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# Vaccine uptake in caregivers family members and patients with dementia and relationship with severity of dementia and caregiver burden: a cross-sectional study

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## Abstract

We cross sectionally evaluated COVID-19 and seasonal flu vaccination rates among 94 dyads consisting of informal caregiver family member and non-institutionalized patient with dementia observed in family-medicine practice in Zagreb, Croatia. COVID-19 vaccination rates in caregivers (78.7%) and patients with dementia (82.9%) were significantly higher than in general population. Caregiver and patient COVID-19 vaccination status (CVS) did not correlate. Among caregivers, seasonal flu vaccination ( $P = 0.004$ ) but no other investigated factors related to caregiving or dementia severity showed significant association with CVS. Among patients with dementia, CVS was significantly associated with lower number of caregiver hours dedicated per week ( $P = 0.017$ ), higher caregiver SF-36 role emotional HRQoL ( $P = 0.017$ ), younger patient age ( $P = 0.027$ ), higher MMSE ( $P = 0.030$ ), higher Barthel index ( $P = 0.006$ ), absence of neuropsychiatric symptoms of agitation and aggression ( $P = 0.031$ ), lower overall caregiver burden ( $P = 0.034$ ), lower burden of personal strain ( $P = 0.023$ ) and lower burden of frustration ( $P = 0.016$ ). Caregiving and severity of dementia-related factors significantly affect patient, but not caregiver CVS.

**Keywords** Alzheimer disease · Dementia · Caregiver burden · SARS-CoV-2 · Vaccination

## Introduction

Dementia and mild cognitive impairment without dementia may affect 6% and 17% of elderly patients encountered in the family-medicine practice [1, 2], and prevalence of these disorders is expected to further increase with the aging of the population [3]. These patients are often cared for by their family members who need to reorganize themselves to adapt to the newly imposed responsibilities.

Caregiving for family member with dementia affects all aspects of living, imposes substantial burden and can negatively reflect on health related quality of life (HRQoL), especially if a patient exhibits pronounced neuropsychiatric symptoms [4, 5].

Patients with dementia are an especially vulnerable group for development of complications associated with SARS-CoV-2 infection, and experience substantially higher mortality in comparison to age and sex matched COVID-19 patients [6]. Introduction of SARS-CoV-2 vaccination reduced the occurrence of severe and critical COVID-19 presentations but factors like vaccine hesitancy, waning effects of vaccination and non-efficient immunization of elderly patients with comorbidities still remain important problems in controlling the SARS-CoV-2 infection [7, 8]. Despite importance of COVID-19 vaccination for dementia patients, data on vaccination uptake among caregivers and dementia patients are scarce. Bruno et al. (2022) report that only three quarter (75%) of caregivers were vaccinated and vaccine uptake among caregivers seems to be affected dominantly by worries about potential side effects of vaccines [9].

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Whether and in what extent caregiver and patient vaccination status are affected by characteristics of caregiving, severity of dementia and caregiver burden is unknown at the moment. Thus, we aimed to investigate how was caregiver and patient COVID-19 vaccination status related to these parameters. We hypothesized that higher caregiver burden would negatively affect both caregiver and patient vaccination status.

## Methods

We have evaluated an initial cohort of 131 dyads consisting of one caregiver family member and non-institutionalized patient with dementia chosen from 97,302 insured persons in 60 family-medicine practices in Health-Care Center Zagreb-West in period from October 2017 to September 2018. Patients had diagnosis of dementia established by either neurologist or psychiatrist and had ICD-10 codes F00, F01, F02, F03 or G30 documented in their medical history. Institutionalized patients, those who did not have diagnosis established by a neurologist or a psychiatrist, those whose dominant caregiver was not a family member or did not consent to participate were excluded from the study. Six instruments were used: the 36-item short form health survey (SF-36), the Zarit burden interview (ZBI), the mini mental state examination (MMSE), the Barthel index, the neuropsychiatric inventory-questionnaire (NPI-Q) and a structured questionnaire including general questions about a caregiver and a patient. Data collected were used to investigate HRQoL and caregiver burden and to perform psychometric validation of the ZBI in our cohort of patients, and were published previously [4, 5].

We subsequently performed cross-sectional analysis of COVID-19 and flu vaccination status of caregivers and patients with dementia in March 2023 in caregivers/patients who had available information on COVID-19 vaccination status which we present in the current study. A total of 94 dyads for caregiver and 41 dyads for patient vaccination status were evaluated. Data were obtained from electronic medical records. Caregivers and patients who were alive at the time of analysis and received at least two doses of COVID-19 vaccine were considered fully vaccinated. Caregivers and patients who deceased prior to March 2023 and did not receive COVID-19 vaccination were excluded from analysis. Associations of caregivers' and patients' characteristics, characteristics of caregiving, type and severity of dementia (MMSE, Barthel index, NPI-Q), HRQoL and ZBI with full vaccination status were evaluated. All caregivers provided written informed consent and the study was approved by the Institutional review board. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation

(institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008.

## Statistical methods

Normality of distribution of numerical variables was analyzed using the Shapiro-Wilks test. Due to non-normal distribution, numerical variables were presented as median and interquartile range (IQR) and were compared between groups using the Mann Whitney *U* test. Categorical variables were presented as frequencies and percentages and were compared between groups using the  $\chi^2$ -test. Test for one proportion was used to assess difference in observed and general population reported proportion of vaccinated patients [10]. *P* values < 0.05 were considered statistically significant. All analyses were done using the MedCalc statistical software version 20.114 (MedCalc Software Ltd, Ostend, Belgium).

## Results

We analyzed a total of 94 caregiver-patient dyads for caregiver vaccination status and 41 caregiver-patient dyads for patient vaccination status. Median age was 59.5 years, IQR (53–71), in caregivers and 80 years, IQR (76–84), in patients with dementia, respectively. There were 70 (74.5%) females among caregivers and 61 (64.9%) among patients with dementia, respectively. Caregivers were children of patients in 47 (50%) and spouses in 36 (38.3%) cases. Median score of MMSE test was 15 points, IQR (10–21), Barthel index score 87.5 points, IQR (70–100), and ZBI score 29 points, IQR (19–39).

Among 94 evaluable caregivers, 17 (18.1%) did not receive any, 3 (3.2%) received one, 28 (29.8%) two, 37 (39.4%) three and 9 (9.6%) four COVID-19 vaccine doses. Among 41 evaluable caregivers, 4 (9.8%) did not receive any, 3 (7.3%) received one, 11 (26.8%) two, 18 (43.9%) received three and 5 (12.2%) received four COVID-19 vaccine doses. A total of 29 (31.5%) caregivers and 18 (66.7%) patients with dementia received seasonal flu vaccination.

Percentages of fully COVID-19 vaccinated caregivers (78.7%) and patients with dementia (82.9%) were significantly higher than reported in general Croatian population (55.9% [10]), *P* < 0.001 for both comparisons.

Associations of caregivers' and patients' clinical characteristics with caregivers' vaccination status are presented in Table 1 and Supplementary Table S1. Only one factor was significantly associated with full COVID-19 vaccination of caregivers, and it was seasonal flu vaccination (*P* = 0.004), whereas there was no significant association with any other investigated parameter (including age,

**Table 1** Relationship of caregiver COVID-19 vaccination status with clinical characteristics

Caregiver vaccination status	Fully vaccinated (N=74)	Non fully vaccinated (N=20)	P value
Caregiver age (years)	60.5 IQR (54–71.75)	56 IQR (51.75–70.25)	0.413
Caregiver gender	18/74 (24.3%)	6/20 (30%)	0.606
Male	56/74 (75.7%)	14/20 (70%)	
Female			
Caregiver seasonal flu vaccination	28/72 (38.9%)	1/20 (5%)	0.004 *
Patient seasonal flu vaccination	14/17 (82.4%)	2/4 (50%)	0.228
Patient fully COVID-19 vaccinated	24/29 (82.8%)	4/4 (100%)	1.000
Caregiver education (years)	12 IQR (12–16)	12 IQR (12–14)	0.393
Caregiver employment status	32/74 (43.2%)	10/20 (50%)	0.224
Employed	4/74 (5.4%)	3/20 (15%)	
Unemployed	38/74 (51.4%)	7/20 (35%)	
Retired			
Caregiver relationship with a patient	29/74 (39.2%)	7/20 (35%)	0.877
Spouse	36/74 (48.6%)	11/20 (55%)	
Children	9/74 (12.2%)	2/20 (10%)	
Other			
Living in the same household	62/74 (83.8%)	18/20 (90%)	0.727
Length of caregiving (years)	2.5 IQR (2–3.75)	2 IQR (2–4)	0.805
Hours dedicated per week	56 IQR (40–80.5)	53 IQR (33.75–70)	0.323
Hours of help received per week	20.5 IQR (0–44.25)	35 IQR (13.75–59.25)	0.139
Caregiver anxious-depressive symptoms	10/74 (13.5%)	5/20 (25%)	0.299
Patient age (years)	80 IQR (77–83.75)	80 IQR (74.75–86.5)	0.993
Patient gender	24/74 (32.4%)	9/20 (45%)	0.296
Male	50/74 (67.6%)	11/20 (55%)	
Female			
Patient education (years)	12 IQR (4.25–14)	9 IQR (4–12.5)	0.456
Type of dementia	41/74 (55.4%)	15/20 (75%)	0.277
Alzheimer disease	28/74 (37.8%)	4/20 (20%)	
Vascular dementia	5/74 (6.8%)	1/20 (5%)	
Other			
Duration of dementia (years)	4 IQR (2–5)	4 IQR (2.75–5.25)	0.486
Use of daily care services	18/74 (24.3%)	5/20 (25%)	1.000
MMSE score	15 IQR (10–20)	18.5 IQR (10.75–22)	0.500
Barthel index score	85 IQR (70–100)	90 IQR (68.75–100)	0.929
NPI-Q score	24.5 IQR (12–37.75)	21 IQR (5.75–37.75)	0.647
NPI-Q distress score	15 IQR (6–23.75)	13 IQR (4–20.5)	0.343
Overall ZBI score	29 IQR (19–41.5)	29 IQR (20.25–33)	0.621

\*Statistically significant at level  $P < 0.05$

sex, patient COVID-19 or flu vaccination status, employment, education, relationship with the patient, caregiving characteristics, dementia type and severity, caregiver burden, HRQoL, and other,  $P > 0.05$  for all comparisons).

Associations of caregiver and patient clinical characteristics with patient vaccination status are presented in Table 2 and Supplementary Table S2. Similarly to caregivers, patient COVID-19 full vaccination status was significantly associated with patient seasonal flu vaccination ( $P = 0.007$ ) and had no association with caregiver COVID-19 or flu

vaccination status ( $P > 0.05$  for both comparisons). However, patient COVID-19 full vaccination was significantly associated with lower number of hours dedicated per week ( $P = 0.017$ ), higher SF-36 role emotional HRQoL ( $P = 0.017$ ), younger patient age ( $P = 0.027$ ), higher MMSE ( $P = 0.030$ ), higher Barthel index ( $P = 0.006$ ), absence of neuropsychiatric symptoms of agitation and aggression ( $P = 0.031$ ), lower overall ZBI ( $P = 0.034$ ), lower burden of personal strain ( $P = 0.023$ ) and lower burden of frustration ( $P = 0.016$ ).

**Table 2** Relationship of patient with dementia COVID-19 vaccination status with clinical characteristics

Patient vaccination status	Fully vaccinated ( <i>N</i> =34)	Non fully vaccinated ( <i>N</i> =7)	<i>P</i> value
Caregiver age (years)	54 IQR (49–68)	64 IQR (55–78)	0.083
Caregiver gender	11/34 (32.4%)	2/7 (28.6%)	1.000
Male	23/34 (67.6%)	5/7 (71.4%)	
Female			
Caregiver seasonal flu vaccination	9/28 (32.1%)	0/4 (0%)	0.303
Caregiver fully COVID-19 vaccinated	24/28 (85.7%)	5/5 (100%)	1.000
Patient seasonal flu vaccination	18/23 (78.3%)	0/4 (0%)	0.007 *
Caregiver education (years)	14 IQR (12–16)	16 IQR (12–16)	0.658
Caregiver employment status	21/34 (61.8%)	3/7 (42.9%)	0.529
Employed	1/34 (2.9%)	0/7 (0%)	
Unemployed	12/34 (35.3%)	4/7 (57.1%)	
Retired			
Caregiver relationship with a patient	12/34 (35.3%)	3/7 (42.9%)	0.554
Spouse	17/34 (50%)	4/7 (57.1%)	
Children	5/34 (14.7%)	0/7 (0%)	
Other			
Living in the same household	25/34 (73.5%)	7/7 (100%)	0.315
Length of caregiving (years)	2 IQR (1–3)	2 IQR (1.5–3)	0.465
Hours dedicated per week	41 IQR (31.25–66.5)	70 IQR (58–84)	0.017 *
Hours of help received per week	25.5 IQR (2.5–48.75)	40 IQR (7–44)	1.000
Caregiver anxious-depressive symptoms	4/34 (11.8%)	0/7 (0%)	1.000
Patient age (years)	77 IQR (71–81)	82 IQR (82–83.5)	0.027 *
Patient gender	7/34 (20.6%)	2/7 (28.6%)	0.637
Male	27/34 (79.4%)	5/7 (71.4%)	
Female			
Patient education (years)	12 IQR (6.5–12)	12 IQR (8–13)	0.957
Type of dementia	18/34 (52.9%)	4/7 (57.1%)	0.665
Alzheimer disease	14/34 (41.2%)	2/7 (28.6%)	
Vascular dementia	2/34 (5.9%)	1/7 (14.3%)	
Other			
Duration of dementia (years)	3.5 IQR (1–4)	4 IQR (3–4.5)	0.455
Use of daily care services	8/34 (23.5%)	3/7 (42.9%)	0.361
MMSE score	20.5 IQR (15–23.75)	15 IQR (8.5–19)	0.030 *
Barthel index score	100 IQR (91.25–100)	80 IQR (77.5–87.5)	0.006 *
NPI-Q score	17.5 IQR (8.5–27.5)	17 IQR (13–28)	0.488
NPI-Q distress score	12.5 IQR (5.25–20.25)	13 IQR (8.5–19)	0.532
Overall ZBI score	25 IQR (14.25–33.25)	33 IQR (27.5–47.5)	0.034 *

\*Statistically significant at level  $P < 0.05$

## Discussion

To the best of our knowledge our study is the first to investigate relationship between COVID-19 vaccination of caregivers/patients with caregiving and dementia characteristics, as well as caregiver burden and HRQoL. There are several important points we would like to emphasize.

There is a high proportion of fully vaccinated caregivers which corresponds to data reported in the literature [9]. Similar was observed for patients with dementia in our study. As we show these proportions are high above general population. Nevertheless, caregivers' and patients' vaccination status are not mutually correlated and are determined by different factors. Also, a substantial proportion of caregivers

did not receive vaccination (18.1%) despite providing caregiving for their very vulnerable family members.

Seasonal flu vaccination was important predictor of COVID-19 vaccination status in both caregivers and patients with dementia, although proportion of flu vaccinated persons was much lower among caregivers than patients with dementia. Seasonal flu vaccination was only significant predictor of caregiver COVID-19 vaccination status supporting the negative attitudes toward vaccination and personality traits could play much more important role than caregiving and characteristics of patients with dementia themselves.

On the opposite, caregiving and dementia-related factors significantly affected COVID-19 vaccination of patients with dementia. It is of special interest that higher caregiver burden,



especially subsets of burden of personal strain and frustration (assessed by ZBI), lower HRQoL in the role emotional domain (assessed by SF-36), higher cognitive impairment (assessed by MMSE test), lower functional status (assessed by Barthel index), and presence of neuropsychiatric symptoms of agitation and aggression (assessed by NPI-Q) significantly reflected on patient vaccination status. Similar was observed for older age of patients and higher numbers dedicated per week. Thus, both caregiver and patient-related aspects of dementia and caregiving affect the COVID-19 vaccination of patients. These observations highlight the possibilities to recognize subgroups of caregivers with high COVID-19 vaccine hesitancy towards patient vaccination and to tailor specific interventions that could be implemented in the family care practice. These subgroups would be caregivers providing care for patients with more severe functional limitations, higher cognitive impairment and more pronounced neuropsychiatric symptoms of agitation/aggression with high caregiving burden. These interventions would probably need to be targeted both towards changing caregivers' attitudes towards vaccination, as well as towards providing additional opportunities to assist in the care of difficult patients (in-home vaccination, emotional counseling, third person assistance, etc.).

Main limitations of our work are cross-sectional study design and inability to establish causality between observed associations and medium size sample. Results obtained in our cohort of urban dwelling caregivers and patients of white race from Croatian capital city might not be translatable to rural and contexts of other regions. Although our results are indicative that more frail patients (with higher cognitive impairment and higher functional dependency) were less likely to receive COVID-19 vaccination, we did not use specific frailty scales to evaluate frailty to properly evaluate this phenomenon. Nevertheless, our results have important implications on recognition of caregivers and patients with COVID-19 vaccine hesitancy and may help in designing targeted interventions aimed at improvement of vaccination rates.

In conclusion, COVID-19 vaccination rate of caregivers and patients with dementia is higher than in general population, but with substantial proportion of both not being vaccinated. Caregiver and patient vaccination status do not correlate and caregiving- and severity of dementia- related factors significantly affect patient, but not caregiver vaccination rates.

**Supplementary Information** The online version contains supplementary material available at <https://doi.org/10.1007/s40520-023-02443-6>.

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**Author contributions** JL, IJ and ML contributed to the study design. JL and MH performed material preparation and data collection. Analysis were performed by KB and ML. The first draft of the manuscript was written by JL. All authors read, critically revised and approved the final version of the manuscript.

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**Availability of data and materials** Data are available per reasonable request from the corresponding author.

## Declarations

**Conflict of interest** All authors declare they have no conflict of interest.

**Ethical approval and informed consent** The study was approved by the Institutional Review Board. All caregivers provided written informed consent for the study. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008.

**Consent for publication** All caregivers provided written informed consent for publication.

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