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

**Running title:** Long-term COVID-19 sick leave

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**Number of characters in the title (spaces included):** 136

**Number of characters in the running title (spaces included):** 29

**Number of words in the abstract:** 246

**Number of words in the main body:** 2,260

**Number of references:** 31

**Number of tables:** 2

**Number of figures:** 1

# Abstract

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

*Methods:* Patients aged 18-65 years who were diagnosed with COVID-19 in one of 1,255 general practices in Germany between March 2020 and February 2021 were included in this study. Long-term sick leave was defined as sick leave of at least four weeks. The association between these 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 [13.0] years). The prevalence of long-term sick leave was 5.8%. 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 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.

**Keywords:** long-term sick leave; COVID-19; coronavirus disease; general practices; Germany

# Introduction

Coronavirus disease (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, dyspnea, 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 around 3.7 million and 90,500, respectively (World Health Organization, 2021). Thus, future research should aim at the better characterization of the epidemiology and the consequences of COVID-19 in this country.

For a substantial proportion of COVID-19 patients, symptoms may last more than three weeks. This persistence of symptoms is referred to as post-COVID syndrome. It is estimated that between 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. As a matter of 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, one study using data collected in a UK medical center 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 1,240 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 this 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 already 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. Three percent of all practices in this country are 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 (EphMRA) Anatomical Therapeutic Chemical (ATC) classification system. The assessment of the quality of these data is based on several 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

Patients diagnosed with COVID-19 in one of 1,255 general practices in Germany between March 2020 and February 2021 were included in this study. 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 a statutory health insurance. Data pertaining to those with a private health insurance were not included in the analysis, as self-employed people frequently opt for a private health insurance (Busse and Blümel, 2014), and sick leave may not be necessary in 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, it was defined as sick leave of at least four weeks for the purposes of this study.

## 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 the diagnosis of COVID-19. These disorders included 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 K46), 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 sick leave was analyzed 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. There were 51.7% of women, and the mean (standard deviation) age was 41.5 (13.0) years (**Table 1**). The most common conditions were hypertension (13.5%), depression (12.2%), and gastritis and duodenitis (11.7%). The prevalence of long-term sick leave (i.e., sick leave lasting at least four 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 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 more than 1,250 general practices in Germany showed 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 knowledge of the authors, this is one of the largest studies to have investigated the prevalence of long-term sick leave in people affected by the 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 one other study has analyzed the prevalence of long-term sick leave in individuals diagnosed with COVID-19. This study of 150 patients with noncritical COVID-19 in France revealed that 19.7% and 11.2% respectively were on sick leave 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 1,911 healthcare workers living in Spain found a median sick leave period of 20 days (Suárez-García et al., 2020). Another study of 4,408 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 findings of this study conducted in Germany 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 this 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 male counterparts. This finding is relatively unexpected because previous research tends to suggest 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), and this 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 = 3,064 patients with COVID-19) revealed that older age increases the risk of several complications (i.e., acute respiratory distress syndrome, acute kidney injury, acute cardiac injury, and shock) (Tiruneh et al., 2021), and the return to work might thus be more difficult in older adults than in younger populations. Third, 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 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), and since some of these disorders 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 a particular risk of severe COVID-19 and COVID-19 complications. Furthermore, there is some evidence showing 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 the ability to work following the diagnosis of COVID-19. 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 the diagnosis of COVID-19 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

Based on the findings of this study, the vast majority of working-age adults followed in general practices in Germany returned to work in the month following their diagnosis of COVID-19. Nonetheless, barriers to the 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 various 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 two major strengths of this study. However, this study is also subject to several limitations, which should be acknowledged at this point. 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 cutoff of four 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 sick leave was around 6% in this sample of approximately 31,000 COVID-19 patients followed in general practices in Germany. Sex, age, and several disorders (i.e., 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.

# Funding source

This research did not receive any specific grants from funding agencies in the public, commercial, or not-for-profit sectors.

# 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, Susanne van der Beck, and Marcel Konrad 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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# Tables and Figures

**Three step flow diagram. 

Box one: "Patients with at least one visit to one of 1,255 general practices in Germany between March 2020 and February 2021. N = 2,864,341"

Box two: "Patients diagnosed with COVID-19. N = 46,050"

Box three: "Patients in the age range 18-65 years and with a statutory health insurance. N = 30,950"**

**Figure 1.** Selection of study patients

**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.

**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)* |  | |  | |  |
| Age 18-25 | 2.6 | | Reference | |  |
| Age 26-35 | 2.9 | | 1.10 (0.87-1.39) | | 0.429 |
| Age 36-45 | 5.1 | | 1.84 (1.48-2.29) | | <0.001 |
| Age 46-55 | 7.5 | | 2.68 (2.17-3.29) | | <0.001 |
| Age 56-65 | 10.7 | | 3.71 (3.01-4.58) | | <0.001 |
| *Disorders diagnosed within 12 months prior to the diagnosis of COVID-19a* | | | | | |
| 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 |

Abbreviations: CI confidence interval; COVID-19 coronavirus disease; 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 four weeks.

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