Social Isolation, depression, and Alzheimer's Disease and Related Dementias among the U.S. elderly during COVID-19

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INTRODUCTION -- By September 2021, 41 million individuals in the United States contracted SARS-CoV2, leading to around 650,000 deaths, representing 12% of the all-cause mortality in the 20 months since the start of the pandemic. Eight out of ten U.S. COVID19 deaths are among person aged 65 years and older.[1] The public health impact of the pandemic may be even higher when additional non-COVID-19 morbidity and mortality induced by the pandemic are included.

Physical activity and mental and social engagement are proven to be protective against rapid decline in cognitively impaired individuals.[2] However, the pandemic has upended established norms of care. Following the March 13th, 2020, federal emergency declaration in response to the pandemic, many states implemented a series of policies including non-essential business closures, school closures and stay-at-home orders to induce social distancing and curb the transmission of the virus. Most states also implemented targeted social distancing policies to specifically protect the elderly against the virus, including extended nursing home visitation bans, which almost completely socially isolated the elderly living in assisted care and long-term care facilities.

Pandemic-induced dramatic social isolation may have disparately impacted the cognitively impaired. Not only is physical activity and social engagement protective against rapid decline in cognitively impaired individuals, but social isolation can make healthcare access in the pandemic environment very challenging for the cognitively impaired patient population who frequently suffer from comorbidities such as cardiovascular disease, diabetes, depression, and anxiety. Non-urgent healthcare delivery was suspended or limited to telehealth modalities to ease the burden on healthcare systems overwhelmed by COVID care needs. Cognitively impaired, quarantined, elderly individuals may be less able to access health and social care via telehealth modalities, without help. Moreover, frequently used services like brain imaging, laboratory testing, and physical and mental therapies to diagnose, monitor and manage disease progression in patients with cognitive impairment cannot be easily provided via telehealth, and may lead to delayed diagnoses and suboptimal clinical management of cognitive impairment, Alzheimer's disease and related dementias (ADRD), and comorbidities of depression and anxiety. Socially isolated patients with mild cognitive impairment (MCI) or ADRD, living independently, may find their medication management, prescribed medication modification and/or new medication initiation more challenging. Many elderly patients or their caregivers may also voluntarily forgo in-person non-COVID care due to the potential risk of contracting the virus while visiting a healthcare facility. Finally, families may choose to care for their cognitively impaired elderly at home – either by delaying planned transitions to skilled nursing facilities (SNF) or transitioning family

members from SNFs to home to prevent infection, which may disrupt routines and access to therapies available in assisted living facilities. While mandated and voluntary social isolation of the elderly may have helped lower the transmission of the virus, these measures may have also restricted elderly persons ability to engage in physical, mental, and social engagement, and access timely non-COVID care.

For the first 10 months of the pandemic, non-pharmaceutical interventions like social distancing and mask wearing were the only means to keep viral transmission in check. The first COVID-19 vaccine (Pfizer-BioNTech) was approved for emergency use by the U.S. Food and Drug Administration (FDA) on December 11, 2020.[3] Vaccines manufactured by Moderna and Johnson & Johnson were approved on December 18, 2020 and February 27, 2021 respectively.[4,5] These vaccines have significantly helped flatten the COVID-19 trajectory in the U.S.[6] After an extended period of social disruption, the state COVID-19 vaccination campaigns have allowed many older Americans to socially engage again safely for the first time since the start of the pandemic.

PAST LITERATURE -- Small sample survey studies of family caregivers of dementia patients in Italy, Spain and Turkey found worsening of preexisting symptoms in over half of the patients, new onset of behavioral and psychological symptoms in a quarter of the patients and modifications to pre-pandemic medication regimes in a quarter of patients within one month of state mandates.[7,8,9] However, health care delivery, societal structures and the trajectory of the pandemic and related social distancing policies have differed greatly in the United States. No literature this far has examined the impact of renewed social engagement made possible by the COVID-19 vaccination campaigns on the mental health of the elderly with ADRD.

OBJECTIVE AND CONTRIBUTION – First, to examine the impact of the COVID-19 pandemic on the incidence of new depression and progression in patients with pre-pandemic ADRD diagnoses in the U.S. Second, we examine the impact of renewed social engagement on the mental health of elderly patients with cognitive impairment since the rollout of the state COVID-19 vaccination campaigns.

DATA -- Using prescription claims data from Symphony health data, capturing 92% of retail pharmacy claims for over 280 million patients in the U.S., between January 2020-August 2021, this study contributes to the existing literature on non-COVID-19 related health effects of the pandemic in three ways. First, we examine changes in the incidence of depression among older adults during the pandemic. Using the near-universe of patients of ages 65+ years with pre-pandemic ADRD diagnoses and piecewise linear multiple regression discontinuity framework, we examined how the onset of the pandemic related shutdowns in spring 2020, followed by state re-openings in summer 2020, and then the rollout of the COVID-19 vaccinations was associated with depression among older adults with ADRD. Second, we examine the role of social isolation

of the elderly as the mechanism explaining the association between the onset of the pandemic and increased incidence of depression, and disease progression among individuals with pre-pandemic ADRD diagnoses. We capture social isolation using two different proxy measures – (1) state/national-level implementation and relaxation of social distancing policies (emergency declaration and stay-at-home orders as used in Gupta et. al, 2020, data on nursing visitation bans, suspension of non-urgent medical care and official state re-openings collected from state gubernatorial sites), and (2) measures of mobility to assisted living and long-term care facilities constructed using cell phone 'pings' from 29 million mobile phones from SafeGraph. The SafeGraph data have been extensively used to measure social distancing,[10,11,12] transmission of COVID-19,[13] and trends in visits to specific locations during the pandemic.[14,15,16] We examine mobility trends using Point of Interest (POI) data for each state starting from 2018 and until the current time and identify assisted living and long-term care facilities using 2-digit U.S. Census NAICS codes). These cellphones based "foot traffic" data more directly capture the extent of social contact of older adults residing in assisted/long-term care facilities with the 'outside world' throughout the pandemic. Third, we examine whether renewed social engagement since the start of the state vaccination campaigns, captured using the timing and rate of state/county vaccination rates from the CDC COVID-19 Vaccine Tracker data and mobility measures to senior living facilities, is associated with reduced incidence of new and continued depression in ADRD patients.

RESULTS -- We find that the shutdown policies at the onset of the pandemic were associated with sharp decline in mobility to senior living facilities (see Exhibit 1), and increased incidence of depression among the elderly ADRD patients. Prior to the shutdowns in response to the pandemic in the spring of 2020, i.e., between January 1, 2020 – March 13, 2020, nearly 714 ADRD patients per 100,000 patients with any prescription claim in the Symphony Health database, received an antidepressant prescription each week. Our initial regression discontinuity results find that relative to the antidepressant use trend in the pre-pandemic period, the post-period trend was higher by 8.075 per 100,000 people (95% CI, 2.073 to 14.08; $P = 0.009$). The increase in trend of antidepressant use was stronger among elderly ADRD female, non-Black and non-Medicaid patients (refer Table 1). The intercept shift in antidepressant use after closures was also positive but was only significant at the 10-percent level for the full sample (24.06 per 100 000 people; 95% CI, -2.419 to 50.53; $P = 0.07$), with statistically significant level shift up for only the white (28.63; 95% CI, 0.436 to 56.82; $P = 0.04$) patients. State re-openings in the early part of the summer, were associated with significant declines in both level and trend of antidepressant use among the elderly ADRD population, in line with increased mobility to nursing homes and reduced isolation, again except for in the male, Black and Medicaid population. Finally, mobility to senior living facilities increased following the rollout of COVID-19 vaccines and is associated with small *increases* in both the level and trend of antidepressant use in full elderly ADRD sample as well, except the Hispanic subpopulation. At least some of

this small increase, in antidepressant use in this vulnerable population, about one-fourth in magnitude of the level and trend increase associated with the shutdowns in spring 2020, may be due to their ability to seek needed medical care more safely after vaccination rollout. Event study analyses exploiting the variation in exact timing and intensity of state stay-at-home orders, re-openings and vaccination campaigns support these findings and suggest that policies aimed at reducing the transmission of the virus may have been associated with increased isolation and related adverse non-COVID health outcomes among the vulnerable elderly ADRD patient population. In line with expectation, mobility to senior living facilities appears to be positively associated with state COVID-19 vaccination rates. With nationwide full vaccination rates still being around 65% of the population, mobility to senior living facilities continues to be below the pre-pandemic level, putting the elderly at continued risk of social isolation, related depression, and (progression of) ADRD.

Exhibit 1. Mobility to Long-term care facilities during the COVID-19 pandemic

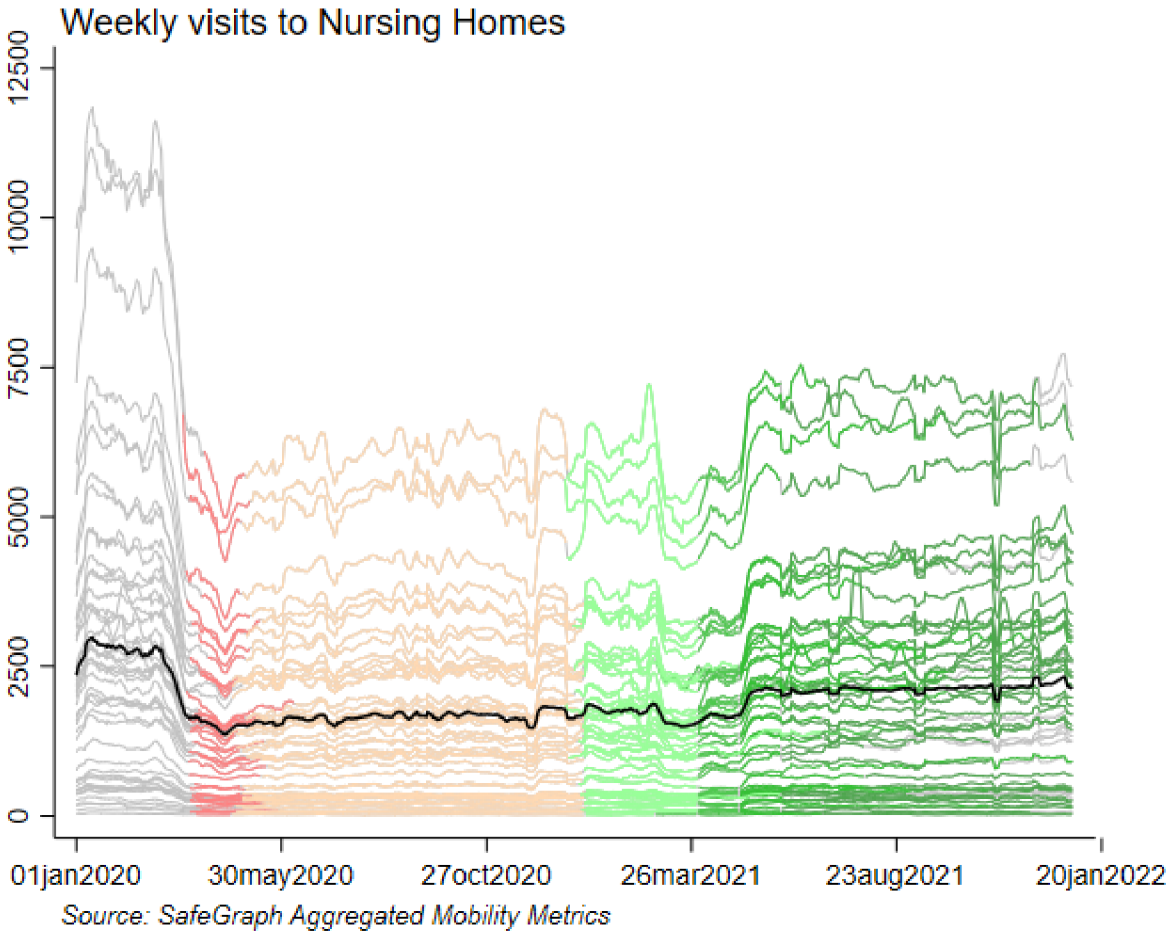
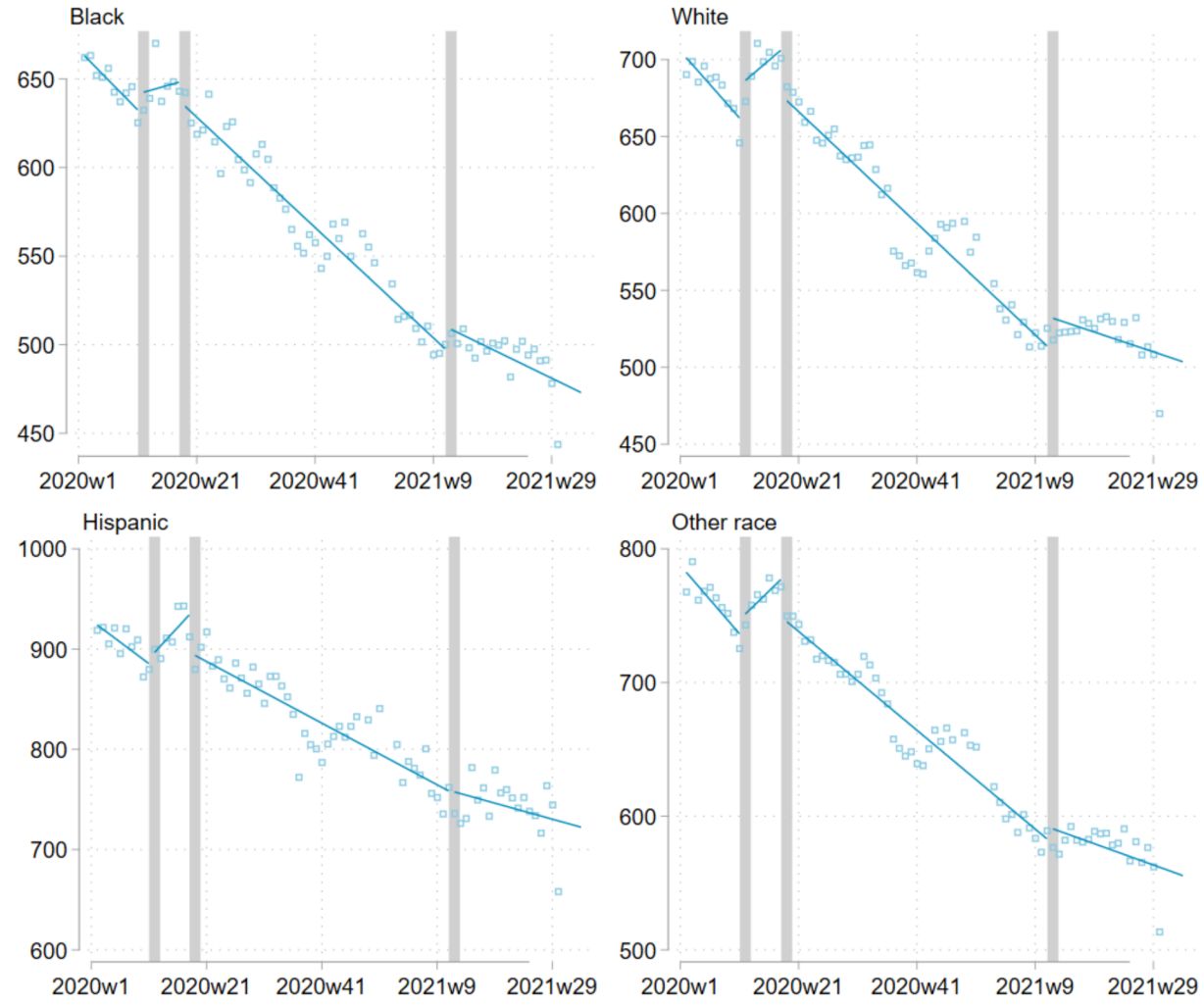


Exhibit 2. Number of Unique Baseline ADRD Patients per 100K, receiving antidepressant prescriptions each week.



Notes. Figures present raw scatter plots and piecewise linear regression discontinuity based fitted lines of antidepressant use among patients with prior ADRD diagnoses associated with the start of shutdowns in Spring 2020 in response to the pandemic, state re-openings following closures in Summer 2020 and COVID-19 vaccination rollout at the start of 2021, using antidepressant prescription claims data from Symphony Health. State closure and reopening policies and vaccination rollout serve as proxies for social isolation of elderly during the COVID-19 pandemic.

Exhibit 3: Number of Unique Baseline ADRD Patients per 100K, receiving antidepressant prescriptions each week, by patient race.



Source: Symphony (January, 2020 - August, 2021)

Notes. Figures present raw scatter plots and piecewise linear regression discontinuity based fitted lines of antidepressant use among patients with prior ADRD diagnoses associated with the start of shutdowns in Spring 2020 in response to the pandemic, state re-openings following closures in Summer 2020 and COVID-19 vaccination rollout at the start of 2021, using antidepressant prescription claims data from Symphony Health. State closure and reopening policies and vaccination rollout serve as proxies for social isolation of elderly during the COVID-19 pandemic.

Exhibit 4. Number of Unique Baseline ADRD Patients per 100K, of ages 65+ receiving antidepressant prescriptions each week, by patient race.



Source: Symphony (January, 2020 - August, 2021)

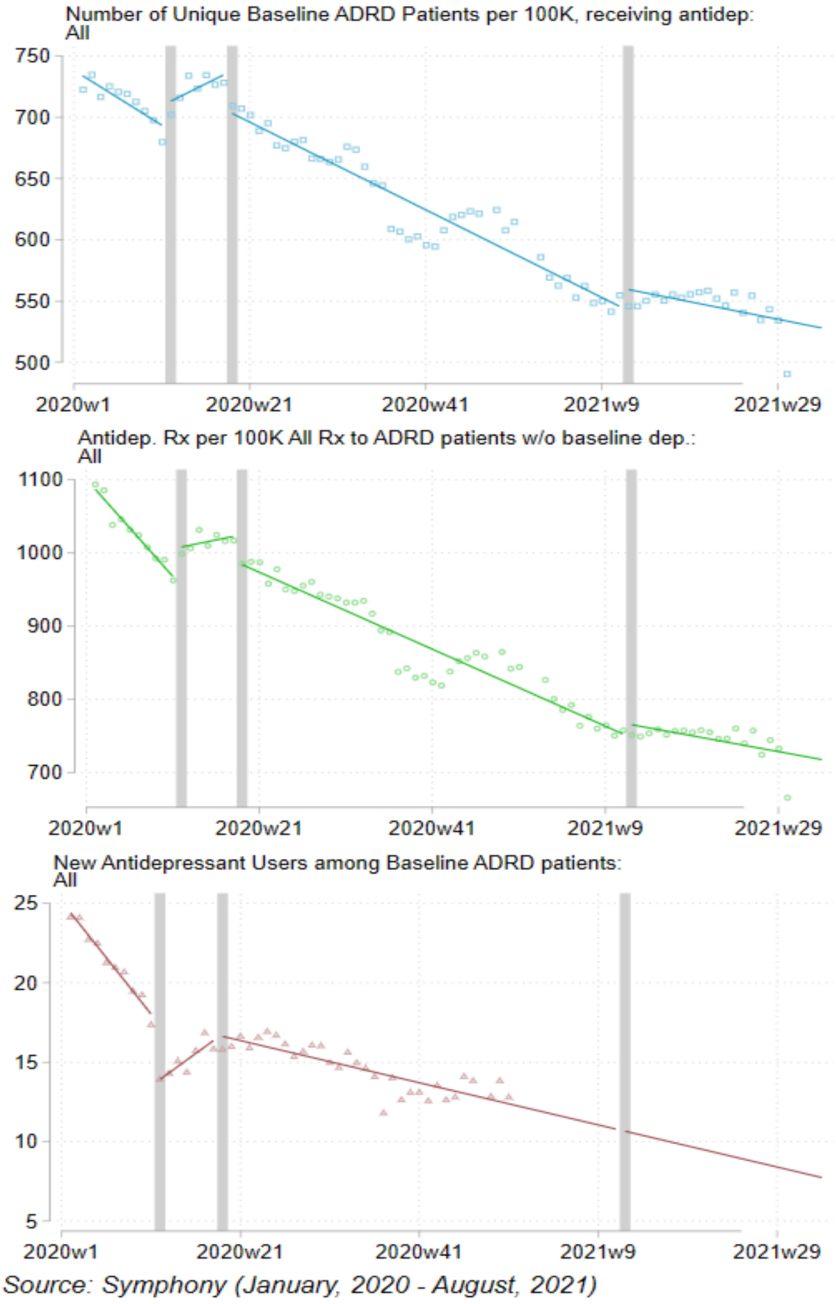
Notes. Figures present raw scatter plots and piecewise linear regression discontinuity based fitted lines of antidepressant use among patients with prior ADRD diagnoses associated with the start of shutdowns in Spring 2020 in response to the pandemic, state re-openings following closures in Summer 2020 and COVID-19 vaccination rollout at the start of 2021, using antidepressant prescription claims data from Symphony Health. State closure and reopening policies and vaccination rollout serve as proxies for social isolation of elderly during the COVID-19 pandemic.

Table 1: Piecewise linear regression discontinuity estimates of the effect of COVID-19 related events on the number of unique patients per 100K, with baseline ADRD diagnosis who were prescription dispensed antidepressant prescriptions each week.

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)
	All	**Female**	**Male**	**Black**	**White**	**Hispanic**	**Other Race**	**Medicare**	**Medicaid**	**Cash**	**Private**
Intercept before the onset of the pandemic	689.0***	820.4***	506.5***	629.2***	657.7***	881.3***	731.4***	755.0***	464.6***	208.9***	485.5***
	(9.399)	(11.592)	(6.951)	(7.687)	(10.009)	(14.616)	(9.325)	(9.403)	(24.653)	(4.360)	(12.425)
Trend before the onset of the pandemic	-4.491***	-5.797***	-2.971***	-3.386***	-4.354***	-4.298*	-5.123***	-4.308***	-5.020	-4.833***	-7.105***
	(1.515)	(1.868)	(1.120)	(1.239)	(1.613)	(2.356)	(1.503)	(1.515)	(3.973)	(0.703)	(2.002)
Δ trend associated with shutdowns at the onset of pandemic	8.075	12.45	2.917	4.338	7.643	10.51	9.418	7.609	7.033	5.786	13.30
95% LCI	2.073	5.043	-1.522	-0.571	1.252	1.181	3.464	1.605	-8.709	3.002	5.362
95% UCI	14.08	19.85	7.355	9.247	14.03	19.85	15.37	13.61	22.77	8.570	21.23
p-value	0.00900	0.00100	0.194	0.0820	0.0200	0.0280	0.00200	0.0140	0.376	0	0.00100
Δ intercept associated with shutdowns at the onset of pandemic	24.06	27.20	20.09	13.23	28.63	15.54	19.88	24.16	20.20	27.23	33.58
95% LCI	-2.419	-5.450	0.510	-8.424	0.436	-25.63	-6.384	-2.322	-49.25	14.94	-1.424
95% UCI	50.53	59.86	39.67	34.89	56.82	56.72	46.15	50.65	89.64	39.51	68.58
p-value	0.0740	0.101	0.0440	0.227	0.0470	0.454	0.136	0.0730	0.564	0	0.0600
Δ trend associated with re-openings	-7.160	-10.88	-2.637	-4.065	-6.915	-9.289	-7.991	-6.853	-6.982	-2.144	-8.838
95% LCI	-12.36	-17.29	-6.480	-8.315	-12.45	-17.37	-13.15	-12.05	-20.61	-4.555	-15.71
95% UCI	-1.964	-4.470	1.205	0.184	-1.382	-1.209	-2.836	-1.655	6.646	0.266	-1.969
p-value	0.00800	0.00100	0.175	0.0600	0.0150	0.0250	0.00300	0.0110	0.310	0.0800	0.0120
Δ intercept associated with re-openings	-35.05	-52.31	-13.94	-14.48	-36.02	-46.53	-35.69	-40.23	-18.32	-17.83	-40.12
95% LCI	-59.60	-82.59	-32.09	-34.56	-62.16	-84.71	-60.04	-64.80	-82.72	-29.22	-72.58
95% UCI	-10.49	-22.03	4.220	5.601	-9.874	-8.351	-11.33	-15.67	46.08	-6.438	-7.668
p-value	0.00600	0.00100	0.130	0.155	0.00800	0.0180	0.00500	0.00200	0.572	0.00300	0.0160
Δ trend associated with COVID-19 vaccine rollout	2.147	2.359	1.804	1.490	2.339	1.472	2.102	1.161	6.511	0.432	1.715
95% LCI	0.954	0.887	0.922	0.514	1.068	-0.384	0.918	-0.0330	3.380	-0.122	0.137
95% UCI	3.341	3.831	2.687	2.467	3.610	3.328	3.287	2.355	9.642	0.986	3.293
p-value	0.00100	0.00200	0	0.00300	0	0.118	0.00100	0.0570	0	0.124	0.0340
Δ intercept associated with COVID-19 vaccine rollout	17.31	22.24	10.94	14.15	21.70	2.104	11.22	17.66	69.03	-0.681	41.00
95% LCI	2.381	3.822	-0.103	1.937	5.805	-21.11	-3.589	2.721	29.87	-7.607	21.26
95% UCI	32.24	40.65	21.98	26.36	37.60	25.32	26.04	32.59	108.2	6.246	60.74
p-value	0.0240	0.0190	0.0520	0.0240	0.00800	0.857	0.135	0.0210	0.00100	0.845	0
Observations	78	78	78	78	78	78	78	78	78	78	78
Baseline DV mean	713.7	852.3	522.8	647.8	681.7	904.9	759.5	778.6	492.2	235.5	524.6

Notes. Author's calculation based on piecewise linear regression discontinuity based fitted lines of antidepressant use among patients with prior ADRD diagnoses associated with the start of shutdowns in Spring 2020 in response to the pandemic, state re-openings following closures in Summer 2020 and COVID-19 vaccination rollout at the start of 2021, using antidepressant prescription claims data from Symphony Health. State closure and reopening policies and vaccination rollout serve as proxies for social isolation of elderly during the COVID-19 pandemic.

Appendix Figure 1. Other antidepressant prescribing outcomes to ages 65+ ADRD patients



[1] https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/older-adults.html

[2] Gupta, Sumedha. "Impact of Volunteering on Cognitive Decline of the Elderly." *The Journal of the Economics of Ageing* 12 (November 1, 2018): 46–60. https://doi.org/10.1016/j.jeoa.2018.01.002.

[3] Food and Drug Administration. Emergency Use Authorization (EUA) for an Unapproved Product Review Memorandum [Internet]. 2020. Available from: https://www.fda.gov/media/144416/download

[4] Food and Drug Administration. FDA Takes Additional Action in Fight Against COVID-19 By Issuing Emergency Use Authorization for Second COVID-19 Vaccine [Internet]. FDA. FDA; 2020 [cited 2021 Mar 25]. Available from: https://www.fda.gov/news-events/press-announcements/fda-takes-additional-action-fight-against-covid-19-issuing-emergency-use-authorization-second-covid

[5] Food and Drug Administration. FDA Issues Emergency Use Authorization for Third COVID-19 Vaccine [Internet]. FDA. FDA; 2021 [cited 2021 Mar 25]. Available from: https://www.fda.gov/news-events/press-announcements/fda-issues-emergency-use-authorization-third-covid-19-vaccine

[6] Gupta, Sumedha, Jonathan Cantor, Kosali I. Simon, Ana I. Bento, Coady Wing, and Christopher M. Whaley. "Vaccinations Against COVID-19 May Have Averted Up To 140,000 Deaths In The United States." *Health Affairs*, August 18, 2021, 10.1377/hlthaff.2021.00619. https://doi.org/10.1377/hlthaff.2021.00619.

[7] Cagnin A, Di Lorenzo R, Marra C, Bonanni L, Cupidi C, Laganà V, Rubino E, Vacca A, Provero P, Isella V, Vanacore N, Agosta F, Appollonio I, Caffarra P, Pettenuzzo I, Sambati R, Quaranta D, Guglielmi V, Logroscino G, Filippi M, Tedeschi G, Ferrarese C, Rainero I, Bruni AC and SINdem COVID-19 Study Group (2020) Behavioral and Psychological Effects of Coronavirus Disease-19 Quarantine in Patients With Dementia. *Front. Psychiatry* 11:578015. doi: 10.3389/fpsyt.2020.578015

[8] Barguilla, Ainara, Aida Fernández-Lebrero, Isabel Estragués-Gázquez, Greta García-Escobar, Irene Navalpotro-Gómez, Rosa María Manero, Víctor Puente-Periz, Jaume Roquer, and Albert Puig-Pijoan. "Effects of COVID-19 Pandemic Confinement in Patients With Cognitive Impairment." *Frontiers in Neurology* 11 (November 24, 2020): 589901. https://doi.org/10.3389/fneur.2020.589901.

[9] Rainero, Innocenzo, Amalia C. Bruni, Camillo Marra, Annachiara Cagnin, Laura Bonanni, Chiara Cupidi, Valentina Laganà, et al. "The Impact of COVID-19 Quarantine on Patients With Dementia and Family Caregivers: A Nation-Wide Survey." *Frontiers in Aging Neuroscience* 12 (2021): 507. https://doi.org/10.3389/fnagi.2020.625781.

[10] Jay J, Bor J, Nsoesie EO, Lipson SK, Jones DK, Galea S, et al. Neighbourhood income and physical distancing during the COVID-19 pandemic in the United States. Nat Hum Behav. 2020 Dec;4(12):1294–302.

[11] Allcott H, Boxell L, Conway J, Gentzkow M, Thaler M, Yang D. Polarization and public health: Partisan differences in social distancing during the coronavirus pandemic. J Public Econ. 2020 Nov 1;191:104254.

[12] Chang S, Pierson E, Koh PW, Gerardin J, Redbird B, Grusky D, et al. Mobility network models of COVID-19 explain inequities and inform reopening. Nature. 2021 Jan;589(7840):82–7.

[13] Gao S, Rao J, Kang Y, Liang Y, Kruse J, Dopfer D, et al. Association of Mobile Phone Location Data Indications of Travel and Stay-at-Home Mandates With COVID-19 Infection Rates in the US. JAMA Netw Open. 2020 Sep 1;3(9):e2020485.

[14] Goolsbee A, Syverson C. Fear, Lockdown, and Diversion: Comparing Drivers of Pandemic Economic Decline 2020 [Internet]. National Bureau of Economic Research; 2020 Jun [cited 2021 Jan 20]. Report No.: w27432. Available from: https://www.nber.org/papers/w27432

[15] Jay J, Bor J, Nsoesie EO, Lipson SK, Jones DK, Galea S, et al. Neighbourhood income and physical distancing during the COVID-19 pandemic in the United States. Nat Hum Behav. 2020 Dec;4(12):1294–302.

[16] Cantor JH, Sood N, Bravata DM, Pera MF, Whaley CM. The Impact of the COVID-19 Pandemic and Policy Response on Health Care Utilization: Evidence from County-level Medical Claims and Cellphone data | NBER [Internet]. National Bureau of Economic Research; 2020 [cited 2021 Mar 25]. Report No.: w28131. Available from: https://www.nber.org/papers/w28131