provide support for activities of daily living in older people with disabilities and psychological problems.[9] These innovative strategies can create a new geriatrics in parallel with traditional face-to-face care for the elderly.

Maintaining social connectivity will help us remain healthy in the current pandemic situation. On April 16, Captain Tom Moore, a 99-year-old army veteran, walked the last 10 laps from 100 backyard lengths as he reached his 100-year-old birthday to raise money for the National Health Services in the UK.[10] This gesture encouraged people worldwide and conveyed to the elderly "You'll never walk alone," as he sang. It is necessary to change the message from "just stay home" to "avoid close contact and maintain a physically, mentally, and socially active lifestyle."

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Drug interactions with potential antivirals used for COVID-19 in older persons

Dear Editor,

Older persons are increasing in proportion globally, and retain important social and economic roles. Unfortunately, they experience disproportionately high mortality from severe coronavirus disease 2019 (COVID-19) infection.[1] Cunningham *et al*. have succinctly highlighted the challenges and potential treatment options.[2] We feel that these options have specific considerations in older adults. To optimize clinical care, we need to be prudent in all areas: clinically, pharmacologically and ethically. In particular, we will highlight the impact of polypharmacy on older adults when potential antivirals for COVID-19 are used.

Although no specific antivirals for COVID-19 infections have been proven to be effective in randomized controlled trials, off-label, compassionate and experimental use of several drugs are common, especially for severe infection.[3] The risks for severe COVID-19 infection and mortality concurrently increase with age. Similarly, chronic obstructive pulmonary disease, cardiovascular diseases, cerebrovascular diseases, cognitive disorders, chronic kidney disease, chronic liver disease, hyperlipidemia, hypertension, diabetes mellitus and hypothyroidism are all more common in older persons. Multimorbidity interacts significantly with frailty.[4] Not surprisingly, treatment of multiple comorbid conditions necessitates the use of multiple medications.

In the presence of both polypharmacy and multimorbidity, antiviral administration in older adults carries an elevated risk of harm from drug–drug and drug–disease interaction. With regard to drug–drug interactions, we show several commonly-used medications in older persons and their interaction with antiviral medications repurposed for COVID-19 (Table 1).[5,6] In addition, aging involves progressive organ impairments that affect drug clearance and pharmacokinetics. For instance, in the presence of moderate-to-severe hepatic impairment, antiviral medications should be avoided. Similarly, in the presence of severe renal dysfunction, i.v. remdesivir is to be used with caution in view of the accumulation of excipient sulfobutylether-β-cyclodextrin. Whereas chloroquine and hydroxychloroquine might require dose attenuation, as they have some clearance through the kidneys.

Table 1 Interactions between commonly used medications in older persons with potential antivirals used for COVID-19

	CQ/HCQ	RDV	TCZ	LPV/r	IFN-beta
Antihyperlipidemics	—	—	Decrease level of antihyperlipidemics (CYP3A4 substrates)	Increased risk of rhabdomyolysis Simvastatin, lovastatin: Contraindicated Atorvastatin, rosuvastatin: Decrease dose Fluvastatin, pravastatin: Least interactions	—
Antihypertensives					
ACEI/ARB	—	—	—	—	—
Beta-blockers	Increase beta-blocker levels	—	—	Increase beta-blocker levels	—
Calcium-channel blockers	Diltiazem and Verapamil increase CQ level	—	Decrease level of calcium-channel blockers (CYP3A4 substrates)	Increase calcium-channel blocker levels	—
Diuretics	—	—	—	Increase indapamide level	—
Antidiabetic medications	Augment effects of hypoglycemic agents	—	—	—	—
Anticoagulants					
Warfarin	—	—	Decrease warfarin level (CYP3A4 substrate)	Decrease warfarin level	—
DOACs	—	—	Decrease drug levels of some DOACs (CYP3A4 substrates)	Increase DOAC levels and toxicity due to CYP3A4 and P-glycoprotein inhibition mechanisms: Avoid concurrent use	—
Antiplatelets	—	—	Decrease drug levels of some antiplatelets (CYP3A4 substrates)	Increase ticagrelor level: Avoid concurrent use Decrease of clopidogrel's active metabolite: Avoid concurrent use Prasugrel use preferred	—
Analgesics	—	—	—	Increase drug levels of opioids	—
Antidepressants (mirtazapine, escitalopram, fluvoxamine)	Potential additive QT prolongation	—	—	Increase drug levels of mirtazapine, escitalopram, fluvoxamine	—
Antipsychotics (olanzapine, quetiapine, risperidone)	Increase level of risperidone Potential additive QT prolongation	—	—	Decrease level of olanzapine Increase level of quetiapine, risperidone, haloperidol	—
Cognition enhancers (donepezil, rivastigmine, memantine)	Potential additive QT prolongation with donepezil	—	—	—	—
Gastrointestinal agents (proton pump inhibitors, antacids)	Decrease CQ levels via adsorption antacids. Separate administration of antacids and CQ by at least 4 h	—	—	—	—
Hypnotics	—	—	Decrease drug levels of some hypnotics (CYP3A4 substrates)	Increase zopiclone and zolpidem levels	—
Respiratory agents	—	—	—	Increase salmeterol level: Avoid concurrent use Decrease theophylline level	—
Thyroxine	Increase TSH	—	—	Decrease thyroxine efficacy	—

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; CQ, chloroquine; DOAC, direct oral anticoagulants; HCQ, hydroxychloroquine; IFN, interferon; LPV/r, lopinavir/ritonavir; RDV, remdesivir; TCZ, tocilizumab; TSH, thyroid-stimulating hormone.

The surge of COVID-19 is not currently stopping. Although no age group is spared, older persons are a vulnerable population. Their care should remain optimal through personalizing clinical care and medications. Unfortunately, antiviral medications have not been proven to be clinically effective against COVID-19, and observational data of treatment effects on older persons are limited. Consequently, any potential antivirals for COVID-19 should be prescribed very carefully, considering drug–drug interactions, drug–disease interactions and the balance of benefit versus harm.

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