# Rationale for integrating a COVID-19 case report form into cardiovascular research

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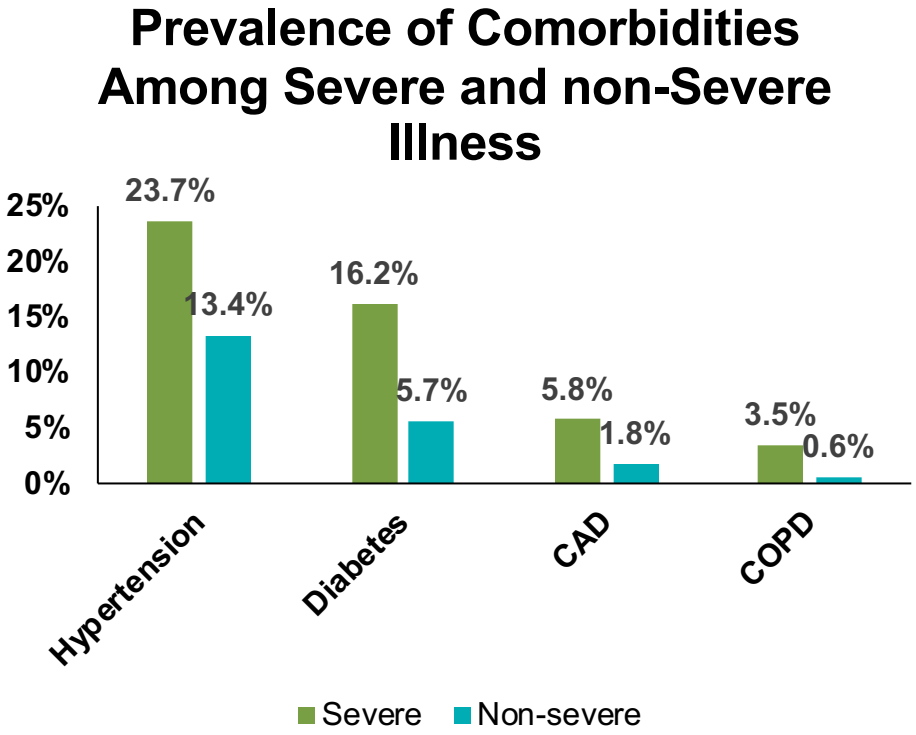
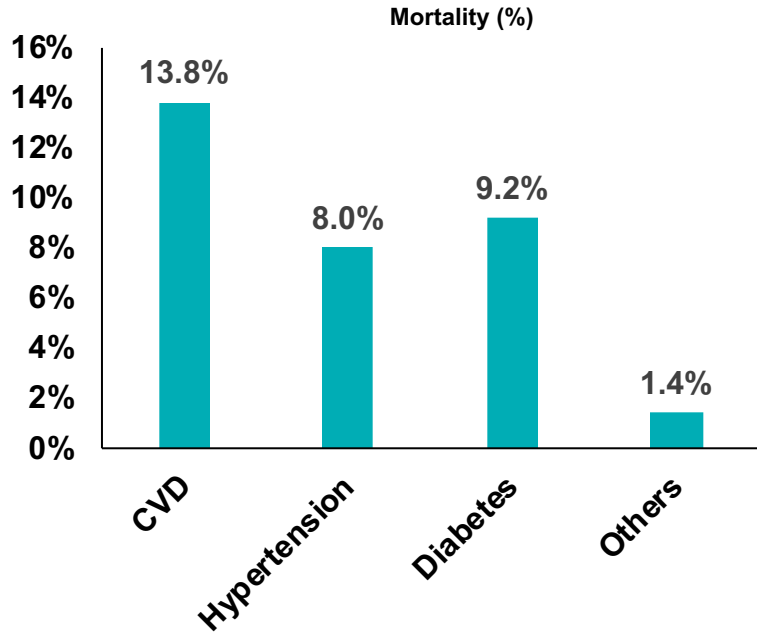
# Patients with Cardiometabolic Diseases Especially Vulnerable to COVID-19



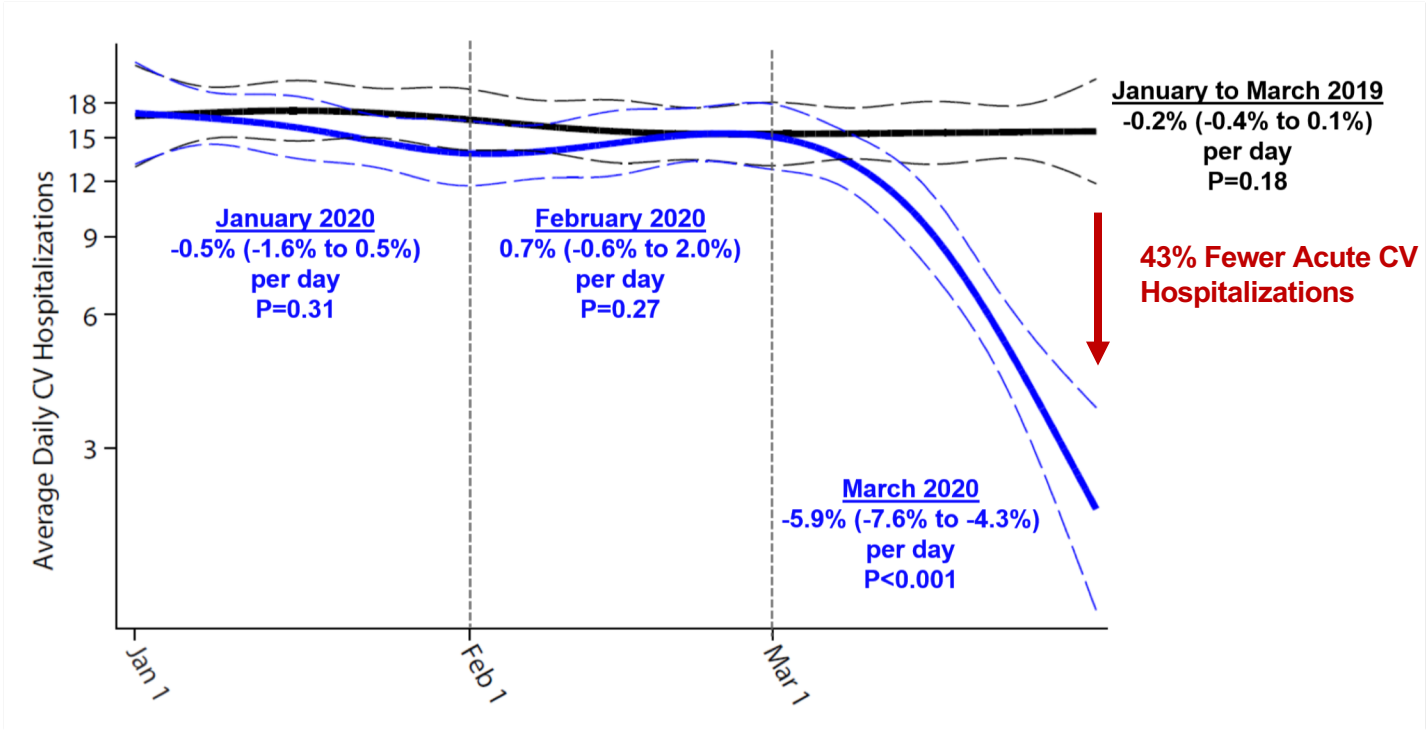




Guan et al. NEJM, 2020

# Cardiovascular Complications

- Venous or arterial thromboses
- Cardiac arrhythmias including atrial fibrillation, bradyarrhythmias, and VT/VF
- Cardiomyopathy
- Acute cardiac injury reflected by elevation in troponin
- Acute coronary syndrome
- Shock

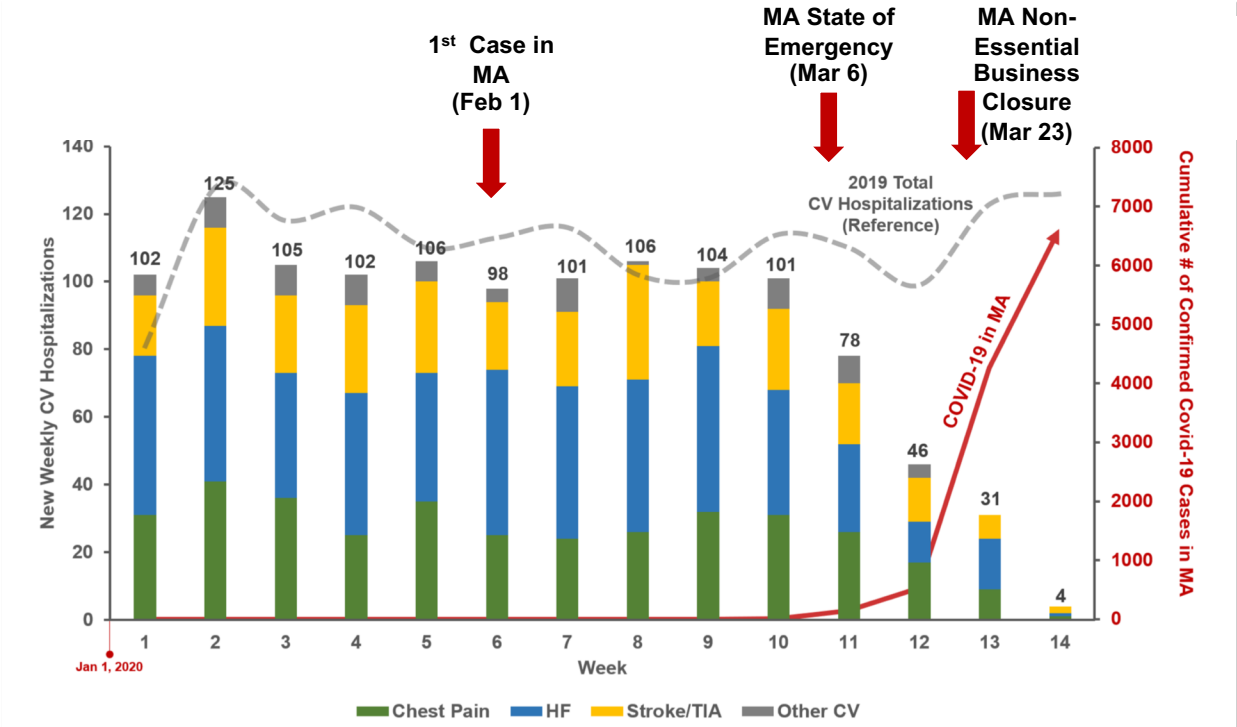
# Global Disruption of Acute CV Care: Mass General Brigham Experience




JACC JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

Bhatt AS, Moscone A, McElrath EE, Varshney AS, Claggett BL, Bhatt DL, Januzzi JL, Butler J, Adler DS, Solomon SD, Vaduganathan M. 2020 [Epub Ahead of Print]

# “Missing” Patients with Acute MI, Stroke, and HF During the Pandemic

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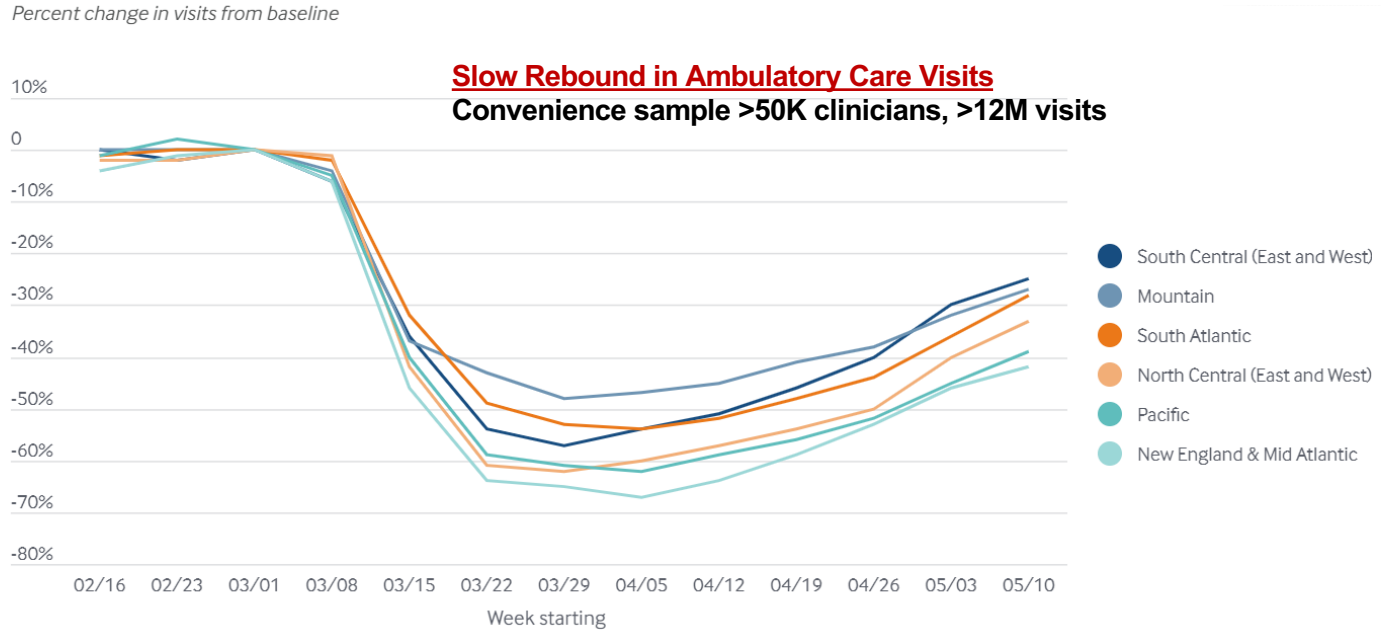
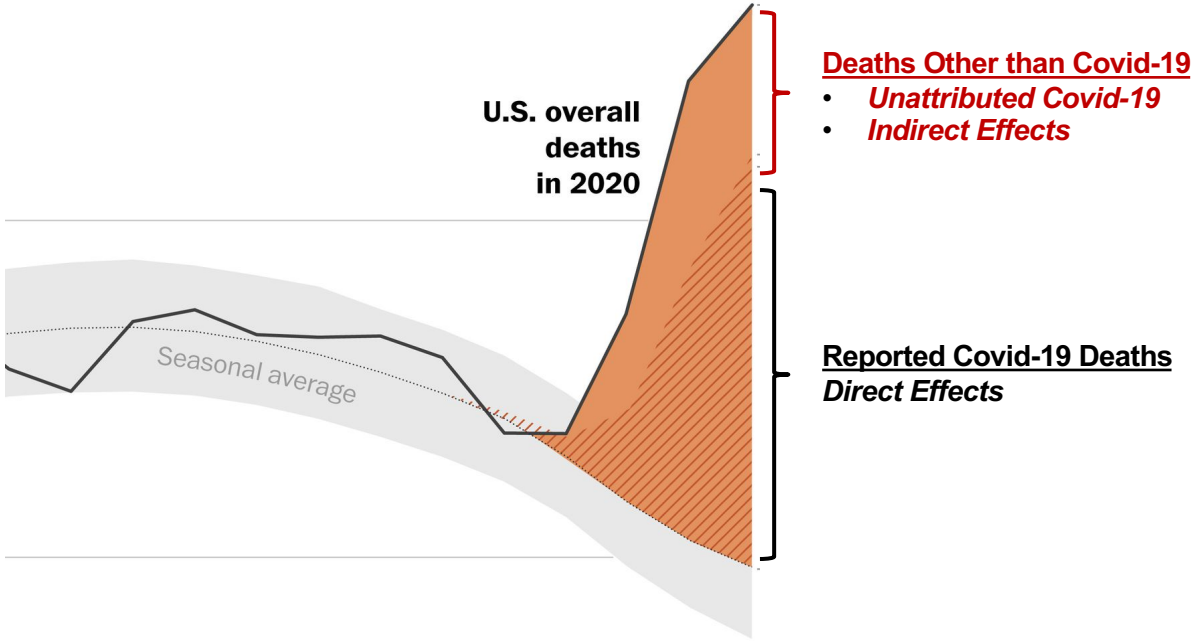
# Restructuring of Ambulatory Care of Chronic Medical Conditions Across US




Mehrotra A et al., Commonwealth Fund, May 19, 2020

# Excess Deaths Unexplained by Covid-19

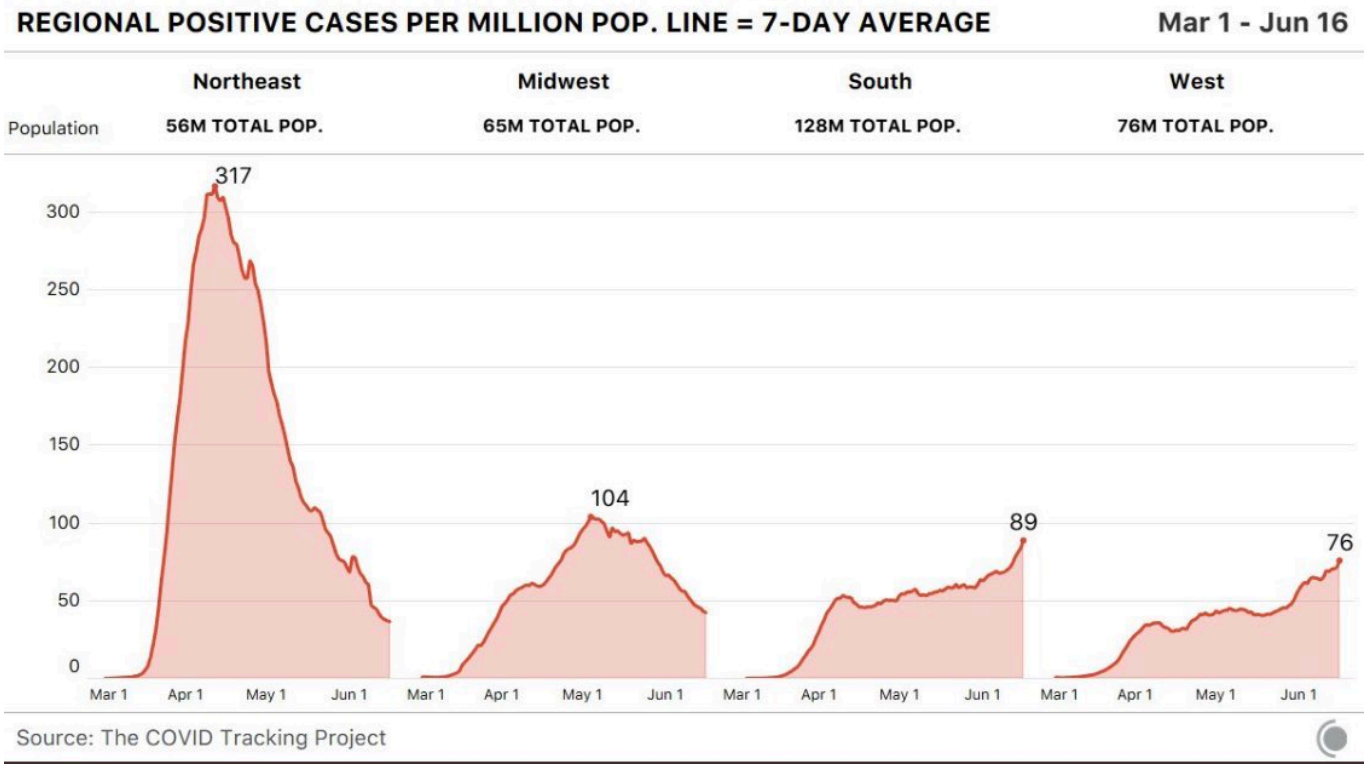



Brown E, Tran AB, Thebault R. Washington Post 2020

# COVID-19 is not going away!

- **COVID-19 disproportionately effects patients at high cardiovascular risk, including those enrolled in clinical trials by design.**
- **COVID-19 will impact trial participants who contract SARS-CoV2 but also those who are indirectly affected by the pandemic (see below)**
- **We expect COVID-19 to impact both clinical care and clinical trials for the next 12-18 months (and possibly longer) with likely multiple waves in various locations across the globe**

# Geographic “Waves” of the Covid-19 Pandemic



# Rationale for Uniform Data Collection

- **Individual trials will collect adverse events related to COVID-19, but capture may not be uniform and may miss patients who don't "present" with clear symptoms or who are not hospitalized.**

- **There is a growing appreciation for the highly variable COVID-19 presentations and important cardiac and vascular complications.**

- **The long-term sequelae of COVID-19 infection on patients with advanced cardiovascular disease is unknown.**

- **Pooled data across trials could inform future trial design.**

A pragmatic, uniform collection of COVID-19-related data across multiple trials is urgently needed.

# New FDA Guidance for Statistical Considerations in the Context of COVID-19 provides compelling rationale for Collection of COVID-19 related data

- **“Sponsors should also proactively plan to address the impact of COVID-19 on the ability to meet the trial objectives.”**

- **“Sponsors should conduct sensitivity analyses examining differences in baseline characteristics and post-baseline events (including endpoints and adverse events) between the originally enrolled participants [Pre-COVID] and the additional participants [Post-COVID] to understand the impact of the change in recruitment, including changes to recruitment locations and time of recruitment.”**

- **“It is important to capture specific information at the participant level, describing the context and/or reasons for post-baseline events as they relate to COVID-19, such as discontinuation of treatment, withdrawal from the trial, use of alternative or rescue treatments, missed endpoint ascertainment, and the use of alternative endpoint ascertainment methods”**

# Heart Failure Collaboratory COVID Data Collection Objectives

- **To provide a general framework for standardized data collection related to COVID-19 across cardiovascular clinical trials.**
- **To pool anonymized data in a registry of CV patients within clinical trials during the pandemic in order to**
    - Assess the effect of COVID-19 and the effect of the pandemic and alterations in care on patients with advanced cardiovascular disease
    - To inform the trials and regulatory community on the influence of the pandemic on ongoing trials
    - To assess factors that influence risk of COVID-19 disease in the HF population
    - To provide a mechanism to understand the long-term implications of COVID-19 infection on our high-risk cardiovascular patients
- **To encourage assessment of the true burden of COVID-19 disease through serologic testing in our clinical trials**

# Implementation

- **Development of a standardized case report form for collection of data from all participants (not just those who present with AEs related to COVID-19).**

- **Data collection could be done using trial-specific platforms and contributed to the registry.**

- **Data collected will be paired with a limited amount of previously collected data from trials (demographics, comorbidities, targeted medications).**

# COVID-19 Sample Data Collection Elements

- COVID-19 symptoms and testing.
- COVID-19 related endpoints.
- Influence of the pandemic on medication changes.
- Influence of the pandemic on healthcare access/interactions.
- Influence of the pandemic on patient behavior.
- Serological information (when available).

For all questions related to timing, the COVID-19 pandemic refers to on or after 1 DEC 2019.
Questions listed in red are considered optional.

## SECTION A: GENERAL INFORMATION

1. COVID-19 Data Collection ID: ___ ___ ___ ___ - ___ ___ ___ - ___

## SECTION B: COVID-LIKE ILLNESS SYMPTOMS AND EXPOSURE

Did you experience any of the following symptoms since our last contact?

| | COVID-19 Symptoms/Exposure | Present |
|---|---|---|
| 1. | Fevers or chills? | ☐ YES ☐ NO ☐ UNK<br>If yes, maximal temperature you remember: _____ °F or _____ °C |
| 2. | New or Worsening Cough<br>a. Dry<br>b. Productive | ☐ YES ☐ NO ☐ UNK<br>☐ YES ☐ NO ☐ UNK |
| 3. | If Yes to cough, indicate Frequency:<br>a. Occasional, several per hour or less<br>b. Constant (every 15 minutes or greater) | ☐ YES ☐ NO ☐ UNK<br>☐ YES ☐ NO ☐ UNK |
| 4. | New or worsened shortness of breath | ☐ YES ☐ NO ☐ UNK |
| 5. | Diarrhea | ☐ YES ☐ NO ☐ UNK |
| 6. | Altered or reduced sense of smell or taste | ☐ YES ☐ NO ☐ UNK |
| 7. | Muscle aches/Severe fatigue | ☐ YES ☐ NO ☐ UNK |
| 8.. | Chest pain or tightness | ☐ YES ☐ NO ☐ UNK |
| 9. | Sore throat | ☐ YES ☐ NO ☐ UNK |

## SECTION C: COVID-LIKE ILLNESS TESTING AND TREATMENT

| | Testing and Treatment | Present | DESCRIPTION |
|---|---|---|---|
| 1. | Have you been tested for COVID-19? (test with a swab in the nose) | ☐ YES ☐ NO ☐ UNK | If yes, which month: _____ |
| 2. | *If yes to #1*,Have you been told that you have tested positive for COVID-19? | ☐ YES ☐ NO ☐ UNK | |
| 3. | Have you been told that you might have had COVID-19/have symptoms suggestive of COVID-19? | ☐ YES ☐ NO ☐ UNK | |
| 4. | Have you been tested for prior COVID-19 exposure or infection (presence of antibodies in your blood)?" | ☐ YES ☐ NO ☐ UNK | If yes, which month: _____ |
| 5. | Have you been told that you have antibodies in your blood that suggest you were previously exposed COVID-19 infection? (test with a blood sample with a skin prick or needle) | ☐ YES ☐ NO ☐ UNK | |
| 6. | Did you get the "flu" or influenza shot/vaccine this season? | ☐ YES ☐ NO ☐ UNK | If yes, which month: _____ |

## SECTION D: MEDICATION USE DURING COVID-19 PANDEMIC

| | Medication Use | | |
|---|---|---|---|
| 1. | Are you currently prescribed an ACEI/ARB/ARNI? (list drug names here) *If no or unknown* to #1, skip to #3. | ☐ YES ☐ NO ☐ UNK | If yes, which one?<br>☐ ACEI (captopril, lisinopril, enalapril, fosinopril)<br>☐ ARB (valsartan, losartan, candesartan)<br>☐ ARNI (sacubitril/valsartan)<br>☐ Unknown |
| 2. | Did you stop taking your ACEI/ARB/ARNI at any time during COVID-19 pandemic? | ☐ YES ☐ NO ☐ UNK | If yes, why?<br>☐ Instructed by my doctor<br>☐ Self-discontinued<br>☐ Unknown/other |
| 3. | Are you currently/have you taken a NSAID (naproxen, ibuprofen, celecoxib) during the COVID-19 pandemic? *If no or unknown* to #3, skip to #5. | ☐ YES ☐ NO ☐ UNK | |

# What can sponsors do?

- Consider collection of participant level data in ongoing trials related to COVID-19 (from both participants with known disease and those without)

- Agree to pool common core data elements in a broad registry of patients enrolled in CV clinical trials (even beyond HF)

- Consider for serologic testing of trial participants to assess burden of COVID-19 disease within trial

# Potential Benefits

## To Individual Trials and Sponsors

- **Assessement of disease burden within the trial may inform analysis plans and interpretation of results (especially results that are potentially affected by the epidemic)**
- **Access to a broader COVID-19 related pooled dataset of patients with heart failure**

## To the Heart Failure Community

- **High quality data on the influence of COVID-19 on patients with advanced heart disease can be a resource to inform the HF community and the clinical trials community**
- **Ongoing trials have a unique opportunity to assess the relationship between COVID-19 disease and cardiovascular outcomes (though each individual trial will be underpowered)**

# Collective Opportunity

- COVID-19 and its direct effects are likely to persist and may have longstanding cardiopulmonary sequela.
- Concerns about a “second wave” or multiple waves and overlap with seasonal influenza.
- Opportunity to contribute broadly to our understanding of the effect of the pandemic on our patients and our clinical trials in a uniform, prospective way.

A unique collaborative effort that epitomizes the mission of the Heart Failure and Valve Collaboratories