

Monitoring the Safety of the 2009 H1N1 Influenza Vaccine in Near Real-Time: Learnings from PRISM

Brookings Roundtable on Active Medical Product
Surveillance
October 22, 2010

Brookings Roundtable on Active Medical Product Surveillance

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Roundtable Agenda

- Dan Salmon, National Vaccine Program Office, U.S. Department of Health and Human Services
- Richard Platt, Department of Population Medicine, Harvard Medical School and Harvard Pilgrim Health Care Institute
- Robert Ball, Office of Biostatistics and Epidemiology, Center for Biologics Evaluation and Research, U.S. Food and Drug Administration
- Discussion and Questions

HHS Rapid Response to a Public Health Need: H1N1 Vaccine Safety Surveillance Using PRISM

Daniel A. Salmon, PhD, MPH
Director of Vaccine Safety
National Vaccine Program Office
U.S. Department of Health and Human Services

H1N1 Vaccine Safety: Microcosm of the Vaccine Safety Challenge

- Response to H1N1 is the largest mass vaccination program in recent history
 - Public concern regarding vaccine safety
 - Reported safety concerns include
 - Vaccine production was “rushed”
 - Vaccine “inadequately tested”
 - 1976 experience with Guillain-Barré Syndrome
-



Uncertainties in Planning Safety Monitoring for H1N1

- What type of vaccine would be used (adjuvanted or non-adjuvanted)
- How many doses would be needed
- Who would be high priority groups
- How vaccine would be distributed



National Vaccine Advisory Committee (NVAC) Recommendation for H1N1 Safety Monitoring

Enhance active surveillance
for signal confirmation and
evaluation of possible
associations between
vaccines and adverse events



Why Does Size Matter for Active Surveillance?

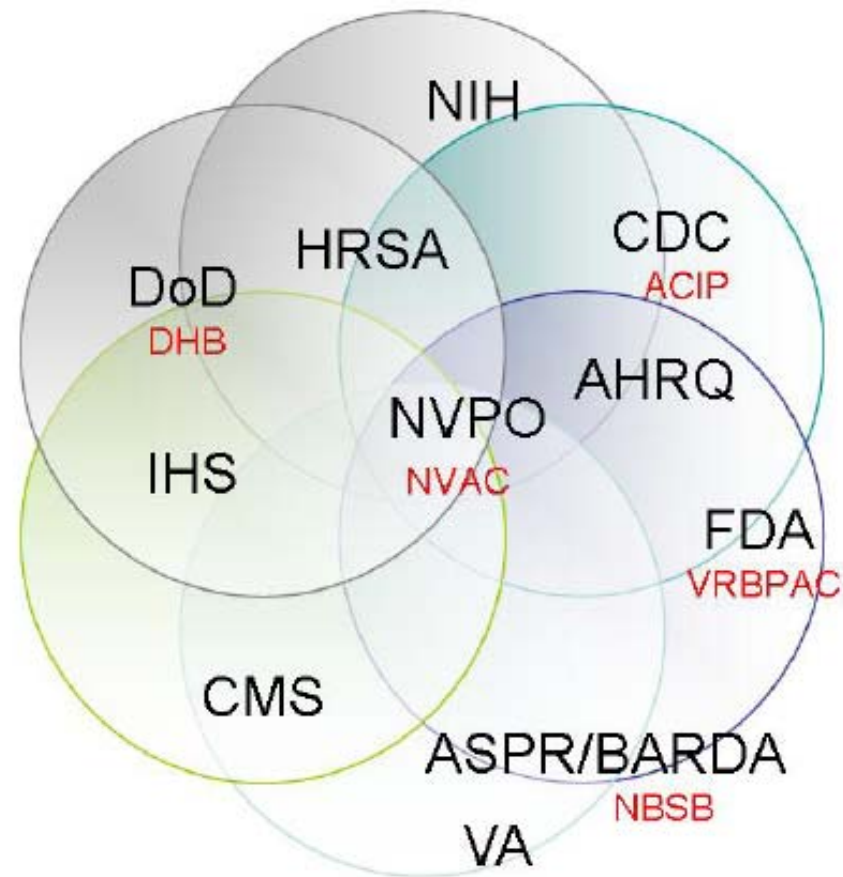
- Examine rare events
- Study subpopulations
- Timeliness



Federal Plans to Monitor Immunization Safety for the Pandemic 2009 H1N1 Influenza Vaccination Program

Federal Immunization Safety Task Force

U.S. Department of Health and Human Services
 Agency for Healthcare Research and Quality
 Centers for Disease Control and Prevention
 Food and Drug Administration
 Health Resources and Services Administration
 Indian Health Service
 National Institutes of Health
 Department of Defense
 Department of Veterans Affairs



<http://www.flu.gov/professional/federal/fed-plan-to-mon-h1n1-imm-safety.pdf>

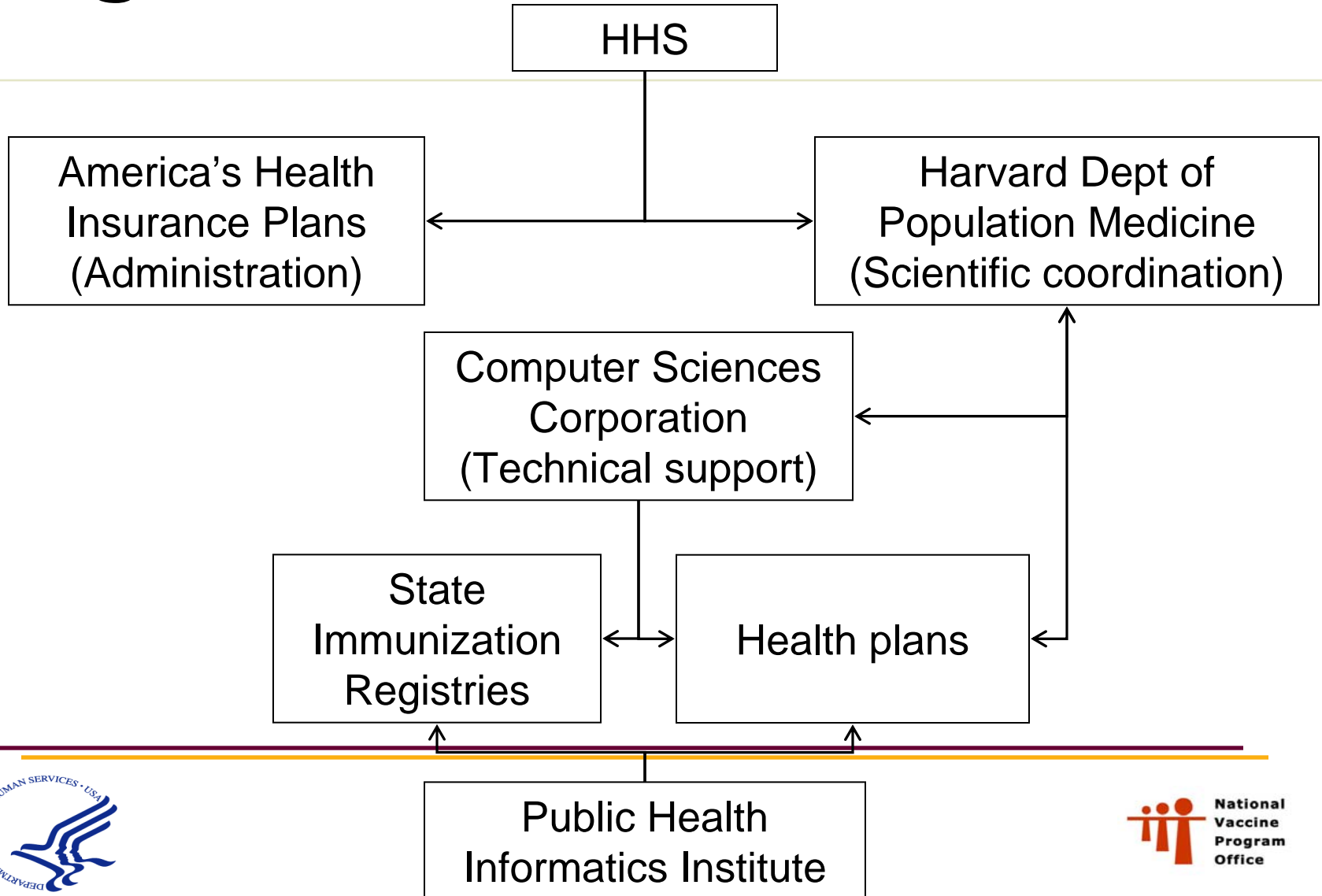
Advisory Committees in Red



Collaborators – Partial List

- **National Vaccine Program Office**
 - Daniel Salmon
 - Kirsten Vannice
- **Centers for Disease Control and Prevention**
 - Frank deStefano
- **Food and Drug Administration**
 - Robert Ball
- **America's Health Insurance Plans**
 - Kevin Fahey
 - Barbara Lardy
 - Victor Rhee
- **Public Health Informatics Institute**
 - Ellen Wild
 - Bill Brand
 - Elaine Lowery
 - Therese Hoyle
 - Alan Hinman
 - David Ross
- **Harvard Pilgrim Health Care Institute**
 - Richard Platt
 - Tracy Lieu
 - Grace Lee
 - Jeff Brown
 - Melisa Rett
 - Charlene Gay
 - Katherine Yih
 - Yury Vilik
- **Health Information Systems Consulting**
 - Robert Rosofsky
- **EpiPatterns**
 - Yinong Young-Xu
- **Computer Sciences Corporation**
 - Daniel Foltz
 - Jim Van Dyke
 - Aurelia Ford
 - Jim Roddy
 - John Manson
 - Vic Tandon
- **Cigna**
 - Therese Conner
 - Anthony Sumner
 - Daniel Carmody
 - Ha Nguyen
 - Mark Regine
 - Jason Cooper
- **Aetna**
 - Claire Spettell
 - Cheryl Walraven
 - Joaquim Fernandes
 - Yihai Liu
- **Healthcore (Wellpoint, BC/BS)**
 - Peter Wahl
 - Alex Cannon
 - Lori Meyers
 - Greg Daniel
 - Chris Hetrick
- **Humana**
 - David Nau
 - Yihau Xu
 - Amy Ball
- **Arizona State Immunization Information System**
 - Lisa Rasmussen
 - Roger Volp
 - Richard Bradley
- **Florida Shots**
 - Susan Lincicome
 - Pete Garner
- **Georgia Registry of Immunization Transactions and Services**
 - Tracy Culbreath
 - Elizabeth Sullivan
 - Michelle Conner
 - Archie Banks
 - Andre Wilson
- **Michigan Care Improvement Registry**
 - Therese Hoyle
 - Ian Hancke
- **Minnesota Immunization Information Connection**
 - Emily Peterson
 - Diana Jaeger
- **New York State Immunization Information System**
 - Loretta Santilli
- **New York City, Citywide Immunization Registry**
 - Vikki Papadouka
 - Rezaul Kabir
 - Luiz Homem de Mello
- **Pennsylvania Statewide Immunization Information System**
 - Frank Caniglia
 - Mike Jamula
- **Wisconsin Immunization Registry**
 - Dan Hopfensperger

Organizations in PRISM



Assessment of Immunization Information Systems (IIS)

- Rapid survey of state immunization programs through Association of Immunization Managers (AIM)
 - Intention to use IIS for H1N1
 - % of public and privately delivered vaccine anticipated to be captured by IIS
 - Anticipated timeliness of IIS
 - History of linking to health plan databases on individual level (HEDIS reporting)
- In depth interviews with selected states



State immunization registries

- Participating states
 - MI, FL, GA, PA, AZ, WI, MN, NY, NYC
- Total ~11 million persons in the participating health plans



Health plans

- Selection criteria
 - Ability to rapidly assemble data
 - Ability to update data every 1-2 weeks
- Participating health plans
 - Aetna, CIGNA, Humana, HealthCore (WellPoint plans in CA, NY, CO; BCBS in MI)
- Total ~35 million persons

PRI SM Aims

- Link health plan data and state immunization registry data in new H1N1 vaccine safety surveillance network
- Conduct continuous active surveillance for pre-specified outcomes
- Provide timely information on *unanticipated* potential adverse events



The Post-Licensure Rapid Immunization Safety Monitoring (PRISM) Network

for the PRISM team

Richard Platt, MD, MSc,
Professor and Chair of the Department of Population
Medicine, Harvard Medical School and the Harvard
Pilgrim Health Care Institute

Active Surveillance Systems

used for H1N1 Vaccine Safety Surveillance, U.S., 2010

System	Organizer	Population
Vaccine Safety Datalink	CDC	9 million (managed care)
Defense Medical Surveillance System	DoD/FDA/ CDC	2.6 million (military)
National Claims History File	CMS/FDA	46 million (elderly, disabled)
Veteran Patients & VA Employee and Volunteers	VA	1 million (veterans and feds)
Indian Health Service	IHS/FDA	1.8 million (all ages)
Post-Licensure Rapid Immunization Monitoring (PRISM)	FDA/NVPO /CDC	35 million (health plans)

Comparison of PRISM and VSD

	VSD	PRISM
Year started	1991	2009
Total cohort size	9.5 million	35 million
Participants	8 HMOs	4 national health plans and 9 state imm registries
Vaccines studied	All new vaccines	H1N1
Advantages	Experience; timeliness; access to charts	Size; state immunization registry data

H1N1 Vaccine Outcomes Monitored

- Neurologic
 - Guillain-Barré Syndrome
 - Bell's palsy
 - Seizures
 - Central nervous system demyelinating diseases
 - Neuropathies
 - Encephalomyelitis
 - Ataxia
- Myocarditis*
- Allergy including anaphylaxis
- Pregnancy**
 - Spontaneous abortion
 - Pre-eclampsia
 - Stillbirth

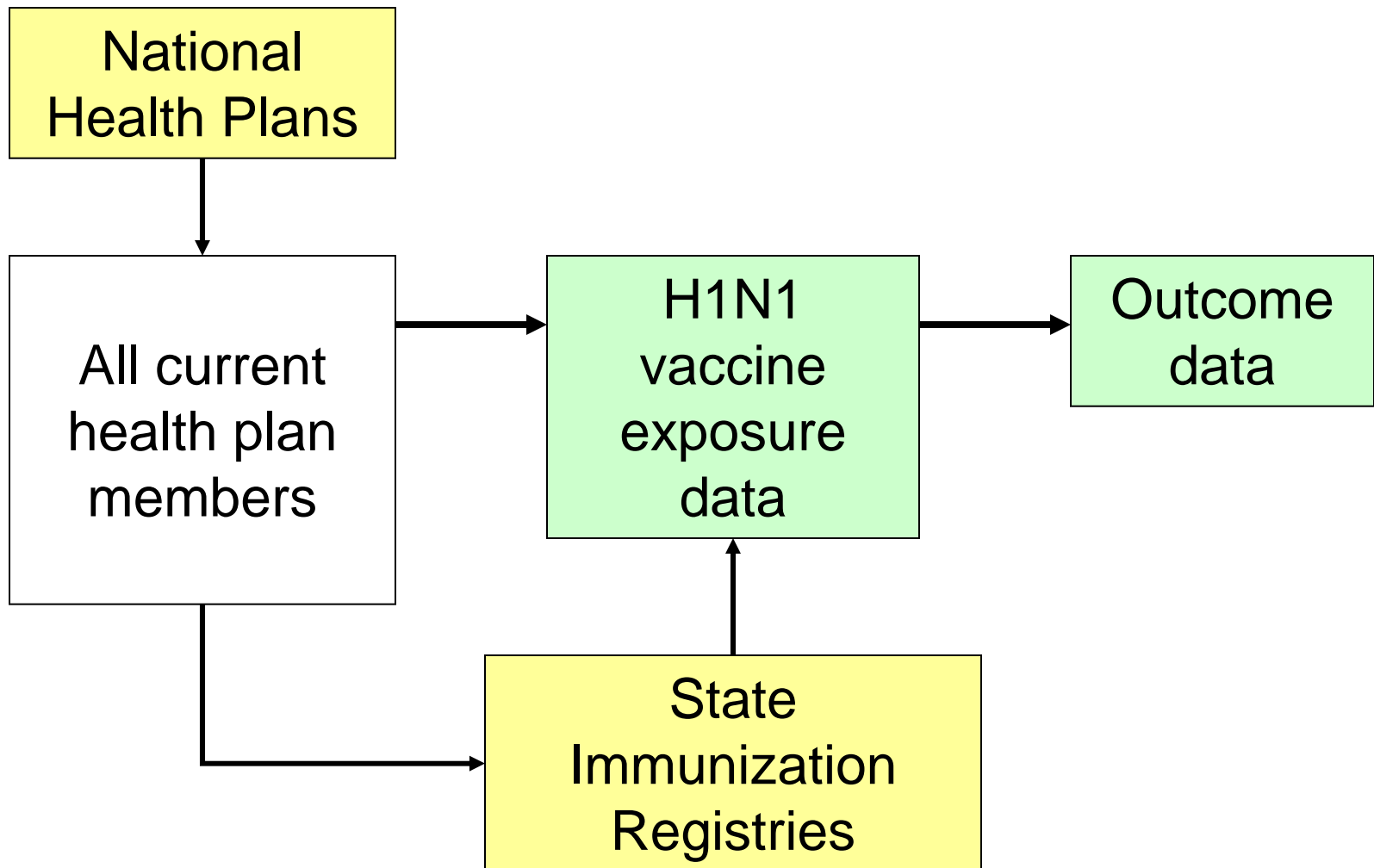
* After live vaccine only

** End of season only

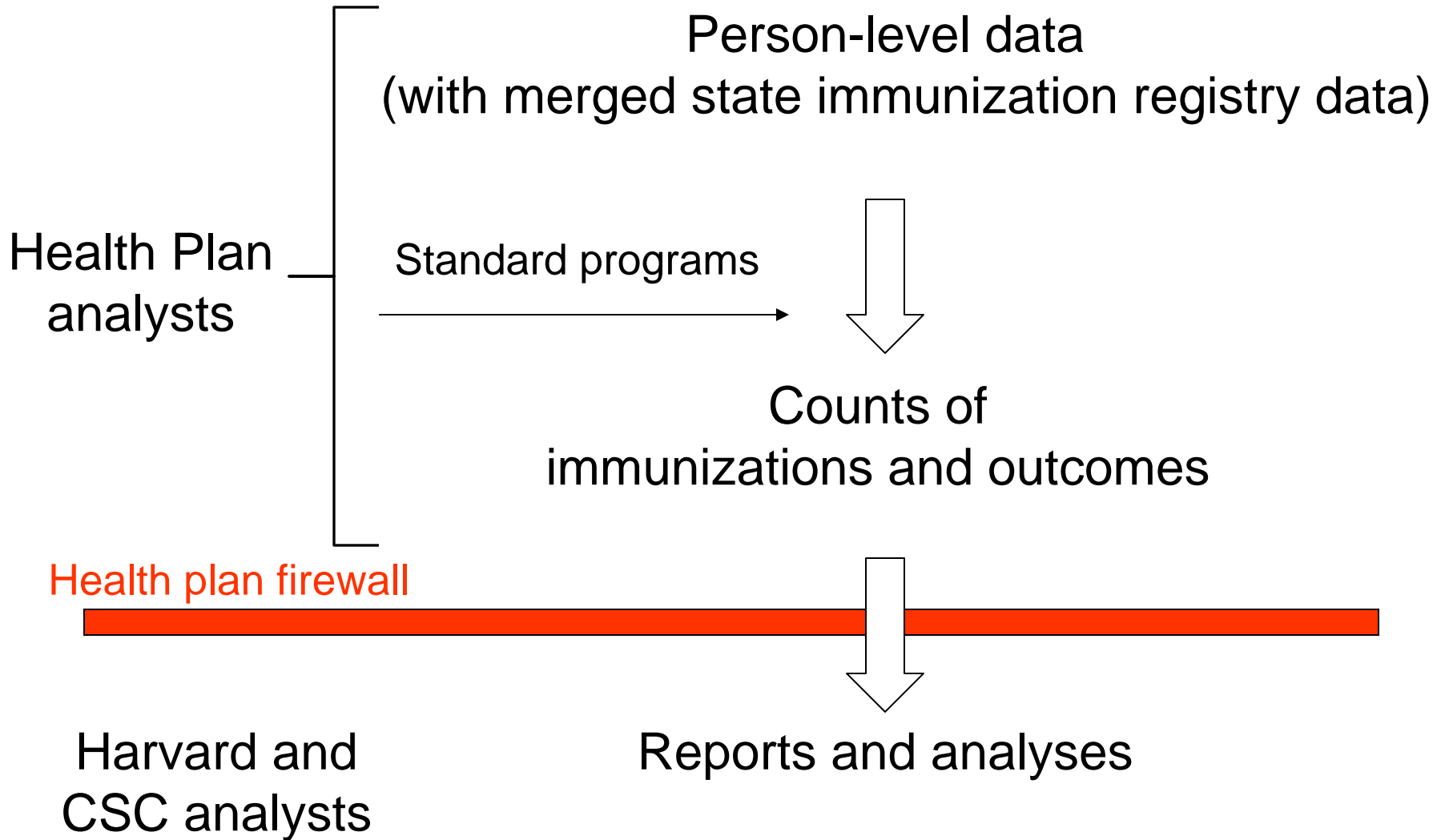
Three novel features of PRISM

- Full population linkage between health plans and state registries
- Use of freshhest possible claims, e.g., pre-adjudicated
- Classified as not research
 - No IRB oversight
 - Health plans and states encouraged to use the HIPAA public health exemption for exchange of Protected Health Information

PRISM – Current season surveillance



PRISM Data Flow



PRISM H1N1 Vaccine Doses*

data through 8/7/2010

	Children (<18)	Adults (≥ 18)	All ages
Inactivated or unknown vaccine type*	1.3 M	1.6 M	2.9 M
Live attenuated*	104,000	52,000	156,000
Total	1.4 M	1.7 M	3.1 M

* Live H1N1 vaccine is not distinguishable from inactivated in claims data, nor in data from all state registries

Contribution of States' Immunization Registry Data

% of vaccine doses* identified via:

	State registry	Health plan claims	Both
H1N1 vaccine	80%	37%	17%
Seasonal TIV	52%	68%	20%

* First doses only

Persons Monitored After H1N1 Vaccination

- PRISM ~3.1 million
- VSD ~1.6 million
- CMS ~3.3 million
- DoD ~1.3 million
- IHS ~0.3 million
- VA ~0.3 million

Next Steps

- End-of-season analyses
- Combine data on Guillain-Barré Syndrome from PRISM, VSD, and other systems

Next Steps for Vaccine Safety Surveillance

Robert Ball, MD, MPH, ScM
Director, Office of Biostatistics and Epidemiology,
Center for Biologics Evaluation and Research, U.S.
Food and Drug Administration

PRISM 2 Network Goals for 2010-11

- Re-design the PRISM Network for long-term sustainability
- Evaluate one vaccine and at least two outcomes of interest
- Develop statistical methods

Re-design for Sustainability

- Bring the PRISM Network under Mini-Sentinel
- Develop the operational framework
 - Identify 25 health outcomes of interest
 - Categorize vaccine exposure and outcomes; develop framework
 - Needs assessment

Re-design for Sustainability

- Evaluate the performance characteristics of PRISM
- Find all available complementary data sources

Evaluate One Vaccine and Two or More Outcomes

- Candidates include influenza, human papillomavirus (HPV) vaccine
- Anaphylaxis is one requested outcome for evaluation
- Validate vaccine – event pairs

Develop Statistical Methods

- Assess data mining methods, especially pattern recognition approaches
- Enhance methods for causal inference in sequential analysis

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