

# **Dutch healthcare professionals' opinion on vaccination and education to prevent infections in immunocompromised patients: A mixed-method study with recommendations for daily practice.**

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## ABSTRACT

### Background

The fast-growing population of immunocompromised patients (ICP) is more vulnerable to infectious diseases, demanding strategies to protect them. These strategies seem inconsistent in available guidelines and in practices. We aim to evaluate healthcare professionals' (HCP) opinions on vaccination to reduce the number and severity of infections in ICP.

### Methods

A mixed-method study, with an exploratory sequential design, was performed. Medical specialists from various departments in a tertiary care center in the Netherlands were invited for semi-structured interviews to explore their perspective on preventive care of ICP. Topics that play a substantial role in daily practice for ICP were translated into a survey to gain insight into what extent opinions were generalizable to Erasmus Medical Center.

### Results

Surveys were completed by 689 HCP (43% of the invitees), 269 of them treated at least two ICP weekly on average and were considered eligible for further analysis. Quantitative data showed that according to 80 percent of HCP, preventive care for ICP can be improved. Education was chosen by 40 percent as the most important intervention to reduce the number and severity of infections. Vaccinations were valued as important by seventeen percent of HCP. Except for influenza, vaccinations were not regularly discussed during routine consultations. Difficulties to administer vaccinations were experienced by 75 percent of HCP.

### Conclusion

According to our respondents, education is the most promising intervention to reduce the number and severity of infections in ICP. To reach a higher vaccine uptake, we recommend HCP to address vaccinations more frequently during consultations and to search for solutions to alleviate barriers to vaccinate.

## INTRODUCTION

Continuously evolving treatment strategies for chronic diseases result in limited disease burden and better survival rates in patients. Part of these diseases or their treatments result in an immunocompromised state, defined as a diminished function of the immune system. This makes the heterogeneous group of immunocompromised patients (ICP) more vulnerable to infectious diseases (1-2). Several pharmacological and non-pharmacological strategies are available to decrease the number and severity of infections.

While most pharmacological approaches rely on their product characteristics, successful immunization relies both on the patients' immune system and on vaccine characteristics. An interaction between numerous cells, receptors and cytokines is required to mount an effective immune response (3-4) – hampered in ICP. Furthermore, vaccine-safety should be considered, especially for live-attenuated vaccines – as in ICP these vaccines might induce serious adverse events (5).

Strategies to prevent infections in ICP, such as vaccination and education, are often mentioned in (international) guidelines (6). These guidelines are usually concentrated to a specific disease or treatment and might differ on international, national and hospital level. In practice, this results in heterogeneous patient management. Moreover, awareness of the immunocompromised state in both healthcare professionals (HCP) and ICP, as well as availability of the vaccination status, seems suboptimal (7-9).

With this mixed-method study, we assess opinions of HCP on strategies to prevent infections in ICP and corroborate these findings in a tertiary care center. This involves HCP from multiple departments as well as HCP with various levels of experience and interactions with ICP. By addressing possible improvements from the HCP perspective, we formulate suggestions and recommendations to optimize preventive care for this vulnerable group of patients.

## METHODS

### Study design and population

This mixed-method study was conducted from December 2015 to December 2017 in the Erasmus Medical Center (EMC), Rotterdam. This 1320 bed hospital is considered as the largest tertiary center in the Netherlands (10). We used an exploratory sequential design, consisting of semi-structured interviews with medical specialists, followed by a hospital-wide survey containing closed-ended questions. The interviews were used to discover key topics that play a role in preventive care for ICP. Subsequently, using surveys, we tested whether colleagues share these opinions (11). In this study, HCP are defined as a comprehensive term for medical specialists, residents (both in training and not in training), physician researchers as well as nurse practitioners (NP) and nursing consultants (NC).

### Qualitative data collection and analysis

We invited medical specialists from various departments (Supplementary Table 1), who are actively involved in preventive care for ICP, by e-mail for interviews held between December 2015 and April 2016. One researcher (WJ, ♂) conducted the semi-structured interviews while another researcher (LD, ♀) made field notes. Both researchers are medical doctors with an additional position at the in-house travel clinic. After informed consent was signed and the purpose of the study was introduced, 30-minute interviews were held in interviewees' or researchers' offices and audio was recorded. A topic list, based on clinical experience, guidelines and literature (9), (12-15), was used to assess: field of work of HCP; characteristics of ICP within their department; availability and usage of guidelines; practices with regards to prevention of infections, in particular vaccination and education; presence of any barriers to vaccinate; and suggestions for improvements in preventive care. After data saturation was reached, data was transcribed ad verbatim by either LD, MH, WJ or KW. Transcripts were read and key themes were manually labeled by LD and WJ (open coding). Overarching ideas were discussed in the research group, and subcategories were generated for a broader understanding of the key categories by constant comparison (axial coding) (16).

### Quantitative data collection and analysis

Recurrent themes from the qualitative part of the study were used as a framework for the major topics in the survey with closed-ended questions. The main topics of the survey were: characteristics of ICP; vaccination practices; preventive care; knowledge and awareness of the immunocompromised state; usability of guidelines; and management of travel plans. A draft survey was piloted with one medical specialist (EG), three residents, two NPs and a medical student. We used LimeSurvey (17), an online survey tool, to invite 1723 HCP that possibly treat ICP (refer to Supplementary Table 1 for a list of invited departments). The survey was set-up using unique one-time use invites and was available from November 27, 2017 until December 20, 2017. To increase the response rate, we requested interviewed HCP to bring the survey to the attention of their colleagues and we sent out two reminders.

Baseline characteristics of all respondents were recorded. To select a study population that was representative for HCP that routinely treat ICP, successive data was collected from respondents who, on average, treated two or more ICP weekly. Data was analyzed with IBM SPSS Statistics 24 (18) and represented with Graphpad Prism 5 (19).

Descriptive methods were used to summarize the survey findings. To assess whether differences in opinions exist between specific groups of HCP (e.g. nurses versus medical doctors), we used a Mann-Whitney test. P-values < 0.05 were considered significant.

### Ethics

Written informed consent was obtained from all interviewed HCP. Data obtained in this research was stored on a local drive that was only accessible to LD and WJ. Referrals to natural subjects

were coded. LimeSurvey data was stored on Erasmus MC servers. A statement of implicit informed consent at return of the survey was included on the first page of the survey. In consultation with the Medical Ethical Research Committee of Erasmus MC, this study was exempted from review according to the Dutch Medical Research Involving Human Subjects Act (20). No plausible harm to participants could arise from this study. The study complied with the Netherlands Code of Conduct for Scientific Practice from the Netherlands Federation of University Medical Centers (21).

## RESULTS

The qualitative component of this study resulted in twelve interviews with middle aged medical specialists, seven males and five females. A third of the interviewees was already acquainted with the researchers. Fifteen specialists were invited. Non-participation ( $n = 3$ ) was due to limited affinity with the topic. Two specialists referred to a colleague. The interviews resulted in four main topics being: characteristics of HCP and ICP; daily practices and responsibilities; travel opportunities and precautions; suggestions for improvement.

The quantitative component resulted in a response rate of 40 percent ( $n = 689$ ) (baseline characteristics shown in Supplementary Table 2). As shown in Figure 1, our main results comprised data of HCP treating more than two ICP weekly ( $n = 269$ ).

We first describe the qualitative results including quotations of medical specialists, followed by the quantitative results supported with figures.

### Qualitative results

#### *Characteristics of HCP and ICP*

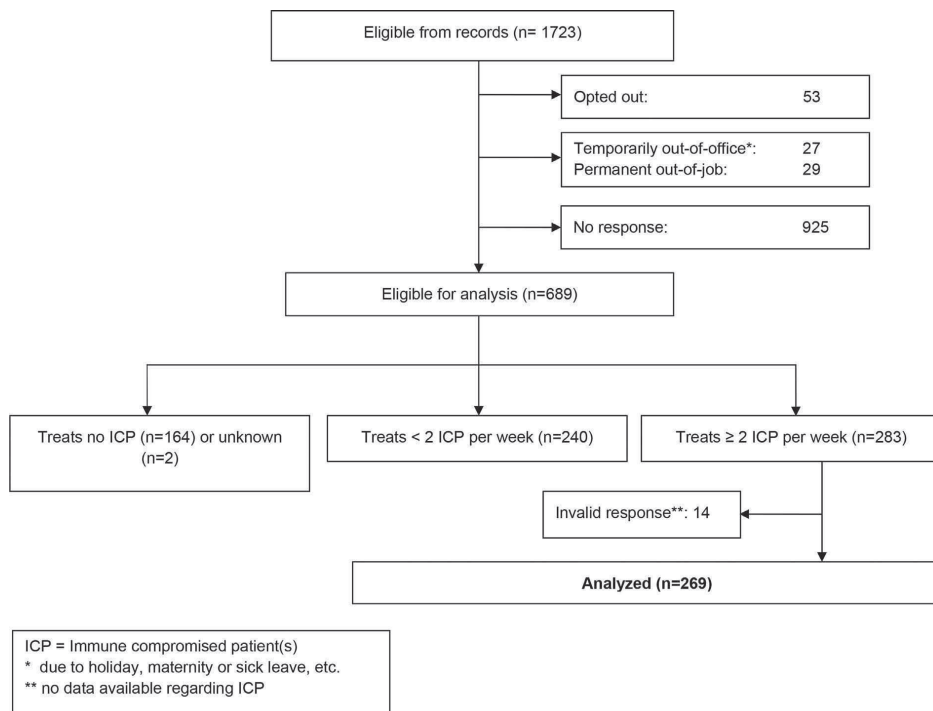
Interviewees described heterogeneity in the immunocompetence of their patient populations. Some medical specialists stated that they often diagnose and initiate treatment in immunocompetent patients; others stated that they treat patients using immunosuppressive therapies (e.g. biologicals), initiated in another, often secondary care, center.

“More than half of our immunocompromised patients become immunocompromised by the medication we start.” (ZS004)

#### *Daily practices and responsibilities*

Interviewees iterated the fact that ICP have to adapt to a substantial amount of information with regards to therapy, preventive measures and life rules. This education is provided predominantly during consultations, complemented by guidebooks and newsletters. Several medical specialists mentioned the complementary role that is appointed to NP and NC for educating ICP:

“We implemented a dedicated consultation hour with an experienced resident in training. A NP is involved to take care of the follow up” (ZS007)



**Figure 1.** Flowchart according to CONSORT statement for quantitative component. Consolidated Standards of Reporting Trials (CONSORT) flowchart delineating the number of eligible healthcare professionals for the quantitative component of this mixed-method study. ICP = Immunocompromised patient(s) \*due to holiday, maternity or sick leave, etc. \*\*no data available regarding ICP.

One of the preventive measures stated is vaccination, preferably done during a screening period, ahead of surgical interventions and/or start of immunosuppressive therapy. Most interviewees questioned the effectiveness and the extent of protection of vaccinations:  
 “... everyone struggles with the same question: is it (the sum of vaccinations administered to ICP) too much or too little?” (ZS003)

Interviewees underlined the need to consider to vaccinate their patients. Almost all specialists stated that they advise ICP to get a yearly influenza vaccination at their general practitioner. Some raised questions about whose role and responsibility it is to administer and register vaccinations. “The treating physician should take the responsibility for vaccinations that are medically indicated, in case of traveling: it’s the patients’ responsibility.” (ZS005)

*Travel opportunities and precautions*

Interviewees mentioned that the quality of life of their patients has improved over the last years, increasing possibilities and willingness to travel. In some situations, treating physicians discourage patients to travel outside Western countries, particularly due to the risk of travel-related

infections. Occasionally, patients ask their physician for travel advice, while others travel to tropical countries without prior notice.

"We see quite some second or third generation people (with a history of migration) travelling to visit their grandparents without notification. I consider it as a tropical journey, in their opinion it's not, it remains a risk." (ZS008)

### *Suggestions for improvement*

To the opinion of interviewees, there is room for improvement:

"Infections are a problem, progress remains to be made." (ZS001)

Mentioned areas of concern in preventive care are: accessibility of specialized vaccination clinics; frequency of interdisciplinary consultations; expense coverage of vaccinations; limited evidence and recommendations on vaccinations and antibiotic prophylaxis in guidelines. Some medical specialists are not informed about the overall vaccination status:

"... the vaccination status of my patient? I got no clue!" (ZS005)

## **Quantitative results**

### *Characteristics of HCP and ICP*

Relevant characteristics of HCP are given in Table 1. The quantitative results concerning heterogeneity of immunocompromised states at first contact with HCP correspond to the interview data. More than half of the patients were considered to be moderately (score 3) to severely (score 4) immunocompromised at first presentation, as scored on a five point Likert scale, ranging from not immunocompromised to worst stage of immunosuppression. Thirteen percent of the patients were considered to be not immunocompromised at their first presentation.

We asked HCP to evaluate their own knowledge and the knowledge of their patients about strategies to prevent infections in ICP. The HCP scored themselves a mean score of 7 (SD 1.66) and patients a mean score of 5 (SD 1.89) on a 1–10 scale (1 = very bad and 10 = excellent).

### *Daily practices and responsibilities*

The majority of respondents (71%) agreed it is the treating physician and their team's responsibility to administer vaccinations in case they consider it as a part of adequate treatment for the ICP. As shown in Figure 2, the majority of HCP (84%) are aware of guidelines containing recommendations regarding vaccinations and other preventive strategies that are applicable to their work field. In contrast to the qualitative results, to less than fifteen percent of respondents, the available guidelines are insufficient to be used in preventive care for ICP.

A comprehensive overview of the reported frequency of discussing vaccinations at distinct departments is represented in Figure 3. In line with the qualitative data, influenza is the most frequently discussed vaccine and is addressed in the consultations of 70 percent of respondents. When HCP

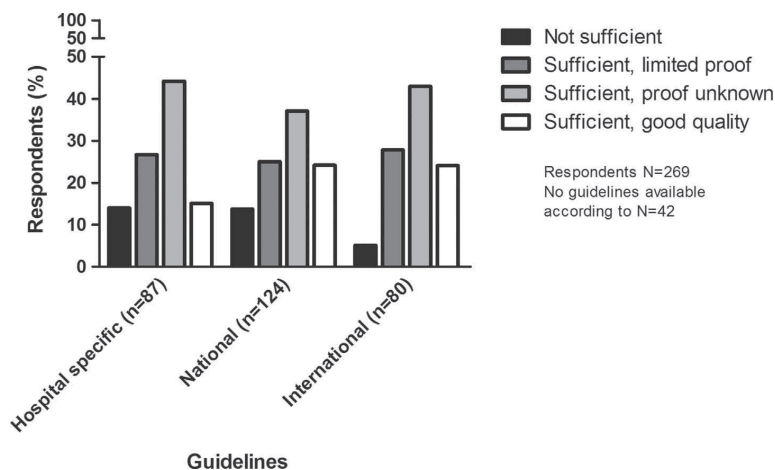
Table 1. Baseline characteristics of HCP (who treat &gt; 2 ICP per week) and ICP per department

HCP age	Internal Medicine	Pediatrics/ Neonatology	Acute Medicine	Pulmonology	Neurology/ Neurosurgery	Gastro-entery	Surgery	Dermato-logy	Cardiology	Rheumato-logy	Other	Mean
Age (mean, yrs)	38,6	42,8	37,5	38,2	40,2	39,2	42,2	39,9	43,1	44,3	42,9	40
<b>HCP gender</b>												<b>Total</b>
Female	58 (68,2)	39 (78,0)	14 (53,8)	11 (50,0)	12 (63,2)	13 (72,2)	8 (66,7)	7 (63,6)	5 (62,5)	5 (71,4)	7 (70)	179 (66,5)
<b>Profession*</b>												<b>Total</b>
Residents, physicians (in training)	34 (40,0)	8 (16,0)	10 (38,5)	7 (31,8)	7 (36,8)	7 (38,9)	2 (16,7)	3 (27,3)	1 (12,5)	1 (14,3)	2 (20)	82 (30,5)
(Physician) researchers	2 (2,4)	1 (2,0)	0	0	2 (10,5)	3 (16,7)	0	1 (9,1)	0	0	0	9 (3,3)
Medical specialists	31 (36,5)	28 (56,0)	12 (46,2)	7 (31,8)	6 (31,6)	6 (33,3)	6 (50,0)	7 (63,6)	4 (50,0)	3 (42,9)	6 (60)	116 (43,1)
Nurse practitioners/nursing consultants	18 (21,2)	13 (26,0)	4 (15,4)	8 (36,4)	4 (21,1)	2 (11,1)	4 (33,3)	0	3 (37,5)	3 (42,9)	2 (20)	62 (23,0)
<b>Years after graduation</b>												<b>Mean</b>
Years (mean, yrs)	13,5	16,9	11,6	13,3	15,6	13,9	17	15,6	18,8	21,3	18,9	15
<b>Patients' age categories*</b>												<b>Total</b>
<18 yrs (%)	1 (1,2)	50 (100)	5 (19,2)	0	1 (5,2)	0	0	0	1 (12,5)	0	0	58 (21,6)
18-35 yrs (%)	0	0	0	1 (4,5)	2 (10,5)	6 (33,3)	0	0	0	1 (14,3)	4 (40)	14 (5,2)
35-65 yrs (%)	69 (81,2)	0	16 (61,5)	16 (72,7)	14 (73,7)	11 (61,1)	8 (66,7)	7 (63,6)	7 (87,5)	6 (85,7)	5 (50)	159 (59,1)
>65 yrs (%)	15 (17,6)	0	5 (19,2)	5 (22,7)	2 (10,5)	1 (5,6)	4 (33,3)	3 (27,3)	0	0	1 (10)	36 (13,4)
<b>Nr. (% of total participants)</b>	85 (31,6)	50 (18,6)	26 (9,7)	22 (8,2)	19 (7,1)	18 (6,7)	12 (4,5)	11 (4,1)	8 (3,0)	7 (2,6)	10 (3,7)	269 (100)

\* Reported as n (%)



consider vaccinating their ICP, up to 75 percent indicated that they experience difficulties. Most important barriers to vaccinate were timing issues (42%), logistical obstacles (30%) and financial problems (19%). Timing issues included short time to start of immunosuppressive therapy or transplantation. Concerns of limited interdisciplinary consultations raised by the interviewees, were not shared by the surveys' respondents, as 84 percent was satisfied with the frequency of consultations with other HCP regarding care for ICP (176 out of 209). Most HCP consulted their colleagues weekly to monthly (28%) or monthly to few times a year (32%).



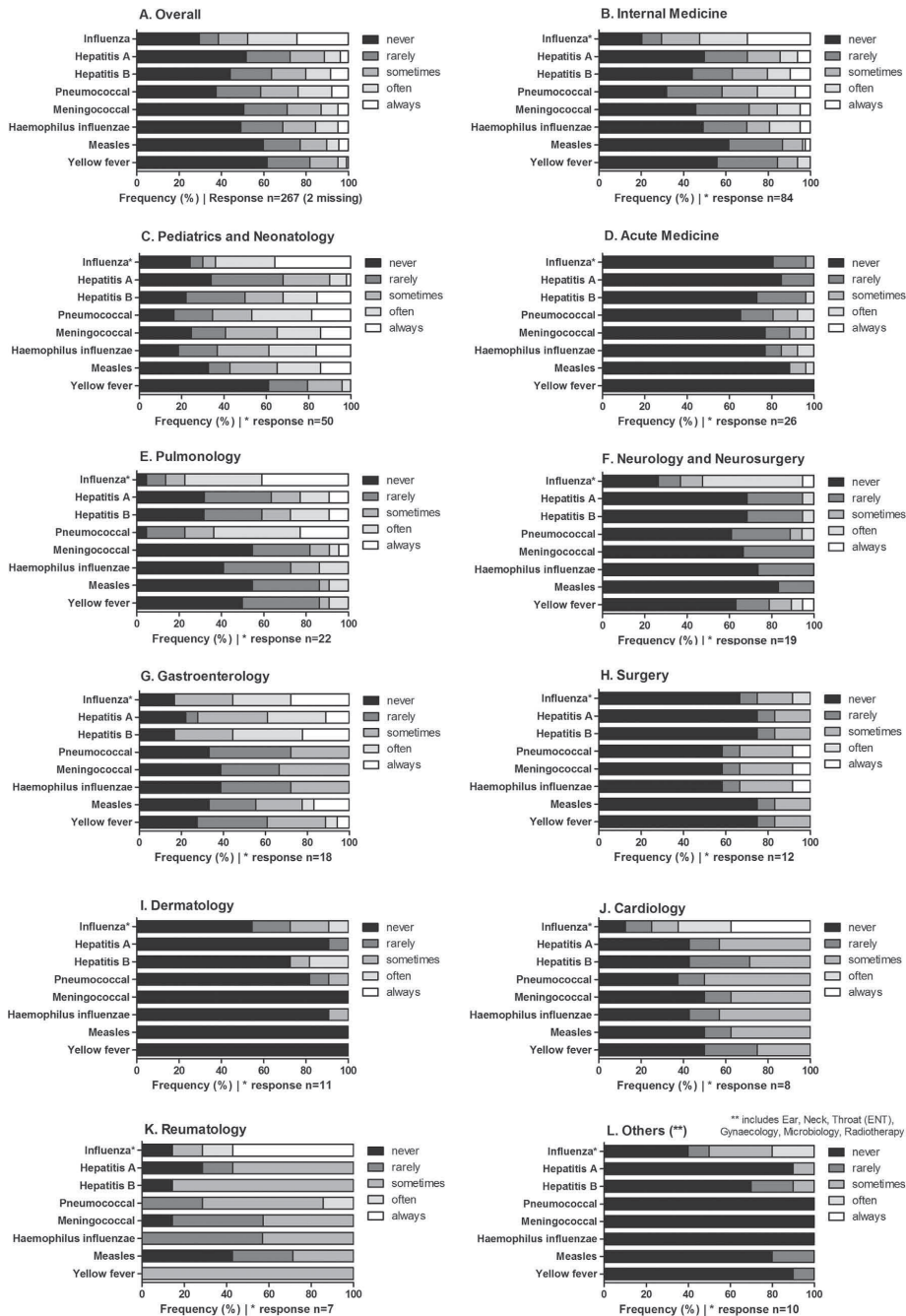
**Figure 2.** Availability and opinion of HCP on guidelines that discuss preventive measures. Availability and opinion of HCP on hospital specific, national and international guidelines that discuss preventive measures to prevent infections in ICP. According to 42 respondents, no guidelines addressing care for ICP were available to them. One answer per guideline category was allowed. HCP = Healthcare professional(s). ICP = Immunocompromised patient(s).

### *Travel opportunities and precautions*

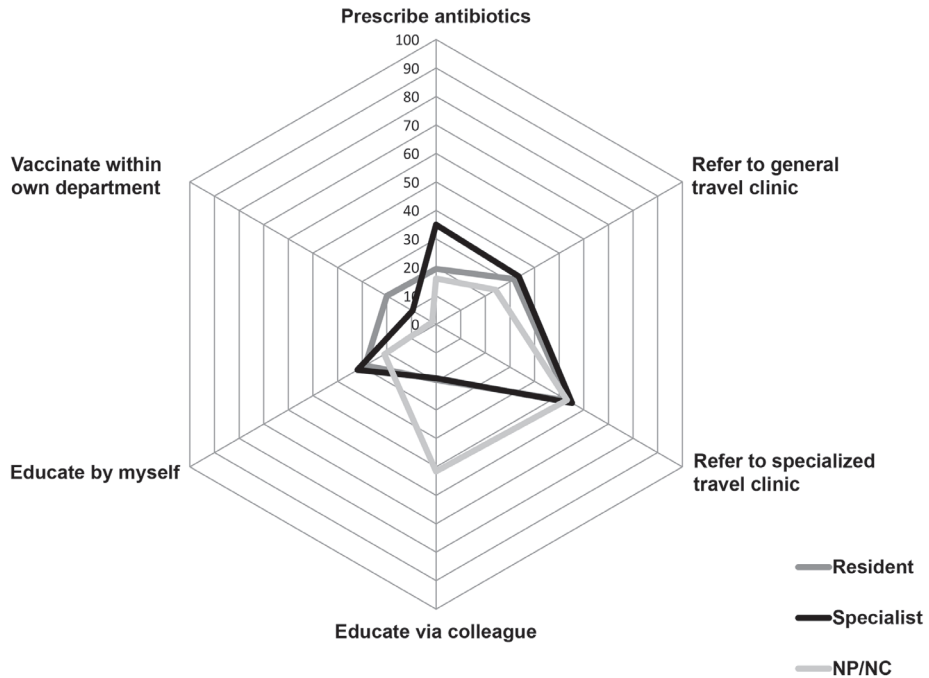
The majority of HCP (65%) indicated to regularly discuss travel plans during their consultations. The topic seems to be discussed most frequently at the departments of Rheumatology, Gastroenterology and Pulmonology and least frequently at the departments of Surgery, Dermatology and Acute Medicine (Supplementary Figure 1). Nurses reported to discuss travel plans more often than doctors do ( $p = 0.001$ ). The follow-up actions of HCP in case ICP informed them about their travel plans are summarized in Figure 4. The majority of respondents indicated to refer their patients to a specialized travel clinic.

3.2.4. Suggestions for improvements

In line with the qualitative data, 80 percent of HCP agreed that there is room for improvement with regards to the prevention of infections in ICP (data available from 248 HCP). Up to 40 percent agreed that education is the most important tool to reduce the number and severity of infections in ICP. To other respondents, refining infection control in the hospital (16%); usage of (prophylactic) medication (13%); or vaccination (13%) is of most importance. According to seventeen percent, the infections they face are not preventable; two percent answered that there are no or few infections.



**Figure 3.** Frequency of discussing vaccinations during consultations. The frequency of discussing vaccinations by HCP during patient consultations, represented as overall (A) and per department (B–L). The number of responses, represented by the responses for influenza vaccine, is shown below the graphs.



**Figure 4.** Infographic follow-up actions of HCP if ICP has travel plans. Infographic showing follow-up actions of HCP if their ICP indicate they have travel plans. Results are shown per type of profession. HCP = Healthcare professional(s). ICP = Immunocompromised patient(s). NP/NC = nurse practitioner/nurse consultant.

## DISCUSSION AND CONCLUSION

This mixed-method study showed that according to the majority of HCP, there are opportunities to further enhance prevention of infections in ICP. Education, as method to optimize knowledge, was chosen by forty percent as the most promising method. Accordingly, HCP graded the knowledge of their patients as insufficient. In addition, one out of seven HCP agreed that ICP could benefit from vaccinations as method to prevent infections. Despite being recommended in guidelines and valued as important, vaccinations are not discussed by default during consultations. Moreover, even when recommended in guidelines, many HCP experience timing issues and other barriers to vaccinate their ICP.

The agreement of HCP from different specialties on the added value of education as method to prevent infections is striking. Vaccination as strategy seems less important to HCP, which might be explained by the limited evidence of vaccine effectiveness in specific populations, as reported in the interviews. Furthermore, the limited ability to prevent a wide range of infections might play a role. Addressing behavior by education therefore seems to transcend the effects that vaccinations induce by means of preventing a smaller number of infectious diseases. On one hand, individualized education is time consuming, while on the other hand, the heterogeneity of ICP

is a complicating factor in the provision of general applicable information. Limited frequency of discussing vaccinations during consultations might be due to short time. In addition, difficulties in timing, logistics and finances, could withhold HCP to discuss vaccinations and act accordingly. In comparison to studies that tested knowledge of HCP with closed-ended questions (9, 22), the HCP in this study rated themselves 'rather good' on knowledge about methods to prevent infections. The variation in the reported frequencies of discussing vaccinations seems in line with studies where immunization histories indicated vaccination rates of 24–70 percent for recommended vaccinations (12). Several strategies are known to reduce the number or severity of infections in ICP. For example, in post-transplantation patients, both influenza vaccination and early antiviral treatment reduced the severity of influenza infections (23). In splenic patients, pneumococcal vaccination, sufficient knowledge level about risks and the usage of prophylactic antibiotics, were associated with a reduction of overwhelming post splenectomy infections (24). Previous studies showed that vaccine uptake increases both in case HCP promotes vaccination and if the ICP has sufficient knowledge on recommended and contraindicated vaccinations (25), (26). Since the frequency of discussing vaccinations and the estimated knowledge of ICP were low in our study, this warrants further attention.

Based on our findings we suggest addressing the following:

First, and according to the data of this study most importantly: integrating a method of education in preventive care of ICP could support reducing the number and severity of infections in this patient population.

Second, efforts should be made to reach a higher vaccine uptake for vaccinations that are known to contribute in the prevention of infections for ICP, by discussing them more frequently during consultations. Especially, during the first HCP visit, still a substantial part of ICP is not yet immunocompromised, and is at that time more likely to mount an effective immune response to vaccination.

In order to increase knowledge and achieve a higher vaccine uptake in ICP, the following interventions are suggested: telephone support programs by HCP (27); targeted information campaigns (28); solid online information resources (29); electronic health record patient portal messages (30), (31); involvement of pharmacists as educators (32); automated telephone communication (33). The optimal strategy to educate ICP remains to be investigated.

Third, we propose to actively track down barriers to vaccinate and solve them in a multidisciplinary approach, incorporating HCP, policy makers, insurance companies and other funding suppliers. Timing issues, which can only partly be resolved due to possible short intervals between diagnosis and start of immunosuppressive therapy, could diminish if acted upon in secondary and primary care centers. We suggest healthcare centers to support HCP by alleviating logistical barriers such as starting a dedicated vaccination clinic or appoint HCP in a consulting role for ICP and vaccination advice.

In addition, we want to stress the importance for HCP to be aware of risks involved with international travel. Travel-associated risks can be integrated in patient education, as increasing

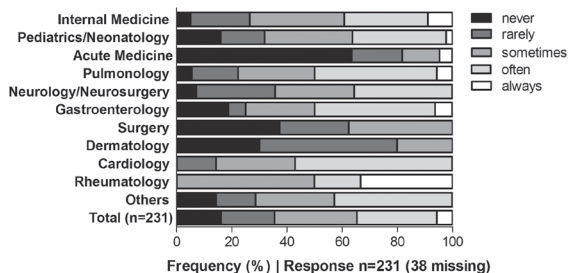
quality of life in ICP due to evolved treatment strategies might increase the willingness to travel (34). Studies showed that up to two-third of ICP travelled to high risk destinations while being immunocompromised, while only 55 to 69 percent sought pre-travel advice (14,35).

For this study, some limitations have to be taken in mind when interpreting the results. The study was conducted in a single tertiary care center, limiting the external validity to other centers. For the interviews, we only invited medical specialists, for their clinical experience as senior HCP. This approach has left the opinions of nurses and residents unnoticed, partly redressed by involving them in pilot-testing of the surveys. Internal validity was strengthened by inviting all HCP that possibly treat ICP; it however resulted in small number of responses for some departments. We therefore chose to display the HCP as one group, highlighting remarkable results per subgroup. Following HCP's opinions, education is considered as most important strategy to reduce the number and severity of infections in ICP. Improved levels of knowledge of ICP about their immunocompromised state; risks for infections; and recommended and contraindicated vaccinations could contribute to the prevention of infections. The optimal method to deliver education is an important topic to elaborate on in future research. In parallel, solving issues that retain HCP to vaccinate could increase the frequency of discussing vaccinations and the vaccine uptake. As the immunocompromised population is increasing, we encourage HCP to contribute to integrative approaches that implement education, vaccinations and other measures to prevent infections.

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**Supplementary figure 1.** Frequency of discussion travel plans during consultation

The frequency of discussing travel plans by HCP during patient consultations, represented per department and overall.

**Supplementary table 1.** List of involved departments

	Qualitative component	Quantitative component
<b>Departments</b>	<b>Specialization of interviewees (n)</b>	<b>Invited departments</b>
<i>As named in analyses</i>		<i>As named in EMC</i>
Acute Medicine		Emergency medicine
Acute Medicine		Intensive Care
Cardiology	Heart transplantations (1)	Cardiology
Dermatology	Immunosuppressive therapies (1)	Dermatology
Ear, nose and throat		Ear, nose and throat
	IBD (1)	
Gastroenterology	Liver transplantations (1)	Gastroenterology
Gynaecology		Gynaecology
Gynaecology		Obstetrics & Gynaecology
Internal Medicine		Geriatrics
	Asplenia (1)	
Internal Medicine	Stem cell transplantations (1)	Haematology
Internal Medicine	Primary immunodeficiencies (1)	Immunology
	HIV (1)	
Internal Medicine	Renal transplantations (1)	Internal Medicine
Medical Microbiology		Medical Microbiology
Neurology/neurosurgery		Neurology/Neuroscience
Neurology/neurosurgery		Neurosurgery
Other		Other departments
Pediatrics		Pediatric surgery
Pediatrics	Various (1)	Pediatrics
Pulmonology	Lung transplantations and CF (1)	Pulmonology
Radiotherapy		Radiotherapy
Rheumatology	Immunosuppressive therapies (1)	Rheumatology
Surgery		Surgery
Urology		Urology

IBD = inflammatory bowel disease, HIV = human immunodeficiency virus, CF = cystic fibrosis