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.

Potential for Drug Interactions and Polypharmacy From Treatment of COVID-19 in Long-Term Care

The COVID-19 pandemic has brought to public attention significant vulnerabilities of older adults living in long-term care (LTC).[1,2] This is due not only to the direct risk of COVID-19 and its potential complications but also the potential for inappropriate polypharmacy.[3] Acute illnesses, of all types, commonly add medications to the profile and therefore increase the threat of drug-drug interactions (DDIs) and polypharmacy. Prescribers often fail to think of these issues when in the midst of treating an acute problem. Residents in LTC are at increased risk of medication-related errors, with approximately 800,000 preventable medication-related errors occurring each year in this care setting.[4] Bundles of medications ("COVID cocktails") prescribed to treat COVID-19 can include antibiotics, anticoagulants, systemic corticosteroids, inhaled therapies, and nutritional supplements. Some of these therapies have evidence of benefit in COVID-19, whereas many do not.[5] COVID cocktails can increase risk of medication errors, drug interactions, and pill burden. Risk can be longer term if medications for COVID-19 are not reviewed or discontinued after the acute illness resolves. Cocktails and other therapies for acute illness have the potential for serious consequences, with state survey tag F757 among them.[6]

We sought to evaluate the impact of COVID-19 cocktails on polypharmacy, preventable medication-related problems, such as drug-drug and drug-disease interactions, and persistence of time-limited medications.

Methods

A retrospective cohort study was performed on all residents with an *International Classification of Diseases, Tenth Revision* (*ICD-10*), code for COVID-19 over 6 months in 41 facilities of a single LTC chain. Demographics, record of medications started for COVID-19, and date of COVID diagnosis were collected. Medication regimens were reviewed for new DDIs with significance based on the clinical skills of the team. The number of scheduled medications at ±30 days from COVID diagnosis date were counted to assess if medication regimens were permanently increased after COVID resolved. The date of COVID-19 diagnosis was considered day zero. Descriptive statistics characterized the data.

Results

There were 759 individuals (51.4% women) diagnosed with COVID-19 during the 6-month window, with data available for 751 residents. Baseline characteristics included an average age of 75.5 ± 12.6, with 133 residents (17.7%) younger than 65 years and 204 (27.3%) older than 85 years.

Almost half of the residents (n=324, 43%) diagnosed with COVID had at least 1 medication initiated. In this medication-added cohort, the average number of medications added was 2.62 ± 1.5 and median number added was 2 (range 1-7). Antibiotics (21.8%; n=164) and corticosteroids (17.7%; n=133) were the most commonly started.

Five hundred sixty-five residents had evaluable data concerning increased medication burden 30 days post COVID-19 diagnosis. Ninety-four residents had fewer medications at 30 days; 198 residents had no change in number of medications. However, 237 (41.9% of the evaluable cohort) had at least 1 additional medication at day 30+. The most common persisting at day 30+: vitamin C, zinc, albuterol, prednisone, and dexamethasone. One-hundred fifty residents (19.9%) 30 days post-COVID were on 2 or more additional medications.

We identified 145 residents (19.5%) with a clinically significant DDI, most commonly increased risk of bleeding, potential for QTc prolongation, additive serotonergic burden, and decreased therapeutic effects due to concomitant administration (eg, chelation or absorption issues; Table 1).

Discussion

We present the first attempt to characterize polypharmacy occurring after COVID-19 diagnosis in the LTC population. It is reflective of the polypharmacy that can be typical in the treatment of acute illness.[6] More than half the residents received at least 1 new medication on COVID-19 diagnosis. Nearly one-third of the original cohort had at least 1 medication still on the profile at 30 days. These cocktails, on average, increased the medication regimen by 2 medications. From these newly initiated COVID-19 medications, close to 20% of residents experienced a new significant DDI related to their new regimen.

Antimicrobials were the most prevalent class of medications prescribed for COVID-19, which is consistent with reviews in community and hospital settings.[7,8] Post hoc reflection noted that several anticoagulants started on the day of COVID diagnosis had new indications (eg, "anticoagulation") at 30 days, potentially making discontinuation difficult.

We recognize several limitations. We were unable to determine efficacy or safety outcomes from these medication regimens, and we limited the scope of our evaluation to *ICD-10* coding; thus, we were unable to characterize patients prescribed medication cocktails for COVID-19 prophylaxis. This is a common occurrence from our own clinical experience in LTC. Our data were pulled from LTC facilities within a single state (Texas), potentially limiting generalizability. However, our results are consistent with other analyses.[7–10]

Polypharmacy and its consequences increase with each additional medication, especially when multiple medications are added all at once, and is a risk factor for adverse outcomes in those with COVID-19.[11] However, this is not simply a "COVID issue" and occurs with many acute illnesses in LTC. Thankfully, opportunities exist to mitigate the issues characterized. Stop dates should be used for every acute-illness medication, not only antimicrobials. Anticoagulants, inhalers, supplements, and PRNs being used for time-limited illness should also include stop dates. This can be especially important if medications prescribed are a diversion risk (eg, promethazine with codeine cough syrup). Current medication regimen should be reviewed prior to starting a new therapy. Consultant pharmacists are ideal members of the health care team to assist with this. Considerations of pill burden, DDIs, and drug-disease interactions should be as important as symptom control.

Conclusions and Implications

Almost half of the LTC residents within our cohort experienced polypharmacy because of their COVID-19 diagnosis and 1 in 5 had a new, potentially dangerous DDI. There is an important opportunity to better care for residents in LTC diagnosed with any acute illness. Clinicians must consider important DDIs, polypharmacy, and

The authors declare no conflicts of interest.

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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