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Caregiver Burden Among Patients with COVID-19: A Systematic Literature Review of Real-World Evidence

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INTRODUCTION

- Studies show that the Coronavirus Disease 2019 (COVID-19) significantly affects the health-related quality of life (HRQoL), work productivity and activity of patients and their families[1-3].
- A significant gap exists in systematically reviewing the impact of patients' COVID-19 illness on their informal caregivers.
  - Informal caregivers defined as individuals providing care to family or friends with physical, cognitive, or mental health conditions without receiving financial compensation[4].

OBJECTIVE

- To systematically synthesize real-world evidence (RWE) characterizing the burden of the patient's COVID-19 illness on their informal caregivers.

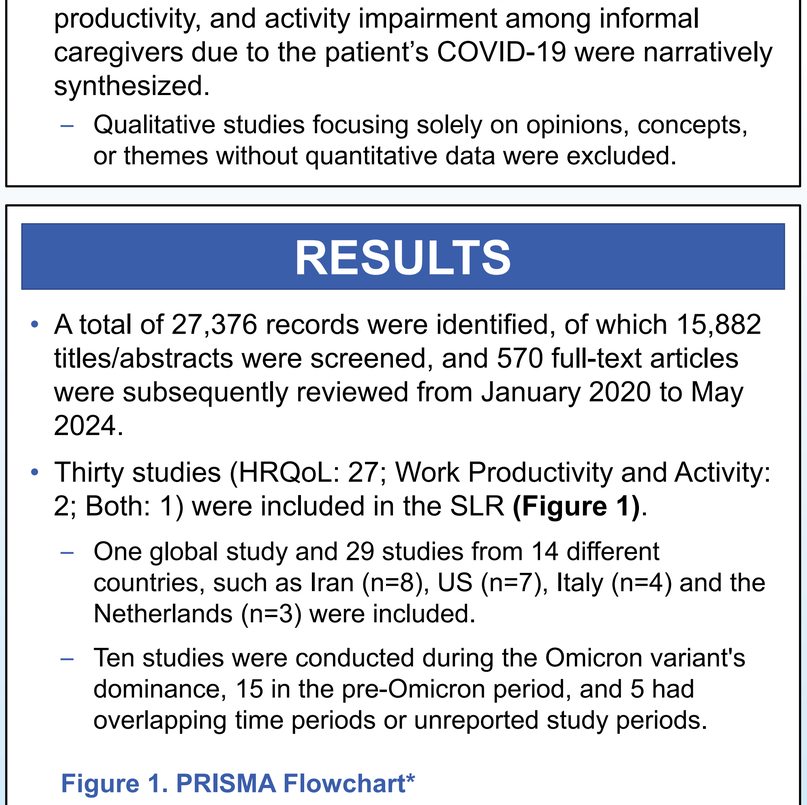
METHODS

- A systematic literature review (SLR) was conducted using six databases, identifying human studies published in English language from January 1, 2020, to May 31, 2024.
- Two independent reviewers performed screening and full-text review based on the PICOS criteria outlined in an a priori protocol.
- Quantitative RWE studies assessing HRQoL, work productivity, and activity impairment among informal caregivers due to the patient's COVID-19 were narratively synthesized.
  - Qualitative studies focusing solely on opinions, concepts, or themes without quantitative data were excluded.

RESULTS

- A total of 27,376 records were identified, of which 15,882 titles/abstracts were screened, and 570 full-text articles were subsequently reviewed from January 2020 to May 2024.
- Thirty studies (HRQoL: 27; Work Productivity and Activity: 2; Both: 1) were included in the SLR **(Figure 1)**.
  - One global study and 29 studies from 14 different countries, such as Iran (n=8), US (n=7), Italy (n=4) and the Netherlands (n=3) were included.
  - Ten studies were conducted during the Omicron variant's dominance, 15 in the pre-Omicron period, and 5 had overlapping time periods or unreported study periods.

Figure 1. PRISMA Flowchart*



*PRISMA template was adapted from Page et al. The PRISMA 2020 statement

RESULTS (continued)

Impact on Caregiver's Work Productivity and Activities – 3 Studies

- In Iran [n=425], the reported mean (SD) daily hours and number of days of informal caregiving were 5.29 (2.98) hours and 15.5 (7.77) days, respectively[5].
  - The most difficult caregiving activities were indoor (32.5%), outdoor (26.4%), personal (22.1%), and taking patients to formal care centers (19.1%)[5].
  - 72.0% of the patients reported complete or very much dependency on their informal caregivers[5].
- In the UK [n=360], the reported mean (SD) and median (IQR) weekly hours of caregiving were 21.3 (19.9) and 15.0 (8.0-28.0) hours, respectively[6].
  - The mean (SD) weekly caregiving hours ranged from 19.7 (19.8) hours for patients with <1 year of long COVID [n=161], to 27.0 (17.5) hours for those with an unknown duration of long COVID [n=41][6].
  - 22.8% of caregivers reported having reduced paid or unpaid work hours to accommodate their caregiving[6].
- In the Netherlands [n=197; 104 caregivers working before patient's ICU admission due to COVID-19], 27.9% of caregivers experienced work-related problems at 12-month follow-up[7].
  - 6.7% of caregivers worked less hours than before patient's ICU admission, 2.9% retired early, 7.7% were still on sick leave, and 10.6% stopped working completely[7].

Impact on Caregiver's HRQoL – 28 Studies

- Twenty-eight studies assessed HRQoL outcomes, predominantly psychological burden, using more than 34 standard patient-reported outcome (PRO) measures and/or specific questionnaires.
  - Most commonly used PRO measures included Hospital Anxiety and Depression Scale (HADS; 7 studies), Impact of Event Scale (IES)-6 items or revised scale (7 studies), Generalized Anxiety Disorder 7-Item (GAD-7; 4 studies).
  - Approximately two-thirds of the caregivers of COVID-19 patients experienced worsening HRQoL and increased psychological issues.

EQ-5D-5L – 3 Studies

- EQ-5D mean utility scores among caregivers ranged from 0.64 to 0.92 depending on the severity of the patient's illness, and the recovery/follow-up period **(Table 1)**.
  - EQ-5D and EQ-VAS scores showed significant negative effects on caregivers of patient with severe COVID-19 compared to those caring for mild or moderate cases, as well as at baseline compared to follow-up at 1-3 weeks.

Table 1. EQ-5D-5L Scores

Study (Country)	Wiertz 2024 (Netherlands)		Zhou 2023 (China)		
Measure	EQ-5D-5L (Dutch version)		EQ-5D-5L (Chinese version)		
Study Population	Caregivers of post-ICU patient (aged median [IQR]: 62 [57-68] yrs)		Caregivers of pediatric patients (aged 0-18 yrs)		
Cohort	Post-ICU at 3 months	Post-ICU at 12 months	With or Without COVID-19	COVID-19 Severity	COVID-19 Recovery
No. of Caregivers	57	37	Without: 231 With: 861	Mild: 311 Moderate: 389 Severe: 161	F/U: 258
EQ-5D mean (SD)	0.84 (0.15)	0.87 (0.12)	Without: 0.88 With: 0.77	Mild: 0.80 Moderate: 0.79 Severe: 0.64	BL: 0.69 F/U: 0.92
EQ-VAS mean (SD)	78.2 (13.2)	75.8 (14.6)	Without: 83.6 With: 72.2	Mild: 76.5 Moderate: 71.4 Severe: 65.7	BL: 62.0 F/U: 85.8

BL, baseline; EQ-5D-5L, EuroQoL 5-Dimension 5-Level; F/U, follow-up at 1-3 weeks; ICU, intensive care unit; IQR, inter quartile range; SD, standard deviation; VAS, visual analogue scale. Note: Martins 2023 (Brazil) did not report overall EQ-5D-5L scores

Stress/Post-traumatic Stress Disorder (PTSD) – 13 Studies

- Different PRO measures such as the IES-6/IES-R, the Depression, anxiety, and stress scale-21 (DASS-21), the Perceived Stress Scale (PSS-10) etc. assessed stress/PTSD.
  - Moderate-to-high stress was reported among 5.1% [Netherlands; post-ICU at 3 vs. 12 months: 28.1% vs. 5.1%][8] to 95.7%[11] of caregivers.
  - PTSD was reported among caregivers of ICU COVID-19 patients [IES-6 mean 12.6][12], and deceased patients [IES-R mean: 36.1 vs 20.4 in survivors; $P < 0.001$][13].

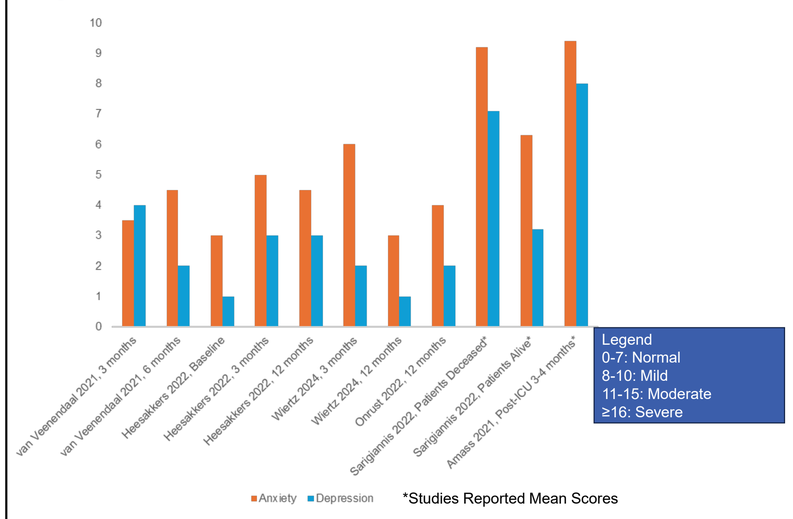
*IES ≥ 10: Significant symptoms of PTSD; IES-R ≥ 33: Diagnosis of PTSD

RESULTS (continued)

Anxiety/Depression – 16 Studies

- Anxiety and Depression were assessed using different PROs including the HADS, GAD-7, Patient Health Questionnaire-9 (PHQ-9), DASS-21.
  - Anxiety was reported among up to 81.8%[14] of caregivers (including up to 29.9% with severe anxiety[15]).
  - Depression was reported among up to 47.6%[12] of caregivers (including low depression up to 86.4%[16], and high depression up to 14.1%[15]).
  - Although the HADS median scores (4 studies)[7,8,17,18] reported normal levels for both domains, the mean scores (2 studies)[12,13] were high among caregivers of deceased patients or those with severe illness **(Figure 2)**.

Figure 2. HADS Median Scores



Overall Caregiver burden – 16 Studies

- Sixteen studies reported moderate caregiver burden, assessed using PROs such as Novak and Guest's Caregiver Burden Inventory (CBI, 4 studies), the Zarit CBI (4 studies), the Short-Form 12 (1 study), SF-20 (1 study), the life changes due to Covid-19 questionnaire (1 study).

CONCLUSIONS

- **RWE studies characterize HRQoL outcomes using various PROs, highlighting the significant humanistic burden among caregivers of patients with COVID-19.**
- **Heterogeneity of studies (e.g., population characteristics, different PROs administered, and outcomes assessed) precluded quantitative synthesis and meta-analysis.**
- **Limited data exist to assess the impact on the work productivity of caregivers due to patient's COVID-19.**

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Disclosures

M.D.F. and V.L.W. are employees of Pfizer Inc., and each held Pfizer stock or stock options at the time of the study. S.V. and A.S. are employees of HealthEcon Consulting, Inc., which was a paid contractor to Pfizer.

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