HEALTH POLICY STATEMENT

ACC Health Policy Statement on Cardiovascular Disease Considerations for COVID-19 Vaccine Prioritization

A Report of the American College of Cardiology Solution Set Oversight Committee

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PREFACE

The American College of Cardiology (ACC) has a long history of developing documents (e.g., decision pathways, health policy statements [HPS], appropriate use criteria) to provide members with guidance on both clinical and nonclinical topics relevant to cardiovascular care. In most circumstances, these documents have been created to complement clinical practice guidelines and to inform clinicians about areas where evidence may be new and evolving or where sufficient data may be more limited. Despite this, numerous care gaps continue to exist, highlighting the need for more streamlined and efficient processes to implement best practices in service to improved patient care.

Central to the ACC's strategic plan is the generation of "actionable knowledge"—a concept that places emphasis on making clinical information easier to consume, share, integrate, and update. To this end, the ACC has evolved from developing isolated documents to developing integrated "solution sets." Solution sets are groups of closely related activities, policy, mobile applications, decision support, and other tools necessary to transform care and/or improve heart health. Solution sets address key questions facing care teams and attempt to provide practical guidance to be applied at the

point of care. They use both established and emerging methods to disseminate information for cardiovascular conditions and their related management. The success of the solution sets rests firmly on their ability to have a measurable impact on the delivery of care. Because solution sets reflect current evidence and ongoing gaps in care, the associated tools will be refined over time to best match changing evidence and member needs.

HPS represent a key component of solution sets. The methodology for HPS is grounded in assembling a group of experts to develop content that addresses key policy issues facing our members. Topics selected for HPS vary widely, but connect to scientific, quality, and/or advocacy efforts within the ACC. HPS are not written to provide clinical guidance; rather, they are intended to advocate a position, be informational in nature, and apprise stakeholders of the ACC's stance on healthcare policies and programs.

Ty J. Gluckman, MD, FACC
Chair, ACC Solution Set Oversight Committee

INTRODUCTION

The coronavirus disease 2019 (COVID-19) has had a devastating impact on healthcare systems around the world, with nearly 99 million cases and 2.1 million associated deaths as of January 2021 ([1]). As such, the rapid development and availability of multiple vaccines are welcome in the long and arduous fight against COVID-19. A coherent vaccine allocation policy promoting the greatest benefit for the greatest number would prioritize individuals with the highest risk for adverse outcomes of COVID-19 ahead of lower-risk populations. There are numerous factors that influence the risk for adverse outcomes in COVID-19, including the exposure risk for contracting COVID-19 and the clinical risk for adverse health outcomes with infection. The phased rollout of the vaccines by the Centers for Disease Control and Prevention (CDC) mirrors this framework by prioritizing older age groups and patients with significant medical comorbidities ([2]). The guidance specifies that during the Phase 1c allocation, all patients from 16 to 64 years of age with medical conditions that increase the risk for severe COVID-19 infection should receive the vaccine. Although the guidance specifies that heart conditions, hypertension, diabetes, obesity, and smoking are examples of such high-risk medical conditions, further delineation of varying levels of risk among patients with cardiovascular disease (CVD) is absent.

As the largest professional society of cardiovascular (CV) professionals in the United States, the ACC aims to offer specific guidance about how CV conditions contribute to the risk for adverse outcomes with COVID-19 infection to inform its membership and the patients they serve. In this policy document, we: 1) outline the overall

considerations of both exposure and clinical risk needed for vaccine allocation efforts; 2) present the specific evidence and risk considerations related to CVD and COVID-19; and 3) propose a schema of CV risk to incorporate into vaccine allocation decisions.

METHODOLOGY

To provide this policy document, the American College of Cardiology convened a writing group with expertise in CVD, epidemiology, and risk assessment. We conducted a literature review of published reports relating to CVD and COVID-19. Where the literature was absent, we achieved consensus among the writing group. However, in some cases, there was insufficient evidence and/or experience to present an informed opinion, which needs to be considered in the interpretation of this document.
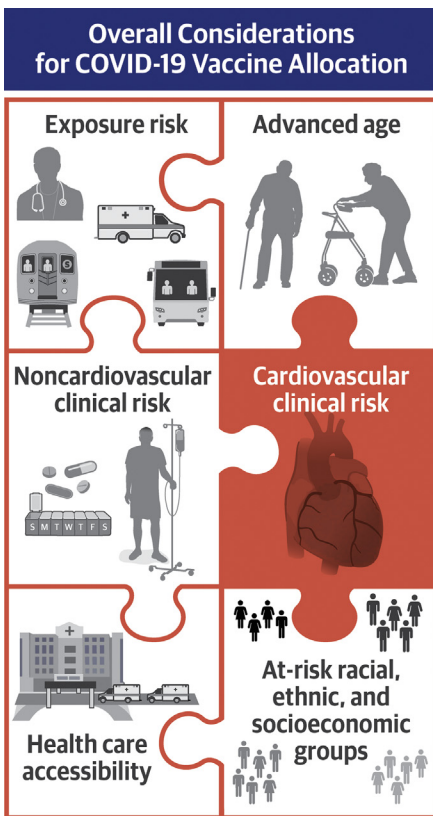
We attempted to include data from geographically diverse areas, when available, recognizing that variability in COVID-19 testing, treatment strategies, and the prevalence of CV conditions can affect estimates of prevalence. It is also noteworthy that most published data have been retrospective in nature and have been conducted at various timepoints during the pandemic. As such, we attempted to emphasize data from larger meta-analyses, when available. It should be noted that our recommendations are based on limited data collected since the pandemic onset. Future recommendations may change over time with higher-quality data.

OVERALL CONSIDERATIONS FOR VACCINE ALLOCATION DECISIONS

Although the focus of this document is the specific clinical risk associated with CV risk factors and disease in COVID-19, it is important to place these recommendations into the broader context of vaccine allocation decisions (**Central Illustration**). These decisions should incorporate both the exposure risk for COVID-19 infection and the clinical risk of experiencing severe COVID-19–related health outcomes. In addition, there are glaring disparities in COVID-19 outcomes between racial/ethnic groups and different socioeconomic status levels, partly due to differential exposures and clinical risks and partly due to overall inequities in health care access and social determinants of health. All of these factors warrant consideration in vaccine allocation decisions.

Exposure risk for COVID-19 correlates with the amount of time spent interacting closely with others and on the number of these interactions. As such, exposure risk is higher among health care workers, first responders, public transportation employees, and other "essential" workers. Evidence suggests that this risk can be reduced by adherence to CDC recommendations for mask-wearing and social distancing ([3]). Frequency of health care system

CENTRAL ILLUSTRATION   Considerations for Prioritization of COVID-19 Vaccination Allocation

Overall Considerations for COVID-19 Vaccine Allocation

- Exposure risk
- Advanced age
- Noncardiovascular clinical risk
- Cardiovascular clinical risk
- Health care accessibility
- At-risk racial, ethnic, and socioeconomic groups

Cardiovascular Clinical Risk for Severe COVID-19 Outcomes

(Increasing Risk for Severe COVID-19 Outcomes — from bottom to top)

Recent, unplanned hospitalization for CVD (<6 months)	Pulmonary hypertension, NYHA class III/IV	ACHD, physiological Stage C or D
High-grade PAD	1- or 2-vessel obstructive CAD with angina; or triple-vessel or left main obstructive CAD	Heart failure, Stage C, NYHA class III/IV; heart failure, Stage D; or heart transplant
Morbid obesity	2+ poorly controlled cardiovascular risk factors (hypertension, diabetes, obesity)	Poorly controlled insulin-dependent diabetes ± complications
Malignant tachyarrhythmia, high burden	Pulmonary hypertension, NYHA class I/II	ACHD, physiological Stage A or B
Low-grade or fully revascularized PAD	1- or 2-vessel obstructive CAD without angina; fully revascularized CAD; or nonobstructive CAD	Heart failure, Stage B or Stage C, NYHA class I/II
Obesity	Poorly controlled hypertension	Insulin-dependent diabetes
Overweight	Hypertension	Non-insulin-dependent diabetes

Poorly controlled hypertension is defined as >140/90 mm Hg. Poorly controlled diabetes is defined using A_{1c} >10%. Overweight is defined as BMI 25–29 kg/m²; obese as BMI 30–40 kg/m², and morbidly obese as BMI >40 kg/m². Obstructive CAD is defined using ≥70% obstruction in major epicardial arteries, ≥50% in left main coronary artery. High-grade PAD is defined using ABI ≥0.5. Malignant tachyarrhythmia includes atrial fibrillation with poor rate control and/or VT with prior ICD therapy or antiarrhythmic medication. ACHD = adult congenital heart disease; ABI = ankle brachial index; BMI = body mass index; CAD = coronary artery disease; CVD = cardiovascular disease; NYHA = New York Heart Association; PAD = peripheral arterial disease; VT = ventricular tachycardia.

interaction is another factor that may be considered to influence exposure risk among patients. For example, patients with advanced CVD may require long-term stays in nursing homes or rehabilitation centers. As such, their risk of COVID-19 exposure may increase. Finally, the local prevalence rates of COVID-19 infection, which vary by community, also influence exposure risk.

Clinical risk for severe COVID-19 infection appears to correlate with both advanced age and pre-existing medical conditions. Advanced age in itself, with its decreased physiological reserve, leads to a higher susceptibility to contracting COVID-19 and experiencing its complications (4,5). Additionally, advanced age is a surrogate for more numerous comorbidities, resulting in greater risk and worse outcomes. Reports by the CDC demonstrate that compared with patients 18 to 29 years of age with COVID-19, those over 75 years of age have an 8-fold higher risk of hospitalization and 220-fold higher risk of death (6). As such, the current CDC phased allocation model prioritizes

patients with advanced age for early vaccination, which is in accordance with the CV-related risk related to advanced age.

Pre-existing medical conditions, particularly when 2 or more co-occur, also significantly increase the risk for severe COVID-19 outcomes. In a large systemic review of the literature including 202,005 patients with COVID-19, the case fatality rate (CFR) rose incrementally with the number of comorbidities: whereas patients with 1 medical comorbidity experienced a CFR of 6%, patients with 6 or more comorbidities experienced a CFR of 21% (7). In addition to multimorbidity, there are data demonstrating the adverse effects of frailty in patients with COVID-19. A multicenter European study of 1,564 adult subjects assessed using the clinical frailty scale (1 to 2 = fit; 3 to 4 = vulnerable, but not frail; 5 to 6 = initial signs of frailty but with some degree of independence; and 7 to 9 = severe or very severe frailty) found that higher levels of frailty were associated with worse adjusted 7-day mortality,

independent of age and comorbidity (8). Given this collective evidence, older patients with multiple comorbidities, including CV conditions, and/or frailty should be considered at high risk and thus prioritized for COVID-19 vaccination.

Finally, it is imperative to recognize the racial, ethnic, and socioeconomic disparities that may influence the risk for adverse outcomes, including mortality, in COVID-19 (9-11). Reports from the CDC show that compared with age-adjusted standardized mortality rates, the risk of death from COVID-19 increased by nearly 3-fold in Blacks, non-Black Hispanics/Latinos, and American Indians/Alaskan Natives (12). The reasons behind these disparities are multifactorial. First, the exposure risk among these populations tends to be higher, given the higher prevalence of multigenerational households and "essential" jobs necessitating more frequent contact with the public. Second, patients in racial and ethnic minority populations have a higher prevalence of CV risk factors and disease and therefore are at higher clinical risk compared with those without comorbidity (13,14). Higher transmission rates are also observed among those who experience social inequalities (15). Third, healthcare accessibility is another important driver of these disparities. The number of hospitals, intensive care unit (ICU) beds, and other resources important to the care of patients with COVID-19 vary by region of the country and are typically lower in communities of color, settings of poverty, and rural locations. As such, the demand for resources may outweigh the supply, affecting the triage and management of patients COVID-19 (16).

A coherent vaccine allocation strategy will consider the exposure risks and clinical risks of given individuals and populations. In addition, it will take into account those demographic populations that, for a variety of reasons, have additional risks that lead to higher rates of COVID-19 infection and severe health outcomes. Finally, the vaccine allocation strategy should balance the use of complex, multifactorial risk stratification with the exigency of operationalizing the most rapid and efficient plan to achieve population immunity and blunt community spread.

CVD AND OUTCOMES IN COVID-19

With the broad context of considerations for COVID-19 vaccine allocation articulated, we now focus on the specific contributions of CV conditions to COVID-19 infection and severity. Numerous multinational studies have demonstrated that CVD and its related risk factors are associated with high morbidity and mortality in patients with COVID-19 infection (17-26). Furthermore, the association between CVD and poor outcomes in COVID-19 has been demonstrated to exist independent of potential confounders (27). In a large meta-analysis of 21 multinational studies inclusive of 11,766 COVID-19 cases, CVD was an independent predictor of severe COVID-19, even after controlling for age and sex (relative risk [RR]: 1.8; 95% CI: 1.1 to 2.7) (28). Additionally, the presence of CVD is a key risk factor for the CV complications of COVID-19, which are also associated with increased morality (29,30). Below, we review the available data regarding the prevalence and association of specific CV conditions and risk factors with outcomes in patients with COVID-19.

Hypertension

Since the earliest cohort studies from China, hypertension has been consistently reported as a common CV comorbidity in patients with COVID-19 (31-34). In a large U.S. cohort study using hospital claims data for 11,721 patients across 38 states, pre-existing hypertension was noted in 46.7% of COVID-positive patients (21). In a critically ill cohort of 257 patients from New York City, the prevalence of pre-existing hypertension among patients in the ICU was even higher, at 63.0% (35).

Although the baseline prevalence of hypertension varies significantly by geographic region, multinational data have consistently demonstrated worse outcomes associated with COVID-19 in patients with pre-existing hypertension (23,33). In a large meta-analysis from China inclusive of 1,567 patients, patients with pre-existing hypertension had higher odds of severe COVID-19 infection compared with those without pre-existing hypertension, although the criteria for severe disease were poorly defined (odds ratio [OR]: 2.46; 95% CI: 1.46 to 2.46) (32). In another large meta-analysis from China inclusive of 1,527 patients, the proportion of patients with pre-existing hypertension was higher in those admitted to the ICU compared with patients not in ICUs (28.8% and 14.1%, respectively; RR: 2.03; 95% CI: 1.54 to 2.68) (31). A large single-center cohort study among 2,877 patients in China hospitalized with COVID-19 demonstrated a greater than 3-fold increase in mortality among patients with pre-existing hypertension (4.0% vs. 1.1%), even after controlling for age, sex, and other CVDs and risk factors (adjusted hazard ratio [HR]: 2.12; 95% CI: 1.17 to 3.82) (36). Importantly, patients with untreated hypertension had significantly higher mortality compared with those with well-controlled hypertension (7.9% vs. 3.2%; adjusted HR: 2.17; 95% CI: 1.03 to 4.57). In a single-center cohort from Wuhan, China, inclusive of 803 patients with hypertension and COVID-19, increased systolic blood pressure was associated with the development of heart failure (HR per 10 mm Hg: 1.89; 95% CI: 1.15 to 3.13) (37). Although the majority of these studies are from China, we believe that these associations are likely generalizable to other geographic populations, including those in the United States. Therefore, patients with hypertension, and

especially those with poorly controlled disease with older age and additional comorbidities, should be considered to have elevated risk of adverse outcomes associated with COVID-19.

Diabetes

Diabetes mellitus is a highly prevalent CV risk factor among patients with COVID-19. In a large cohort study using medical record data including 31,461 patients from 24 U.S. healthcare systems, diabetes was present in 15% of patients with COVID-19 (9). In this analysis, diabetes was the second most common medical comorbidity overall, aside from pre-existing pulmonary disease, which was prevalent in 17.5% of patients (9). Among hospitalized patients, large cohort studies from different areas of the United States demonstrate even higher prevalence, ranging from 25.2% to 35.8% (21,35,38,39). Although the prevalence of diabetes at baseline varies significantly by country, cohort studies from various nations around the world all demonstrate diabetes to be a prevalent comorbidity in patients with COVID-19 (33,34,40,41).

Limited data demonstrate an association between diabetes and adverse outcomes in COVID-19. A large meta-analysis inclusive of patients hospitalized with COVID-19 in China demonstrated ICU patients to have a higher prevalence of diabetes compared with non-ICU patients (11.7% vs. 4.0%) (31). In a large global meta-analysis inclusive of 18,012 patients with COVID-19, diabetes was associated with increased mortality from COVID-19 (OR: 2.50; 95% CI: 1.74 to 3.59) (23). In a large population-based study in England, pre-existing diabetes was associated with higher odds of in-hospital death after adjusting for age, sex, and comorbidities (OR: 3.51; 95% CI: 3.16 to 3.90 for type 1 diabetes and OR: 2.03; 95% CI: 1.97 to 2.09 for type 2 diabetes) (42). Similar associations were observed in a population-based study from Scotland (43).

The severity of diabetes is also related to adverse outcomes in COVID-19 (44). In a population-based study among over 16,000 patients with diabetes in England, those with a glycosylated hemoglobin (HbA_{1c}) level greater than 10% had higher mortality compared with those with an HbA_{1c} level between 6.5% and 7.0% (HR: 2.23; 95% CI: 1.50 to 3.30) (45). Patients with insulin dependence, poor glycemic control, and/or microvascular and macrovascular complications from diabetes should be considered at especially high risk for adverse outcomes associated with COVID-19.

Obesity

Obesity is a highly prevalent CV risk factor in the United States, and as such, much of the data for adverse outcomes in patients with obesity and COVID-19 come from cohort studies in the United States. Among 11,721 patients hospitalized for COVID-19 across 38 states, 16% of patients were obese (body mass index [BMI] ≥ 30 kg/m^2) (21). However, in certain regions, obesity is even more prevalent. Two New York City cohort studies demonstrated obesity in approximately one-third of inpatients admitted with COVID-19 (38,39). In a cohort study of critically ill patients admitted to the ICU in New York City, 46% of patients were obese (26).

Small studies have demonstrated that pre-existing obesity has been consistently associated with adverse outcomes in COVID-19. Among 393 patients hospitalized for COVID-19 in New York City, patients with obesity were more likely to be intubated compared with patients without obesity (43.4% vs. 31.9%) (38). Even among a cohort of young adults with COVID-19, morbid obesity (BMI >40 kg/m^2) was independently associated with death or mechanical ventilation during hospitalization (46). A larger national study using hospital claims data from the majority of states also showed this association of obesity with a greater need for mechanical ventilation (18.3% vs. 15.7%) (21). Interestingly, in a cohort study of 6,916 patients from Kaiser Permanente hospitals in California, the association between BMI and mortality related to COVID-19 was J-shaped, with higher risks in patients with either low or elevated BMIs (47). Specifically, low BMI (<18.5 kg/m^2) was associated with worse outcomes (RR: 1.81; 95% CI: 0.99 to 3.30), likely due to frailty or cachexia related to comorbid conditions (47). In addition, compared with patients with BMIs of 18.5 to 24 kg/m^2, those with BMIs of 40 to 44 kg/m^2 or greater than 45 kg/m^2 had a progressive increase in risk for mortality in multivariable models controlling for age, sex, and numerous CV comorbidities (RR: 2.68; 95% CI: 1.43 to 5.04; and RR: 4.18; 95% CI: 2.12 to 8.26, respectively). Although data from other nations are limited, a large-scale population study from England demonstrated an increasing likelihood of COVID-19 hospitalization with increasing BMI (48), thus supporting the U.S. data. Accordingly, we recognize obesity as an important CV risk factor and postulate the risk of obesity to be incremental, such that patients with morbid obesity are at the highest risk for poor outcomes associated with COVID-19. Furthermore, it is important to recognize that obesity contributes to other risks such as hypertension, diabetes, sleep apnea, and secondary pulmonary hypertension.

Atherosclerotic Cardiovascular Disease

Although the data from China demonstrated pre-existing atherosclerotic cardiovascular disease (ASCVD) in only a small minority of patients with COVID-19, studies from the United States demonstrate ASCVD to be a more common CV comorbidity, likely due to higher baseline prevalence (40). Data from inpatients and outpatients with COVID-19 in a large New York City health system reported an 8.6% prevalence of pre-existing coronary artery

disease (CAD) and an 8.1% prevalence of peripheral artery disease (PAD) (49). In another New York City cohort of 393 patients hospitalized with COVID-19, the prevalence of pre-existing CAD was even higher, at 13.7% (38).

The presence of ASCVD has been shown in multiple analyses to be associated with adverse outcomes with COVID-19 infection. In a federated electronic medical record analysis of multiple U.S. centers, prior myocardial infarction was associated with higher odds of death from COVID-19 (OR: 1.97; 95% CI: 1.64 to 2.35). Among 8,438 patients from a large hospital system in New York City, the presence of pre-existing CAD was associated with higher risk for outcomes of mechanical intubation and death compared with the absence of CAD (RR: 1.88; 95% CI: 1.52 to 2.35 and RR: 2.24; 95% CI: 1.98 to 2.55, respectively) (49). Importantly, the presence of PAD was an equally important CV risk factor for intubation and death in this cohort (RR: 1.82; 95% CI: 1.45 to 2.29; and RR: 1.64; 95% CI: 1.42 to 19.1, respectively). Studies from China confirm this association. In a cohort of 1,590 patients hospitalized for COVID-19, pre-existing CAD, present in 16% of the cohort, was associated with significantly higher odds of in-hospital death in a multivariable model controlling for other relevant risk factors (HR: 4.28; 95% CI: 1.14 to 16.13) (50). At the present time, data supporting a connection between cerebrovascular disease and adverse COVID-19 outcomes are lacking. Nonetheless, the presence of ASCVD appears to be a clear risk factor for poor outcomes in COVID-19. Furthermore, we believe that patients with extensive, high-risk ASCVD are the most susceptible to adverse outcomes.

Cardiac Dysrhythmia

The risk of COVID-19 infection to patients with pre-existing cardiac dysrhythmias has not been well defined. However, patients with marginally controlled heart rhythm disorders may be at increased risk for exacerbations of their underlying conditions if infected with COVID-19. Interestingly, an association between atrial fibrillation (AF) and elevated angiotensin-converting enzyme 2 (ACE2) levels has led to speculation that patients with known AF may have a higher risk for morbidity and mortality associated with COVID-19 (51–53). Certain populations with AF have a higher risk for morbidity and mortality from arrhythmia recurrence, which COVID-19 seems to provoke (54,55). For example, patients with a known history of a tachycardia-induced cardiomyopathy or diastolic heart failure exacerbation related to AF should be considered at high risk. Those patients in persistent or permanent AF or flutter with marginal rate control should also be considered at higher risk than those who are well rate-controlled and prioritized appropriately. Data regarding other supraventricular tachycardias are less clear. Notably, despite the known thrombotic

complications of COVID-19, anticoagulant therapy before admission, commonly used to prevent stroke in patients with AF, does not appear to have an impact on mortality in hospitalized patients (56,57).

The effect of COVID-related illness on patients with pre-existing ventricular arrhythmias has not been reported in large series. Clinical experience suggests that pulmonary decompensation from any cause can be associated with recurrent ventricular arrhythmias including ventricular tachycardia (VT) and ventricular fibrillation (VF) and therapy from implanted cardioverter-defibrillators (ICDs) (54,58). Markers that might reasonably be expected to confer increased risk include a history of appropriate ICD therapy for VT or VF or a requirement for longitudinal treatment with an antiarrhythmic medication to achieve clinical suppression. Patients in those categories should reasonably be considered at high risk for adverse outcomes with COVID-19.

Heart Failure

In distinction to many other CVDs, there is robust evidence for poor outcomes in COVID-19 in the presence of pre-existing heart failure. Among a cohort of 31,461 patients with COVID-19 across the United States, 7.3% had a history of heart failure (9). Compared with those who survived, those who died had a significantly higher proportion of pre-existing heart failure (30.8% vs. 6.3%). In a multivariable model controlling for relevant demographic and CV risk factors, pre-existing heart failure was independently associated with death in this cohort (OR: 1.42; 95% CI: 1.21 to 1.67). These findings have been replicated in 2 large New York City cohorts as well (49,59). In an analysis of 1,212,153 patients with heart failure who were included in the Premier health care database, patients with heart failure who were hospitalized for COVID-19 had markedly greater risk for in-hospital mortality in multivariable analysis (OR: 14.48; 95% CI: 12.23 to 17.12) (60). In multivariable models for the outcomes of death or mechanical ventilation, pre-existing heart failure was also a significant independent risk factor (OR: 8.04; 95% CI: 7.10 to 9.12). Notably, these associations were persistent over 2 distinct time periods in the pandemic, although overall mortality was lower later in the pandemic. Therefore, heart failure is a clear, established risk factor for poor outcomes, and patients who are decompensated and/or those with poor functional status should be considered at the highest risk.

Prior Heart Transplant

Patients who have undergone heart transplantation are at elevated risk for poor outcomes of COVID-19, likely in part due to their immunosuppressed status. Although there are no large studies to date in the heart transplant population, numerous case series from around the world

demonstrate poor outcomes in the context of COVID-19 infection. In a cohort study from Italy inclusive of 47 patients with prior heart transplants, the CFR was nearly double that of patients without a history of transplant (29.7% vs. 15.4%) (61). In a case series of 21 patients with a history of heart transplant in Germany, of the 38.1% who required mechanical ventilation, 87.5% died (62). Small U.S. cohort studies have shown similarly poor outcomes. Among 13 patients with a history of heart transplantation in Michigan, 6 required ICU admission and 2 died (63). In a slightly larger New York City cohort of 28 patients with prior heart transplants and COVID-19, 22 required hospitalization, of whom 7 required mechanical ventilation and 7 died (64). Given these data and the immunosuppressed status of these patients, patients with a history of heart transplantation are at especially high risk for COVID-19. Patients who are actively listed for heart transplants in the hospital or at home should also be presumed to be at high risk. Furthermore, those patients with durable mechanical support, such as left ventricular assist devices, should also be presumed to be at high risk, regardless of transplant candidacy.

Pulmonary Hypertension

Patients with pulmonary hypertension (PH) have an increased risk of death with COVID-19 infection, though the data are limited. One group surveyed 77 U.S. PH comprehensive care centers, noting that although the incidence of COVID-19 infection in patients with PH was similar to that of the general U.S. population (2.9 per 1,000 patients), their rates of hospitalization were higher, at 30% (65). Furthermore, mortality was significantly higher compared with the general population, at 12%. The authors allude to the important point that in addition to the potential direct harm associated with COVID-19, patients with PH had fewer clinic visits and limited diagnostic testing during the pandemic, indicating potential indirect effects on disease progression and monitoring. Although there are no studies that examine the impact of PH severity on disease outcomes, it is likely that those patients with advanced disease and/or those undergoing lung transplant evaluation are at especially high risk for poor outcomes with COVID-19.

Adult Congenital Heart Disease

There are very limited data thus far on the association between adult congenital heart disease (ACHD) and outcomes in patients with COVID-19. Given the variable anatomy and functional status associated with different forms of ACHD, the risk for poor outcomes in COVID-19 is heterogeneous within this population. A single-center New York City cohort study examined outcomes among 53 patients with congenital heart disease, 43 (81%) of whom were adults (66). Seven patients (5.7%) died of COVID-19 in this cohort. Patients who were classified as physiological stages C or D, indicating more clinically severe disease, had significantly higher mortality than those with better clinical status (OR: 19.4). Notably, 36% of patients with ACHD had associated heart failure (40% of adults), 11% had PH, and 17% were obese, all of which significantly increased the risk for death in this cohort, whereas lesion type and lesion complexity were not associated with outcomes. Although larger multicenter studies are needed, patients with ACHD, especially those with concomitant heart failure and/or PH and those with poor physiological stage, are at the highest risk with COVID-19 infection.

Prevalent Noncardiac Comorbidities in CVD Populations

There are many patients with pre-existing CVD who have important coexisting medical conditions that together likely influence the risk for morbidity and mortality in COVID-19. For example, patients with CVD and comorbid pulmonary disease are likely to have poor outcomes with COVID-19, given the severe impact of the virus on both organ systems. Similarly, patients with CVD and comorbid chronic kidney disease are likely to experience poor outcomes. Furthermore, patients with CVD and active and prior malignancies likely represent a high-risk group, given their poor performance status, immunocompromised status, and/or hypercoagulability, which may portend CV complications associated with COVID-19 (67). Pregnant women with CVD should also be considered high risk, given the potential for pregnancy to decompensate certain CVDs, such as heart failure, that may be exacerbated in the setting of COVID-19 infection. In addition to other non-CV comorbidities, other behaviors may amplify CV risk, such as smoking, medical noncompliance, and alcohol or substance abuse. Although these interactions are all important to consider, more data are needed to make recommendations for these specific populations.

PROPOSED COVID-19 VACCINATION ALLOCATION AND PRIORITIZATION BY CV RISK

Based on epidemiological evidence to date defining the morbidity and mortality of COVID-19 and the expert consensus of the writing group, we outline a proposed vaccine allocation schema with regard to CV risk (**Central Illustration**). Our proposed vaccine allocation schema outlines key CV clinical risk considerations within the broader context of key overall risk considerations, including exposure, disparities, health care access, advanced age, and multimorbidity. Individual risk should be determined by their highest-risk CV condition.

Importantly, this schema does not suggest that individuals with lower-risk CV conditions should delay or avoid receiving the vaccine. Rather, its intent is to

emphasize that those with relatively higher-risk CV conditions should prioritize their receipt of the vaccine. Accordingly, their care teams should encourage prompt vaccination and proactively address any barriers or hesitancy that the patient may be facing.

Patients with CV risk factors and disease are at variable risk for adverse outcomes in COVID-19 based on the severity of their comorbidities. Patients with more advanced CVD are at higher risk compared with those with well-controlled CV conditions (36,66). For example, those patients with poorly controlled hypertension, insulin-dependent diabetes, or diabetes with microvascular and/or macrovascular complications as a result of poor glycemic control should be considered higher risk compared with patients who are medically optimized. Similarly, patients with morbid obesity should be considered higher risk compared with patients who are overweight. Patients with high-risk or symptomatic ASCVD, including CAD or PAD, should be considered at higher risk compared with patients with asymptomatic or fully revascularized disease. In patients with a history of cardiac dysrhythmia, those with poorly controlled or poorly tolerated AF/flutter should be considered at higher risk. Furthermore, those patients with a history of VT or VF previously requiring ICD therapy and/or longitudinal treatment with an antiarrhythmic medication should be considered at higher risk as well. Among patients with heart failure, those with worse functional status (i.e., New York Heart Association class III/IV) and those requiring recent hospitalization or an urgent visit for worsening heart failure should be considered higher risk compared with those patients who are well-compensated on medical therapy and infrequently hospitalized. Patients with heart failure who are being considered for or are already listed for a heart transplant should be considered at especially high risk, given their advanced, decompensated disease. Additionally, patients with a history of a heart transplant should be considered higher risk, given their immunosuppressed status, especially those in the immediate postoperative state and at the highest intensity of immunosuppression. Although there are less data in the PH population, patients with moderate-severe PH should be considered higher risk, especially those who are decompensated and being considered or listed for lung transplant. Patients with ACHD with advanced physiological stage, indicating more advanced disease, should be prioritized. We hope that this document can be used to guide COVID-19 vaccine allocation and patient outreach in the context of prolonged demand-supply mismatch as we enter Phase 1c.

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APPENDIX 1. AUTHOR RELATIONSHIPS WITH INDUSTRY AND OTHER ENTITIES (RELEVANT)—ACC HEALTH POLICY STATEMENT ON CARDIOVASCULAR DISEASE CONSIDERATIONS FOR COVID-19 VACCINE PRIORITIZATION

To avoid actual, potential, or perceived conflicts of interest that may arise as a result of industry relationships or personal interests among the writing committee, all members of the writing committee, as well as peer reviewers of the document, are asked to disclose all current healthcare-related relationships, including those existing 12 months before initiation of the writing effort. The Solution Set Oversight Committee reviews these disclosures to determine which companies make products (on market or in development) that pertain to the document under development. Based on this information, a writing committee is formed to include a majority of members with no *relevant* relationships with industry (RWI), led by a chair with no *relevant* RWI. RWI is reviewed on all conference calls and updated as changes occur. Author RWI pertinent to this document is disclosed in the table below, and peer reviewer RWI is disclosed in Appendix 2. Additionally, to ensure complete transparency, authors' *comprehensive disclosure information*— including RWI not pertinent to this document—is available in the Supplemental Appendix. Disclosure information for the ACC Solution Set Oversight Committee is available online, as well as the ACC disclosure policy for document development.

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APPENDIX 2. REVIEWER RELATIONSHIPS WITH INDUSTRY AND OTHER ENTITIES (COMPREHENSIVE)— ACC HEALTH POLICY STATEMENT ON CARDIOVASCULAR CONSIDERATIONS FOR COVID-19 VACCINE PRIORITIZATION

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