



Kaiser Permanente Surveillance

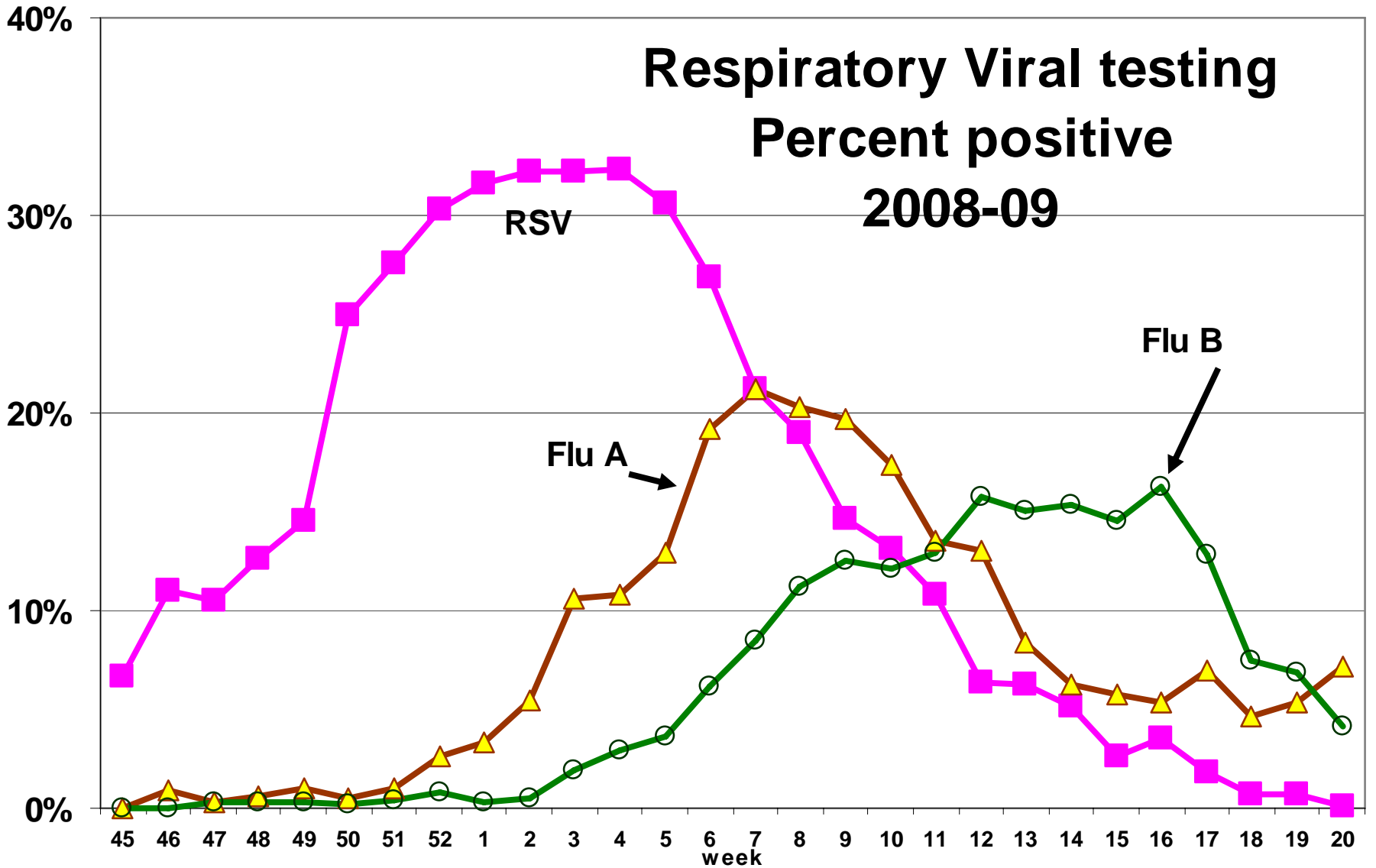
Roger Baxter, MD
Kaiser Permanente
Vaccine Study Center



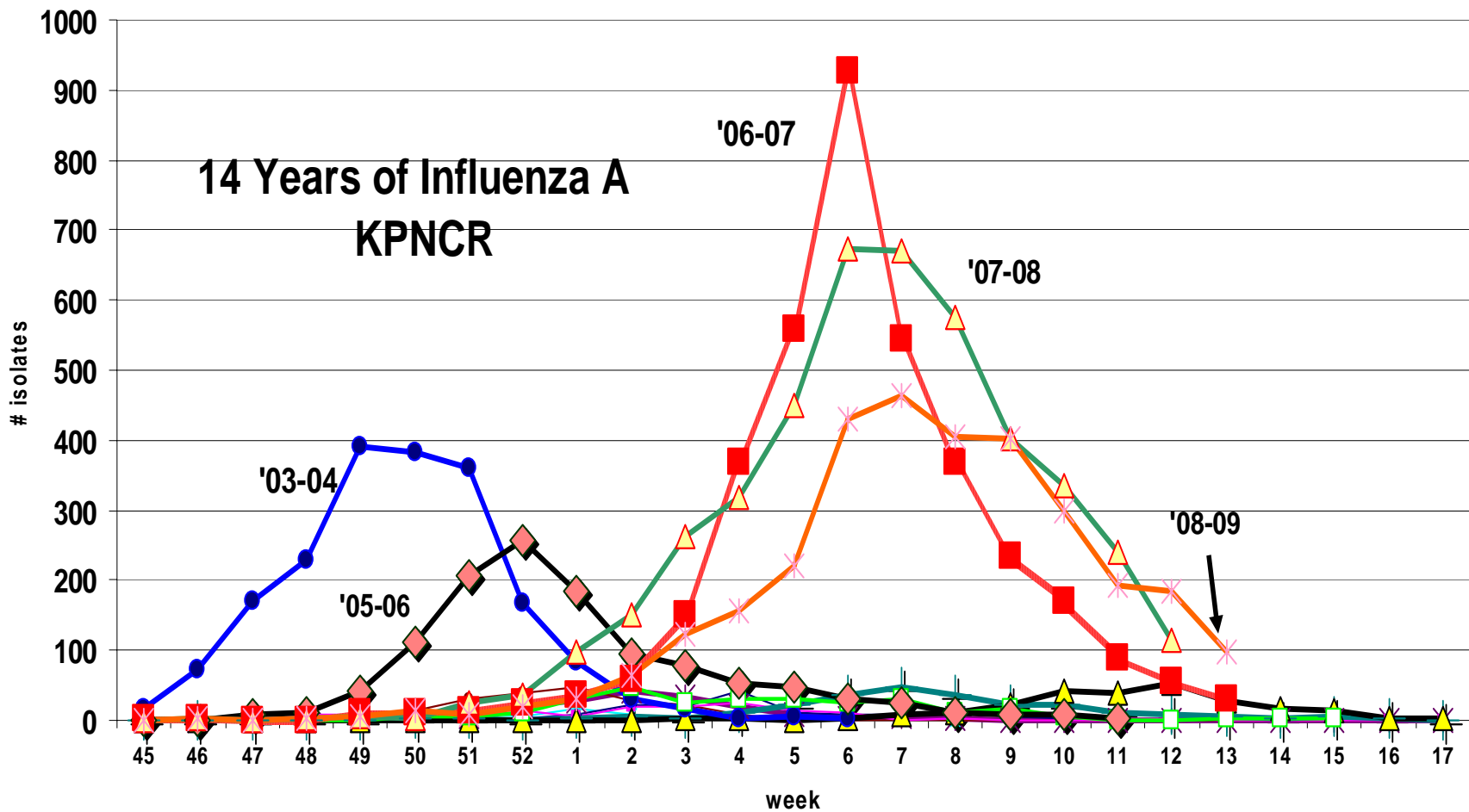
Since 1996, KP has been following Influenza and RSV isolates

- 1996-2005: Direct Fluorescent Antibody (DFA) and culture
- Beginning in 2006: RT-PCR for RSV, Flu A and B
- Lab data is collated weekly (Sat-Sun)

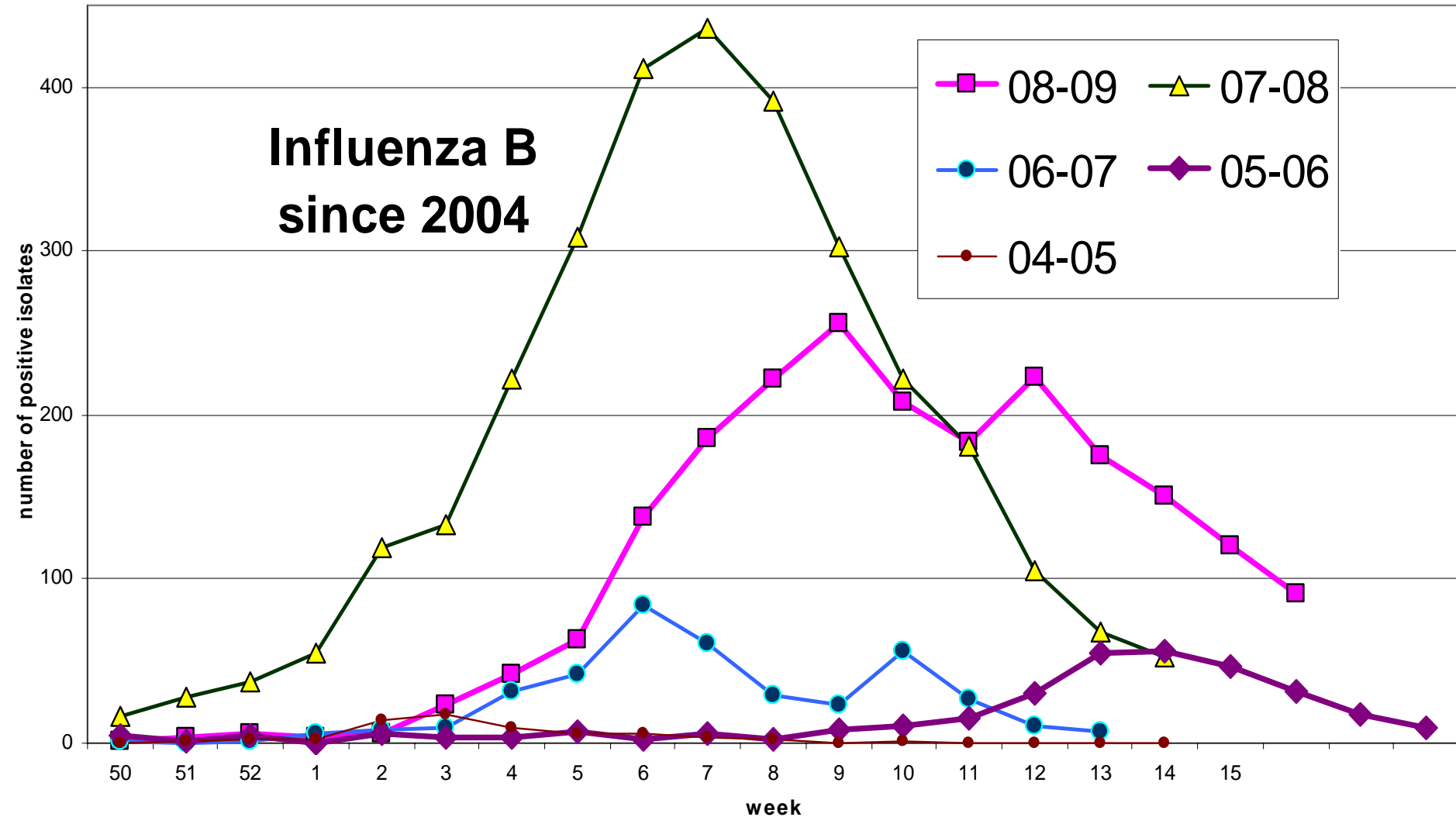
Respiratory Viral testing Percent positive 2008-09



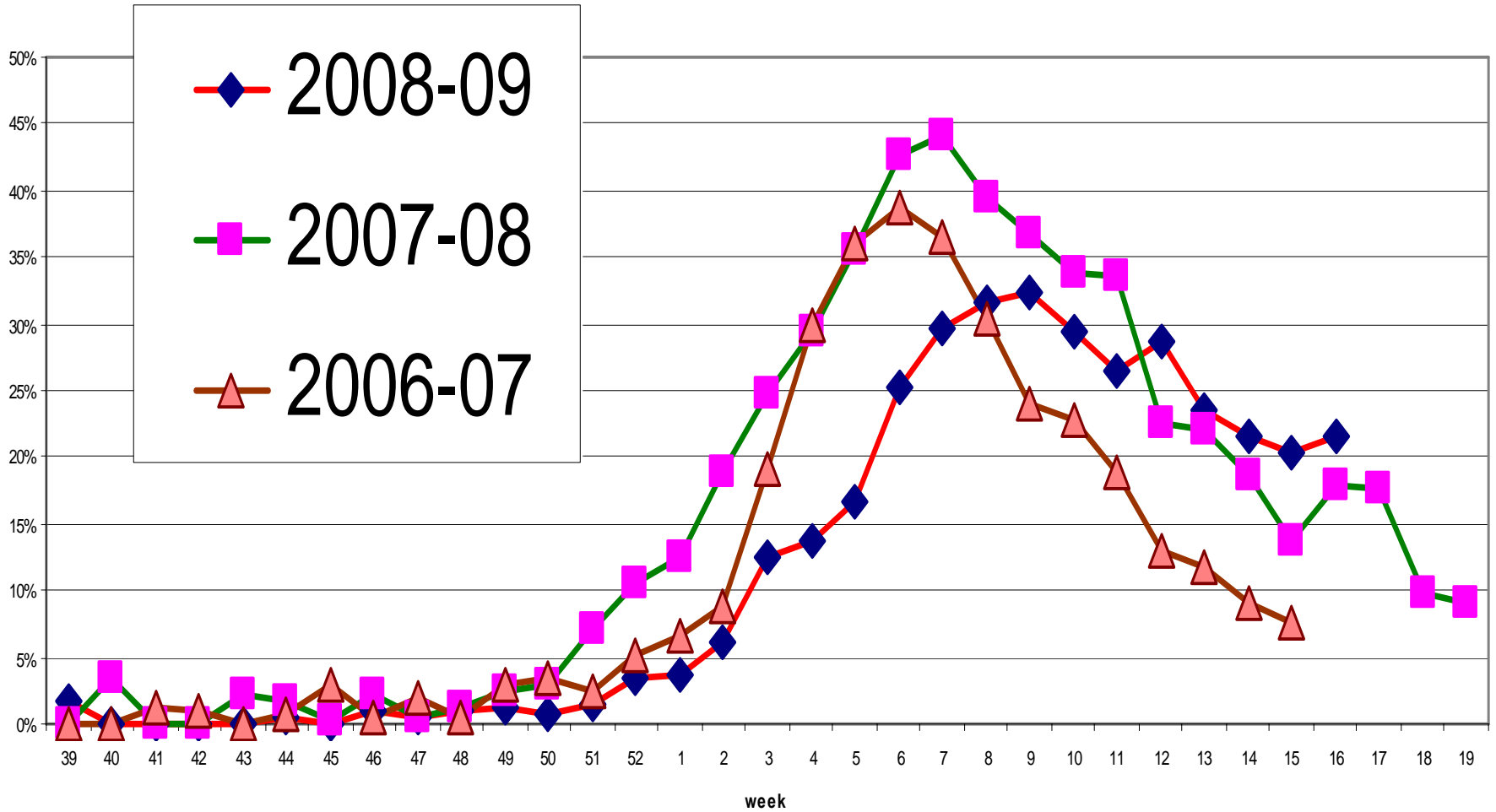
14 Years of Influenza A KPNCR



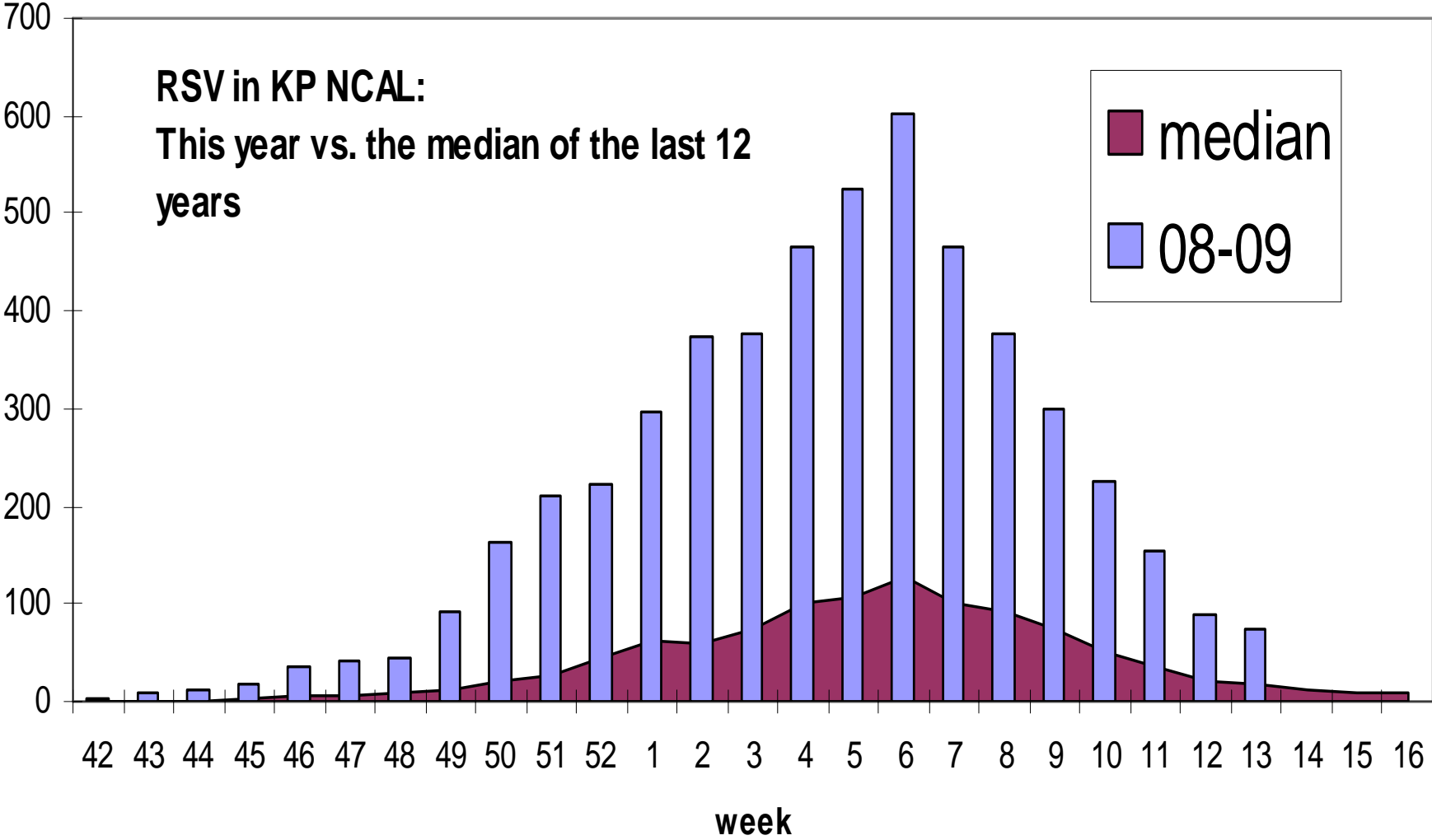
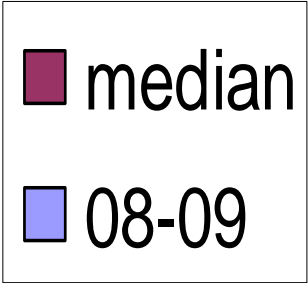
Numbers positive per week



Flu A + B percent positive 2006-09

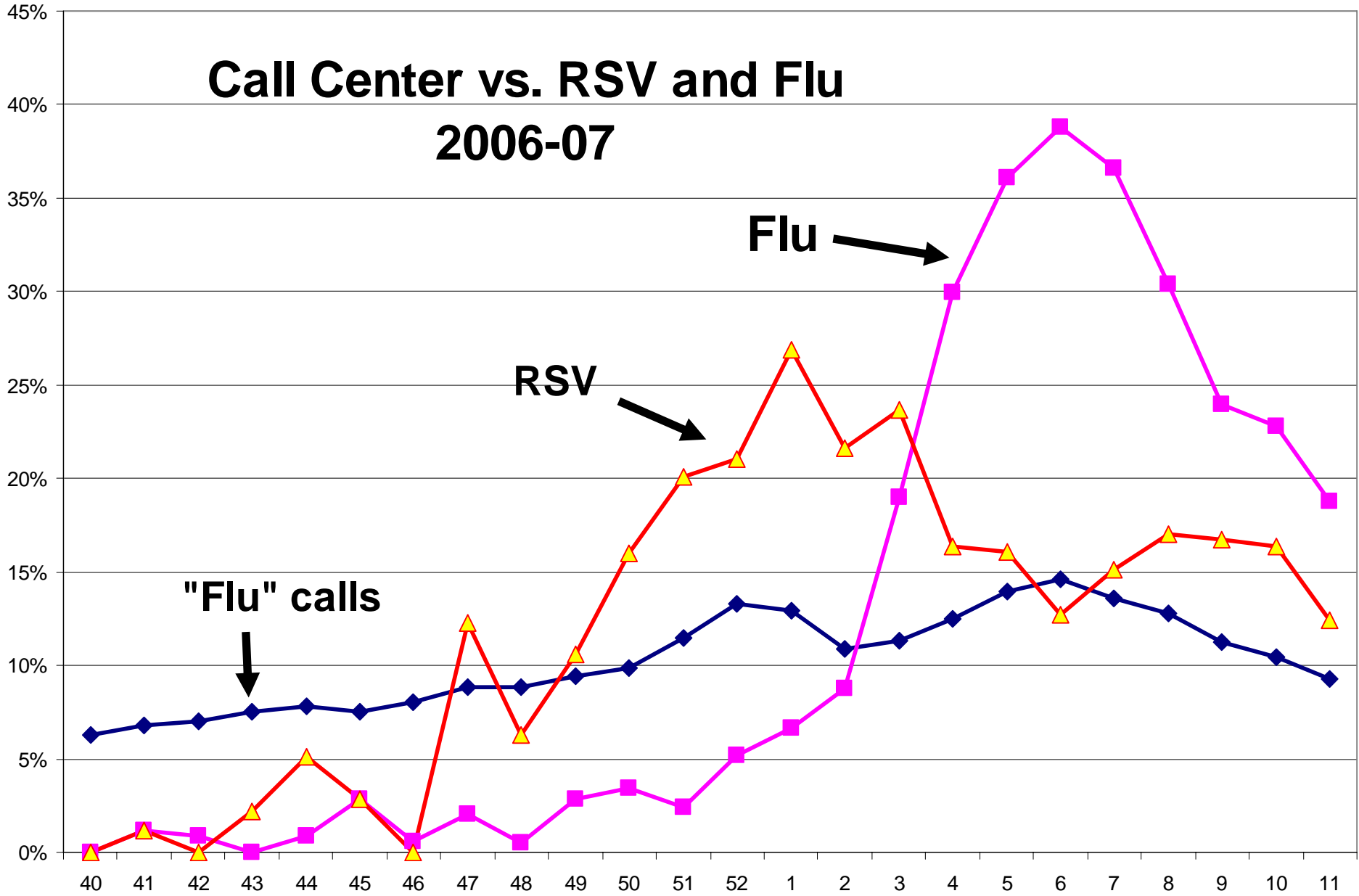


**RSV in KP NCAL:
This year vs. the median of the last 12
years**

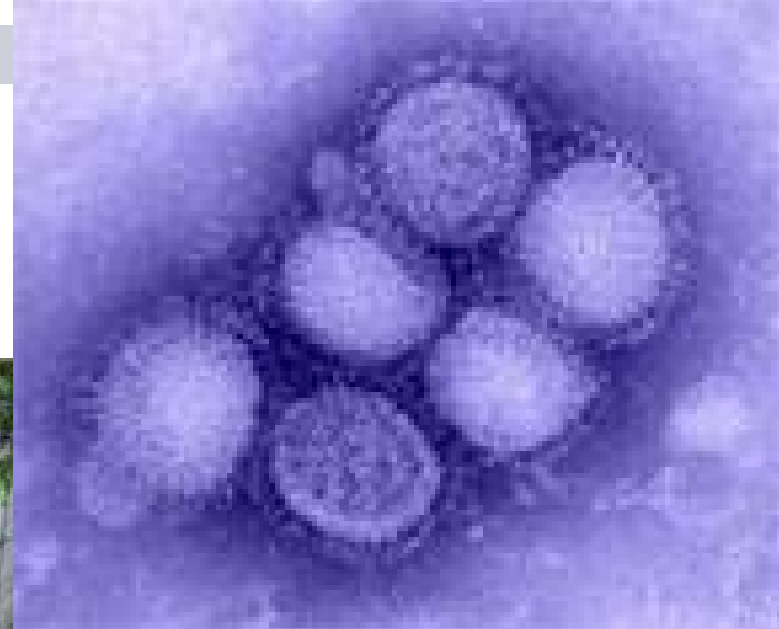


Call Center vs. RSV and Flu

2006-07

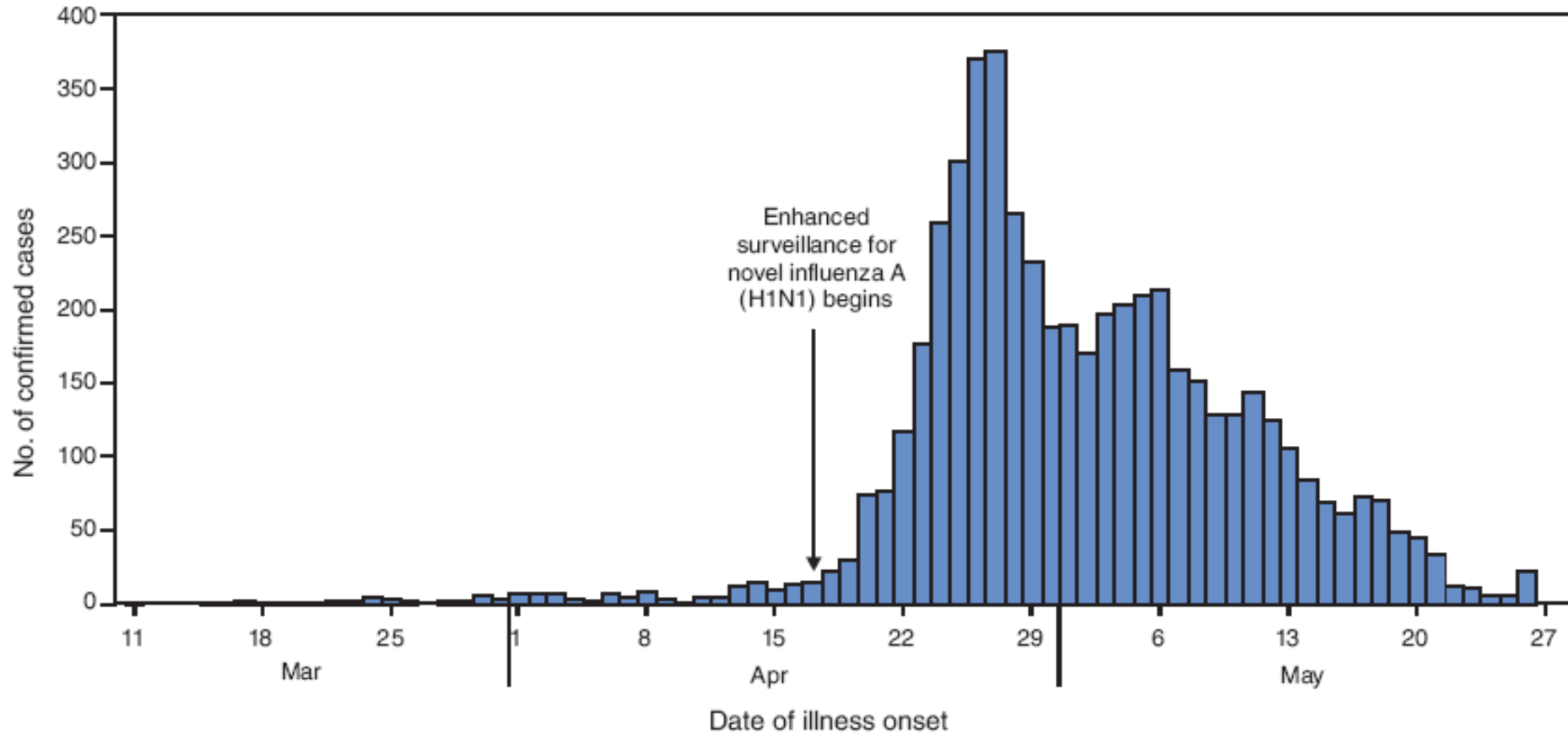


Swine flu



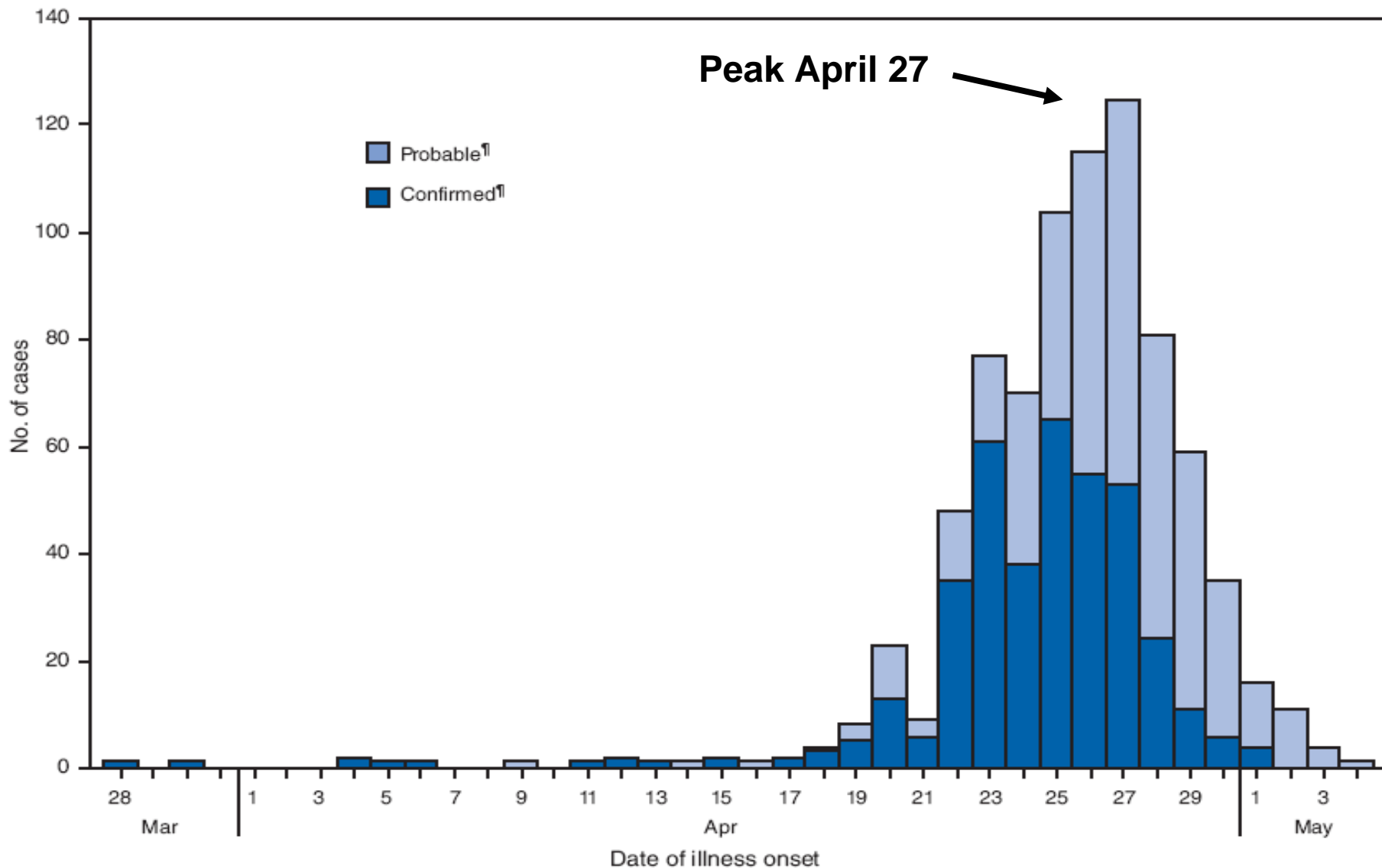
Mexican outbreak of Swine H2

FIGURE 2. Number (N = 5,305) of laboratory-confirmed cases of novel influenza A (H1N1) virus infection,* by date of illness onset — Mexico, March–May 2009

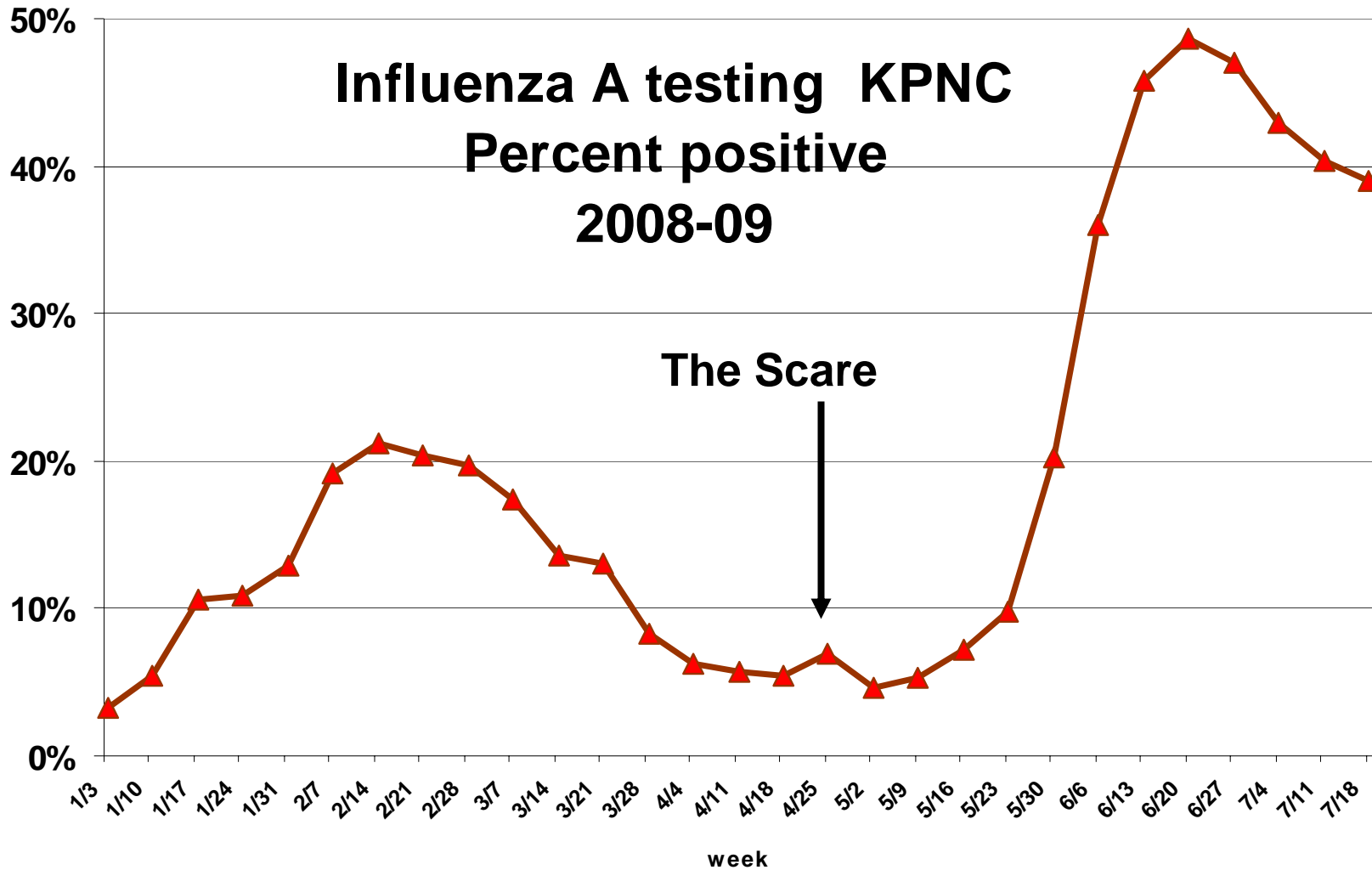


Swine Flu in US April 2009

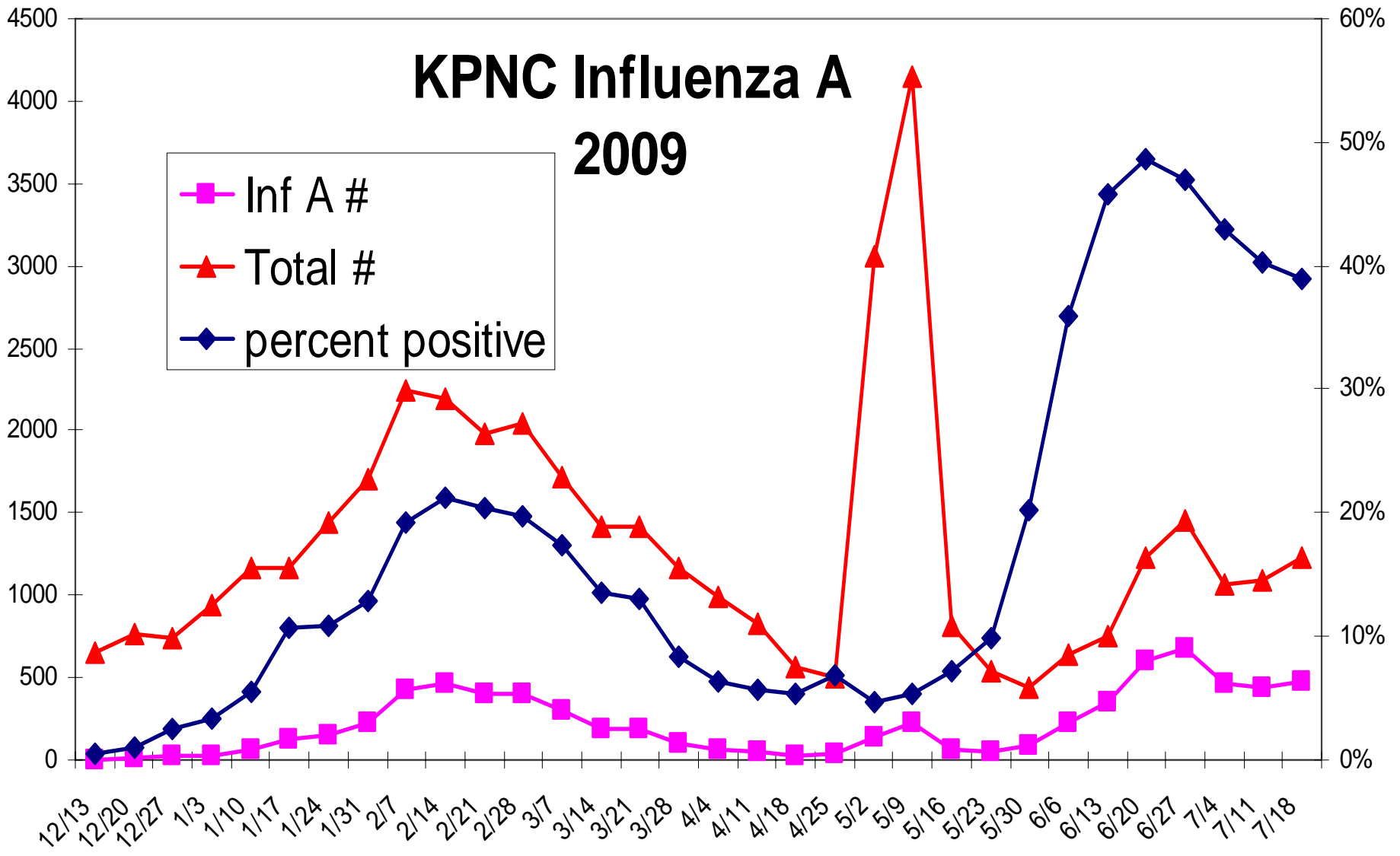
FIGURE 2. Number of confirmed (N = 394)* and probable (N = 414)[†] cases of novel influenza A (H1N1) virus infection with known dates of illness onset — United States, March 28–May 4, 2009[§]



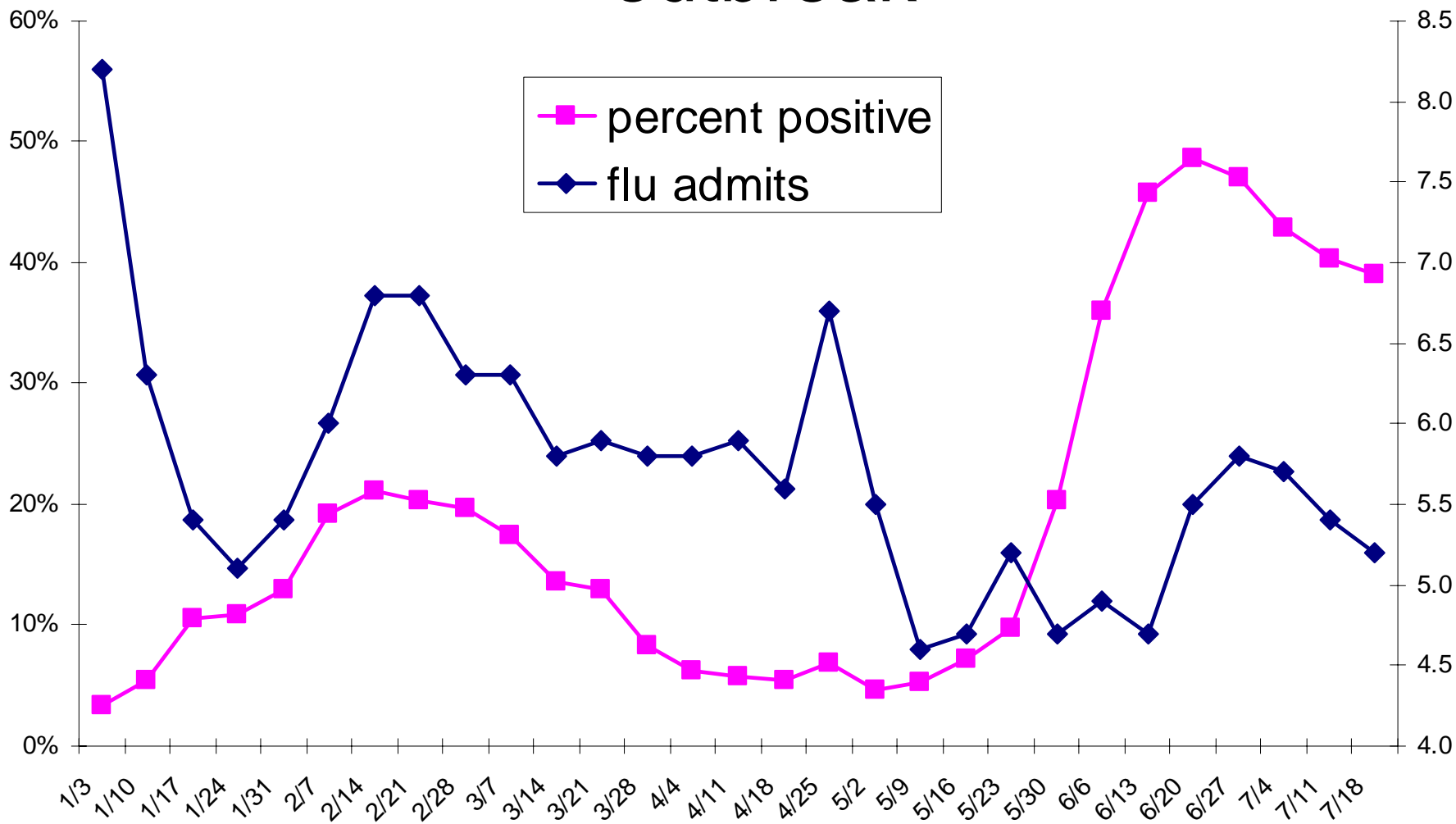
Flu during the Swine outbreak (KP NCAL)



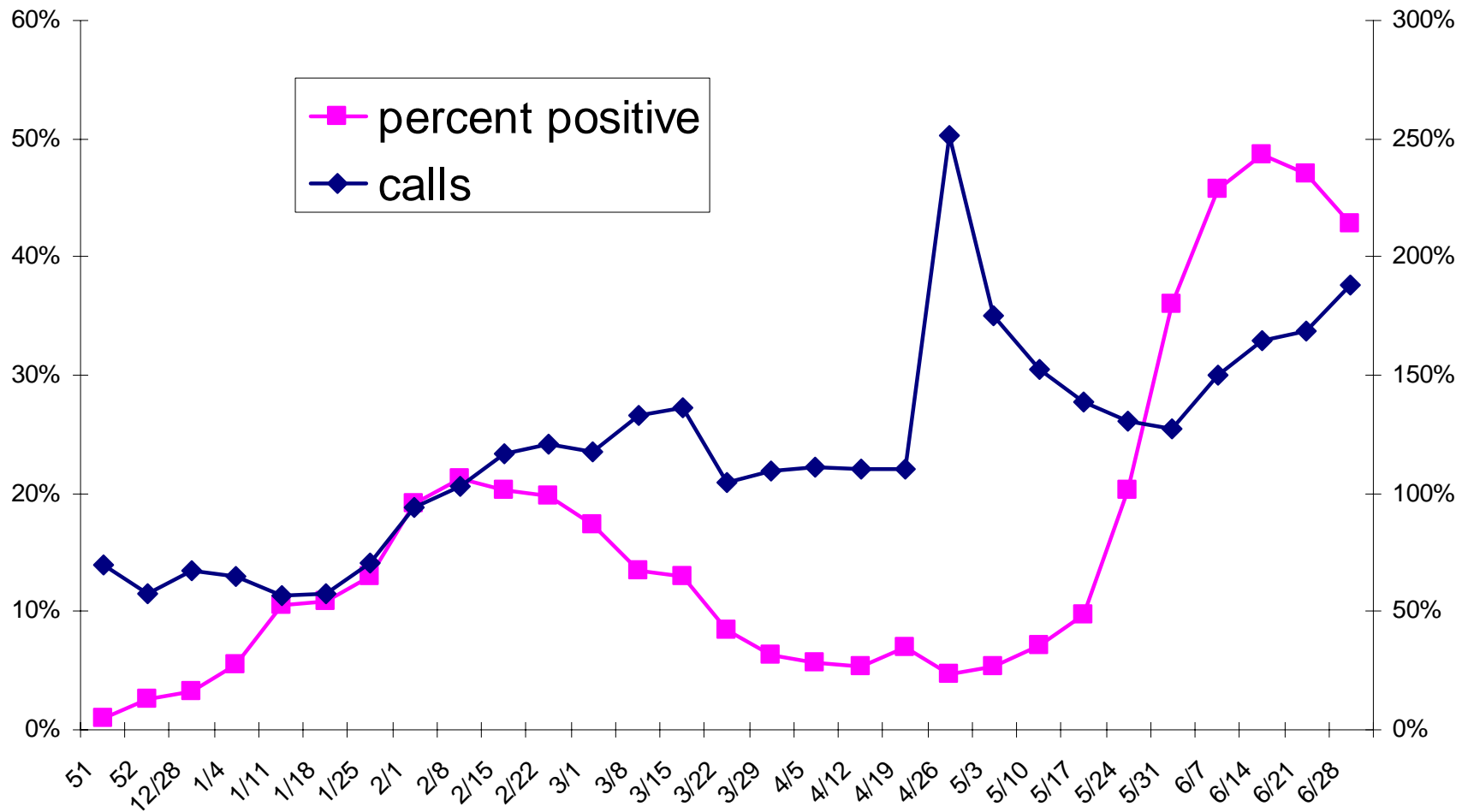
Pandemic H1 2009



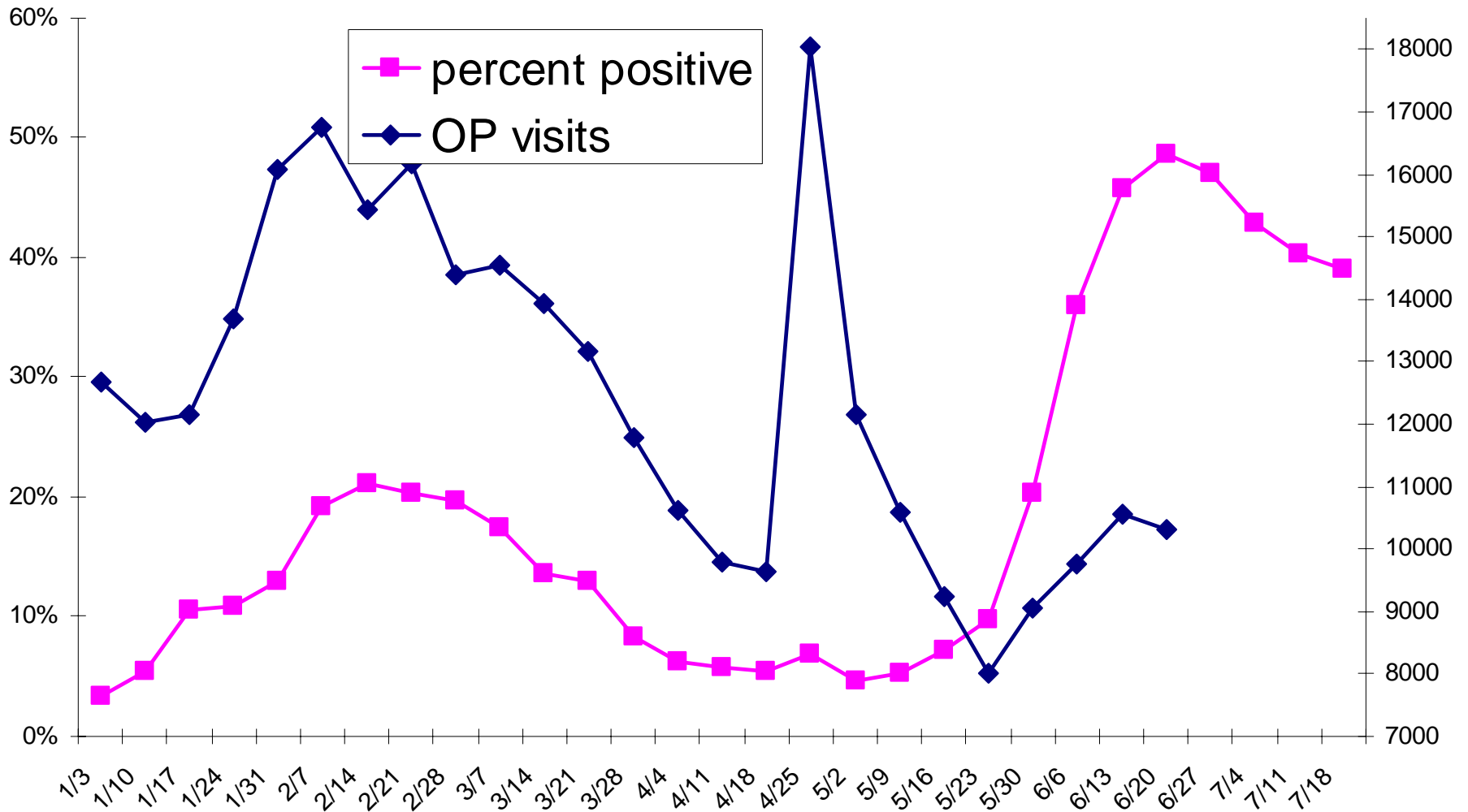
Percent of Hospital admissions from pneumonia and influenza during Swine outbreak



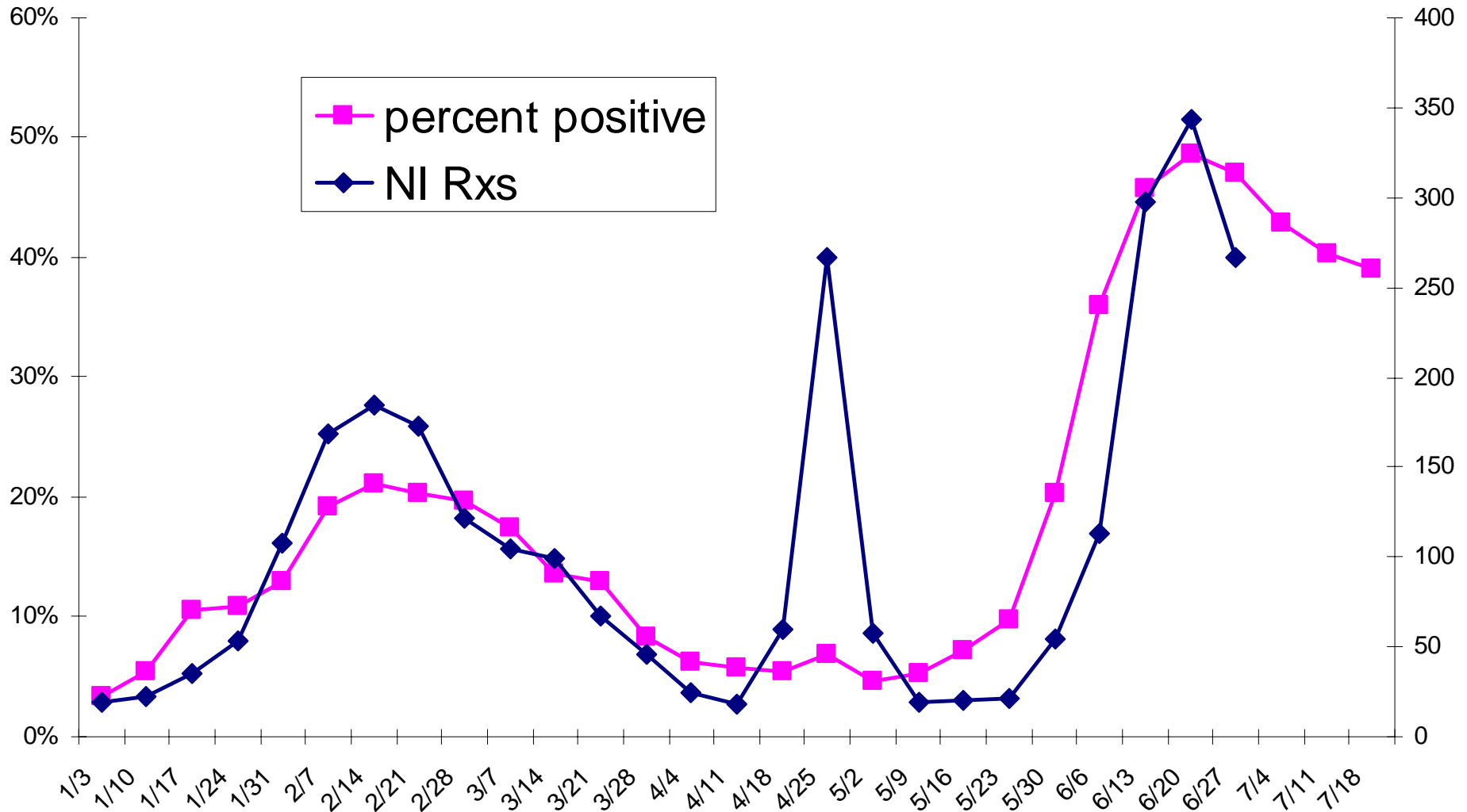
Calls to Kaiser about flu



Outpatient medical visits for fever, URI, and influenza

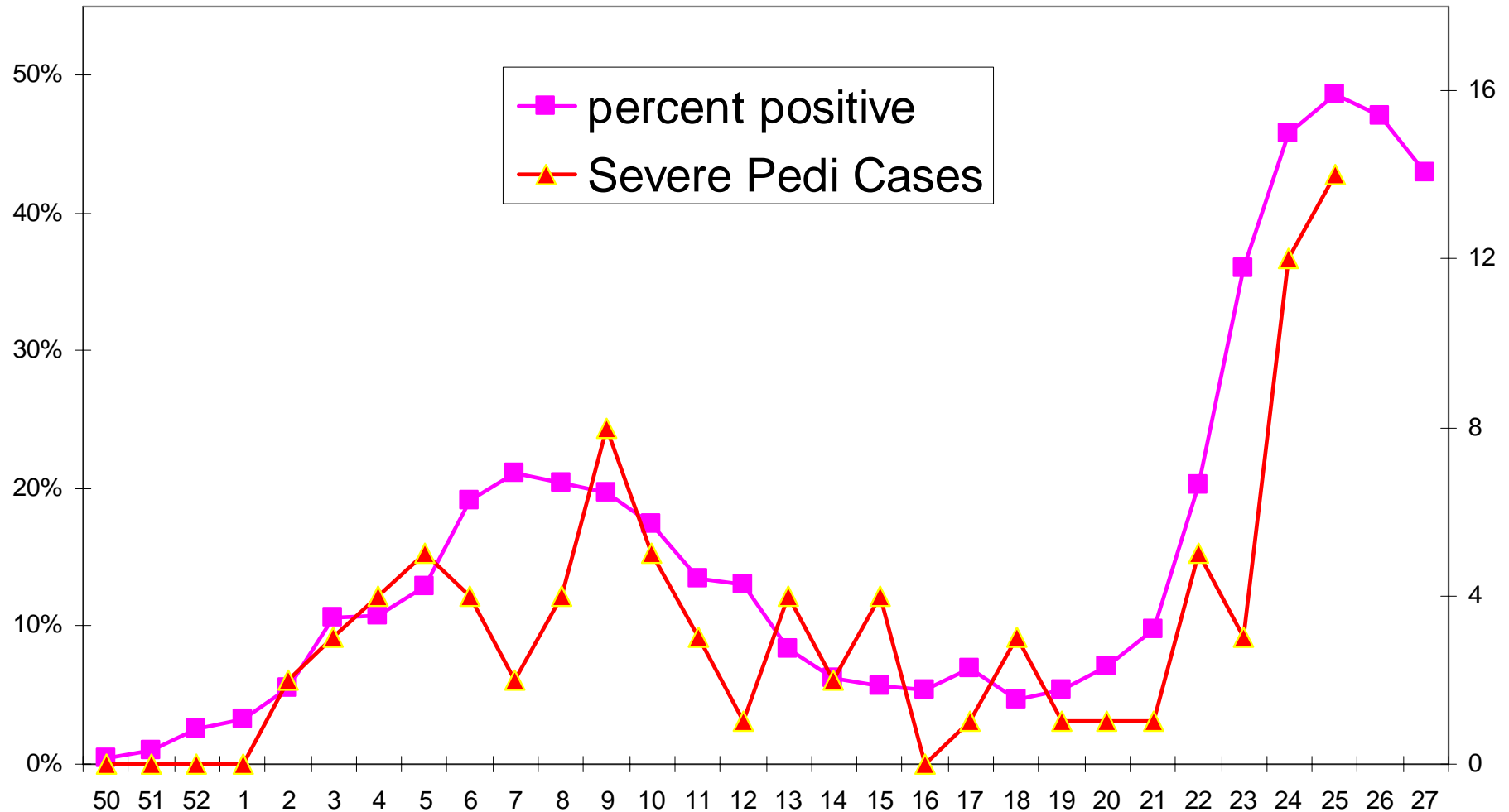


Neuraminidase use in KPNC 2009



Severe Pediatric Influenza in CA

(thanks to Janice Louie and Cynthia Jean at DPH)





Conclusions

- Laboratory and utilization data can track influenza outbreaks
- Utilization data (call, visits, drugs and hospitalizations) are highly susceptible to public concerns about virulence



Subtyping is extremely helpful, but there are limited resources.

- Planning is underway to determine the best way to use our surveillance for the possibility of a pandemic later this year.
 - Limit testing
 - Limit subtyping
 - Treat based on epidemiology



Does the Flu Vaccine prevent death in the Elderly?: a new approach

**Bruce Fireman, Janelle Lee, Ned Lewis
Roger Baxter**




Vaccine Study Center





Conflicts of interest

- Roger Baxter receives research grants from Sanofi Pasteur, GSK, MedImmune, Novartis, and Protein Sciences



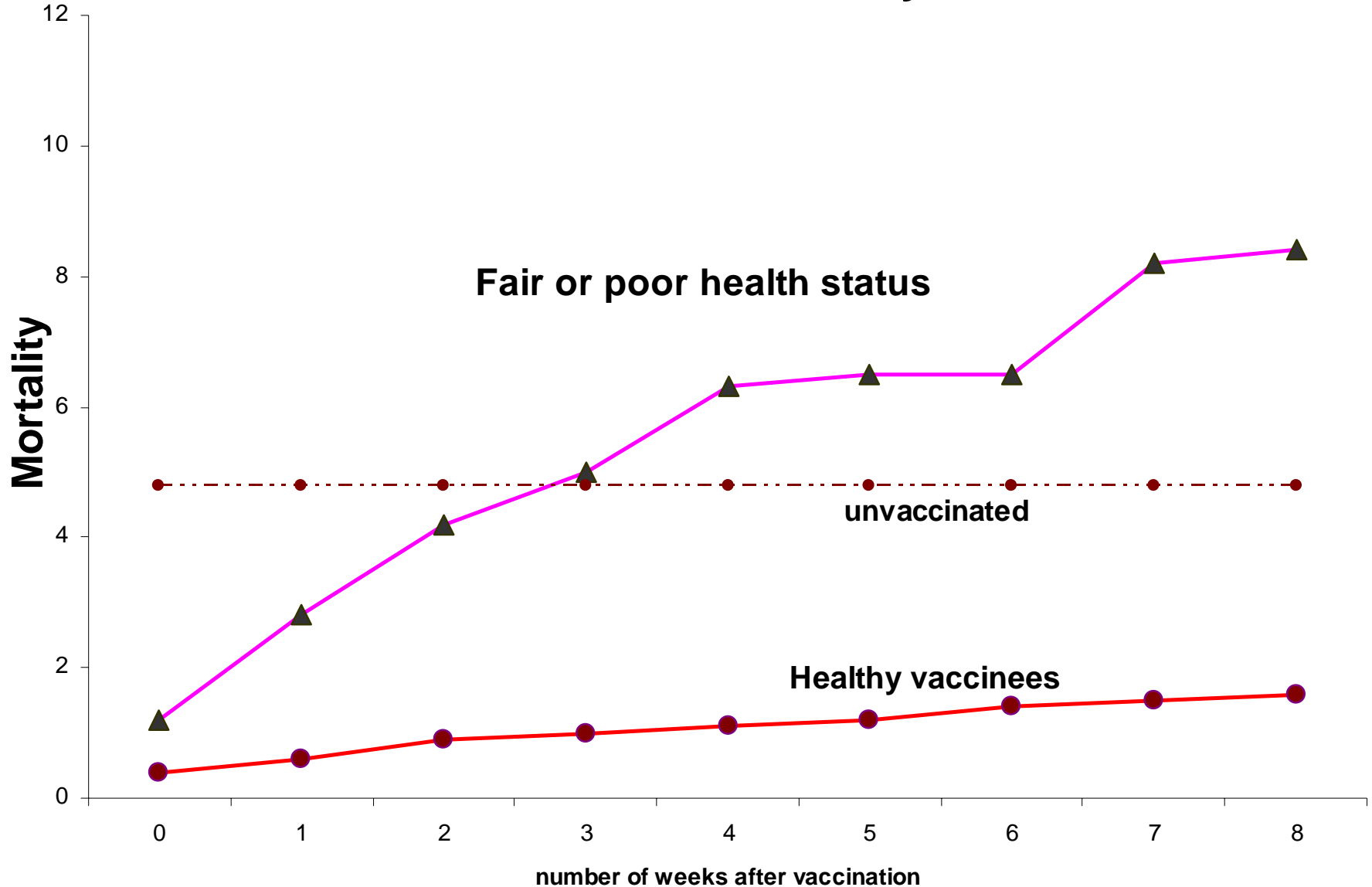
How well does the flu vaccine prevent mortality in the elderly?


- No good randomized controlled studies
- Observational studies show effectiveness over 50%
- This is not plausible, as excess flu mortality is only about 10% overall
- Overestimates are probably due to selection bias

Usual observational studies

- Compare mortality in vaccinated vs. unvaccinated, and adjust for potential confounders
- We look at it differently: people who die were unlikely to have gotten the vaccine.
- This makes the vaccine look great, but may reflect differences in vaccinated vs. unvaccinated rather than vaccine effectiveness

Can selection bias be overcome by adjusting for confounders? Probably not



- 
- Mortality rises in a similar slope after vaccination, in healthy and unhealthy people.
 - This trend upwards means selection bias is constantly changing, and would be very difficult to overcome with adjustment.

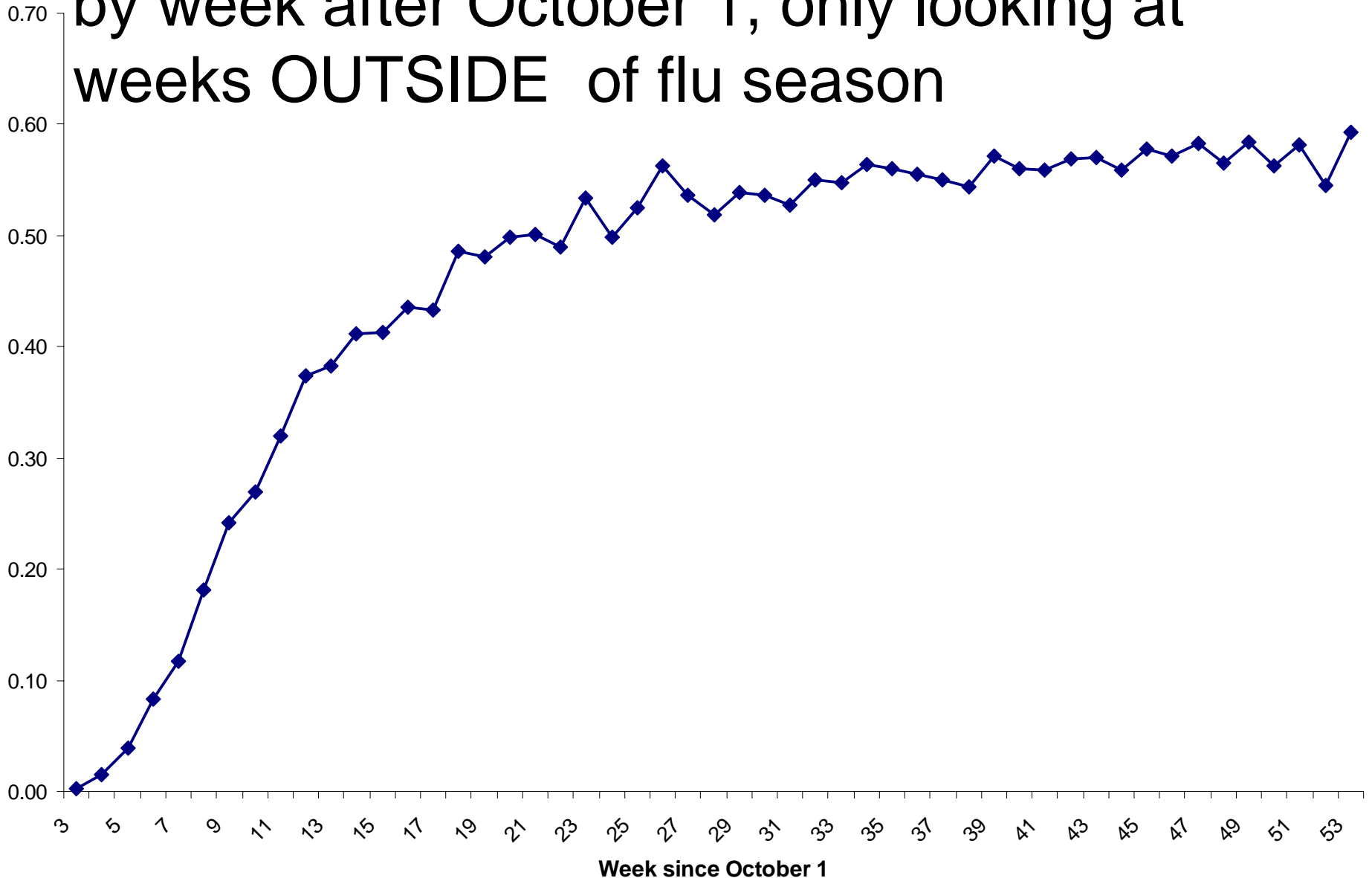


We tried a new approach:

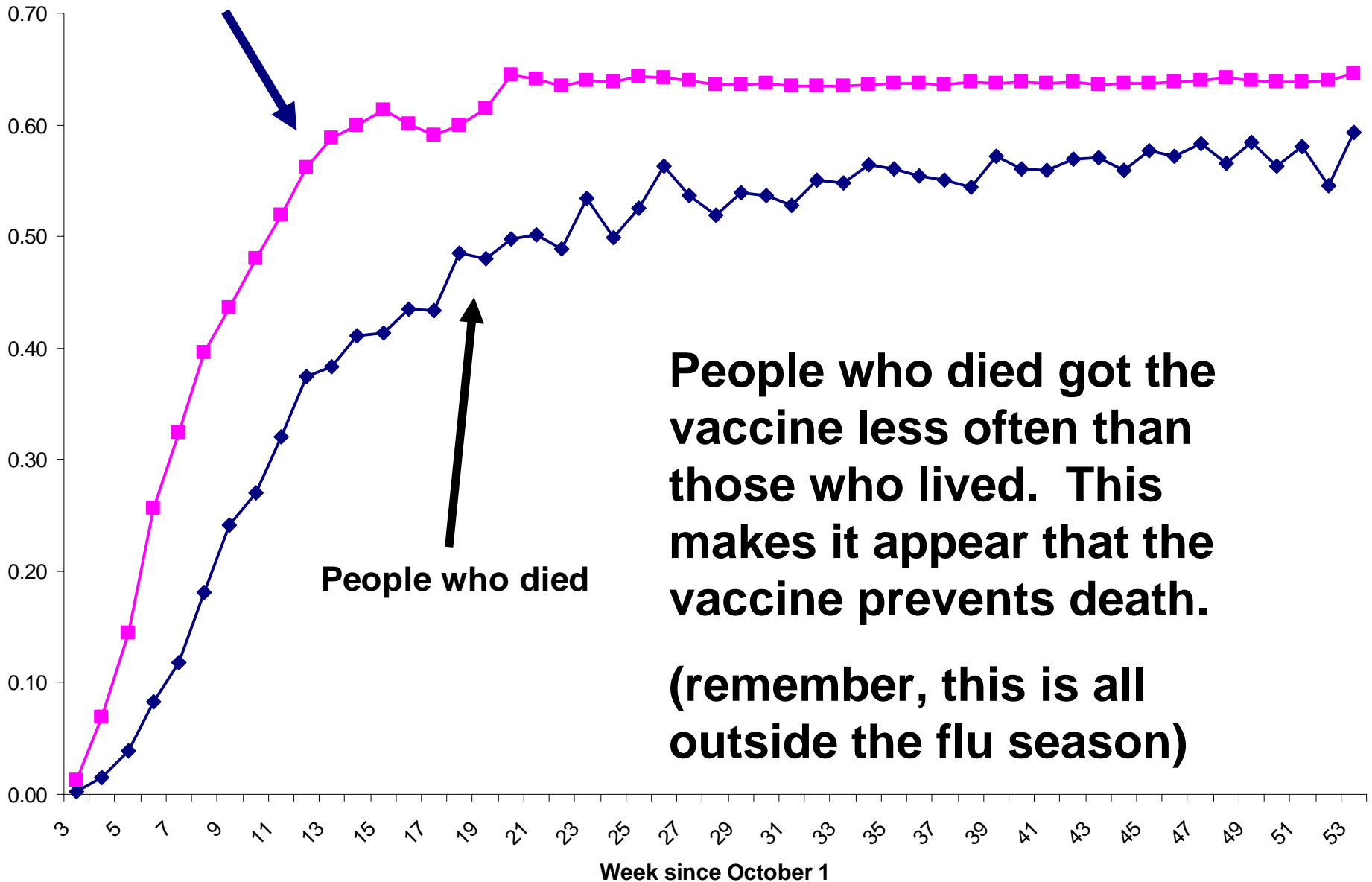
Difference-in-differences method

- We traced the trajectory of apparent “VE” when flu is not circulating, and adjusted for it.
- “Vaccine effectiveness” during these times is actually a measure of selection bias.

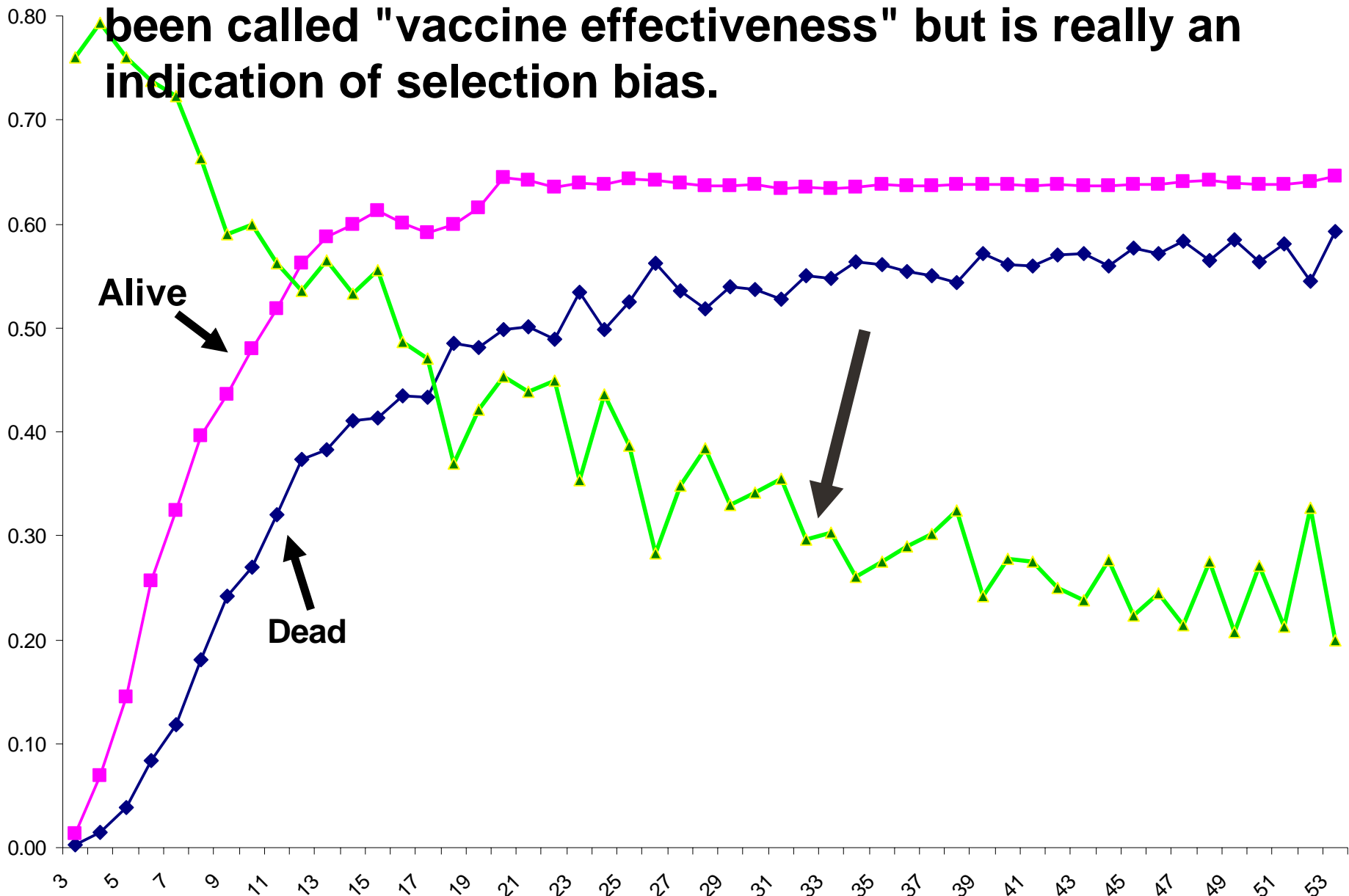
Proportion of decedents vaccinated by week after October 1, only looking at weeks OUTSIDE of flu season



Proportion of living people vaccinated (age and sex matched to those who died).



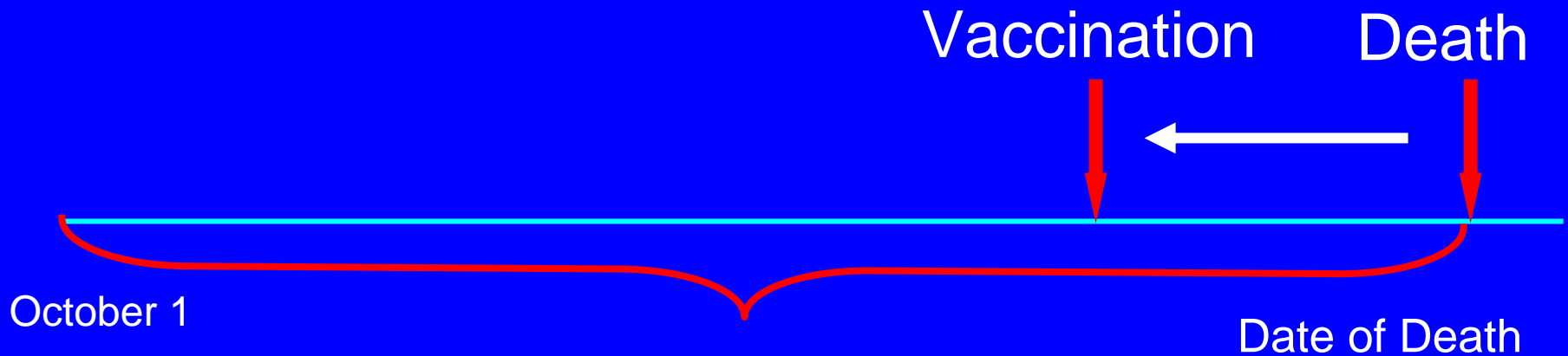
The difference between dead and alive person vaccination rates OUTSIDE FLU SEASON. This has been called "vaccine effectiveness" but is really an indication of selection bias.



Case-centered method

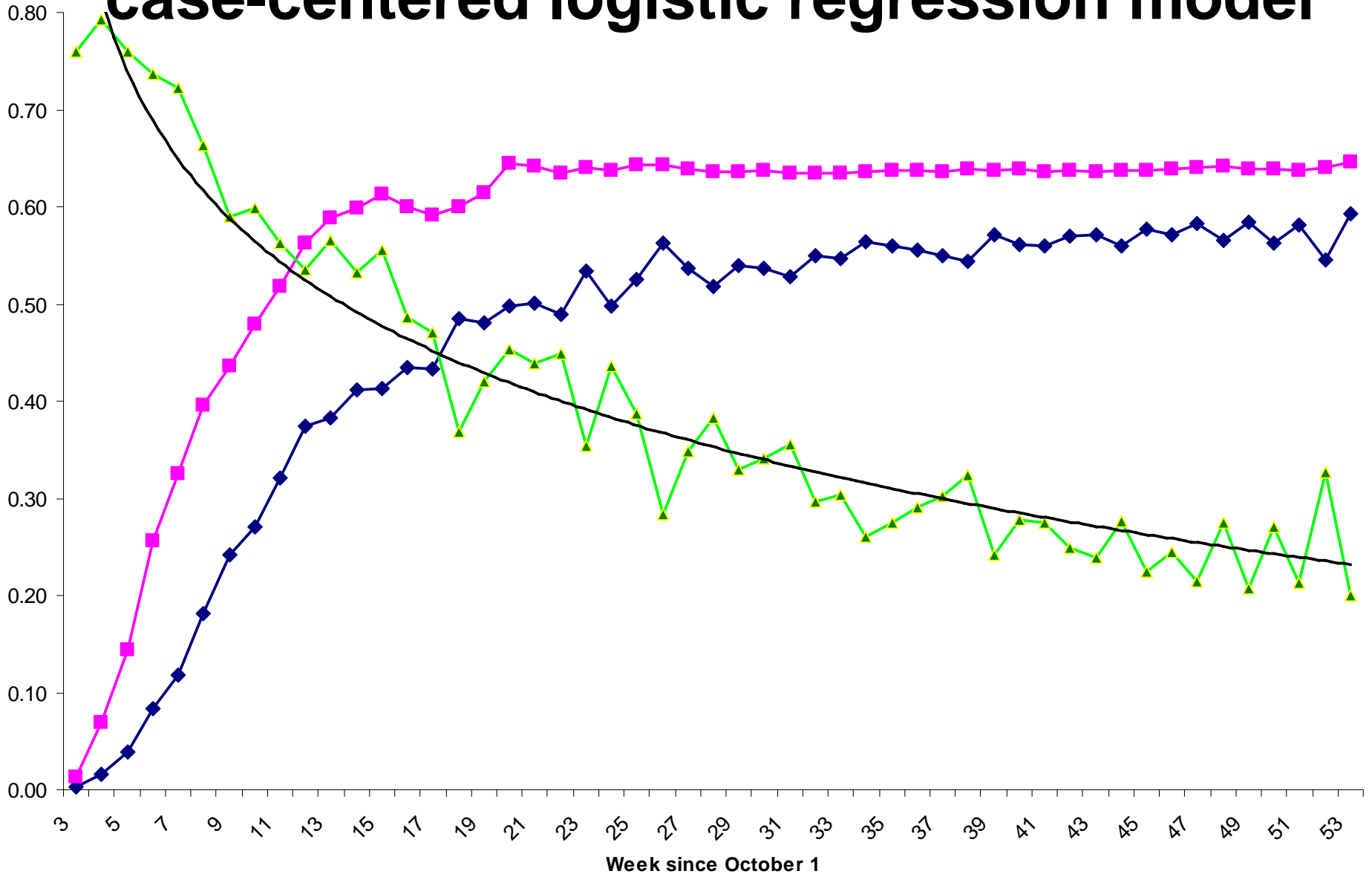
- We fit a logistic regression model to the dataset with one record for each death
- Compares odds of vaccination in decedents to the odds expected based on survivors

Case-centered method simplified

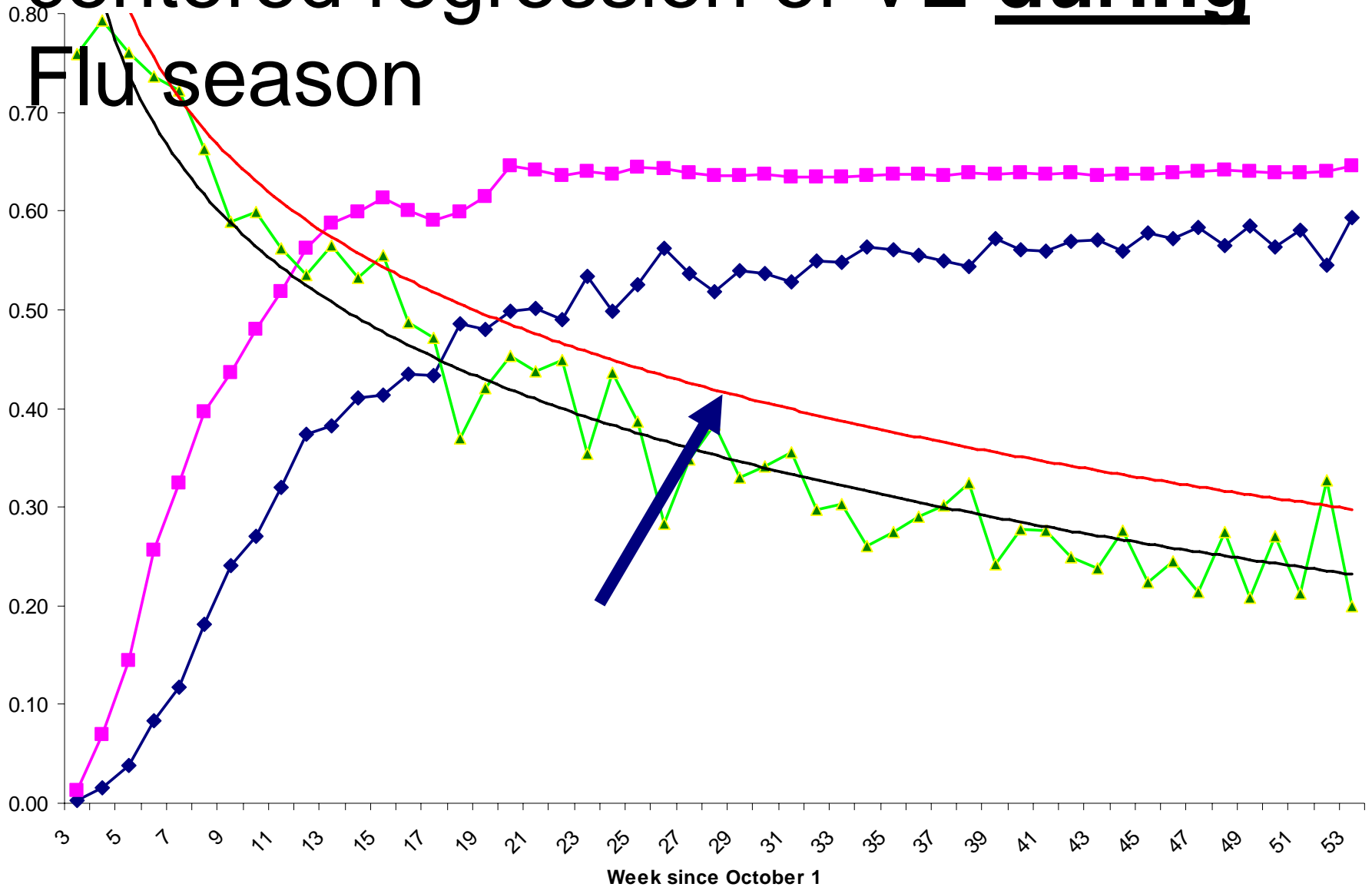


- Was the decedent vaccinated?
- What was vaccine coverage in her age/sex group?

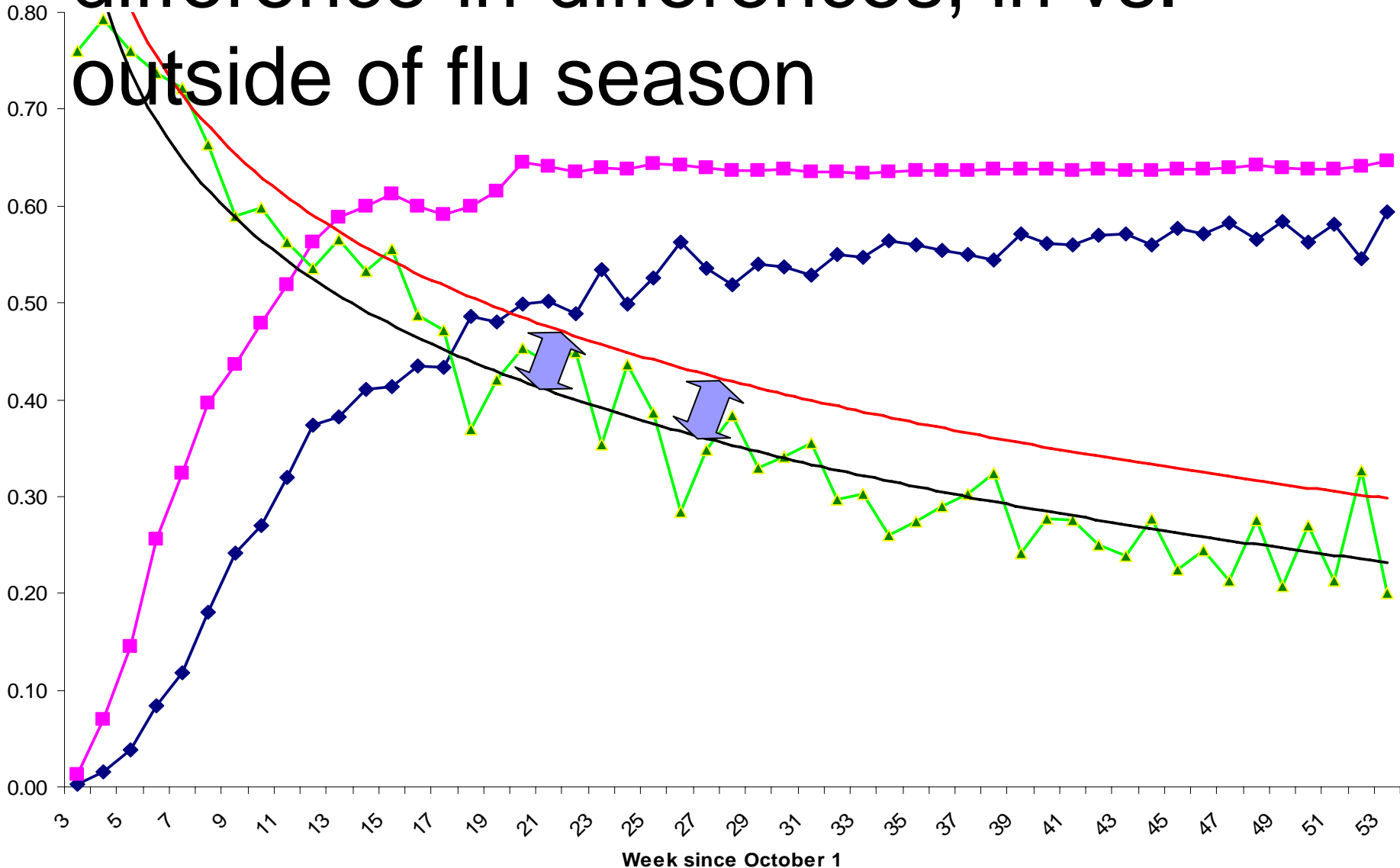
The smooth curve is the "VE" fit to our case-centered logistic regression model



The upper curve is the case-centered regression of VE during Flu season



True Vaccine Effectiveness is the difference-in-differences, in vs. outside of flu season





Difference-in-differences

- This approach bypasses the attempt to adjust for confounding due to underlying morbidity or frailty.
- Instead we focus on the difference in vaccine effect inside vs. outside the flu season.

Flu Vaccine effectiveness in people over 65

Cause of death	Age Group	N of Deaths	VE (%)	95% CI for VE (%)	<i>P</i> value
All causes	65 & up	61,436	4.6	0.7, 8.3	0.0212
All causes	65-79	29,743	5.3	-0.3, 10.6	0.0641
All causes	80 & up	31,693	3.9	-1.6, 9.0	0.1606
CVD or Respiratory	65 & up	31,798	8.5	3.3, 13.4	0.0017
Other causes	65 & up	29,638	0.1	-5.9, 5.8	0.9632

4.6% seems low

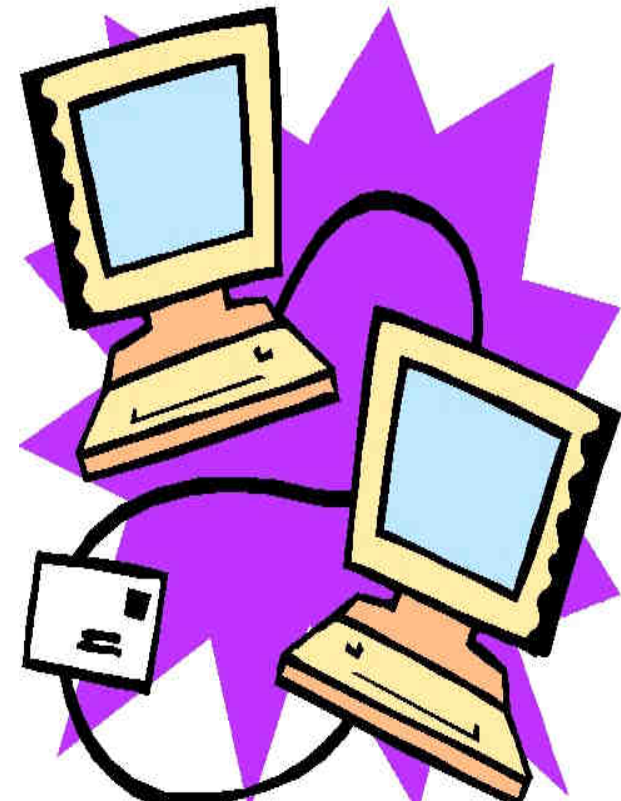
- Estimate of excess mortality due to influenza in KP: 7.8%, but we are vaccinating 63% of the population.
- If we weren't vaccinating anybody, then excess mortality would be about 10%.
- If excess mortality is truly 10% (in a bad season), then 4.6% overall means that flu vaccine prevents approximately 46% of all excess deaths ***that can be attributed to influenza.***



Supplemental slides

Kaiser Permanente and the Vaccine Safety Datalink (VSD)

- A collaboration between CDC and 8 managed care organizations
- Enrollment of over 8 million
 - Over 2% of the American population



VSD Principal Investigators At MCOs

Northwest KP, Portland OR

- Allison Naleway, PhD

Kaiser Permanente NCAL, Oakland CA

- Roger Baxter, MD
- Nicky Klein, MD, PhD

UCLA /SCAL Kaiser Permanente, CA

- Steven Jacobsen, MD, PhD
- S. Michael Marcy, MD
- Marlene Lugg, Dr.Ph

Group Health Cooperative, Seattle WA

- Lisa Jackson, MD, MPH

Marshfield Clinic Rsch. Foundation Marshfield WI

- Edward Belongia, MD

Health Partners Rsch Foundation Minneapolis MN

- Jim Nordin, MD

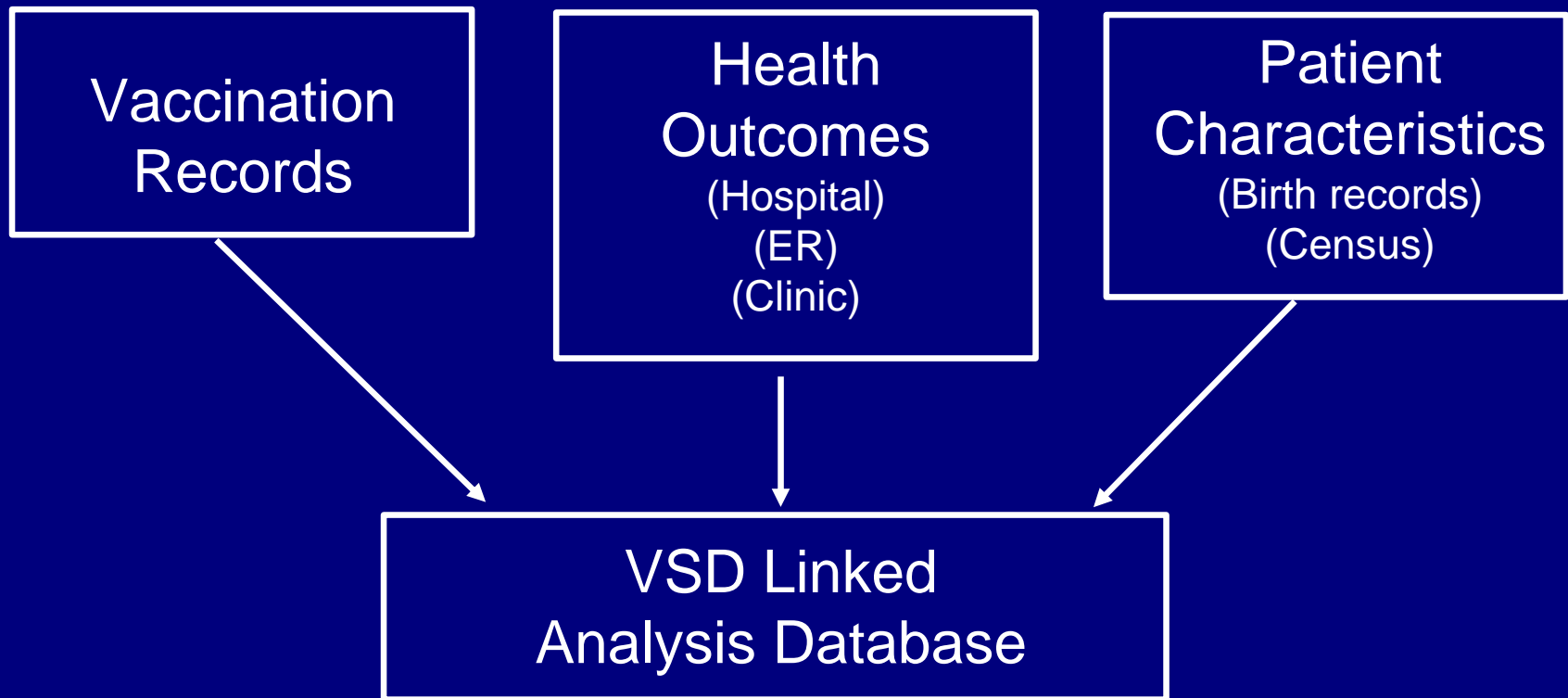
Kaiser Permanente of Colorado

- Simon Hambidge, MD, PhD
- Jason Glanz, MS, PhD

Harvard Pilgrim Boston MA

- Tracy Lieu, MD, MPH
- Richard Platt, MD, MSc

VACCINE SAFETY DATALINK (VSD) Overview





VSD Strategic Priorities

- Evaluate safety of:
 - newly licensed vaccines
 - new recommendations for existing vaccines
 - vaccines in high-risk populations
- Develop new methodologies for vaccine safety assessment
- Test hypotheses suggested by signals from VAERS



VSD Achievements:

Rapid Cycle Analysis

- Increased likelihood of febrile seizure 7-10 days after MMRV compared with MMR+V

Seizures within 42 days of Vaccine, 2000-2008
12-23 Months of Age



Other VSD Achievements:

- Confirmed association between RotaShield® and Intussusception
- No association between:
 - Hepatitis B vaccine and multiple sclerosis, optic neuritis, or RA
 - MMR and increased risk of IBD among children
 - Childhood vaccinations and type 1 diabetes

Rapid Cycle Analysis Studies

- Menactra
- Rotateq
- MMRV
- Tdap
- Flu vaccines
- HPV
- Zostavax





VSD - Strengths

- Large sample size
- Electronic medical records data available for epidemiology studies
- Can calculate incidence rates and attributable risks
- Relatively quick and timely



VSD - Limitations

- Dynamic cohorts – loss to follow up
- Expensive
- Not large enough for some hypotheses
- Difficult to study VAEs with delayed or insidious onset
- MCO members generally well-vaccinated so can be difficult to find unbiased controls