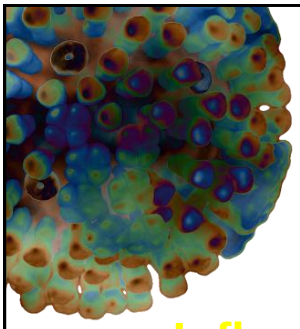


Influenza Vaccine Program Effectiveness in the United States

National Influenza Vaccine Summit
May 2012

Carrie Reed, DSc
Influenza Division

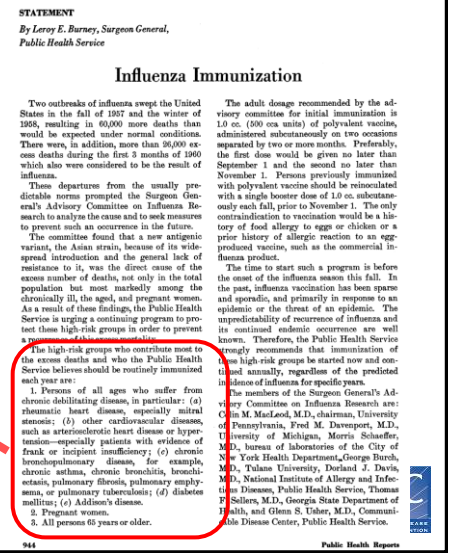
Disclaimer

- **The findings and conclusions in this presentation have not been formally disseminated by CDC and do not represent any agency determination or policy**
- **I have no financial conflicts of interest**

2010: 50th Anniversary of First Influenza Vaccine Recommendation

The high-risk groups who contribute most to the excess deaths and who the Public Health Service believes should be routinely immunized each year are:

1. Persons of all ages who suffer from chronic debilitating disease, in particular: (*a*) rheumatic heart disease, especially mitral stenosis; (*b*) other cardiovascular diseases, such as arteriosclerotic heart disease or hypertension—especially patients with evidence of frank or incipient insufficiency; (*c*) chronic bronchopulmonary disease, for example, chronic asthma, chronic bronchitis, bronchiectasis, pulmonary fibrosis, pulmonary emphysema, or pulmonary tuberculosis; (*d*) diabetes mellitus; (*e*) Addison's disease.
2. Pregnant women.
3. All persons 65 years or older.



STATEMENT

By Leroy E. Burney, Surgeon General, Public Health Service

Influenza Immunization

Two outbreaks of influenza swept the United States in the fall of 1957 and the winter of 1958, resulting in 60,000 more deaths than would be expected under normal conditions. There were, in addition, more than 26,000 excess deaths during the first 3 months of 1960 which also were considered to be the result of influenza.

These departures from the usually predictable norms prompted the Surgeon General's Advisory Committee on Influenza Research to analyze the cause and to seek measures to prevent such an occurrence in the future.

The committee found that a new antigenic variant, the Asian strain, because of its widespread introduction and the general lack of resistance to it, was the direct cause of the excess number of deaths, not only in the total population but most markedly among the chronically ill, the aged, and pregnant women. As a result of these findings, the Public Health Service is urging a continuing program to protect these high-risk groups in order to prevent a recurrence of this excess mortality.

The high-risk groups who contribute most to the excess deaths and who the Public Health Service believes should be routinely immunized each year are:

1. Persons of all ages who suffer from chronic debilitating disease, in particular: (*a*) rheumatic heart disease, especially mitral stenosis; (*b*) other cardiovascular diseases, such as arteriosclerotic heart disease or hypertension—especially patients with evidence of frank or incipient insufficiency; (*c*) chronic bronchopulmonary disease, for example, chronic asthma, chronic bronchitis, bronchiectasis, pulmonary fibrosis, pulmonary emphysema, or pulmonary tuberculosis; (*d*) diabetes mellitus; (*e*) Addison's disease.
2. Pregnant women.
3. All persons 65 years or older.

The adult dosage recommended by the advisory committee for initial immunization is 1.0 cc. (500 cca units) of polyvalent vaccine, administered subcutaneously on two occasions separated by two or more months. Preferably, the first dose would be given no later than September 1 and the second no later than November 1. Persons previously immunized with polyvalent vaccine should be reinoculated with a single booster dose of 1.0 cc. subcutaneously each fall, prior to November 1. The only contraindication to vaccination would be a history of food allergy to eggs or chicken or a prior history of allergic reaction to an egg-produced vaccine, such as the commercial influenza product.

The time to start such a program is before the onset of the influenza season this fall. In the past, influenza vaccination has been sparse and sporadic, and primarily in response to an epidemic or the threat of an epidemic. The unpredictability of recurrence of influenza and its continued endemic occurrence are well known. Therefore, the Public Health Service strongly recommends that immunization of these high-risk groups be started now and continued annually, regardless of the predicted incidence of influenza for specific years.

The members of the Surgeon General's Advisory Committee on Influenza Research are: Colin M. MacLeod, M.D., chairman, University of Pennsylvania, Fred M. Davenport, M.D., University of Michigan, Morris Schaeffer, M.D., bureau of laboratories of the City of New York Health Department, George Burch, M.D., Tulane University, Dorland J. Davis, M.D., National Institute of Allergy and Infectious Diseases, Public Health Service, Thomas F. Sellers, M.D., Georgia State Department of Health, and Glenn S. Usher, M.D., Communicable Disease Center, Public Health Service.

944 Public Health Reports

Influenza vaccination recommendations over time

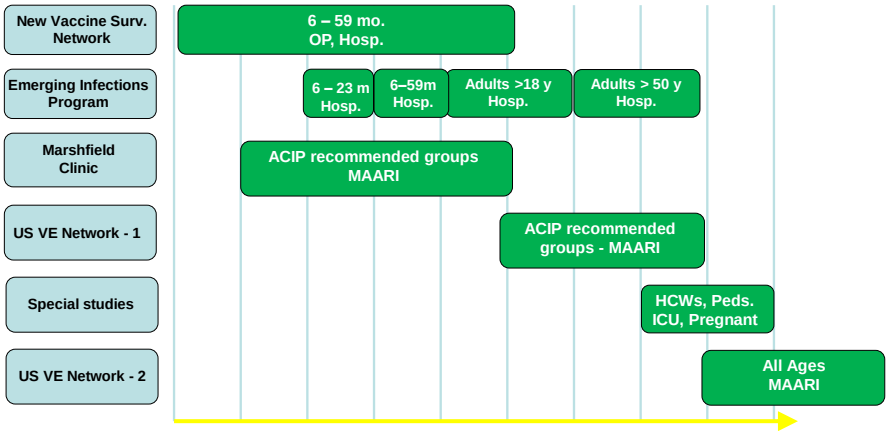
Before 2000:	**Persons aged 65 or older** **Persons with high-risk chronic medical conditions** **Pregnant women in the second or third trimester** **Household contacts of the above** **Health care workers**
2000:	**Adults 50 and older**
2004:	**Children aged 6—23 months** **Household contact of children aged 0--23 months** **Women who will be pregnant during influenza season**
2006:	**Children aged 6—59 months** **Household contacts of children aged 0—59 months**
2008:	**All children aged 6 months—18 years**
2010:	**All persons > 6 months in the US**

During the last decade…

- More people getting vaccinated with influenza vaccines
- Greater use of vaccines in persons at high risk of complications
- More awareness of the need for vaccination
- Some skepticism of the value of influenza vaccination

Are influenza vaccines effective in preventing influenza-associated illnesses each year?

Influenza Division program to measure influenza vaccine effectiveness in the U.S.



During the last decade…

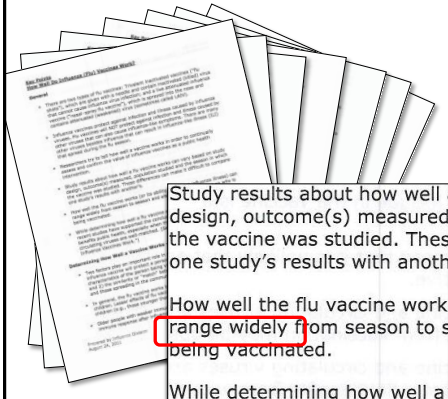
- More people getting vaccinated with influenza vaccines
- Greater use of vaccines in persons at high risk of complications
- More awareness of the need for vaccination
- Some skepticism of the value of influenza vaccination

Are influenza vaccines effective in preventing influenza-associated illnesses each year?

Yes.

… but the effectiveness of vaccines varies by season, population, and outcome measured

And, communication of influenza vaccine effectiveness is difficult



Study results about how well a flu vaccine works can vary based on study design, outcome(s) measured, population studied and the season in which the vaccine was studied. These differences can make it difficult to compare one study's results with another's.

How well the flu vaccine works (or its ability to prevent influenza illness) can range widely from season to season and also can vary depending on who is being vaccinated.

While determining how well a flu vaccine works is challenging, in general, recent studies have supported the conclusion that influenza vaccination benefits public health, especially when the viruses in the vaccine and circulating viruses are well-matched. (See "Current Efforts to Study How Well Influenza Vaccines Work.")

Influenza Vaccine Program Effectiveness Project

- **Question: Are influenza vaccine programs effective in reducing influenza-associated health outcomes in the population?**
- **Goal: Estimate the number of averted influenza-associated outcomes that result from influenza vaccination in the United States**

Influenza Vaccine Program Effectiveness Project

- **Advantages:**
  - **Consistent and systematic approach across seasons**
  - **Uses data collected as core program activities (Influenza Division and Immunization Services Division)**
  - **Estimates can be updated annually**
  - **Illness/outcomes averted may be easier and more meaningful way to communicate value of vaccine?**

Project Phases

Phase 1: Develop the model

Phase 2: Apply the model to previous years' data (2005-2010)

Phase 3: Run the model following each influenza season to estimate the effect of vaccination annually

Phase 4: Apply economic data to the model to estimate costs/costs averted

Use the model to address programmatic questions (e.g. value of new vaccines vs. existing vaccines)

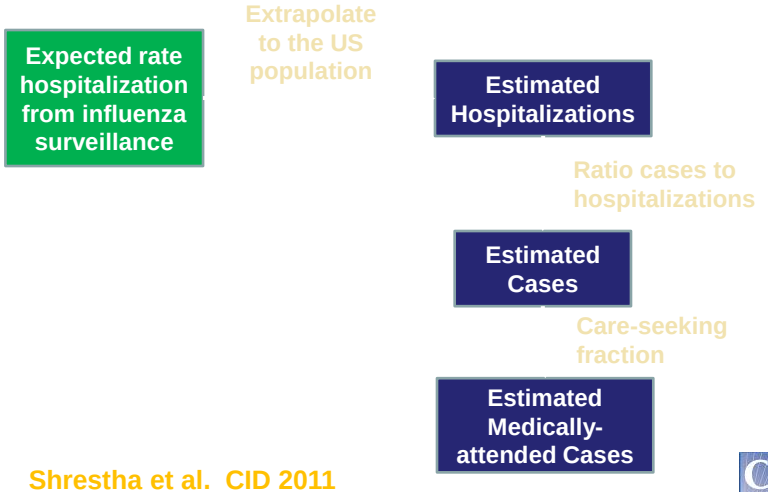
Influenza Vaccine Program Effectiveness Methods

1. **Estimate observed annual burden of influenza-associated outcomes**
2. **Estimate observed risk of influenza-associated outcomes among susceptible individuals**
   - **Using data on annual vaccine coverage and vaccine effectiveness**
3. **Calculate expected burden of influenza-associated outcomes in population with no vaccination**
4. **Calculate difference in outcomes attributable to vaccination program**

1. Estimating annual US burden of influenza

- Outcomes
  - Illness
  - Medically-attended illness
  - Hospitalization
- Stratified by month and age group
- Five past influenza seasons (2005–2010)

1. Estimating annual US burden of influenza



Shrestha et al. CID 2011

2. Risk of influenza outcomes if susceptible

- Influenza-related outcomes measured among persons at risk for influenza:
  - Hospitalizations
  - Outpatient visits
  - Deaths
  - Many influenza-related outcomes
  - Population at risk = population not protected from effective vaccination or having prior illness
  - Effective vaccination = VE x VC

Example: Population at risk

Month	VE	VC*	Pop at risk	Est. Illness
September	60%	15%	= 1000*(1-60%*15%) = **910**	0
October	60%	10%	= (910-0)*(1-60%*10%) = **855**	5
November	60%	5%	= (855-5)*(1-60%*5%) = **825**	10
December	60%	5%	= (825-10)*(1-60%*5%) = **790**	20
January	60%	2%	= (790-20)*(1-60%*2%) = **761**	40

Example: Risk among susceptibles

Month	Pop. at risk	Est. Illness	Risk of illness
September	**910**	**0**	0/910 = **0%**
October	**855**	**5**	5/855 = **0.6%**
November	**825**	**10**	10/825 = **1.2%**
December	**790**	**20**	20/790 = **2.5%**
January	**761**	**40**	40/761 = **5.3%**

3. Estimated burden if no vaccination

- **Apply same risk of outcome among susceptible persons, by month**
- **Greater population susceptible because no vaccination**
  - **Remove persons protected due to illness each month, but no longer remove persons vaccinated**

Example: Estimated burden without vaccination

Month	Risk of illness	Pop. at risk (no vaccination)	Expected Illnesses
September	**0%**	**1000**	=1000 * 0% = **0**
October	**0.6%**	= 1000-0 = **1000**	=1000 * 0.6% = **6**
November	**1.2%**	= 1000-6 = **994**	= 994 * 1.2% = **12**
December	**2.5%**	= 994-12 = **982**	= 982 * 2.5% = **25**
January	**5.3%**	= 982-25 = **957**	= 957 * 5.3% = **50**

4. Calculate net impact of vaccine program

- **Difference between expected outcomes without vaccination and estimated annual burden**
- **Using the illness example presented earlier:**

  93 expected without vaccination

  – 75 observed

  18 averted illnesses

Draft Results: Averted Outcomes

Influenza Vaccine Program Effectiveness Project

Year	Ilnesses	Medically-attended illness	Hospitalization
2005-06	1,620,856	680,760	16,029
2006-07	873,539	366,886	7,273
2007-08	2,139,830	898,728	21,292
2008-09	1,713,955	719,861	11,621
2010-11	4,834,888	2,030,653	40,764
Five Season Total	11,183,068	4,696,888	96,979

Summary

- **Substantial annual averted disease burden from the influenza vaccination program**
  - **Varies by season**
  - **Varies by age group**
  - **Due to variability in VC, VE, annual disease burden**
- **Expect that effects will be greater, as analysis does not yet account for any indirect protection of unvaccinated persons**

Conclusions

- Having a standardized framework to evaluate program impact
  - Allows comparison across seasons to examine impact of changes in burden, VE, and VC
  - Helps identify and prioritize data needed to routinely evaluate program impact
- Program improvements will be made by
  - increasing coverage in non-elderly persons
  - improving effectiveness of vaccines, especially in elderly persons

Influenza Vaccine Program Effectiveness Team

- Deliana Kostova
- Carrie Reed
- Po-Yung Cheng
- Martin Meltzer
- Paul Gargiullo
- In Kyu Kim
- David Shay
- Lyn Finelli
- Jim Singleton
- Joe Bresee

Questions?

BACKUP SLIDES

Annual and age-group variation in parameters

Age group	Vaccine coverage	Vaccine effectiveness	Hospitalization rates (per 100,000)
6 mos–4 yrs	35–59%	35–63%	71–115
5–19 yrs	15–38%	35–63%	9.6–17
20–64 yrs	20–31%	35–63%	8.2–25
65+ yrs	66–70%	25–39%	39–203

Draft Results: Averted Illnesses

Year	All ages	0-4 yrs	5-19 yrs	20-64 yrs	65+ yrs
2005-06	1,620,856	354,430	238,609	342,974	684,843
2006-07	873,539	260,233	168,409	214,505	229,391
2007-08	2,139,830	325,172	276,834	632,665	905,159
2008-09	1,713,955	485,677	554,869	424,402	249,007
2010-11	4,834,888	758,633	1,066,858	1,604,536	1,404,860
Five Season Total	11,183,068	2,184,145	2,305,579	3,219,082	3,473,260

Draft Results: Medically-attended Illness

Year	All ages	0-4 yrs	5-19 yrs	20-64 yrs	65+ yrs
2005-06	680,760	148,861	100,216	144,049	287,634
2006-07	366,886	109,198	71,152	90,092	96,344
2007-08	898,728	136,572	116,270	265,719	380,167
2008-09	719,861	203,984	233,045	178,249	104,583
2010-11	2,030,653	318,626	448,080	673,905	590,041
Five Season Total	4,696,888	917,241	968,763	1,352,014	1,458,769

Draft Results: Hospitalizations

Year	All ages	0-4 yrs	5-19 yrs	20-64 yrs	65+ yrs
2005-06	16,029	2,471	654	2,314	10,590
2006-07	7,273	1,814	465	1,447	3,547
2007-08	21,292	2,267	759	4,269	13,997
2008-09	11,621	3,386	1,521	2,864	3,850
2010-11	40,764	5,289	2,925	10,827	21,724
Five Season Total	96,979	15,227	6,324	21,721	53,708