

# Vaccination Against SARS-Cov-2 among Patients with Parkinson's Disease Based on the Results of COVPARK-LT Study

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**Summary.** *Background.* COVID-19 in patients with Parkinson's disease leads to worsening of symptoms and development of severe/critical conditions; its long-term consequences are still being investigated. Data on vaccination against SARS-Cov-2 in Parkinson's disease are inconsistent. There are no publications on this topic regarding Lithuania.

*Materials and methods.* The retrospective study COVPARK-LT was performed in Vilnius University Hospital Santaros Clinics in 2022. Methods: analysis of anonymous data from electronic patient histories obtained during consultations for Parkinson's disease in the out-patient department (form E025).

*Objective.* To investigate COVID-19 vaccination status and associated factors in patients with Parkinson's disease.

*Results.* 173 patients were enrolled, 68 males (39.3%) and 105 females (60.7%), the average age of the cohort was  $67.99 \pm 1.34$  years, the duration of Parkinson's disease was  $7.73 \pm 0.54$  years. The rate of vaccination against SARS-Cov-2 with at least one dose was 85.6% among study patients and 69.8% in the general population. The rate of full vaccination against SARS-Cov-2 was 81.5% in COVPARK-LT and 33.4% in the general population. The rate of laboratory-proven COVID-19 was 20% (N=5) in the non-vaccinated group of the cohort and 22.3% (N=33) in the vaccinated group ( $p=0.087$ ). COVID-19 vaccine-negativity was associated with the history of vaccination against non-SARS-Cov-2 infections (odds ratio, OR: 0.18,  $p < 0.01$ ), vaccination against influenza (OR: 0.21,  $p < 0.01$ ), male gender (OR: 0.68,  $p < 0.05$ ), male age (OR: 0.88,  $p < 0.05$ ), duration of Parkinson's disease (OR: 1.1,  $p < 0.001$ ), and Parkinson's disease stage according to Hoehn-Yahr (OR: 0.51,  $p < 0.05$ ).

*Conclusions.* The rate of vaccination against SARS-Cov-2 was higher in the COVPARK-LT cohort patients than in the general population in Lithuania. Non-vaccinated status was positively associated with female gender, younger age in men and earlier stage of Parkinson's disease according to Hoehn-Yahr staging. Vaccinated status was associated with vaccination against other infectious diseases (influenza, tick-borne encephalitis, pneumococcus). The rate of COVID-19 in the COVPARK-LT cohort did not differ between non-vaccinated and vaccinated patients with Parkinson's disease.

**Keywords:** Parkinson's disease, COVID-19, SARS-CoV-2, vaccination.

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## BACKGROUND

Numerous studies have investigated clinical and pathological aspects of COVID-19 in patients with Parkinson's disease (PD) over the last three years. It has been demonstrated that SARS-CoV-2 can cause clinical variations ranging from asymptomatic or mild (such as nasal obstruction, etc.) to more severe or even critical COVID-19 complex (22.9 vs. 1.0%,  $p < 0.001$  [1]), especially in compli-

cated PD. In clinical trials, PD patients with COVID-19 were elderly with advanced stage (76.69±9.21 years; Hoehn-Yahr stage 3-5 as 65.3% [1]), but it has been demonstrated that SARS-CoV-2 can lead to deterioration of motor and non-motor symptoms of PD and quality of life regardless of its pre-infectious stage [2]. Data on the mortality from COVID-19 in PD are controversial: Zhang et al. (2020) compared 78,355 non-PD COVID-19 patients with 694 COVID-19 patients with PD and found an increased mortality even after adjusting and matching for age and sex [3]; a systematic review by Artusi et al. (2021) on a total of 1061 PD patients with confirmed COVID-19 showed a higher hospitalization rate, case fatality and mortality [3]; a multicenter German study by Scherbaum et al. (2021) showed that the prevalence and mortality of COVID-19 was higher in PD than in non-PD in-patients [3]; an increase of PD long-term mortality was determined by Fedeli et al. (2022) [4]. A detailed review by Fearon et al. (2021) led to conclusion that COVID-19 mortality is probably not increased in PD patients [5]. The Columbia University Medical Center cohort study (Xu et al., 2022) [6] and the Lombardy community-based case-control study (Fasano et al., 2021) did not find sufficient evidence that PD is an independent risk factor for severe COVID-19 and death [7]. The long-term consequences of COVID-19 in PD are still being investigated, and pro-degenerative qualities of SARS-CoV-2 remain an important research target, but to date most authors agree that the rate of psychiatric complications and long-term COVID-19 in PD is higher than that of patients without PD [1, 2]. That is why vaccination against SARS-Cov-2, which helps to prevent or alleviate clinical symptoms of the infection and causes a higher likelihood of asymptomatic infection and a lower rate of "long COVID-19" and hospitalization [8–9], plays a key preventive role. Global and national health authorities have formulated recommendations for PD patients to be vaccinated against COVID-19, but real-life data on vaccination against SARS-Cov-2 in Parkinson's disease are inconsistent. In the study by Zhou et al., COVID-19 vaccination rate in patients with PD was 54.0%, which was significantly higher than the general population level [10]; the authors analyzed the reasons for vaccine acceptance using a self-reported survey and determined a significant relationship between vaccination and fear of COVID-19 (77.5%), trust in the efficacy (82.9%) and safety (66.8%) of COVID-19 vaccine, and trust in the government (70.3%) [10]. Concern about the impact of the vaccine on PD (67.4%) was the most common reason for COVID-19 hesitancy [10]. COVID-19 vaccines in PD patients showed similar types and incidence of side effects as in the general population [11, 12]. EudraVigilance database reported only a few cases of transient movement disorders after COVID-19 vaccination (mostly tremor) [13], and there were case reports of worsening motor and non-motor symptoms of PD in patients treated with both deep brain stimulation (DBS) and duodenal levodopa [12]. We found no publications on vaccination against SARS-CoV-2 in PD regarding the situation in Lithuania.

## MATERIALS AND METHODS

The retrospective study COVPARK-LT was performed in Vilnius University Hospital Santaros Clinics (VUHSC) in 2022. Permission to use medical data for retrospective analysis was obtained from the hospital administration.

**Objective:** To investigate the vaccination status for COVID-19 and associated factors in patients with Parkinson's disease.

**Method:** Analysis of anonymous data from electronic patient histories obtained during consultations for Parkinson's disease in the out-patient department (form E025).

Diagnoses (according to ICD-10) included:

- G20 (Parkinson's disease);
- G20+U07.1 (COVID-19 disease, virus identified);
- G20+U07.2 (COVID-19 disease, virus not identified);
- G20+U07.3 (case history of COVID-19 disease);
- G20+U07.4 (post-COVID condition);
- G20+U07.5 (multisystem inflammatory syndrome associated with COVID-19 disease)

The retrospective anonymous data we analyzed included: gender, age (years), PD stage according to Hoehn-Yahr, PD duration since diagnosis (years), vaccination status (fact of vaccination against SARS-CoV-2, number of doses, fact of vaccination against influenza, tick-borne encephalitis, *Streptococcus pneumoniae*), and diagnosis of COVID-19.

**Inclusion criteria:** age >18 years, diagnosis of idiopathic Parkinson's disease, duration of PD more than 2 years verified in the same centre (covering the accessible time frame for vaccination against COVID-19 since 2020), accessible data about vaccination against SARS-CoV-2, and fact of COVID-19.

There were no exclusion criteria. The patients were divided into two groups according to the fact of vaccination and comparison was made between groups.

## Statistics

Statistical analyses were performed using *MS Excel* and *R Commander* (R-3.5.0). Chi-square test and Fisher's exact test were used to compare categorical variables and Student's t-test was used for continuous variables. Univariate logistic regression analyses were used to explore potential factors associated with negative SARS-CoV-2 vaccine status, and variables with  $p < 0.05$  were further entered into a multivariate analysis. A two-tailed  $p < 0.05$  was defined as statistically significant.

## RESULTS

The study enrolled 173 patients, 68 males (39.3%) and 105 females (60.7%), with stage 1-5 PD of Hoehn-Yahr scale. The average age was 67.99±1.34 years and did not

differ in the incidence of COVID-19 ( $p=0.086$ ) or between vaccinated and non-vaccinated groups ( $p=0.059$ ). The duration of PD was  $7.73\pm 0.54$  years. The rate of vaccination against SARS-Cov-2 among COVPARK-LT patients with at least one dose of vaccine was 85.6% ( $N=148$ ). 81.5% of patients ( $N=141$ ) received at least two doses and 66% received the full recommended vaccination ( $N=114$ ). 22% ( $N=38$ ) of patients in COVPARK-LT had documented COVID-19 and 86.8% of these were vaccinated ( $N=33$ ). The non-vaccinated group had a higher percentage of women (72%,  $N=18$  vs. 58.8%,  $N=87$ ,  $p<0.05$ ) and fewer patients with advanced PD (stages 3-5 of Hoehn-Yahr scale; 44% vs. 46.62%,  $p<0.05$ ). The distribution of patients in the COVPARK-LT cohort according to stages of PD in the vaccinated and non-vaccinated

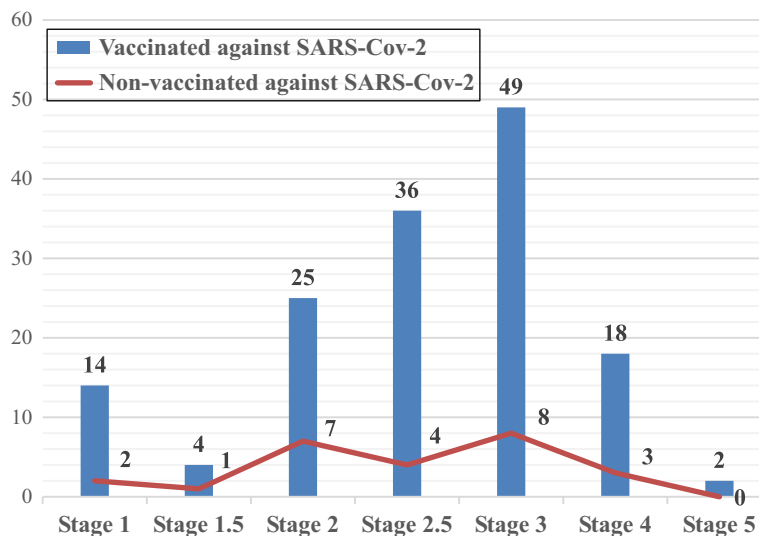


Fig. Number of vaccinated and non-vaccinated patients by Hoehn-Yahr Parkinson's disease staging in COVPARK-LT

groups is presented in Fig. The rate of laboratory-proven COVID-19 was 20% ( $N=5$ ) in the non-vaccinated group of the cohort and 22.3% ( $N=33$ ) in the vaccinated group ( $p=0.087$ ). The average age of men was  $58.14\pm 3.16$  in the non-vaccinated group and  $63.57\pm 2.17$  in the vaccinated group ( $p=0.008$ ). 19% ( $N=33$ ) of the enrolled patients were vaccinated against other infections during the data collection period: 13.3% ( $N=23$ ) against influenza, 9.9% ( $N=17$ ) against tick-borne encephalitis, and 2.3% ( $N=4$ ) against Streptococcus pneumoniae. No adverse events from SARS-Cov-2 vaccines in the COVPARK-LT cohort were reported in the e-registry during the study period.

The results of logistic regression are presented in the Table. In univariate analysis, COVID-19 vaccine-negative status was significantly associated with history of vaccination against non-SARS-Cov-2 infections (OR: 0.18, 95% CI: 0.023-0.443,  $p<0.01$ ), vaccination against influenza (OR: 0.21, 95% CI: 0.096-0.618,  $p<0.01$ ), male gender (OR: 0.68, 95% CI: 0.456-0.902,  $p<0.05$ ), male age (OR: 0.88, 95% CI: 0.621-0.997,  $p<0.05$ ), duration of PD (OR: 1.1, 95% CI: 1.044-1.171,  $p<0.001$ ), and stage of PD (OR: 0.51, 95% CI: 0.267-0.961,  $p<0.05$ ). Multivariate analysis showed that SARS-CoV-2 vaccine-negative status was independently associated with history of vaccina-

tion against non-SARS-Cov-2 infections (OR: 0.14, 95% CI: 0.018-0.581,  $p<0.05$ ), male age (OR: 0.57, 95% CI: 0.358-0.884,  $p<0.05$ ) and stage of PD (OR: 0.78, 95% CI: 0.594-0.997,  $p<0.05$ ).

## DISCUSSION

The vaccination rate against SARS-Cov-2 among study patients was 85.6% exceeding the rate in the general population in Lithuania (69.8%; range 79.3-90.6% in people older than 35 years) [14]. The rate of full vaccination against SARS-Cov-2 in the COVPARK-LT cohort was 81.5% and was higher than in the general population (33.4%, with inverse gradient in people above 35 years of age: 42.7% in 35-44 years-age group gradually decreasing to 27.5% in the age group above 80 years) [14]. In comparison, a recent study in China showed that COVID-19 vaccination rate in PD was 54%, which is lower than that of the general elderly [10]. It is reasonable to assume that the accessibility to medical care in large cities could improve the rate of vaccination, but Zhou et al. reported that the acceptance rate of COVID-19 vaccination of PD in Shanghai was much lower compared to the national rate (38.4% vs. 67.3%) due to broader socioeconomic status, including in-

Table. Factors associated with COVID-19 vaccine-negative status

	Univariate analysis		Multivariate analysis	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Vaccination against non-SARS-Cov-2 infections	0.18 (0.023-0.443)	<0.01	0.14 (0.018-0.581)	<0.05
Vaccination against influenza	0.33 (0.216-0.618)	<0.05	1.086 (0.256-2.584)	0.825
Gender (male)	0.68 (0.456-0.902)	<0.05	0.87 (0.442-0.999)	0.062
Age (male)	0.88 (0.621-0.997)	<0.05	0.57 (0.358-0.884)	<0.05
Parkinson's disease duration	1.1 (1.044-1.171)	<0.05	1.01 (0.964-1.127)	0.076
Stage of Parkinson's disease	0.51 (0.267-0.961)	<0.05	0.78 (0.594-0.997)	<0.05

Abbreviations: OR - odds ratio; CI - confidence interval.

come, education, and international exchanges [10]. Fründt et al. analyzed the results of the German Care4PD study and showed that COVID-19 vaccination rates and acceptance were generally high, but higher in PD patients with professional long-term care compared with PD patients without long-term professional care (64.3% with professional care and 52.3% without professional care, respectively) [15]. Our study enrolled PD patients who were consulted in the out-patient department of the VUHSC for Parkinson's disease and other movement disorders not less than twice (in 2020 and in 2022); this fact may to some extent increase patients' trust in novelties and modern therapeutic measures. Both Chinese and German studies were based on patient survey data [10, 15]. The data in COVPARK-LT were collected not from self-administered surveys, but from out-patient consultation forms (based on e-registration and referrals), so the data on the fact of vaccination is more reliable. On the other hand, the limitations of the COVPARK-LT study include potential selection bias, as all participants were from a single center.

Studies have shown that vaccination against COVID-19 can significantly reduce the risk of symptomatic COVID-19, severe illness, and death [6, 8–10, 15]. The rate of COVID-19 in the COVPARK-LT cohort did not differ between non-vaccinated and vaccinated patients with Parkinson's disease. COVPARK-LT included PD patients who did not undergo or survived COVID-19 and did not include fatal outcomes because the study did not aim to analyze all the outcomes of COVID-19. This methodological issue may have an impact on the reported incidence rate of COVID-19 between vaccinated and non-vaccinated PD patients; the study is ongoing and further data will be collected. Vaccine-negative status in COVPARK-LT was associated with negative history of vaccination against non-SARS-Cov-2 infections, female gender, younger age of male patients, earlier stage and longer duration of PD. The study by Zhou et al. [10] showed a similar association between low COVID-19 vaccination rates and negative influenza vaccination history, longer duration of PD disease, and gender association [10]. Considering the above evidence, we recommend that PD patients, regardless of the stage of disease, should be vaccinated against COVID-19, unless there are specific contraindications.

## CONCLUSIONS

The rate of vaccination against SARS-Cov-2 among patients of the COVPARK cohort was higher than in the age-adjusted general population in Lithuania. The non-vaccinated status was associated with female gender, younger age in men, and earlier stage of PD according to Hoehn-Yahr staging. The vaccinated status was associated with vaccination against other infectious diseases (influenza, tick-borne encephalitis, pneumococcus). The rate of COVID-19 in the COVPARK-LT cohort did not differ between non-vaccinated and vaccinated patients with Parkinson's disease.

## Declarations

**Ethical approval.** The authors confirm that the permission from the authorities of Vilnius University Hospital Santaros Clinics was obtained, and the approval of the ethic review board was not required for this work.

**Conflict of interest.** The authors declare no competing interests.

## References

1. Wu L, Shen J, Jiang Y, Shen X, Wang P, Nie X, et al. Clinical characteristics and outcome of COVID-19 patients with Parkinson's disease: a hospital based case-control study in Shanghai, China. *Front Aging Neurosci* 2023; 15: 1138418. <https://doi.org/10.3389/fnagi.2023.1138418>
2. Taquet M, Sillett R, Zhu L, Mendel J, Camplisson I, Dercon Q, et al. Neurological and psychiatric risk trajectories after SARS-CoV-2 infection: an analysis of 2-year retrospective cohort studies including 1 284 437 patients. *Lancet Psychiatry* 2022; 9(10): 815–27. [https://doi.org/10.1016/S2215-0366\(22\)00260-7](https://doi.org/10.1016/S2215-0366(22)00260-7)
3. Krey L, Huber MK, Höglinger GU, Wegner F. Can SARS-CoV-2 infection lead to neurodegeneration and Parkinson's disease? *Brain Sci* 2021; 11(12): 1654. <https://doi.org/10.3390/brainsci11121654>
4. Fedeli U, Casotto V, Barbiellini Amidei C, Saia M, Tiozzo SN, Basso C, et al. Parkinson's disease related mortality: long-term trends and impact of COVID-19 pandemic waves. *Parkinsonism Relat Disord* 2022; 98: 75–7. <https://doi.org/10.1016/j.parkreldis.2022.04.011>
5. Fearon C, Fasano A. Prevalence and outcomes of COVID-19 in Parkinson's disease: acute settings and hospital. *Int Rev Neurobiol* 2022; 165: 35–62. <https://doi.org/10.1016/bs.irm.2022.03.001>
6. Xu Y, Surface M, Chan AK, et al. COVID-19 manifestations in people with Parkinson's disease: a USA cohort. *J Neurol* 2022; 269(3): 1107–13. <https://doi.org/10.1007/s00415-021-10784-3>
7. Fasano A, Cereda E, Barichella M, Cassani E, Ferri V, Zecchinelli AL, et al. COVID-19 in Parkinson's disease patients living in Lombardy, Italy. *Mov Disord* 2020; 35(7): 1089–93. <https://doi.org/10.1002/mds.28176>
8. Antonelli M, Penfold RS, Merino J, Sudre CH, Molteni E, Berry S, et al. Risk factors and disease profile of post-vaccination SARS-CoV-2 infection in UK users of the COVID Symptom Study app: a prospective, community-based, nested, case-control study. *Lancet Infect Dis* 2022; 22(1): 43–55. [https://doi.org/10.1016/S1473-3099\(21\)00460-6](https://doi.org/10.1016/S1473-3099(21)00460-6)
9. Byambasuren O, Stehlik P, Clark J, Alcorn K, Glasziou P. Effect of COVID-19 vaccination on long covid: systematic review. *BMJ Med* 2023; 2(1): e000385. <https://doi.org/10.1136/bmjmed-2022-000385>
10. Zhou Y, Lin Z, Wan X, Liu J, Ding J, Zhang C, et al. COVID-19 vaccine acceptance and hesitancy in patients with Parkinson's disease. *Front Public Health* 2022; 10: 977940. <https://doi.org/10.3389/fpubh.2022.977940>
11. Bloem BR, Trenkwalder C, Sanchez-Ferro A, Kalia LV, Alcalay R, Chiang HL, et al. COVID-19 vaccination for persons with Parkinson's disease: light at the end of the tunnel? *J Parkinsons Dis* 2021; 11(1): 3–8. <https://doi.org/10.3233/JPD-212573>

12. Imbalzano G, Ledda C, Artusi CA, Romagnolo A, Montanaro E, Rizzone MG, et al. SARS-CoV-2 vaccination, Parkinson's disease, and other movement disorders: case series and short literature review. *Neurol Sci* 2022; 43(9): 5165–8. <https://doi.org/10.1007/s10072-022-06182-w>
13. EudraVigilance database [last revised 2023 Apr 30]. Available from: <https://www.ema.europa.eu/en/human-regulatory/research-development/pharmacovigilance/eudravigilance>
14. Valstybės duomenų agentūra. COVID-19 Lietuvoje [last revised 2023 Apr 30]. Available from: <https://koronastop.lrv.lt/lt/statistika-lietuvoje>
15. Fründt O, Hanff AM, Mai T, Kirchner C, Bouzanne des Mazery E, Amouzandeh A, et al. Impact of COVID-19 pandemic on (health) care situation of people with Parkinson's disease in Germany (Care4PD). *Brain Sci* 2021; 12(1): 62. <https://doi.org/10.3390/brainsci12010062>

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#### PARKINSONO LIGA SERGANČIŲ ASMENŲ VAKCINACIJA NUO SARS-COV-2 VIRUSO, REMIANTIS COVPARK-LT TYRIMO REZULTATAIS

##### Santrauka

*Įvadas.* COVID-19 pacientams, sergantiems Parkinsono liga, sukelia simptomų pasunkėjimą ar grėsmingų / kritinių komplikacijų išsivystymą. Šios infekcijos ilgalaikiai padariniai dar tiriami. Duomenys apie vakcinaciją nuo SARS-Cov-2, sergant Parkinsono liga, yra nevienalyčiai. Lietuvoje tokių duomenų nėra skelbta.

*Tiriamieji ir tyrimo metodai.* Retrospektyvinis tyrimas COVPARK-LT atliktas Vilniaus universiteto ligoninės Santaros

klinikų Neurologijos centre 2022 m. Metodas: nuasmenintų duomenų analizė, šaltinis – ambulatorinės neurologo konsultacijos dėl Parkinsono ligos aprašas E025.

*Tikslas:* ištirti vakcinuotumą nuo COVID-19 ir susijusius veiksnius pacientams, sergantiems Parkinsono liga.

*Rezultatai.* Į tyrimą įtraukti 173 pacientai (tarp jų 68 vyrai, 39,3 %); vidutinis kohortos dalyvių amžius –  $67,99 \pm 1,34$  m., Parkinsono ligos trukmė –  $7,73 \pm 0,54$  m. Pacientų vakcinuotumas nuo SARS-Cov-2 bent viena doze buvo 85,6 %, o bendros Lietuvos populiacijos – 69,8 %. Pilnai vakcinuoti nuo SARS-Cov-2 buvo 81,5 % COVPARK-LT pacientų ir 33,4 % Lietuvos gyventojų. Laboratoriniais tyrimais patvirtinta, kad COVID-19 sirgo 20 % ( $N = 5$ ) neskiepytų ir 22,3 % ( $N = 33$ ) skiepytų kohortos asmenų ( $p = 0,087$ ). Nevakcinuotumas nuo COVID-19 buvo susijęs su vakcinuotumu nuo ne SARS-Cov-2 infekcijų (OR: 0,18,  $p < 0,01$ ), vakcinuotumu nuo gripo (OR: 0,21,  $p < 0,01$ ), vyriška lytimi (OR: 0,68,  $p < 0,05$ ), vyrų amžiumi (OR: 0,88,  $p < 0,05$ ), Parkinsono ligos trukme (OR: 1,1,  $p < 0,001$ ) ir stadija pagal Hoehn ir Yahr skalę (OR: 0,51,  $p < 0,05$ ).

*Išvados.* COVPARK-LT kohortos pacientų vakcinuotumas nuo SARS-Cov-2 viršijo Lietuvos bendros populiacijos vakcinuotumą. Nevakcinuotumas buvo tiesiogiai susijęs su moteriška lytimi, jaunesniu vyrų amžiumi ir lengvesne Parkinsono ligos stadija pagal Hoehn ir Yahr skalę. Vakcinuotumas buvo tiesiogiai susijęs su vakcinuotumu nuo kitų infekcijų (gripo, erkinio encefalito, pneumokokinės infekcijos). Vakcinuoti ir nevakcinuoti COVPARK-LT kohortos asmenys COVID-19 sirgo vieno- dvi dažnai.

**Raktažodžiai:** Parkinsono liga, COVID-19, SARS-Cov-2, vakcinacija.

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