



# **Studying the Natural History of COVID-19: Risk of Arterial and Venous Thrombotic Events in the Sentinel System**

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# Need for Real-World Evidence on COVID-19

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- **Numerous limitations of existing data:**
  - Bulk of evidence from case reports, series
  - Limited sample sizes from single centers
  - Inherent biases (selection, misclassification), lack of control of confounders
- **Sentinel offers unique opportunity for real-world evidence on COVID-19**
  - Epidemiology, natural history of COVID-19
  - Effects of chronic medications taken in ambulatory setting on course of COVID-19
  - Safety, effectiveness of COVID-19 therapies

# Sentinel COVID-19 Natural History Master Protocol

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- **Provides approaches to identify COVID-19 patients in the Sentinel System**
- **Delineates variables relevant to such analyses**
  - Feasibility of collection of these variables within Sentinel's Data Partners
  - Proposed code lists for variables
- **Considers potential limitations of methods, approaches to address**
  - Biases (selection, misclassification, protopathic)
  - Unmeasured confounding variables
  - Generalizability

# Reports of Abnormalities in Blood Coagulation

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- **Arterial, venous thrombotic events**
  - Arterial occlusion (acute MI, ischemic stroke), even at younger ages
  - Venous thromboembolism (DVT/PE, microthrombi on autopsy)
- **Coagulopathy**
  - ↑ D-dimer, fibrinogen levels
  - Disseminated intravascular coagulation

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**Assembled team, formulated Aims, applied methods from Master Protocol**

# Sentinel Coagulopathy Workgroup: Specific Aims

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- **Aim 1:** Determine 90-day incidence of arterial and venous thrombotic events (evaluated separately) with COVID-19 and risk of death within 90 days of an event.
  - Hypothesis: Events will occur within 90 days of COVID-19 diagnosis and may result in death.
- **Aim 2:** Evaluate patient characteristics present prior to COVID-19 diagnosis as risk factors for arterial and venous thrombotic events (evaluated separately).
  - Hypothesis: Characteristics that promote endothelial injury, stasis of circulation, and hypercoagulability will be risk factors for thrombosis.
- **Aim 3:** Compare 90-day risk of arterial and venous thrombotic events (evaluated separately) between health plan members with COVID-19 and those with influenza.
  - Hypothesis: Risk of thrombotic events will be higher with COVID-19 than influenza.

# Significance of Study Aims

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## Biological

- Gain insights into risk factors for thrombotic events with COVID-19
- Determine if risk of events is higher for COVID-19 vs. influenza

## Clinical

- Identify interventions to ↓ risk of thrombotic events with COVID-19
- Identify high-risk subgroups to inform decisions, enroll in future trials

## Public Health

- Modifying risk factors for thrombotic events could prevent their development and prolong survival

# Sentinel Coagulopathy Workgroup Activities to Date

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- **Developed study protocol**
- **Establishing collaborations with multiple Sentinel Data Partners**
  - Integrated delivery system, claims partners
  - Increase sample size, enhance generalizability, permits evaluation of lab data
  - Allows for limited chart review to confirm PPVs of ICD-10-based outcomes
- **Working with Reagan-Udall Foundation**
  - Promote parallel analyses, enhance scientific validity



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## Sentinel COVID-19 Coagulopathy Working Group

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