Supplementary Online Content

Gilstrap L, Zhou W, Alsan M, Nanda A, Skinner JS. Trends in mortality rates among Medicare enrollees with Alzheimer disease and related dementias before and during the early phase of the COVID-19 pandemic. *JAMA Neurol*. Published online February 28, 2022. doi:10.1001/jamaneurol.2022.0010

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This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix 1. Data Description

Link to Data Downloads:

https://www.nber.org/research/data/mortality-rates-among-medicare-enrollees-alzheimer-disease-and-related-dementias-during-early-phase

A. Medicare Excess Mortality

The Medicare data comprises four time-periods, all of whom have full Part A and B Medicare coverage and are not enrolled in an HMO plan during the period.

The first control time-period is for people who were alive and age 65+ on March 1, 2019. The data analysis covers March 1 through July 31, 2019. The second is for people who are alive and age 65+ on August 1, 2019; the analysis again ranges for 5 months until December 31, 2019. The third (treatment) cohort is for people alive on March 1 2020 and age 65+ with the analysis beginning March 1, 2020 and finishing July 31, 2020; similarly for the fourth cohort that ranges from August 1 2020 to December 31, 2020.

For the summary statistics shown in Table 1, we merged time-periods 1 and 2 into "2019" (conditional on being alive and age 65+ as of March 1, 2019) and time-periods 3 and 4 into "2020" (again conditional on being alive and age 65+ as of March 1, 2020)

For the HRR level adjusted mortality rates: the methods we used were:
(i) Combined 2019 and 2020 populations to get the population percentage (decimal) for cells age 65-74, male, age 75-84 male, age 85+ male, age 65-74 female, age 75-84 female, age 85+ female.

(ii) For each period/each group/each HRR, calculate the crude mortality rate for each of the 6 cells above.

(iii) Merge (i) and (ii); the adjusted mortality rate for each cell is equal to the share of each group in the population times the crude mortality rate within each cell

(iv) Multiply by 100 to get the age-sex adjusted mortality rate (percentage) for each HRR.

B. Disease categories and nursing home status

These were calculated in as follows:

a) The definition of Alzheimer's Disease and Related Dementias (ADRD) comes from the Chronic Conditions Warehouse (CCW) algorithm corresponding at least one inpatient, SNF, HHA, HOP, or Carrier claim with a DX code DX G30.0, G30.1, G30.8, G30.9 (any DX on the claim). See https://www2.ccwdata.org/web/guest/condition-categories for further details. We limit the designation to data from 1 year (the CCW designation allows for measures over 3 year.)

b) We employed the Yun et al. (2010) algorithm to identify beneficiaries with any nursing facility service. During the cohort (or cohorts) in question, we identify nursing home patients if the beneficiary had any one of the following:
(i) Any claim with POS codes (place of service codes: 31, 32,33) using Medicare Carrier file.
(ii) Any claim with CPT codes (99301, 99302, 99303, 99311, 99312, 99313, 99315, 99316, 99379, 99380, G0066) using Medicare Carrie and Outpatient file
(iii) Any SNF claim using Medicare SNF file.

c.) We included 3 critical comorbidities:

Heart Failure: At least 1 inpatient, HOP, or Carrier claim with DX code: DX I09.81, I11.0, I13.0, I13.2, I50.1, I50.20, I50.21, I50.22, I50.23, I50.30, I50.31, I50.32, I50.33, I50.40, I50.41, I50.42, I50.43, I50.810, I50.811, I50.812, I50.813, I50.814, I50.82, I50.83, I50.84, I50.89, I50.9 (any DX on the claim)

Chronic Obstructive Pulmonary Disease and Bronchiectasis: At least 1 inpatient, SNF, HHA OR 2 HOP or Carrier claims with DX codes: DX J40, J41.0, J41.1, J41.8, J42, J43.0, J43.1, J43.2, J43.8, J43.9, J44.0, J44.1, J44.9, J47.0, J47.1, J47.9 (any DX on the claim)

Diabetes: At least 1 inpatient, SNF, HHA OR 2 HOP or Carrier claims with DX codes as follows: DX E08.00, E08.01, E08.10, E08.11, E08.21, E08.22, E08.29, E08.311, E08.319, E08.321, E08.3211, E08.3212, E08.3213, E08.3219, E08.329, E08.3291, E08.3292, E08.3293, E08.3299, E08.331, E08.3311, E08.3312, E08.3313, E08.3319, E08.339, E08.3391, E08.3392, E08.3393, E08.3399, E08.341, E08.3411, E08.3412, E08.3413, E08.3419, E08.349, E08.3491, E08.3492, E08.3493, E08.3499, E08.351, E08.3511, E08.3512, E08.3513, E08.3519, E08.3521, E08.3522, E08.3523, E08.3529, E08.3531, E08.3532, E08.3533, E08.3539, E08.3541, E08.3542, E08.3543, E08.3549, E08.3551, E08.3552, E08.3553, E08.3559, E08.359, E08.3591, E08.3592, E08.3593, E08.3599, E08.36, E08.37X1, E08.37X2, E08.37X3, E08.37X9, E08.39, E08.40, E08.41, E08.42, E08.43, E08.44, E08.49, E08.51, E08.52, E08.59, E08.610, E08.618, E08.620, E08.621, E08.622, E08.628, E08.630, E08.638, E08.641, E08.649, E08.65, E08.69, E08.8, E08.9, E09.00, E09.01, E09.10, E09.11, E09.21, E09.22, E09.29, E09.311, E09.319, E09.321, E09.3211, E09.3212, E09.3213, E09.3219, E09.329, E09.3291, E09.3292, E09.3293, E09.3299, E09.331, E09.3311, E09.3312, E09.3313, E09.3319, E09.339, E09.3391,E09.3392, E09.3393, E09.3399, E09.341, E09.3411, E09.3412, E09.3413, E09.3419,E09.349, E09.3491, E09.3492, E09.3493, E09.3499, E09.351, E09.3511, E09.3512, E09.3513, E09.3519, E09.3521, E09.3522, E09.3523, E09.3529, E09.3531, E09.3532, E09.3533, E09.3539, E09.3541, E09.3542, E09.3543, E09.3549, E09.3551, E09.3552, E09.3553, E09.3559, E09.359, E09.3591, E09.3592, E09.3593, E09.3599, E09.36, E09.37X1, E09.37X2, E09.37X3, E09.37X9, E09.39, E09.40, E09.41, E09.42, E09.43, E09.44, E09.49, E09.51, E09.52, E09.59, E09.610, E09.618, E09.620, E09.621, E09.622, E09.628, E09.630, E09.638, E09.641, E09.649, E09.65, E09.69, E09.8, E09.9, E10.10, E10.11, E10.21, E10.22, E10.29, E10.311, E10.319, E10.321, E10.3211, E10.3212, E10.3213, E10.3219, E10.329, E10.3291, E10.3292, E10.3293, E10.3299, E10.331, E10.3311, E10.3312, E10.3313, E10.3319, E10.339, E10.3391, E10.3392, E10.3393, E10.3399, E10.341, E10.3411, E10.3412, E10.3413, E10.3419, E10.349, E10.3491, E10.3492, E10.3493, E10.3499, E10.351, E10.3511, E10.3512, E10.3513, E10.3519, E10.3521, E10.3522, E10.3523, E10.3529, E10.3531, E10.3532, E10.3533, E10.3539, E10.3541, E10.3542, E10.3543, E10.3549, E10.3551, E10.3552,

E10.3553, E10.3559, E10.359, E10.3591, E10.3592, E10.3593, E10.3599, E10.36, E10.37X1, E10.37X2, E10.37X3, E10.37X9, E10.39, E10.40, E10.41, E10.42, E10.43, E10.44, E10.49, E10.51, E10.52, E10.59, E10.610, E10.618, E10.620, E10.621, E10.622, E10.628, E10.630, E10.638, E10.641, E10.649, E10.65, E10.69, E10.8, E10.9, E11.00, E11.01, E11.10, E11.11, E11.21, E11.22, E11.29, E11.311, E11.319, E11.321, E11.3211, E11.3212, E11.3213, E11.3219, E11.329, E11.3291, E11.3292, E11.3293, E11.3299, E11.331, E11.3311, E11.3312, E11.3313, E11.3319, E11.339, E11.3391, E11.3392, E11.3393, E11.3399, E11.341, E11.3411, E11.3412, E11.3413, E11.3419, E11.349, E11.3491, E11.3492, E11.3493, E11.3499, E11.351, E11.3511, E11.3512, E11.3513, E11.3519, E11.3521, E11.3522, E11.3523, E11.3529, E11.3531, E11.3532, E11.3533, E11.3539, E11.3541, E11.3542, E11.3543, E11.3549, E11.3551, E11.3552, E11.3553, E11.3559, E11.359, E11.3591, E11.3592, E11.3593, E11.3599, E11.36, E11.37X1, E11.37X2, E11.37X3, E11.37X9, E11.39, E11.40, E11.41, E11.42, E11.43, E11.44, E11.49, E11.51, E11.52, E11.59, E11.610, E11.618, E11.620, E11.621, E11.622, E11.628, E11.630, E11.638, E11.641, E11.649, E11.65, E11.69, E11.8, E11.9, E13.00, E13.01, E13.10, E13.11, E13.21, E13.22, E13.29, E13.311, E13.319, E13.321, E13.3211, E13.3212, E13.3213, E13.3219, E13.329, E13.3291, E13.3292, E13.3293, E13.3299, E13.331, E13.3311, E13.3312, E13.3313, E13.3319, E13.339, E13.3391, E13.3392, E13.3393, E13.3399, E13.341, E13.3411, E13.3412, E13.3413, E13.3419, E13.349, E13.3491, E13.3492, E13.3493, E13.3499, E13.351, E13.3511, E13.3512, E13.3513, E13.3519, E13.3521, E13.3522, E13.3523, E13.3529, E13.3531, E13.3532, E13.3533, E13.3539, E13.3541, E13.3542, E13.3543, E13.3549, E13.3551, E13.3552, E13.3553, E13.3559, E13.359, E13.3591, E13.3592, E13.3593, E13.3599, E13.36, E13.39, E13.40, E13.41, E13.42, E13.43, E13.44, E13.49, E13.51, E13.52, E13.59, E13.610, E13.618, E13.620, E13.621, E13.622, E13.628, E13.630, E13.638, E13.641, E13.649, E13.65, E13.69, E13.8, E13.9 (any DX on the claim)

All measures are specific to the calendar year.

C. Sample Size for ADRD and non-ADRD Medicare Enrollees During March-December 2019 and March-December 2020

	ADRD 2019	ADRD 2020	Non-ADRD 2019	Non-ADRD 2020
Overall Crude and Adjusted Mortality Rates				
Overall Crude Mortality	2,412,124	2,308,234	24,540,628	24,379,902
Overall Adjusted Mortality	2,412,124	2,308,234	24,540,628	24,379,902
Nursing Home Residents Crude and Adjusted Mortality Rates				
Crude Mortality, Nursing Home Residents	1,074,880	934,454	871,865	647,346
Adjusted Mortality, Nursing Home Residents	1,074,880	934,454	871,865	647,346
Demographic Subgroups Adjusted Mortality Rates				
Adjusted Mortality, Men	881,105	852,268	11,008,476	10,948,021
Adjusted Mortality, Women	1,531,019	1,455,966	13,532,152	13,431,881
Adjusted Mortality, Asian Patients	65,014	64,374	692,097	701,992
Adjusted Mortality, Black Patients	222,528	211,830	1,654,093	1,593,543
Adjusted Mortality, Hispanic Patients	136,945	133,122	1,213,001	1,200,286

eAppendix 2. Confidence Intervals and Testing for Trend and Underlying Differences in Regional Mortality Rates Prior to the COVID-19 Pandemic

A. Confidence Intervals:

We use the delta method (Casella & Berger, 2002, p. 240-45) to estimate the variance of excess mortality. First, m_1 is the estimated mortality rate in 2020, while m_0 is the corresponding mortality rate in 2019; the ratio is an approximation of the true excess mortality ratio equal to μ_1 (the true mortality rate in 2020) divided by μ_0 (the corresponding true mortality rate in 2019):

$$E\left[\frac{m_1}{m_0}\right] \approx \frac{\mu_1}{\mu_0}$$

This approximation holds for relatively small variances around the estimated means such that the denominator does not approximate zero. We also use a first-order Taylor-series approximation (or the delta method) to approximate the variance of the ratio:

$$Var\left[\frac{m_1}{m_0}\right] \approx \left(\frac{\mu_1}{\mu_0}\right)^2 \left\{\frac{Var(\mu_1)}{\mu_1^2} + \frac{Var(\mu_0)}{\mu_0^2} - 2\frac{Cov(\mu_0, \mu_1)}{\mu_0\mu_1}\right\}$$

Given temporally independent draws (so the covariance is assumed to be zero), we used this approximation (based on sample sizes and crude fractions) to calculate all 95% confidence intervals for all 4 groups (ADRD, non-ADRD, ADRD nursing home residents, and non-ADRD nursing home residents) overall and by subgroup. This approach is also used to calculate confidence intervals for HRR-specific excess mortality.

B. Testing for trend in region-specific mortality rates:

One concern is that the measures of excess mortality we observe do not adjust for underlying trends in mortality that have continued for several years before 2020. Our primary concern was with regard to region-specific mortality trends, so that (for example) HRRs in Quintile 1 COVID-19 exposure were experiencing a baseline decline in mortality trends that were more rapid than for Quintile 5. For this reason, we used Medicare claims data from the Dartmouth Atlas Project (www.dartmouthatlas.org) using crude mortality from 2012-2018 by region and for the US overall; these were for the entire elderly population including Medicare Advantage. There was a negative trend in mortality of roughly 1.5% annually, but this trend was consistent across the 5 early quintiles of the US, as shown in the Figure below – we did not detect any significant difference across quintiles. While we do not believe that the comparisons across quintiles are biased, our estimates of excess mortality might be viewed as overly conservative; projecting the trend forword would suggest a null hypothesis of no effect of COVID-19 on mortality would be 0.985 rather than 1.000.

Mortality Rate for the 65+ Population in the US and by Quintile of Early Covid-19 Exposure, 2012-2018
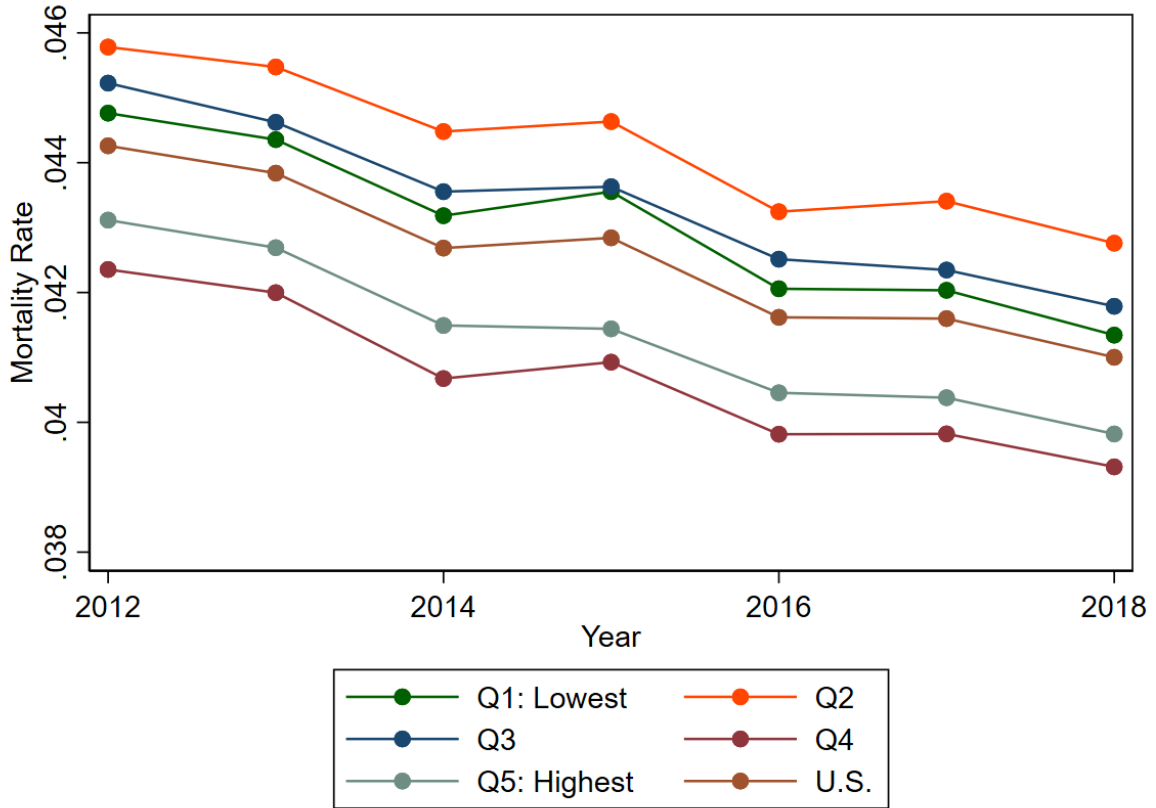
Notes: The mortality rates include both fee-for-service and Medicare Advantage patients.

eAppendix 3. Values and Ranges of Average Daily Cases per 100,000 for Quintiles of Community Exposure

The HRR-level Covid-19 data was constructed using the New York Times' county-level COVID-19 data stream and a county crosswalk provided by the University of Missouri. Using 2010 census data, we determined the populations of both counties and HRRs, and distributed COVID deaths and cases to HRRs proportionally, by the percentage of a county's population living in that HRR; e.g., if 20% of County X's population lived in HRR Y, and County X experienced 10 COVID deaths, 2 deaths would be attributed to HRR Y. As the New York Times data provided cumulative deaths by date, we estimated deaths during periods by subtracting totals from the prior period, i.e., determining deaths between August and December by subtracting the cumulative count as of December 31st from the cumulative count as of July 31st.

Further background information and daily/weekly prevalence and incidence rates and all underlying data are described here:
https://dataverse.dartmouth.edu/dataset.xhtml?persistentId=doi:10.21989/D9/ACQURP

Table A.2: Average daily rate of new cases per day (averaged over 14 days):

Early Period (March-July)

Quintile	Number of HRRs	Average	Minimum	Maximum
1 (Lowest)	94	3.1	0.5	5.0
2	61	6.2	5.1	7.6
3	53	9.0	7.7	10.4
4	39	11.6	10.4	12.9
5 (Highest)	59	16.7	12.9	28.9

Late Period (August-December 2020)

Quintile	Number of HRRs	Average	Minimum	Maximum
1 (Lowest)	57	18.3	7.1	22.9
2	49	25.4	23.0	27.4
3	53	31.3	27.5	35.9
4	54	38.7	35.9	42.3
5 (Highest)	77	52.1	42.5	92.6

eAppendix 4. Nursing Home Resident Demographic Characteristic Comparison, 2019-2020

	ADRD		p-value 2019 vs. 2020	Non-ADRD		p-value 2019 vs. 2020
	2019	**2020**		**2019**	**2020**	
Nursing Home Residents (1,000)	1,075	934		872	647	
Mean age, y (SD)	83.56 (8.39)	83.41 (8.50)	<0.001	79.67 (8.84)	79.66 (8.99)	0.4945
Female sex, % (SD)	65.74 (47.46)	65.75 (47.45)	<0.001	62.42 (48.43)	61.2 (48.73)	<0.001
Race/ethnicity, % (SD)						
Asian	1.956 (13.84)	1.964 (13.88)	0.683	1.67 (12.81)	1.55 (12.35)	<0.001
Black	10.01 (30.01)	10.19 (30.25)	<0.001	7.6 (26.50)	7.99 (27.11)	<0.001
Hispanic	4.93 (21.65)	5.1 (22.00)	<0.001	3.63 (18.70)	3.57 (18.55)	0.049
White	81.8 (38.35)	81.32 (38.98)	<0.001	85.32 (35.39)	85.03 (35.68)	<0.001
Other	1.31 (11.37)	1.43 (11.87)	<0.001	1.78 (13.22)	1.86 (13.51)	<0.001
Medicaid recipient, % (SD)	36.51 (48.15)	38.55 (48.67)	<0.001	26.62 (44.20)	29.37 (45.55)	<0.001
Disabled, % (SD)	15.13 (35.83)	16.03 (36.69)	<0.001	19.32 (39.48)	20.97 (40.71)	<0.001
End-stage renal disease, % (SD)	2.06 (14.20)	2.07 (14.24)	0.619	3.14 (17.44)	3.38 (18.07)	<0.001
Chronic Conditions, % (SD)						
Lung disease	35.49 (47.85)	34.07 (47.39)	<0.001	41.28 (49.23)	39.5 (48.89)	<0.001
Diabetes	38.51 (48.66)	38.66 (48.70)	0.0293	41.52 (49.28)	42.12 (49.38)	<0.001
Cardiovascular	59.81 (49.03)	59.26 (49.14)	<0.001	61.04 (48.77)	60.79 (48.82)	0.002

eReference

Casella, G., R.L. Berger, Statistical Inference (2nd Edition), Duxbury Advanced Series, 2002.