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Original Article

Duration of mild acute SARS-CoV-2 infections with Omicron depending on previous vaccinations and infections – Using data of the German DigiHero cohort study from post-pandemic winters 2022/2023 and 2023/2024

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ABSTRACT

Objectives: Protection against severe course of SARS-CoV-2 infection after COVID-19 vaccination or infection was extensively studied. It is unknown whether this effect also translates into shortened duration of mild infections. We assessed the duration of symptoms depending on vaccination status and previous SARS-CoV-2 infections among individuals with a mild course of infection.
Methods: For two post-pandemic winters (2022/2023 and 2023/2024), in total 13,615 participants of the German DigiHero study reported their SARS-CoV-2 infections from September to March. Via negative binomial regression adjusting for sociodemographic factors, we studied the association of infection duration (days with symptoms and in bed) with number of vaccinations, prior SARS-CoV-2 infections, and time since last vaccination/and infection.
Results: We noted no major differences in infection duration depending on the number of vaccinations and time since last infection for short mild infections (≤21 days with symptoms). Per 6 months since the last vaccination, symptom duration and days spent in bed increased by 2 % and 4 %. The risk of long mild SARS-CoV-2 infections (> 21 days with symptoms) was higher for individuals with no prior SARS-CoV-2 infection (Odds Ratio: 1.98; 95 % confidence interval [1.43; 2.76]), but not for vaccinations (OR: 0.98; 95 % CI [0.74; 1.33]).
Conclusions: There was no indication of reduced duration of symptoms during short mild infections depending on the number of vaccinations and time since the last SARS-CoV-2 vaccination or infection. A prior SARS-CoV-2 infection was protective against prolonged disease in mild SARS-CoV-2 infections.

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Introduction

Background

As of November 2021, Omicron has been classified as the fifth SARS-CoV-2 variant of concern (VOC) by the World Health Organization (WHO) [1]. Omicron has a higher transmissibility compared to previous VOCs [2]. Given its immune evading properties, protection offered by vaccines or previous infections are limited [2].

Several studies demonstrated that two doses of mRNA vaccines achieved only 33–52 % protection against Omicron after 3–6 months and onwards decreased further [3–6]. Compared to the third dose, vaccine effectiveness (VE) of the fourth dose against Omicron infection peaked in the first month with 57 % and decreased to 22 % after 3 months (meta-analysis: [7]). Immunity against Omicron induced by a previous SARS-CoV-2 infection was similarly investigated, revealing a protection against both reinfection and symptomatic disease of 45 % and 44 % (meta-analysis [8]).

Unlike protection against infection, VE remained high against severe course of disease, hospitalization and the need for intensive care treatment in Omicron infections [6,9]. A recent meta-analysis reported that VE against severe infections with Omicron was relatively high at 64 % and 71 % for single and multiple times boosted individuals, respectively [10]. Similarly, meta-analyses suggested a protective effect of previous SARS-CoV-2 infections against severe course of disease (hospitalization or death) for Omicron [8,11].

Less evidence is available on whether vaccination and prior SARS-CoV-2 infections also shorten the duration of milder courses of disease, not requiring hospitalization. Two cohort studies estimated the duration of symptoms for SARS-CoV-2 infections with Omicron [12,13]. Only one of the studies assessed a possible association with increasing time since the last vaccination [14], though this could not be analyzed in great detail as only a small number of infected individuals was included. Further, no studies assessed the effects of previous SARS-CoV-2 infections.

As SARS-CoV-2 has turned into an endemic pathogen, it adds to the seasonal burden of acute respiratory infections (ARI) [15,16]. In a previous publication, we estimated the excess ARIs related to SARS-CoV-2 in Germany in a post-pandemic winter season at 21 % [17]. In July 2021, vaccination prioritization was abolished and vaccination became freely accessible for everyone in Germany [18]. Since the end of the pandemic in May 2023, the German Standing Committee on Vaccination (STIKO) recommends an initial immunization against SARS-CoV-2 for all individuals over 18 years, achieved via three antigen contacts with the virus (through vaccination or infection) [19,20]. Since winter 2022, recommendations suggested at least one booster vaccination for individuals aged between 18 and 59 and at least two booster shots for the elderly above 60 [20]. This was updated in 2024, with the STIKO recommending yearly booster for individuals above 60 [21].

Objectives

We aimed to investigate the association between vaccination status and previous SARS-CoV-2 infection history with the duration of mild SARS-CoV-2 infections. In addition, we analyzed the association with increasing time since vaccination and infection.

Methods

Study design and study participants

This study used data from the German population-based cohort for digital health research (DigiHero, DRKS Registration-ID: DRKS00025600). The study design of DigiHero was described elsewhere [22]. In brief, participants from 13 federal states were recruited via postal letters; the following study participation takes place online only. Inclusion criteria for the selection of potential study participants were year of birth between 1936 and 2003, main residence in the selected city/municipality, no blocking notice in register for addresses. Further, there is an option to register directly via the DigiHero website without having received an invitation for all individuals over 18. The study was approved by the Ethics Committee of the Martin Luther University Halle-Wittenberg (2020–076). Informed consent from all participants was obtained during the online registration process.

Questionnaires and study size

Data on SARS-CoV-2 infections during the winter season of September 2022 to March 2023 and COVID-19 vaccinations were collected via an online-questionnaire over the course of March to May 2023. This survey was sent to 70,538 participants registered in DigiHero. Individuals reporting infections were asked whether they conducted a test and if yes, to report the result. Those, who reported their first SARS-CoV-2 infection in this time window, were asked about the symptom duration and the number of days spent in bed during infection in a follow up questionnaire. Data on SARS-CoV-2-infections during the winter season of September 2023 to March 2024 were obtained via another online-questionnaire during April and May 2024 sent to 80,593 DigiHero participants. In this questionnaire, every individual reporting a SARS-CoV-2 infection was asked about symptom duration and number of days spent in bed. In winter 2023/2024, individuals only reported the month of SARS-CoV-2 vaccinations received during that winter plus the total number of ever received SARS-CoV-2 vaccinations. A detailed outline on the exclusion criteria and response is depicted in a flowchart (Fig. 1).

Variables

The study was conducted in Germany during the dominance of the Omicron variant [23]. In previous analyses only 1 % of the infected in the DigiHero sample were admitted to the hospital [24]. Therefore, we considered the reported SARS-CoV-2 infections as mild, but subdivided these into two groups: those with reported symptoms shorter than 21 days (short mild infections) and those with a reported symptom duration of over 21 days (long mild infections). For vaccination status, three vaccine doses were considered as having received a single booster and four or more vaccine doses as multiple boosters. We further considered the type of immunity, divided into two main groups: only vaccinated and hybrid immunity (vaccinated and previously infected with SARS-CoV-2; no respondents were only infected). These groups were further stratified by the number of received booster doses. The collected data were merged with information on sociodemographic characteristics obtained in the baseline questionnaire. Education was categorized into low, medium and high, using the International Standard Classification of Education (ISCED-97) [25]. Further, individuals were categorized according to net household income and social class determined via the Winkler-Index, as described in a previous paper [17]. Further details on all relevant outcome variables and covariates can be found in the appendix (Appendix).

Statistical analysis

In a descriptive analysis of the study population and of SARS-CoV-2 infected individuals, we show frequencies and percentages. As in a previous study, analyses on symptom duration were conducted for all individuals reporting a mild infection with a recovery within 21 days [13]. We report the mean number of days with

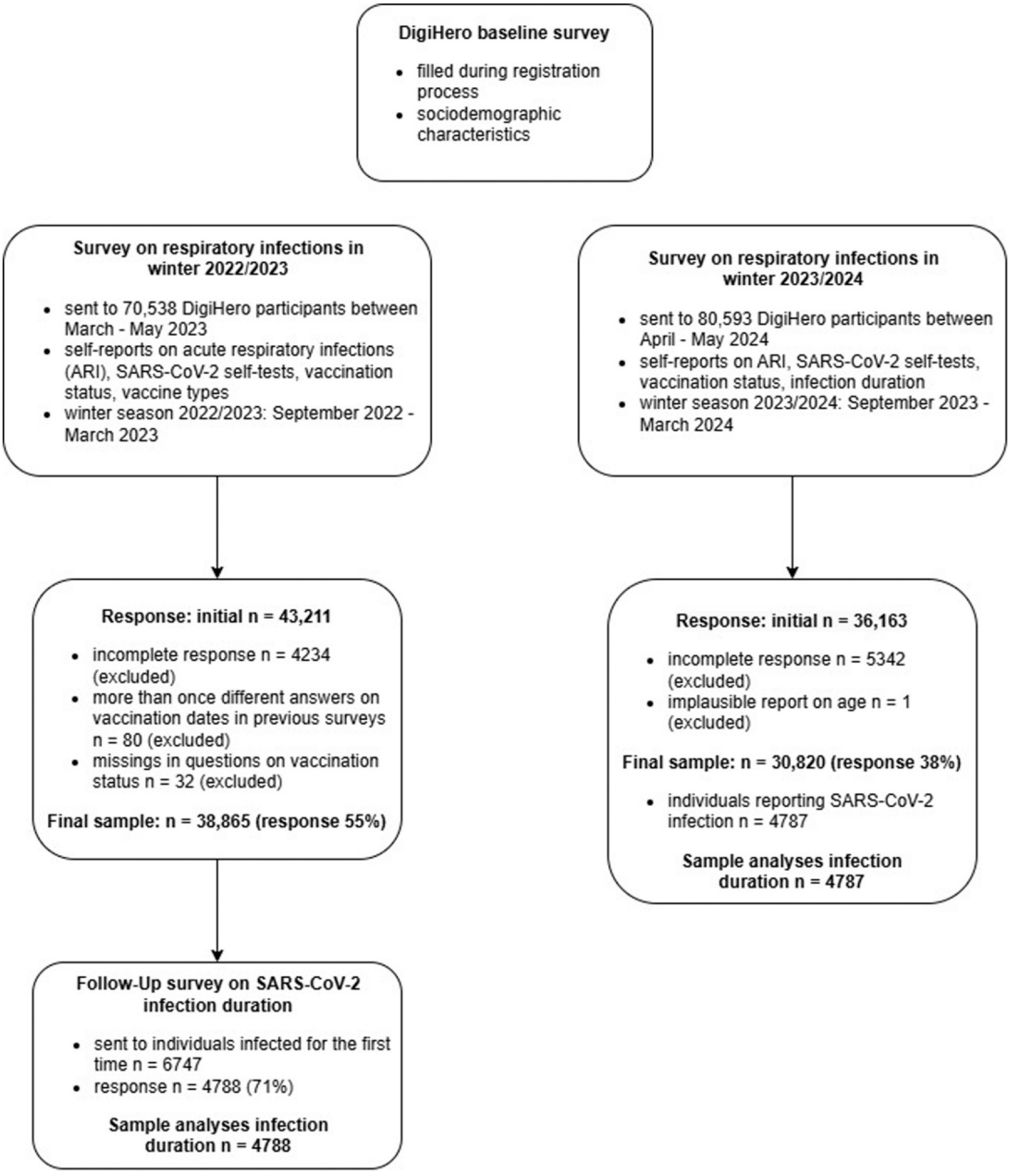

Fig. 1. Flowchart of the two surveys: in winter 2022/2023[a] and winter 2023/2024[b]. [a] September 2022 to March 2023; [b] September 2023 to March 2024.

symptoms and days spent in bed during an episode of COVID-19 stratified by the number of received vaccinations. We further calculated the time since the last received SARS-CoV-2 vaccine, and for reinfected individuals, the time since the last SARS-CoV-2 infection in months. The relative duration of symptoms and days spent in bed during infection were determined depending on the number of received vaccine doses, time since last vaccination and infection, previous SARS-CoV-2 infection history and sociodemographic factors using a negative binomial model. This association was additionally analyzed regarding time since last vaccination, time since last infection and age using generalized additive models (GAMs) adjusted for the number of vaccinations. Two model types using different smoothing methods were fitted: first, splines model using Restricted Maximum Likelihood (REML); (2) second, model using Locally Weighted Scatter Plot Smoothing (LOESS). Further, we assessed the association between long mild infections (recovery > 21 days) and the aforementioned vaccination variables and SARS-CoV-2 infection history, via a logistic regression adjusting for sociodemographic factors. All regression analyses were repeated, assessing the potential effect of a single booster dose compared to multiple booster doses and the type of immunity on short mild infection duration and the risk of long mild infections. All models have been checked for multicollinearity by assessing the Variance Inflation Factors (VIF) and tolerance. Regression results are presented as estimates and corresponding 95 % confidence intervals of the estimates. GAM model figures present estimates and corresponding point-wise 95 % confidence intervals. Statistical analysis was conducted in R version 4.2.2 using the packages “MASS”, “mgcv”, and “gam” [26–28]. Further details on statistical models can be found in the appendix (Appendix).

Table 1
Sociodemographic characteristics of individuals infected for the first time or for a repeated time[c] in winter 2022/23 and winter 2023/2024.

Characteristic	Value	Winter 2022/2023[a]			Winter 2023/2024[b]		
		Infection in winter 2022/2023 N [%] (n = 9740)	First-infections N [%] (n = 6747)	Reinfection N [%] (n = 2586)	Infection in winter 2023/2024 N [%] (n = 4787)	First-infections N [%] (n = 1123)	Reinfection N [%] (n = 2482)
Sex	Female	6236 [64.0]	4107 [60.9]	1865 [72.1]	3357 [70.1]	773 [68.8]	1874 [75.5]
	Male	3430 [35.2]	2591 [38.4]	712 [27.5]	1214 [25.4]	342 [30.5]	585 [23.6]
	Diverse	6 [0.1]	5 [0.1]	1 [0.0]	/	/	/
	Missing	68 [0.7]	44 [0.7]	8 [0.3]	216 [4.5]	8 [0.7]	23 [0.9]
Age Group	18–29	771 [7.9]	454 [6.7]	271 [10.5]	221 [4.6]	35 [3.1]	112 [4.5]
	30–39	1495 [15.3]	882 [13.1]	545 [21.1]	652 [13.6]	117 [10.4]	366 [14.7]
	40–49	1762 [18.1]	1043 [15.5]	627 [24.2]	808 [16.9]	139 [12.4]	491 [19.8]
	50–59	2541 [26.1]	1793 [26.6]	638 [24.7]	1300 [27.2]	296 [26.4]	738 [29.7]
	60–69	2088 [21.4]	1641 [24.3]	390 [15.1]	1101 [23.0]	335 [29.8]	547 [22.0]
	≥ 70	997 [10.2]	877 [13.0]	101 [3.9]	481 [10.0]	195 [17.4]	198 [8.0]
	Missing	86 [0.9]	57 [0.8]	14 [0.5]	224 [4.7]	6 [0.5]	30 [1.2]
N of Household members	1	1635 [16.8]	1236 [18.3]	362 [14.0]	916 [19.1]	279 [24.8]	431 [17.4]
	2	4820 [49.5]	3608 [53.5]	1050 [40.6]	2189 [45.7]	618 [55.0]	1132 [45.6]
	3	1571 [16.1]	1013 [15.0]	479 [18.5]	733 [15.3]	131 [11.7]	441 [17.8]
	4	1231 [12.6]	648 [9.6]	500 [19.3]	554 [11.6]	70 [6.2]	351 [14.1]
	≥ 5	367 [3.8]	173 [2.6]	169 [6.5]	173 [3.6]	20 [1.8]	100 [4.0]
	Missing	116 [1.2]	69 [1.0]	26 [1.0]	222 [4.6]	5 [0.4]	27 [1.1]
Education	Low	241 [2.5]	146 [2.2]	80 [3.1]	104 [2.2]	21 [1.9]	53 [2.1]
	Medium	2841 [29.2]	1927 [28.6]	794 [30.7]	1357 [28.3]	322 [28.7]	715 [28.8]
	High	6193 [63.6]	4349 [64.5]	1602 [61.9]	2905 [60.7]	729 [64.9]	1585 [63.9]
	Missing	465 [4.8]	325 [4.8]	110 [4.3]	421 [8.8]	51 [4.5]	129 [5.2]
Net household equivalent Income	Below 1250€	836 [8.6]	533 [7.9]	250 [9.7]	392 [8.2]	94 [8.4]	208 [8.4]
	1250 - < 1750€	1865 [19.1]	1269 [18.8]	515 [19.9]	879 [18.4]	230 [20.5]	463 [18.7]
	1750 - < 2250€	1393 [14.3]	828 [12.3]	495 [19.1]	669 [14.0]	125 [11.1]	384 [15.5]
	2250 - < 3000€	2417 [24.8]	1718 [25.5]	613 [23.7]	1188 [24.8]	291 [25.9]	645 [26.0]
	3000 - < 4000€	2173 [22.3]	1635 [24.2]	462 [17.9]	963 [20.1]	257 [22.9]	509 [20.5]
	4000 - < 5000€	90 [0.9]	66 [1.0]	23 [0.9]	47 [1.0]	8 [0.7]	26 [1.0]
	≥ 5000€	59 [0.6]	39 [0.6]	19 [0.7]	41 [0.9]	9 [0.8]	19 [0.8]
	Missing	907 [9.3]	659 [9.8]	209 [8.1]	608 [12.7]	109 [9.7]	228 [9.2]
Social class	Lower class	858 [8.8]	561 [8.3]	253 [9.8]	430 [9.0]	104 [9.3]	226 [9.1]
	Middle class	4279 [43.9]	2852 [42.3]	1234 [47.7]	1990 [41.6]	479 [42.7]	1092 [44.0]
	High class	3499 [35.9]	2533 [37.5]	841 [32.5]	1648 [34.4]	412 [36.7]	885 [35.7]
	Missing	1104 [11.3]	801 [11.9]	258 [10.0]	719 [15.0]	128 [11.4]	279 [11.2]
Federal state	Baden-Württemberg (only city of Stuttgart)	121 [1.2]	76 [1.1]	39 [1.5]	68 [1.4]	15 [1.3]	38 [1.5]
	Bavaria	860 [8.8]	557 [8.3]	252 [9.7]	386 [8.1]	94 [8.4]	217 [8.7]
	Berlin	127 [1.3]	95 [1.4]	25 [1.0]	66 [1.4]	14 [1.2]	37 [1.5]
	Brandenburg	852 [8.7]	603 [8.9]	227 [8.8]	381 [8.0]	102 [9.1]	210 [8.5]
	Hamburg	145 [1.5]	104 [1.5]	36 [1.4]	70 [1.5]	20 [1.8]	35 [1.4]
	Lower Saxony	580 [6.0]	435 [6.4]	135 [5.2]	558 [11.7]	59 [5.3]	137 [5.5]
	Mecklenburg-Western Pomerania	564 [5.8]	422 [6.3]	123 [4.8]	235 [4.9]	64 [5.7]	138 [5.6]
	Rhineland-Palatinate	1290 [13.2]	944 [14.0]	276 [10.7]	544 [11.4]	130 [11.6]	321 [12.9]
	Saarland	361 [3.7]	264 [3.9]	90 [3.5]	158 8 [3.3]	42 [3.7]	80 [3.2]
	Saxony	1678 [17.2]	1049 [15.5]	526 [20.3]	728 [15.2]	184 [16.4]	424 [17.1]
	Saxony-Anhalt	2345 [24.1]	1588 [23.5]	666 [25.8]	1197 [25.0]	301 [26.8]	698 [28.1]
	Schleswig-Holstein	650 [6.7]	508 [7.5]	131 [5.1]	261 [5.5]	94 [8.4]	136 [5.5]
	Other	27 [0.3]	15 [0.2]	10 [0.4]	95 [2.0]	3 [0.3]	9 [0.4]
	Missing	140 [1.4]	87 [1.3]	50 [1.9]	40 [0.8]	1 [0.1]	2 [0.1]

[a] September 2022 to March 2023.
[b] September 2023 to March 2024.
[c] In winter 2022/2023 individuals directly reported whether they had ever been infected with SARS-CoV-2. In contrast, in 2023/2024 previous infection history was determined by infections reported in previous questionnaires.

Results

Response and characteristics of study participants

Between March and May 2023, 43,211 DigiHero participants reported on their respiratory infections in the winter season 2022/2023. Individuals with incomplete questionnaires (n = 4234) were excluded from the analysis In addition, individuals who more than once gave different answers on vaccination dates in previous questionnaires (n = 80) or who did not report an answer to all questions regarding vaccination were excluded (n = 32), resulting in a final sample size of 38,865 for the winter season 2022/2023 (response 55 %). Between April and May 2024, 30,821 individuals provided complete questionnaires on respiratory infections in the winter season 2023/2024. Due to implausible reports regarding age, one person was excluded, resulting in a final sample size of 30,820 for winter season 2023/2024 (response 38 %). Comparison between the two samples revealed some differences in sociodemographic characteristics (Table S1).

SARS-CoV-2 infections were classified according to self-reported positive testing results. While in winter 2022/2023 testing was conducted for 79 % of all reported ARI, this number decreased to 55 % in winter 2023/2024.

25 % of the participants reported an infection with SARS-CoV-2 during winter 2022/2023. Out of these, 69 % reported that this was their first infection (Table 1). In winter 2023/2024, 16 % of the participants reported a positive test for SARS-CoV-2, with 23 % of these individuals being infected for the first time and 52 % reinfected,

Table 2
Duration of acute SARS-CoV-2 infections, by number of previous vaccinations, Including only individuals who reported a recovery within 21 days. Data on infections reported in winter 2022/2023 include only first-infected individuals. Data on infections reported in winter 2023/2024 include first and reinfections.

Number of vaccinations	Infected N	Infected % [95 % CI*]	Mean number of days with symptoms [95 % CI*]	Mean number of days in bed [95 % CI*]
Winter 2022/2023[a] [n = 4184]				
0	120	2.9 [2.4; 3.4]	7.8 [6.8; 8.9]]	2.9 [2.4; 3.4]
1–2	235	5.6 [4.9; 6.4]	8.3 [7.6; 9.0]	2.6 [2.3; 3.0]
3	2585	61.8 [60.3; 63.3]	8.8 [8.6; 9.0]]	3.0 [2.9; 3.1]
4	1126	26.9 [25.6; 28.3]	8.2 [7.9; 8.5]]	2.3 [2.1; 2.4]
> 4	111	2.7 [2.2; 3.2]	8.5 [7.4; 9.6]	2.2 [1.7; 2.8]
Missing	7	0.2 [0.1; 0.4]	11.9 [5.7; 18.0]	4.7 [1.3; 8.1]
Winter 2023/2024[b] [n = 4415]				
0	122	2.8 [2.3; 3.3]	8.4 [7.6; 9.1]	3.3 [2.8; 3.8]
1–2	302	6.8 [6.1; 7.6]	9.0 [8.5; 9.5]	3.8 [3.5; 4.1]
3	1930	43.7 [42.2; 45.2]	8.9 [8.7; 9.1]	3.8 [3.6; 3.9]
4	715	16.2 [15.1; 17.3]	9.2 [8.8; 9.5]	3.5 [3.3; 3.8]
> 4	350	7.9 [7.2; 8.8]	9.3 [8.8; 9.9]	3.6 [3.2; 4.0]
Missing	996	22.6 [21.3; 23.8]	9.0 [8.8; 9.3]	4.0 [3.8; 4.2]

* CI – Confidence interval.
[a] September 2022 to March 2023.
[b] September 2023 to March 2024.

based on answers to previous questionnaires in DigiHero, while for 25 % of the infected individuals the previous history of SARS-CoV-2 infections was not available.

Outcome data

Participants reported a recovery within 21 days for 4184 (87 % of individuals reporting symptom duration; n = 4788 infections) and 4415 (92 % of individuals reporting symptom duration; n = 4787 infections) SARS-CoV-2 infections in winter 2022/2023 and winter 2023/2024, respectively. We observed a mean symptom duration of 8.6 days [95 % CI: 8.4; 8.7] (winter 2022/2023) and 9.0 days [95 % CI: 8.9; 9.1] (winter 2023/2024) and a mean of 2.8 days [95 % CI: 2.7; 2.9] (winter 2022/2023) and 3.8 days [3.7; 3.9] (winter 2023/2024) spent in bed during infection among those with symptoms ≤ 21 days (short mild infections). The majority of individuals reporting symptom durations had received mRNA vaccines only (72 % winter 2022/2023; 54 % winter 2023/2024). A smaller part had received both vector and mRNA vaccines over time (24 % in winter 2022/2023; 17 % in winter 2023/2024). For winter 2023/2024, no data on vaccine type was available for 29 % of the sample.

Main results

Short mild infections (symptom duration ≤21 days)

We compared the mean reported symptom duration and mean number of days spent in bed depending on the number of previous SARS-CoV-2 vaccinations (Table 2). There was a difference between three and four vaccinations in 2022/23 but not in 2023/24, consistent with the notion of waning vaccine protection over time (given the substantially shorter time since last vaccination for participants with fourth vaccination in 2023/2023 compared to 2023/2024, Table S2). At the same time, the effect was not very strong and even less pronounced for the mean duration of symptoms. An additional stratification by time since infection revealed also no consistent association between the time and the reported duration of mild infections for either winter season, suggesting no major effect of increased reporting time in either winter season (Table S3).

In multivariable analysis of the relative infection duration, which was conducted separately for each winter season, the number of vaccinations was not associated with the symptom duration and number of days spent in bed (Table 3). However, there was a

Table 3
Association of sociodemographic variables and vaccination status with symptom duration and days spent in bed during infection. Relative durations are presented from multivariable negative binomial regression adjusted for all displayed variables. After exclusion of individuals who did not recover within 21 days or had missing data on any of the sociodemographic variables, 3352 (winter 2022/2023) and 2765 individuals (winter 2023/2024) were included in the analysis. Size of the individual groups in brackets. Data on infections reported in winter 2022/2023 include only first-infected individuals. Data on infections reported in winter 2023/2024 include first and reinfections.

Characteristic	Relative Duration [95 % CI*] Symptom duration	Days spent in bed during infection
Winter 2022/2023[a] [n = 3352]		
Sex		
Female [Ref.] (n = 1984)	1.00	1.00
Male (n = 1368)	0.83 [0.79; 0.86]	0.72 [0.67; 0.77]
Age (per additional 10 years)	0.98 [0.97; 1.00]	0.87 [0.85; 0.89]
Social class		
Lower class (n = 273)	1.07 [0.99; 1.16]	1.08 [0.94; 1.23]
Middle class (n = 1598)	1.07 [1.02; 1.12]	1.13 [1.04; 1.21]
High class [Ref.] (n = 1481)	1.00	1.00
Number of vaccinations (per additional vaccination)	1.01 [0.96; 1.06]	0.96 [0.89; 1.04]
Time since last vaccination (per additional 6 months)	1.02 [0.98; 1.06]	1.04 [0.98; 1.11]
Winter 2023/2024[b] [n = 2765]		
Sex		
Female [Ref.] (n = 2016)	1.00	1.00
Male (n = 749)	0.91 [0.88; 0.95]	0.82 [0.76; 0.87]
Age (per additional 10 years)	1.01 [1.00; 1.03]	0.95 [0.93; 0.97]
Social class		
Lower class (n = 268)	1.14 [1.07; 1.21]	1.32 [1.19; 1.46]
Middle class (n = 1331)	1.05 [1.01; 1.09]	1.10 [1.04; 1.18]
High class [Ref.] (n = 1166)	1.00	1.00
Number of vaccinations (per additional vaccination)	1.00 [0.97; 1.04]	1.04 [0.98; 1.10]
Time since last vaccination (per additional 6 months)	1.01 [0.99; 1.03]	1.04 [1.00; 1.07]
Previous SARS-CoV-2 infection		
Yes [Ref.] (n = 1903)	1.00	1.00
No (n = 862)	1.18 [1.14; 1.23]	1.25 [1.17; 1.34]

* CI – Confidence interval.
[a] September 2022 to March 2023.
[b] September 2023 to March 2024.

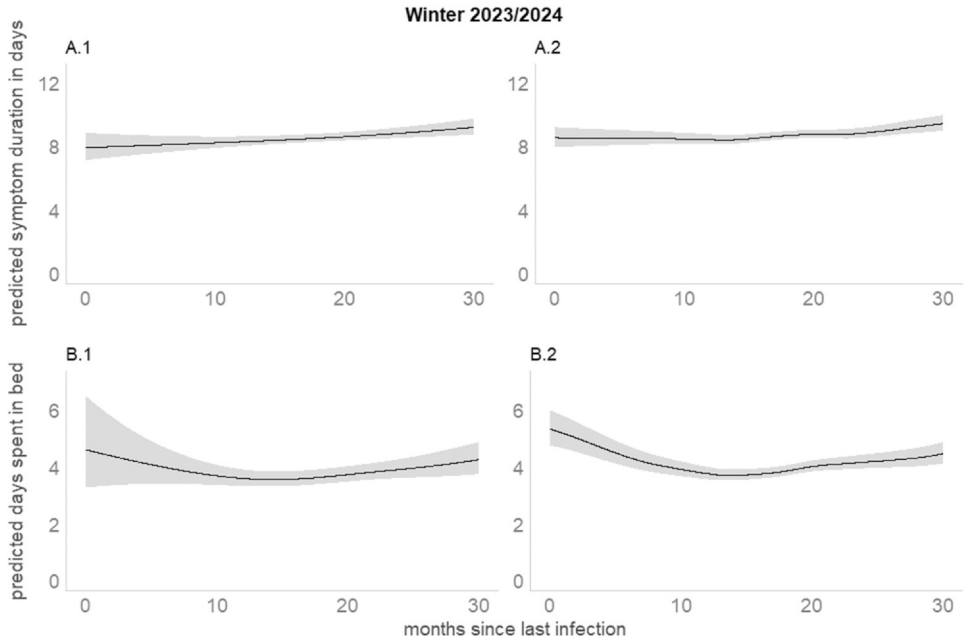

Fig. 2. Association of time since last infection with symptom duration (A) and days spent in bed (B) during mild acute SARS-CoV-2 infections in winter 2023/2024[a]. (1 – splines model using R package "mgcv"; 2 – LOESS model using R package "gam"; gray bands representing the point-wise 95 % confidence interval of the predicted symptom duration in days and days spent in bed, respectively; a – September 2023 to March 2024).

Table 4
Association of sociodemographic variables and vaccination status with long SARS-CoV-2 infections with Omicron. Odds Ratios for long SARS-CoV-2 infections with Omicron are presented from multivariable logistic regression adjusted for all displayed variables. Infections with symptom durations over 21 days were classified as long infections (winter 2022/2023 n = 604; winter 2023/2024 n = 281). After exclusion of individuals with missing data on any of the sociodemographic variables, 3835 (winter 2022/2023) and 2930 individuals (winter 2023/2024) were included in the analysis. Size of the individual groups in brackets. Data on infections reported in winter 2022/2023 include only first-infected individuals. Data on infections reported in winter 2023/2024 include first and reinfections.

Characteristic	Odds Ratio [95 % CI*]
Winter 2022/2023[a] [n = 3835]	
Sex	
Female [Ref.] (n = 2315)	1.00
Male (n = 1520)	0.68 [0.55; 0.84]
Age (per additional 10 years)	0.99 [0.92; 1.06]
Social class	
Lower class (n = 320)	1.19 [0.84; 1.68]
Middle class (n = 1831)	1.00 [0.82; 1.24]
High class [Ref.] (n = 1684)	1.00
Number of vaccinations (per additional vaccination)	0.86 [0.69; 1.06]
Time since last vaccination (per additional 6 months)	1.01 [0.86; 1.19]
Winter 2023/2024[b] [n = 2930]	
Sex	
Female [Ref.] (n = 2146)	1.00
Male (n = 784)	0.66 [0.44; 0.97]
Age (per additional 10 years)	1.10 [0.97; 1.25]
Social class	
Lower class (n = 286)	1.30 [0.73; 2.21]
Middle class (n = 1421)	1.38 [0.98; 1.97]
High class [Ref.] (n = 1223)	1.00
Number of vaccinations (per additional vaccination)	0.98 [0.74; 1.33]
Time since last vaccination (per additional 6 months)	0.95 [0.80; 1.14]
Previous SARS-CoV-2 infection	
Yes [Ref.] (n = 1989)	1.00
No (n = 941)	1.98 [1.43; 2.76]

* CI – Confidence interval.
[a] September 2022 to March 2023.
[b] September 2023 to March 2024.

marginal effect of time since vaccination, with both increasing slightly by 2 % and 4 % (per 6 months) in winter 2022/2023 and by 1 % and 4 % in winter 2023/2024. This effect was almost linear for both symptom duration and days spent in bed (Fig. S1A, Fig. S2A). An analysis comparing single and multiple times boosted individuals revealed a slight reduction of the number of days spent in bed of 9 % for multiple times boosted individuals (Table S4). In individuals with hybrid immunity, multiple booster doses marginally shortened the duration of symptoms and number of days spent in bed by 4 % and 5 %. However, this effect was not observed in only vaccinated individuals. In reinfected individuals the time since last infection marginally increased both symptom duration and number of days spent in bed by 3 % and 4 % per 6 months (Table S5). This association was linear for symptom duration and showed minor quadratic tendencies for days spent in bed (Fig. 2). In both winters, the reported duration of mild SARS-CoV-2 infections was lower for men and individuals belonging to a higher social class. A higher age was associated with a small decrease in the relative number of days spent in bed of 13 % per 10 years of age in winter 2022/2023 (Table 3). This effect was smaller in winter 2023/2024. The decrease was steeper for higher ages (Fig. S2B). Individuals with no prior SARS-CoV-2 infection before winter 2023/2024 reported an increased symptom duration and a higher number of days spent in bed of 18 % and 25 % compared to individuals reporting a reinfection with SARS-CoV-2 (Table 3).

Long mild infections (symptom duration > 21 days)

In both winters, the time since last vaccination was not associated with the risk of long mild Omicron infections (recovery > 21 days) (Table 4). Stratification by number of vaccinations and time since last vaccination revealed no consistent effect either (Table S6). A reduced risk for long mild infections was observed for multiple times boosted DigiHero participants (Table S7). In the stratified analysis, compared to single time boosted individuals, a lower percentage of multiple times boosted individuals reported a long mild infection (Table S6). However, this effect was not observed in only vaccinated individuals (Table S7). In individuals with hybrid immunity, compared to a single booster, multiple booster doses further

decreased the risk of reporting long mild infections by 28 %. In reinfected individuals, the time since last infection was not associated with the risk of reporting long mild infections (Table S8). In both winters, the risk of long mild infections was lower for men and individuals with a higher social class (Table 4). Compared to reinfected individuals, individuals with no prior SARS-CoV-2 infection history were almost twice as likely to report long mild infections. Only in winter 2023/2024, an increase in age by 10 years was associated with an increased risk of long mild infections by 10 %. For winter 2022/2023, we noted a slightly increased risk of reporting long mild infections for middle-aged individuals, which decreased again with higher age (Fig. S3).

Discussion

Our analyses showed that the number of vaccinations, time since vaccination and time since last infection had either none or only a marginal negative association with the duration of short mild SARS-CoV-2 infections. On the other hand, we observed a strong association between a prior SARS-CoV-2 infection and the risk of reporting a long mild SARS-CoV-2 infection.

Effect of the number of previous vaccinations

So far, only a small number of studies focused on the symptom duration of milder SARS-CoV-2 infections in a sample representing the general population [12,13]. The effect of boosting was small and inconsistent in our study – partly in contrast to previous studies. Using a prospective approach, Menni et al. observed a bigger reduction and reported a mean symptom duration of 8.3 days for double vaccinated individuals and a reduced symptom duration of 4.4 days for triple vaccinated individuals [13]. While infection duration was reported retrospectively in the DigiHero sample, in a previous analysis, we assessed whether means and standard deviations of the reported symptom durations and days spent in bed in the data of 2022/2023 depend on the time between infection and filling out the questionnaire [17]. We assumed that less specific reporting would be more common for longer recall times, and we did not observe any time trend. We clearly cannot exclude the possibility of recall bias, but also were not able to confirm it in our sample. Hence, the difference between prospective and retrospective design might not be the only explanation for the only small observed effect of boosting in the current study.

Effects of previous SARS-CoV-2 infections and time since last infection

The DigiHero sample reporting disease durations in winter of 2022/2023 consisted only of first-infected individuals, hence we could not report the effect of previous infections in that season. In reinfected individuals, an increased time since the last infection was associated with a marginal increase in symptom duration and days spent in bed. For the first 10 months since last infection a small decrease in days spent in bed was noted, with an increase following after. Individuals without prior SARS-CoV-2 infection reported an increased symptom duration and number of days spent in bed for short mild infections (recovery within 21 days). Further, a history of previous SARS-CoV-2 infections was associated with a substantial protection against long mild infections (recovery > 21 days). Previously, prior SARS-CoV-2 infections were found to be associated with a shortened symptom duration for pre-Omicron SARS-CoV-2 infections [29,30]. For Omicron, one study reported that the likelihood of experiencing longer infection durations (defined as > 70th percentile of overall symptomatic duration distribution) was reduced by 15 % (BA.2 variant: recovery > 13 days; OR [95 % CI 0.54; 1.29]) and 34 % (XBB variant: recovery > 12 days; OR [95 % CI 0.40; 1.06]) for individuals who had experienced previous SARS-CoV-2 infections [31]. Following the WHO declaring the end of the COVID-19 pandemic in the beginning of May 2023 [32], mandatory testing was abolished and with it self-testing rates decreased in the population. We also saw this in the DigiHero data. Overall, it is possible that some individuals have been falsely labeled as first-infected. Therefore, the true level of protection of immunity induced by previous SARS-CoV-2 infections might be even higher.

Effects of time since last vaccination

An increased time since the last SARS-CoV-2 vaccination was associated with reporting a slightly longer infection duration. Another study suggested protection levels offered by booster vaccination against mild Omicron infections to be low [33]. Our results similarly showed almost no effect for mild Omicron infections, as the expected increase of the reported infection duration with increasing time since vaccination was minimal. Further, there was no association between the risk of long mild infections and time since last vaccination. The previously mentioned study by He et al. assessed the symptom duration of mild Omicron infections in individuals that had received their booster vaccination over one year prior to infection compared to individuals who had received their booster within the same year [14]. They reported no obvious difference in symptom duration between the two groups. These and our results suggest that vaccination status might have almost no effect on the reported duration of short mild Omicron infections (recovery within 21 days). We think this is an important information. There is clear evidence that vaccination decreases the risk of infection, an effect which diminishes over time within less than one year [34]. Further, vaccination protects against severe course of infection, including hospitalization, ventilation or mortality [6,9], likely for a longer time. On the other side, there could be expectation in the society that there is also shortening of symptoms in mild infections in those vaccinated. When the expectation is not met, it could lead to hesitancy against vaccination even among those with a higher risk of severe course of disease. Therefore, we consider the information on duration of mild infections in vaccinated individuals an important part of public health messages. At the same time, more studies are needed to establish the evidence.

Effects of boosting and hybrid immunity

In the first post-pandemic winter 2022/2023, we observed a decreased risk of reporting a long mild Omicron infection for multiple boosted individuals. This result suggests that for mild infections without previous SARS-CoV-2 infection history, an increased protection against higher symptom durations is achieved only from the fourth vaccine dose onward. A previous study, which assessed the likelihood of developing Post-COVID-19 in individuals with hybrid immunity, also reported an increased protection after the fourth SARS-CoV-2 vaccination [35]. Similarly, we noted a slight further decrease in the risk of long mild infections for individuals with hybrid immunity that had been boosted multiple times compared to single boosted reinfected individuals. Another explanation could be possible waning of protection offered by vaccination with the fourth dose being the most recent. While we adjusted for time since last vaccination, there could be some residual effect.

Our results suggest that in vaccinated individuals, the history of previous SARS-CoV-2 infections has a bigger influence on infection duration than the number of received vaccine doses and the time point of vaccination. A possible explanation could be the difference in the induction of SARS-CoV-2 specific tissue resident memory T cells [36]. This subset of memory T cells persists in epithelial barrier tissues, like the respiratory epithelium, and enables quick protective responses upon pathogen contact. It has been shown that tissue

resident T cells are mainly induced after natural infection rather than after vaccination [36].

Effects of sociodemographic factors

Looking at potential risk factors for reporting longer symptom durations and more days spent in bed during Omicron infections, male sex was determined to be protective. This was still the case in the analysis assessing the risk for long mild infections. Several studies showed men to be at a higher risk for severe outcomes such as hospitalization and death [37,38]. However, our results suggest that this might not be the case for milder SARS-CoV-2 infections with Omicron. This is in line with a study, that reported women had a higher risk to progress from an asymptomatic to a mildly symptomatic Omicron infection than men (OR: 1.37 [95 % CI: 1.37; 1.42]) [39]. A study conducted during the early pandemic, found that IgG antibody levels did not differ between men and women for mild SARS-CoV-2 infections, though for severe cases more women had displayed relatively high antibody levels and were shown to have a stronger IgG antibody production in early disease stages [40]. This difference in antibody levels might partly explain the higher risk for severe infections for men and why this is not the case for mild diseases. On the other hand, we cannot rule out the possible influence of differential reporting by sex. Increasing age was observed to be slightly protective against spending a longer time in bed during a SARS-CoV-2 infection. Our results suggest that a higher age might be associated with reporting a shorter duration of mild SARS-CoV-2 infections. On the other hand, our analysis focusing on the risk of reporting long mild infections revealed a minor increased risk of 10 % per 10 years of age for infections reported in winter 2023/2024, but not in winter 2022/2023. A higher social class was associated with reporting a shorter duration of symptoms and a reduction of days spent in bed during a short mild SARS-CoV-2 infection.

Role of dominant Omicron sub-lineages

Different Omicron sub-lineages have been the dominant cause of SARS-CoV-2 infections in the two post-pandemic winter seasons (XBB in winter 2022/2023 and JN.1 in winter 2023/2024). One study reported that having received an adapted SARS-CoV-2 vaccine had no influence on the symptom duration of infections with the XBB sub-lineage [31]. While we found no study assessing the duration of infection with the JN.1 variant, it has been reported that self-reported symptom profiles were similar to previous variants [41].

Limitations

Our study has several limitations. First, our data relied on self-reports of the number of days with symptoms and days spent in bed during an Omicron infection. Data collection was conducted retrospectively, but as previously mentioned we saw no major influence of increasing reporting time on the self-reported symptom duration and days spent in bed. While in winter 2022/2023, we asked participants to report exact vaccination dates, in winter 2023/2024 individuals were only required to report the month of administration for both vaccination and infection dates. Therefore, analysis on the influence of the time since the last vaccination and last infection on the duration of mild SARS-CoV-2 infections are possibly less accurate for infections reported in winter 2023/2024. However, as results regarding time since last vaccination were similar for both winters, we believe this inaccuracy to have only a minor effect. As we did not inquire about possible SARS-CoV-2 infections occurring during the summer months in 2023, the group labelled as previously not infected might have included some individuals who actually had gotten infected during that time. SARS-CoV-2 infections were reported according to self-administered positive test results. As self-testing is associated with a certain risk of false-negative results, we cannot rule out the possibility of our data excluding some false-negative SARS-CoV-2 infections. Further, as the perceived risk of SARS-CoV-2 decreased in the population after the pandemic ended, so did testing frequency. Hence, we might have excluded hidden SARS-CoV-2 infections for which no test was conducted. We did not exclude hospitalized individuals. However, the DigiHero population consists of mostly generally healthy individuals as in previous analyses, only 1 % had to be admitted to the hospital [24]. Hence, we believe this number to be small. Given the overall low recruitment proportion, there is a big potential for selection bias. In another study, we demonstrated that while reminders in the invitation are helpful to increase overall sample size, those responding to reminders are similar to those who responded first [42]. We also had some non-response among those recruited, but within the study sample, the response was high. While our study requires that participants have internet access, in a previous study, we demonstrated that results were similar between an online only study and a study allowing participation on either paper or online [43]. Our sample is not representative for the German population in terms of for example education, but our main interest was in the comparison within the sample of the DigiHero study, and this comparison is less affected by the lack of overall representativity. Lastly, our study did not include any direct biological measurements of immunity levels and hence cannot make assertions on the underlying mechanisms of immunological responses.

Conclusions

We observed no association between an increasing number of previous vaccinations and the duration of mild SARS-CoV-2 infections with Omicron with a recovery within 21 days. There was nearly no indication of protection depending on the time since the last SARS-CoV-2 vaccination or infection. Previous infections were associated with shortening of symptoms and days spent in bed for infections lasting ≤ 21 days and even stronger with the risk of prolonged symptoms (> 21 days). This indicates that the burden related to SARS-CoV-2 might be progressively decreasing in the endemic phase.

Ethical Approval

Not Applicable.

Authors contribution

Conceptualization, Nadine Glaser, Sophie Diexer, Bianca Klee, Janka Massag, Laura Pfrommer, Cornelia Gottschick and Rafael Mikolajczyk; Data curation, Oliver Purschke; Formal analysis, Nadine Glaser; Funding acquisition, Mascha Binder, Thomas Frese, Matthias Girndt, Jessica Hoell, Irene Moor, Jonas Rosendahl, Michael Gekle, Daniel Sedding and Rafael Mikolajczyk; Investigation, Nadine Glaser, Sophie Diexer, Bianca Klee and Cornelia Gottschick; Methodology, Nadine Glaser, Cornelia Gottschick and Rafael Mikolajczyk; Project administration, Mascha Binder, Thomas Frese, Matthias Girndt, Jessica Hoell, Irene Moor, Jonas Rosendahl, Michael Gekle, Daniel Sedding, Cornelia Gottschick and Rafael Mikolajczyk; Software, Oliver Purschke; Supervision, Rafael Mikolajczyk; Visualization, Nadine Glaser; Writing – original draft, Nadine Glaser; Writing – review & editing, Nadine Glaser, Sophie Diexer, Bianca Klee, Janka Massag, Laura Pfrommer, Mascha Binder, Thomas Frese, Matthias Girndt, Jessica Hoell, Irene Moor, Jonas Rosendahl, Michael Gekle, Daniel Sedding, Cornelia Gottschick and Rafael Mikolajczyk

Informed consent statement

Informed consent was obtained from all subjects involved in the study.

Institutional review board statement

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Ethics Committee of the Martin Luther University Halle-Wittenberg (registration number 2020–076).

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jiph.2025.102746.

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