Implications of COVID-19 in an Ageing Population

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Summary

- Coronavirus disease 2019 (COVID-19) encompasses a broad spectrum of clinical presentation and disease severity. Globally, case fatality rates demonstrate a strong age-related gradient.
- Baseline medical comorbidities present in patients with severe disease and death include hypertension, cardiovascular disease, and diabetes. Importantly, causative association for individual comorbid conditions have not been established. There is inadequate evidence regarding either beneficial or harmful effects of angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), and non-steroidal anti-inflammatory drugs (NSAIDs).
- Non-COVID medical issues of concern in the elderly include a trend to delayed presentation and management of other acute medical issues, including acute coronary syndromes and stroke, and the sequel of elective surgery postponement.
- Whilst residential aged-care facilities remain a particularly vulnerable setting for COVID-19 transmission, health policies of social distancing and visitor restriction aimed at limiting transmission also increase risk of symptoms of depression and anxiety in susceptible individuals. Adaptive models of care such as Telehealth consultations can facilitate ongoing management of regular comorbidities and maintain contact between patient, family, and clinicians when isolation is imposed.
- SARS-CoV-2 vaccine may not translate into lasting immunity in an elderly population due to immunosenescence. The indiscriminate use of non-validated therapies to treat COVID-19, such as hydroxychloroquine and azithromycin, should be discouraged in the elderly outside a registered clinical trial due to increased risks of adverse effects common to most drugs when used in the elderly (eg. QT-interval prolongation, ventricular tachyarrhythmia, and sudden cardiac death).
- Asymptomatic transmission remains a constant threat to the elderly population and has implications for infection control measures; community surveillance must go beyond targeting only symptomatic individuals.

Introduction

Coronavirus disease 2019 (COVID-19) encompasses a broad clinical spectrum caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Since the identification of a novel coronavirus causing a cluster of pneumonia cases in Wuhan, China, significant insight into the epidemiology, transmission, and clinical presentation has been achieved (1).

Amidst rapidly accumulating global data, a particularly vulnerable group emerging is the elderly population. Accumulating evidence indicates a strong age-related gradient for risk of severe disease, hospitalisation, and death (2).

Recent modelling indicates early case identification and social restriction strategies implemented across Australia have been effective in reducing and delaying the projected peak of COVID-19 infection (3). However, in the absence of chemoprophylaxis, effective vaccine or proven treatment options, a prolonged campaign of community surveillance is likely required for early case detection to limit morbidity and mortality and mitigate overwhelming healthcare system capacity. Such surveillance is particularly imperative given the degree of asymptomatic transmission within our community is likely underestimated. The elderly population and those with multi-morbidity will continue to be disproportionately vulnerable.

This review focuses on the evolving risk of COVID-19 in an ageing population and the associated increased mortality and morbidity, both physical and psychological. It is targeted at clinicians involved in the routine care of our elderly. The scope of this review does not encompass the acute diagnosis and management of COVID-19.

Methods

We have identified relevant literature via a PubMed and Medline review, including original articles, topic reviews, and societal guidelines to formulate an evidence-based synopsis of COVID-19 in the elderly population. Suitable articles since case identification through to the present were included in the review.

COVID-19 in an Aging Population

Globally, as of April 28, 2020, there have been 2,954,222 confirmed cases and 202,597 deaths caused by COVID-19 (4). Australia has been comparatively spared due to rapid implementation of border restrictions, social distancing measures, and contract tracing. As of April 29, 2020, there are 6,731 cases and 84 deaths from COVID-19 (5). The median age of Australian deaths secondary to COVID-19 is 79 years.

Individuals identified at greatest risk of severe disease, hospitalisation and death from COVID-19 are the elderly (with risk increasing continuously from 60-years of age, and much higher over 70-years) and those with underlying medical comorbidities (6). One model-based analysis demonstrated hospitalisation estimates for COVID-19 increased with age: 1.04% for those aged 20-29 years, increasing to 18.4% for those aged 80 years and older (2). There is also a strong age gradient for COVID-19 mortality. Case fatality rates for patients with confirmed COVID-19 in China were 8.0% amongst patients aged 70-79 years and 14.8% for patients aged ≥80 years in comparison to 2.3% for

the entire cohort of confirmed cases (7). Case fatality rates in Italy also demonstrated a strong age association, with 12.8% and 20.2% amongst patients aged 70-79 years and ≥80 years, respectively (8).

Based on recent modelling (2), when infection fatality rates (assuming a uniform attack rate by age group) were applied to the Australian population (9), it is projected that if 0.5 million Australians were infected with COVID-19, that 66% of deaths would occur in those aged 70 years and older. Eight-eight percent of deaths would occur in Australians aged 60 years and older. Refer to **Box 1** (adapted from Glynn. (10)).

Advancing age is emerging as the strongest predictor of COVID-19 associated morbidity and mortality (11, 12). The individual contributions related to frailty and underlying physiological changes associated with aging or to multi-morbidity remains uncertain. Given Australia's ageing population (21.4% are aged 60 years and older), an evolving public health policy in response to the COVID-19 pandemic must address the needs of this vulnerable population (9). **Figure 1** summarises some of the key factors in assessing the impact of COVID-19 in an elderly population.

Specific Populations

Protecting Older Health Care Workers

In Italy, an estimated 20% of health care professionals have become infected (13). In the United Kingdom, of 1,654 healthcare workers screen between March 10 and 31, 2020, 14% (240 of 1,654) were positive (14). In Victoria, a reported 165 health care workers have been infected (where the source was known, 12 cases were thought to have been acquired in the workplace). Importantly, these figures do not account for the degree of asymptomatic transmission within our healthcare facilities.

In Australia in 2018, the average age of practicing general practitioners and specialists was 51.1 and 49.9 years, respectively (15). This creates complex challenges to strained health infrastructure and resources to ensure the allocating of vulnerable staff to 'non-COVID' roles whilst maintaining ongoing input of years of valuable clinical experience.

Long-Term Care Facilities

Residents of long-term care facilities are generally elderly, multi-morbid, and restricted in their capacity to self-isolate. The WHO has estimated up to half of COVID-19 related deaths in Europe are residents of aged care facilities (16). In Australia, 12 residence of the Newmarch House (Sydney) have now died from COVID-19 (17).

Importantly, of the 48 residents of one American residential facility who tested positive for SARS-CoV-2, 27 (56%) were asymptomatic at the time of testing, with a further 24 subsequently developing symptoms (18). Given that greater than half of the confirmed cases were asymptomatic at the time of testing, this highlights that infection control measures targeting symptomatic patients only are inadequate. However, the ideal surveillance strategy remains uncertain.

Key strategies outlined by the American-based Centers for Disease Control and Prevention (CDC) for the prevention of COVID-19 in long-term care facilities include: training facility staff and visiting health care workers in adequate use of personal protective equipment (PPE), ensuring adequate

supply of PPE, discouraging visitation of symptomatic people, and early identification and isolation of cases through liberal screening to prevent transmission (19). Aerosol generating procedures, such as nebulised therapy (eg. salbutamol or normal saline nebulisers), should be prohibited, to the extent of confiscating relevant medication vials. In the currently climate, such preventative measures are all we have to rely on until medication or vaccination are available.

Guidance for residents, facilities and health care workers are available to assist management during the COVID-19 (**Box 2**).

Impact of Medical Comorbidities

Comorbidities associated with more severe disease include hypertension, cardiovascular disease, diabetes, obesity, and malignancy. A review of 5,700 patients hospitalised in the New York area with COVID-19 (median (IRQ) age: 63 (52-75) years), the most prevalent comorbidities were hypertension, obesity, and diabetes (proportion of patients: 56.6%, 41.7%, and 33.8%, respectively) (20).

Characterisation of 1,591 Italian patients (median (IQR) age: 63 (56-70) years) with COVID-19 requiring intensive care unit (ICU) support, 68% had at least one comorbidity (21). Most frequent comorbidities were: with hypertension (49%), cardiovascular disease (21%), hypercholesterolaemia (18%), and diabetes (17%). Only a minimal proportion had a prior diagnosis of chronic obstructive pulmonary disease (4%). In the largest case series from China involving 1,099 patients across 30 provinces, hypertension was the most common comorbidity (6).

Several mechanisms between diabetes and COVID-19 have been postulated, including the role of angiotensin converting enzyme 2 (ACE2) expression on pancreatic β cells and of the dipeptidyl peptidase-4 (DPP-4) enzyme, a functional receptor for the virus responsible for Middle East respiratory syndrome (MERS). Importantly, however, such mechanisms remain hypothetical in the absence of current evidence (22).

Interestingly, chronic respiratory diseases, such as asthma and chronic obstructive pulmonary disease (COPD), appear to be underrepresented comorbid conditions in patients infected with SARS-CoV-2 when compared to global prevalence estimates for these conditions (23). Whilst several mechanism have been postulated to explain this unanticipated finding, it remains uncertain.

What is important to bear in mind for the above studies and others, is that it remains unclear with regards to the contributing role of a particular medical comorbidity, another associated comorbidity, or indeed medication prescribed for the treatment of the comorbidity, in predisposing to either SARS-CoV-2 infection or disease severity and mortality. Causative associations for individual comorbid conditions have not been established. Importantly, in many studies, baseline characteristics in COVID-19 patients were unadjusted for potential confounders (eg. age).

Cardiovascular complications of COVID-19

Amongst patients hospitalised with COVID-19, evidence of myocardial injury is common, leading to increased morbidity and mortality. In one of the larger studies involving 416 patients hospitalised for COVID-19 in Wuhan, China, 82 (19.7%;) had biochemical evidence of cardiac injury. Patients with myocardial injury also had a higher morality rate (51.2% versus 4.5%; $p<0.001$) (24). These patients were older (median age (range): 74, 34-95 versus 64, 21-95; $p<0.001$) and had more comorbidities.

Postulated causes include myocarditis, stress-induced cardiomyopathy, systemic inflammatory response syndrome (SIRS), ischaemic to cardiac microvascular or pericardial supply (plaque rupture or supply-demand imbalance). Cardiovascular risk factors cardiovascular disease are prevalent amongst patients with COVID-19, as detailed above, and are more prevalent with patient age (11). However, the exact case of myocardial injury remains unknown.

Heart failure has also been observed in hospitalised COVID-19 patients, and is associated with increased mortality (11). Data remains limited on incidence and aetiology.

Disability-free Survival

It is too early to comprehensively evaluate lasting morbidity in COVID-19 survivors. Given the increased risk of hospitalisation and morbidity amongst the elderly, a key focus heading forward of any public health strategy must be on implementing systems for the long-term surveillance and management of those who recover from the acute effects of COVID-19 only to face lasting disabilities into the future.

Uncertainty Regarding use of Regular Medications

The angiotensin converting enzyme 2 (ACE2), an enzyme that counters renin-angiotensin-aldosterone system (RAAS) activation, is co-opted by the SARS-CoV-2 to gain entry into human epithelial cells (25). ACE2 is expressed in multiple organs, including heart, kidney and respiratory alveolar epithelium, the primary target of SARS-CoV-2 (26). There is conflicting theoretical concerns as to whether treatment with RAAS inhibiters, primarily ACE inhibitors and angiotensin receptor blockers (ARBs), could lead to altered ACE2 activity and/or levels, enhanced binding and entry of SARS-CoV-2 into respiratory epithelial cells, or increased disease severity in a patient with confirmed COVID-19 (27). A contrasting theory is that increased ACE2 activity could be degrading Angiotensin II and lead to beneficial effects.

In a single-centre study from Wuhan, China, of 362 patients (median (IQR) age: 66 (59-73) with comorbid hypertension hospitalised for COVID-19, of which 115 patients (31.8%) were taking ACE inhibitors or ARBs, the use of ACE inhibitors or ARBs were not associated with either increased disease severity or mortality (28). The proportion of patients on ACE inhibitors or ARBs with severe and non-severe disease was not statistically different (33% versus 31%; p=0.65), nor between non-survivors and survivors (27% and 33%; p=0.34). In a larger retrospective multi-centre study of 1,128 adult patients hospitalised for COVID-19 across Hubei Province, China, of which 188 were taking either an ACE inhibitors or ARB, they observed a lower risk of all-cause mortality in the ACE inhibitor/ARB group versus the non-ACE inhibitor/ARB group (adjusted hazard ratio (95%CI): 0.42, 0.19-0.92; P =0.03) (29).

Currently, clinical data and experimental evidence is lacking to inform of either adverse or beneficial outcomes from continued use of ACE inhibitors and ARBs in the setting of COVID-19 (27). Given the well-established benefits in cardiovascular disease, relevant societal bodies have recommended continuation of a patient's regular RAAS antagonists in the absence of proven risk (30-34). The indiscriminate discontinuation of ACE inhibitors or ARBs may lead to decompensation and hospitalisation in patients receiving therapy for heart failure. Refer to **Box 3** for summary of Societal Recommendations.

There is a multicentre, randomised, double-blind, placebo-controlled phase 2 clinical trial of commencing the ARB losartan in both an inpatient (ClinicalTrials.gov identifier: NCT04312009) and an outpatient setting in patients with confirmed COVID-19 (ClinicalTrials.gov identifier: NCT04311177). However, further prospective epidemiological clinical trials are desperately required to inform the safety of continuing ACE inhibitor and ARBs in patients with COVID-19.

Concerns raised regarding non-steroidal anti-inflammatory drugs (NSAIDs) in COVID-19 were based on case reports only (35). Given current lack of clinical studies to evaluate risk, NSAIDs should not be discontinued. Similarly, initiation of NSAIDs in the absence of contraindications does not need to be avoided in patients with COVID-19 (36-38).

Unintended Consequences: Non-COVID Medical Issues of the COVID-19 Pandemic

A secondary consequence to emerge from the COVID-19 pandemic is the alterations in delivery of usual standards of care for non-COVID medical issues, including primary care and preventative medicine (eg. cancer screening).

A trend towards delayed presentation and management of acute medical issues, including acute coronary syndromes and strokes, has been observed. Despite timely reperfusion being standard of care for ST-segment elevation myocardial infarction (STEMI) (39, 40), there has been an observed reduction in cardiac catheterisation laboratory STEMI activations in America by 38% (41), in Spain by 40 % (42), and Northern Italy (43). Similar observations are occurring for stroke (44). The delay in presentation, if patients present at all, for these time-critical issues is thought secondary to fear of contracting COVID-19 infection from hospitalisation (45).

The National COVID-19 Clinical Evidence Taskforce, an Australian collective of expert panels endorsed by major societal bodies, is currently formulating evidence-based clinical guidelines to assist in the management of a range of medical conditions in the context of the COVID-19 pandemic (46). Australian and New Zealand cardiovascular healthcare providers have drafted a consensus statement to advocate novel healthcare delivery models to support patients with pre-existing cardiovascular disease during the COVID-19 pandemic (30).

Elective procedures

To reduce transmission risk and preserve resources, including personal protective equipment (PPE) and hospital beds, most counties have undertaken periods of suspending all non-essential procedures and elective surgery. The Australian Government implemented restrictions on all non-urgent (category 1 and urgent category 2) elective surgery from March 26, 2020 and subsequently eased restrictions on April 27, 2020 (47, 48). Whilst the term ‘elective’ implies a lack of urgency, it does not translate into an absence or morbidity and mortality if the procedure is delayed, as highlighted by accumulating case reports (45). Surgical colleges have published guidelines to assist hospitals to triage non-emergent surgical procedures during the uncertainty of COVID-19 (49-51).

Digital Revolution for Health Care Delivery

Adaptive models of health care delivery, such as Telehealth consultations, have rapidly been adopted to ensure ongoing delivery of essential health care services (52). Facilitating transition to digital health care delivery for both community and residential patients will face challenges in an aging population for multiple reasons. These include technology literacy, infrastructure restrictions, and underlying cognitive impairment. Globally, greater than 50 million people have dementia (53). There also remains the risk of privacy breaches and data insecurity.

This transition has been facilitated by the Australian Government's release on March 13, 2020, as part of the COVID-19 National Health Plan, of new temporary Medicare Benefits Schedule (MBS) Telehealth item numbers (54).

Psychological Impact of Isolation

Elderly are more susceptible to social disconnection and isolation, leading to increased symptoms of anxiety and depression (55). A review of quarantine measures for COVID-19 identified quarantine duration, inadequate supplies, financial concerns, and infection fears as some of the key triggers for psychological distress (56). The loss of direct connection with routine health care providers from inability to have in-person interactions will also intensify distress and anxiety.

Unaddressed psychological and emotional distress has also been shown in prior pandemics to transition to reduce compliance with social distancing measures (57). An effective COVID-19 public health responses must incorporate a campaign of education and awareness, risk assessment, and evidence-based interventions to address evolving mental health concerns, with a particular focus on people living with dementia and their caregivers (58).

Advanced Care Planning and Palliative Care

When health system capacity is overwhelmed by demanded, triaging is inevitable, with the elderly and frail are unlikely to be offered intensive care management both due to resource scarcity and reduced ability to survive prolonged intubation from COVID-19-associated pneumonia (59). There are guidelines available to assist with an ethical framework for resource allocation during disaster management (60, 61). A key aspect of responsible health care provision in the age of COVID-19 is prioritising advanced care planning (62, 63).

The delivery of effective psychological and physical symptom relief remains an underlying humanitarian principle, even during a crisis. Palliative care delivery and family visitation and grieving is especially challenging during a pandemic setting. Local (64) and international (65) guidelines are available to facilitate this process.

COVID-19 and Immunity in the Elderly

Longitudinal serological prevalence measurements are urgently required to establish extent and duration of immunity to SARS-CoV-2 infection. This has implications is evaluating the potential of heard immunity. Based on an estimated basic reproduction number (R_0) for SARS-CoV-2 of 2.2 (66), 60% of the population would need protective immunity to mitigate against future substantial COVID-19 outbreaks (67). It also remains uncertain if reinfection is possible, and the nature and degree of

immunity required to protect against reinfection. Estimates from related coronaviruses suggest immunity was present after 1 year (68, 69).

Interruption of the global covid-19 pandemic will likely rely on the development of an effective vaccine. The influenza vaccine is regarded as best practice for influenza prevention in the elderly. Whilst more than 100 candidate SARS-CoV-2 vaccines are in development (70), the most ambitious estimates are 6 to 12 months until efficacy results from a phase 3 expansion trial are known (71). There are also efforts by the WHO to centralise vaccine development to ensure immunological responses to various vaccines are uniformly measured. Importantly, activation of the immune system, in response to either wild-type infection or vaccination, may not translate into lasting immunity in the elderly due to immunosenescence, the gradual deterioration of immunological response with age (72). However, the elderly should be prioritised in receiving a SARS-CoV-2 vaccine.

Risks of Unproven Medication in the Elderly

There is no evidence-based treatment for COVID-19 (73). Drugs proposed for management of COVID-19 include the antimalarial drugs (chloroquine and hydroxychloroquine), antivirals (lopinavir, ritonavir, and remdesivir), interferon-beta, and the IL-6 pathway inhibitor tocilizumab (74). In Australia, the ASCOT (Australasian COVID-19 Trial: ACTRN12620000445976) will study two drugs, lopinavir/ritonavir and hydroxychloroquine, across more than 70 hospitals in Australia and 11 hospitals in New Zealand (75). The World Health Organization (WHO) is overseeing a large global trial, called SOLIDARITY, focusing on four potential therapies (remdesivir; lopinavir/ritonavir; lopinavir/ritonavir with interferon-beta; chloroquine and hydroxychloroquine) (76).

It is important to be mindful of the well-established adverse side effects of these medications. Hydroxychloroquine and azithromycin independently increase risk of adverse cardiac events (eg. QT-interval prolongation, ventricular tachyarrhythmia, and sudden cardiac death). On April 24, 2020, the American-based Food and Drug Administration (FDA) issued a 'Drug Safety Communication' for Hydroxychloroquine and chloroquine and discouraged administration outside a hospital or clinical trial setting (77). The elderly are more predisposed to adverse effects of these medications. Overall, the indiscriminate use of non-validated therapies to treat COVID-19 should be discouraged in the elderly outside a registered clinical trial due to risk of established harm.

Conclusion: Projecting the COVID-19 Period

The projected course of the COVID-19 pandemic remains uncertain. Within the space of just 5 months, SARS-CoV-2 has infected in excess of 2.9 million of the world's population, of which 202,597 (6.9%) have died (4). Globally, case fatality rates have demonstrated a strong age-related gradient. Australians aged over 65 year and those with comorbidities remain disproportionately vulnerable to hospitalisation and death. They are also at heightened risk of psychological distress from prolonged social distancing measures and the transition from trusted in-person health care delivery to digital platforms. Psychological health strategies must form an integral part of any COVID-19 public health response.

Results of prospective clinical trials are desperately needed to guide continuation of common prescription medications (eg. Ace inhibitors and ARBs), establish efficacy of chemoprophylaxis or

pharmacotherapy options, and SARS-CoV-2 vaccine development, mindful of immunosenescence in the elderly.

With the COVID-19 risk projected to remain a public health concern, both locally and globally, for many months to come, strategies of addressing the asymptomatic transmission of SARS-CoV-2 in the community are required. The elderly population remain especially vulnerable to bearing the burden of substantial morbidity and mortality.

Box 1: Projected Australian deaths according to age group if 0.5 million SARS-CoV-2 infections occurred. (Adapted from Glynn (10)).

Age Range (years)	Proportion of total population (%)[1]	Infection fatality ratio (%)[2]	Number of deaths if 0.5 million infected	Proportion of deaths (%)
0 – 9	12.56	0·00161%	1	<1
10 – 19	12.05	0·00695%	4	<1
20 – 29	14.45	0·0309%	22	<1
30 – 39	14.48	0·0844%	61	1
40 – 49	12.91	0·161%	104	2
50 – 59	12.14	0·595%	361	8
60 – 69	10.30	1·93%	994	28
70 – 79	7.06	4·28%	1,511	33
≥ 80	4.02	7·80%	1,568	34

1. Australian population data from Australian Bureau of Statistics (9).
2. Infection fatality ratios from Verity et al. (2).

Figure 1: Key aspects of COVID-19 in an elderly population.

Box 2: Clinical resources for care of the elderly during COVID-19*

Australian Resources

- Australian Government Department of Health: COVID-19 Resources
  - https://www.health.gov.au/resources/collections/novel-coronavirus-2019-ncov-resources
- Australian & New Zealand Society for Geriatric Medicine: COVID-19 Resources
  - https://anzsgm.org/resources/covid-19/
- National COVID-19 Clinical Evidence Taskforce
  - https://covid19evidence.net.au/

International Resources

- World Health Organisation (WHO)
  - https://www.who.int/emergencies/diseases/novel-coronavirus-2019
- American Geriatrics Society (AGS): COVID-19 Information Hub
  - https://www.americangeriatrics.org/covid19
- British Geriatrics Society (BGS): Resource Series - Coronavirus and older people
  - https://www.bgs.org.uk/resources/resource-series/coronavirus-and-older-people
- European Geriatric Medicine Society (EuGMS): Task Force on COVID-19
  - https://www.eugms.org/news/read/article/490.html
- Centers for Disease Control and Prevention (CDC): Long-term Care Facilities, Nursing Homes
  - https://www.cdc.gov/coronavirus/2019-ncov/hcp/long-term-care.html

*Websites reviewed April 29, 2020.

Box 3: Summary of Societal recommendations for the use of ACE inhibitors and ARBs in patients with COVID-19. (Adapted from Bavishi et al. (78)).

Professional Society	Release Date	Position Statement
CSANZ, NHF, HBPRCA, ANZSCTS https://www.mja.com.au/journal/2020/cardiovascular-disease-and-covid-19-australiannew-zealand-consensus-statement	April 3, 2020	"Given the well-established beneficial effects of ACEI/ARB in patients with hypertension, heart failure and CVD, it is the strong recommendation of the authors and numerous national and international societies that these medications should be continued as indicated."
HFSA, ACC, and AHA https://www.acc.org/ latest-in-cardiology/articles/ 2020/03/17/08/59/hfsa-acc-ahastatement-addresses-concerns-reusing-raas-antagonists-in-covid-19	March 17, 2020	"The HFSA, ACC, and AHA recommend continuation of RAAS antagonists for those patients who are currently prescribed such agents for indications for which these agents are known to be beneficial, such as heart failure, hypertension, or ischemic heart disease. In the event patients with cardiovascular disease are diagnosed with COVID-19, individualized treatment decisions should be made according to each patient's hemodynamic status and clinical presentation. Therefore, be advised not to add or remove any RAAS-related treatments, beyond actions based on standard clinical practice."
ESC Council on Hypertension https://www.escardio.org/ Councils/Council-onHypertension-(CHT)/News/ position-statement-of-the-esccouncil-on-hypertension-onace-inhibitors-and-ang	March 13, 2020	"The Council on Hypertension strongly recommend that physicians and patients should continue treatment with their usual anti-hypertensive therapy because there is no clinical or scientific evidence to suggest that treatment with ACEi or ARBs should be discontinued because of the Covid-19 infections."
ESH https://www.eshonline.org/ spotlights/esh-stabtementon-covid-19/	March 12, 2020	• "In stable patients with COVID-19 infections or at risk for COVID-19 infections, treatment with ACEIs and ARBs should be executed according to the recommendations in the 2018 ESC/ESH guidelines." • "The currently available data on COVID-19 infections do not a support a differential use of RAS blockers (ACEI or ARBs) in COVID-19 patients."
Hypertension Canada https://hypertension.ca/ wp-content/uploads/2020/03/ 2020-30-15-Hypertension-CanadaStatement-on-COVID-19-ACEi-ARB.pdf	March 13, 2020	• "However, there is no evidence that patients with hypertension or those treated with ARB or ACE inhibitor antihypertensive therapy are at higher risk of adverse outcomes from COVID-19 infection." • "We endorse patients with hypertension to continue with their current blood pressure treatment."
The Canadian Cardiovascular Society and the Canadian Heart Failure Society https://www.ccs.ca/images/ Images_2020/CCS_CHFS_statement_ regarding_COVID_EN.pdf	March 15, 2020	"The Canadian Cardiovascular Society and the Canadian Heart Failure Society strongly discourage the discontinuation of guideline directed medical therapy (GDMT) involving Angiotensin Converting Enzyme Inhibitors (ACEi), Angiotensin Receptor Blockers (ARB) or Angiotensin Receptor Neprilysin Inhibitors (ARNi) in hypertensive or heart failure patients as a result of the COVID-19 pandemic."
International Society of Hypertension https://ish-world.com/news/a/ A-statement-from-theInternational-Society-ofHypertension-on-COVID-19/	March 16, 2020	"[T]here is no good evidence to change the use of ACE-inhibitors or ARBs for the management of raised blood pressure in the context of avoiding or treating COVID-19 infection."
BCS and BSH https://www. britishcardiovascularsociety.org/ news/ACEi-or-ARB-and-COVID-19	March 19, 2020	"[T]he BCS and the BSH…share the view of the European Society of Hypertension and the Renal Association that patients should continue treatment with ACEi and ARB unless specifically advised to stop by their medical team."

Abbreviations: ACC, American College of Cardiology; AHA, American Heart Association; ANZSCTS, Australian and New Zealand Society of Cardiac and Thoracic Surgeons; BCS, British Cardiovascular Society; BSH, British Society for Heart Failure; CSANZ, Cardiac Society of Australian and New Zealand; ESC, European Society of Cardiology; ESH, European Society of Hypertension; HBPRCA, High Blood Pressure Research Council of Australia; HFSA, Heart Failure Society of America; NHF, National Heart Foundation; RAAS, renin angiotensin aldosterone system.

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