Using Freshest Feasible Data for Medical Product Safety Surveillance in Mini-Sentinel: Potential and Challenges

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Harvard Medical School

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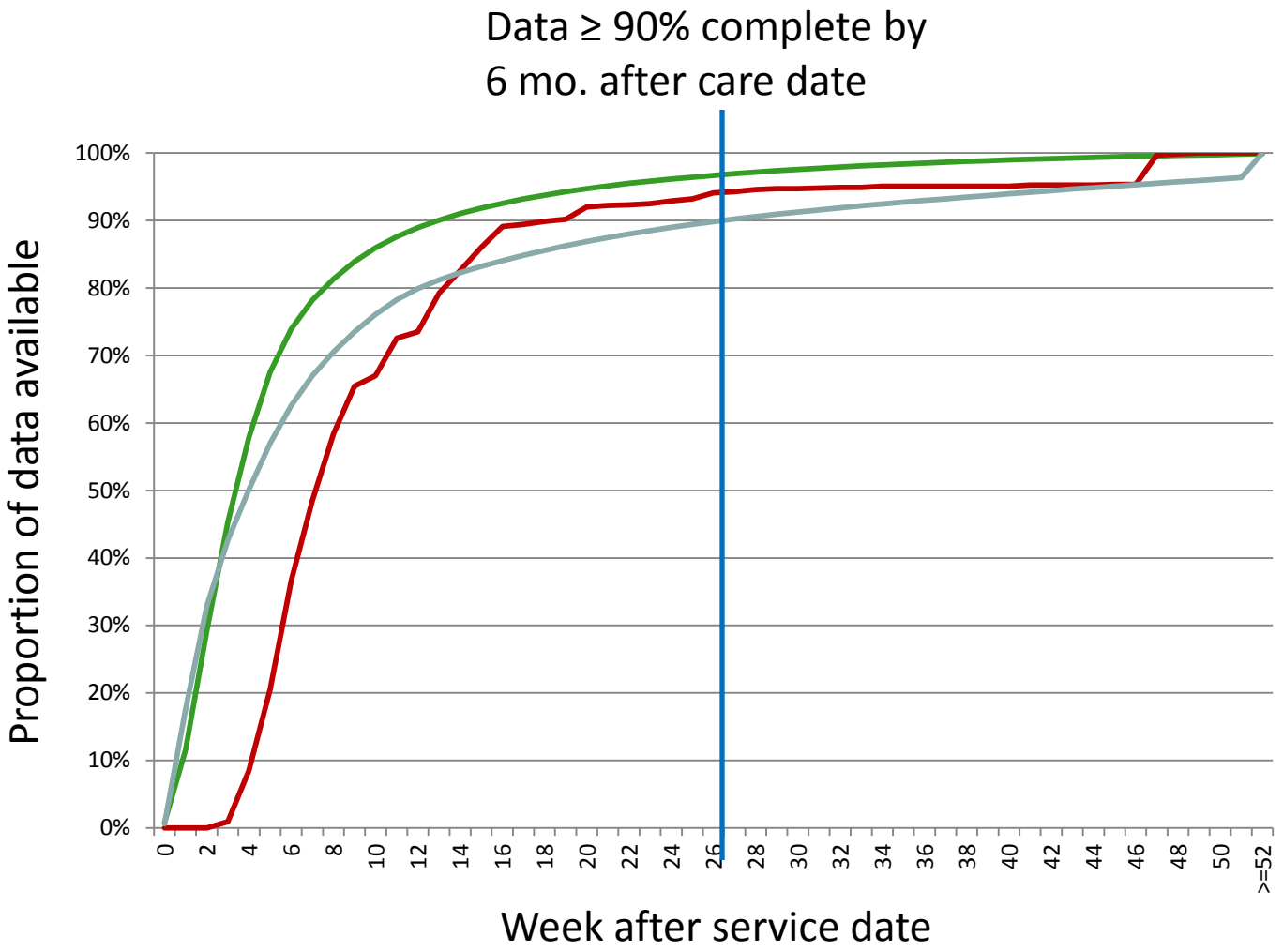
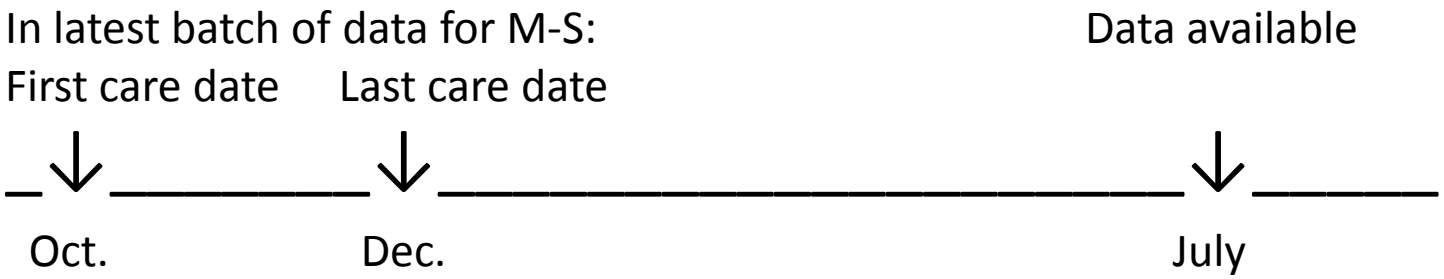
Inpatient claims data lag, 3 data partners



Mini-Sentinel data are relatively complete

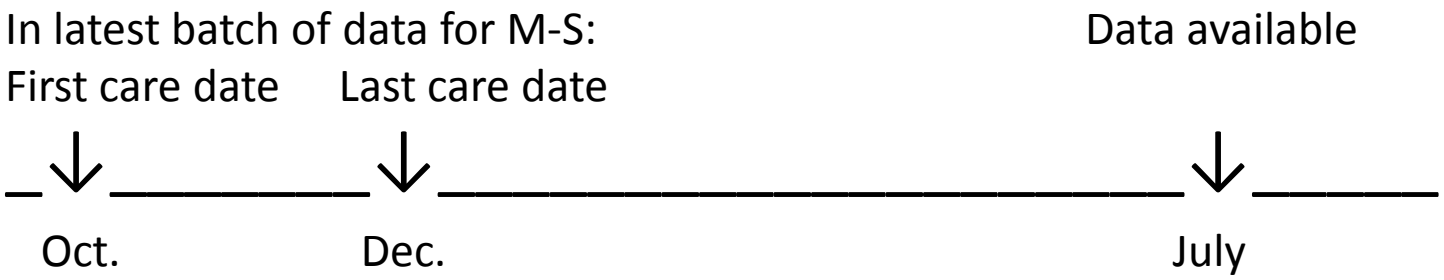
- Data updated on quarterly basis
- Typical example of timing:



- The most recent data typically 6-9 months old

Advantage of mature (less fresh) data

- PRO: data more complete and settled



Pros and cons of mature (less fresh) data

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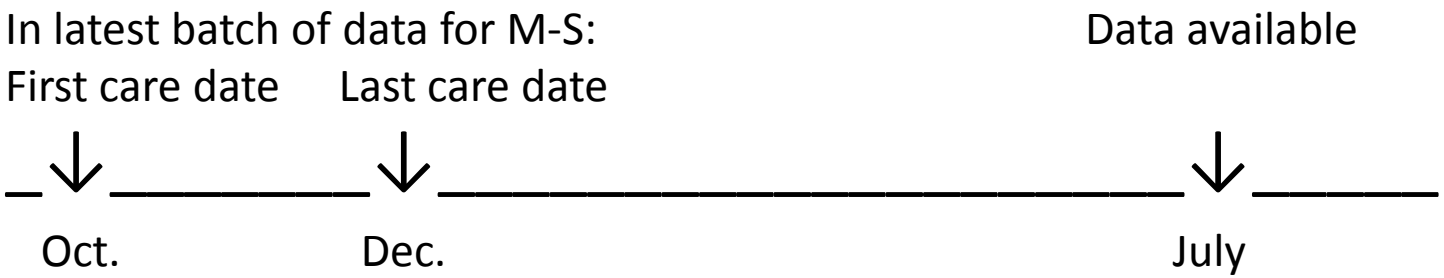

- CON: signal detection delayed

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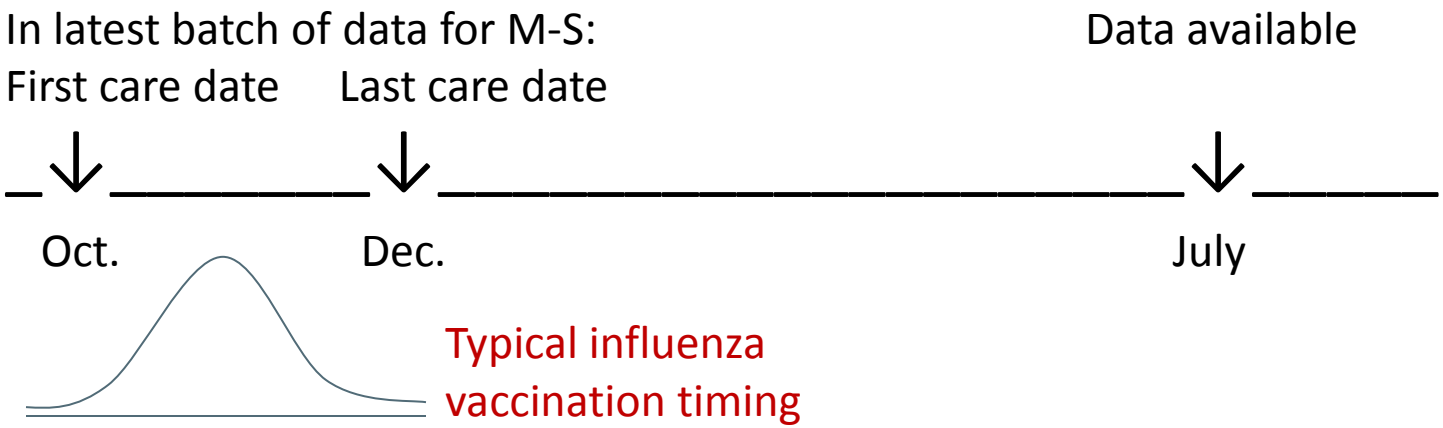
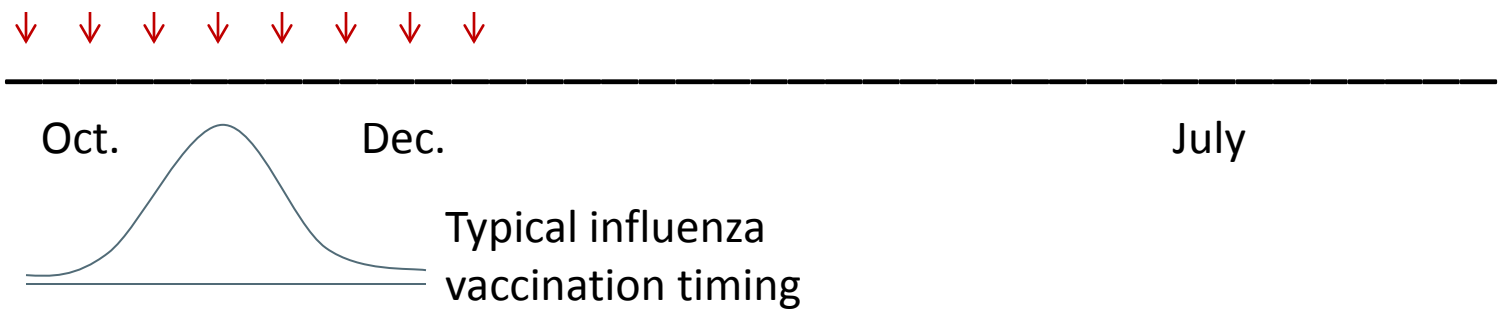


- CON: signal detection delayed
  Especially problematic for influenza vaccine safety monitoring

Challenges of influenza vaccine safety monitoring

Influenza vaccination period relatively short, so data must be available soon after exposure to find safety problems in time to make a difference



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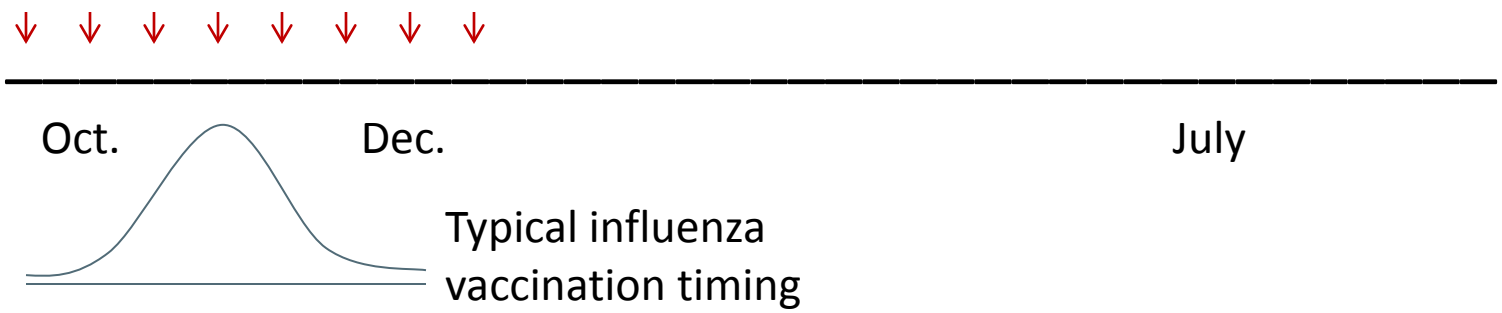
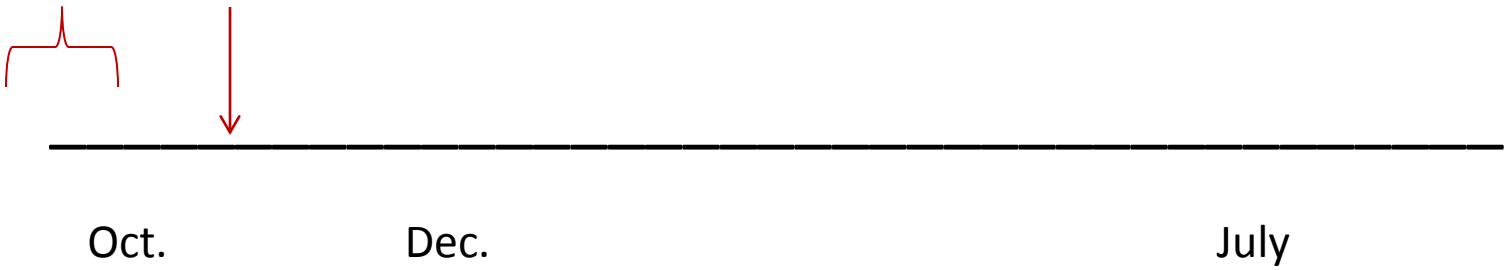


1. Need fresher and frequently updated data
2. Need to adjust for incomplete data

1. Getting fresher and frequent data

Freshest feasible data source is refreshed monthly

- Available toward end of following calendar month (data through Sept. available late Oct., etc.)
- More timely than M-S Distributed Dataset



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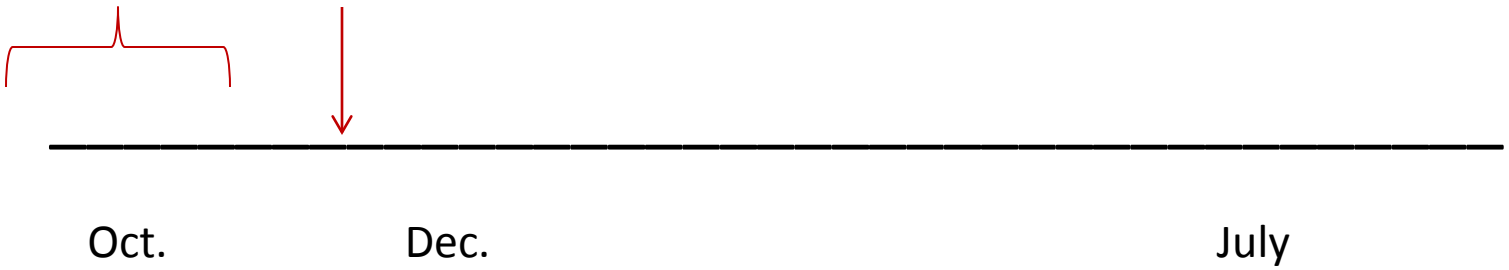

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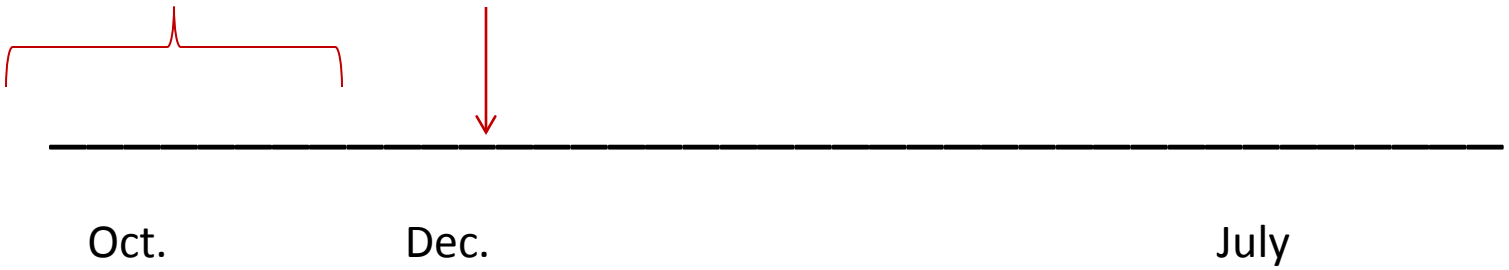

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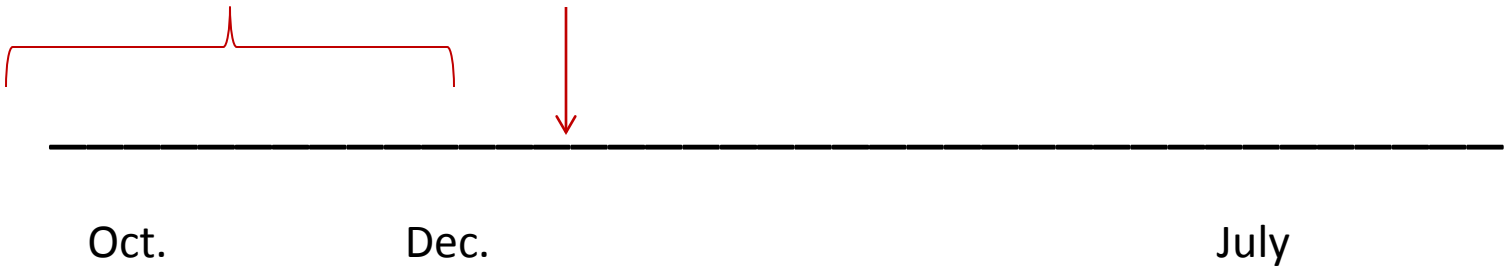


Files to be created for influenza vaccine safety monitoring

SDFs

Sequential Data Files (SDFs)

- Patient-level data, kept by data partners
- Population = persons with medical claim on or after 9/1/2012

SCFs

Sequential Case Files (SCFs)

- Patient-level data, kept by data partners
- Population = persons per current SDFs with health outcome of interest following influenza vaccination

SAFs

Sequential Analysis Files (SAFs)

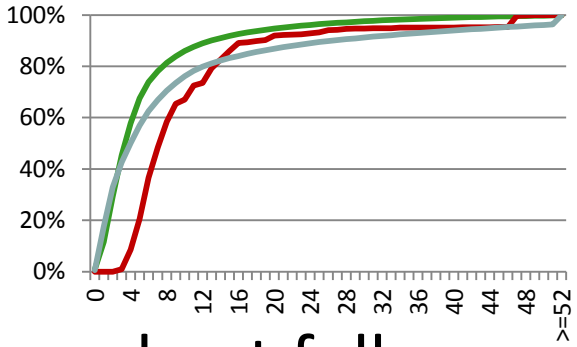
- Aggregate data, sent to M-S Operations Center for analysis
- Vaccination population: vaccination per current SDFs
- Cases population: cases per all SCF versions

Expected timing of data refreshes and analyses

- Monthly but unsynchronized data refreshes by data partners
- Biweekly analyses by Operations Center (in weeks in red)

Week	1	**2**	3	**4**	5	**6**	7	**8**	9
DP1	SDF	**SAF**			SDF	**SAF**			SDF
DP2		SDF	**SAF…**	→		SDF	**SAF…**	→	
DP3			SDF	**SAF**			SDF	**SAF**	
Analysis		yes		yes		yes		yes	

2. Adjusting for incomplete data



Two kinds of "incompleteness"

A. Lag in data availability →
B. Post-vaccination follow-up interval not fully elapsed

To avoid bias, both must be taken into account.

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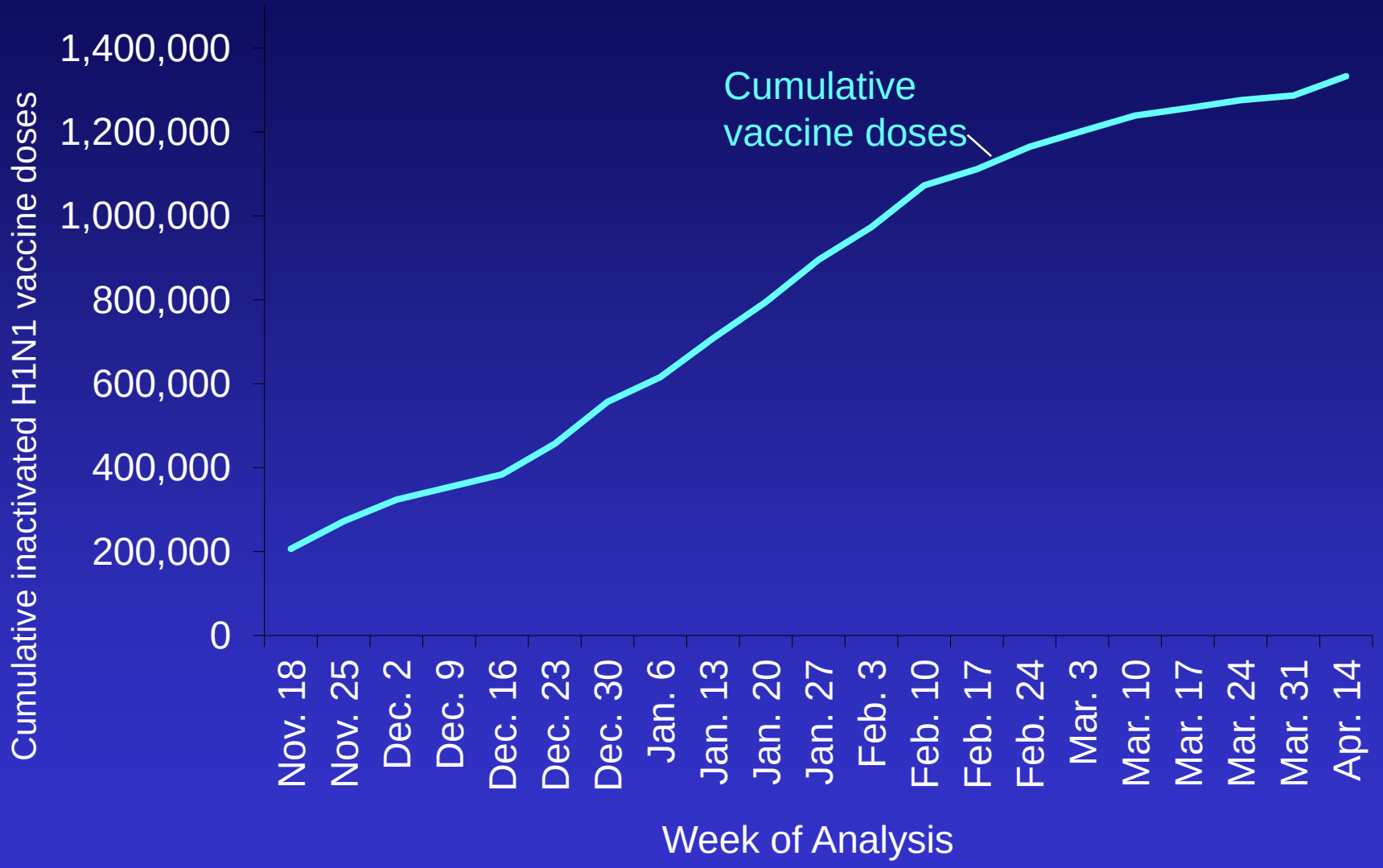
ORIGINAL REPORT

Near real-time vaccine safety surveillance with partially accrued data†

Sharon K. Greene[1]*, Martin Kulldorff[1], Ruihua Yin[1], W. Katherine Yih[1], Tracy A. Lieu[1], Eric S. Weintraub[2] and Grace M. Lee[1,3]

[1]*Department of Population Medicine, Harvard Medical School and Harvard Pilgrim Health Care Institute, Boston, MA, USA*
[2]*Immunization Safety Office, Centers for Disease Control and Prevention, Atlanta, GA, USA*
[3]*Division of Infectious Diseases and Department of Laboratory Medicine, Children's Hospital Boston, Boston, MA, USA*


Cumulative inactivated H1N1 vaccine doses
1,400,000
1,200,000
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800,000
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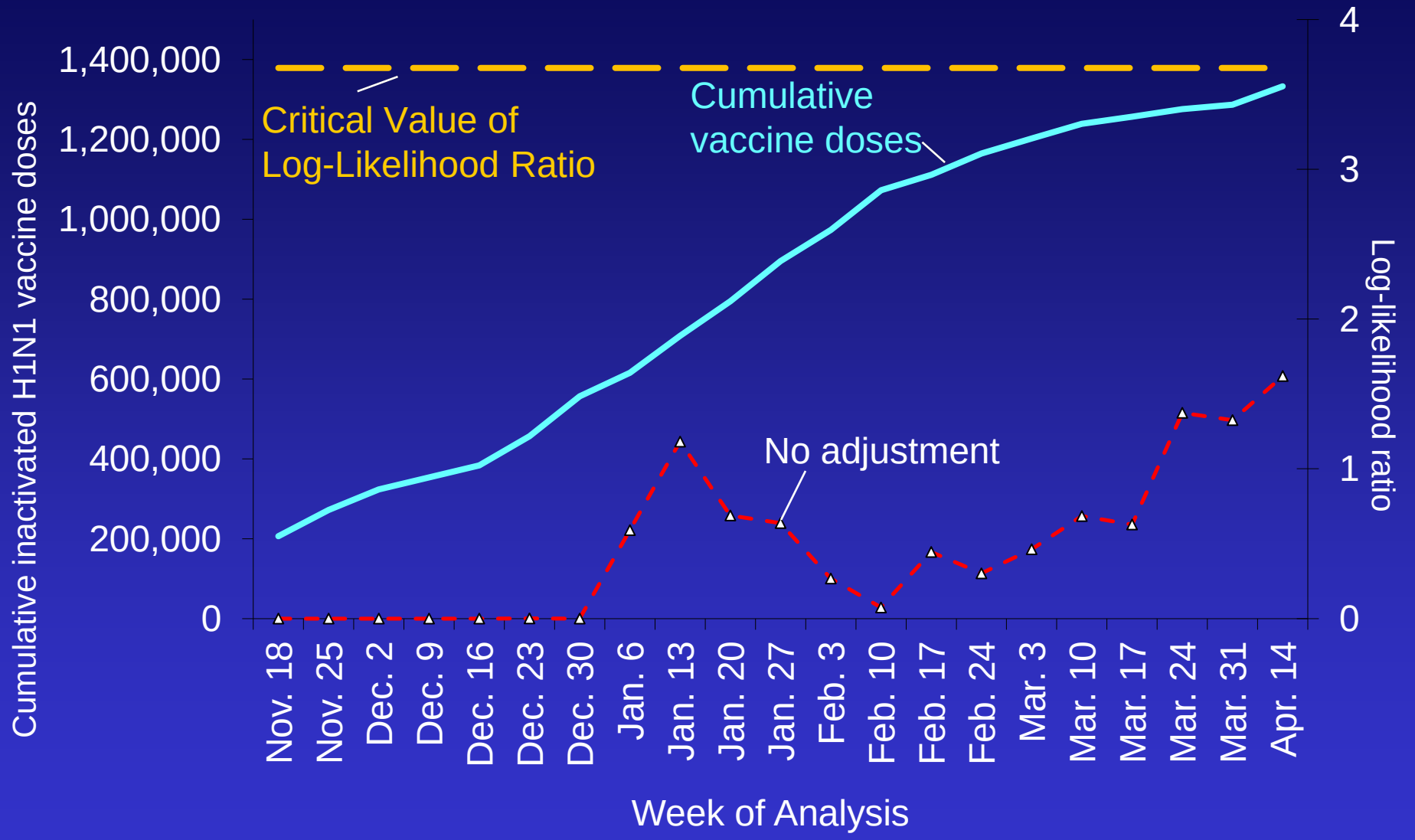
Cumulative vaccine doses
Nov. 18
Nov. 25
Dec. 2
Dec. 9
Dec. 16
Dec. 23
Dec. 30
Jan. 6
Jan. 13
Jan. 20
Jan. 27
Feb. 3
Feb. 10
Feb. 17
Feb. 24
Mar. 3
Mar. 10
Mar. 17
Mar. 24
Mar. 31
Apr. 14
Week of Analysis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Log-likelihood ratio
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3
2
1
0
Critical Value of
Log-Likelihood Ratio
Cumulative
vaccine doses
No adjustment
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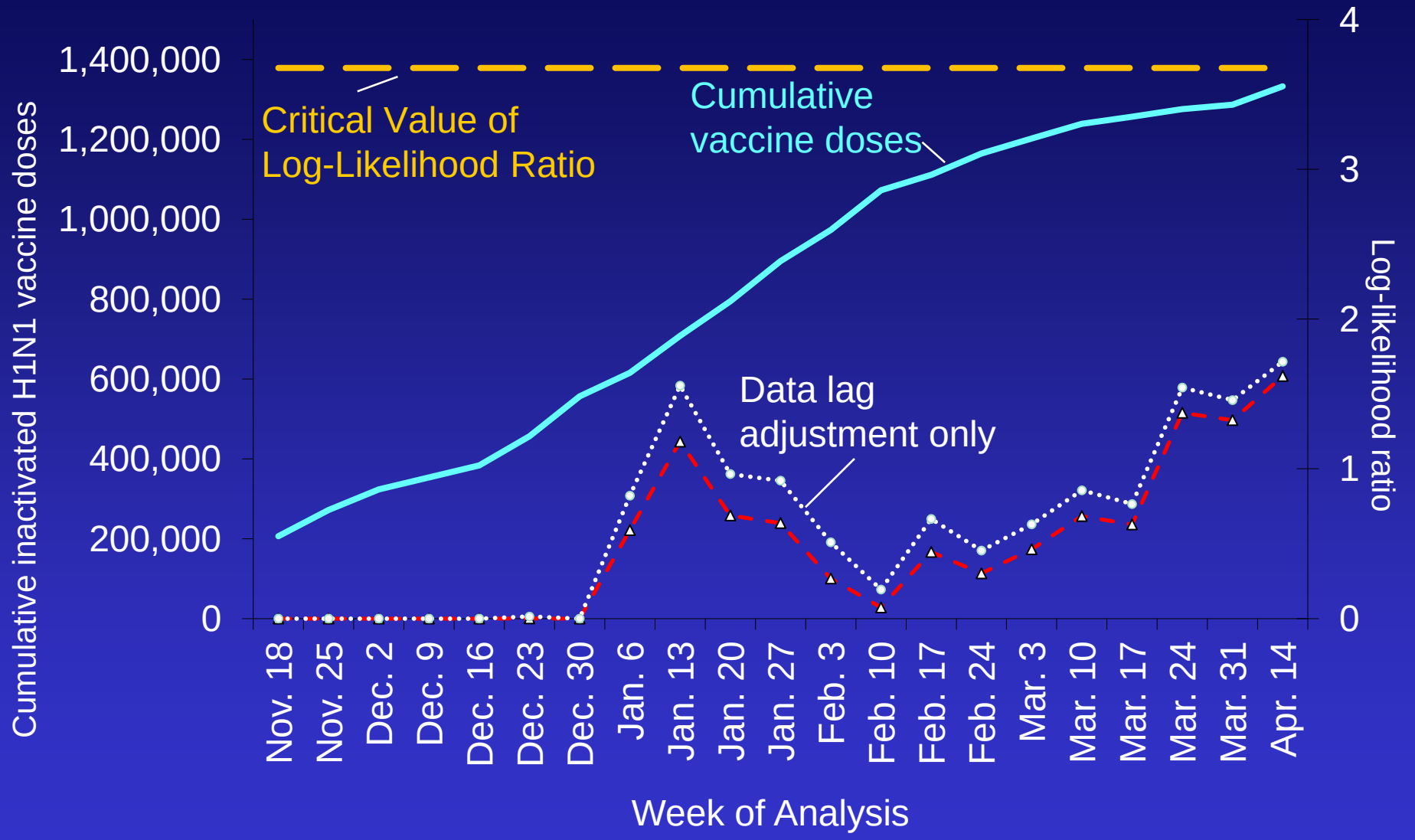
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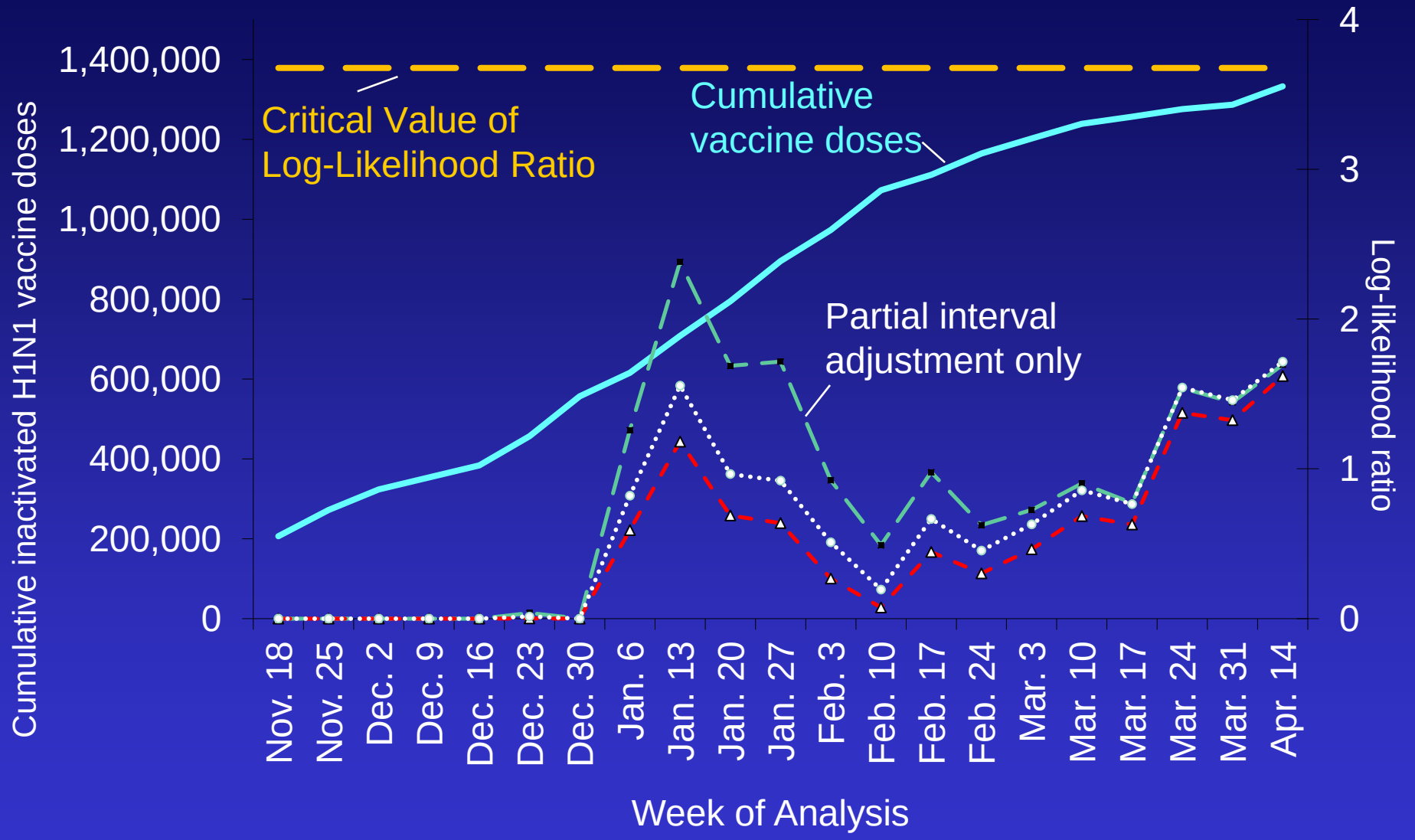
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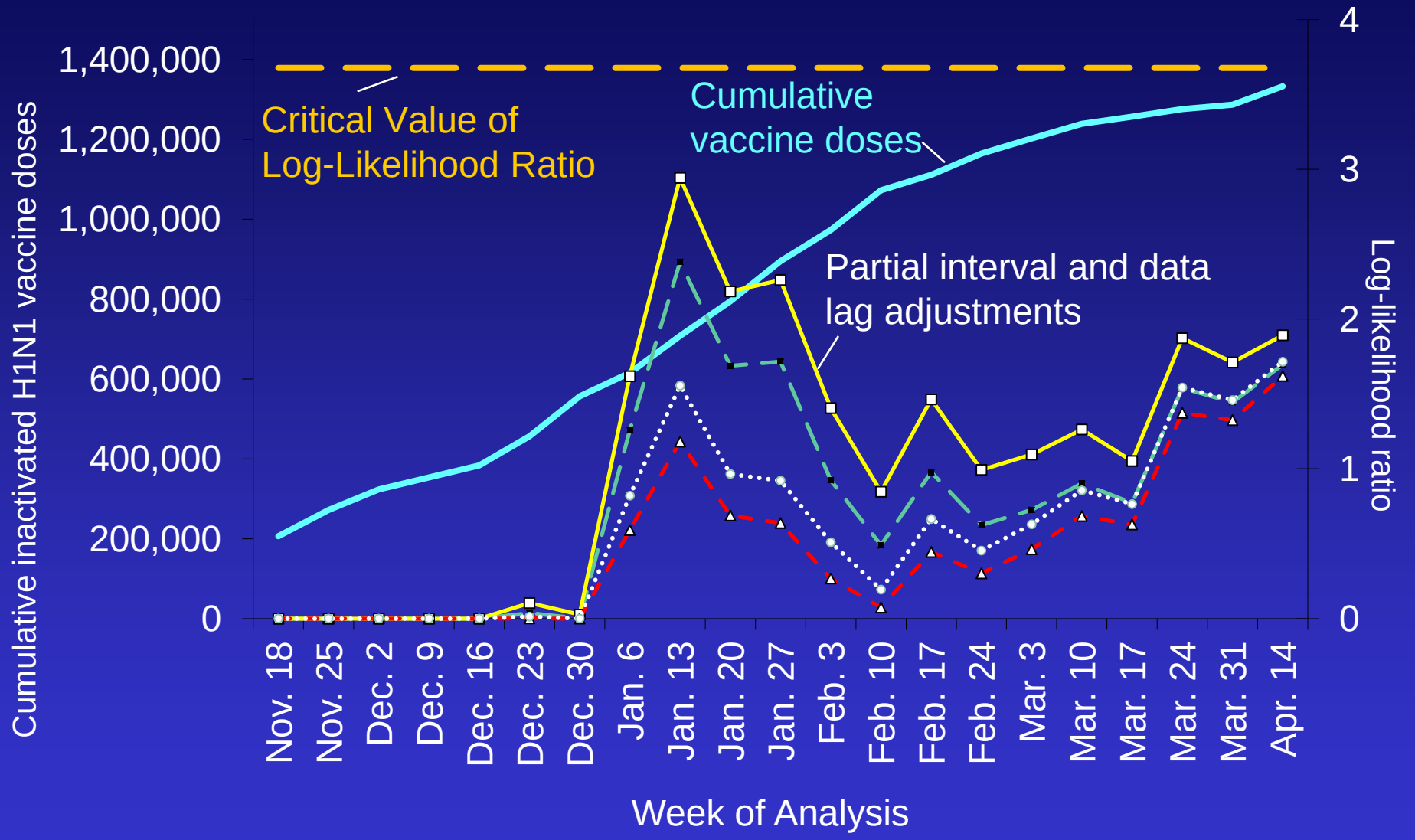
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Conclusion

- PROS of using fresher data
  - Gain in timeliness ~5-8 mo.
  - Necessary for influenza vaccine safety monitoring
- CONS of using fresher data
  - Some loss of accuracy despite adjustments for data incompleteness and flux
  - Takes extra effort to produce these data—more frequent refreshes, different source files, special file structures
  - Each product needs a separate extract
- We *can* use fresher data, but probably not worthwhile to do so on routine basis

What constitutes a comprehensive safety surveillance system?

- Semi-automated routine surveillance, applying general tools with minor adaptations to address the specific product

But also…

- Ability to bring specialized expertise to bear on specific issue(s) that may arise in product lifecycle