Update on Influenza Vaccine Safety Monitoring

Advisory Committee on Immunization Practices
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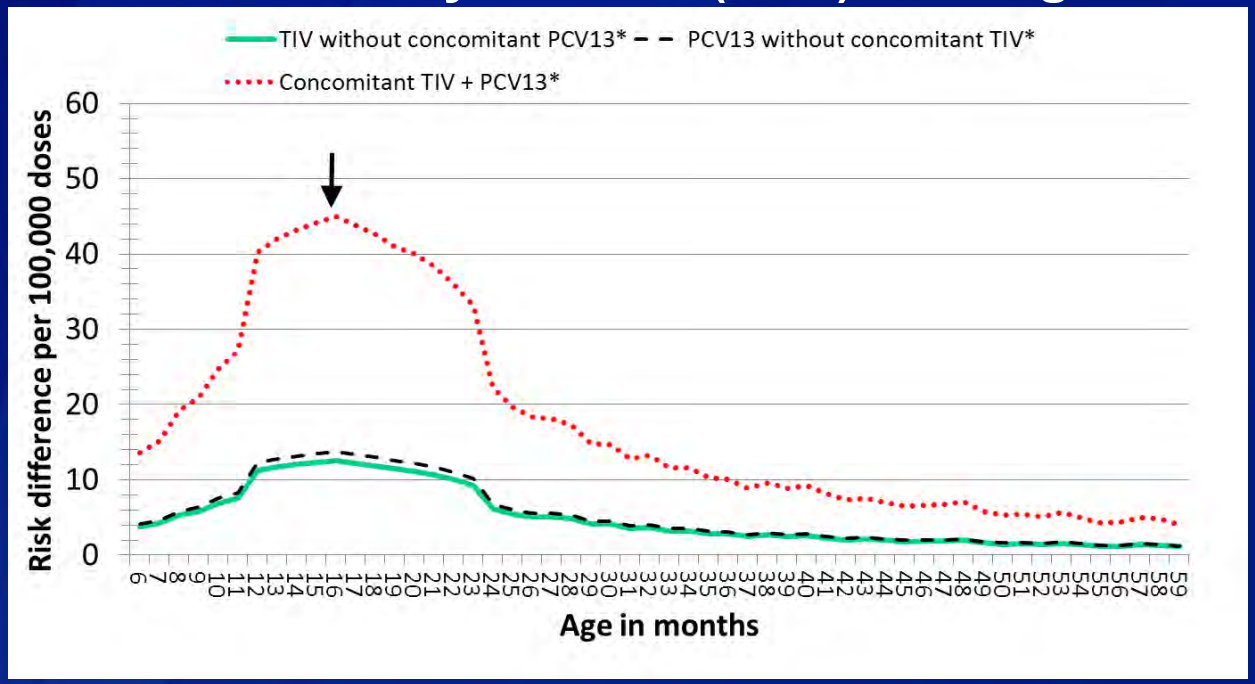
Febrile seizures (2010-11 recap)

- FDA VAERS data mining signaled for Fluzone® and febrile seizure
- Vaccine Safety Datalink (VSD) investigation^



Peak risk difference at 16 months:

45/100,000 concomitant TIV+PCV13 doses
or
~1/2,200

- No policy change was recommended for TIV or PCV13 for 2011-12
- Further investigation is underway to determine if other childhood vaccines may be contributing to the febrile seizures

^ Tse A and Lee G for the VSD
* Vaccines may have been received concomitantly with non-TIV, non-PCV13 vaccines

Febrile seizures (cont.)

- Continued to observe disproportionate reporting for febrile seizures in young children following Fluzone® in VAERS data mining for 2011-12
  - Not unexpected given no formulation change for 2011-12
  - Possibility of stimulated reporting
- Elevated relative risk observed for seizures following TIV in children age 6-23 months in VSD surveillance of automated data for 2011-12
  - Magnitude of risk consistent with risk observed in 2010-11
  - No increased risk in children 24-59 months old

Guillain-Barré syndrome (GBS)

- Temporally associated GBS cases following influenza vaccination have been observed/reported; gastrointestinal and upper respiratory infections are known risk factors
- No disproportionate reporting for GBS following TIV or LAIV in VAERS data mining for 2011-12 (same for 2010-11)*
- No elevated risk for GBS following TIV or LAIV in VSD surveillance of automated data for 2011-12 (same for 2010-11)

* A/California/7/09 (H1N1) strain included in 2010-11 and 2011-12 vaccines

2009 H1N1 vaccine and GBS

- "End of season" analyses for GBS following 2009 H1N1 inactivated monovalent vaccine
  - Small statistically significant increased risk observed in some surveillance systems
  - Variable results across surveillance systems and when using different study methodologies
- When sample size was large enough to detect a small increased risk, risk for GBS following 2009 H1N1 inactivated monovalent vaccine was similar to risk observed for U.S. seasonal TIV in some past seasons*†;
- But substantially lower than risk observed following 1976 swine influenza vaccine

* Lasky et al. The Guillain-Barré syndrome and the 1992-1993 and 1993-1994 influenza vaccines. N Engl J Med. 1998;339:1797-802.
† Juurlink et al. Guillain-Barré syndrome after influenza vaccination in adults: a population-based study. Arch Intern Med. 2006;166:2217-21

Summary of GBS results from U.S. 2009 H1N1 vaccine safety surveillance systems*

Vaccine safety system	Study design†	RR/OR (95% CI)	Risk Diff (95% CI) Additional cases per million doses
EIP GBS surveillance	Unvaccinated control	1.57 (1.02, 2.21)	0.74 (0.04, 1.56)
	Self control (var. window)	2.1 (1.2, 3.5)	1.5 (0.3, 3.4)
	Self control (fixed window)	3.0 (1.4, 6.4)	2.8 (0.6, 7.4)
VSD	Self control	4.4 (1.3, 14.2)	5.0 (0.5, 9.5)
	Case-centered	2.0 (0.5, 8.1)	3.4 (-6.4, 7.6)
PRISM	Self control	2.50 (0.42, 15.0)	Estimated at 2-3 additional cases per million doses
	Case-centered	1.15 (0.07, 18.6)	
CMS	Self control	2.41 (1.14, 5.11)	2.84 (0.21, 5.48)
DoD	Self control	1.90 (0.63, 5.72)	
VA	Historic control	3.89 (0.44, 14.04)	
	Self control	3.86 (0.00, ∞)^	

* Adapted from Vellozi at ICPE 2011 and Sandhu at VRBPAC 2011; † All cases chart confirmed;
^ Upper bound undetermined due to a small number of cases

Allergy/anaphylaxis

- Recommendations for egg allergic patients updated for 2011-12*
- No disproportionate reporting for allergy or anaphylaxis following TIV or LAIV in VAERS data mining for 2011-12

Allergy/anaphylaxis reports in VAERS following influenza vaccination in egg allergic patients (2010-11 vs. 2011-12)

	2010-11 Vaccine type (N)	2011-12 Vaccine type (N)
Non-anaphylactic allergic reaction	TIV (15) LAIV (0)	TIV (15) LAIV (1)
Anaphylaxis	TIV (3) LAIV (0)	TIV (0) LAIV (1)†

* http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6033a3.htm

† Patient was an 8 year old child with egg allergy, other known food allergies and atopic dermatitis who ate eggs the morning of vaccination, prior to vaccination; had been eating eggs several times a week for several weeks prior as part of allergist recommended desensitization protocol

High-dose and intradermal TIV

- High-dose TIV (2011-12) – 2nd season of use
  - 600 VAERS reports after high-dose TIV (88% non-serious)
    - During 2010-2011 VAERS received 672 reports after high-dose TIV (91% were non-serious)
  - No new safety concerns identified
- Intradermal TIV (2011-12) – 1st season of use
  - 51 VAERS reports after intradermal TIV (96% non-serious)
  - No safety concerns identified

Note: Review includes U.S. reports only. Serious report is defined as life threatening or resulting in death, permanent disability, hospitalization, or extension of an existing hospitalization

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Thank You

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