (0.3–1.0) ^o	
Non-European					
Educational degree ^a (years of study)					
Lower education (<12 years)	0.8 (0.6–1.1)				
Secondary education (12 years)	Reference				
Higher education (>12 years)	1.2 (0.9–1.6)				
Unknown	0.7 (0.2–2.3)				
Employment				Reference	
Full-time				0.7 (0.4–1.2)	
Part-time				1.3 (0.9–1.8)	
Not working					
Net monthly family income					
<1500 euro				0.8 (0.6–1.1)	1.2 (0.6–2.4)
1500–3000 euro				Reference	Reference
>3000 euro				1.2 (0.8–1.7)	2.7 (1.4–5.3)**
Unknown income				0.5 (0.3–0.8)**	1.0 (0.4–2.2)
Physical activity					
Never		Reference	Reference		
Occasionally (≤2 times/week)		0.5 (0.2–1.0)*	1.4 (1.0–2.1) ^o		
Frequently (>3 times/week)		1.0 (0.7–1.6)	1.4 (1.1–1.9)*		
Smoking					
No smoking			Reference	Reference	
Smoker			0.9 (0.6–1.2)	1.0 (0.7–1.6)	
Ex-smoker			1.2 (0.9–1.6)	1.5 (1.1–2.1)*	

Multivariate logistic regression with backwards selection.

^aEducation: Lower Education = no secondary school diploma, Secondary education = secondary school diploma achieved, higher education = university of university college diploma achieved. CI: confidence interval, CKD: chronic kidney disease COPD: chronic obstructive pulmonary disease, DM: diabetes mellitus, SOT: solid organ transplantation, ^o p < 0.1; * p < 0.05; ** p < 0.01; *** p < 0.001

information for influenza and pneumococcal vaccination were occupational health professionals, family and friends.

Discussion

Less than 10% of the patients were vaccinated against diphtheria-tetanus, influenza and pneumococcal disease. Overall, 29% of the subjects were vaccinated against diphtheria-tetanus, 10% against pertussis, 44% against influenza, 32% against pneumococcal disease and 24% of patients

with HIV and 31% of patients with CKD were vaccinated against hepatitis B.

For influenza, the vaccination coverage is far below the WHO/EU target of 75% for risk groups.^{27,28} Similarly, the WHO European region reported coverage rates of mostly below 40% for people with chronic illnesses in 14 other European countries.¹⁵ For pneumococcal vaccination, other studies also reported low coverage rates ranging from 7% in Italy to 50% in immunocompromised patients in the United states and 60% in high-risk groups in Catalonia (Spain).^{17–19,29}

Table 4. Reasons for non-vaccination.

N = 367	Diphtheria-tetanus (n = 86)	Influenza (n = 157)	Pneumococcus (n = 138)
	n(%)	n(%)	n(%)
Concerns and doubts			
Concerns about safety	1 (1.2)	20 (12.7)	1 (0.1)
Doubts about necessity of vaccination	8 (9.3)	10 (6.4)	2 (1.4)
Doubts about effectiveness of vaccination	-	10 (6.4)	-
Opposition to vaccination	-	14 (8.9)	5 (3.6)
Afraid of needle	-	1 (0.6)	-
Does already take a lot of medication	-	1 (0.6)	-
Information			
Not aware of the recommendation	33 (38.4)	4 (2.5)	111 (80.4)
Discouraged by physician	-	4 (2.5)	-
Assumed not to be necessary since absence of injuries	4 (4.6)	-	-
Practical reasons			
Having forgotten to get the vaccine	25 (29.1)	1 (0.6)	3 (2.2)
I have not received vaccine yet, but will get it in the future	-	64 (40.7)	2 (1.4)
Vaccine is too expensive	-	-	1 (0.7)
Not given due to medical condition/treatment	-	3 (1.9)	-
Lack of time	-	1 (0.6)	-
No reason	12 (14.0)	23 (14.6)	13 (9.4)

A possible reason for low coverage rates is that patients at risk are closely monitored by a specialist and therefore less often consult a general practitioner, which is the preferred vaccinator in Belgium. Specialists often do not approach patients about vaccination as this is considered the general practitioner's task.¹ A vaccination recommendation by a specialist could thus have a substantial impact on the vaccination rate.

In accordance with other studies, we observed that people over the age of 65 are better vaccinated against influenza and pneumococcal disease.^{16,18,29-31} Similarly, an Irish study found coverage rates of 28% against influenza and 16% against pneumococcus in adults at risk below 65 years of age and 60% against influenza and 36% against pneumococcus in adults above the age of 65.¹⁸ It has been suggested that most countries are more devoted to vaccinating older rather than younger risk groups.¹⁶ Nevertheless, younger patients with chronic diseases are also at increased risk of complications, and neither recommendations nor uptake of vaccination should be different. Coverage for pneumococcal vaccination in diabetes patients might be low because they are not specifically mentioned as risk-group in the Belgian recommendations. However, it was generally recognized that this was a mistake as there is sufficient evidence that diabetes patients are at increased risk of pneumococcal disease.^{32,33} Furthermore, SOT patients, who are the most immunocompromised, and COPD patients were more likely to be vaccinated against pneumococcal disease and influenza compared to patients with heart failure. Likewise, other studies report higher coverage rates in patients who are immunocompromised or suffer from a lung disease.^{17,18,29} Possibly, more attention is paid to their influenza and pneumococcal vaccination status due to the risk of COPD exacerbation. Since influenza has been associated with worsening of preexisting heart disease, one might also expect a higher coverage in

patients with heart failure,³⁴ but in contrast with some other studies, we did not observe this trend.^{18,19,29}

Given the low vaccination coverage rates for all recommended vaccines, it is clear that more effort is needed to monitor the vaccination status of patients at risk more closely. This starts with systematic registration and documentation of vaccination. We only found documented proof of any vaccination in less than 70% of the patients, but self-reported vaccination rates were higher. Although we cannot exclude recall bias, we attribute this difference mainly to issues with recordkeeping. Access to a central vaccination register is essential for both patients and healthcare providers to keep an overview of the vaccination status.³⁵ Patients are often being followed up by different physicians (specialist, occupational health physicians, general practitioners) and vaccination records may become fragmented or lost. There is a central vaccine register (Vaccinnet) in Flanders (Belgium) which could resolve this issue, but it is not yet being used systemically for vaccines that are not available free of charge in Flanders. Therefore, registration of influenza, pneumococcal and (adult) hepatitis B vaccines is incomplete or missing, even for risk groups. Only the Tdap vaccine is provided free of charge to all.

In addition, physicians should address reasons for non-vaccination. In terms of influenza vaccination, concerns about effectiveness and side effects were important drivers for a lower uptake. Giese *et al.* reported not deeming vaccination necessary as the main reason for non-vaccination against influenza in adult risk patients below 65 years of age.¹⁸ The most prevalent reason for non-vaccination against pneumococcal disease was not being aware of the recommendation. We found that less than 30% of all patients claimed to have received information about the pneumococcal vaccine. Similarly, according to a large European survey in people above 65 years, 54% stated that their physician had not recommended pneumococcal vaccination.³⁶ As we, and others, observed a strong positive association between the recommendation of a particular vaccine by a physician and the coverage rate of this vaccine, we urge all physicians to discuss this with their patients.^{18,30} Furthermore, as some patients claimed to have forgotten the vaccination, a timely reminder by their physician would be beneficial.

Based on these findings, we advocate well-organized multi-intervention vaccination campaigns in which improving recordkeeping of administered vaccines and vaccination recommendations to patients by healthcare professionals are key components. Other studies showed a significant increase in vaccination uptake as a result from such an approach.^{37,38} The guide to Tailoring Immunization Programs (TIP) from the World Health Organization could be used to tailor interventions to lower local barriers to vaccination.³⁹ Moreover, specific education in vaccinology for medical doctors and nurses should increase specialists' awareness of the issue and encourage them to recommend vaccines. Currently, vaccine education is limited in the training of physicians and nurses.

A strength of this first survey is that it assesses vaccination coverage of recommended vaccines in a large and diverse group of at-risk patients. Vaccination data in at-risk groups are scarce and often not monitored. Available studies are often limited to

a particular vaccine in a certain risk group. However, there are some limitations to this survey as well. Firstly, not all recommended vaccines for adult at-risk patients are covered in the study. This includes vaccination against meningococcal disease, varicella, measles, mumps and rubella, which are only recommended in particular subgroups of our patient groups. Secondly, the external validity of the study may be limited as only patients attending a tertiary care hospital were surveyed. Studies on documented vaccination coverage of community at-risk patients are needed to assess follow-up of vaccination recommendation at population level. Nevertheless, we believe that surveys in such hospitals are important as they are responsible for teaching and training of health care workers and should set an example for other care settings. Thirdly, there is a possibility of selection bias, particularly in the HIV group. Patients who were not therapy compliant, recently diagnosed or changing therapy during the recruitment period were not approached as resolving those issues was considered more important than study participation. Another drawback is the frequent lack of documentation. Since we only considered documented vaccination, our estimates are a lower boundary, which may well be an underestimation of the true coverage rates. We chose not to include self-reported data because studies have shown that recall bias by patients is large and such vaccination coverage rates are often overestimated.⁴⁰ Finally, we did not achieve the sample size of 250 patients in all groups due to time and logistical limitations. This resulted in an increase of the 95% CI width of coverage rates of up to one third in the smallest group (i.e. CKD, n = 138).

We conclude that vaccination coverage of recommended vaccines in clinical risk groups is beneath the desired level. Efforts should be made to closely monitor the vaccination status of vulnerable groups. There is need for systematic vaccination registration, communication about vaccination by physicians and vaccination campaigns tailored to the at-risk groups.



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