FDA/CMS Vaccine Safety Projects Using Medicare Data

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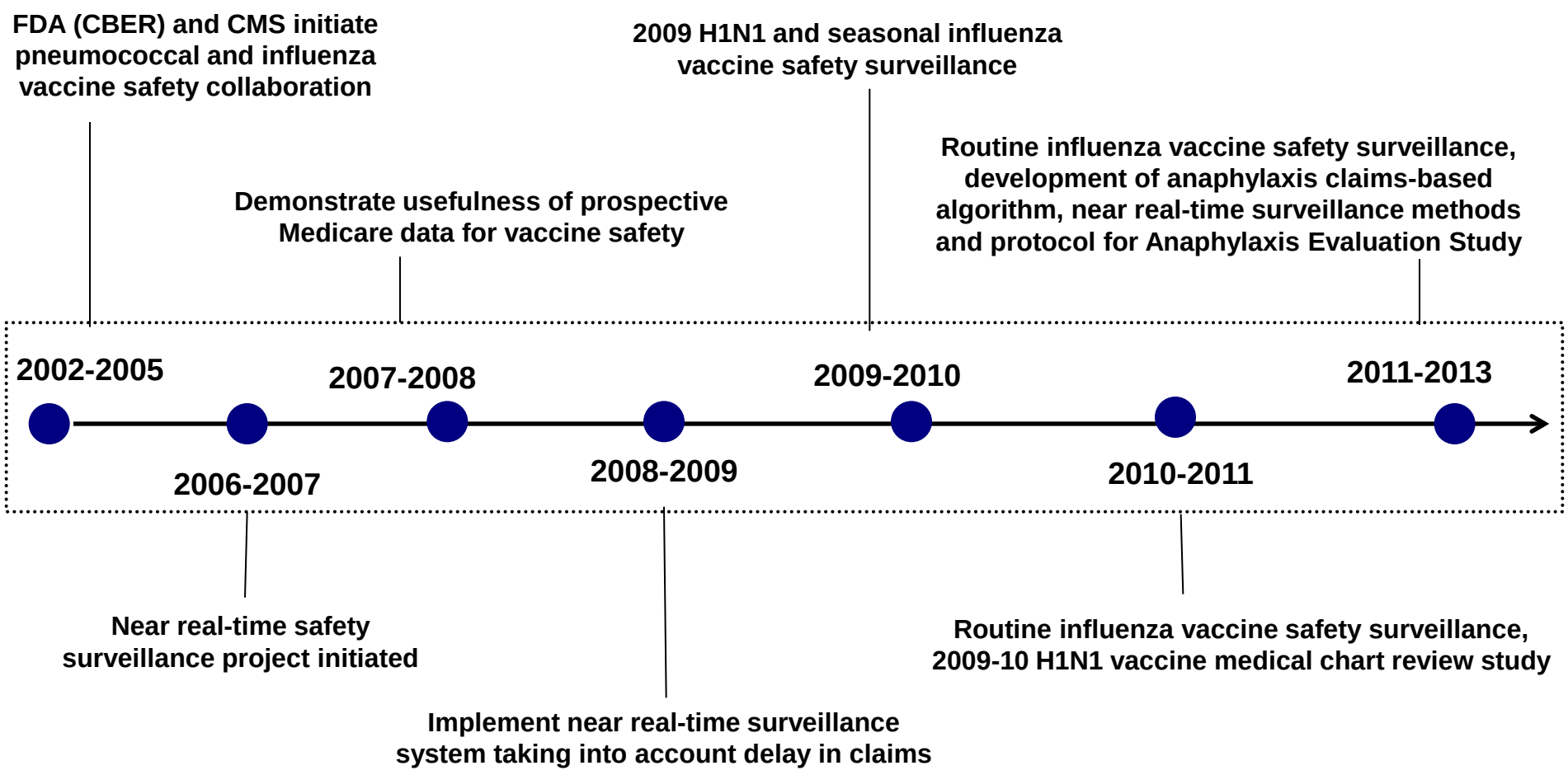
Sukhminder K. Sandhu, PhD, MPH, MS
FDA/CBER/OBE

Background

- Existing data systems for vaccine safety evaluation using managed care networks underrepresent the elderly and may have insufficient statistical power to evaluate uncommon serious adverse events.
- Medicare is government health insurance for
  - 43 million persons[1] age ≥65 years
  - 9 million persons[1] age <65 with disability or end stage renal disease vaccine
- Initially focused on active surveillance methods for adverse events after influenza vaccination, e.g., Guillain-Barré Syndrome (GBS)
  - GBS associated with the 1976-77 swine influenza vaccine[2,3]

[1] Data for April 2013
[2] Am J Epidemiol. 1979;110:105-123.
[3] Am J Epidemiol. 1991;133:940-51.

Project History
Vaccine Safety



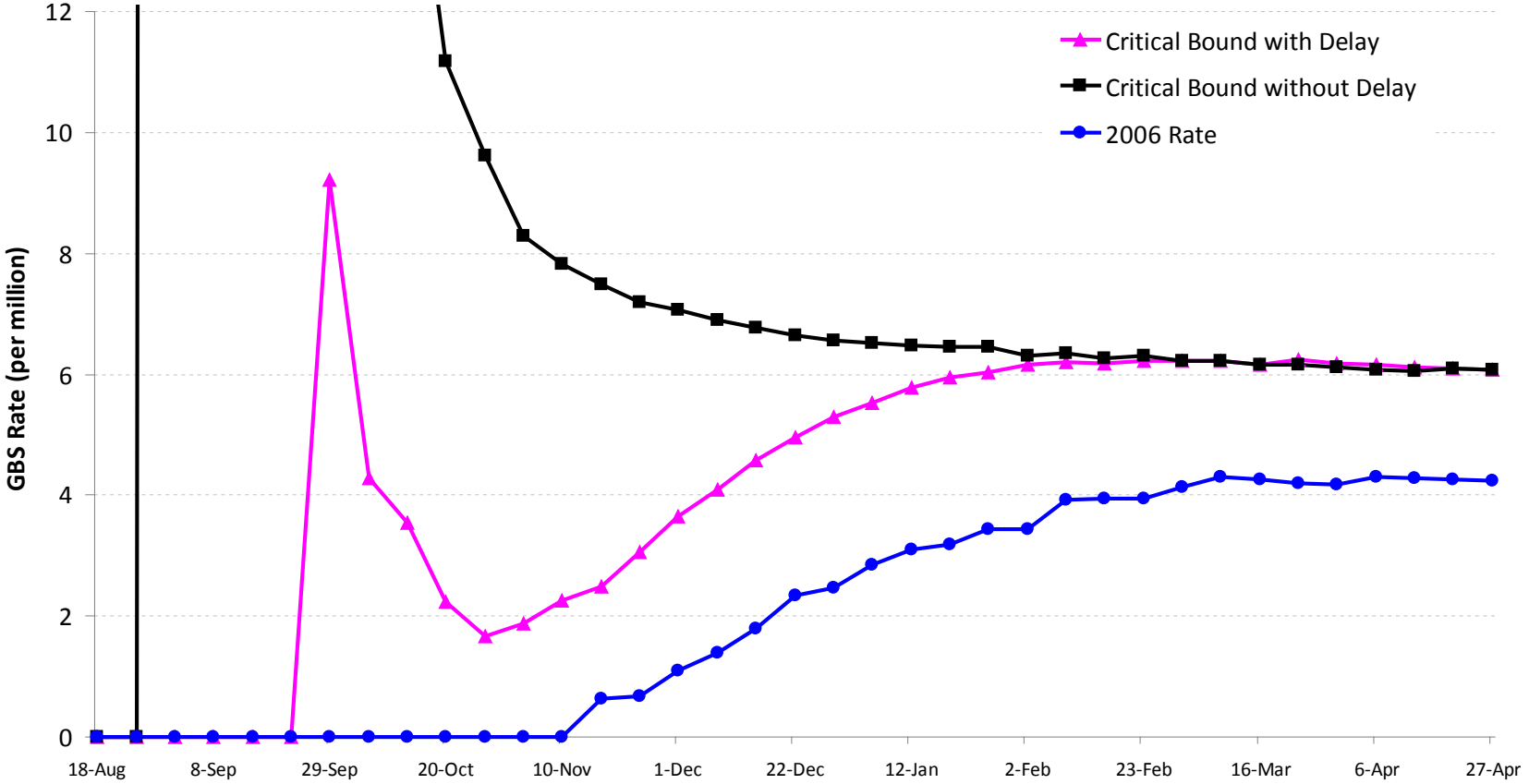
Vaccine Safety Studies Using CMS Data

- Near real-time surveillance
  - Active surveillance for signal detection
  - Conduct in near real-time vs. waiting for all of data to accumulate
  - May “look” at the same data multiple times as it accumulates over time
- Epidemiologic studies
  - Signal evaluation and confirmation
- Methodological studies
  - Refinement of methodologies to conduct vaccine safety

CMS Near Real-time Surveillance

- Updating Sequential Probability Ratio Test (USRPT) used to account for repeated testing and delay in claims
- Primary Analysis
  - 0–42 day risk window
  - All seasonal influenza vaccines
  - All ages
- Secondary Analyses: Variation of risk windows, age groups and vaccine type
- Signal defined as observed GBS rate higher than critical limit for primary analysis (based on historical comparator of prior influenza seasons)

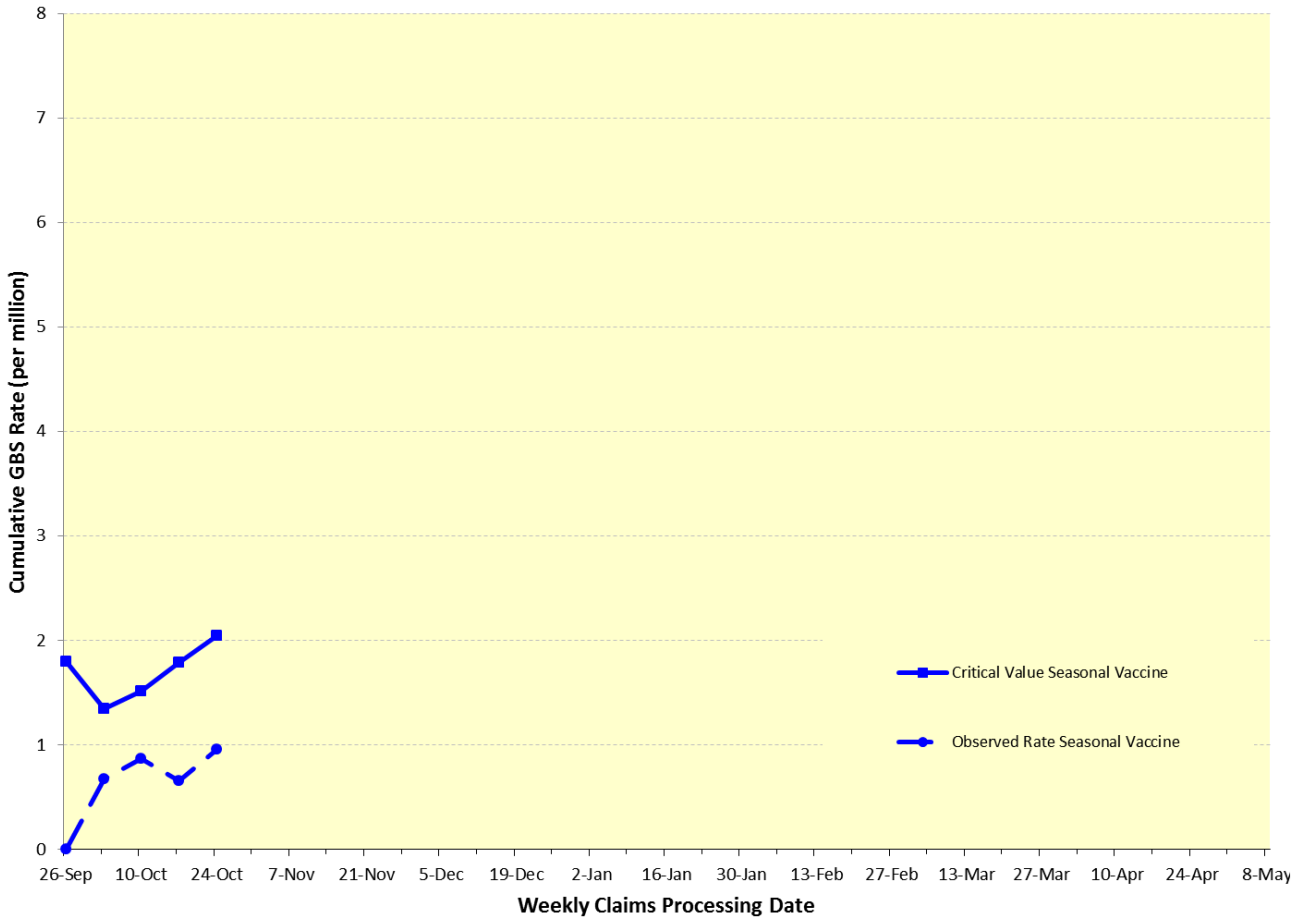
Adjustment for Claims Delay Optimizes Critical Limits to Facilitate Early Signal Detection



Signal Evaluation Plan

- Internal technical evaluation
  - Data quality assurance checks
  - Alternative methodologies for analysis
  - Temporal clustering
  - Sensitivity analyses
  - Risk vs. benefit assessment
- Communication of signal and early evaluation results to Immunization Safety Task Force (ISTF)
- Follow-up epidemiologic studies, including medical record review if necessary and feasible

CMS Near Real-time Influenza Vaccine Surveillance Results, 2009–10



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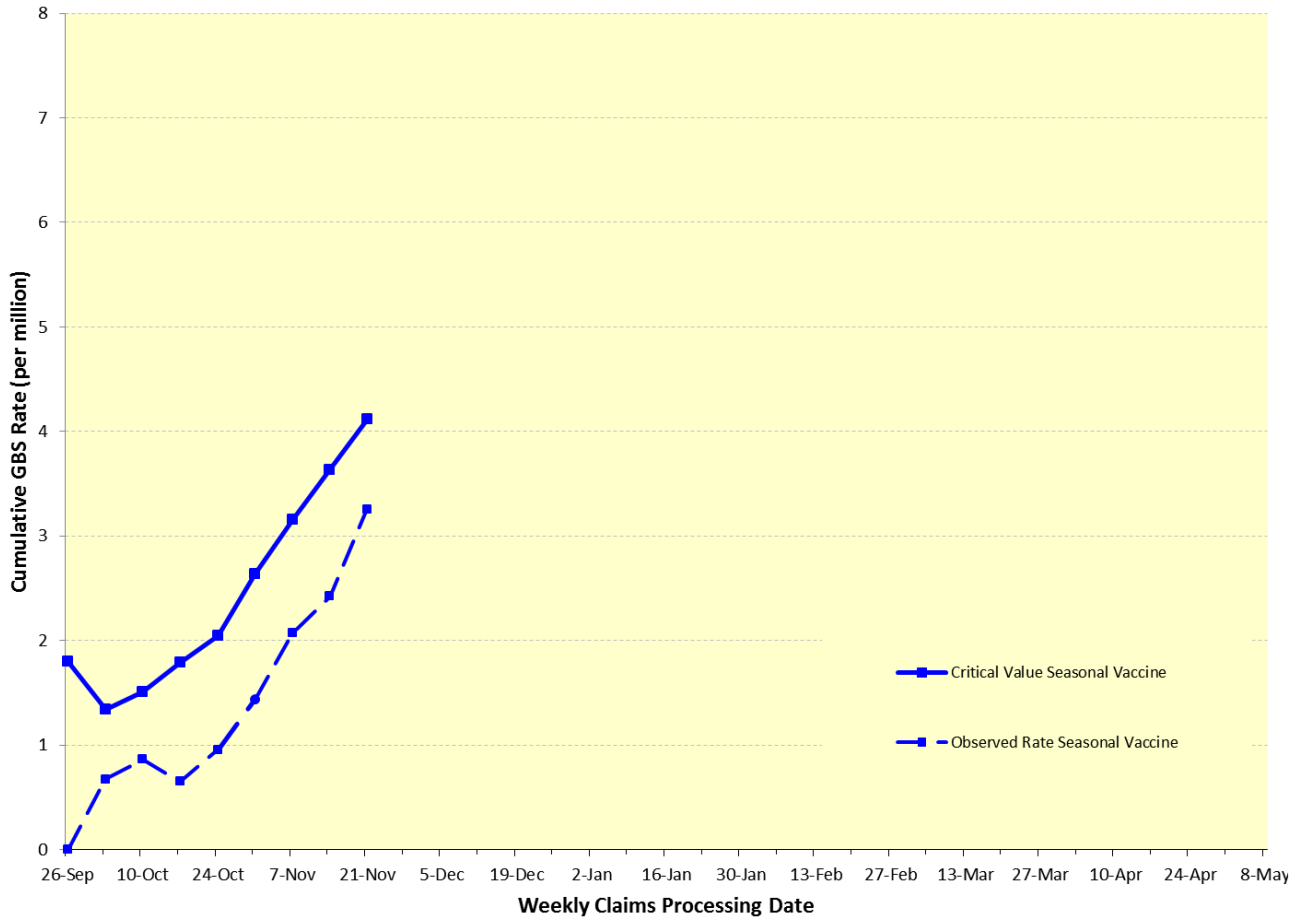

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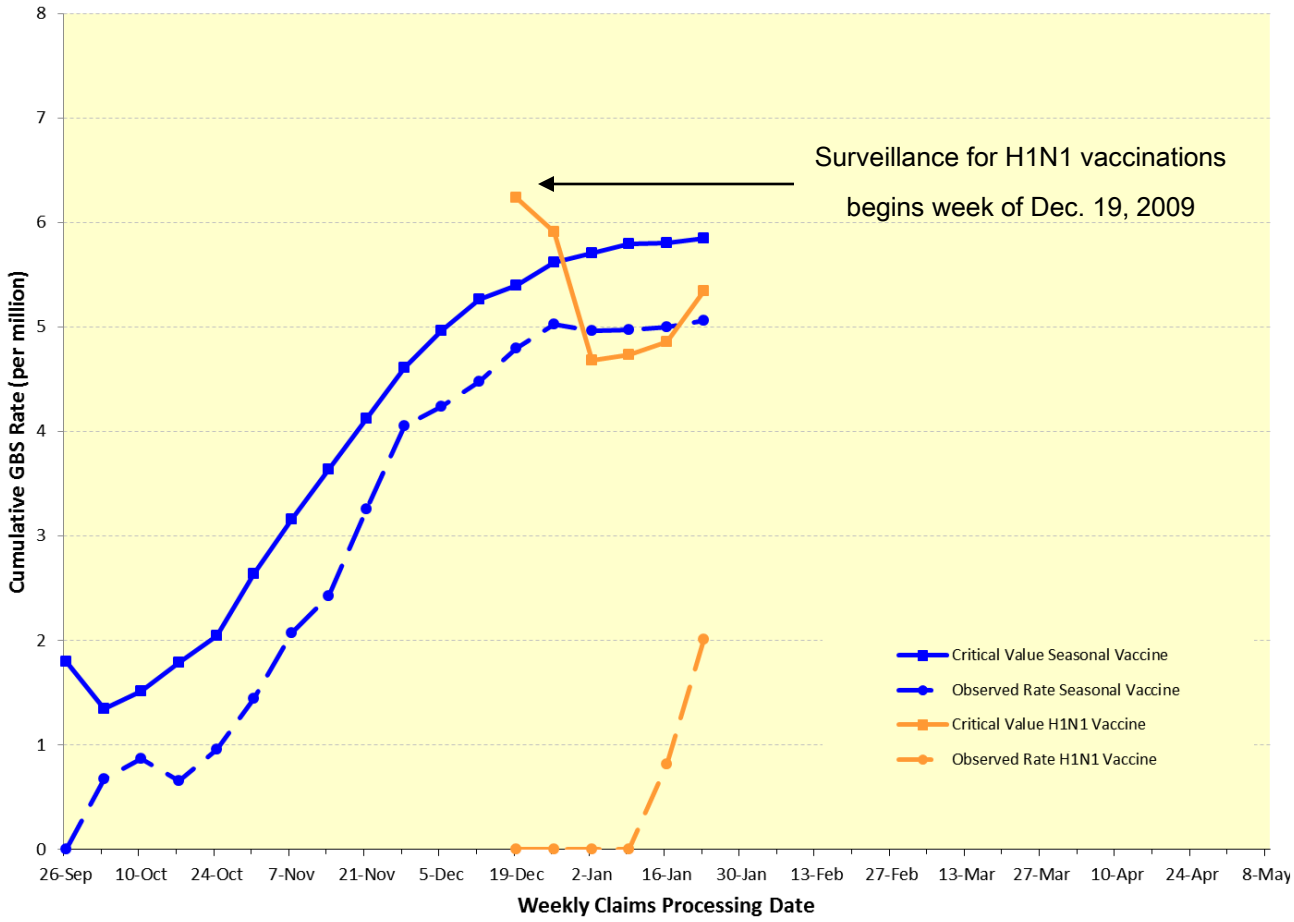

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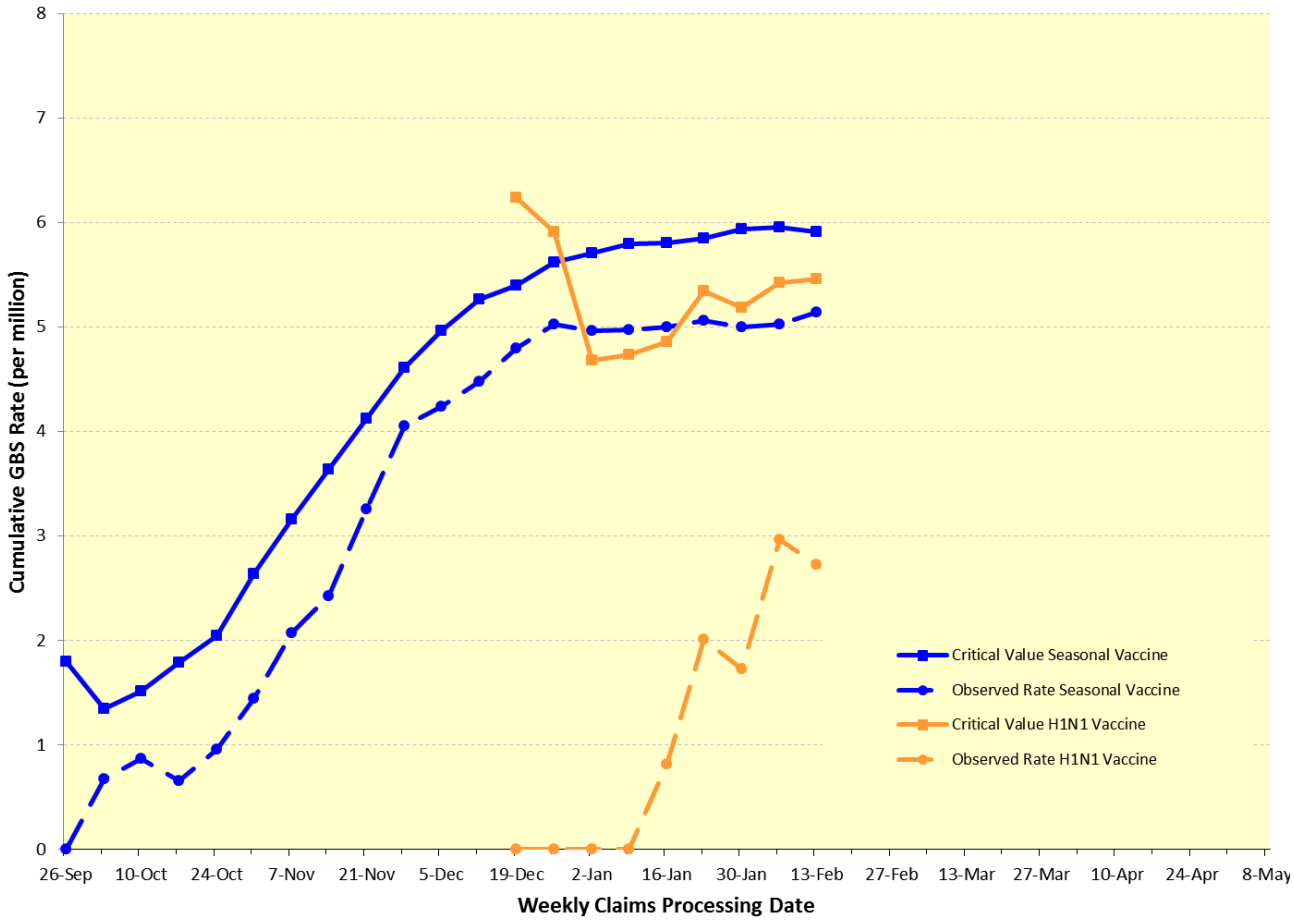

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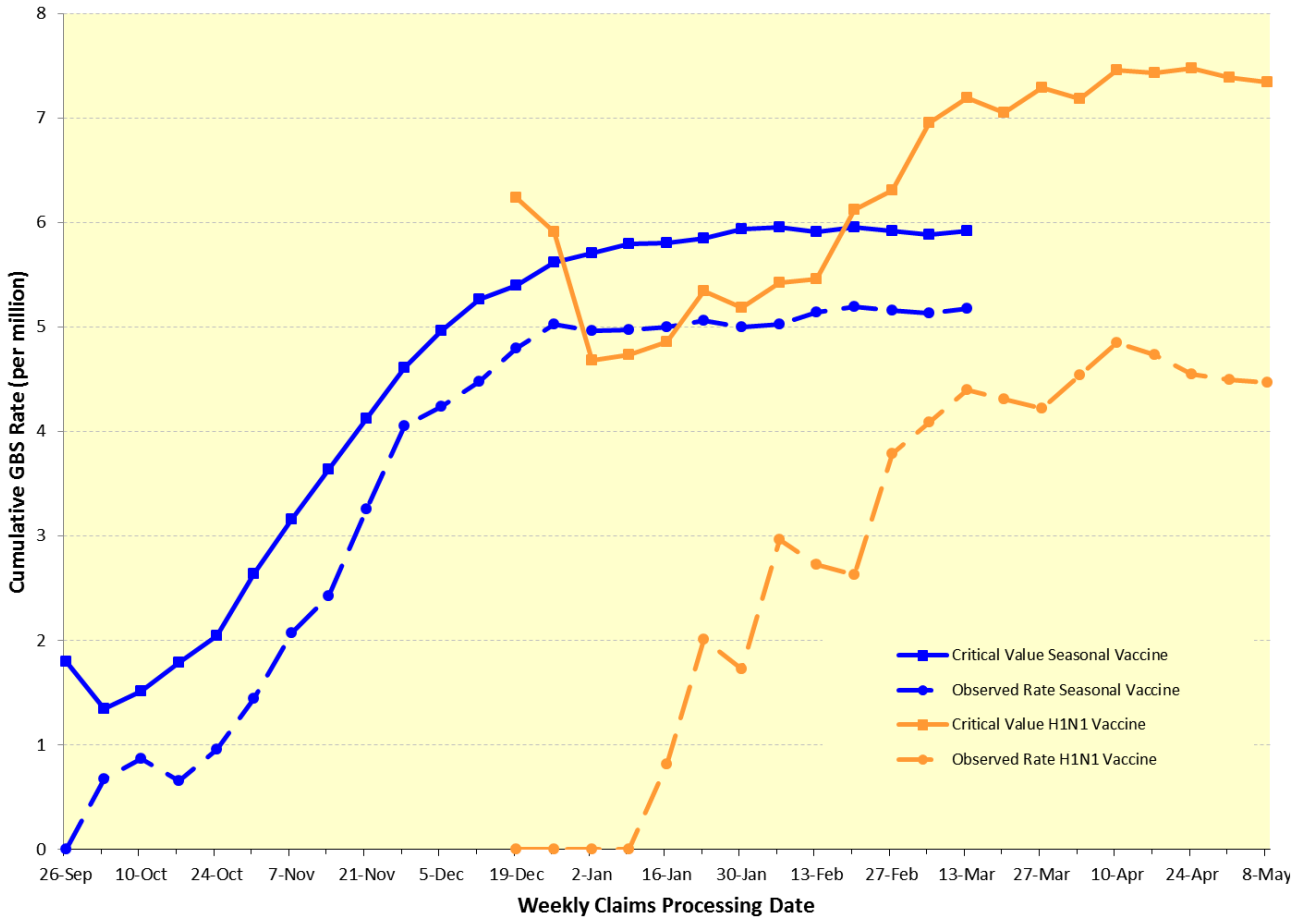

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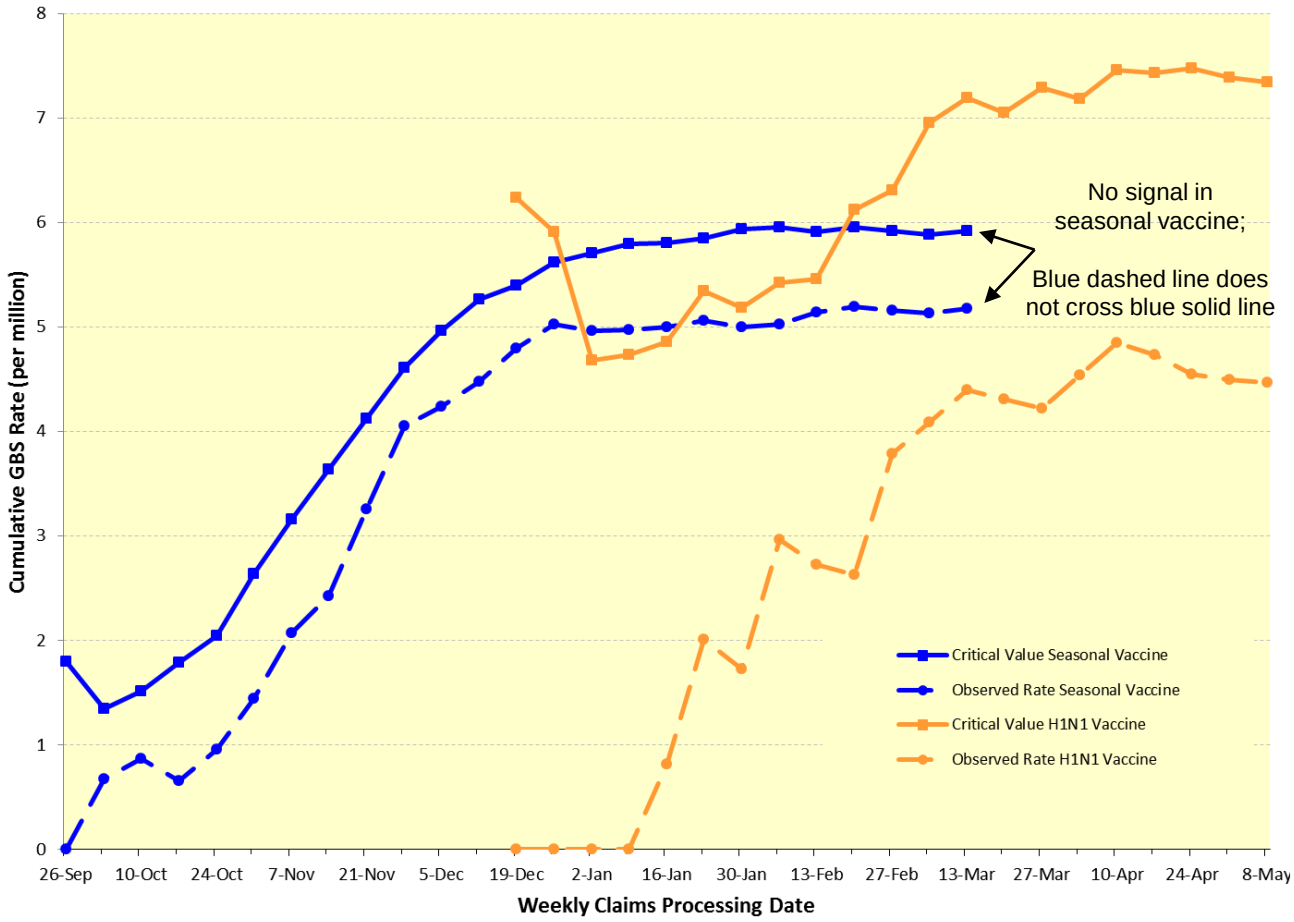

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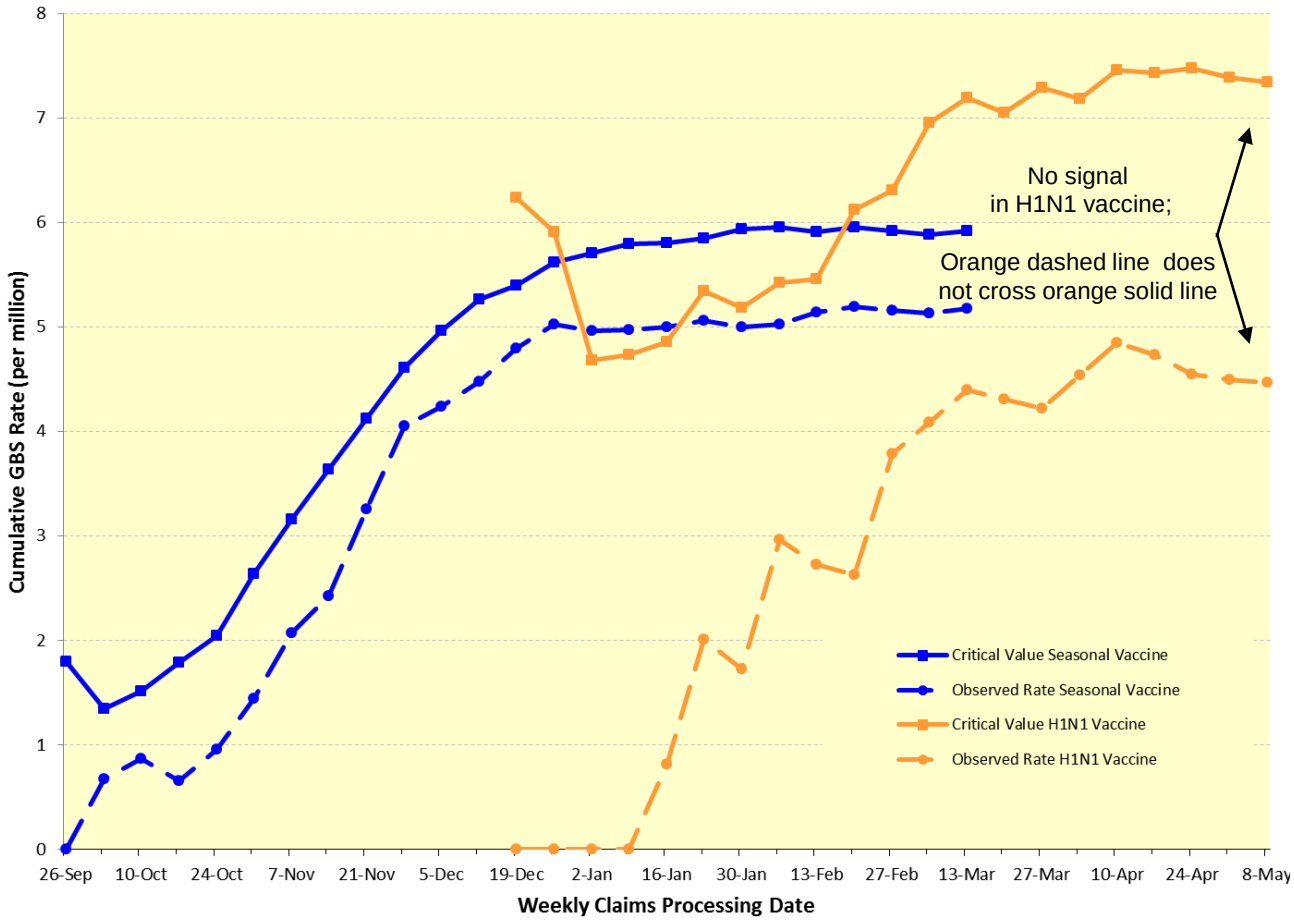

Influenza Vaccine Near Real-Time Safety Surveillance for Guillain-Barré Syndrome, 2009-10

- Claims-based data as of 7/30/2010 indicated
  - 14 million seasonal influenza vaccinations
    - Relative risk of 1.16 during 42 days after vaccination
    - Slightly higher (1.17-1.22) during 0-21 and 7-21 days after vaccination
  - 3 million H1N1 vaccinations
    - Relative risk of 1.14 during 42 days after vaccination
    - Slightly higher (1.34-1.42) during 0-21 and 7-21 days after vaccination
- No signal in Medicare claims-based data
- Medical record review performed in support of HHS Meta Analysis; conducted SCRI analyses in-house suggesting evidence of slight increase in risk (RR=2.36, 1.13-4.94)[1]

[1] Am J Epidemiol. 2013 May 6. [Epub ahead of print]; PMID: 23652165

Influenza Vaccine Near Real-Time Safety Surveillance Expansion

- Refinement of USPRT methodology to monitor for additional adverse events of interest (e.g., anaphylaxis)
  - Risk interval with a historical comparator
  - Pilot in 2013/14 influenza season
- Development of “CMS-specific” claims-based algorithm for anaphylaxis
- Anaphylaxis Medical Record Review Study to
  - Validate claims-based algorithm
  - Assess the safety of H1N1 containing vaccines
    - H1N1-containing vaccines: 2010/11-2011/12 influenza seasons
    - Non H1N1-containing vaccines: 2008/09-2009/10 influenza seasons

Summary

- FDA, in collaboration with CMS and Acumen, have developed an active surveillance system that monitors GBS risk after flu vaccination in near real-time. The 2009 H1N1 pandemic and vaccine put this monitoring system into practice and it is used every flu season.
- FDA has the capacity to perform validation through chart-confirmation and epidemiological studies of GBS and other adverse event signals identified using active surveillance on the Medicare population.
- Refinement of methodologies and expansion to anaphylaxis for near real-time monitoring after influenza vaccine continues; possible expansion to other exposures, outcomes and data sources (e.g., Medicaid).

Additional FDA/CMS Biologic Safety/Effectiveness Projects using Medicare Data

- Blood Safety Projects
  - Utilization of blood products among the elderly
  - Immune Globulins and thrombotic events
  - Transfusion-Related Acute Lung Injury (TRALI) studies
  - Babesiosis occurrence among elderly
  - New blood safety codes to improve active surveillance of different blood safety issues in the US
- Tissue Safety Projects
  - Corneal transplantation project
- Influenza Vaccine Effectiveness (in collaboration with CDC)
- Modeling Uptake of MCMi Interventions using Empirical Influenza Vaccination Data
- Quantitative Bias Analysis

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