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RESEARCH ARTICLE

The course of neuropsychiatric symptoms and psychotropic drug use in Dutch nursing home patients with dementia during the first wave of COVID-19: A longitudinal cohort study

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Abstract

Objective: To describe the course of neuropsychiatric symptoms in nursing home residents with dementia during the step-by-step lifting of restrictions after the first wave of the COVID-19 pandemic in the Netherlands, and to describe psychotropic drug use (PDU) throughout the whole first wave.

Methods: Longitudinal cohort study of nursing home residents with dementia. We measured neuropsychiatric symptoms using the Neuropsychiatric Inventory-Questionnaire (NPI-Q). From May to August 2020, the NPI-Q was filled in monthly. Psychotropic drug use was retrieved from the electronic prescription system, retrospectively for the months February to April and prospectively for the months May to August.

Results: We followed 252 residents with dementia in 19 Dutch nursing homes. Agitation was the most prevalent type of neuropsychiatric symptom at each assessment. Overall, the prevalence and severity of agitation and depression significantly decreased over time. When considering more in detail, we observed that in some residents specific neuropsychiatric symptoms resolved (resolution) while in others specific neuropsychiatric symptoms developed (incidence) during the study period. For the majority of the residents, neuropsychiatric symptoms persisted over time. Psychotropic drug use remained stable over time throughout the whole first wave of the pandemic.

Conclusions: At group level, lifting the measures appeared to have beneficial effects on the prevalence and severity of agitation and depression in residents with dementia. Nevertheless, on an individual level we observed high heterogeneity in the course of neuropsychiatric symptoms over time. Despite the pressure of the pandemic and the restrictions in social contact imposed, PDU remained stable.

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KEYWORDS

BPSD, COVID-19, lockdown, neuropsychiatric symptoms, nursing homes, psychotropic drugs

Key points

- The prevalence of agitation, depression and anxiety was high in patients with dementia during imposed restrictions in the first wave of COVID-19.
- During step-by-step lifting of restrictions on social contact in nursing homes, depression and agitation decreased.
- Despite the pressure of the pandemic and the social restrictions imposed, psychotropic drug use (PDU) remained stable in Dutch NHs.

1 | INTRODUCTION

People with dementia living in NH frequently display neuropsychiatric symptoms neuropsychiatric symptoms (NPS), with a 2-year cumulative prevalence of up to 96%.¹ NPS are defined as behavioral and psychological problems – including agitation, aggression, depression, psychosis and apathy – and can be elicited by a multitude of causes, both related to disease or extrinsic factors.^{2,3} Importantly, these symptoms can pose a heavy burden on the resident and his or her surroundings and decrease the quality of life.⁴ In more than half of the NH residents with dementia, psychotropic drugs are prescribed, in particular antidepressants, benzodiazepines and antipsychotics.⁵

When the COVID-19 pandemic reached the Netherlands, NH residents were strongly affected.⁶ The mortality risk in NH residents living in The Netherlands with a proven COVID-19 infection was high in the first wave of the pandemic.⁷ in particular in residents with dementia.⁸ As many of their European counterparts, the Dutch government decided that from March 19th 2020 all NHs had to take restrictive measures.⁹ These measures included a national NH visiting ban in order to minimize the interaction between residents and others. The visitor ban proved to be a double-edged sword: crucial to curb the rising infection rate and mortality, but at the cost of social contact. Previous studies in this area have underscored the vital importance of social interaction for the quality of life of the NH residents.¹⁰⁻¹² The behavior of residents with dementia is strongly influenced by contact with others, social activities, and the general surroundings.^{4,13,14} Therefore, it is probable that the COVID-19 induced restrictions in social contact affect the prevalence and expression of neuropsychiatric symptoms of residents with dementia.

A limited number of largely retrospective studies have been conducted to examine to what extent the restrictions in social contact imposed by the measures influenced NPS and PDU in people with dementia. It was found that, except for psychotic behavior, all NPS increased.¹⁵⁻²⁰ Two studies reporting on PDU found an increase in the proportion of dementia patients using psychotropic drugs, in particular antipsychotic drugs.^{21,22}

Notably, these studies only included dementia patients living at home^{17-19,22} or in a retirement home.²⁰ It is challenging to extrapolate these results to the NH population, as the severity of dementia

and behavioral problems in NH residents is likely to be much higher.²³ NH professionals participating in a survey during the first COVID-19 wave reported that the effect of lockdown differed per individual: they noted an increase in some residents and a decrease in others.²⁴ However, none of these studies investigated NPS and PDU over time on individual resident level.

Therefore, the aim of this study was to describe the course of NPS in a cohort of NH residents with dementia from May 2020 until August 2020 during and after the first wave of COVID-19. In this period the COVID-19 restrictions were lifted step-by-step in the Netherlands. We describe both changes in the overall prevalence of NPS in general and the course of NPS within the study population in more detail, defining the incidence, persistence, and resolution of separate NPS over time. Secondly, we describe PDU over time between February 2020 and August 2020, throughout the whole first wave of COVID-19.

2 | METHODS

2.1 | Design

We performed a longitudinal cohort study, comprised of both prospective and retrospective data. Data collection started in May 2020, in a period with severe restrictions in social contact. Retrospective data was collected from February 2020 - before the lockdown - and onwards, and prospective data collection continued during the decrease of the restrictions until August 2020.

2.2 | Setting and participants

Data was collected at psychogeriatric units of 19 NHs, a convenience sample of units in NHs associated with the vocational training for elderly care physician (ECP) in Amsterdam. Residents lived in the north or central part of the Netherlands, comprising both rural and urban areas. Inclusion criteria were: a reported diagnosis of dementia in the medical chart and admittance to the psychogeriatric unit before January 1st 2020. Residents were excluded if they were expected to die within a month after the start of the study in May 2020.

2.3 | Measurements

Data was collected and pseudonymized by elderly care physicians (ECPs) in training, further referred to as 'ECPs'.²⁵

In May 2020, ECPs obtained patient characteristics, gender, age, and type of dementia from the medical chart. Severity of dementia was estimated by the ECP using the Global Deterioration Score (GDS).²⁶ A GDS score of 1–3 was classified as 'mild', GDS 4–5 was classified as 'moderate' and GDS 6–7 'severe'.

Once a month in May, June, July, and August, the ECPs filled in a case report form on the pandemic-related restrictions on social contact in NHs, NPS and PDU for every resident. Furthermore, PDU data was collected retrospectively for the months February, March and April 2020.

2.3.1 | Neuropsychiatric symptoms

We used the Neuropsychiatric Inventory-Questionnaire Neuropsychiatric Inventory-Questionnaire (NPI-Q), a validated questionnaire, to measure the occurrence (present or absent) and severity (mild, moderate, or severe) of NPS in residents with dementia.²⁷ The NPI-Q includes 12 scales of behavior: delusions, hallucinations, agitation/ aggression, depression, anxiety, euphoria, apathy, disinhibition, irritability, repetitive motor behavior, nighttime disturbances, and appetite/changes in eating habits.

We categorized NPS into five types of challenging behavior as defined by the Dutch Multidisciplinary guideline problem behavior in dementia² namely: depression, anxiety, apathy, psychotic behavior, and agitation. For depression, anxiety, and apathy, the corresponding single NPI-Q items were used. Following previous studies, the symptoms delusions and hallucinations were combined in a new scale for psychotic behavior and agitation was defined as a combination of the symptoms agitation/aggression, disinhibition, and irritability.²⁸ For the combined scales psychotic behavior and agitation 'present' was defined if at least one of the individual NPI-Q symptoms was present at that assessment. To determine the severity of these combined scales, the mean of the respectively two or three subscales was calculated at each assessment. Euphoria, repetitive motor behavior, nighttime disturbances, and appetite/changes in eating habits were not analyzed over time. However, to get an overview of the complete NPI-Q over time, the proportion of the residents who showed any of the 12 symptoms was calculated for each assessment and referred to as 'NPI-Q Total'.

2.3.2 | PDU

PDU was retrieved from the electronic prescription system. For prospectively collected PDU, the reference date was set on the day of the NPI-Q assessments and the reference date for retrospective PDU was respectively in week eight (February), 12 (March), 17 (April) 2020. PDU was grouped into antipsychotics, antidepressants, benzodiazepines and anti-dementia drugs, and dichotomized to either present or absent. Among as needed prescriptions, only as needed benzodiazepine use was included in the analysis.

2.4 | Analysis

We used IBM SPSS Statistics 26th Edition for statistical analysis. Baseline characteristics and measurements were analyzed by means of descriptive statistics. We reported percentages per group for dichotomous or ordinal data, and mean and standard deviation for continuous variables.

We used logistic generalized estimating equation (GEE) with an exchangeable correlation structure to assess longitudinal changes in point prevalence for each NPS and PDU. The Friedman test was used to analyze the severity of the NPS over time. Since the Friedman test cannot be conducted on participants with missing data, these analyses were done in the population with complete data at each assessment. Results are presented with 95% confidence intervals (CI) and all reported p values are two-sided. We applied Bonferroni correction because of multiple comparisons within each NPS.

To gain more insight into the course of NPS within the population, we calculated resolution, persistence, and incidence for every interval between two successive assessments.^{1,29} Resolution described the proportion of residents showing an NPS at one assessment, but absence of the NPS in the next. Persistence was defined as the proportion of residents showing a specific NPS at two succeeding assessments. Resolution and persistence together make 100%. Incidence describes the population that developed an NPS between two assessments and was calculated over residents not showing the specific symptom at the previous assessment. The cumulative prevalence is the proportion of participants who showed an NPS atleast one assessment during the study period (4 months). The cumulative incidence is defined as the ratio of participants without a specific NPS at the start of the study, who developed this in a succeeding assessment. To calculate the percentages of the parameters for each interval, complete data at every assessment is needed. Therefore, these analyses were performed on participants with complete data at each assessment.

2.5 | Ethical approval

The Dutch Medical Ethics Review Committee (METC) of the Amsterdam University Medical Center (UMC), location VUmc approved the study protocol. Residents were followed by their own ECP. A legal representative received a letter with information and the purpose of the study and could object against use of data for this study.

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FIGURE 1 Flowdiagram of included residents

3 | RESULTS

3.1 | Participants

At baseline, 265 residents met the inclusion criteria of whom 252 were included in this study (Figure 1). During the study, the number of residents decreased to 240, 234 and 221 in respectively June, July, and August due to death, relocation, or unknown reasons (Figure 1). In June, there was missing data for 17 residents. Among these 17 residents, one had died after the third assessment, but before the end of the study. Thus, 221 residents survived the study, and a total of 205 (92.8%) had complete data for each assessment.

The mean age of residents was 84 years (SD 9) and 71.4% were female. Alzheimer's disease was the most prevalent type of dementia (41.3%) and the majority of the residents were suffering from severe dementia (69.8%). All resident characteristics are presented in Table 1.

3.2 | Restrictions in social contact

In March, April and May, for all residents (100%) restrictions in social contact were reported compared to February. In August, 54.8% of

TABLE 1 Resident characteristics in May 2020 (n = 252)

	Residents included at baseline	Ν
Age, mean (SD)	84 ⁹	
Female gender (%)	71.4	180
Type of dementia (%)		
Alzheimer	41.3	104
Vascular	15.9	40
Mixed	13.5	34
Other	7.9	20
Not specified	21.4	54
Severity of dementia (%)		
Mild/Moderate	30.2	76
Severe	69.8	176

the residents still had to deal with these restrictions induced by the COVID-19 pandemic. The rate of specific COVID-19 related measures causing restrictions in social contact per time point is depicted in Table 2.

TABLE 2 COVID-19 related measures with consequences on social contact for nursing home (NH) residents with dementia (compared to pre-COVID: february 2020)

	May (N = 252)	Jun (N = 223)	Jul (N = 234)	Aug (N = 221)
Any restrictions	100.0	100.0	91.0	54.8
Restricted visiting policy	88.1	98.2	84.6	47.5
Changes in nursing staff ^a	23.0	13.4	6.0	6.3
Deployment of other care practitioners ^b	59.9	35.4	15.4	3.2
COVID-19 infection at the ward ^c	22.2	9.0	4.3	4.9
Freedom of movement of the $\ensuremath{resident}^d$	40.9	30.9	32.9	13.6

Note: multiple restrictions could be in force for individual residents at the same time.

Abbreviation: NH, nursing homes.

^aExamples of changes in nursing staff due to the COVID-19 pandemic were: shortage in staff caused by illness; constantly, alternating temporary workers. Consequences of these changes and shortage was that residents could no longer receive their daily care.

^bDuring the lockdown, care practitioners other than the nursing staff (e.g. physiotherapists, physicians, activity guides, ergo therapists, speech therapists) were not allowed in all NHs.

^cMeasures taken during an COVID-19 infection at the ward were: the whole ward in isolation, isolating residents at their room, no isolation restrictions for the resident or other measures.

^dExamples of restrictions in freedom of movement were: except from the unit, the NH was closed for the resident, specific public areas in the NH were closed for the resident, the courtyard was closed for the resident.

We observed that all taken restrictions in social contact and the process of lifting them was heterogeneous between NHs. A strict visitors ban was in force for most residents until the beginning of June. In August, visits were still restricted in some way in almost half (47.5) of the residents. The allowance to move freely in and around the NH was limited in 40.9% of residents in May, but reduced considerably to 13.6% in August. Additionally, almost 60% of the NH care practitioners not involved in direct (medical) care (e.g. physio-therapists or psychologists) were not allowed to visit residents in May; only online contact was possible. This percentage decreased substantially to less than 4% in August.

3.3 | Neuropsychiatric symptoms

The prevalence of all NPS from May until August is shown in Figure 2 and Table S1. In May, agitation was the most prevalent type of challenging behavior (75%), followed by apathy (38%), anxiety (36%) and depression (34%). Psychotic behavior was the least prevalent (28%).

Longitudinal change in the prevalence of NPS are summarized in Table S2 GEE analyses revealed that the number of residents showing any NPS (NPI-Q Total) significantly decreased over time (OR 0.36; CI 0.23–0,57; p < 0.001). In addition, we observed a significant decrease in prevalence over time from May until August for agitation (74.6%–60.2%; OR 0.52; CI 0.39–0.70; p < 0.001) and depression (34.1%–19.9%; OR 0.48; CI 0.35–0.65; p < 0.001). The severity of depression and agitation also decreased significantly during the study period (p < 0.001, Table S3). For apathy, anxiety, and psychotic behavior, no significant changes over time were found in prevalence and severity (Tables S2 and S3).

In Table 3, we present resolution, persistence, and incidence of specific NPS at each successive interval. Although agitation and



FIGURE 2 Neuropsychiatric symptoms over time

depression decreased over time, the incidence rate fluctuated (16.1%-21.1% for agitation and 6.6%-13.2% for depression). For apathy, anxiety, and psychotic behavior, the overall prevalence averaged. Still, the NPS resolved in some residents (resolution) and developed in others (incidence). At each interval, persistence was higher than resolution for all types of NPS.

3.4 | PDU

Figure 3 shows point prevalence of PDU in the 252 included residents between February 2020 and August 2020. PDU remained largely stable over time: rates of antidepressant use lied between 24.4% and 25.4% and antipsychotic drug use between 21.0% and 22.9%. A slight, non-significant change over time was observed in daily benzodiazepine use; 13.7% in February increasing to 16.1% in June and decreasing to 13.7% in August. The rate of as needed prescriptions of

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TABLE 3	Frequency	parameters (of neuropsych	iatric symp	toms (NPS)	of residents	with complete	e data at e	ach assessm	ent (N = 205	()				
	Мау	May - Jun			Jun	lul - nul			Jul	Jul - Aug			Aug		
	Prevalence	Resolution ^a	Persistence ^b	Incidence ^c	Prevalence	Resolution ^a	Persistence ^b	Incidence ^c	Prevalence	Resolution ^a	Persistence ^b	Incidence ^c	Prevalence	Cum prev ^d	Cum inc ^e
	(u) %	(N/u) %	(N/u) %	(N/u) %	(u) %	(N/u) %	(N/u) %	(N/u) %	(u) %	(N/u) %	(N/u) %	(N/u) %	(u) %	(u) %	(N/u) %
Depression	32.2 (66)	42.4 (28/66)	57.6 (38/66)	11.5 (16/ 139)	26.3 (54)	37.0 (20/54)	63.0 (34/54)	13.2 (20/ 151)	26.3 (54)	48.1 (26/54)	51.9 (28/ 54)	6.6 (10/ 151)	18.5 (38)	45.9 (94)	20.1 (28/ 139)
Anxiety	32.2 (66)	27.3 (18/66)	72.7 (48/66)	10.1 (14/ 139)	30.2 (62)	25.8 (16/62)	74.2 (46/62)	14.7 (21/ 143)	32.7 (67)	32.8 (22/67)	67.2 (45/67)	12.3 (17/ 138)	30.2 (62)	50.7 (104)	27.3 (38/ 139)
Apathy	38.0 (78)	44.9 (35/78)	55.1 (43/78)	21.3 (27/ 127)	34.1 (70)	35.7 (25/70)	64.3 (45/70)	13.3 (18/ 135)	30.7 (63)	31.7 (20/63)	68.3 (43/63)	12.7 (18/ 142)	29.8 (61)	59.5 (122)	34.6 (44/ 127)
Psychotic behavior	27.8 (57)	35.1 (20/57)	64.9 (37/57)	7.4 (11/ 148)	23.4 (48)	14.6 (7/48)	85.4 (41/48)	11.5 (18/ 157)	28.8 (59)	39.0 (23/59)	61.0 (36/59)	11.6 (17/ 146)	25.9 (53)	42.9 (88)	20.9 (31/ 148)
Agitation	73.2 (150)	11.3 (17/ 150)	88.7 (133/ 150)	18.2 (10/ 55)	69.8 (143)	13.3 (19/ 143)	86.7 (124/ 143)	16.1 (10/ 62)	65.4 (134)	23.9 (32/ 134)	76.1 (102/ 134)	21.1 (15/ 71)	57.1 (117)	82.4 (169)	34.5 (19/ 55)
Abbreviations ^a Proportion o ^b Proportion o	: Cum Inc, cu f the residem f residents w	umulative inci ts with a pres ith a present	dence; Cum Pr sent NPS at th NPS at the fir	ev, cumulati e first assess st assessmer	ive prevalenc sment to resi nt to resident	e; neuropsyc dents withou ts with a pres	hiatric symptor It a present NP sent NPS at th	ms. ⁹ S at the ne» e next asses	kt assessmen ssment.	نې					

^cProportion of residents without a present NPS at the first assessment to residents with a present NPS at the next assessment.

"Proportion of resident without a present NPS in May to residents that developed a NPS at least one successive assessment.

^dProportion of the resident that had a present NPS at least at one assessment.

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FIGURE 3 psychotropic drug use (PDU) over time

benzodiazepines also increased slightly from 11.7% in February to 13.7% in May and decreased to 11.2% in June. Remarkably, as needed prescriptions afterwards increased again to 13.7% August (Table S4). However, these changes over time are all non-significant.

The prescription rate of anti-dementia drugs was very low throughout the study period (2.4%–3.6%). At the beginning of the pandemic (February 2020), nine residents used cholinesterase inhibitors. During the study, two residents discontinued the use and in one resident a cholinesterase inhibitor was started. None of the residents used memantine.

4 | DISCUSSION

To our knowledge, this is the first longitudinal prospective cohort study examining the course of NPS in residents with dementia on a monthly base during the step-by-step easing of restrictions in NHs after the first wave of COVID-19. Agitation was the most prevalent type of behavior at each assessment. We observed a significant decrease of the prevalence and severity of depression and agitation over time. The overall point prevalence of anxiety, apathy, and psychotic behavior did not change significantly over time. When considering the pattern of NPS in more detail, we observed that in some residents specific NPS resolved (resolution) while in others NPS developed (incidence) during the study period. However, for the majority of residents the NPS persisted over time. Remarkably, the prescription of psychotropic drugs remained largely stable throughout the whole first wave of COVID-19.

Previous studies on the effect of the COVID-19 induced restrictions on NPS in patients with dementia living at home,^{17–20,22} reported that except for psychotic behavior, all NPS increased during the pandemic compared to before the pandemic. The data collection in our study started during severe restrictions in social contact. If these restrictions would induce an increase in NPS, one would expect a high prevalence of NPS during the severe restrictions and a decrease in prevalence when lifting the restrictions.

For agitated behavior, we indeed observed a high prevalence of all agitation subscales in May, during severe restrictions in social contact. This prevalence appears to be higher than reported in two Geriatric Psychiatry_WILEY_⁷

previous studies in the Dutch NH setting before the COVID-19 pandemic.^{1,30} Furthermore, overall agitation significantly decreased when the restrictions in social contact were lifted whereas under normal circumstances, the overall prevalence of agitation tends to increase over time.¹ Therefore, our results suggest that the lockdown negatively affected agitated behavior in NH residents with dementia. However, in the majority of individual residents, agitation still persisted, similarly to patterns in pre-COVID studies.^{1,31} Furthermore, we observed that for some NH residents, agitation developed when the restrictions in social contact were relieved, as reflected in the incidence of agitation in June, July and August (16%–21%). Possibly, these are the residents described by professionals who benefitted from the restrictions during the lockdown.²⁴

In line with our agitation results, the prevalence of depressive symptoms significantly decreased over time. This also may be attributed to the lifting of the restrictions in social contact as the prevalence of depression during the restrictions in social contact was higher than reported in studies before the COVID-19 pandemic,^{1,30} and decreased after lifting of the restrictions in social contact. But under pre-COVID-19 circumstances depressive symptoms in NH residents with dementia also tend to decrease somewhat over time.^{1,32}

For anxiety, psychotic behavior, and apathy we found no significant change over time. Conversely, at all timepoints the prevalence of anxiety was relatively high compared to pre-pandemic studies.^{1,30} Possibly, symptoms of anxiety are less related to the restrictions in social contact but more a result of the threat of a pandemic as a whole.³³ Still, symptoms of anxiety fluctuated; in 26%–33% of the residents, anxiety resolved during each interval. The overall prevalence of psychotic behavior and apathy appeared to stay in a narrow range whereas resolution and incidence showed an intermittent course. Taken together, the specific NPS scores at group level can provide a comprehensive overview of effects over time, but may mask individual variability. Our results underscore the findings by Leontjevas et al.²⁴ who reported that the effect of the restrictions in social contact on NPS differed per individual.

As psychotropic drugs in residents with dementia are often prescribed to treat NPS, an increase in NPS could also induce an increase in PDU. Interestingly, we found that PDU remained largely stable in NH throughout the whole first wave of COVID-19 induced restrictions in social contact and the prevalence of PDU is in line with a recent study in Dutch NH conducted before the pandemic.⁵ These results differ from findings in community-dwelling patients with dementia in other countries reporting an increase in PDU.^{21,22} Apparently, the high prevalence of NPS did not induce an increase in psychotropic drug prescriptions in NH residents. We consider this a positive result, in line with the recommendations in guidelines to prefer non-pharmacological interventions over PDU.^{2,3}

The strength of this study is that, despite the high workload in NHs during the first wave of COVID-19, we were able to prospectively collect data on NPS using a validated questionnaire on a monthly basis in a large cohort of NH residents with dementia. Moreover, we were able to retrieve data on PDU throughout the whole first wave of the pandemic. The proportion of residents with complete data at each ⁸ WILEY Geriatric Psychiatry

assessment was high. To this respect, we were able to describe the course of NPS over 4 months in detail, including fluctuations per NPS as reflected in incidence, resolution, and persistence.

Inevitably, this study also has several limitations that must be considered when interpreting our results. First, as data collection started during the lockdown, NPI-Q scores from before the lockdown are lacking. As a consequence, we do not know whether the observed decrease of agitation and depression during lifting the restrictions in social contact was indeed preceded by an increase in these symptoms after imposing the restrictions. Second, we used the short NPI-Q instead of the more commonly used Neuropsychiatric Inventorynursing homes (NPI-NH). A drawback from the NPI-Q as compared to the NPI-NH is that it cannot distinguish clinically relevant symptoms. Therefore, our results could overestimate the prevalence of clinically relevant NPS. Nevertheless, given the already excessive workload in most NHs, we considered the brief and reliable NPI-Q more feasible for this study. Third, as the ECPs and nursing staff had to fill in the NPI-Q questionnaires, they were more aware of the presence of NPS. This awareness could have positively influenced the course of NPS, the so-called Hawthorne effect.³⁴ Lastly, as a result of the observed large variety in restrictions in social contact and range in lifting the measures, it was not possible to analyze the effects of particular restrictions on the NPS.

5 CONCLUSION AND IMPLICATIONS

In the period the restrictions in social contact were diminished in NHs in The Netherlands, residents with dementia showed a significant decrease of prevalence and severity of depression and agitation. The prevalence of agitation at baseline is higher than previous studies conducted in NHs and the downward trend in prevalence contrasts with the natural development. Thus, it is likely that lifting the measures indeed had a beneficial effect on agitated behavior. For depression, the high prevalence during maximum restrictions and the subsequent decline also suggests a relation with lifting the restrictions. Despite the pressure of the pandemic and the restrictions in social contact imposed, PDU remained stable in NHs.

This study showed that NPS manifest and develop heterogeneously in residents with dementia during a period of time with a continuously changing environment. Some residents will suffer from the social isolation and the changing environment. Others might even benefit from less external stimuli due to restrictions in social contact. In case of new restrictions, nursing home professionals need to be alert for changes in NPS of residents. Policy makers should take the effects on NPS in residents with dementia into consideration when imposing restrictions in social contact on NH residents.

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AUTHOR CONTRIBUTIONS

Study concept and design: Eefje M. Sizoo, Martin Smalbrugge. Acquisition of data: Claire L. Brederveld, Helma Timmer. Analysis and interpretation of data: Eefie M. Sizoo, Josi A. Thunnissen, Anouk M. van Loon, Claire L. Brederveld, Helma Timmer, Simone Hendriks, Martin Smalbrugge. Drafting of the manuscript: Eefje M. Sizoo, Josi A. Thunnissen, Anouk M. van Loon, Claire L. Brederveld. Critical revision of the manuscript for important intellectual content: Eefie M. Sizoo. Josi A. Thunnissen, Anouk M. van Loon, Claire L. Brederveld, Helma Timmer, Simone Hendriks, Martin Smalbrugge.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

ETHICS STATEMENT

The Dutch METC of the UMC in Amsterdam UMC, location VUmc approved the study protocol.

DATA AVAILABILITY STATEMENT

Due to the nature of this research, residents included in this study did not agree for their data to be shared publicly, so supporting data is not available.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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