Prevalence of, and factors associated with, long-term COVID-19 sick leave in working-age patients followed in general practices in Germany

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ABSTRACT

Objectives: To investigate the prevalence of, and the factors associated with, long-term sick leave in working-age patients diagnosed with COVID-19 in general practices in Germany.

Methods: Patients aged 18–65 years diagnosed with COVID-19 in any of 1255 general practices in Germany between March 2020 and February 2021 were included in the study. Long-term sick leave was defined as sick leave of at least 4 weeks. The association between predefined independent variables and long-term sick leave was studied using an adjusted logistic regression model.

Results: This study included 30 950 patients diagnosed with COVID-19 (51.7% women, mean (standard deviation) age 41.5 ($\pm$13.0) years). The prevalence of long-term sick leave was 5.8%. Female sex, older age, and several conditions (noninfective enteritis and colitis; reaction to severe stress, and adjustment disorders; atopic dermatitis; mononeuropathies; reflux diseases; diabetes mellitus; and hypertension) were positively and significantly associated with long-term sick leave.

Conclusion: Long-term sick leave was relatively rare in COVID-19 patients followed in general practices in Germany. These results should be confirmed or invalidated in other settings and countries.

Introduction

COVID-19 is a respiratory infection that emerged in China in December 2019 (Zu et al., 2020) and was declared a global pandemic in March 2020 (Cucinotta and Vanelli, 2020). Common clinical manifestations include fever, cough, dyspnoea, malaise, and fatigue (da Rosa Mesquita et al., 2020). As of June 24, 2021, more than 179 million individuals had contracted COVID-19, and approximately 3.9 million related deaths had been recorded (World Health Organization, 2021). In Germany, the number of confirmed cases and deaths is approximately 3.7 million and 90 500, respectively (World Health Organization, 2021). In this context, research is required to better characterize the epidemiology and the consequences of COVID-19 in this country.

For a substantial proportion of COVID-19 patients, symptoms may last more than 3 weeks. This persistence of symptoms is referred to as post-COVID syndrome. It is estimated that be-

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tween 10% and 35% of individuals will develop post-COVID syndrome, with fatigue being the most frequent symptom (Pavli et al., 2021). Interestingly, COVID-19 is not only associated with a wide range of symptoms of a potentially chronic nature but is also a risk factor for poor physical health (Tanji et al., 2021), impaired mental well-being (Xiong et al., 2020), and increased disability (Pizarro-Pennarolli et al., 2021). Taken together, these various complications of COVID-19 may negatively impact the ability of working-age patients to work; in fact, a large number of studies have reported high rates of sick leave in workers affected by COVID-19 (Alquézar-Arbé et al., 2020; Calvo-Bonacho et al., 2020; Carvalho-Schneider et al., 2021; COVIDSurg Collaborative, 2021; Groenewold et al., 2020; Khorasanee et al., 2021; Merkin et al., 2020; Prezant et al., 2020; Suárez-García et al., 2020). For example, 1 study using data collected in a UK medical centre in March and April 2020 found that 39% of physicians were absent at least once due to sickness and that absences due to sickness amounted to 1240 days in the overall sample (Khorasanee et al., 2021). Despite this extensive literature, however, little is known about long-term COVID-19 sick leave (i.e., sick leave lasting for at least several weeks) and the populations at particular risk.

Therefore, the goal of our study was to investigate the prevalence of, and the factors associated with, long-term COVID-19 sick leave in working-age patients followed in general practices in Germany.

Materials and methods

Database

Data from the Disease Analyzer database (IQVIA) were used for this study. Details on this database are available in the literature (Rathmann et al., 2018). To summarize, the Disease Analyzer database contains demographic, diagnosis, and prescription data collected in general and specialized practices in Germany, with 3% of all practices in the country included in the database. Diagnosis data are coded using the German adaptation of the International Classification of Diseases, 10th revision (ICD-10), and prescription data using the European Pharmaceutical Marketing Research Association's Anatomical Therapeutic Chemical classification system. Assessment of data quality includes criteria such as completeness of documentation and linkage between diagnoses and prescriptions. Finally, previous research has shown that the Disease Analyzer database offers a representative panel of practices in Germany (Rathmann et al., 2018).

Study population

Our study included patients diagnosed with COVID-19 in any of 1255 general practices in Germany between March 2020 and February 2021. Given that the population of interest of this study corresponded to working-age adults, participants had to be aged 18–65 years. Moreover, participants had to have statutory health insurance. Data on those with private health insurance were not included in the analysis, as self-employed people frequently opt for private health insurance (Busse and Blümel, 2014), and sick leave may not be necessary for this group of workers. The selection of study patients is displayed in Figure 1.

Long-term sick leave

As there is no clear consensus on the definition of long-term sick leave, for the purposes of this study, it was defined as sick leave of at least 4 weeks.
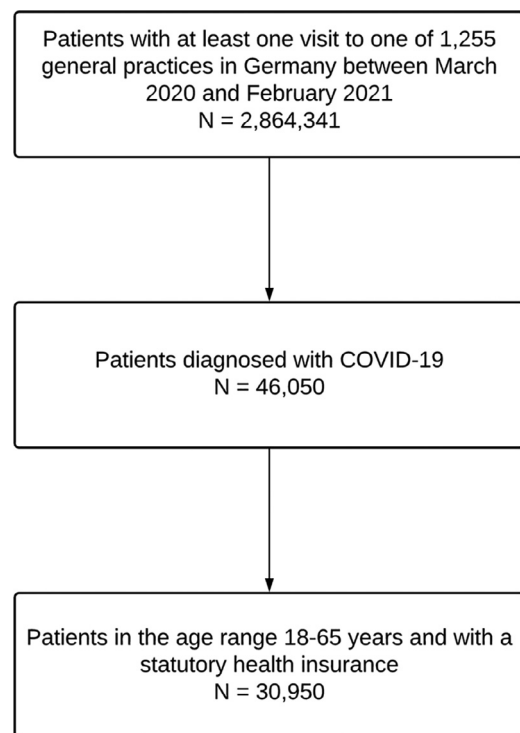

Figure 1. Selection of study patients

Demographic and clinical variables

Demographic variables included sex and age. Clinical variables included all disorders diagnosed in at least 3% of patients within 12 months prior to COVID-19 diagnosis. These disorders were: hypertension (ICD-10: I10); depression (F32 and F33); gastritis and duodenitis (K29); thyroid gland disorders (E00-E07); atopic dermatitis (L20-L30); reaction to severe stress, and adjustment disorders (F43); lipid metabolism disorders (E78); chronic sinusitis (J32); somatoform disorders (F45); sleep disorders (F51 and G47); chronic headache (G43 and G44); obesity (E66); osteoarthritis (M15-M19); reflux diseases (K20-K22); asthma (J45 and J46); allergic rhinitis (J30); noninfective enteritis and colitis (K50-K52); diabetes mellitus (E10-E14); phlebitis and thrombosis (I80-I84); cardiac arrhythmias (I76-I79); anxiety disorders (F41); mononeuropathies (G56-G59); spondylitis (M47); and vitamin D deficiency (E55).

Statistical analyses

The demographic and clinical characteristics of the study population were studied. The prevalence of long-term sick leave was estimated by dividing the number of patients on long-term sick leave by the total number of patients. Finally, the association of demographic and clinical variables with long-term sick leave was analysed using an adjusted logistic regression model. The results are presented as odds ratios (ORs) and 95% confidence intervals (CIs). P-values <0.05 were considered statistically significant. All analyses were performed using SAS 9.4.

Results

This study included a total of 30 950 patients diagnosed with COVID-19. Of these patients, 51.7% were women, and the mean (standard deviation) age was 41.5 ($\pm$13.0) years (Table 1). The most common conditions were hypertension (13.5%), depression (12.2%),

Table 1
Demographic and clinical characteristics of the study population (N = 30 950)

Variable	Value
Sex	
Women	51.7
Men	48.3
Age (in years)	
Mean (standard deviation)	41.5 (±13.0)
18-25	14.3
26-35	22.5
36-45	21.6
46-55	23.2
56-65	18.4
Disorders diagnosed within 12 months prior to the diagnosis of COVID-19	
Hypertension	13.5
Depression	12.2
Gastritis and duodenitis	11.7
Thyroid gland disorders	11.4
Atopic dermatitis	9.5
Reaction to severe stress, and adjustment disorders	9.3
Lipid metabolism disorders	8.2
Chronic sinusitis	7.4
Somatoform disorders	7.2
Sleep disorders	6.5
Chronic headache	6.4
Obesity	6.1
Osteoarthritis	6.1
Reflux diseases	6.1
Asthma	5.2
Allergic rhinitis	4.7
Noninfective enteritis and colitis	4.6
Diabetes mellitus	4.3
Phlebitis and thrombosis	4.0
Cardiac arrhythmias	3.8
Anxiety disorders	3.7
Mononeuropathies	3.5
Spondylitis	3.4
Vitamin D deficiency	3.0

Abbreviation: COVID-19 coronavirus disease.

and gastritis and duodenitis (11.7%). The prevalence of long-term sick leave (i.e., sick leave lasting at least 4 weeks) was 5.8% in the overall sample. Finally, the results of the adjusted logistic regression analysis are displayed in Table 2. In terms of demographic characteristics, female sex (OR = 1.19; male sex: reference) and older age (36–45 years: OR = 1.84; 46–55 years: OR = 2.68; 56–65 years: OR = 3.71; 18–25 years: reference) were positively and significantly associated with the odds of taking long-term sick leave. In terms of clinical characteristics, there was a significant relationship between long-term sick leave and noninfective enteritis and colitis (OR = 2.02), reaction to severe stress, and adjustment disorders (OR = 1.68), atopic dermatitis (OR = 1.27), mononeuropathies (OR = 1.27), reflux diseases (OR = 1.24), diabetes mellitus (OR = 1.21), and hypertension (OR = 1.19).

Discussion

Main findings

This cross-sectional study, including almost 31 000 patients with COVID-19 from across more than 1250 general practices in Germany, found that 5.8% of patients were on long-term sick leave between March 2020 and February 2021. It was also observed that female sex, older age, and several conditions (i.e., noninfective enteritis and colitis; reaction to severe stress, and adjustment disorders; atopic dermatitis; mononeuropathies; reflux diseases; diabetes mellitus; and hypertension) were positively and significantly associated with the risk of long-term sick leave. To the best of the authors' knowledge, this is one of the largest studies to have investigated the prevalence of long-term sick leave in people affected by COVID-19.

Interpretation of findings

One major finding of this study is that the rate of long-term sick leave in COVID-19 patients followed in general practices in Germany was slightly higher than 5%. To date, only 1 other study has analysed the prevalence of long-term sick leave in individuals diagnosed with COVID-19. This study of 150 patients with non-critical COVID-19 in France revealed that 19.7% and 11.2%, respectively, were on sick leave for 30 and 60 days after the onset of the disease (Carvalho-Schneider et al., 2021). Although they do not directly assess the proportion of patients on long-term sick leave, other pieces of research have focused on the mean or median period of sick leave. For example, a study including 1911 health-care workers living in Spain found a median sick leave period of 20 days (Suárez-García et al., 2020). Another study of 4408 emergency medical system responders and 11 230 firefighters from the United States estimated that the mean duration of medical leave was 19.8 days for those with suspected COVID-19 and 25.3 days for those with confirmed COVID-19 who later returned to work (Prezant et al., 2020). The discrepancy between the findings of the previous French study (Carvalho-Schneider et al., 2021) and the present German study's findings may be due to the different settings in which these studies were carried out. Patients included in the French study were treated for COVID-19 in an academic university hospital, whereas our study included individuals followed in general practices. Thus, it is likely that the proportion of participants with severe COVID-19 was lower in the German sample than in the French one.

Interestingly, sex, age, and several chronic disorders were positively and significantly associated with long-term sick leave. First, women were more likely to take long-term sick leave than their

Table 2

Association between demographic and clinical variables and long-term sick leave in COVID-19 patients followed in general practices in Germany

Variable	Proportion of patients on long-term sick leave (%)	OR (95% CI)	P value
Total	5.8		
Sex			
Female	6.5	1.19 (1.07-1.31)	<0.001
Male	5.1	Reference	
Age (in years)			
18–25	2.6	Reference	
26–35	2.9	1.10 (0.87-1.39)	0.429
36–45	5.1	1.84 (1.48-2.29)	<0.001
46–55	7.5	2.68 (2.17-3.29)	<0.001
56–65	10.7	3.71 (3.01-4.58)	<0.001
Disorders diagnosed within 12 months prior to the diagnosis of COVID-19[a]			
Noninfective enteritis and colitis	12.3	2.02 (1.70-2.40)	<0.001
Reaction to severe stress, and adjustment disorders	11.6	1.68 (1.46-1.92)	<0.001
Atopic dermatitis	9.2	1.27 (1.10-1.47)	0.001
Mononeuropathies	11.1	1.27 (1.04-1.57)	0.022
Reflux diseases	11.2	1.24 (1.05-1.47)	0.013
Diabetes mellitus	11.3	1.21 (1.00-1.48)	0.048
Spondylitis	12.3	1.21 (0.99-1.49)	0.063
Hypertension	10.5	1.19 (1.04-1.36)	0.010
Chronic headache	8.2	1.19 (1.00-1.42)	0.056
Phlebitis and thrombosis	11.0	1.17 (0.96-1.42)	0.114
Somatoform disorders	9.9	1.13 (0.96-1.34)	0.132
Sleep disorders	10.1	1.11 (0.94-1.32)	0.218
Chronic sinusitis	7.7	1.11 (0.94-1.32)	0.218
Allergic rhinitis	7.6	1.11 (0.89-1.37)	0.360
Obesity	9.1	1.08 (0.90-1.29)	0.433
Asthma	8.8	1.06 (0.87-1.30)	0.540
Depression	8.6	1.05 (0.91-1.21)	0.506
Gastritis and duodenitis	8.1	1.05 (0.91-1.21)	0.534
Lipid metabolism disorders	9.9	1.04 (0.89-1.21)	0.638
Vitamin D deficiency	8.9	1.03 (0.81-1.31)	0.823
Osteoarthritis	11.2	1.02 (0.87-1.21)	0.784
Cardiac arrhythmias	8.4	1.02 (0.81-1.27)	0.892
Anxiety disorders	8.8	1.02 (0.73-1.15)	0.469
Thyroid gland disorders	8.1	0.99 (0.86-1.14)	0.910

OR: odds ratio.

The adjusted logistic regression model included all demographic and clinical variables displayed in the table.

Long-term sick leave corresponded to sick leave of at least 4 weeks.

[a] The reference column corresponds to patients without the disorder of interest.

male counterparts. This finding is relatively unexpected because previous research suggests that male sex is a risk factor for severe COVID-19 and COVID-19 complications (Vahidy et al., 2021). That being said, persistent fatigue after COVID-19 is more common in women than in men (Townsend et al., 2020), which might explain why the prevalence of long-term sick leave was higher in women than in men. Second, there was a positive relationship between increasing age and long-term sick leave. A systematic review and meta-analysis of 12 studies (N = 3064 COVID-19 patients) revealed that older age increases the risk of several COVID-19 complications (i.e., acute respiratory distress syndrome, acute kidney injury, acute cardiac injury, and shock) (Tiruneh et al., 2021) and thus return to work might be more difficult in older adults than in younger populations. Third, several conditions (noninfective enteritis and colitis; reaction to severe stress, and adjustment disorders; atopic dermatitis; mononeuropathies; reflux diseases; diabetes mellitus; and hypertension) were associated with increased odds of long-term sick leave. Since noninfective enteritis and colitis, atopic dermatitis, mononeuropathies, and reflux diseases involve immunological dysregulations (Elzinga et al., 2019; Lee et al., 2018; Miraglia del Giudice et al., 2006; Rieder et al., 2010), some of which may require the use of immunotherapies (Catalan-Serra and Brenna, 2018; Léger et al., 2016; Werfel and Biedermann, 2015), people affected by these conditions may display a disrupted immunological response when exposed to a pathogen and may be at particular risk of severe COVID-19 and COVID-19 complications. Furthermore, there is some evidence that both diabetes mellitus

and hypertension are associated with severe COVID-19 and related complications (Abdi et al., 2020; Lippi et al., 2020), suggesting that these diseases could have long-lasting effects on ability to work following COVID-19 diagnosis. Finally, there was a significant association between reaction to severe stress, and adjustment disorders, and long-term sick leave. One hypothesis is that individuals with this psychiatric condition may have more difficulty adjusting to a COVID-19 diagnosis than the general population, resulting in a delayed return to work after the acute phase of the disease.

Public health implications and directions for future research

Our study found that the vast majority of working-age adults followed in general practices in Germany returned to work in the month following their COVID-19 diagnosis. Nonetheless, barriers to return to work should be identified in people on long-term sick leave, and public health measures reducing these barriers should be implemented. These measures may include the possibility to work from home or to work flexible hours. In terms of future research, long-term sick leave in adults with COVID-19 should be studied in other settings and countries. In addition, further studies are needed to gain a better understanding of the factors that significantly impact the odds of long-term sick leave.

Strengths and limitations

The large sample size and the use of data collected in general practices are 2 major strengths of this study. However, this study is

also subject to several limitations. First, sick leave may have been initiated in other settings (e.g., pulmonology practices and hospitals), and sick leave-related data may have been undocumented in some general practices, indirectly leading to an underestimation of the prevalence of long-term sick leave. Second, there is no consensus on the definition of long-term sick leave, and the use of a cut-off of 4 weeks may have impacted the results of this study. Third, no information was available on COVID-19 severity and COVID-19 complications, although these variables likely help predict the odds of taking long-term sick leave.

Conclusion

The prevalence of long-term sick leave was 5.8% in this sample of approximately 31 000 COVID-19 patients followed in general practices in Germany. Sex, age, and several disorders (noninfective enteritis and colitis; reaction to severe stress, and adjustment disorders; atopic dermatitis; mononeuropathies; reflux diseases; diabetes mellitus; and hypertension) were significantly associated with the risk of long-term sick leave. Further research is warranted to corroborate or invalidate the study results in other settings and countries.

Conflicts of interest

The authors declare no competing financial interests.

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Ethical approval

German law allows the use of anonymous electronic medical records for research purposes under certain conditions. According to this legislation, it is not necessary to obtain informed consent from patients or approval from a medical ethics committee for this type of observational study that contains no directly identifiable data. Because patients were only queried as aggregates and no protected health information was available for queries, no Institutional Review Board approval was required for the use of this database or the completion of this study.

Author contributions

Louis Jacob contributed to the design of the study, managed the literature searches, wrote the first draft of the manuscript, and corrected the manuscript. Ai Koyanagi, Lee Smith, Christian Tanislav, Marcel Konrad, and Susanne van der Beck corrected the manuscript. Karel Kostev contributed to the design of the study, performed the statistical analyses, and corrected the manuscript. All authors contributed to and have approved the final manuscript.

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