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Table 1
Top 10 Drug-Drug/Drug-Disease Interactions Seen in Study Population

Drug-Drug or Drug-Disease	Adverse Physiologic Effect
Levofloxacin + cations (eg, zinc, calcium)	Decreased serum concentration of levofloxacin resulting in reduced effectiveness when given within 2 h of each other
Azithromycin + simvastatin or atorvastatin	Increased risk of myopathies
Aspirin + anticoagulation (eg, enoxaparin, apixaban)	Increased risk for bleeding
Aspirin + dexamethasone or prednisone	Increased risk for gastrointestinal ulceration and bleeding
Albuterol + carvedilol or metoprolol	Attenuation of albuterol bronchodilatory effects
Hydroxychloroquine + azithromycin	QTc prolongation potential
Azithromycin + donepezil	QTc prolongation potential
Anticoagulation + SSRI or SNRI (eg, sertraline, duloxetine)	Increased risk for bleeding
Alzheimer's dementia + dexamethasone or prednisone	Behavioral issues (eg, agitation, aggression), insomnia
Diabetes mellitus type 2 + dexamethasone or prednisone	Loss of blood glucose control

SNRI, serotonin and norepinephrine reuptake inhibitors; SSRI, selective serotonin reuptake inhibitor.

appropriate stop dates for treatment of time-limited acute illnesses. Keeping pill burden in mind is also important, especially when using unproven therapies for both treatment and prophylaxis of acute illness, such as COVID-19. Polypharmacy can lead to adverse outcomes, and a more cautious and evidence-based approach for treating COVID-19, or any acute illness, is needed.

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Changing Dynamics of COVID-19 Deaths During the SARS-CoV2 B.1.617.2 (Delta Variant) Outbreak in England and Wales: Reduced COVID-19 Deaths Among the Care Home Residents



To the Editor:

Care homes and long-term care facilities (LTCFs) worldwide plunged into crisis during the initial stages of COVID-19 pandemic caused by SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2).^{1,2} Numerous preventive measures were taken to reduce the COVID-19 infections among the care home residents and to improve the outcomes.^{3–5}

The Office of National Statistics reported a sharp increase in the COVID-19 deaths among care home residents in England and Wales during the initial stages of the pandemic.⁶ The COVID-19 surge since early June 2021 was predominantly due to the Delta variant (SARS-CoV2 B.1.617.2), but the outcomes of COVID-19 deaths among care home residents have not been described.

Methodology

In this observational study, we analyzed the nationwide data of care home deaths in England and Wales between March 7, 2020, and November 26, 2021, during the COVID-19 pandemic using data from the UK Office of National Statistics.^{7,8}

We performed an analysis of the COVID-19 deaths occurring at the places of death, including care homes, in terms of total weekly COVID-19 deaths during 3 comparative periods of March 7–August 28, 2020; August 29, 2020–May 28, 2021; and May 29–November

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26, 2021. We also performed further analysis of the proportion of deaths occurring at care homes that were due to COVID-19 during each of those 3 periods.

Statistical Analysis

The relative risk (RR), 95% CI, and *P* values were calculated to compare the outcomes during the 3 study periods. Statistical comparisons of these outcomes were made between each preceding study period.

Results

Table 1 shows the distribution of the total COVID-19 deaths (*n* = 153,179) in England and Wales. There were 220,092 care home deaths from all causes and 33,329 deaths due to COVID-19 in care homes from March 7, 2020, to November 26, 2021.

During March 7–August 28, 2020 (first wave), a total of 15,414 COVID-19 deaths (29.8%) occurred in care homes. There was a significant decrease in the percentage of COVID-19 deaths occurring in care homes relative to the total COVID-19 deaths [16,603 (19.2%); RR 0.64, 95% CI 0.63–0.65; *P* < .001] during August 29, 2020–May 28, 2021. Furthermore, COVID-19 deaths occurring in care homes decreased significantly [1312 (8.9%); RR 0.46, 95% CI 0.43–0.48; *P* < .001] during the Delta variant surge (May 29–November 26, 2021) compared with prior periods.

Table 1 also shows that during March 7–August 28, 2020, COVID-19 was responsible for 20.0% (15,514/76,906) of all care home deaths, which significantly declined to 18.5% (RR 0.92, 95% CI 0.90–0.93; *P* < .001) during August 29, 2020–May 28, 2021, and then further to 2.5% (RR 0.13, 95% CI 0.12–0.14; *P* < .001) during May 29–November 26, 2021. During the first surge (Figure 1), up to 43.6% of the weekly COVID-19 deaths occurred at care homes, with associated decreases in deaths occurring in hospitals. The significant decline in the proportion of weekly COVID-19 deaths in care homes during the Delta variant surge compared with prior surges is

associated with the significantly increased proportion of COVID-19 deaths occurring in hospitals (Table 1, Figure 1).

Discussion

Our study indicates that during the first wave (March 7–August 28, 2020), COVID-19 had a devastating effect on care homes, with 29.8% of all COVID-19 deaths occurring in care homes. Overall, 20% of deaths in care homes were due to COVID-19. During the second wave, there was a slight, but significant, decrease in the COVID-19 deaths occurring in care homes. The deaths due to COVID-19 occurring in care homes showed a significantly sharp decline (from 19.2% to 8.9%) during the Delta variant surge, as well as since the second surge (18.5% vs 2.5%).

The findings of our study for the first wave is similar to prior reports of the UK Office of National Statistics, which highlighted the higher number of deaths in care homes during the second wave than the first wave.⁶

The reduced death rates in the care homes during the Delta variant surge are most likely due to the infection control and protective measures implemented in the care homes by applying lessons learned from the previous surges.^{3,4} The greater adoption of COVID-19 vaccination among care home residents is also a major contributory factor for reduced deaths during the Delta variant surge.⁹ The immunity from previous SARS-CoV2 infections may also be a potential contributory factor for reduced deaths during the Delta variant surge.¹⁰ The increased hospital deaths we noted during the Delta variant surge are probably due to a relative increase in COVID-19 mortality among persons living in the community compared with persons living in care homes.

Limitations of our study are that it is an observational study of publicly reported data and that the generalizability of the findings is limited to the England and Wales population. The other limitation of our study is that we are unable to determine the proportion of deaths that occurred in care homes after transfer from a hospital, as those data are not publicly available.

Table 1
Total SARS-CoV2 Deaths in England and Wales, Place of Death, and the Percentage of Deaths due to COVID-19 (at Each Place of Death) During March 7, 2020–November 26, 2021

	Study Period		RR (95% CI); <i>P</i> Value*	May 29–November 26, 2021, <i>n</i> (%)	RR (95% CI); <i>P</i> Value*
	March 7–August 28, 2020, <i>n</i> (%)	August 29, 2020–May 28, 2021, <i>n</i> (%)			
Total deaths from all causes (<i>n</i> = 1,025,282)	299,844 (100)	456,847 (100)		268,591 (100)	
Total deaths due to COVID-19 (<i>n</i> = 153,179)	51,740 (17.3)	86,627 (19.0)	1.099 (1.088–1.110); <i>P</i> < .001	14,812 (5.5)	0.291 (0.286–0.296); <i>P</i> < .001
Place where the COVID-19 deaths occurred					
Hospital (acute or community, not psychiatric)	32,731 (63.3)	62,653 (72.3)	1.143 (1.135–1.152); <i>P</i> < .001	11,968 (80.8)	1.117 (1.107–1.127); <i>P</i> < .001
Care home	15,414 (29.8)	16,603 (19.2)	0.643 (0.631–0.656); <i>P</i> < .001	1312 (8.9)	0.462 (0.438–0.488); <i>P</i> < .001
Home	2432 (4.7)	5451 (6.3)	1.339 (1.278–1.403); <i>P</i> < .001	1297 (8.8)	1.392 (1.313–1.475); <i>P</i> < .001
Hospice	730 (1.4)	1315 (1.5)	1.076 (0.984–1.177); <i>P</i> = .11	129 (0.9)	0.574 (0.479–0.687); <i>P</i> < .001
Other communal establishment	228 (0.4)	292 (0.3)	0.765 (0.644, 0.909); <i>P</i> = .002	24 (0.2)	0.481 (0.317–0.729); <i>P</i> = .001
Elsewhere	205 (0.4)	313 (0.4)	0.912 (0.765–1.087); <i>P</i> = .30	82 (0.6)	1.532 (1.202–1.953); <i>P</i> = .001
Deaths due to COVID-19/deaths from all causes, <i>n/n</i> (%)					
Care home (<i>n</i> = 33,329)	15,414/76,906 (20.0)	16,603/89,954 (18.5)	0.921 (0.903–0.939); <i>P</i> < .001	1312/53,232 (2.5)	0.134 (0.126–0.141); <i>P</i> < .001
Hospital (<i>n</i> = 107,352)	32,731/120,273 (27.2)	62,653/206,411 (30.4)	1.115 (1.103–1.128); <i>P</i> < .001	11,968/116,191 (10.3)	0.339 (0.333–0.346); <i>P</i> < .001
Home (<i>n</i> = 9180)	2432/82,713 (2.9)	5451/129,926 (4.2)	1.427 (1.361–1.496); <i>P</i> < .001	1297/79,066 (1.6)	0.391 (0.368–0.415); <i>P</i> < .001
Hospice (<i>n</i> = 2174)	730/12,261 (6.0)	1315/18,317 (7.2)	1.206 (1.105–1.316); <i>P</i> < .001	129/12,126 (1.1)	0.148 (0.124–0.177); <i>P</i> < .001
Elsewhere (<i>n</i> = 600)	205/6441 (3.2)	313/10,612 (2.9)	0.927 (0.779–1.102); <i>P</i> = .39	82/7035 (1.2)	0.395 (0.311–0.503); <i>P</i> < .001
Other communal establishments (<i>n</i> = 544)	228/1250 (18.2)	292/1627 (17.9)	0.984 (0.841–1.151); <i>P</i> = .84	24/941 (2.6)	0.142 (0.095–0.214); <i>P</i> < .001

*Statistical comparisons were performed with the prior comparison period.

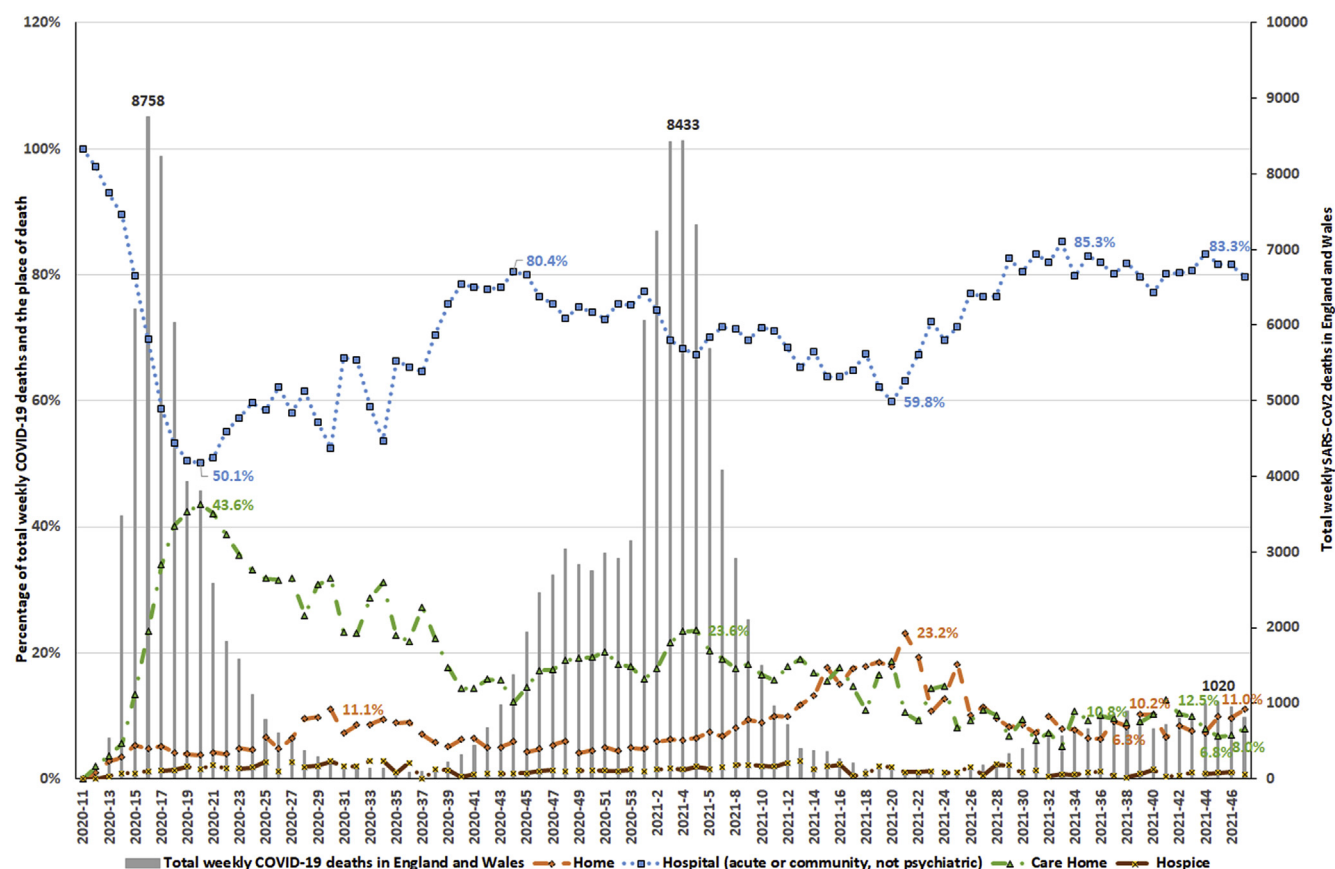


Fig. 1. Proportion of weekly COVID-19 deaths based on the place of death (primary axis) and total weekly deaths (secondary axis). Since the Delta variant surge in June 2021, the proportion of COVID-19 deaths occurring in hospitals increased significantly. There is also a significant decline in the proportion of weekly COVID-19 deaths in care homes during the Delta variant surge compared with prior surges. During the first surge, up to 43.6% of weekly COVID-19 deaths occurred at care homes, with associated decreases in deaths occurring in hospitals.

In summary, we observed that a significantly lower number of COVID-19 deaths occurred in care homes and that during the Delta variant surge in England and Wales, the number of care home deaths caused by COVID-19 was significantly lower than the prior surges. Furthermore, care home residents are at the highest risk for mortality because of advanced age and comorbidities; therefore, continuous monitoring and research on COVID-19 preventive interventions is an absolute necessity to further improve the outcomes.

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