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Frequency and temporal evolution of COVID-19 vaccination rate among oncological patients undergoing 18F-FDG-PET

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ABSTRACT

Purpose: To evaluate the temporal evolution of vaccination against COVID-19 in a Swiss oncological cohort.

Methods: History of complete vaccination (i.e. at least two vaccine doses) against COVID-19 of patients undergoing oncological 18F-FDG PET/CT between February and September 2021 (n = 2613) was taken. Vaccination rate was compared with age-matched national data from the Swiss Federal Office of Public Health. Subgroup differences in temporal evolution of vaccination rate were analyzed by fitting a generalized linear model and determined by significant interaction between, sex, oncological diagnosis, and month of examination.

Results: Rate of complete vaccination against COVID-19 steadily increased and reached 81 % in September 2021. The fraction of vaccinated patients in the oncological cohort was higher in the beginning and approached the fraction in the age-matched general Swiss population at the end of the study period. Month of exam ($p < 0.001$) was the only significant predictor of the vaccination rate.

Conclusion: Vaccination rate against COVID-19 in a Swiss oncological cohort increased steadily from February to September 2021. Compared to the age-matched general population it was higher in the beginning and similar by the end of the study period.

Ethics approval: Trial registration: BASEC 2021-00444, Ethikkommission Zürich (Cantonal Ethics Committee Zurich), Switzerland, registered February 24th 2021.

1. Introduction

In a global effort to fight the COVID-19 pandemic, vaccines have proven to be effective in reducing COVID-19 incidence, hospital admissions and severe health related events including death [1]. Although heterogeneous, some studies reported an elevated risk for severe COVID-19 related outcomes in cancer patients [2–4]. Despite being proposedly vulnerable to COVID-19, patients with malignancy were often explicitly excluded from key clinical trials due to cancer therapy including immunomodulatory treatment [5]. With the advent of COVID-19 vaccines however, cancer patients were still prioritized to receive the vaccines in many countries. In general, high efficacy and safety of the vaccine and a sufficiently high acceptance and accessibility of the vaccine in the population are necessary for the success of any vaccination program. Yet, available data on frequency of COVID-19 vaccination in cancer patients is limited.

^{18}F-fluorodeoxyglucose (18F-FDG) - positron emission tomography (PET) is a frequently used imaging modality for staging and therapy monitoring in a multitude of oncological diseases [6], with a large number of patients undergoing imaging, especially in Switzerland [7]. Patients are referred to 18F-FDG-PET imaging

Abbreviations: 18F-FDG, ^{18}F-Fluorodeoxyglucose; Astra-Zeneca, AZD1222; SMN, Suspicion for Malignant Neoplasm; FOPH, Swiss Federal Office of Public Health; IQR, Interquartile Range; Moderna, mRNA-1273 Vaccine; PET, Positron Emission Tomography; Pfizer-BioNTech, BNT162b2 Vaccine; Sinopharm, BIBP-CorV Vaccine.

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by a broad array of medical specialties treating cancer, therefore resulting in a large cohort of cancer patients.

Consequently, our study aimed to systematically review the frequency and temporal evolution of vaccination against COVID-19 in an oncological cohort of patients undergoing 18F-FDG-PET, compare it with the general population, and further to identify subgroups of cancer patients with a comparably low vaccination rate.

2. Methods

2.1. Study population

This retrospective, single-center, observational study included patients undergoing clinically indicated oncological 18F-FDG PET/CT between February and September 2021. Clinical data including age, sex, underlying diagnosis with indication for 18F-FDG PET/CT, and information about COVID-19 vaccination including type of vaccine (BNT162b2 [Pfizer-BioNTech], mRNA-1273 [Moderna], AZD1222 [Astra-Zeneca], and BIBP-CorV [Sinopharm]) were recorded. For reference, national data on the prevalence of fully vaccinated (i.e. having received at least two vaccine doses) residents in Switzerland was retrieved from the Swiss Federal Office of Public Health, (FOPH), (data available at https://www.covid19.admin.ch/en/vaccination/persons, accessed November 23rd 2021). To age-match the study cohort, only patients aged 50 years and older were included in the reference cohort. Written informed consent for the scientific use of medical data was obtained from all patients. The study was approved by the local ethics committee.

2.2. Statistical analysis

All statistical analyses were performed in the open-source statistics software R (version 4.1.0, R Foundation for Statistical Computing, Vienna, Austria) [8]. Categorical variables are expressed as frequency distribution. Continuous variables are presented as mean ± standard deviation if normally distributed or median (interquartile range [IQR]) otherwise. The fraction of vaccinated patients was calculated by calendar week and calendar month. National weekly data on the fraction of fully vaccinated people was averaged by month. To assess for subgroup differences in temporal evolution of vaccination fraction, a generalized linear model was fitted. Specifically, sex, oncological diagnosis and month of examination were implemented as predictors, while the fraction of fully vaccinated patients was used as response variable. Assumptions of the model were checked visually with various plots (residuals against fitted values, scale-location plot of square root of residuals against fitted values, normal quantile–quantile plot, Cook's distances against leverage/[1-leverage]). A p-value of < 0.05 was considered statistically significant.

3. Results

3.1. Study cohort

Two thousand six hundred thirteen patients were retrospectively included. The median age was 65 (IQR 55 – 74) years. The most frequent indication for imaging was melanoma (719 / 2613, 28 %) followed by lung cancer (525 / 2613, 20 %) and various ear, nose and throat cancers (247 / 2613, 10 %). Overall, 1759 / 2613 (67 %) patients were vaccinated when undergoing 18F-FDG-PET imaging. Of the vaccinated patients 941 / 1759 (60 %) had received Pfizer-BioNTech, 624 (40 %) had received Moderna and 4 / 1759 (0.2 %) had received Sinopharm or Astra-Zeneca. Demographic data of the cohort are summarized in Table 1.

Table 1
Demographic data of study subjects (n = 2613).

Female/male, n (%)	1081 (41 %) / 1532 (59 %)
Age, years	65 (IQR 55 – 74)
Overall vaccinated / unvaccinated	1759 (67 %) / 854 (33 %)
Vaccine received	
Pfizer-BioNTech	941 (60 %)
Moderna	624 (40 %)
Sinopharm	3 (0.2 %)
Astra-Zeneca	1 (0.1 %)
Indication for imaging	
Melanoma and other skin cancer	719 (27 %)
Lung cancer	525 (20 %)
Ear, nose, throat cancer	247 (10 %)
Lymphoma	180 (7 %)
Breast cancer	145 (6 %)
Colorectal cancer	85 (3 %)
Suspicion for malignant neoplasm	77 (3 %)
Pancreatic cancer	55 (2 %)
Esophageal cancer	46 (2 %)
Other cancer	534 (20 %)

Values are given as absolute numbers and percentages in parenthesis or median (Interquartile Range [IQR].

3.2. Temporal evolution of COVID-19 vaccination rate

During the study period from February to September 2021, the fraction of vaccinated patients increased steadily (Fig. 1). At the beginning of the study period in February 2021, one month after the initiation of the national COVID-19 vaccination campaign in Switzerland in January 2021, 21 % of all patients were fully vaccinated, i.e. had received at least two shots of vaccine (Table 2). This number increased steadily to 54 % in May and reached 81 % in September 2021. The fraction of fully vaccinated patients in the oncological cohort was higher than in the age-matched general Swiss population in the beginning and similar by the end of the study period (Fig. 2).

3.3. Influence of time, sex and diagnosis on vaccination rate

Analyzing the time course of the fraction of fully vaccinated patients, the generalized linear model revealed that month of exam and "suspicion for malignant neoplasm (SMN)" as the indication for undergoing 18F-FDG-PET imaging were significant predictors of the vaccination rate. Specifically, vaccination rate increased on average by 0.09 ($p < 0.001$) with every additional month. Furthermore, patients with SMN exhibited on average a 0.14 ($p = 0.02$) lower vaccination rate as opposed to the average vaccination rate of all patients (after adjusting for month). We found no significant effect of male sex ($p = 0.4$) or of indications for 18F-FDG-PET imaging other than SMN ($p > 0.06$). The time course of the fraction of fully vaccinated patients is visualized in Fig. 3.

4. Discussion

In our study, we assessed the time course of the rate of vaccination against COVID-19 in an oncological cohort. Our major findings are as follows: First, the vaccination rate in our cohort increased steadily from February to September 2021. Second, vaccination rates were higher in our oncological cohort than in the age-matched general population in the beginning and similar by the end of the study period. Third, we found a significantly lower vaccination rate in patients with SMN compared to patients with oncological diseases. Fourth we could not identify a difference in vaccination rates for sex or the underlying malignant diseases.

To this point, data available on COVID-19 vaccination rate in cancer patients remains sparse with only few studies reporting

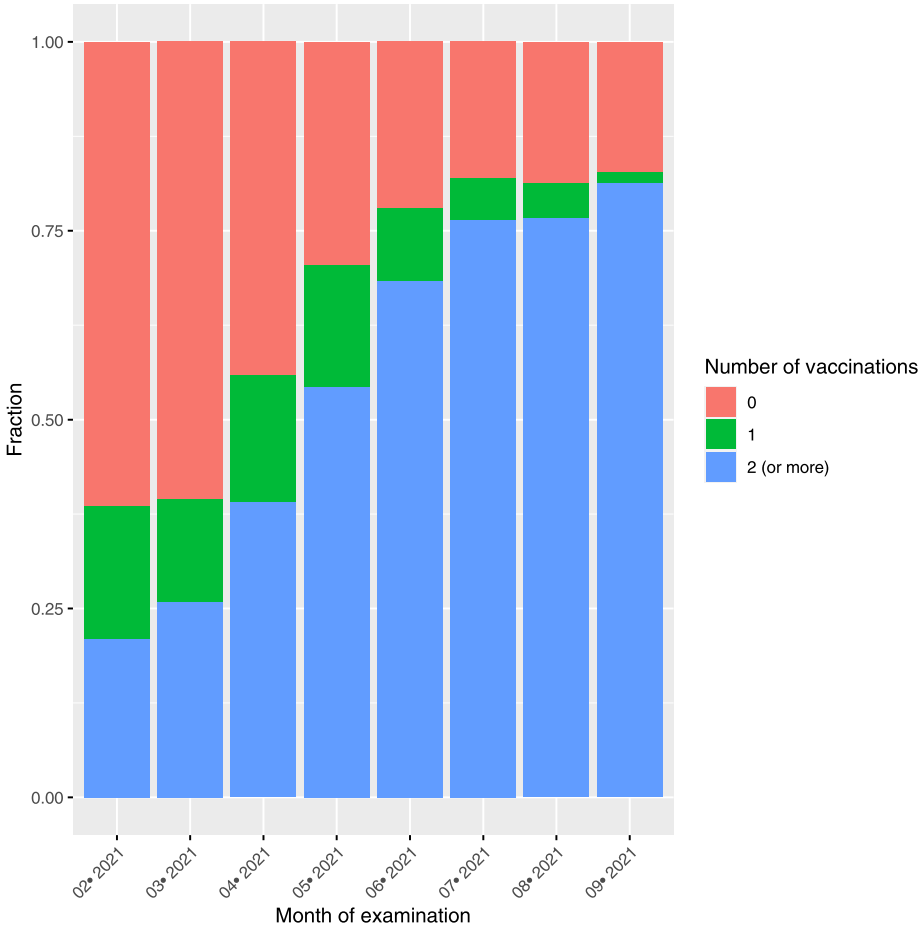

Fig. 1. Temporal evolution of the fraction of vaccinated patients as bar plots. The fractions of unvaccinated patients (red), patients having received one dose (green) and at least two doses (blue) of COVID-19 vaccine are illustrated monthly over the study period. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 2
Fraction of fully vaccinated patients by month.

		Fully vaccinated		
Month of exam	***n***	**all**	**female**	**male**
February	30	21 %	22 %	20 %
March	91	26 %	26 %	25 %
April	162	39 %	35 %	42 %
May	222	54 %	50 %	58 %
June	305	68 %	66 %	70 %
July	318	76 %	73 %	79 %
August	282	77 %	74 %	78 %
September	52	81 %	83 %	79 %

Values are given as absolute numbers and percentages.

willingness to receive the vaccine [9–11] and even fewer evidence reporting the real world prevalence of vaccination [12]. To our knowledge, our study represents the first description of COVID-19 vaccination rate in cancer patients in Switzerland. As cancer patients are amongst the most vulnerable to COVID-19 infections and some reports show decreased efficacy of the vaccines – possibly due to immunosuppressant effects of cancer therapy - widespread adoption of vaccination is of utmost importance. To this respect, we observed high acceptance of the vaccine in our cohort, a promising finding for an effective strategy to conquer COVID-19 overall and decrease the incidence of COVID-19-associated severe events in oncological patients. Our findings parallel the increased acceptance of COVD-19 vaccination found in cancer patients in a global survey including 21,294 patients with serious comorbidities by Tsai et al. [13] and are comparable to a similar cohort of 1073 cancer patients in Australia of which 65.2 % had received at least one dose by August 2021 [14]. Vaccination rate was lower in patients with SMN than in oncological diagnoses. This might be since a large fraction of these patients may not have an established diagnosis of cancer at the time of 18F-FDG-PET. These patients may therefore not have been enforced to get vaccinated in the same manner patients with proven cancer have been at the same time.

Our study has some limitations. As it is a single-center study, generalizability is inherently reduced. Although the cohort included a wide range of oncological diagnoses, not all cancers are routinely imaged with 18F-FDG-PET. Explicitly, tumors which do not generally display a high rate of glucose metabolism, especially non-solid malignancies, neuroendocrine tumors, or prostate cancer are not part of the study and this constitutes a selection bias. Further, we compared our cohort to an age-matched subgroup of the overall Swiss population without correcting for the actual distribution of age, as this data was unavailable. The comparably high vaccination rates in our cohort might therefore be overestimated to some extent.

Our results suggest overall high vaccination rates in cancer patients in Switzerland, which steadily increased from February to September 2021. We found higher vaccination rates in cancer patients than in the age-matched general population at the beginning of the study period, a promising finding for the successful and effective progress of the COVID-19 vaccination campaigns in patients with cancer.

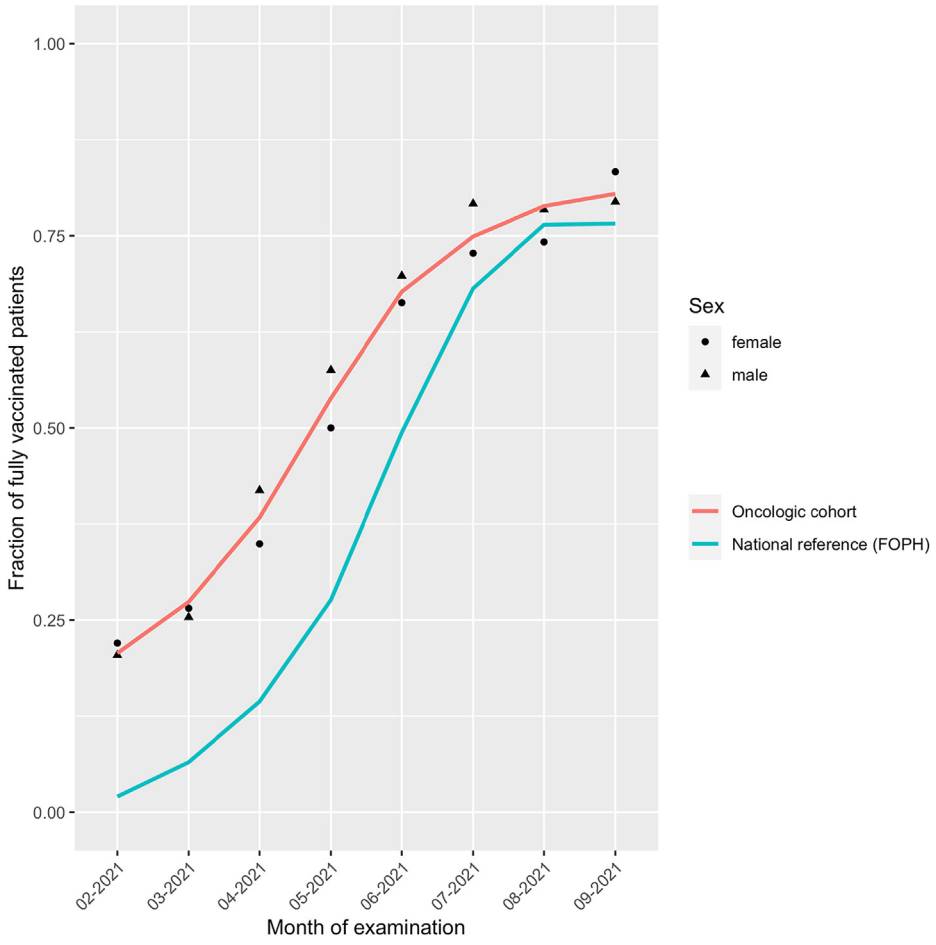

Fig. 2. Temporal evolution of the monthly fraction of fully vaccinated patients, separately for women (circles) and men (triangles) of the study cohort (red) and national data of patients aged 50 years and older as a reference (turquoise, data from the Federal Office of Public Health in Switzerland [FOPH], data on sex unavailable). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Data availability

Data will be made available on request.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Stephan Skawran reports financial support was provided by Palatin Foundation, Switzerland. Michael Messerli reports financial support was provided by Iten-Kohaut Foundation, Switzerland. Michael Messerli reports financial support was provided by CRPP AI Oncological Imaging Network of the University of Zurich. Martin W. Huellner reports financial support was provided by CRPP AI Oncological Imaging Network of the University of Zurich. Martin W. Huellner reports financial support was provided by GE Healthcare. Martin W. Huellner reports financial support was provided by Alfred and Annemarie von Sick legacy for translational and clinical cardiac and oncological research. The University Hospital of Zurich holds a research agreement with GE Healthcare (unrelated to current study).

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Availability of data and material

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable eth-

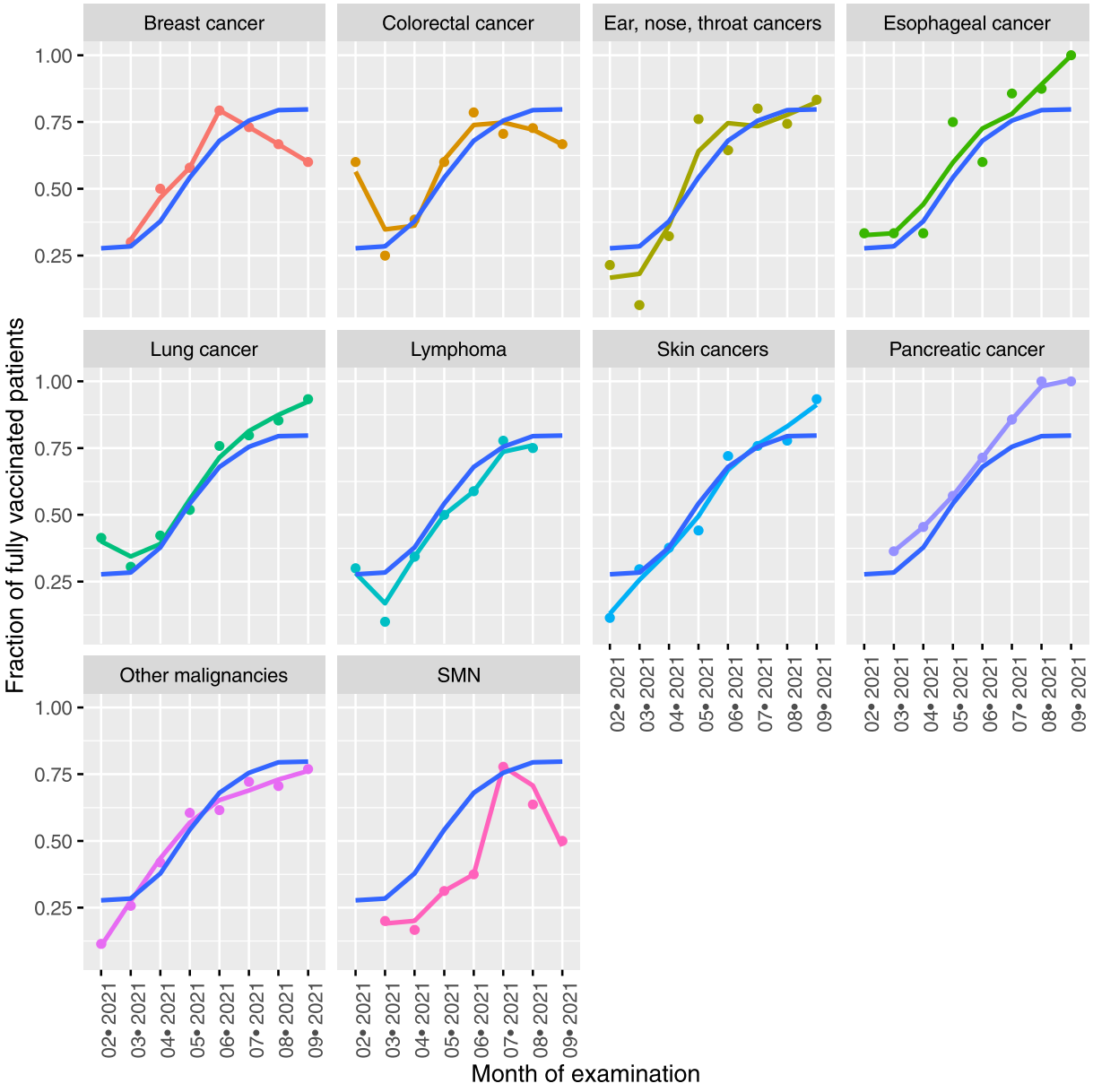

Fig. 3. Time series of the monthly fraction of fully vaccinated patients, separately for the various indications for 18F-FDG-PET imaging. Data are shown with a locally fitted regression line of the overall cohort (blue). SMN: Suspicion for malignant neoplasm. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

ical standards. This retrospective study protocol was approved by the local institutional ethics committee and written informed consent for the scientific use of medical data was obtained from all patients (Trial No. BASEC-Nr. 2021-00444).

Consent for publication

Not applicable.

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