



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



JAMDA

journal homepage: www.jamda.com

Brief Report

Short- and Long-Term Mortality and Mortality Risk Factors among Nursing Home Patients after COVID-19 Infection



Johannes A. Booij MD^{a,*}, Julie C.H.Q. van de Haterd MD^b, Sanne N. Huttjes MD^a, Rogier H.P.D. van Deijck MD, PhD^a, Raymond T.C.M. Koopmans MD, PhD^{c,d}

^a De Zorggroep, Region Venlo (EBC), Venlo, the Netherlands

^b Department of Radiology and Nuclear Medicine, Radboud University Medical Center, Nijmegen, the Netherlands

^c Department of Primary and Community Care: Center for Family Medicine, Geriatric Care, and Public Health, Radboud University Medical Center, Nijmegen, the Netherlands

^d De Waalboog, Joachim en Anna, Center for Specialized Geriatric Care, Nijmegen, the Netherlands

A B S T R A C T

Keywords:

Nursing home patients
SARS-CoV-2
long-term care facility
mortality
advanced care planning

Objective: To assess short- and long-term mortality and risk factors in nursing home patients with COVID-19 infection.

Design: Retrospective 2-center cohort study.

Setting and Participants: Dutch nursing home patients with clinically suspected COVID-19 infection confirmed by reverse transcription-polymerase chain reaction testing.

Methods: Data were gathered between March 2020 and November 2020 using electronic medical records, including demographic characteristics, comorbidities, medical management, and symptoms on the first day of suspected COVID-19 infection. Mortality at 30 days and 6 months was assessed using multivariate logistic regression models and Kaplan-Meier analysis. At 6 months, a subgroup analysis was performed to estimate the mortality risk between COVID-negative patients and patients who survived COVID-19. Risk factors for mortality were assessed through multivariate logistic regression models.

Results: A total of 321 patients with suspected COVID-19 infection were included, of whom 134 tested positive. Sixty-two patients in the positive group died at 30 days, with a short-term mortality rate of 2.9 (95% CI 1.7–5.3). Risk factors were fatigue (OR 2.6, 95% CI 1.3–6.2) and deoxygenation (OR 2.9, 95% CI 1.3–7.6). At 6 months, the mortality risk was 2.1 (95% CI 1.3–3.7). Risk factors for 6-month mortality were shortness of breath (OR 2.7, 95% CI 1.3–7.0), deoxygenation (OR 2.5, 95% CI 1.1–6.5) and medical management (OR 4.5, 95% CI 1.7–25.8). However, among patients who survived COVID-19 infection, the long-term mortality risk was not sustained (OR 1.0, 95% CI 0.4–2.7).

Conclusions and Implications: Overall, COVID-19 infection increases short- and long-term mortality risk among nursing home patients. However, this study shows that surviving COVID-19 infection does not lead to increased mortality in the long term within this population. Therefore, advanced care planning should focus on quality of life among nursing home patients after COVID-19 infection.

© 2022 AMDA – The Society for Post-Acute and Long-Term Care Medicine.

Since the first presentation of SARS-CoV-2 (COVID-19) in the Netherlands in February 2020, more than 15,000 long-term care patients died within the first 3 months of the pandemic alone.¹ To date, only a few studies have assessed the impact of COVID-19 on nursing home patients, showing that COVID-19 infection increases short-term mortality.^{2–4} Within this population, especially patients with

Parkinson disease, cognitive impairment, or dementia, overall frailty, chronic kidney disease, diabetes, and male sex are at risk.^{2,5,6}

Regarding long-term effects, a study by Rooney et al found that physical functioning and fitness are impaired within the general population after 12 months of follow-up.⁷ Another study found that patients who experienced COVID-19 infection had persisting complaints such as fatigue, muscle weakness, difficulty sleeping, and depression, up to 6 months after infection.⁸ The impact of surviving COVID-19 on physical functioning is presumably similar or possibly even higher in frail older individuals and could have an effect on long-term mortality, as suggested by Soldevila et al.⁶ However, to our knowledge, no studies have yet investigated the consequences of

This research did not receive any funding from agencies in the public, commercial, or not-for-profit sectors.

* Address correspondence to Johannes A. Booij, MD, De Zorggroep, region Venlo (EBC), 5900 AR Venlo, the Netherlands.

E-mail address: robin.booij@dezorggroep.nl (J.A. Booij).

<https://doi.org/10.1016/j.jamda.2022.06.005>

1525-8610/© 2022 AMDA – The Society for Post-Acute and Long-Term Care Medicine.

COVID-19 infection on long-term mortality among nursing home patients after COVID-19 infection. Therefore, we aimed to assess mortality as well as risk factors for short-term mortality and long-term mortality in nursing home patients with COVID-19.

Methods

Study Design and Population

Between March and November 2020, a retrospective, 2-center cohort study was conducted in 2 Dutch long-term care organizations with a total of 2500 eligible patients, including patients under the care of an older adult care physician or general practitioner, who were living in hospice settings, somatic departments, and dementia special care units within a nursing home.⁹ Patients who were admitted to a unit for geriatric rehabilitation or a hospice-unit were not eligible due to short-stay, chance of loss to follow-up, or short life expectancy. As the medical records of patients under the care of a general practitioner were not accessible, these patients were not included. Patients with a clinical suspicion of COVID-19 infection based on a physician's assessment and for whom reverse transcription-polymerase chain reaction (PCR) test results were available were included. Patients who were suspected of COVID-19 infection but tested negative were defined as controls. All patients had a follow-up period of 30 days after the first suspicion of COVID-19 infection to document 30-day mortality. All patients who were alive after 30 days were followed for an additional 5 months to document 6-month mortality (Figure 1). Patients who tested positive and were still alive 30 days after the first suspicion of COVID-19 infection were defined as survivors. Patients who initially tested negative but later tested positive during the first 30 days were included in the COVID-positive group, where new baseline parameters were defined. Patients who tested negative at baseline but tested positive for COVID-19 between 30 days and 6 months of follow-up were excluded (Figure 1).

Data Collection

An infection log was recorded by each center by including all patients with a clinical suspicion of COVID-19 infection, testing dates and results, and clinical signs and symptoms, as advised by the Dutch Association of Elderly Care Physicians (Verenso).¹⁰ Electronic medical records were used to obtain data regarding demographic

characteristics, comorbidities, and medical management. We registered comorbidities that were considered potential risk factors for severe illness or mortality due to COVID-19 infection in the general population conforming to the International Classification of Primary Care.^{11–16} These comorbidities included lung disease, cardiovascular disease, cardiovascular risk factors, cerebrovascular disease, neurocognitive disorders, diabetes mellitus, kidney disease, liver disease, cancer, autoimmune disease, and hematologic disorders. Medical management was defined as curative care or palliative care. Palliative care was defined as life-prolonging treatment, such as resuscitation, hospitalization, antibiotic treatment, artificial nutrition, and hydration, are withheld.¹⁷ We reported clinical symptoms on the first day of suspected COVID-19 infection, namely nasal congestion, sore throat, cough, shortness of breath, malaise or fatigue, myalgia, headache, dizziness, diarrhea, nausea or vomiting, and loss of taste and/or smell, and clinical parameters, including blood pressure, pulse, temperature, respiratory rate, oxygen saturation, and consciousness.

Ethical Approval

This research concerned a retrospective analysis of routine anonymized patient data, and no patients were subjected to procedures or were required to follow rules of behavior in our research. Therefore, ethical approval was not obtained.¹⁸

Statistical Analyses

Descriptive and frequency analyses were performed for demographic characteristics and clinical signs and symptoms. COVID-19-positive and -negative patients were compared using χ^2 or Fisher exact tests for nonnormally distributed data, for categorical variables. Age distribution was compared using a Mann-Whitney U test.

Mortality was estimated from the day of the first suspicion to the time of follow-up at 30 days and 6 months. Here, we compared overall mortality between all COVID-19-positive and -negative patients at 30 days and 6 months, as well as a subgroup analysis to estimate mortality of COVID-positive patients who survived COVID-19 infection, compared with patients who tested negative at baseline. Odds ratios for mortality were calculated using univariate and multivariate logistic regression. Independent risk factors were selected based on significantly different variables resulting from univariate analysis. The results were corrected

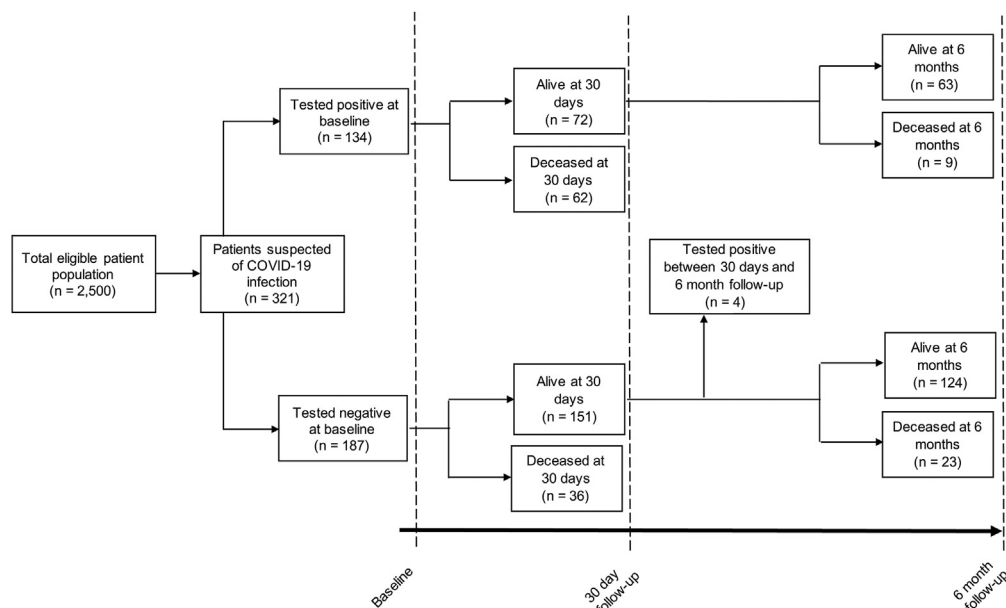


Fig. 1. Overview of patient groups and follow-up.

for confounders (ie, age and sex). In addition, Kaplan-Meier analysis was performed to compare survival at 6 months, and statistical significance was tested using log-rank test.

To investigate potential risk factors for mortality at 30 days and 6 months among COVID-positive patients, an univariate logistic regression was first performed including all documented clinical signs and symptoms, medical history, and medical management. Statistically significant variables were then included in a multivariate logistic regression model. The results were controlled for age and sex. Confidence intervals were calculated using a bootstrap analysis of 5000 samples. All analyses were performed using IBM SPSS Statistics for Windows, Version 27.0 (2020).

Results

Baseline Characteristics

Overall, 321 patients suspected of COVID-19 infection were included. In total, 134 patients (41.7%) tested positive. At inclusion, there were no statistically significant differences between COVID-19-positive and -negative patients regarding demographic characteristics and comorbidities. Patients who tested positive were significantly more likely to present with fever, malaise, or fatigue.

COVID-19-negative patients more often presented with symptoms of sore throat or headache (Table 1). None of the suspected patients with COVID-19 were lost to follow-up due to discharge to another care facility or (temporary) hospital admission. Between 30 days and 6 months of follow-up, 4 COVID-19-negative patients tested positive and were excluded from the 6-month mortality analysis.

Thirty-Day Mortality

Sixty-two patients (46.3%) in the COVID-19-positive group had died at 30 days (Figure 1). Patients who tested positive for COVID-19 were 3.6 times more likely to have died within 30 days than patients who tested negative (OR 3.6, 95% CI 2.3–6.2). Multivariate analysis showed that after correction for statistically significant different variables at baseline (ie, headache, sore throat, fatigue, and fever; Table 1), increased mortality risk for COVID-19-positive patients persisted (OR 2.9, 95% CI 1.7–5.3).

Risk Factors for 30-Day Mortality in Patients with COVID-19

Univariate analysis showed a statistically significant associated higher mortality risk at 30 days for COVID-19-positive patients with

Table 1
Baseline Characteristics of Nursing Home Patients Who Tested Positive or Negative for COVID-19, at Time of Inclusion and at 30 Days

	Characteristics at Time of Inclusion			Characteristics at 30 D		
	COVID-19 Positive (n = 134)	COVID-19 Negative (n = 187)	P Value	COVID-19 Positive (ie, Survivors, n = 72)	COVID-19 Negative (n = 147)	P Value
Age, mean (SD)*	85.1 (8.0)	83.4 (9.4)	.197	85.1 (8.7)	83.1 (9.6)	.152
Age group, n (%)						
≥85 y	74 (55.2)	98 (52.4)	.618	43 (59.7)	75 (51.0)	.225
Sex, n (%)						
Male	53 (39.6)	70 (37.4)	.700	25 (34.7)	55 (37.4)	.697
Comorbidity, n (%)						
Lung disease	20 (14.9)	31 (17.1)	.600	10 (13.9)	19 (12.9)	.843
Cardiovascular disease	58 (43.3)	78 (41.7)	.779	29 (40.3)	57 (38.8)	.831
Cardiovascular risk Factors	87 (64.9)	117 (62.6)	.665	48 (66.7)	91 (61.9)	.492
Cerebrovascular Disease	46 (34.3)	59 (31.6)	.601	19 (26.4)	49 (33.3)	.297
Neurocognitive disorder	102 (76.1)	141 (75.4)	.882	53 (73.6)	112 (76.2)	.677
Diabetes mellitus	36 (26.9)	54 (28.9)	.692	20 (27.8)	39 (26.5)	.845
Kidney disease	32 (23.9)	29 (15.5)	.059	13 (18.1)	23 (15.6)	.651
Liver disease	2 (1.5)	0 (0.0)	.940	1 (1.4)	0 (0)	.329
Cancer	17 (12.7)	24 (12.8)	.969	9 (12.5)	21 (14.3)	.718
Auto-immune disease [†]	8 (6.0)	11 (5.9)	1.000	5 (6.9)	6 (4.1)	.511
Hematologic disorder [†]	3 (2.2)	0 (0.0)	.072	1 (1.4)	0 (0)	.329
Symptoms at first suspicion of COVID-19 infection, n (%) [‡]						
Nasal congestion	32 (23.9)	37 (19.8)	.379	18 (25.0)	31 (21.1)	.514
Sore throat	7 (5.2)	24 (12.8)	.023	4 (5.6)	19 (12.9)	.095
Cough	90 (67.2)	106 (56.7)	.058	49 (68.1)	79 (53.7)	.043
Shortness of breath	43 (32.1)	42 (22.5)	.054	19 (26.4)	32 (21.8)	.447
Malaise or fatigue	78 (58.2)	84 (44.9)	.019	35 (48.6)	65 (44.2)	.540
Myalgia [†]	5 (3.7)	2 (1.1)	.133	2 (2.8)	2 (1.4)	.462
Headache [†]	0 (0.0)	7 (3.7)	.044	0 (0.0)	6 (4.1)	.082
Dizziness [†]	2 (1.5)	2 (1.1)	1.000	2 (2.8)	2 (1.4)	.462
Diarrhea	11 (8.2)	20 (10.7)	.457	7 (9.7)	17 (11.6)	.682
Nausea or vomiting	15 (11.2)	21 (12.8)	.657	9 (12.5)	19 (12.9)	.929
Loss of taste and/or smell [†]	1 (0.7)	2 (1.1)	1.000	0 (0.0)	2 (1.4)	.320
Clinical parameters at first suspicion of COVID-19 infection, n (%) [‡]						
Hypotensive, ≤100/min [†]	4 (2.9)	10 (5.4)	.268	3 (5.2)	5 (4.4)	.544
Tachycardia, ≥100/min	21 (15.7)	30 (16.0)	.779	10 (17.2)	19 (16.5)	.905
Tachypnea, ≥21/min	24 (17.9)	31 (16.6)	.326	8 (50.0)	23 (54.8)	.745
Deoxygenation, ≤91% SO ₂	41 (30.6)	38 (20.3)	.062	15 (26.8)	27 (24.3)	.729
Fever, ≥38.1°C	72 (53.7)	51 (27.3)	<.001	37 (51.4)	33 (22.4)	<.001
Unconscious	16 (11.9)	25 (13.4)	.621	6 (8.7)	15 (10.9)	.625
Abnormal lung sounds	15 (11.2)	25 (13.4)	.735	6 (66.7)	13 (65.0)	.930
Clinical management, n (%) [†]						
Palliative care	21 (15.7)	37 (19.8)	.345	7 (9.7)	22 (15.0)	.282

*Analyzed using Mann-Whitney U test.

[†]Analyzed using Fisher exact test, all other categorical variables were analyzed using χ^2 .

[‡]Symptoms and clinical parameters were documented at first suspicion of COVID-19 and not included in long-term analysis.

fatigue and deoxygenation. These risk factors remained statistically significant predictors for mortality after correction for confounding, yielding ORs of 2.6 (95% CI 1.3–6.2) for fatigue and 2.9 (95% CI 1.3–7.6) for deoxygenation.

Mortality at 6 Months

At 6 months, 71 COVID-19-positive patients (53.0%) had died vs 59 patients (31.6%) of the patients who tested negative at baseline (Figure 2); this was significantly different (log-rank P value < .001). The long-term mortality risk in patients who tested positive was 2.4 times higher compared with patients who tested negative (95% CI 1.5–3.8), which was sustained after correction for statistically significant different variables at baseline (ie, headache, sore throat, fatigue, and fever; OR 2.1 95% CI 1.3–3.7).

Risk Factors for 6-Month Mortality in Patients with COVID-19

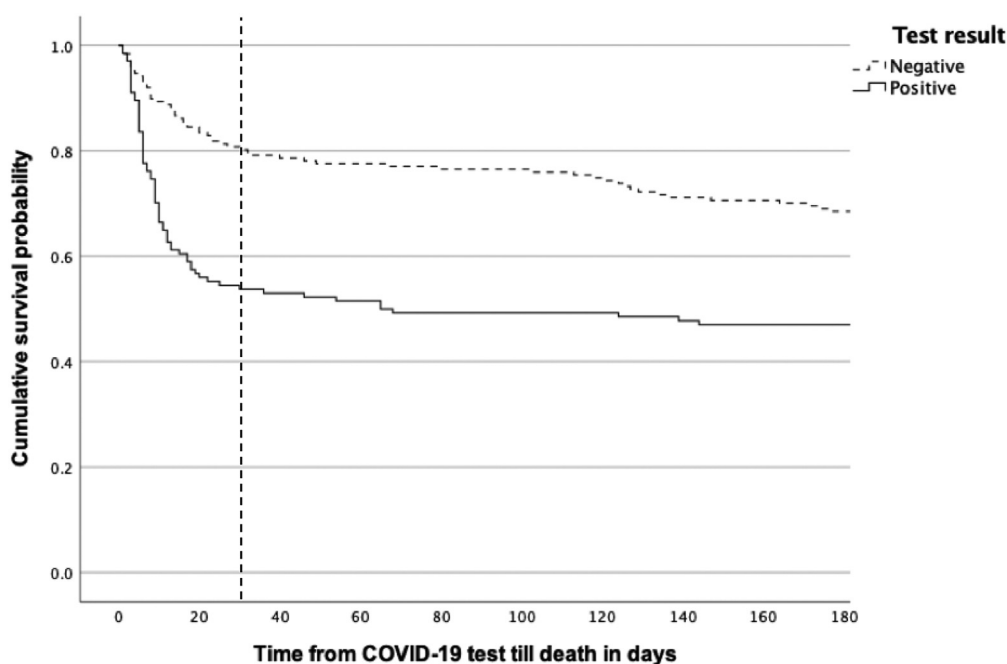
At 6 months, cerebrovascular disease, shortness of breath, deoxygenation, and medical management were associated with higher mortality. After correction for confounding, only shortness of breath (OR 2.7, 95% CI 1.3–7.0), deoxygenation (OR 2.5, 95% CI 1.1–6.5), and medical management (OR 4.5, 95% CI 1.7–25.8) only remained as statistically significant risk factors.

Mortality Risk after COVID-19 Survival

Seventy-two patients in the COVID-19-positive group (53.7%) were still alive after 30 days of follow-up and were therefore labeled survivors (Table 1). Both univariate and multivariate analyses showed that COVID-19 survivors did not have a higher mortality risk at 6-month follow-up than COVID-19-negative patients (multivariate OR 1.0, 95% CI 0.4–2.7).

Discussion

This study shows that COVID-19 infection increases short-term mortality risk, leading to excess mortality, confirming the findings of another Dutch study among nursing home patients.^{1,2} However, compared with an international study conducted in US nursing homes, mortality risk was higher in our study population.⁵ This discrepancy might be explained by differences in the study population, as they also included asymptomatic patients who were tested. Another factor might be differences in medical care and management in Anglo-Saxon countries compared with the Netherlands, where palliative care and treatment limitations are relatively more common and initialized in an earlier phase.^{19,20} To illustrate this, 18% of all patients in our study population were already receiving palliative management. Moreover, during the entire follow-up no patients were admitted to a hospital for symptoms or complications due to COVID-19 infection. Furthermore, nursing home patients with COVID-19 have an overall increased long-term mortality risk of more than 7% compared with patients who do not experience COVID-19-infection. This was also demonstrated in another study among previously hospitalized patients with COVID-19; however, this study was performed outside the setting of a nursing home.²¹ More importantly, our study showed that 6-month mortality was not statistically significant different between patients who survived COVID-19 infection and COVID-negative patients; therefore, surviving COVID-19 does not lead to increased mortality among nursing home patients in the long term. Concerning risk factors for mortality among patients with COVID-19, only fatigue and deoxygenation were statistically significant predictors for 30-day mortality. At 6 months, patients who had experienced shortness of breath or deoxygenation or those who received palliative medical management had an increased mortality risk. As our population size was limited, this study may have lacked power to find other significant risk factors for mortality as demonstrated in larger nationwide studies conducted among nursing home patients.^{2,5,6}



† The vertical dotted line marks the 30-day follow-up period.

Fig. 2. Kaplan-Meier survival curve for mortality between COVID-19 positive and COVID-19 negative patients.

Regarding clinical consequences, the findings of this study can be used to improve advanced care planning in nursing home patients after COVID-19 infection. Generally, advanced care planning is used to guide choices regarding medical management based on clinical and personal preferences. During COVID-19 infection, mortality risk and specific risk factors for mortality can be used to guide advanced care planning. However, as patients who survive infection do not have a prolonged increased mortality risk at 6 months, advanced care planning should focus on quality of life, as frail populations such as nursing home patients presumably experience a similar or even greater disease burden after COVID-19 infection than the general population.^{6–8,15}

Last, there were several limitations in this study. Selection bias could be present as the study was conducted in 2 long-term care organizations in a single region. Moreover, we did not randomly select patients in the nursing homes. Preferably, a control group would have consisted of a randomly selected group not suspected of COVID-19 infection or any other (respiratory) disease, to more accurately estimate excess mortality. Furthermore, we only reported symptoms and clinical parameters on the day of clinical suspicion of COVID-19 infection and PCR testing, whereas other studies included symptoms in the days prior to and after clinical suspicion and testing as well. Moreover, reverse transcription-PCR introduces another limitation, as the literature estimates a median sensitivity of 0.89 (false-negative rates ranging from 0.018 to 0.58); therefore, repeated PCR testing is recommended for patients who initially test negative but who are still suspected of COVID-19 infection.²² Finally, we would like to remark that different strains of SARS-CoV-2 have developed since its first presentation, which were not included in our study, and different mutations might present with different morbidity and mortality.

Conclusion and Implications

Overall, COVID-19 infection increases short- and long-term mortality risk among nursing home patients. However, this study is the first to show that patients who survived COVID-19 did not have a higher long-term mortality risk; therefore, advanced care planning should focus on quality of life among nursing home patients after COVID-19 infection.

Acknowledgments

The authors thank J.S.F. Maurits, MSc for providing assistance with statistical analyses and proofreading. The authors further thank the organizations De Zorggroep, Venlo, the Netherlands, Proteion, Haelen, the Netherlands and Radboud University Medical Center, Nijmegen; Department of Primary and Community Care, Center for Family Medicine, Geriatric Care and Public Health, Nijmegen, the Netherlands, for facilitating this study.

References

1. Centraal Bureau voor Statistiek. Gezondheid in coronatijd. Updated 10-12-2021. 2021. Accessed December 10, 2021. <https://www.cbs.nl/nl-nl/visualisaties/welvaart-in-coronatijd/gezondheid-in-coronatijd>
2. Rutten JJS, van Loon AM, van Kooten J, et al. Clinical Suspicion of COVID-19 in Nursing Home Residents: Symptoms and Mortality Risk Factors. *J Am Med Dir Assoc.* 2020;21:1791–1797.e1791.
3. Chudasama DY, Milbourn H, Nsonwu O, et al. Penetration and impact of COVID-19 in long term care facilities in England: population surveillance study. *Int J Epidemiol.* 2022;50:1804–1813.
4. Garcia-Cabrera L, Perez-Abascal N, Montero-Erassquin B, et al. Characteristics, hospital referrals and 60-day mortality of older patients living in nursing homes with COVID-19 assessed by a liaison geriatric team during the first wave: a research article. *BMC Geriatr.* 2021;21:610.
5. Panagiotou OA, Kosar CM, White EM, et al. Risk Factors Associated With All-Cause 30-Day Mortality in Nursing Home Residents With COVID-19. *JAMA Intern Med.* 2021;181:439–448. <https://doi.org/10.1001/jamainternmed.2020.7968>.
6. Soldevila L, Prat N, Mas MA, et al. The interplay between infection risk factors of SARS-CoV-2 and mortality: a cross-sectional study from a cohort of long-term care nursing home residents. *BMC Geriatr.* 2022;22:123.
7. Rooney S, Webster A, Paul L. Systematic Review of Changes and Recovery in Physical Function and Fitness After Severe Acute Respiratory Syndrome-Related Coronavirus Infection: Implications for COVID-19 Rehabilitation. *Phys Ther.* 2020;100:1717–1729.
8. Huang C, Huang L, Wang Y, et al. 6-month consequences of COVID-19 in patients discharged from hospital: a cohort study. *Lancet.* 2021;397:220–232.
9. Koopmans R, Pellegrom M, van der Geer ER. The Dutch Move Beyond the Concept of Nursing Home Physician Specialists. *J Am Med Dir Assoc.* 2017;18:746–749. <https://doi.org/10.1016/j.jamda.2017.05.013>.
10. Verenso, NVAVG. *Treatment advice COVID-19. Diagnostics, treatment and infection prevention and outbreak management.* 2020. Updated 14/4/2022.
11. Murk JL, van de Biggelaar R, Stohr J, et al. [The first 100 COVID-19 patients admitted to the Elisabeth-Tweesteden Hospital, Tilburg, The Netherlands]. *Ned Tijdschr Geneesk.* 2020;164:D5002.
12. Fang L, Karakiulakis G, Roth M. Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection? *Lancet Respir Med.* 2020;8:e21.
13. Olde Rikkert MGM, Vingerhoets RW, van Geldorp N, et al. [Atypical clinical picture of COVID-19 in older patients]. *Ned Tijdschr Geneesk.* 2020;164.
14. Wang L, He W, Yu X, et al. Coronavirus disease 2019 in elderly patients: Characteristics and prognostic factors based on 4-week follow-up. *J Infect.* 2020;80:639–645.
15. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet.* 2020;395:1054–1062.
16. Centers for Disease Control and Prevention. *The National Diabetes Statistics Report 2020: Estimates of Diabetes and Its Burden in the United States.* Centers for Disease Control and Prevention; 2020.
17. Nederlandse Vereniging van Verpleeghuisartsen (NVVA/Verenso), Sting, Verpleegkundigen en Verzorgenden Nederland (V&VN). *Begrippen en Zorgvuldigheidseisen met betrekking tot de besluitvorming rond het levenseinde in de verpleeghuiszorg.* 2007.
18. Central Committee on Research Involving Human Subjects (CCMO). Non-WMO research: File research. Accessed May 1, 2022. <https://english.ccmo.nl/investigators/additional-requirements-for-certain-types-of-research/non-wmo-research/file-research>
19. van der Steen JT, Kruse RL, Ooms ME, et al. Treatment of nursing home residents with dementia and lower respiratory tract infection in the United States and The Netherlands: an ocean apart. *J Am Geriatr Soc.* 2004;52:691–699.
20. Hendriks SA, Smalbrugge M, Deliens L, et al. End-of-life treatment decisions in nursing home residents dying with dementia in the Netherlands. *Int J Geriatr Psychiatry.* 2017;32:e43–e49.
21. Leijte WT, Wagemaker NMM, van Kraaij TDA, et al. [Mortality and re-admission after hospitalization with COVID-19]. *Ned Tijdschr Geneesk.* 2020;164:D5423.
22. Arevalo-Rodriguez I, Buitrago-Garcia D, Simancas-Racines D, et al. False-negative results of initial RT-PCR assays for COVID-19: a systematic review. *PLoS One.* 2020;15:e0242958.