Validation of claims-based algorithms to identify hospitalized COVID-19 events within the FDA Sentinel System

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- The views expressed in this presentation are those of the presenter and do not necessarily reflect those of the FDA.

Background

- Claims databases are a rich resource of population-based information, but often lack laboratory results, the gold standard for COVID-19 diagnosis.
- There was no specific code for COVID-19 until April 1, 2020, when ICD-10-CM U07.1 was released.
- While coding guidelines were updated, diagnostic test availability and guidance evolved as well.

Objective: Determine the ICD-10-CM code(s) that defines the most valid and complete cohort of patients hospitalized with COVID-19

Methods: Data

FDA Sentinel System Data Partners

- Six data partners participated:
  - Two national claims-based insurers
  - Four integrated delivery systems (IDS)
    - Provide continuum of health care services and have associated health plan

- Selection criteria:
  - Availability of laboratory result data
  - Availability of adjudicated and unadjudicated claims

Methods: Algorithms Evaluated

Five diagnosis code-based algorithms

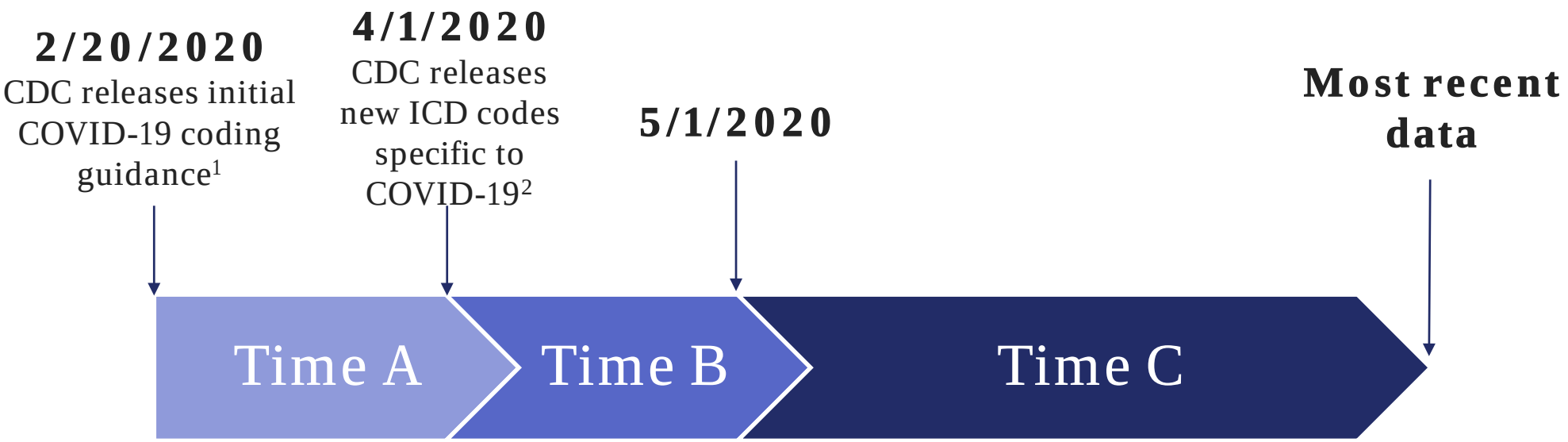
	Algorithm 1	Algorithm 2	Algorithm 3	Algorithm 4	Algorithm 5
U07.1 *COVID-19*	■	■	■	■	■
B97.29 *Other coronavirus as the cause of diseases classified elsewhere*		■	■	■	■
B34.2 *Coronavirus infection, unspecified*			■	■	
J12.81 *Pneumonia due to SARS-associated coronavirus*				■	
B97.21 *SARS-associated coronavirus as the cause of diseases classified elsewhere*				■	
Pneumonia					■
J80 *Acute Respiratory Distress Syndrome*					■

Methods: Algorithms Evaluated

Five diagnosis code-based algorithms

	Algorithm 1	Algorithm 2	Algorithm 3	Algorithm 4	Algorithm 5
U07.1 *COVID-19*		OR	OR	OR	OR
B97.29 *Other coronavirus as the cause of diseases classified elsewhere*			OR	OR	
B34.2 *Coronavirus infection, unspecified*				OR	
J12.81 *Pneumonia due to SARS-associated coronavirus*				OR	AND
B97.21 *SARS-associated coronavirus as the cause of diseases classified elsewhere*					
Pneumonia					OR
J80 *Acute Respiratory Distress Syndrome*					

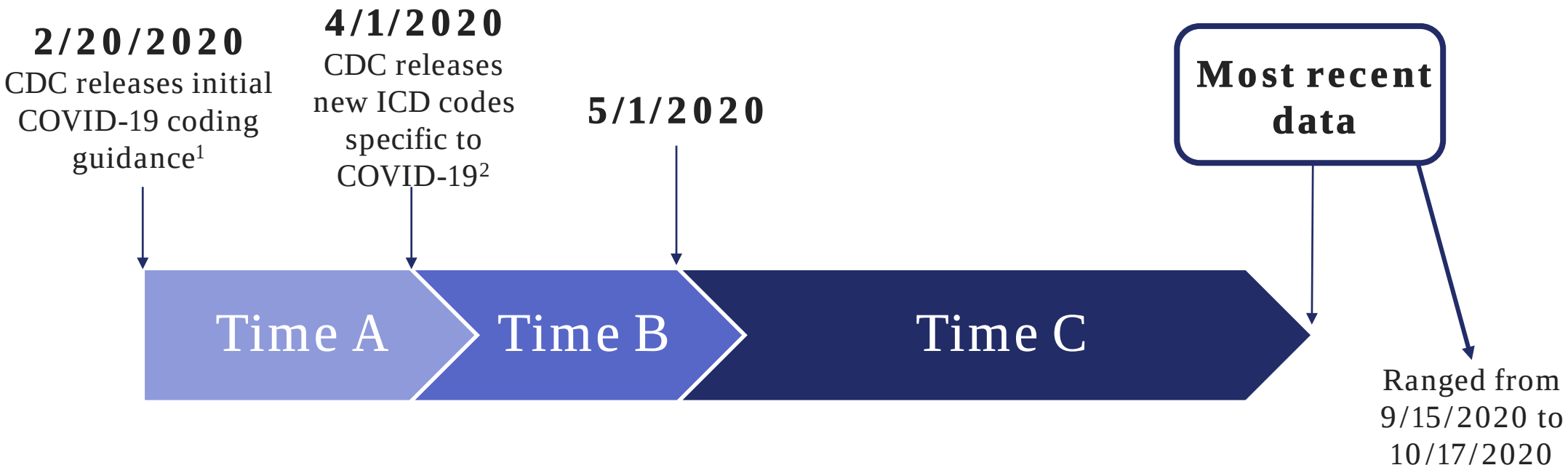
Methods: Study Design



1. ICD-10-CM Official Coding Guidelines - Supplement. Coding encounters related to COVID-19 Coronavirus Outbreak, February 20, 2020 – March 31, 2020. Accessed November 20, 2020. https://www.cdc.gov/nchs/data/icd/ICD-10-CM-Official-Coding-Gudance-Interim-Advice-coronavirus-feb-20-2020.pdf

2. ICD-10-CM Official Coding and Reporting Guidelines, April 1, 2020 through September 30, 2020. Accessed November 20, 2020. https://www.cdc.gov/nchs/data/icd/COVID-19-guidelines-final.pdf

Methods: Study Design



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Methods: Cohort Identification

Algorithm-based cohorts:

- Identify patients with algorithm-defining code(s) during a single inpatient stay
- Classify algorithm-identified patients according to observed COVID-19 nucleic acid amplification (NAA) lab results within ±14 days of inpatient admission date:
  - **Lab-positive**: Any positive NAA test
  - **Lab-negative**: All negative NAA test(s)
  - **NAA test performed, no result to-date**
  - **No NAA test observed**

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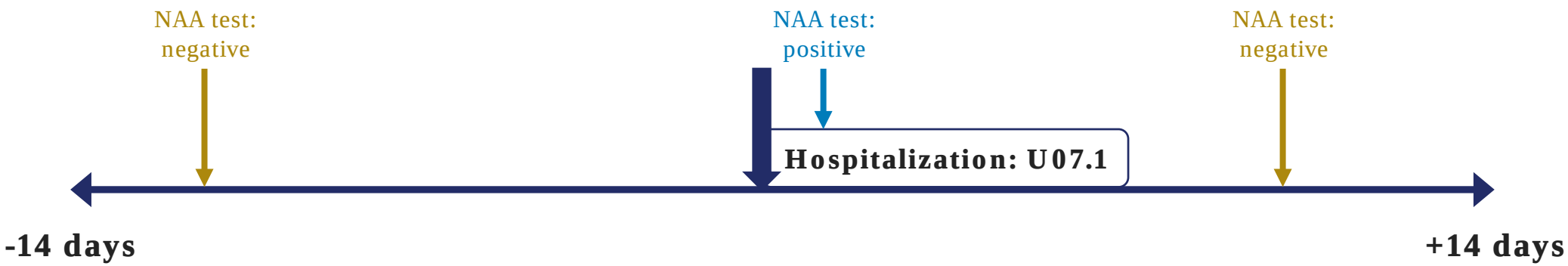

Methods: Cohort Identification

Patients identified via Algorithm 1			
Lab (+) patients	Lab (-) patients	Lab performed, results unknown	Patients with no lab
A	***B***	***C***	***D***

Methods: Statistical Analysis

Patients identified via Algorithm 1			
Lab (+) patients	Lab (-) patients	Lab performed, results unknown	Patients with no lab
A	***B***	***C***	***D***

$$\text{Positive Predictive Value} = \frac{A}{A+B}$$

Methods: Cohort Identification

Lab-based cohorts:

- Identify patients with COVID-19 nucleic acid amplification (NAA) test within ±14 days of **any** inpatient admission (including non-COVID-19 related hospitalizations)
- Classify patients according to NAA result:
  - **Lab-positive**: Any positive NAA test
  - **Lab-negative**: All negative NAA test(s)

Methods: Cohort Identification

Lab-based cohorts:

- Identify patients with COVID-19 nucleic acid amplification (NAA) test within ±14 days of **any** inpatient admission (including non-COVID-19 related hospitalizations)
- Classify patients according to NAA result:
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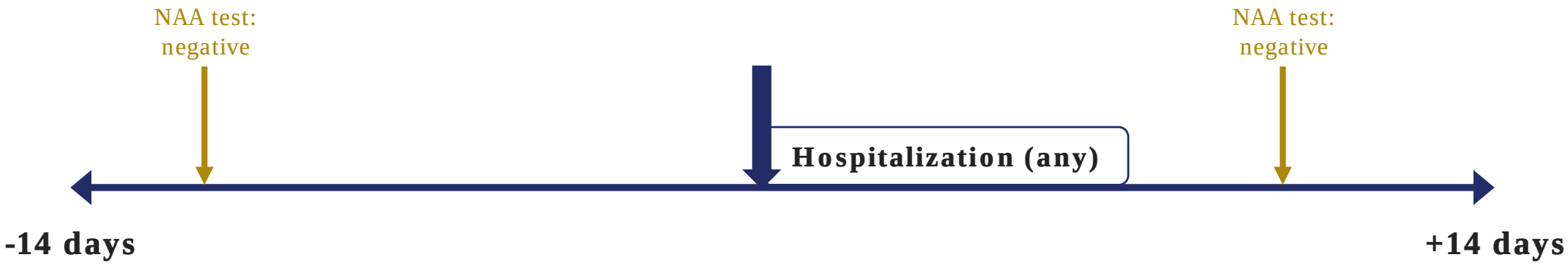

Methods: Cohort Identification

Patients identified via Algorithm 1				Patients with ≥1 NAA test ±14 days of hospitalization	
Lab (+) patients	Lab (-) patients	Lab performed, results unknown	Patients with no lab	Lab (+) patients	Lab (-) patients
A	***B***	***C***	***D***	***X***	***Y***

Methods: Statistical Analysis

Patients identified via Algorithm 1				Patients with ≥1 NAA test ±14 days of hospitalization	
Lab (+) patients	Lab (-) patients	Lab performed, results unknown	Patients with no lab	Lab (+) patients	Lab (-) patients
A	***B***	***C***	***D***	***X***	***Y***

$$\text{Sensitivity} = \frac{A}{X}$$

Methods: Statistical Analysis

Counts, PPV calculations, and sensitivity calculations stratified by:

Time Period

x

- Demographics:
  - Sex
  - Age category
  - Race
  - Ethnicity
- Symptoms:
  - Pneumonia
  - Bronchitis
  - Respiratory infection
  - ARDS
  - Sepsis
  - Cough
  - Shortness of breath
  - Fever

Results

Algorithm 1: U07.1
Algorithm 2: U07.1 or B97.29
Algorithm 3: U07.1 or B97.29 or B34.2
Algorithm 4: U07.1 or B97.29 or B34.2 or J12.81 or B97.21
Algorithm 5: [U07.1 or B97.29] and [pneumonia or ARDS]

Patient counts across algorithms and over time

	Algorithm 1	Algorithm 2	Algorithm 3	Algorithm 4	Algorithm 5
Time A (2/20 - 3/31)	3,644	5,997	6,354	6,474	5,282
Time B (4/1 - 4/30)	12,815	12,945	13,081	13,153	10,389
Time C (5/1 - current)	27,238	27,424	27,588	27,666	19,135
Total	**43,697**	**46,366**	**47,023**	**47,293**	**34,806**

Algorithm 1 (U07.1 alone) captures almost as many patients as the broader algorithms.

Results: Cohort demographics

Algorithm 1: U07.1
Algorithm 2: U07.1 or B97.29
Algorithm 3: U07.1 or B97.29 or B34.2
Algorithm 4: U07.1 or B97.29 or B34.2 or J12.81 or B97.21
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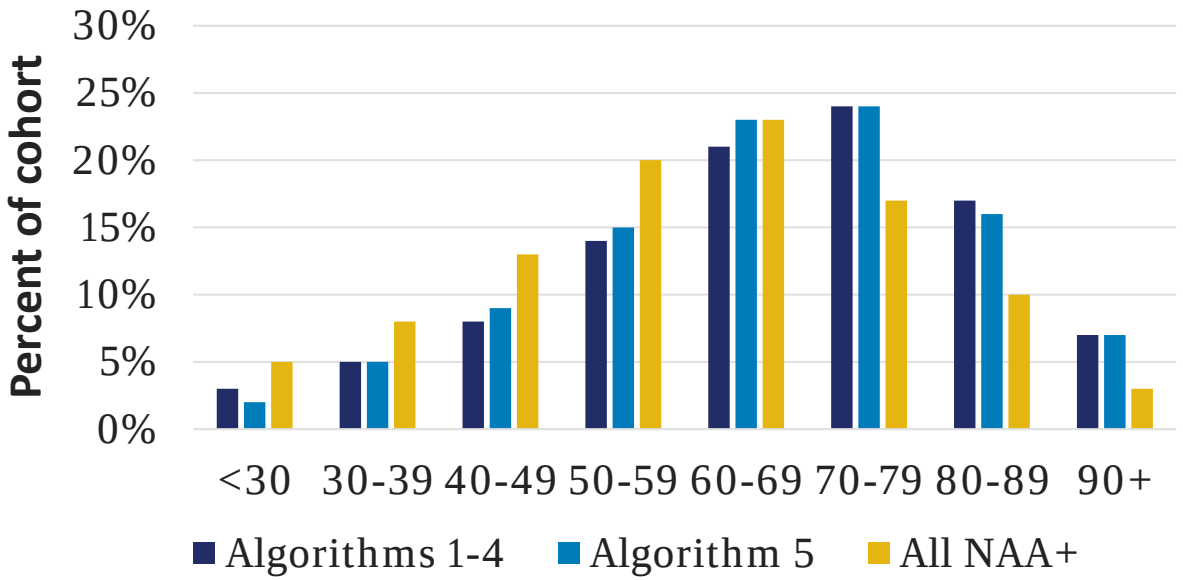
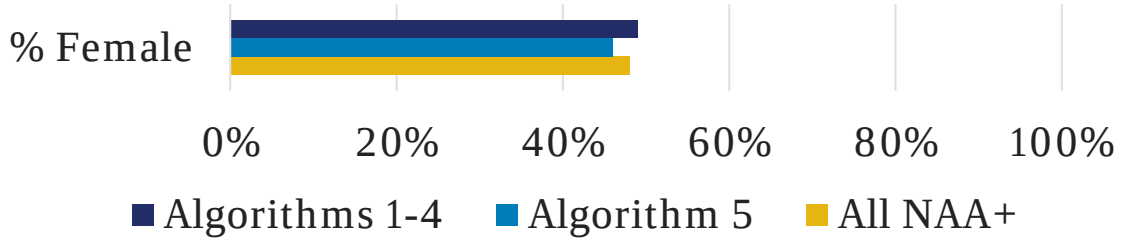
Age distribution



Diagnosis code-based cohorts are slightly older than **lab-based cohort**

Sex distribution



Results: Cohort clinical characteristics

Algorithm 1: U07.1
Algorithm 2: U07.1 or B97.29
Algorithm 3: U07.1 or B97.29 or B34.2
Algorithm 4: U07.1 or B97.29 or B34.2 or J12.81 or B97.21
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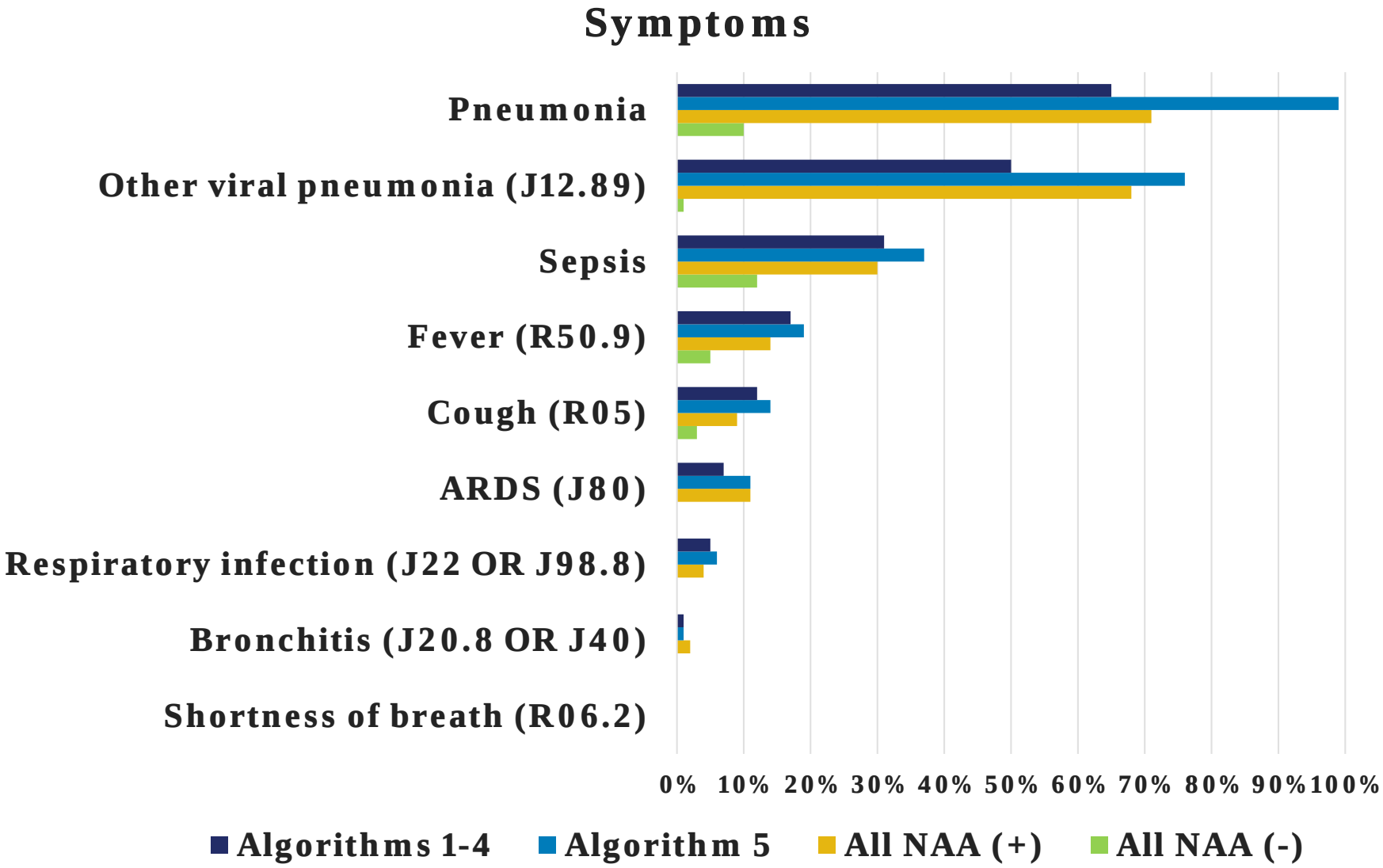


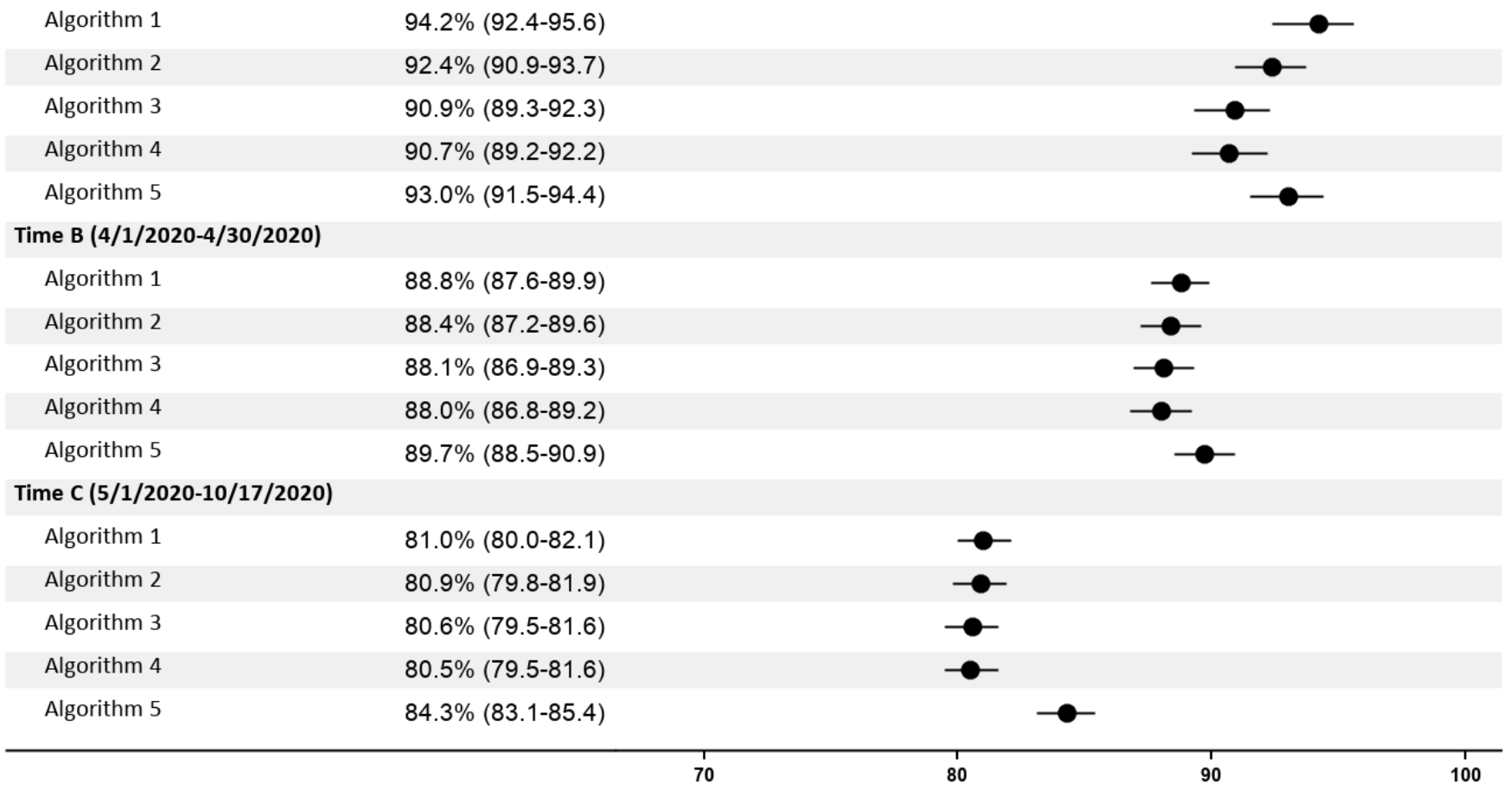
Algorithm-based cohorts (1-4) and lab-based cohort have similar symptoms

Severe COVID-19 cohort (algorithm 5) has a slightly higher prevalence of sepsis, fever, and cough

Results: PPV

Algorithm 1: U07.1
Algorithm 2: U07.1 or B97.29
Algorithm 3: U07.1 or B97.29 or B34.2
Algorithm 4: U07.1 or B97.29 or B34.2 or J12.81 or B97.21
Algorithm 5: [U07.1 or B97.29] and [pneumonia or ARDS]

Results by Time Period	Positive Predictive Value (95% CI)
Time A (2/2/2020-3/31/2020)	
Algorithm 1	94.2% (92.4-95.6)
Algorithm 2	92.4% (90.9-93.7)
Algorithm 3	90.9% (89.3-92.3)
Algorithm 4	90.7% (89.2-92.2)
Algorithm 5	93.0% (91.5-94.4)
Time B (4/1/2020-4/30/2020)	
Algorithm 1	88.8% (87.6-89.9)
Algorithm 2	88.4% (87.2-89.6)
Algorithm 3	88.1% (86.9-89.3)
Algorithm 4	88.0% (86.8-89.2)
Algorithm 5	89.7% (88.5-90.9)
Time C (5/1/2020-10/17/2020)	
Algorithm 1	81.0% (80.0-82.1)
Algorithm 2	80.9% (79.8-81.9)
Algorithm 3	80.6% (79.5-81.6)
Algorithm 4	80.5% (79.5-81.6)
Algorithm 5	84.3% (83.1-85.4)



Aggregated across all data partners, PPV decreases from ~91% in Time A to ~81% in Time C

Results: PPV by data source

Algorithm 1: U07.1
Algorithm 2: U07.1 or B97.29
Algorithm 3: U07.1 or B97.29 or B34.2
Algorithm 4: U07.1 or B97.29 or B34.2 or J12.81 or B97.21
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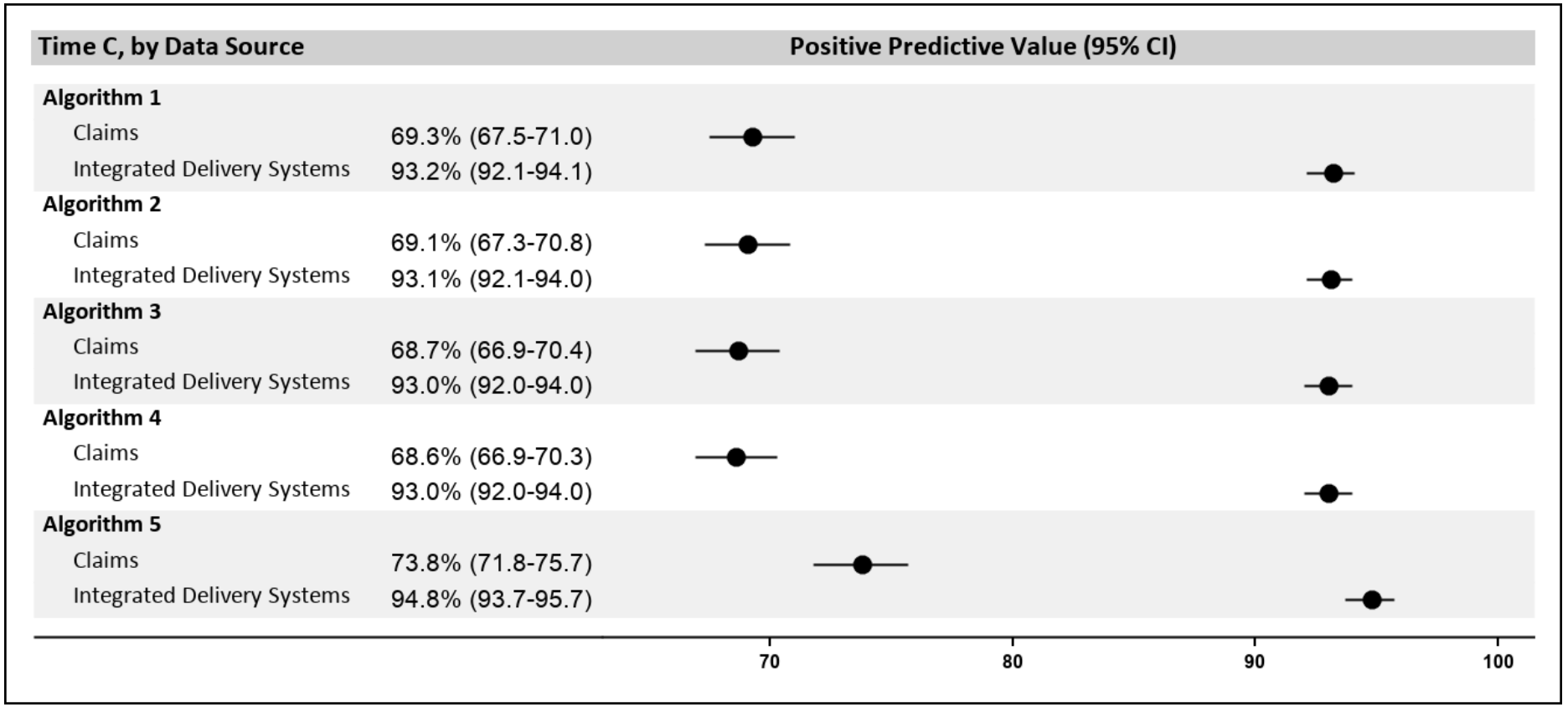

Overall PPV of 81% in Time C actually reflects:

- **69% PPV among claims data partners**
- **93% PPV among integrated delivery systems**

Results: Sensitivity

Algorithm 1: U07.1
Algorithm 2: U07.1 or B97.29
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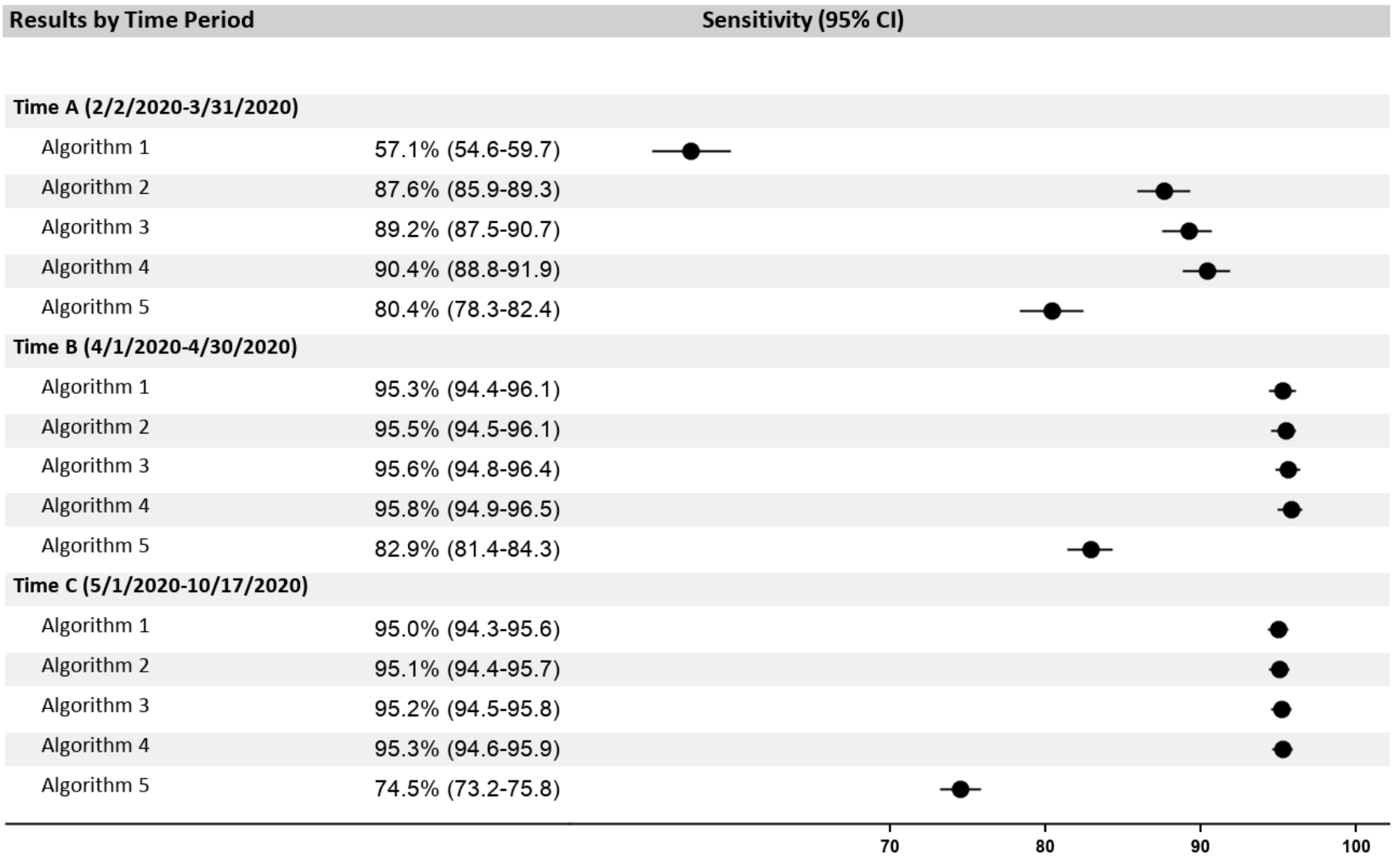
Algorithm 5: [U07.1 or B97.29] and [pneumonia or ARDS]

Results by Time Period	Sensitivity (95% CI)
Time A (2/2/2020-3/31/2020)	
Algorithm 1	57.1% (54.6-59.7)
Algorithm 2	87.6% (85.9-89.3)
Algorithm 3	89.2% (87.5-90.7)
Algorithm 4	90.4% (88.8-91.9)
Algorithm 5	80.4% (78.3-82.4)
Time B (4/1/2020-4/30/2020)	
Algorithm 1	95.3% (94.4-96.1)
Algorithm 2	95.5% (94.5-96.1)
Algorithm 3	95.6% (94.8-96.4)
Algorithm 4	95.8% (94.9-96.5)
Algorithm 5	82.9% (81.4-84.3)
Time C (5/1/2020-10/17/2020)	
Algorithm 1	95.0% (94.3-95.6)
Algorithm 2	95.1% (94.4-95.7)
Algorithm 3	95.2% (94.5-95.8)
Algorithm 4	95.3% (94.6-95.9)
Algorithm 5	74.5% (73.2-75.8)



Time A:

- Lower sensitivity
- U07.1 did not yet exist

Times B & C:

Algorithms 1-4:

- Sensitivity consistent across algorithms
- Sensitivity stable at 95%

Algorithm 5:

- Sensitivity substantially lower than for other algorithms.
- Declines over time

Results: Sensitivity by data source

Algorithm 1: U07.1
Algorithm 2: U07.1 or B97.29
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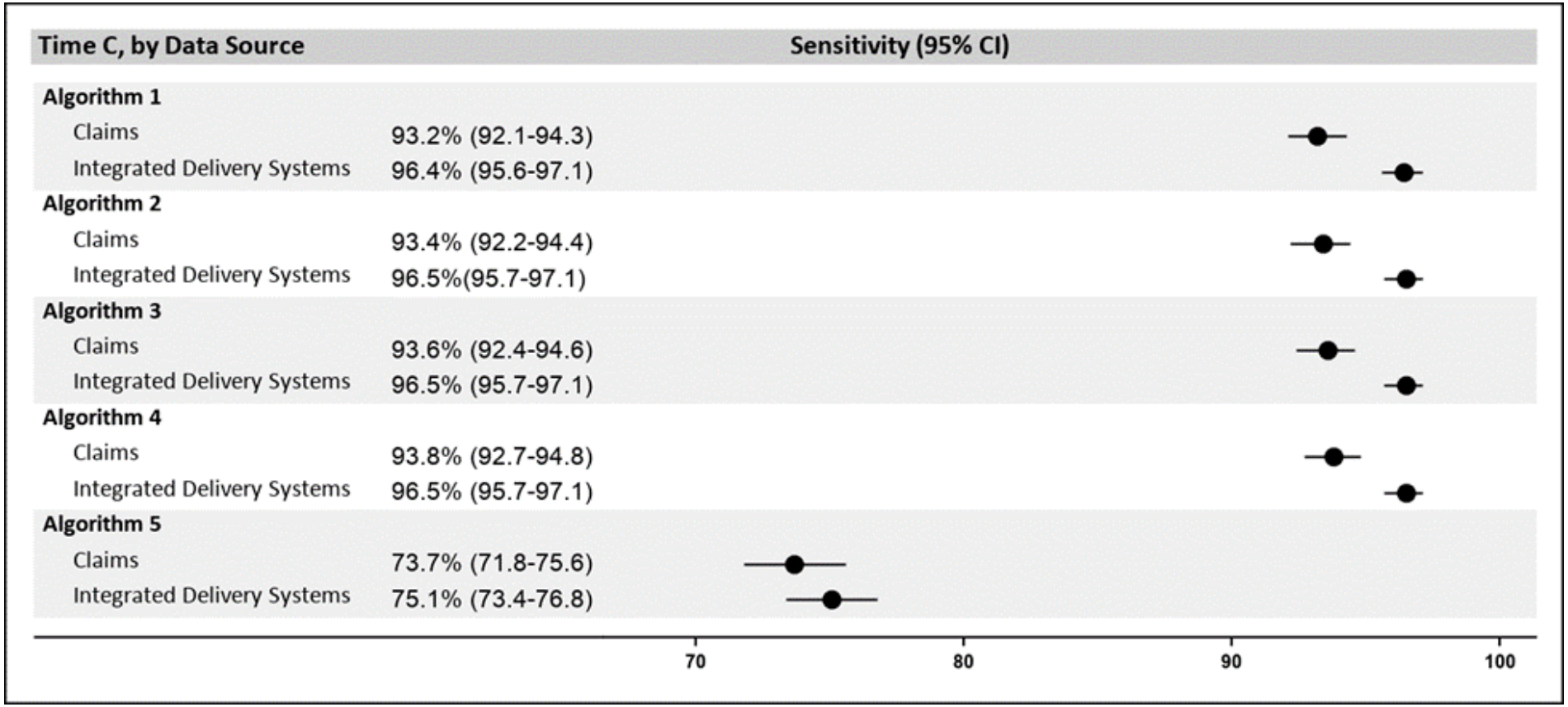
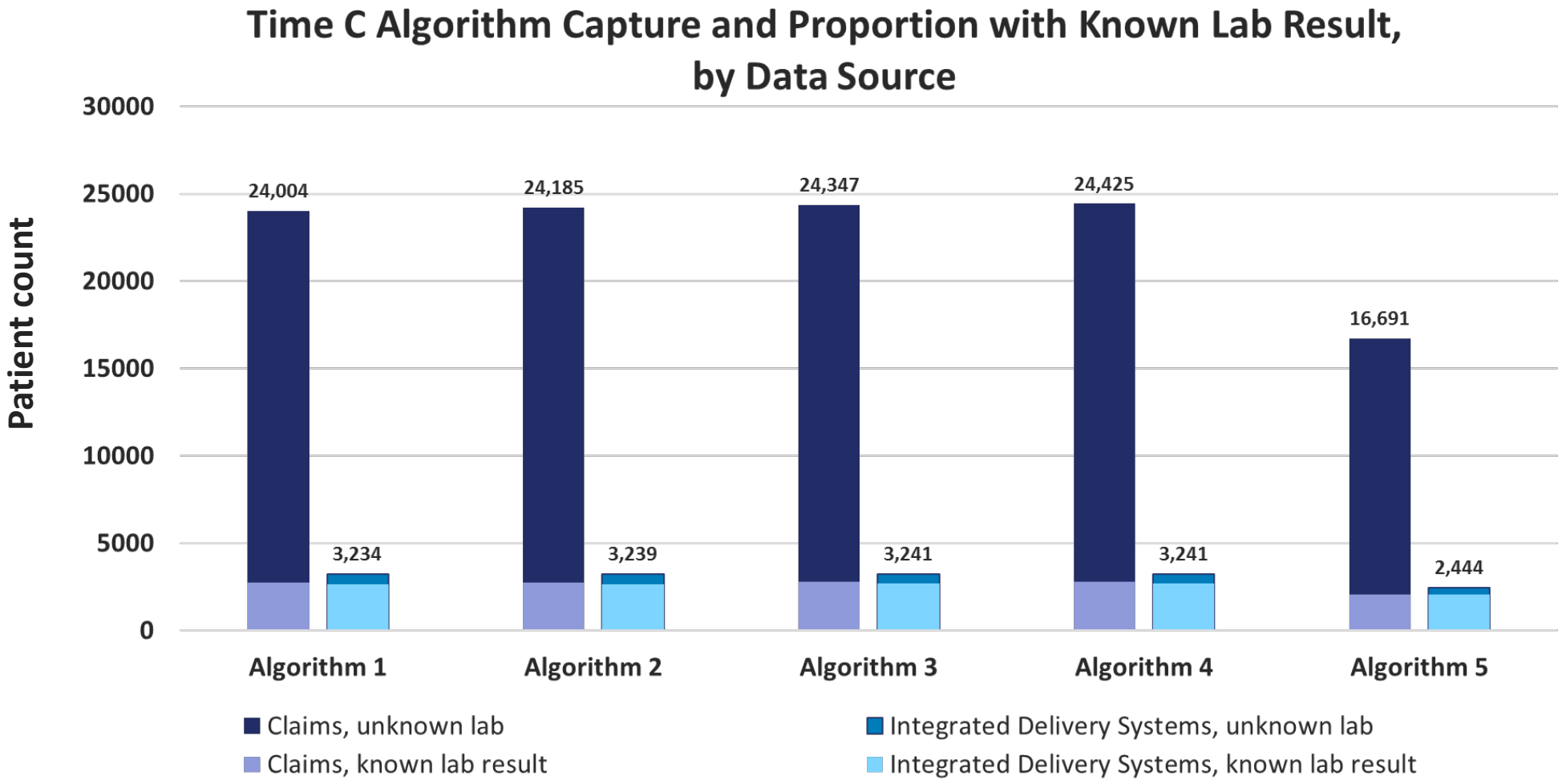
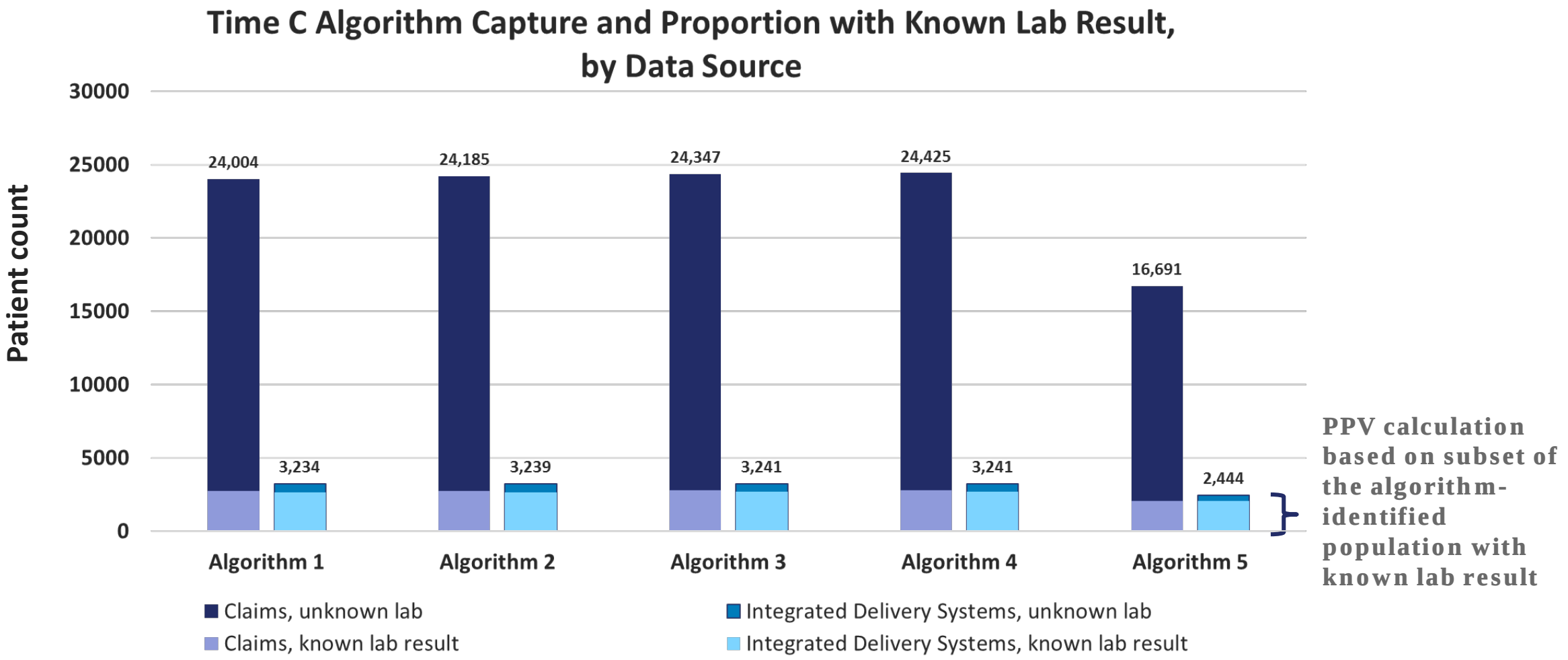


Sensitivity is similar for claims and integrated delivery systems

Results: Interpretation



Results: Interpretation



Results: Limitations

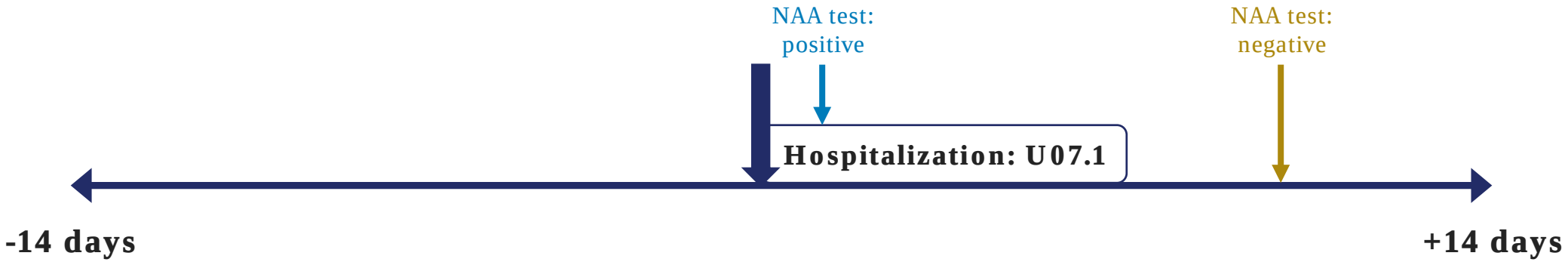
Data capture among claims data partners:

- **Data missingness:** Claims data partners have little inpatient lab data; their lab results come from large national diagnostic laboratories that mostly process outpatient tests.
- **Not at random:** Among hospitalized patients with COVID-19 diagnoses, inpatient lab results are likely to be positive. We believe we are missing some of these inpatient tests.
- **Resulting bias:** In claims data, patients with a negative outpatient test before or after hospitalization for COVID-19 could be misclassified as lab-negative even with a positive inpatient test.

Results: Limitations

Claims: Capture of lab results differs by care setting

Sample misclassified patient:



Results: Limitations

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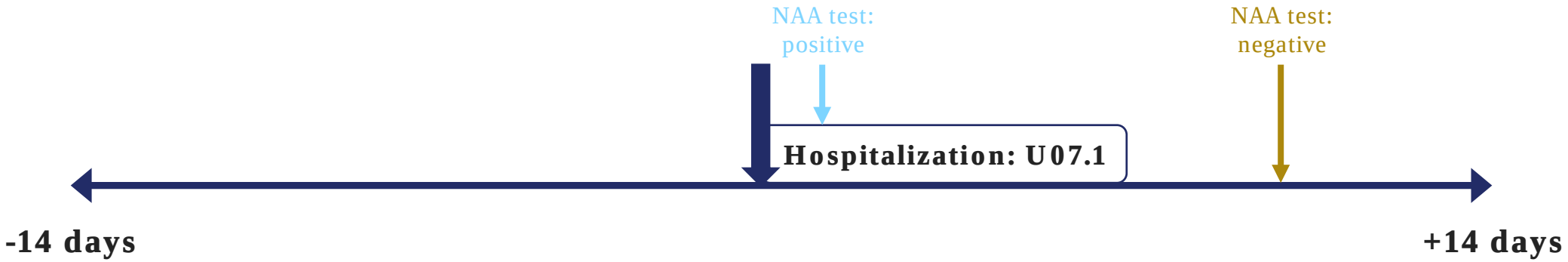

**Inpatient tests are not observed;
patient is classified as algorithm-positive and NAA-negative**

Summary

Findings:

- **U07.1** alone captured almost as many patients as the broader algorithms, with nearly identical PPV (Time C, all data partners: 81% PPV).
- **Observed PPV** of algorithms 1-4 declined across the three time periods.
  - Claims: Observed PPV declined from 93% to 69% over time.
  - Integrated delivery systems: PPV was >90% across all time periods.
- **Sensitivity** was stable at 95% for Times B and C.
- **Algorithm 5,** "severe COVID-19," had a higher PPV and lower sensitivity.

Summary

Conclusions:

- PPV is based on more complete data for integrated delivery systems compared to claims.
- We believe that the observed differences in PPV by health plan type are partly attributable to differences in capture of inpatient laboratory data.
- With a PPV of 81% and sensitivity of 95%, we recommend using U07.1 for inpatient COVID-19 cohort identification in U.S. claims data when complete laboratory results are not available.

Workgroup

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Thank you

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