**The impact of the COVID-19 pandemic on the psychological well-being of caregivers of people with dementia or Mild Cognitive Impairment: A systematic review and meta-analysis**

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**Abstract**

The aim of this systematic review was to investigate the effects of the COVID-19 lockdown on the psychological well-being of caregivers of patients with dementia or Mild Cognitive Impaitrment (PwD/MCI). Electronic databases were searched from inception to Aug 2022 for observational studies investigating COVID-19 lock-down and psychological well-being of caregivers of PwD/MCI. Summary estimates of standardized mean differences (SMD) in psychological well-being scores pre- versus during COVID-19 were calculated using a random-effects model. Fifteen studies including 1702 caregivers (65.7% female, mean age 60.40±12.9 years) with PwD/MCI were evaluated. Five studies found no change in psychological well-being parameters including depression, anxiety, distress, caregiver burden, and quality of life, 10 studies found a worsening in at least one parameter: depression (6 studies, n=1368; SMD=0.40; 95%CI:0.09-0.71; p=0.01, I2=86.8%), anxiety (7 studies, n=1569; SMD=1.35; 95%CI:0.05-2.65; I2=99.2%), caregiver’s distress (6 studies, n=1320, SMD=3.190; 95%CI:1.42-4.95; p<0.0001; I2=99.4%), caregiver’s burden (4 studies, n=852, SMD=0.34; 95%CI:0.13-0.56; p=0.001; I2=54.1%) (p<0.05). There was an increase in depression, anxiety, caregiver burden and distress in caregivers of PwD/MCI during lockdown in the COVID pandemic. This could have longer term consquences, and it is essential that caregivers’ psychological well-being is assessed and supported, to benefit both themselves and those for whom they care.

**Keywords:** COVID-19, psychological well-being, caregivers, dementia, systematic review, meta-analysis

1. **Introduction**

The COVID-19 pandemic has influenced many conditions related to neurodegenerative disease both during the pandemic and beyond. For example, survivors of COVID-19 infection had a higher incidence of new-onset Alzheimer's Disease (AD) and dementia (especially older people) compared to those without COVID-19 and other respiratory infections [1]. Also, COVID-19 was likely a significant contributor to the large increase in deaths from dementia in recent years [2]. Importantly, the COVID-19 pandemic has posed significant social, psychological, emotional, and physical challenges to family members and friends who provide care for people with dementia, thereby creating a crisis for caregivers [3]. 30% of older adults with dementia rely on three or more unpaid caregivers, compared to 23% of older adults without dementia [3]. Therefore, the COVID-19 pandemic per se and its wider psychosocial impact may have affected multiple caregivers.

Efforts to stop the spread of SARS-CoV-2 led to restrictions on in-person contact, including "stay-at-home" recommendations to avoid infection, simultaneously with health service interruptions [4]. Due to the "stay-at-home" recommendations, caregivers endured disrupted daily routines, fewer supportive services for themselves and their care recipient, and reduced social relations [5]. The consequences of the pandemic have been noteworthy in vulnerable populations, increasing existing health inequalities [6]. These consequences will likely build on existing social inequalities and proportionately affect vulnerable populations, such as caregivers.

Lockdown restrictions were associated with worsening neuropsychiatric symptoms in people living with dementia; and those with mild cognitive impairment (MCI) [7-9]. There was a significant emotional burden in caregivers [7-8]. In a nationwide survey in Italy during lockdown in 2020 caregivers (n= 5321) reported a significant increase in anxiety (45.9%), depression (18.6%), irritability (26.2%), and distress (28.9%) during quarantine [10]. Notably, in the one-year follow-up of Italian caregivers (n=85), stress-related symptoms stayed high, including depressive symptoms and feelings of sadness being the most prevalent [11].

The COVID-19 pandemic has posed significant social, psychological, emotional, and physical challenges to caregivers, but detail is lacking on the specific consequences including depression, anxiety, distress, caregiver burden, mental well-being, and quality of life. Importantly, there is currently no meta-analysis investigating how caregivers’ general psychological well-being was affected by the COVID-19 pandemic. Therefore, the aim of this review was to examine the effect of the COVID-19 pandemic on caregivers of people with dementia (PwD) or MCI.

1. **Method**

This systematic review was conducted according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) criteria [12] and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [13]. The present review was pre-registered with PROSPERO [registration number: CRD42022349890].

* 1. **Search strategy**

We searched MEDLINE/PubMed (via Ovid), Embase, Scopus, CINAHL (Cumulative Index to Nursing and Allied Health Literature), PsycINFO, and Web of Science. We built detailed and highly sensitive search strategies combining search terms (free vocabulary words and controlled vocabulary terms) for dementia, COVID-19 and caregivers (full search strategies in Appendix), with the help of an expert librarian, and searched from database inception to 07 Aug 2022.

The search terms used were (dement\* OR Alzheimer\* OR Lewy OR Posterior cortical atrophy OR Binswanger OR Progressive supranuclear palsy OR Frontotemporal disorder\* OR Frontotemporal degeneration OR Corticobasal degeneration OR Corticobasal syndrome OR Mild cognitive impairment) **AND** **(**Caregiver OR Carer OR Caring OR family OR Relative OR Spouse OR Children) **AND** (COVID-19 OR Novel Coronavirus–Infected Pneumonia OR 2019 novel coronavirus OR 2019-nCoV OR SARS-CoV-2). ti,ab.

* 1. **Inclusion and Exclusion criteria**

The included studies were published as (i) conducted during the COVID-19 pandemic, (ii) longitudinal, cohort or case-control observational studies, (iii) involving unpaid/informal caregivers (e.g., family members) or paid caregivers, (iv) involving caregivers for people with a prior diagnosis of dementia or MCI (or other condition defined as cognitive decline which has an increased risk of future dementia), (v) reporting caregiver burden using validated scales [secondary outcomes depression, anxiety, distress using validated scales]

Studies were excluded if they were (i) qualitative or thematic studies, (ii) conference abstracts, (iii) cross-sectional studies, (iv) carried out prior to and not including data during the COVID-19 pandemic, (v) not longitudinal in design, (vi) included caregivers for persons without MCI/dementia, (viii) and when outcomes were not assessed using validated scales.

* 1. **Data extraction and statistical analyses**

The literature search, assessment of inclusion and exclusion criteria, quality of studies, and extraction of data were independently undertaken and verified by two authors (DR, AC). The results were then compared, and, in case of inconsistency, consensus was reached with the participation of a third author (PS). The following information was extracted: 1) characteristics of the study population (e.g., sample size, demographics, country in which the study was performed, date of data collection); 2) setting in which the study was performed (i.e. own home, residential facility); 3) definition of caregivers (paid, unpaid, family member or not, living with the PwD/MCI or not) 4) presence of dementia/MCI, dementia type, 5) value pre COVID-19 (or early in lockdown) and later in lockdown for cognitive impairment severity (MMSE, CDR), patients' neuropsychiatric symptoms using validated scales (e.g. NPI, CBI6), caregivers’ mental health outcomes (e.g., caregiver burden, anxiety, depression) using validated scales.

* 1. **Meta-Analysis Method**

We synthesized the results using a meta-analysis when at least three studies for the same outcome were present. The data were reported as standardized mean differences (SMDs) with their 95% confidence intervals (CIs), under a random-effects model.

In case of a significant heterogeneity (identified as *I²*>=50%), we planned to run meta-regression analyses, but since less than ten studies were present for each outcome, this analysis was not performed. Similarly, sensitivity analyses planned by protocol were not carried out since less than three studies were present for each stratum. Publication bias was assessed using Egger's test and in case of a publication bias a trim-and-fill analysis was planned.

For all analyses, a p-value less than 0.05 was considered statistically significant. All analyses were performed using STATA version 14.0 (StataCorp).

* 1. **Assessment of study quality/risk of bias**

The Risk of Bias in Non-randomized Studies - of Exposure (ROBINS-E) tool was used to assess the risk of bias of the selected studies. ROBINS-E provides a structured approach to assessing the risk of bias in observational epidemiological studies [14]. ROBINS-E was used thorough examination of the strength of evidence about the following categories: Domain 1: Risk of bias due to confounding • Domain 2: Risk of bias arising from measurement of the exposure • Domain 3: Risk of bias in selection of participants into the study (or into the analysis) • Domain 4: Risk of bias due to post-exposure interventions • Domain 5: Risk of bias due to missing data • Domain 6: Risk of bias arising from measurement of the outcome • Domain 7: Risk of bias in selection of the reported result. The risk of bias was recorded as low risk of bias, some concerns, high risk of bias or very high risk of bias. Two researchers independently assessed all items (YC, BA), and disagreements were resolved by consensus in consultation with a third researcher (PS or SDS).

1. **Results**
   1. **Search results**

Of 1489 studies, we examined 73 articles as full texts (Figure 1), excluding 58 articles, mainly due to data being cross-sectional.15 studies were included in the review [11,15-28].

* 1. **Descriptive results (Table 1)**

The majority of the studies (N=12) were conducted in Europe [11, 15, 17-19, 21-26, 28], and three in Asia [16,20,27]. 1702 caregivers of PwD/MCI were included (mean age 60.40 ± 12.9 years, 65.7% female). PwD were older, mean age 76.36 ±9.32 years. Caregivers were more likely to be female than PwD (65.7% vs 52.0%). Almost all caregivers were unpaid (>90%); 52.2% were spouses and were living with PwD together (72.9%).

Two studies did not specify the type of dementia [20,26]. The prevalence of Alzheimer’s disease (AD), vascular dementia, and other dementia were 36.4%, 25.5% and 32.7%, respectively, with 5.4% having MCI. The dementia was reported in nine studies as moderate (27.9%) or severe (18.9%): six studies did not define the severity. Almost all caregivers were unpaid family members (>90% were unpaid or were family) and were living with PwD (72.9%).

Multiple scales were used to describe the impact on caregivers’ psychological well-being Neuropsychiatric Inventory (NPI) (n=5); Caregiver Burden Inventory (CBI) (n=3); Generalized Anxiety Disorder Scale-7 (GAD-7) (n=3); Depression Anxiety and Stress Scale (DASS) (n=2); Zarit Burden Index (ZBI) (n=2), c-Dementia Quality of Life Instrument (n=2). One study each used Hospital Anxiety and Depression Scale (HADS), Patient Health Questionnaire-9 (PHQ-9), CarerQol-7D/ CarerQol-VAS, National Statistics ONS4, Center for Epidemiologic Studies Depression Scale (CED). The lockdown duration varied between 8-61 weeks (mean 23.15 weeks).

Across all studies (summarised in Table 1), there were no changes in psychological well-being in five studies [18,19,21,26,27] and worsening psychological well-being in 10 studies.

* 1. **Meta-analysis (Figure 2)**

There was a significant increase in **depression** (6 studies [11,15,16,20,24,27], n= 1368; SMD=0.401; 95% CI: 0.091 to 0.711; p=0.01; *I2*=86.8%) (**Figure 2a**); in **anxiety** (7 studies [11,15,16,20,24,26,27], N=1569; and SMD=1.357; 95%CI: 0.055-2.659; *I2*=99.2%) (**Figure 2b**), in **caregiver’s burden** (4 studies [11,16,17,25], n=852; SMD=0.34; 95% CI: 0.13 to 0.56; p=0.001; *I2*=54.1%) (**Figure 2c**), and in **caregiver’s distress** (6 studies [20,23-25,27,28], n = 1320; SMD=3.190; 95%CI: 1.423-4.957; p<0.0001; *I2*=99.4%) (**Figure 2d**). There was high heterogeneity across studies for all outcomes (less for caregiver’s burden). The Egger’s test was marginally significant for a possible publication bias for studies of anxiety (p=0.06), but the trim-and-fill analysis left the SMD unchanged. There was no publication bias for any other outcome.

* 1. **Meta-regression and sensitivity analyses**

We pre-planned several meta-regression and sensitivity analyses such as paid vs unpaid caregivers, longitudinal data compared within pandemic vs compared to before the pandemic, different outcome durations, dementia vs MCI, early vs late onset dementia, the time without vs with vaccination. However, the outcomes included less than 10 studies, or the strata did not reach the minimum of four publications, thus these analyses were not possible.

* 1. **Risk of Bias**

The results of the risk of bias assessments are shown in Figure 2. Two studies were rated as very high risk of bias, six studies were rated as high risk of bias, and seven studies were rated as some concerns. Most of the studies had a high or very high level of bias (53.3%). The reasons for this might be due to the absence of those without dementia/MCI (i.e. control group), not evaluating confoundings, and the fact that caregiver’ psychological well-being were evaluated with a caregiver-based telephone interview.

**Table 1. Descriptive data of the included studies**

| **Author(s),**  **Year** | **Country** | **CG/**  **PwD, n** | **Mean**  **age** | **Female, n** | **Characteristics**  **of CG n** | **Mean**  **age** | **Female,**  **n** | **Dementia types** | **Dementia**  **severity** | **Caregiver Measurement** | **Lockdown duration, weeks** | **General Findings** | **RoB** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Altieri et al, 2021  \*DA  [15] | Italy | 84 | 48.7  (11.7) | 71  (84.5%) | Living with PwD (63) Unpaid (84)  Family (84)  -Spouses (10)  11.9% | 78.5 (10.1) | 61  (72.6%) | AD (47)  VAD (26)  FTD (9)  LBD (2) | Severe (29)  Moderate (38)  Mild (17) | HADS scale  CBI  RSA | 8 weeks | -increase in depression level  -high resilience had a negative effect on anxiety | High |
| Bao et al., 2022  \*CB  [16] | China | 177 | 62.5  (10.8) | 78  (44.1%) | Living with PwD (130)  Unpaid (177)  Family (177)  -Spouses (102)  11.9% | 71.0  (8.2) | 100  (56.5%) | AD (105)  DLB (22)  MCI (50) | NA | GAD-7  PHQ-9  PSQI  ZBI | 52 weeks | -increased caregiver burden and worsened psychological states | Some |
| Borges-Machado et al., 2020  \*CB  [17] | Portugal | 36 | 64.94  (13.5) | 15 (41.7%) | NA  Unpaid (36)  Family (36)  -Spouses (22)  61.1% | 74.28  (6.76) | 24 (66.7%) | AD (17)  VAD (2)  FTD (1)  MCI (5)  Others(11) | NA | CarerQol-7D  CarerQol-VAS | 12 weeks | -an increased caregiving burden and a decline in their well-being. | Very high |
| Bussè et al., 2022  \*DACB  [11] | Italy | 85 | 62  (14.6) | 59  (69.4%) | Living with PwD (57) Unpaid (85)  Family (85)  -Spouses (49)  57.6% | 74.62  (11.3) | NA | AD (51)  DLB (26)  FTD (6)  VAD (2) | Severe (18)  Moderate (16)  Mild (51) | CBI  PSQI  DASS-21 | 52 weeks | -Caregiver burden was higher during pandemic and time dependent  -caregivers reported at least one stress-related symptom (depression, irritability, anxiety, and sleep alterations) | Some |
| Carbone et al., 2021  [18] | Italy | 35 | 61.23 (9.91) | 26 (74.28%) | NA  Unpaid (34)  Family(34)  - Spouses (NA) | 82.60 (8.91) | 22 (62.9%) | AD (6)  VAD (13)  Others(16) | Severe (13)  Moderate and Mild (22) | NPI caregiver distress score | 8 weeks | No change was found in caregiver’ distress | High |
| Daley et al., 2022  [19] | United Kingdom | 248 | 70.08 (10.6) | 169  (68.1%) | Living with PwD (157)  Unpaid (248)  Family(248)  -Spouses (197)  79.4% | 77.47 (8.0) | 103 (41.5%) | AD (93)  VAD (37)  Others (118) | Severe (11)  Moderate  (73)  Mild (156) | C-DEMQOL | T1-T2:61 weeks  T2-T3:20 weeks | No change was found in caregiver’ quality of life | Some |
| Fong at al., 2021  \*DA  [20] | Hong Kong | 51 | 53.5 | 44  (86.3%) | Living with PwD (45)  Unpaid (51)  Family(51)  -Spouses (6)  11.8% | NA | NA | NA | NA | GAD-7  CES-D  PSS-10  ZBI | 12 weeks | A significant increase in depression symptom scores; no changes in anxiety, and caregiver distress | Some |
| Giebel et al., 2021  [21] | United Kingdom | 149 | 62 (13) | 118 (79.7%) | NA  Unpaid (149)  Family or friend (149)  -Spouses (NA) | 72 (10) | 14 (37.8) | AD (14)  VAD (8)  Others (15) | NA | PHQ-9  GAD-7 | 12 weeks | No significant changes in mental well-being | High |
| Hicks et al., 2022  [22] | United Kingdom | 114 | 66.1 (13.81) | 76  (69%) | Living with PwD (77)  Unpaid (114)  Family (114)  -Spouses (NA) | 79.5 (8.85) | 79  (58%) | AD (65)  DLB (6)  VAD (16) Others(27) | Severe (5)  Moderate  (25)  Mild (84) | C-DEMQQL carer | 12 weeks | Significant decline in quality of life | Some |
| Manini et al., 2021  \*CD  [23] | Italy | 94 | 64.4  (14.7) | 64  68.1% | Living with PwD (77)  Unpaid (89)  Family (89)  -Spouses (42) | 83.2  (5.5) | 67  (71.3%) | AD (78)  DLB (3)  VAD (3)  FTD (2)  Others(8) | Severe (28)  Moderate  (33)  Mild (33) | Neuropsychiatric Inventory Caregiver Distress Scale | 8 weeks | Significant, but overall modest increased in caregiver distress | High |
| Moretti et al., 2021  \*DA  [24] | Italy | 221 | NA | NA | Living with PwD (NA)  Unpaid (221)  Family (221)  --Spouses (NA) | 75.6 (6.6) | 119  (54%) | VAD (221) | NA | RSS  BDI  HAM-A | 8 weeks | Increased in depression, anxiety, and distress | High |
| Panerai at al., 2020  \*CB  [25] | Italy | 128 | 57.5 | 94  (73.4%) | Living with PwD (NA)  Unpaid (128)  Family (128)  -Spouses (57) | 76 | 67  (52.3%) | AD (31)  VAD (42)  FTD (8)  Others(47) | Severe (22)  Moderate  (47)  Mild (59) | Caregiver Burden Inventory (CBI)  NPI-Q | 8 weeks | An increased in caregiver burden and distress | Very high |
| Perach et al., 2022  \*A  [26] | United Kingdom | 114 | 66.1 (13.8) | 76  (67%) | Living with PwD (77)  Unpaid (NA)  Family (107)  -Spouses (63) | 79.8 (8.9) | 66  (58%) | NA | NA | National Statistics ONS4 | 32.8 weeks | - no significant changes in psychological wellbeing and anxiety | Some |
| Rajagopalan et., 2022  \*DA  [27] | India | 66 | 46.18 (16.11) | 18 (27.24) | Living with PwD (NA)  Unpaid (66)  Family (66)  -Spouses (18) | 67.48 (9.46) | 33 (50.0%) | AD (20)  VAD (9)  FTD (14)  Others(23) | Severe (13)  Moderate  (23)  Mild (30) | NPI-CD  DASS-21 | 21.4 weeks | No significant increase in depression, anxiety, and distress | High |
| Vernuccio et al., 2022  \*CD  [28] | Italy | 100 | NA | NA | Living with PwD (95)  Unpaid (NA)  Family (NA) | 77.1 | 59  (59%) | AD (34)  VAD (13)  DLB (1)  FTD (2)  MCI (28)  Others(22) | Severe (42)  Mild (30) | NPI-CD | 40 weeks  (Between two evaluation time) | Caregivers’ distress increased | Some |
| **Total** | **Asia:3**  **Europe:12** | **1702** | **60.40**  **(12.9)** | **65.7%** | **Living with PwD (72.9%)**  **Unpaid (99.6%)**  **Family (99.2%)**  **--Spouses (52.2%)** | **76.36**  **(9.32)** | **52.0%** | **AD (36.4%)**  **VAD (25.5%)**  **MCI (5.4%)** | **Severe dementia**  **(18.9%)**  **Moderate (27.9%)**  **Mild**  **(53.2%)** |  | **23.15 weeks** | **-5 studies: No changes in wellbeing.**  **-10 studies: Worsening psychological well-being** | **Some: 7**  **High: 6**  **Very High:2** |

Abbreviations: CB: Caregiver Burden; Caregiver Burden Inventory: CBI; CES-D: Center for Epidemiologic Studies Depression Scale; DASS-21: Depression Anxiety and Stress Scale; Hospital Anxiety and Depression Scale: GAD-7: Generalized Anxiety Disorder Scale; HADS; Resilience Scale for Adults: PHQ-9: Patient Health Questionnaire; PSQI: Pittsburgh Sleep Quality Index; ZBI: Zarit Burden Interview; Perceived Stress Scale-10 (PSS-10); HAM-A: Hamilton Anxiety Rating Scale; Beck’s Depression Inventory: BDI; RSS: Relative Stress Scale; ; NPI-CD, Neuropsychiatric Inventory Caregiver Distress; DASS-21, Depression, Anxiety and Stress Scales; Patient Health Questionnaire-9 (PHQ-9). NA: Not applicable

* \* = included in meta-analysis , D: depression, A: anxiety, CB: caregiver’s burden, CD: Caregiver distress

**Figure 1. PRISMA flow-chart**

Studies from databases/registers **(n = 1523)**

Duplicated studies **(n =34)**

**Identification**

Studies included in review **(n = 15)**

Studies excluded **(n = 1416)**

Studies screened **(n = 1489)**

Studies excluded **(n = 58)**

6. other reasons (Interventions studies, Conference presentation, not in English)

(n = 11)

1. not caregivers (n = 1)

3. not longitudinal (n = 29)

poster presentation (n = 6)

4. not a validated scale (n = 8)

2. not patients with dementia (n = 3)

Studies assessed for eligibility **(n = 73)**

**Screening**

**Included**

**Studies included in (meta-analysis)**

Depression: 6 studies

Anxiety: 7 studies

Caregiver’s Burden: 4 studies

Caregiver’s Distress: 6 studies

**Meta-analysis**

**DIS**



1. **Discussion**

In this systematic review and meta-analysis of 15 studies including 1702 caregivers of PwD or MCI, caregiver psychological well-beingparameters worsened during the pandemic for depression, anxiety, caregiver’ burden and caregiver distress. The studies had high heterogeneity and many had a high risk of bias, particularly in outcome measurement, but the results suggest that the impact of COVID on caregivers of PwD or MCI were important, and may have implications for health and social care services in the future.

Depression, anxiety, caregiver' burden and caregiver distress are often interrelated [20,29]; therefore, possible causes will be examined together. First, a previous study found that caregivers reported feeling prepared for typical caregiving responsibilities but felt less prepared for someone else to assume the role of primary caregiver. It is thus likely that being unprepared as the COVID-19 pandemic emerged and took hold both caregiver burden and distress increased [30]. Therefore, when one is diagnosed with dementia, caregivers, specifically unpaid and thus likely family members, should be informed and educated about how they can overcome the problems that may develop in their patients (including extreme situations such as the COVID-19 pandemic, war, disasters).

Globally health systems were not prepared for the COVID-19 pandemic subsequently causing caregivers to be adversely affected. During the COVID-19 pandemic, caregivers reported that they had difficulties in accessing medical services, which is not surprising considering that the COVID-19 pandemic led to the breakdown of health care systems worldwide and a decrease in the quality of health care due to overwhelmed wards or intensive care units. Amongst the most common problems described are discontinuation of specialized medical care, difficulty accessing hospitals, or even appointments and frequent COVID antigen testing. Similarly, a recent European study described some of the frequent issues encountered: some hospitals had to reschedule non-urgent visits for safety measures, or patients cancelled because of the fear of infection [31]. Considering that the average age of dementia patients in our review is 76.36 years and the average age of caregivers is 60.4 years; it appears that caregivers may be concerned not only with dementia or covid-related conditions, but also with other comorbid diseases and conditions associated with their own health problems. Indeed, in one study caregivers stated that they restricted the use of health services for their own health problems during the pandemic owing to fear of being infected with the virus during this process. This subsequently exacerbated existing health conditions among caregivers [32]. There is some evidence that telephone counseling can reduce depressive symptoms and meets the important needs of caregivers of PwD/MCI [33]. Also, a study suggests that online psychoeducational support and specific care guidelines can contribute to the well-being of PwD and caregivers [34]. Therefore, digital interventions for caregivers’ anxiety, depression, and burden should include video and online psychoeducational programs, telephone calls, and messages to reach those with poorer digital resources [29].

The COVID pandemic and lockdown has a considerable impact on PwD as well as their caregivers: a systematic review and meta-analysis investigating the effects of the COVID-19 lockdown on neuropsychiatric symptoms (NPS) in PwD/MCI showed that there was an increase in the worsening of NPS (especially, depression, anxiety, agitation, irritability, and apathy) in the patients during lockdown [7]. An increase in NPS of PwD may explaine why caregivers’ burden and distress increased during pandemic. Indeed, it may be hypothesised that there is a bidirectional relationship between caregiver burden and NPS [35]. The inability to maintain physical activity and social interactions, which are non-pharmacological approaches recommended for NPS prevention, due to forced lockdown at home, and the closure of outpatient rehabilitation centres that provide services such as cognitive training, occupational therapy, and group activities, may have increased the risk for development of NPS [8]. Additionally, the rapid cognitive deterioration in PwD during the pandemic, the inability of these patients to adapt to new living conditions, and the inability of patients to continue their usual daily activities, may have led to the development of NPS [36]. It is clear that NPS are associated with negative caregiver outcomes. Indeed, depressive behaviors were the “most important symptoms” relative to caregiver burden followed by agitation, aggression, sleep disturbances, and apathy [35]. Moreover, NPS may lead to a worse relationship with the caregiver, and this altered relationship may lead the patients with NPS to be more irritable, or those caregivers with a poorer relationship may perceive NPS as more severe or as purposefully provocative behaviours. A study by Perren et al. found that the lower level of spousal caregivers’ well-being and insecure attachment style were associated with increased levels of NPS [37]. Interestingly, inappropriate caregiver's manner has been found to be associated with delusions; the impact of delusions on both the caregiver and patient may be mitigated through pharmacological treatment. Moreover, previous studies have found that distressed caregivers tended to use emotion‐ oriented rather than problem‐focus coping strategies, which may increase patient's behavioral disturbance [38,39]. Caregiver's irritation, anger, or impatience can lead to greater agitation in the patients [40]. One study also reported that caregiver-delivered cognitive stimulation therapy showed significant improvements in cognition, behavioral and psychiatric symptoms and quality of life of PwD [41]. Therefore, training caregivers and combining pharmacological and behavioral and/or family interventions targeting NPS may alleviate patient suffering but also mediate improved caregiver well‐being. However, Bao et al. found that during the one-year COVID-19 lockdown, the change in patients' NPS was not associated with caregiver depression, anxiety, and burden [9]. Thus, it is clear that NPS is not the only factor influencing the psychological well-being of caregivers. Fourth, the lockdown period may be related to loneliness, social isolation, and reduced physical activity caregiver anxiety and detention [9]. Many studies suggest that social contact relieves anxiety and related disorders by activating a neural reward system, regulating the hypothalamic-pituitary-adrenal axis, and regulating and secreting neurotransmitters, including oxytocin and opioids [42]. Physical activity may promote mental health by decreasing anxiety and depression symptoms through downregulating TNF-α and other inflammation parameters [43]. Furthermore, countless hours spent caregiving could precipitate feelings of loneliness and intensify the distress levels of caregivers [44].

Owing to the potential pathways discussed above, the well-being of caregivers for older adults with dementia is especially important to examine during the COVID-19 lockdown. Moreover, depression, anxiety and distress reduced among caregivers after COVID-19 restrictions (i.e., lockdown) ended [24]; which suggests the need for improved support of long-term lockdown strategies/policies specifically for family caregivers. In the present review, we found that almost all caregivers were unpaid family members (>90% were unpaid or were family) and were living with PwD (72.9%). Family caregivers in particular reported higher anxiety, depression, fatigue, sleep disturbance, lower social participation, lower financial well-being, increased food insecurity, and increased financial worries [45]. Although the consequences between the impact of dementia and the caregiver's psychosocial conflict are persistent, increased cognitive impairment or decreased self-care ability and caregiver burden, primarily anxiety, pressure, and distress in maintaining daily routine, also leads to a 'caregiver burden' during the pandemic [17,26].

The strength of our study is that it is the first compilation of results of studies conducted under difficult pandemic conditions, with a rigorous search strategy, two independent reviewers at all stages, and a braod range of relevant outcomes. However, findings from the present study must be interpreted in light of its limitations. First, only a small number of studies could be included for meta-analysis. It is noteworthy that studies focused on negative rather than positive outcomes, which may lead to confirmation bias. Second, nearly all caregivers were unpaid and there was a very small number of paid caregivers /0.4%). Therefore, we cannot generalize our results for paid caregivers. Third, the studies were clinically and statistically heterogeneous; this may be partly due to different time periods between assessments, differences in not only dementia type or severity, but also evaluation of psychological well-being (by using different scales). The other limitation is that the studies’ data cover the first part of the pandemic. Additionally, the variation in impact of COVID-19 and restrictions may be different in different countries, which might be the cause of high heterogeneity and high risk of bias.

1. **Conclusion**

There was an increase in the worsening of depression, anxiety, distress and caregiver burden in caregivers of PwD/MCI during COVID-19 pandemic lockdown. Therefore, there was a negative effect of COVID-19 pandemic on the psychological well-being of caregivers. There is a clear need to further explore potential mechanisms relating to negative outcomes so that caregivers can be supported in any future similar scenarios, and supported with any ongoing symptoms as they continue to care for PwD/MCI, or deal with the grief when their loved one dies.

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