

## Travelling activity and travel-related risks after allogeneic haematopoietic stem cell transplantation – a single centre survey

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### Summary

**BACKGROUND:** Travel activity and travel-related risks of patients after allogeneic haematopoietic stem cell transplantation (allo-HSCT) remain largely unknown. The aim of our study was to examine travel activity after allo-HSCT including travel behaviour and travel patterns.

**METHODS:** We analysed travel characteristics of allo-HSCT recipients by using a retrospective cross-sectional survey. Allo-HSCT patients were asked to complete a questionnaire during their annual health visits from 2010 to 2012.

**RESULTS:** Overall, 118/153 (77%) participating patients reported travel activity for a total of 201 travelling episodes. Travellers versus non-travellers were receiving immunosuppressive treatment in 35.6% versus 65.7% ( $p = 0.002$ ), and had graft-versus-host-disease (GvHD) in 52.5% versus 62.9% ( $p = 0.17$ ). In a multivariate analysis, the time between the transplantation and the survey was the only factor associated with travel activity ( $p < 0.0001$ ) and taking pretravel advice ( $p < 0.0001$ ). In 34.8% of travel episodes pretravel advice was sought. Patients with pretravel advice reported travel-related symptoms more frequently. Minor respiratory (27/201) and gastrointestinal (23/201) symptoms were most frequently indicated. Four percent (8/201) of the patients were hospitalised while travelling.

**CONCLUSION:** We conclude that travelling after allo-HSCT is frequent and linked to the time since transplantation. We could not define specific risks for any destination. Nevertheless, pretravel advice and preparation are highly recommended for immunosuppressed patients.

**Key words:** *Allogeneic haematopoietic stem cell transplantation (allo-HSCT); travel; complications; destination; pretravel advice; risk factors*

### Introduction

Travelling is a challenge for immunosuppressed patients owing to the complex medical conditions and an increased risk of travel-associated infections. Most studies including immunosuppressed travellers have focussed on patients with solid organ transplants (SOTs), HIV infection or various malignancies [1–4]. Type and severity of immunosuppression are highly diverse among these high-risk populations [5, 6].

In 2010, more than 12,000 allogeneic haematopoietic stem cell transplantations (allo-HSCT) were performed in Europe [7]. The continuous increase in survivors after allo-HSCT will likely correlate with the number of high-risk travellers in the near future. After allo-HSCT, immunosuppression is often prolonged, complex and associated with an increased risk of infectious diseases [8, 9]. A profound knowledge regarding travel behaviour is important in order to provide the best recommendations for safe travel.

To the best of our knowledge, to date no guidelines regarding the time and specific conditions for travelling after allo-HSCT have been published. Despite immunosuppression, safety during travel is crucial [10, 11]. For SOT recipients travel to high-infection-risk destinations (Africa, Asia, Middle and South America) should be postponed for at least 1 year post-transplant according to the current recommendations of the Centres for Disease Control and Prevention (CDC) [12]. Travel advice may depend on various factors such as the degree of immunosuppression or the travel destination. Immunosuppression after allo-HSCT is variable and depends on induction treatment, type of transplantation and manipulation of the transplant, status of immune reconstitution, graft-versus-host-disease (GvHD), and immunosuppressive treatments. The CDC considers the presence of active GvHD, the need of on-going immunosuppressive treatment and a post-transplant time less than 2 years as conditions of severe immunosuppression [12]. After allo-HSCT, up to 50% of patients are affected by chronic GvHD [13, 14]. In addition to the requirement for

prolonged intensive immunosuppressive treatment, allo-HSCT recipients with chronic GvHD are regarded as functionally asplenic [15]. These factors significantly increase the risk for infections and associated complications [16, 17].

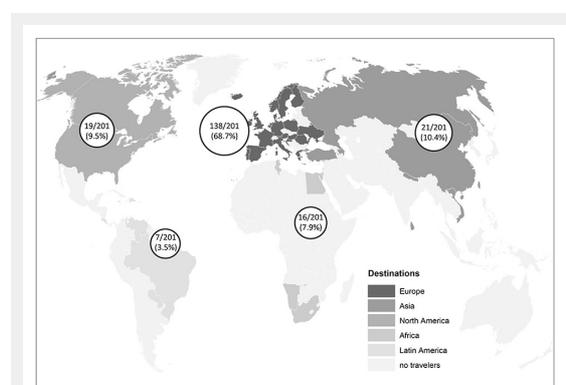
Most studies of immune competent and compromised travellers focused on tropical and subtropical areas [3]. Nevertheless, in European countries also infectious diseases may be challenging as a result of an increase of multidrug-resistant Gram-negative bacteria such as in *Escherichia coli* and *Klebsiella pneumoniae*, with a perceptible north-to-south gradient, reaching up to 50% of clinical isolates in popular travel destinations such as Greece and Italy [18, 19].

Pretravel advice should help to identify specific risks and potential travel-related problems. Among SOT patients fewer than 50% seek pretravel advice [2, 3, 20]. These patients primarily ask general practitioners or transplant physicians for pretravel advice – and not infectious diseases or travel medicine specialists. However, a study among Swiss general practitioners showed that they often do not feel up to the mark to counsel immunosuppressed patients for before travelling [21]. Vaccination is a key topic in pretravel advice and an important preventive strategy to reduce the burden of infectious diseases. Live vaccines are generally considered to be contraindicated in immunosuppressed hosts, including allo-HSCT patients [22]. In addition, the vaccine-induced immune responses are often poor.

Antibiotics for self-treatment by immunocompromised patients should be based on detailed knowledge of the endemic resistance patterns at a particular travel destination. Therefore, instructions concerning risk behaviour, medication and necessary prophylaxis, preferably given by the treating physician, are even more important [1, 20, 21].

The aim of our study was to identify travel patterns and behaviours in patients after allo-HSCT. Our rationale was that a broader understanding of travel behaviour in allo-HSCT patients might help to improve pretravel advice for this complex subset of high-risk travellers.

## Methods



**Figure 1**

Distribution of reported travel destinations. In total 201 travel episodes were reported.

## Study design and participants

We performed a retrospective cross-sectional observational study of travel behaviour in patients older than 18 years after allo-HSCT. Between September 2010 and September 2012 patients attending a routine annual visit at the haematological outpatient clinic of the University Hospital Basel, Switzerland, were asked to complete a questionnaire regarding travelling in the previous year. The questionnaire was filled in at the outpatient clinic without any help of a healthcare worker or study nurse. Information about medication, remission state, grading of GvHD, underlying haematological disease, and time since transplantation were completed from the medical record. Patients with missing baseline information or who answered the questionnaire incorrectly were excluded. All patients provided a written informed consent statement. The study was approved through the local ethics committee (Ethikkomitee beider Basel, EKBB, approved 2010, [www.eknz.ch](http://www.eknz.ch)).

## Questionnaire

The questionnaires included factors of the following four categories:

- I demographics, clinical information including time since transplantation, and immunosuppressive drugs;
- II general travel information including travel activity, details on travel destination, overall duration, purpose, travel companions, and accommodation;
- III pretravel medical advice;
- IV during and after travel – risk behaviour, symptoms and medical advice.

The questionnaire was developed in collaboration with experts in haematology and infectious diseases at the University Hospital Basel (Switzerland) and in travel medicine at the Swiss Tropical and Public Health Institute (Switzerland).

## Definitions

Travel episodes were defined as journeys for 7 days or more to any country outside of Switzerland within the previous year. Multiple travel episodes per questionnaire were possible. Reported countries were grouped into five regions: Europe, Africa, Asia, North America, and Latin America.

Based on guidelines of the CDC [12], we defined active GvHD, concurrent immunosuppressive drugs or transplantation within the previous 2 years as evidence of active immunosuppression.

Risk behaviour while travelling consisted of unprotected sex, receiving tattoos or piercings, bathing in stagnant water, close animal contact, receiving blood transfusions, and risky eating habits (raw meat or fish, and ice cubes).

Health issues were divided into six groups: respiratory (cough, cold, phlegm, sore throat), gastrointestinal (abdominal cramps, diarrhoea), musculoskeletal (arthralgia, rheumatic pains), urinary tract infections, dermatological (skin rashes) and fever.

A personal visit to a healthcare provider (e.g. haematologist, general practitioner, travel medicine specialist) was considered as pre- or post-travel advice.

### Statistical analysis

Primarily descriptive statistics was used for travel destinations. Basic sociodemographic characteristics, type and severity of immunosuppression, the presence of GvHD, and time after allo-HSCT were compared between travelers and non-travellers using the chi-square test for categorical variables and the Mann-Whitney for continuous variables. A multivariate logistic regression model was used to explore predictors of travelling by patients after allo-HSCT. We included age, gender, presence of GvHD, time since transplantation, and immunosuppressive treatment into the model.

Two-tailed p-values of <0.05 were considered significant. Statistical analyses were performed with STATA® 12.0 (Stata Corp., College Station, TX) and GraphPad Prism (version 4.0).

## Results

### Baseline characteristics

The haematological outpatient clinic of the University Hospital Basel, where the questionnaire was distributed, performs around 300 annual check-up visits. During the study period, 217 questionnaires were returned. Thirty question-

**Table 1:** General characteristics of the study population (n = 153).

	Travelers (n = 118)		Non-travelers (n = 35)		p-value
	n	%	n	%	
Median age (years), IQR	47	37–56	54	39–61	0.3
Males, %	72	61	25	71.4	0.261
Immunosuppressive therapy, %	42	35.6	23	65.7	0.002
Graft-versus-host-disease, %	62	52.5	22	62.9	0.168
Underlying disease					
Chronic myeloid leukaemia	21	17.8	4	11.4	
Myelodysplastic syndromes / acute myeloblastic leukaemia	36	30.5	12	34.3	
Non-Hodgkin lymphoma	50	42.4	16	45.7fe	
Hodgkin lymphoma	4	3.4	1	2.9	
Congenital immunodeficiency	1	0.8	1	2.9	
Aplastic anaemia	6	5.1	1	2.9	

IQR = Interquartile range (only for age)

**Table 2:** Characteristics of 201 journeys performed by 118 patients according to the main destination.

	Europe		Africa		Asia		Canada/USA		Latin America		Total	
Number of journeys	138	(100%)	16	(100%)	21	(100%)	19	(100%)	7	(100%)	201	(100%)
Immunosuppressive therapy	51	(36.7%)	8	(50%)	8	(38.1%)	6	(31.6%)	1	(14.3%)		
Graft-versus-host-disease	76	(55.1%)	10	(62.5%)	10	(47.6%)	9	(47.4%)	2	(28.6%)		
Median duration, days (interquartile range)	14	(7–21)	14	(7–14)	12	(7–28)	14	(9–24)	17	(10–28)		
Counselling before journey	43	(31.2%)	8	(50%)	9	(42.9%)	5	(26.3%)	5	(71.4%)	70	(34.8%)
By family doctor	13	(9.4%)	4	(25%)	5	(23.8%)	2	(10.5%)	3	(42.9%)	27	(13.4%)
By haematologist	26	(18.8%)	4	(25%)	4	(19.0%)	3	(15.8%)	2	(28.6%)	39	(19.4%)
By travel clinic	2	(1.4%)	1	(6.3%)	1	(4.8%)	0	(0%)	1	(14.3%)	5	(2.5%)
Other	10	(7.2%)	1	(6.3%)	3	(14.3%)	0	(0%)	0	(0%)	14	(7.0%)
Symptoms during journey <sup>1</sup>	37	(26.8%)	5	(31.3%)	6	(28.6%)	3	(15.8%)	3	(42.9%)	54	(26.9%)
Respiratory	19	(13.8%)	1	(6.3%)	4	(19.0%)	2	(10.5%)	1	(14.3%)	27	(13.4%)
Gastrointestinal	15	(10.9%)	3	(18.8%)	3	(14.3%)	0	(0%)	2	(28.6%)	23	(11.4%)
Fever	4	(2.9%)	0	(0%)	2	(9.5%)	0	(0%)	0	(0%)	6	(3.0%)
Risk during journey <sup>2</sup>	30	(21.7%)	2	(12.5%)	9	(42.9%)	8	(42.1%)	1	(14.3%)	50	(24.9%)
Food	20	(14.5%)	2	(12.5%)	6	(28.6%)	6	(31.6%)	0	(0%)	34	(16.9%)
Symptoms after journey <sup>3</sup>	35	(25.4%)	2	(12.5%)	4	(19.0%)	2	(10.5%)	3	(42.9%)	46	(22.9%)
Respiratory	16	(11.6%)	2	(12.5%)	4	(19.0%)	2	(10.5%)	0	(0%)	24	(11.9%)
Gastrointestinal	10	(7.2%)	1	(6.3%)	2	(9.5%)	0	(0%)	0	(0%)	13	(6.5%)
Fever	1	(0.72%)	0	(0%)	2	(9.5%)	0	(0%)	0	(0%)	3	(1.5%)
Intended behaviour before next journey												
Counseling <sup>4</sup>	48	(34.8%)	6	(37.5%)	5	(23.8%)	5	(26.3%)	4	(57.1%)	68	(33.8%)
Inform about local health care <sup>5</sup>	51	(37.0%)	4	(25%)	6	(28.6%)	7	(36.8%)	3	(42.9%)	71	(35.3%)
Inform about vaccination <sup>6</sup>	65	(47.1%)	9	(56.3%)	11	(52.4%)	8	(42.1%)	5	(71.4%)	98	(48.8%)

Missing data for: <sup>1</sup> 20 journeys, <sup>2</sup> 39 journeys, <sup>3</sup> 37 journeys, <sup>4</sup> 54 journeys, <sup>5</sup> 58 journeys, <sup>6</sup> 47 journeys  
Multiple answers possible for <sup>1,2,3,4</sup>

naires were excluded: in 21 cases because of missing baseline information, 6 patients reported travel duration shorter than 1 week, 3 refused to fill out the questionnaire, and 1 patient reported a journey before the transplantation date. Thus, 187 questionnaires from a total of 153 individuals were finally analysed, and 118/153 (77.1%) patients reported travel activity in the previous year. Table 1 summarises the baseline characteristics of the study participants. The majority of patients (145/153, 94.8%) were in complete remission of their haematological malignancy at the time of travelling.

### Travelling after allo-HSCT

A total of 118/153 (77.1%) reported travel activity, including 201 episodes, mostly for vacation (176/201, 87.6%). Only 15 (7.5%) travel episodes were reported for business purposes. Forty-two percent of the travellers (50/118) declared multiple trips within 1 year prior to the survey. The median reported number of travel episodes was 1 (interquartile range [IQR] 1–2). Most travel episodes were in company (148/201, 73.6%). The accommodation mentioned most was hotel (86/201, 42.8%), followed by privately organised lodging (36/201, 17.9%). European countries were the most common destinations (138/201, 68.7%), followed by Asia (21/201, 10.5%), North America (19/201, 9.5%), Africa (16/201, 8.0%) and Latin America (7/201, 3.5%) (fig. 1). Among European travel destinations, Mediterranean countries dominated (82/201, 40.8% Italy, Spain, France, Portugal and Greece), followed by German speaking neighbour countries (19/201, 9.5% Germany and Austria), Nordic countries (14/201 7.0% Sweden, Norway, Island, Finland, Denmark), Eastern European countries (11/201, 5.5% Ukraine, Rumania, Kosovo, Croatia, Hungary, Poland), Western Europe countries (7/201, 3.5% England, Ireland, Holland) and Canary Islands (5/201, 2.5%). Table 2 shows the characteristics of the 201 travel episodes according to destination. There was a longer median time since transplantation among patients travelling to non-European compared with European destinations (median 9.3 vs 6.5 years,  $p = 0.13$ ).

Among all study participants 22.9% (35/153) reported no travel activity in the previous year. The most common reasons mentioned were “no interest” (12/35, 34.3%), “not feeling well” (12/35 34.3%), “financial reasons” (4/35, 11.4%), and “recommendation not to travel by the treating physician” (3/35, 8.6%).

### Impact on travel activity

In general, travellers showed a significantly longer time since transplantation (median 7.5 years, IQR 5–12) compared with non-travellers (median 3 years, IQR 1–5;  $p < 0.0001$ ). Only 3/201 (1.5%) (France, Israel, Egypt) travel

episodes were within 1 year after transplantation, and 16/201 (8.0%) – 14/16, 87.5% to European countries – within 2 years post-transplant. Also, patients without immunosuppressive treatment were more likely to travel (42/118, 35.6% vs 23/35, 65.7%;  $p = 0.002$ ). Nevertheless, in the multivariate analysis, only time after transplantation was an independent predictor for travel activity after allo-HSCT (odds ratio [OR] 9.056, 95% confidence interval [CI] 2.033–40.337,  $p = 0.004$ ; table 3). Neither presence of GvHD nor concurrent immunosuppressive drugs had a significant influence on travel activity in the multivariate model. These two factors also did not prevent patients from travelling to high-infection-risk continents (table 2).

### Pretravel advice and preparation

In only 34.8% (70/201) of travel episodes was pretravel advice sought. Only in 147 cases a statement regarding intended future travel advice was given. Of those who had sought pre-travel advice, 94.5% (52/55) would do so again and among those refusing it, 82.6% (76/92) would do so in the future. Among the reported travel episodes patients were more likely to seek pretravel advice when taking immunosuppressive treatment (49.3% [36/74] vs 26.8% [34/127],  $p = 0.001$ ), having a shorter time since allo-HSCT (median time 4.5 years vs 11 years,  $p < 0.0001$ ) or GvHD (42.0% [45/107] vs 26.6% [25/94],  $p = 0.025$ ). Travel advice was also requested more frequently for travel to Africa, Asia and Latin America (table 2). A common source for pretravel information was the haematologist (39/201, 19.4%), preferably chosen by travellers with a shorter time since transplantation (3.7 years, IQR = 2.1–5.5), whereas family doctors were asked at a longer time since transplantation (5.3 years, IQR = 4.1–8.4).

For only 24/201 (11.9%) travel episodes, patients reported having received recommendations for vaccination. Also the patients' self-reported vaccination status was often poor. Vaccine status for common vaccines such as tetanus or influenza could be determined in fewer than half of the travel episodes. Table 4 summarises the self-reported vaccine status in travelling allo-HSCT recipients. For future travel, 48.8% (98/201) reported that they would inform themselves about the need of vaccination and 35.3% (71/201) about local healthcare; 33.8% (68/201) indicated they would seek advice from a health professional prior to travel (table 2).

### Travel-related illness

Symptoms were reported in 54/201 (26.9%) cases during travel and in 46/201 (22.9%) after travelling. While travelling, in 27/201 (13.4%) respiratory and in 23/201 (11.4%) gastrointestinal symptoms were reported, compared with 24/201 (11.9%) and 13/201 (6.5%), respectively, after re-

**Table 3:** Multivariate regression analysis of possible predictors for travel activity in 153 patients after allogeneic haematopoietic stem cell transplantation.

	Adjusted odds ratio	95% confidence interval	p-value
Age, per 10 years older	1.132	0.765–1.675	0.536
Female	1.419	0.43–4.68	0.566
Graft-versus-host-disease	1.105	0.299–4.081	0.881
Immunosuppressive treatment	0.386	0.098–1.513	0.172
Transplantation at least 1 year before journey	9.056	2.033–40.337	0.004

turning (table 2). Only six patients reported fever during travel and three post-travelling. Sixteen out of 201 (8.0%) patients required medical advice during their travel, and five of these were hospitalised. Reasons for hospitalisation were febrile respiratory infection (n = 2), petechial skin rash (n = 1), dehydration (n = 1) and surveillance after a car accident (n = 1). In 18/201 (9.0%) travel episodes antibiotics were used, but in only half of these cases had a physician been contacted.

Within 4 weeks after returning home, 17/201 (8.5%) patients required medical advice. Among those six patients were hospitalised, specifically owing to febrile respiratory infection (n = 2), gastrointestinal infection (n = 2), eye problems (n = 1), and persistent musculoskeletal pain (n = 1). Three of these six patients had already been hospitalised at the travel destinations, namely owing to febrile respiratory infection (n = 1), gastrointestinal infection (n = 1), and persistent musculoskeletal pain (n = 1).

Interestingly, gastrointestinal and respiratory symptoms were more frequent among travel episodes with pretravel advice than patients without pretravel advice (p = 0.001 and p = 0.027, respectively). Among travel episodes with gastrointestinal symptoms during travel (34/201, 16.9%), in only five (14.7%) had the patient indicated risky eating and drinking habits. Risk behaviour was slightly higher for travelling outside Europe than across Europe and mostly concerned eating and drinking habits (raw fish or meat, and ice cubes). There was no clear trend for health issues during the journey regarding risk behaviour, gender, time since transplantation, immunosuppressive therapy and GvHD. Overall, reported risk behaviour was low. The most frequent risk behaviour while travelling consisted of risky eating habits (34/201, 16.9%), followed by bathing in stagnant water (16/201, 8.0%). Unprotected sex (2/201, 1%) and blood transfusions (1/201, 0.5%) were rare. Nobody reported receiving tattoos or piercings nor close animal contact.

## Discussion

In our study, more than 75% of the allo-HSCT recipients reported travel activity in the previous year. The time since allo-HSCT was the most important predictor for travel activity. Only a minority did not travel, mainly owing to lack of interest, not feeling well or financial reasons. Most

patients travelled to European countries. Pretravel advice was reported by only one-third of allo-HSCT patients. When travelling in Europe or North America respiratory health issues dominated, whereas among travellers to the subtropics and tropics gastrointestinal symptoms were the most frequent symptoms.

In a Canadian study, solid organ transplant recipients showed less difference in median time after transplantation between travelling and non-travelling patients (5 vs 3 years) [20] compared with our study (7 vs 2 years). We would postulate that allo-HSCT patients waited longer for travel activities, because of the initial severity of disease and GvHD with a prolonged immunosuppressed state. With longer time after allo-SCT, the probability of being immunocompromised decreases, in contrast to the situation for solid organ transplant recipients who have a continuous need for immunosuppressive drugs. In a recent study among HSCT patients, the incidence of international travel increased from 13% to 32% between 1 year and 2 years after transplantation [23]. An American study among patients after SOT and patients with haematological diseases showed that travel-related symptoms in immunosuppressed travellers were mostly minor [1]. In our study, the percentages of reported health issues and the hospitalisation rate were comparable to a recently published study among travelling patients after HSCT where 7% had a travel-related illness and 1.8% needed to be hospitalised. In healthy individuals a similar hospitalisation rate of between 0.5% and 2% has been shown [24–26], fever being the most common reason, which is in accordance with our study. Allogeneic HSCT compared with autologous HSCT does not seem to increase incidence of travel-related illness within the first 2 years. Focusing only on patients after allogeneic HSCT and including patients with a longer time since transplantation may increase the percentages of chronic GvHD. Certain reported health issues in our study could be chronic in nature. In the other study among HSCT recipients, 89% reported having had a good or excellent overall health status before travel, whereas we did not ask patients about their wellbeing before departure. Incidence of reported diarrhoeal infections was slightly lower than in healthy individuals travelling to tropical and subtropical destinations, where diarrhoea is the most frequent health issue, affecting up to every third person [23].

In a study among patients with solid tumours, immunosuppressive treatment had less impact on travel related-illness than the infection risk at destination [20]. Nevertheless, it has to be considered that solid tumour patients typically have a milder degree and shorter duration of immunosuppression compared with those with haematological malignancies.

European studies among healthy individuals focus mostly on travel to the subtropics and tropics where the prevalence of pretravel advice is between 50%–65%, which is comparable to our study participants who visited tropical countries. In our study, travel episodes to high-risk countries had higher percentages of pretravel advice than those to low-risk countries, which is similar to a recently published study among HSCT patients. In this study, however, the number of travellers to low-risk countries seeking medical advice from a healthcare provider was higher than in our

**Table 4:** Self-reported vaccination status in 201 travel episodes among patients after allogeneic haematopoietic stem cell transplantation.

Vaccination type	Self-reported vaccination status	
	n	%
Tetanus	89	44.3%
Influenza	85	42.3%
Hepatitis B	63	31.3%
<i>Streptococcus pneumoniae</i>	50	24.9%
Poliomyelitis	40	19.9%
Hepatitis A	31	15.4%
<i>Neisseria meningitidis</i>	24	11.9%
Rabies	8	4.0%
Typhoid	4	2.0%
Japanese encephalitis	3	1.5%

study. This finding could be explained by the wider range of time since transplantation in our study correlating with the lower probability of seeking pretravel advice. Among healthy individuals reasons for not seeking pretravel advice are prior travel experience to a similar country and assumed level of knowledge [27]. This corresponds with common reasons for patients after HSCT not seeking pretravel advice. Additionally, they mentioned no knowledge about pretravel advice and absence of a recommendation by their primary care physician or transplant coordinator to seek pretravel advice. Two-thirds of those HSCT patients not seeking pretravel advice thought it was unnecessary, a level that was even higher than in a study among travelling SOT patients (38%) [3, 23]. In our study, almost all patients with pretravel advice would contact a physician again, while those without would not do so in the future. This may underline the maintenance of accustomed travel patterns and shows the need to identify travelling patients who do not seek pretravel advice by themselves. Interestingly, it has been recently shown that patients after HSCT were more likely to travel internationally soon after HSCT if they were already used to do so before transplantation. Popular European travel destinations such as Italy and Greece might not be considered as high-risk destinations; nevertheless, the current dramatic increase of multidrug-resistant Gram-negative bacteria should not be underestimated after all when treating immunocompromised hosts. In fact, travel returners may easily become colonised with multidrug-resistant bacteria [28].

In our study, patients with a shorter time after allo-HSCT and with immunosuppressive treatment were more likely to seek pretravel advice. Although these two factors by themselves did not increase the probability for travel-related illness, in our study patients with pretravel advice were more often confronted with health issues during their trip. This phenomenon was also shown in another study among travellers ill after HSCT. Also in our study, multivariate analysis to adjust for other confounders could not be conducted because of the low number of travel-related health issues. It might be that patients with a higher susceptibility for health issues were more likely to seek pretravel advice. We did not ask about their wellbeing prior to their travel episode. It is notable that even half of travellers under immunosuppressive treatment did not contact a health professional prior to travel. This is in line with other studies among immunosuppressed travellers [2, 3]. HSCT patients contacted their haematologist for pretravel advice by far the most often, corresponding to another study among HSCT patients [23]. We did not ask whether Internet sources (such as [www.safetravel.ch](http://www.safetravel.ch)) were contacted. However, specific information on the Internet about allo-HSCT and travel is rare. This may underline the need of personal advice by a health professional prior to travel. Another challenge is that pretravel advice is often sought only within 4 weeks before departure by both immunosuppressed and healthy individuals [1, 27]. Within this time period it might not be possible to reach sufficient vaccine-induced immunity and properly prepare for the trip e.g. localization of emergency rooms. Even if patients after HSCT received reminder telephone calls and vaccination cards based on the updated vaccination guidelines, one-third missed at least one vaccination

set within 14 months post-transplant [29]. Therefore, it is recommendable to check patients' vaccination status regularly and to direct their attention to the need of a repeated immunisation after allo-HSCT.

It might be that to the majority in our study no vaccination was recommended because their protection was already sufficient. Nevertheless, a recently published study among hematopoietic cell transplant physicians showed a large gap between the post-HCT guidelines and clinical practice. Only 38% of patients received the first series of vaccinations within the recommended 6 months after HSCT [30]. The most common reasons to withhold or delay vaccines were current use of steroids (70%) and GvHD (87%). Therefore, patients undergoing allo-HCT had an increased risk for being unvaccinated. Based on International Guidelines from 2009 the Official Swiss vaccination recommendations for HSCT patients propose vaccinating regardless of GvHD (acute or chronic) with nonlive vaccines 6 months after stem cell transplantation [31, 32].

In our study fewer than half of the patients could report on their own vaccination status in spite of a generally positive attitude towards vaccination. This is comparable to healthy individuals showed in a study among European travellers, where over one half could not report their protection against hepatitis A or B [33].

This study has some limitations as a result of its retrospective nature and, therefore, considerable recall bias. Under- and over-reporting of symptoms is possible. Nevertheless, we can assume that severe illness and hospitalisation would be remembered and indicated in the questionnaire. It might be that patients with positive travel experiences were more willing to complete the questionnaire than people with less good holiday memories or no travel activity. As we have not performed an analysis of the people not responding to the questionnaire, we cannot rule out a responder bias. As not much detail on the aetiology of reported diseases could be acquired, a clear association between symptoms and travel is difficult. In addition, this study is from a single centre in Switzerland and, therefore, some results might not be directly transferrable to other centres.

Comparisons between studies among other immunocompromised travellers are difficult, as existing studies focus on travellers from North America, who may prefer other travel destinations closer to their home country. Also among healthy individuals travel related issues are more frequently investigated for countries outside of Europe. Furthermore, the study represents data only from a single institution in Switzerland, where the composition of the population may differ from other transplant centres. For example, travellers visiting their families and friends might be under-represented compared with other countries with more immigration history. This possibility has to be considered, as studies showed that this group of patients is especially susceptible for travel-related diseases because they are less cautious about risk behaviour [34]. We did not ask about the origin of the patients and therefore also did not perform an analysis of visiting friends and relatives as a risk factor.

One important strength of this study is the remarkable number of travel episodes among allo-HSCT patients travelling in Europe; however, certain subgroups, such as travel-

related illnesses, were still rare, so that no clear analysis could be performed.

We conclude that patients after allo-HSCT show unexpectedly high travel activity, increasing further with longer time after transplantation. All patients should be encouraged to contact their haematologist prior to travel, as they are most familiar with the complex medical condition of patients after allo-HSCT. On the other hand, haematologists should ask patients regularly about intended travel plans during their annual health visits. Prevention measures such as vaccination should be discussed early enough between patients and their haematologist. Travelling after allo-HSCT can be considered safe, but nevertheless pre-travel advice is crucial. It would be worth striving for further prospective investigations about travel activity in wider populations among patients after allo-HSCT to improve their travel safety and therefore quality of life.

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Figures (large format)

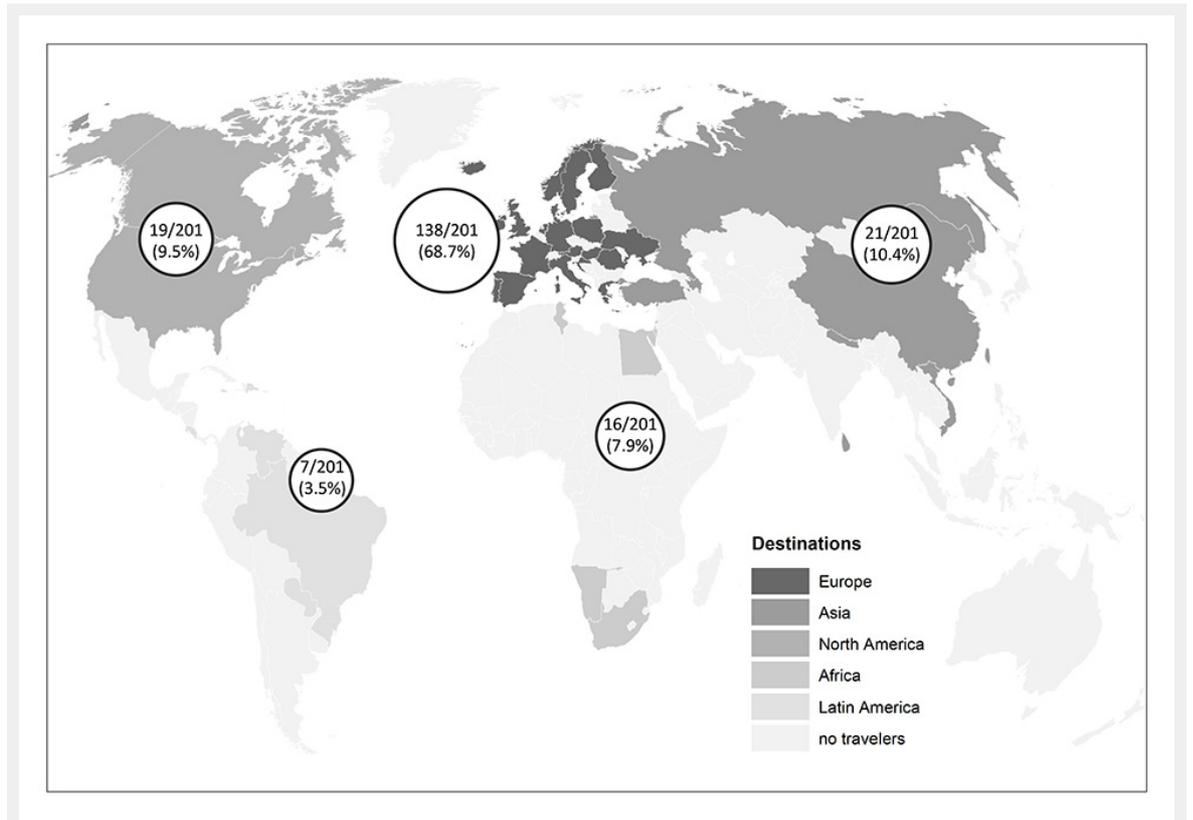


Figure 1

Distribution of reported travel destinations. In total 201 travel episodes were reported.