



Descriptive Assessment of Coagulopathy Among COVID-19 Patients: Feasibility Data Review

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Disclaimer

- These presentations reflect the views of the author and should not be construed to represent FDA's views or policies

Sentinel Coagulopathy Full Study – Specific Aims

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

Primary Outcomes for Aims 1-3: Thrombotic Events

Primary

Arterial Thrombosis

Acute myocardial infarction
Acute ischemic or embolic
stroke



Primary

Venous Thromboembolism

Acute upper/lower deep
venous thrombosis (DVT)
Acute pulmonary embolism
(PE)



**Primary or Secondary Hospital Discharge ICD-10-CM Diagnosis
(Mapped from ICD-9-CM Diagnoses Validated in Sentinel Data)**

Secondary Endpoints for Aims 1-3

1. Ambulatory, ED, or hospital discharge ICD-10-CM of arterial thrombosis (AMI or stroke) or venous thromboembolism (DVT or PE)

2a. **Arterial:** Meet primary outcome or have ambulatory, ED, or hospital discharge ICD-10-CM of angina, TIA, PAD, or amputation

2b. **Venous:** Meet primary outcome or have ambulatory, ED or hospital discharge ICD-10-CM of venous thrombosis of device, implant, or graft

3. Meet primary outcome or dispensed thrombolytic therapy and/or therapeutic anticoagulation therapy during follow-up

4. Intracranial, upper/lower GI tract, or retroperitoneal bleeding

5. Death (any cause)

Methods for Full Study: Study Design / Data Source

- **Design:** Retrospective cohort studies (Aims 1-3)
- **Data Source:** Sentinel System
 - Lab data: COVID-19, influenza, coagulation related labs
 - Thromboembolic events via outpatient and inpatient diagnoses
 - Pre-existing comorbidities, medication exposures at time of diagnosis

Feasibility data request

- To inform sample size calculations for full study
- To provide preliminary information for full study implementation
 - Focused on primary outcomes
- Coagulopathy workgroup provided table shells to be populated by partners
- Data partners used freshest data available to them
- Examined data by type of partner
 - 5 integrated delivery system (IDS)
 - 4 national insurer / claims data

Overview of feasibility data request

- Counts of arterial thrombosis & venous thromboembolic events among health plan members with COVID-19, Jan 20 - July 31, 2020
 - ICD-10 code (U07.1 or B97.29) **OR** molecular amplification test **OR** antigen test; any care setting
- Counts of arterial thrombosis & venous thromboembolic events among health plan members with influenza, October 1, 2018 - April 30, 2019
 - Influenza-specific ICD-10 diagnosis codes (J09-J11); any care setting
- Baseline characteristics of health plan members with COVID-19, Jan 20 - July 31, 2020 (optional; 183-day lookback; ICD-10 diagnosis codes)
- *Other criteria*: 183-days of medical and pharmacy coverage prior to index
- *Events*: Assessed separately; identified within 30 days of index in any care setting

Health plan members with COVID-19, by cohort entry criteria, Jan 20 - July 31, 2020

	Claims		IDS		Overall	
Identification criteria	N=230,023		N=26,547		N=256,570	
Diagnosis code (U07.1 or B97.29)	186,575	81%	6,671	25%	193,246	75%
Molecular amplification test	43,429	19%	7,728	29%	51,157	20%
Antigen test	19	<0.1%	606	2.3%	625	0.2%
Not reported*	0	-	11,542	43%	11,542	4.5%

IDS = integrated delivery system

*One site did not provide complete stratified data; full study will have complete data for this element

Health plan members with COVID-19, by cohort entry criteria, Jan 20 - July 31, 2020

	Claims		IDS		Overall	
Identification criteria	N=230,023		N=15,005		N=245,028	
Diagnosis code (U07.1 or B97.29)	186,575	81%	6,671	44%	193,246	79%
Molecular amplification test	43,429	19%	7,728	52%	51,157	21%
Antigen test	19	<0.1%	606	4%	625	0.3%

IDS = integrated delivery system

Care setting is among those sites that provided complete data for this element

Health plan members with COVID-19, by age and care setting, Jan 20 - July 31, 2020

Overall Total (n=256,570)		
<i>Age (years)</i>		
<20	16,635	6.5%
20-44	88,105	34.3%
45-54	41,607	16.2%
55-64	41,079	16.0%
65-74	29,067	11.3%
75-84	17,861	7.0%
≥85	10,674	4.2%
Not reported*	11,542	4.5%

<i>Location of index lab or diagnosis code</i>		
Ambulatory/outpatient	160,008	62%
Hospital	28,914	11%
ED	24,960	10%
SNF or long-term care	791	0.3%
Unknown / not reported*	41,897	16%

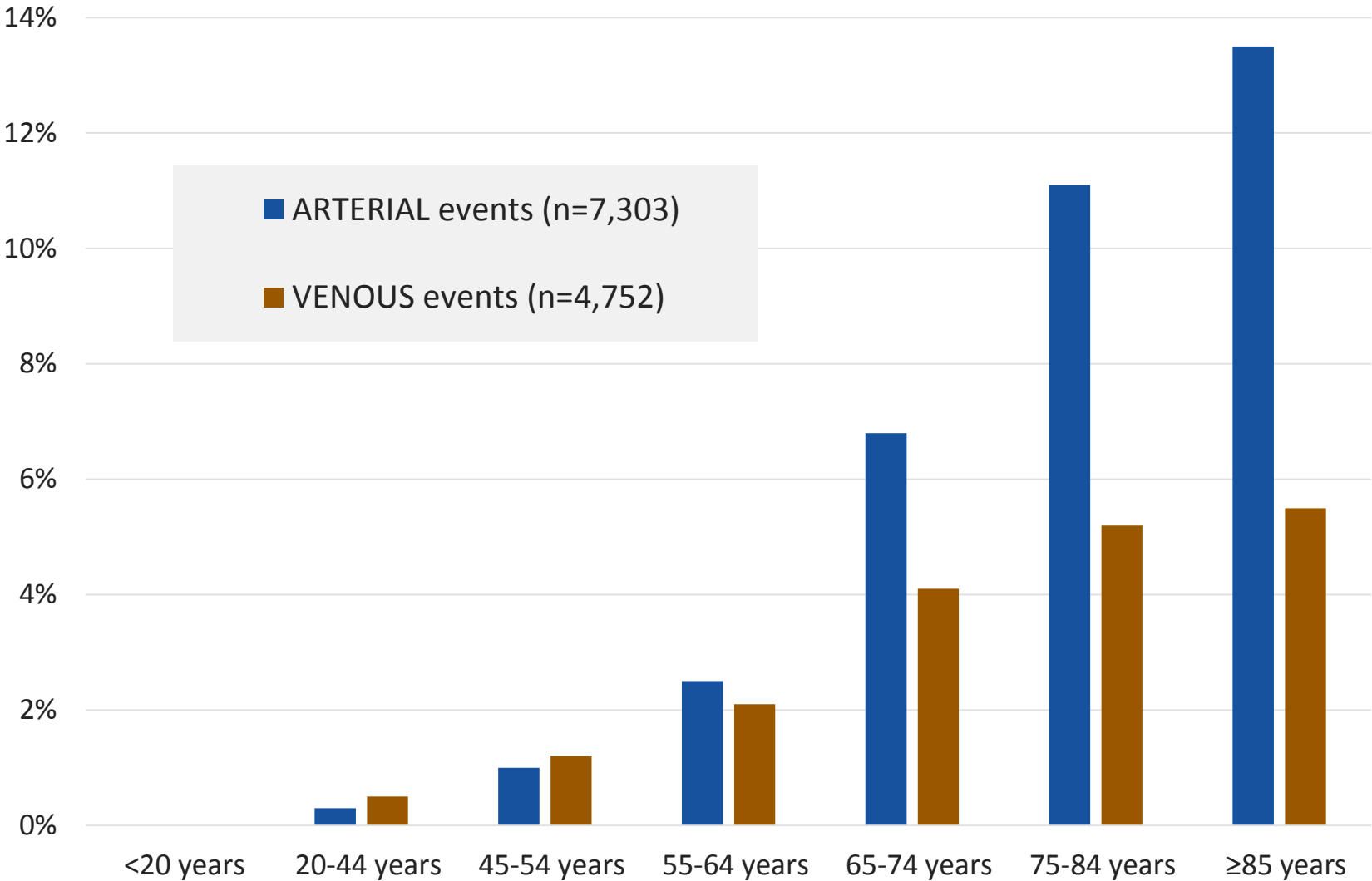
*Full study will have complete data for these elements

Counts of arterial thrombosis and venous thromboembolic events among health plan members with COVID-19, Jan 20 - July 31, 2020

Total COVID	Claims (n=230,023)		IDS (n=26,547)		Overall (n=256,570)	
Arterial events						
	6,844	3.0%	459	1.7%	7,303	2.8%
Venous events						
	4,247	1.8%	505	1.9%	4,752	1.9%

Age differences by Data Partner and partner type likely partly explain the differences in frequency of arterial events

Health plan members with COVID-19 and event of interest, by age, Jan 20 - July 31, 2020



N <10 for those under 20 yrs for both events types

Distribution of care setting of thromboembolic events among health plan members with COVID-19, Jan 20 - July 31, 2020

	Arterial events		Venous events	
	N=7,825		N=5,128	
<i>Location of event</i>				
Ambulatory/outpatient	2,470	31.6%	1,930	37.6%
Hospital	3,787	48.4%	2,300	44.9%
ED	1,468	18.8%	794	15.5%
SNF or Long-term care	58	0.7%	18	0.4%
Other or not reported	42	0.5%	86	1.7%

Some sites counted >1 event / person and reported all locations

Baseline characteristics of health plan members with COVID-19, Jan 20 - July 31, 2020

- **N=150,997**
- 2 claims, 2 IDS partners provided data
- Conditions assessed in 183 days prior to index via ICD-10 diagnosis codes

Hypertension	48,438	32.1%
Cardiovascular disease	55,157	36.5%
Diabetes mellitus	24,831	16.4%
Obesity	23,748	15.7%
Chronic kidney disease	17,124	11.3%
Smoking history	12,395	8.2%
Chronic obstructive pulmonary disease	11,706	7.8%
Cancer	10,052	6.7%
Asthma	9,930	6.6%
Heart failure	9,600	6.4%
Neurological disease	8,791	5.8%
Atrial fibrillation	7,563	5.0%
Chronic liver disease	5,442	3.6%
Cerebrovascular disease	6,636	4.4%
Inherited (primary) thrombophilia	4,250	2.8%
Peripheral arterial disease	5,048	3.3%
Rheumatologic disease	3,982	2.6%
Ischemic stroke	2,835	1.9%
Pregnancy (current)	2,436	1.6%
Venous thromboembolism	2,247	1.5%
Myocardial infarction	1,976	1.3%
Alcohol history	1,919	1.3%
Antiphospholipid antibody syndrome	79	0.1%

Health plan members with influenza, October 1, 2018 - April 30, 2019

	Claims	IDS	Total
Number	791,772	33,852	825,624

<i>Age (years)</i>		
<20	372,098	45.1%
20-44	211,439	25.6%
45-54	81,900	9.9%
55-64	70,556	8.5%
65-74	50,927	6.2%
75-84	27,737	3.4%
≥85	10,967	1.3%

<i>Location of index diagnosis among total</i>		
Ambulatory/outpatient	750,944	91.0%
Hospital	21,000	2.5%
ED	52,423	6.3%
SNF or Long-term care	40	0.0%
Other or unknown	1,217	0.1%

Counts of arterial thrombosis and venous thromboembolic events among health plan members with influenza, October 1, 2018 - April 30, 2019

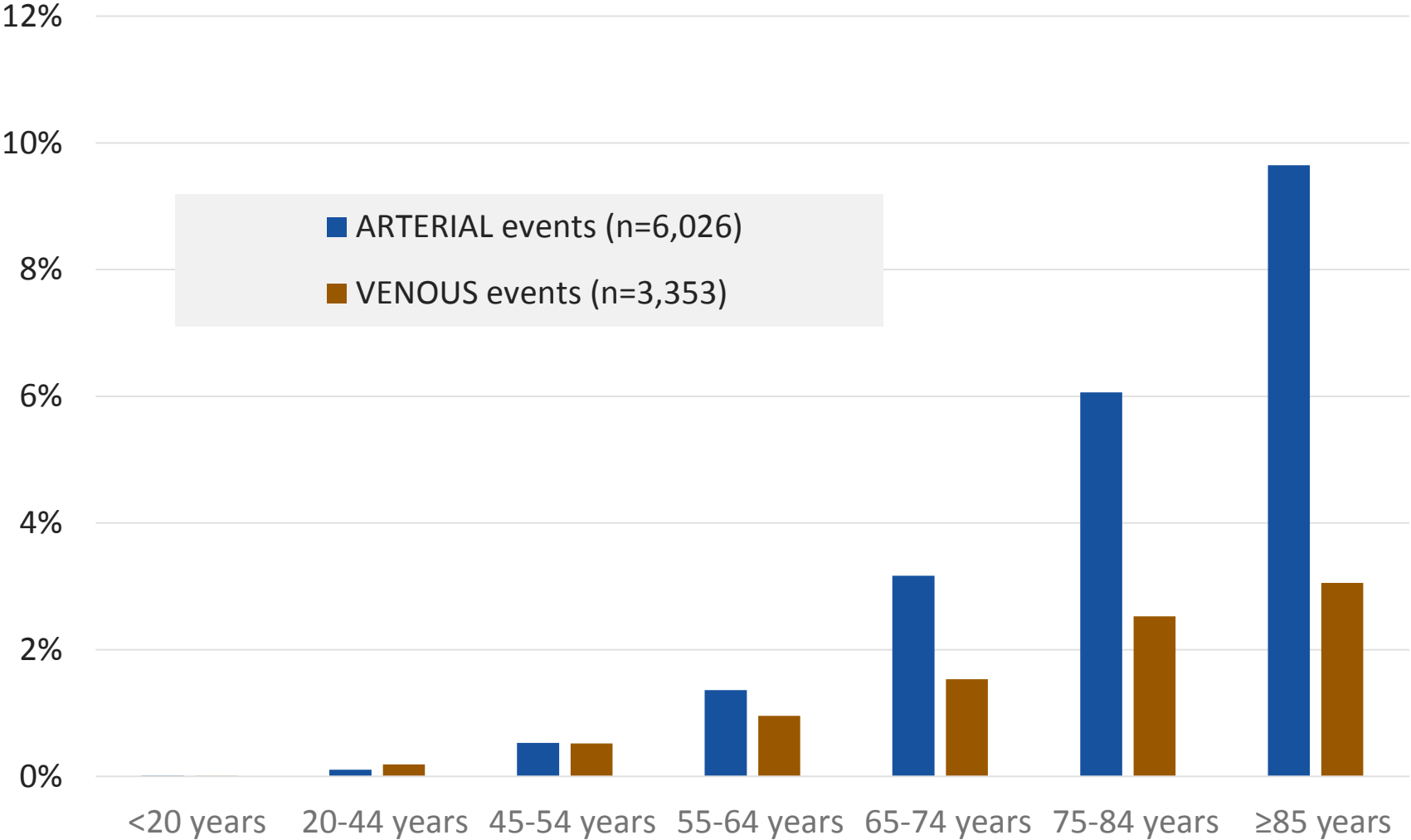
Total influenza	Claims (n=791,772)		IDS (n=33,852)		Overall (n=825,624)	
Arterial events						
	5,744	0.7%	282	0.8%	6,026	0.7%
Venous events						
	3,195	0.4%	158	0.5%	3,353	0.4%

Distribution of care setting of thromboembolic events among health plan members with influenza, October 1, 2018 - April 30, 2019

	Arterial events		Venous events	
	N=6,506		N=3,653	
<i>Location of event</i>				
Ambulatory/outpatient	2,590	39.8%	1,982	54.3%
Hospital	2,768	42.5%	1,122	30.7%
ED	1,116	17.2%	461	12.6%
SNF, long-term care, other	32	0.4%	88	2.4%

Some sites counted >1 event / person and reported all locations

Health plan members with influenza and event of interest, by age, Oct 1, 2018 - April 30, 2019



Conclusions from feasibility data

- Many Sentinel Data Partners able to quickly identify cohorts and events of interest
- Many more COVID-19 patients identified with diagnosis code than lab, with variation by Partner type
- As we defined it, the COVID-19 cohort is relatively young
- The proportion of COVID-19 and influenza patients with an event is relatively low, with more events among older people
 - There are more arterial events than venous events in this preliminary assessment
- For the full study, anticipating including multiple IDS partners and a claims partner:
 - Improve sample size
 - Increase generalizability
 - Enable access to lab data and other data elements more readily available with IDS partners

Thank you to the Data Partners

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Thank You

ICD-10 diagnosis codes used to identify influenza cohort

J09.X1	Influenza due to identified novel influenza A virus with pneumonia
J09.X2	Influenza due to identified novel influenza A virus with other respiratory manifestations
J09.X3	Influenza due to identified novel influenza A virus with gastrointestinal manifestations
J09.X9	Influenza due to identified novel influenza A virus with other manifestations
J10.00	Influenza due to other identified influenza virus with unspecified type of pneumonia
J10.01	Influenza due to other identified influenza virus with the same other identified influenza virus pneumonia
J10.08	Influenza due to other identified influenza virus with other specified pneumonia
J10.1	Influenza due to other identified influenza virus with other respiratory manifestations
J10.2	Influenza due to other identified influenza virus with gastrointestinal manifestations
J10.81	Influenza due to other identified influenza virus with encephalopathy
J10.82	Influenza due to other identified influenza virus with myocarditis
J10.83	Influenza due to other identified influenza virus with otitis media
J10.89	Influenza due to other identified influenza virus with other manifestations
J11.00	Influenza due to unidentified influenza virus with unspecified type of pneumonia
J11.08	Influenza due to unidentified influenza virus with specified pneumonia
J11.1	Influenza due to unidentified influenza virus with other respiratory manifestations
J11.2	Influenza due to unidentified influenza virus with gastrointestinal manifestations
J11.81	Influenza due to unidentified influenza virus with encephalopathy
J11.82	Influenza due to unidentified influenza virus with myocarditis
J11.83	Influenza due to unidentified influenza virus with otitis media
J11.89	Influenza due to unidentified influenza virus with other manifestations