# Vaccines in Adults

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### Vaccines

Continued Medical Education

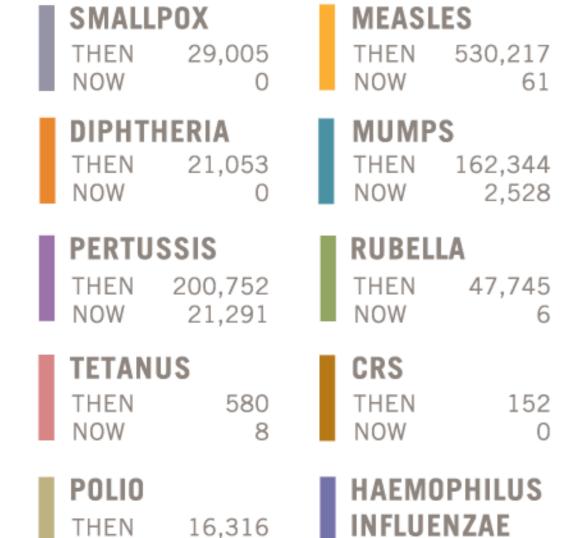


### Vaccines

Continued Medical Education

# **VACCINES WORK**

These bubbles are sized according to the annual number of disease cases in the US during the 1900s versus 2010. We've come so far. It's a reminder that while disease rates are low, most diseases haven't disappeared. This is why we continue to vaccinate.



20,000

270

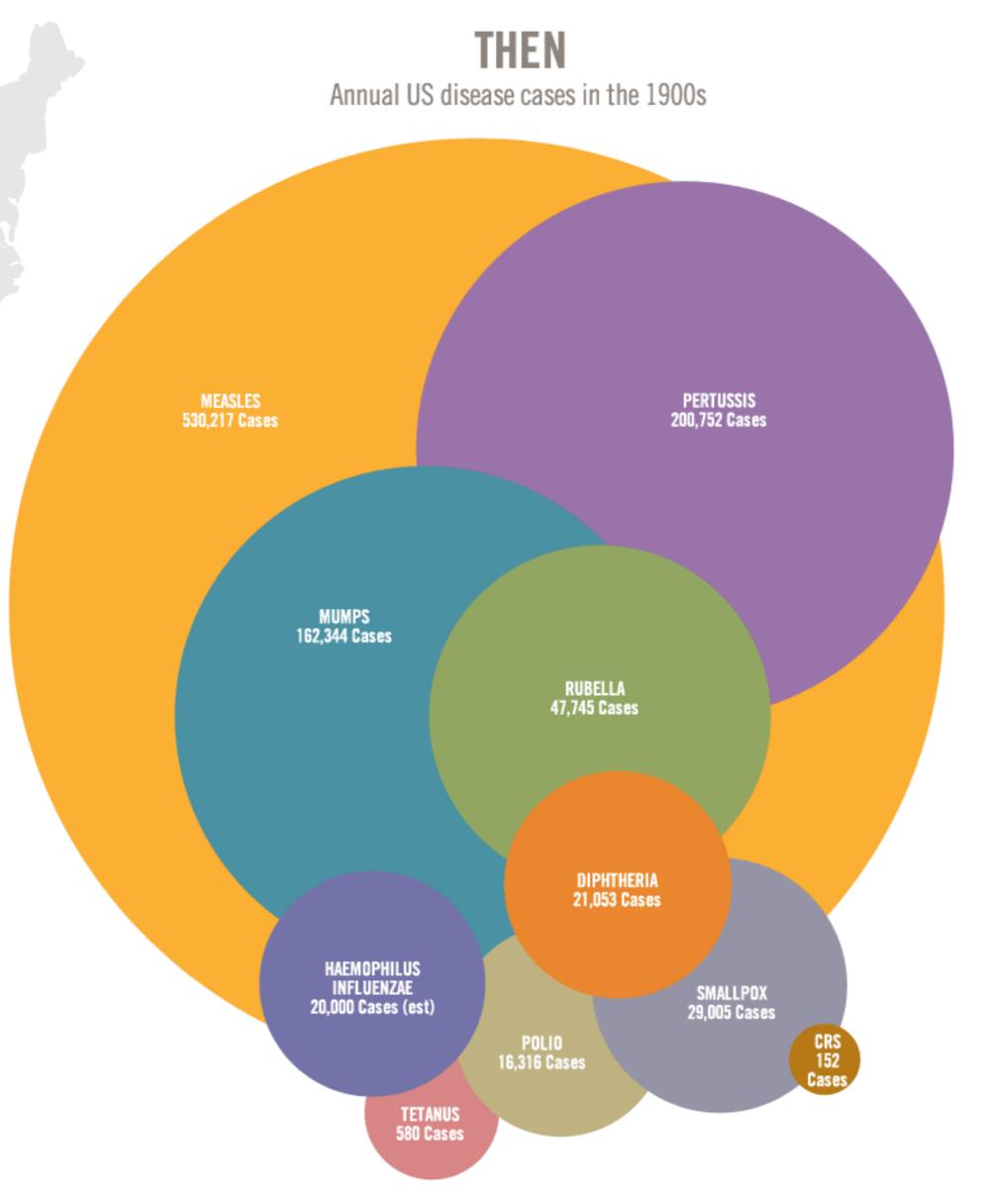
THEN

NOW

16,316

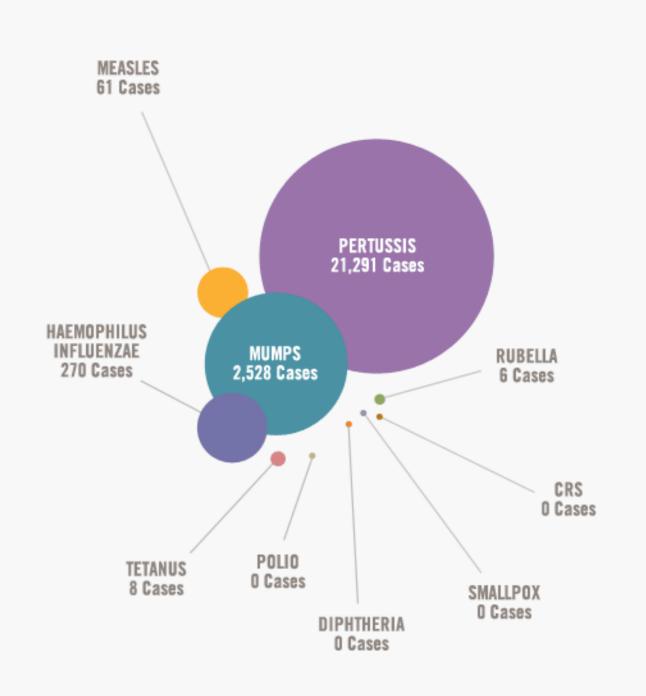
THEN

NOW



#### NOW

US disease cases in 2010



<sup>9.</sup> Centers for Disease Control and Prevention (CDC). Parents Guide to Childhood Immunizations. http://www.cdc.gov/vaccines/pubs/parents-guide/default.htm. Accessed August 15, 2011. 10 CDC. Impact of Vaccines in the 20th & 21st Centuries. http://www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/G/impact-of-vaccines.pdf. Updated January 2011. Accessed August 15, 2011.

FIGURE 1. Crude death rate\* for infectious diseases — United States, 1900–1996†

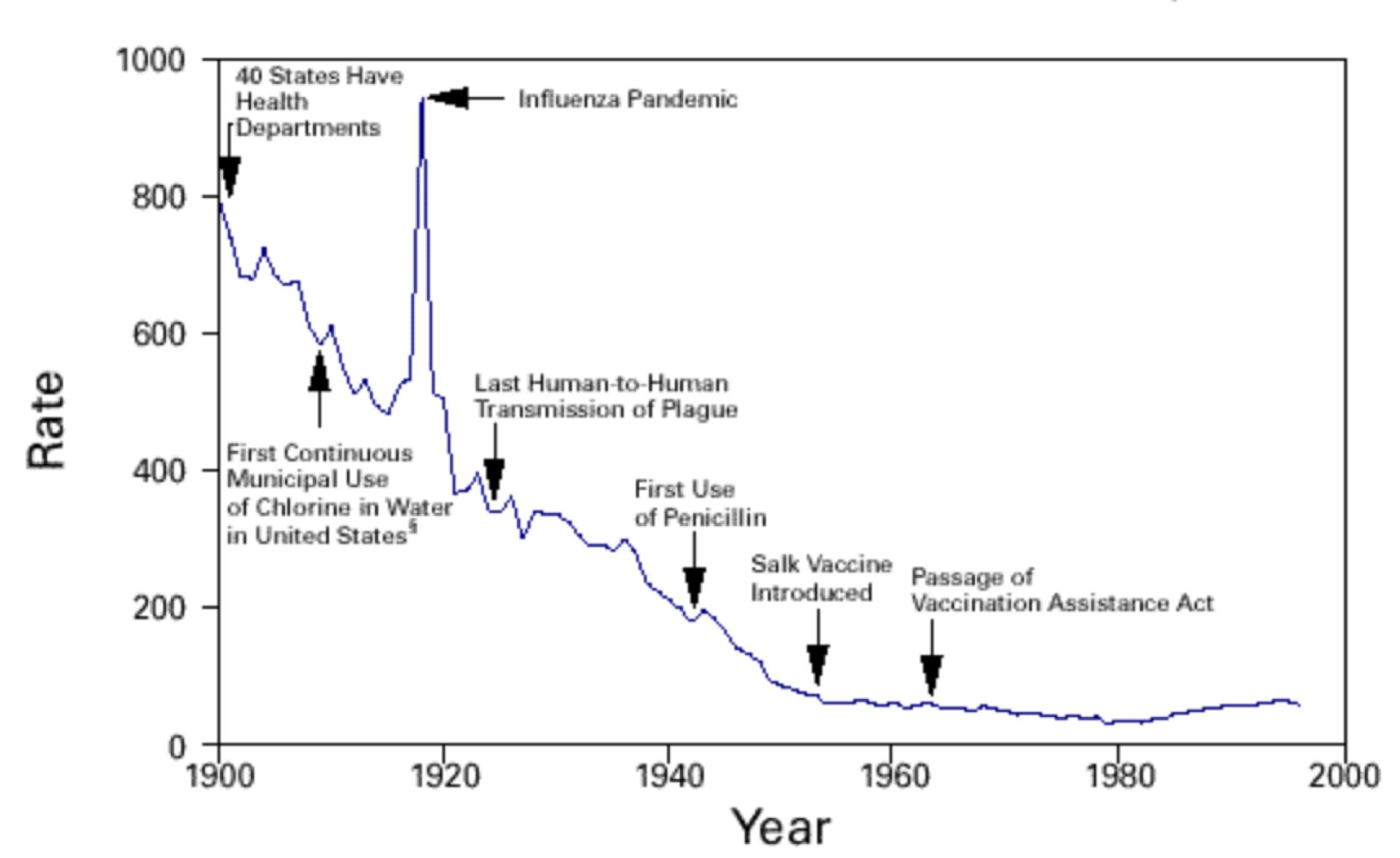
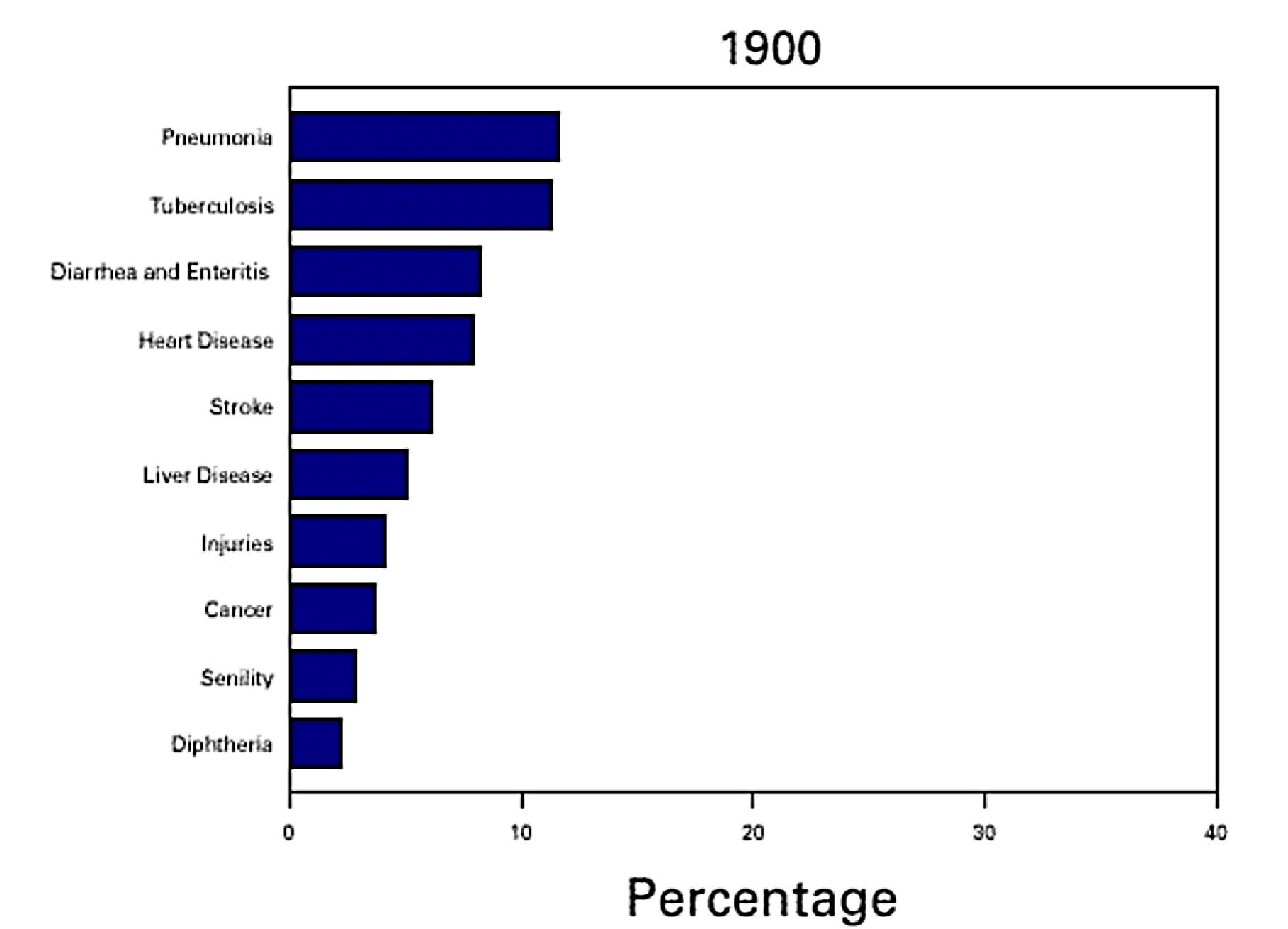
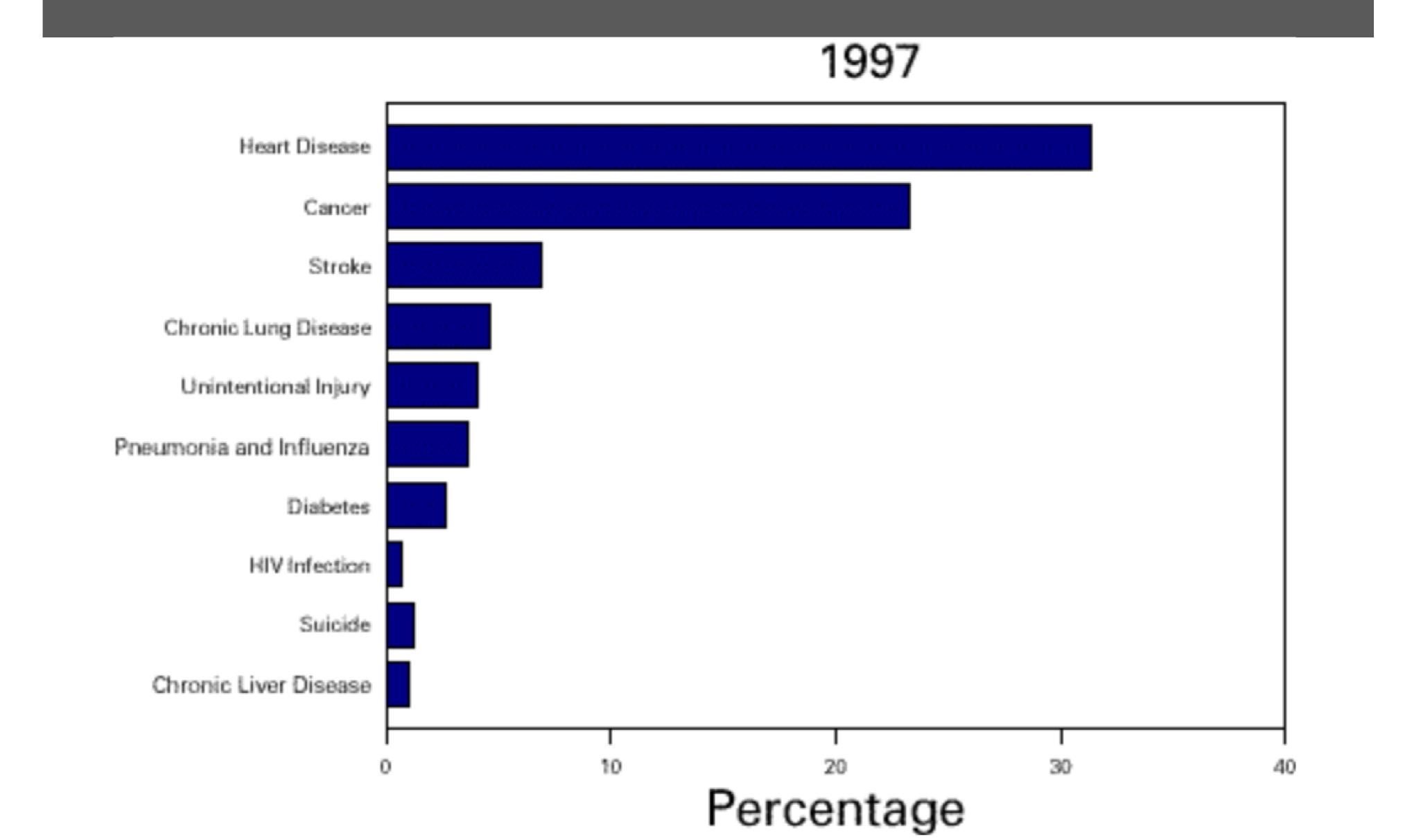


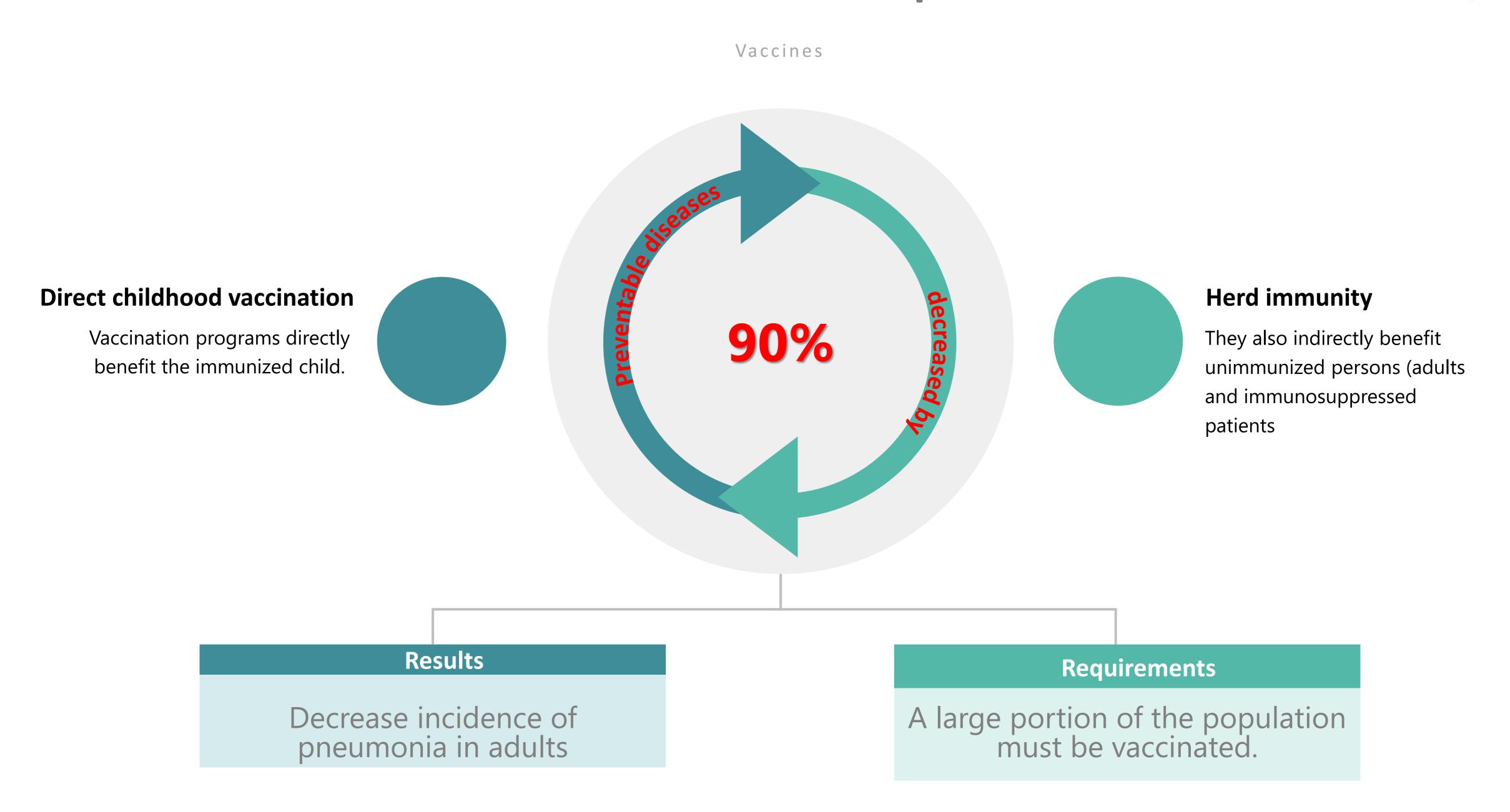
FIGURE 2. The 10 leading causes of death as a percentage of all deaths — United States, 1900 and 1997



# Where we stand "today"



### Immunization is one of the most effective preventive health measures.



### **Herd Immunity**

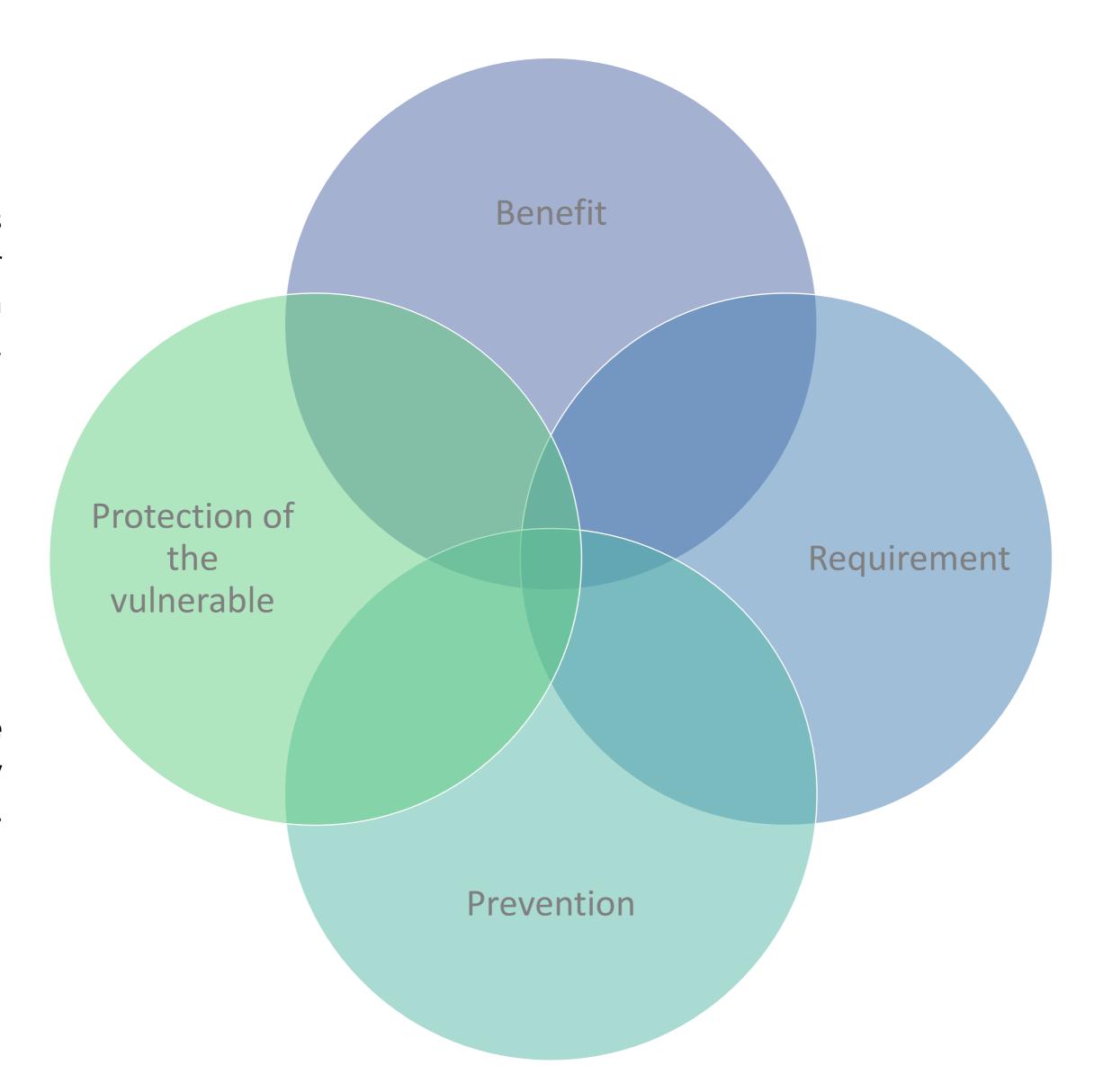
Adult Vaccination

#### Benefit

Community immunity protects children who are too young for immunization and persons with contraindications to vaccines.

#### Requirement

It relies on the majority of the population receiving routinely recommended immunizations.



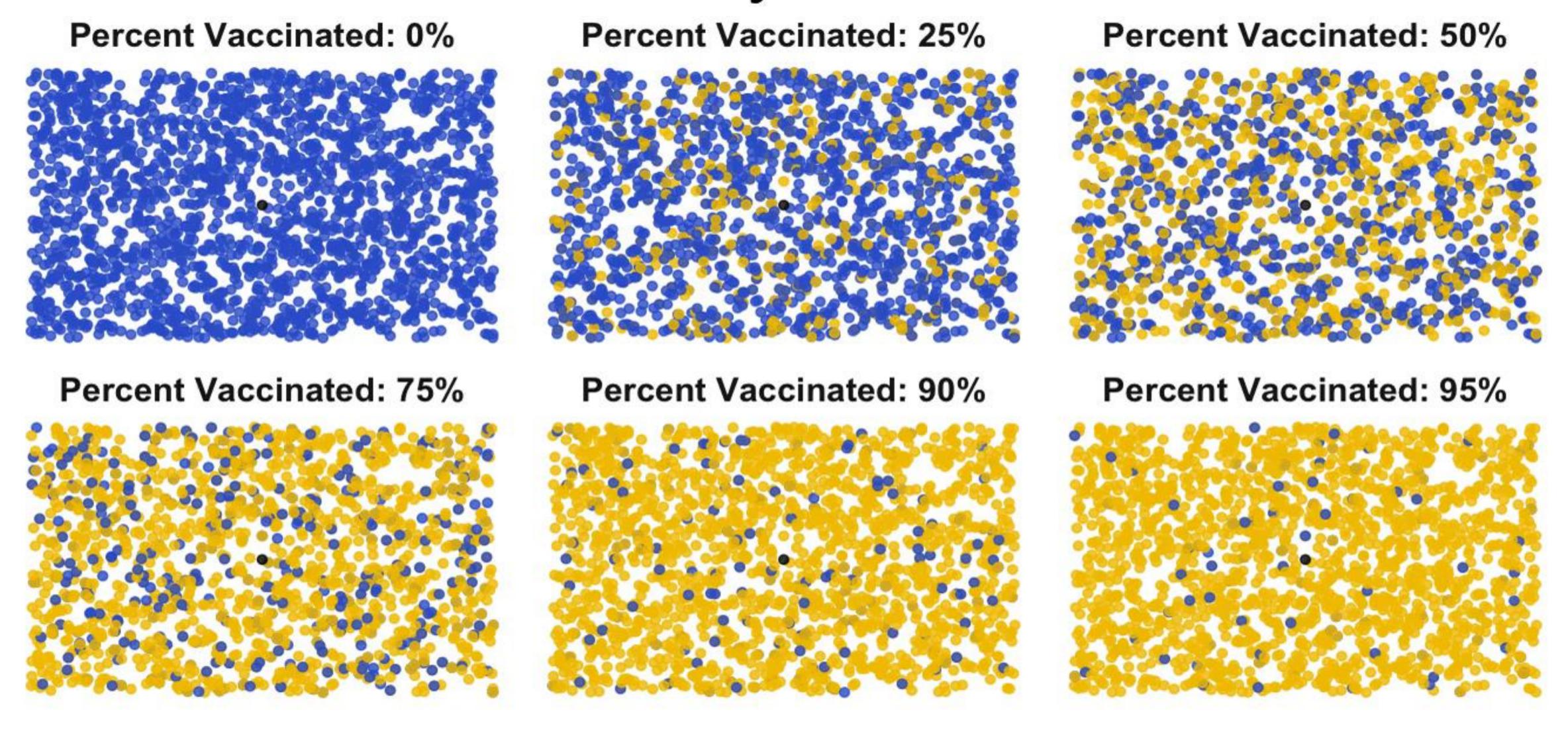
#### **Prevention**

Of paramount importance to the ever increasing population of patients who have impaired immunity, because of excessive morbidity and mortality, and antimicrobial therapy is often less effective than usual.

# Protection of the most vulnerable

Many patients with impaired immunity are unable to mount a protective immune response to active vaccination. Failure to adhere to the recommended immunization schedules, leaves individuals susceptible to lifethreatening diseases.

# Herd Immunity: How It Works



Infected
 Unvaccinated
 Vaccinated

# Vaccination Historical Achievements

- ✓ Global eradication of smallpox
- ✓ Nearly global eradication of polio
- ✓ Drastic decrease in the morbidity & mortality associated with other infectious diseases

As a result, many parents are unaware of the threats that these infectious diseases posed for previous generations, and as such, may believe that vaccinations are no longer necessary for their children.

While health officials maintain that routine childhood vaccines are safe and effective, vaccination refusal has increased in the US the last decade, same as parents expressing concerns about the safety of vaccines.

# Vaccination hesitancy - Adults

2016 NHIS estimates influenza vaccination among adults aged ≥19 years was 45.4% and Tdap vaccination 31.7%.

- Coverage for the adult age-appropriate composite measures including influenza and any tetanus vaccine was low in all age groups:
  - ✓ 14.5% in adults aged 60-64 years
  - ✓ 26.7% in adults aged 19-59 years
- Racial and ethnic differences in vaccination coverage is lower for most vaccinations among non-white compared with white adults.
- All providers should routinely assess adults' vaccination status at every clinical encounter, strongly recommend needed vaccines.

# Vaccination hesitancy - Adults

Adults are at increase risk of:

Illness

Hospitalization

Disability

\*Particularly influenza and pneumococcal disease\*

\*Compliance with adult vaccination schedule is low\*

# Is education the answer?

A 2014 study sought to test the effectiveness of messages designed to reduce vaccine misperceptions. 1759 parents in the US age  $\geq$  18 years with children age -  $\leq$  17 and younger were surveyed. Participants were randomly assigned to a control group or received 1 of 4 interventions:

- ✓ Information from the Centers for Disease Control and Prevention explaining the lack of evidence that MMR causes autism
- ✓ Textual information from the Vaccine Information Statement about the dangers of the diseases prevented by MMR
- ✓ Images of children who have diseases prevented by the MMR vaccine
- ✓ A dramatic narrative from the CDC about an infant who almost died from measles

None of the interventions increased a parent's desire to vaccinate a child.

# Vaccination hesitancy

Parents who are faced with the decision to have their children vaccinated may be more likely to seek information about vaccines via the Internet than through their doctor.

<u>Perceiving danger in vaccines tends to be associated with reluctance to vaccinate.</u> For example, many people believe that vaccines have dangerous side effects, and that exposure to the disease itself would often be preferable to the vaccination.

Now anti-vaccine group want to be referred as "vaccine risk awareness" despite all available safety data.

### Factors that influence immunisation rates

#### Provision of free vaccines

Doctor recommendation

Vaccine safety

Vaccine effectiveness

Vaccine supply

Disease burden and perception of risk

Education and health promotion

Availability of vaccine Injury compensation schemes

School entry and other legislation

> School/childcare exclusion rules for unvaccinated

Parental financial incentives

Financial incentives for doctors

Cultural context

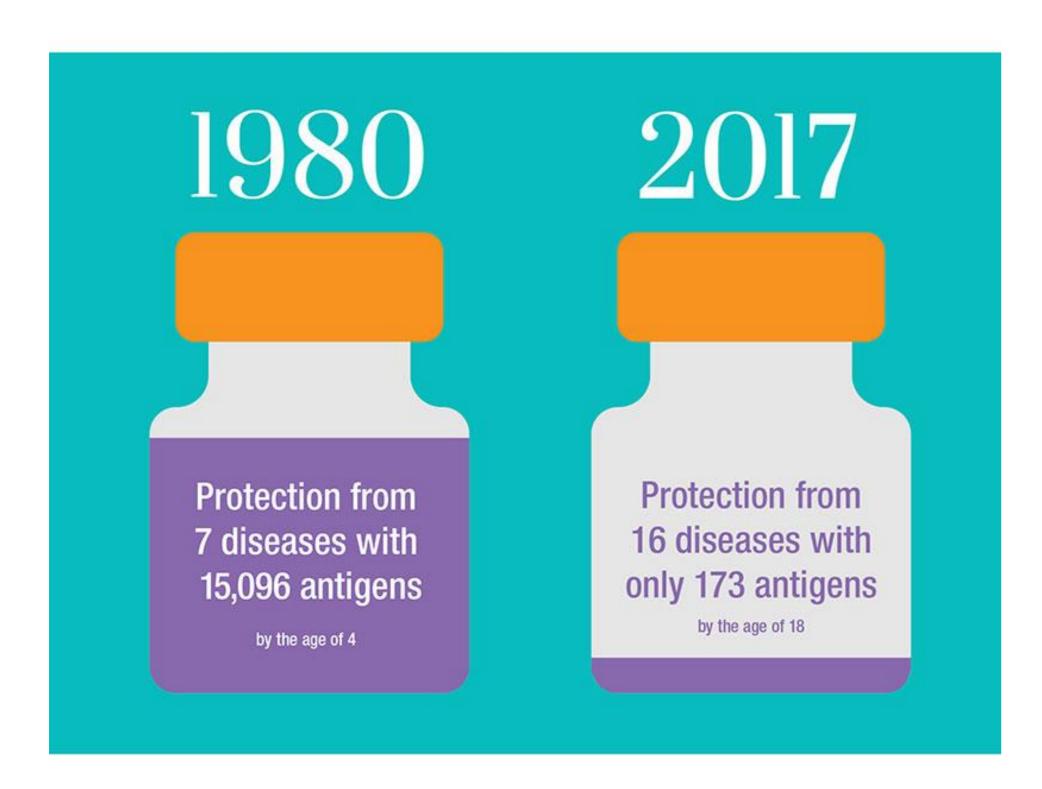
Conscientious objection options with administrative hurdles to claiming these options

### **Adult Vaccines**

Awareness

## Vaccines Today Work Better Than Ever

Since 1980: More protection, fewer antigens.



Based on CDC Recommended Vaccine Schedule U.S. for children birth to 18 years.
Source: Plotkin's Vaccines (Seventh Edition)

#### Safe

Current vaccines are safer and elicit better immune response.

### Available

Available at clinics, medical offices and pharmacies

### Lead by example

Make sure you understand vaccine benefits and vaccinate yourself. If not, most efforts will fail.

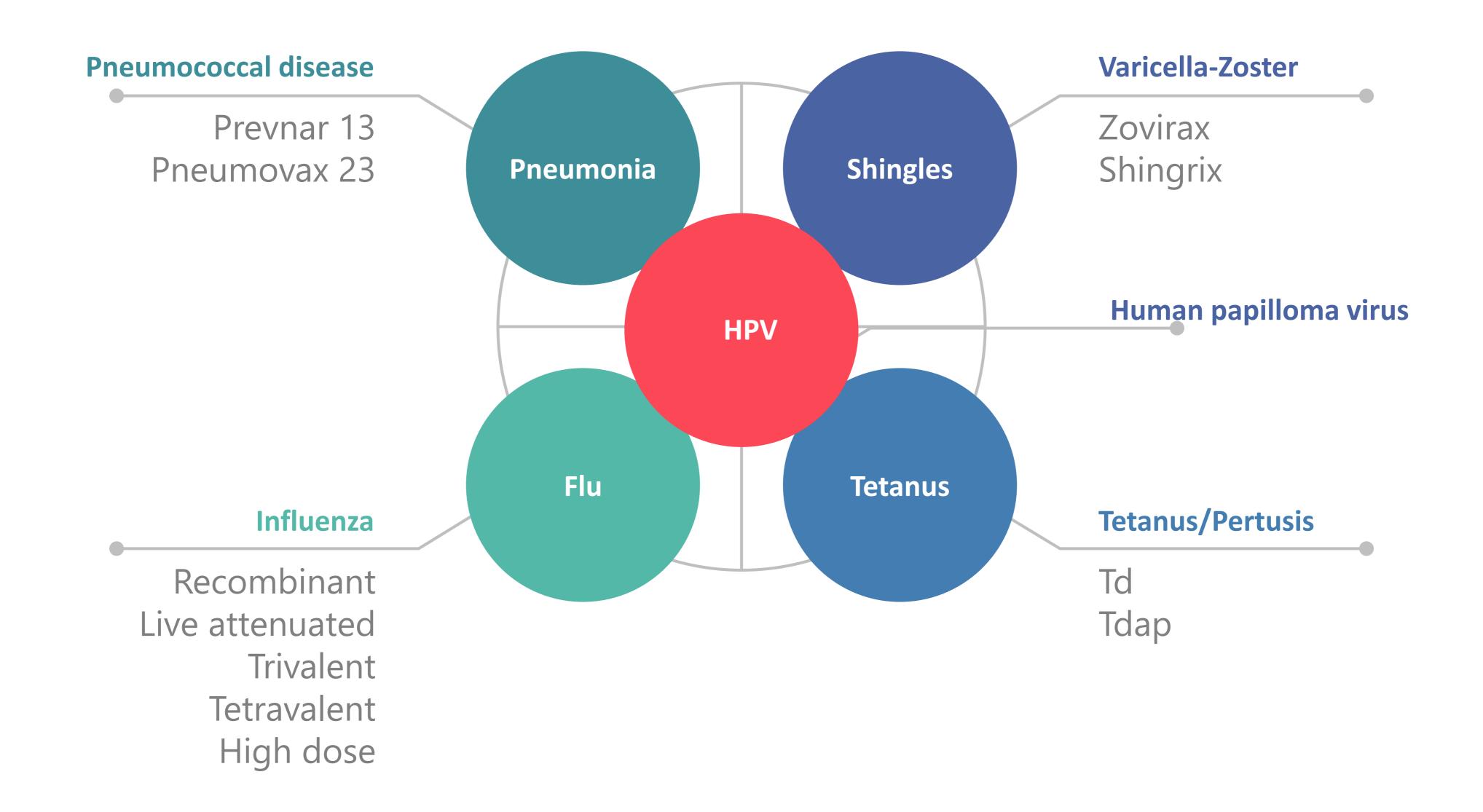
Recommended vaccination for adults with an additional risk factor

necommendation/

for adults who meet age requirement, ₩. Recommende

commended vaccination based on shared

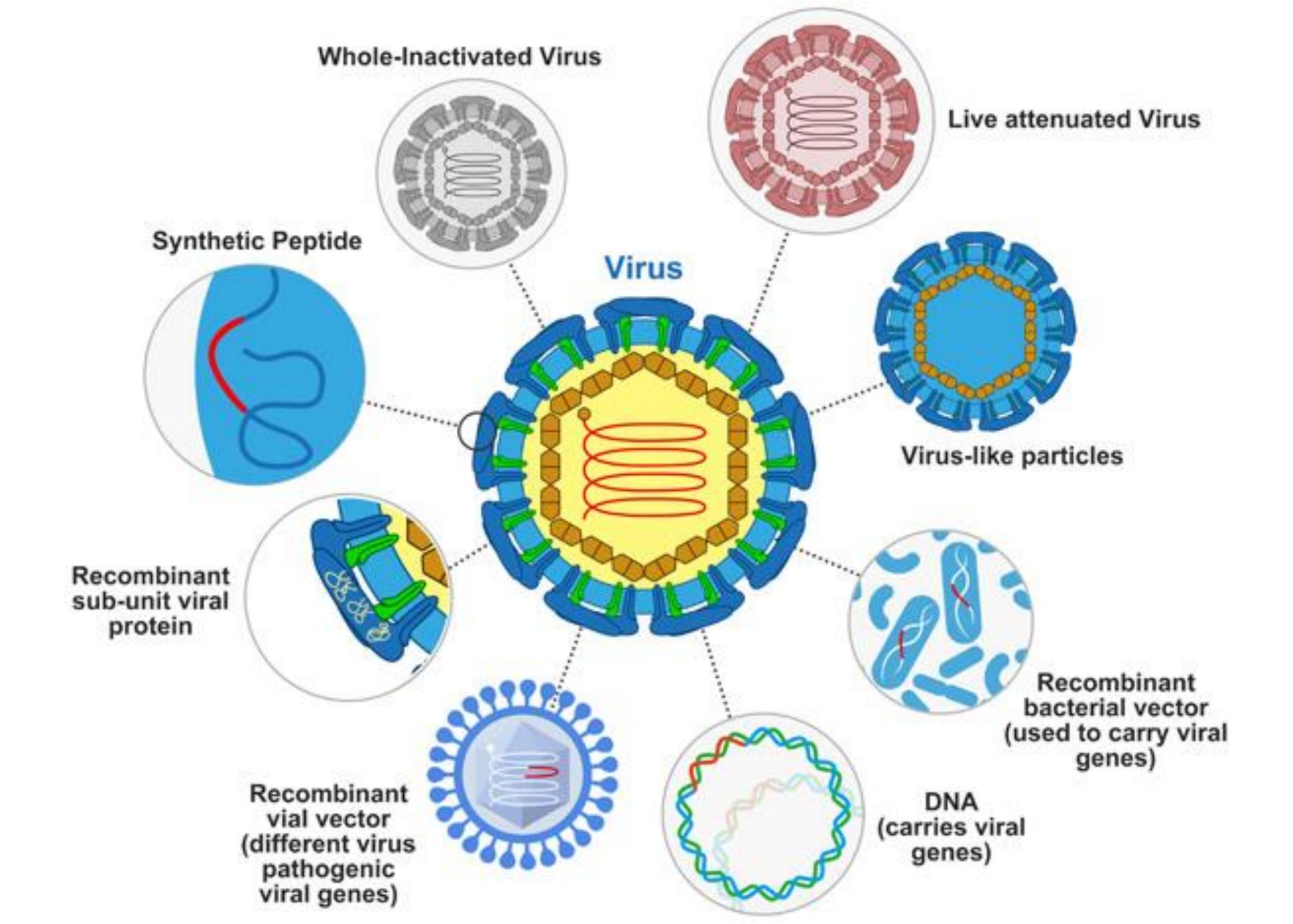
### **Adult Vaccination Recommendations**



# Vaccine Types

There are several different types of vaccines. Based on a number of these factors, scientists decide which type of vaccine they will make. They include:

- ✓ Inactivated vaccines
- ✓ Live-attenuated vaccines
- ✓ Messenger RNA (mRNA) vaccines
- ✓ Subunit, recombinant, polysaccharide, and conjugate vaccines
- ✓ Toxoid vaccines
- ✓ Viral vector vaccines



## Pneumococcus vaccine

Pneumococcal disease is common in young children, but older adults are at greatest risk of serious illness and death.

Invasive pneumococcal disease caused by the serotypes in PCV7 declined by 99% in the United States since 2000.

Unvaccinated people of all ages, including babies too young to get the vaccine, have seen decreases in disease.

Experts estimate PCV13 in the first 3 years of use:

- ✓ Prevented more than 30,000 cases of invasive pneumococcal disease
- ✓ Prevented 3,000 deaths

## Pneumococcus vaccine

Currently 2 vaccines, Prevnar 13 and Pneumovax 23

Before 65 y/o, Pneumovax 23 only if:

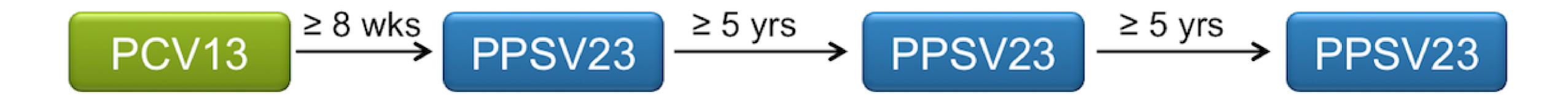
After 65 y/o, Prevnar 13 and Pneumovax 23 independent of medical conditions

- Heart diseases
- Lung disease

When possible, PCV13 should be given first, followed by PPSV23 in 8 weeks for maximum effect. But should not wait more than a year.

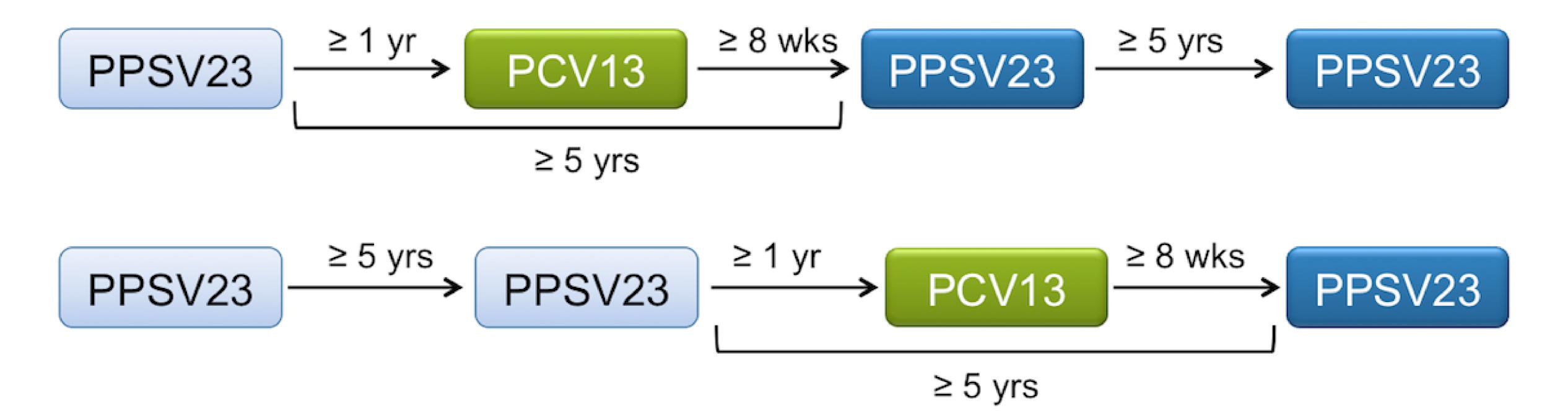
## Pneumococcal Vaccine-Naïve Adults

≥ Age 65



### **PPSV23-Immunized Adults**

≥ Age 65



# Both PCV13 and PPSV23 should be given to adults of any age who have the underlying conditions:

Cerebrospinal fluid leak/Cochlear implant

Functional or anatomic asplenia

Immunocompromising conditions:

- √ Congenital or acquired
- √HIV infection
- ✓ Generalized malignancy (eg, metastatic disease, disease treated with chemotherapy)
- ✓ Hematologic malignancy (eg, leukemia, Hodgkin/non-Hodgkin lymphoma, multiple myeloma)
- ✓ Solid organ transplant
- ✓ latrogenic immunosuppression, including long-term systemic glucocorticoids or radiation
- √ Chronic renal failure/Nephrotic syndrome

- Prior doses count towards doses recommended below and do not need to be repeated.
- If PPSV23 was given previously: (1) Wait 1 year before giving PCV13; (2) For group B, wait at least 5 years before giving a second dose of PPSV23.
- No more than two doses of PPSV23 recommended before 65th birthday and one dose thereafter.
- DO NOT administer PCV13 and PPSV23 at the same visit.

#### A. Smoker, long-term care facility resident, or chronic conditions:

- Heart Disease (excluding hypertension)
- Lung Disease (including asthma)
- Liver Disease (including cirrhosis)
- Diabetes
- Alcoholism

# PPSV

#### B. Immunocompromised:

- HIV Infection
- Chronic Renal Failure
- Nephrotic Syndrome
- Asplenia (including sickle cell)



#### C. CSF Leaks or Cochlear Implants



| Vaccine | Serotypes included  |  |
|---------|---|--|
| PPSV23  | I, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, IOA, IIA, I2F, I4, I5B, |  |
|         | 17F, 18C, 19A, 19F, 20, 22F, 23F, and 33F                 |  |
| PCV7    | 4, 6B, 9V, 14, 18C, 19F, and 23F                          |  |
| PCVIO   | 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, and 23F                |  |
| PCV13   | 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F    |  |

### **Shared serotypes:**

1, 4, 5, 6B, 7F, 9V, 14 (6 total)

## Combined serotypes:

20 unique serotypes, but there is an immune boosting effect when combined

### Pneumococcal contraindications

Don't get <u>PCV13</u> if you have ever had a life-threatening allergic reaction to:

- A shot of the vaccine
- An earlier pneumococcal vaccine called PCV7 (or Prevnar)
- Any vaccine containing diphtheria toxoid (for example, DIaP)

## Don't get PPSV23 if you:

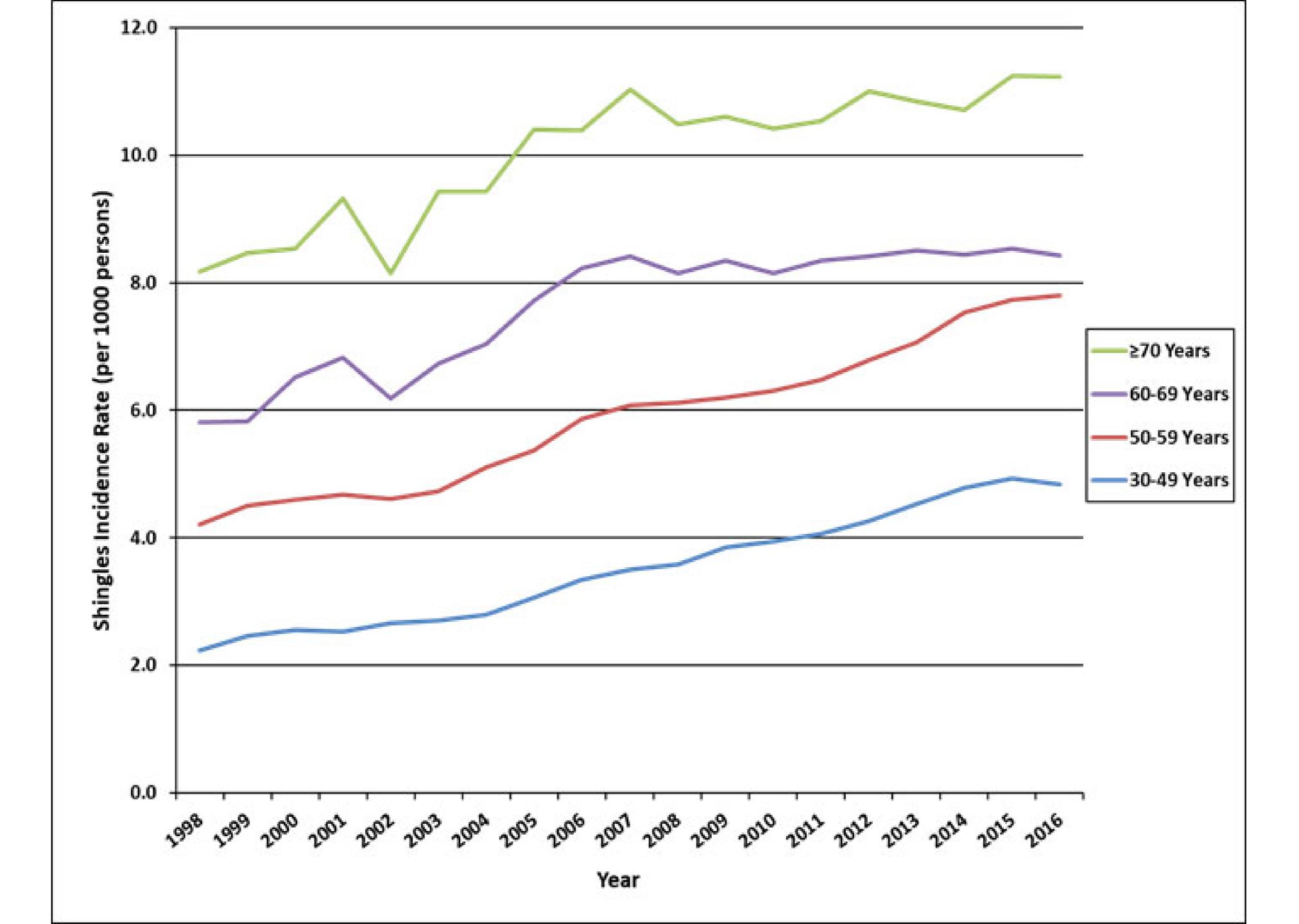
- Ever had a life-threatening allergic reaction to a shot of PPSV23
- Have a severe allergy to any component of the vaccine

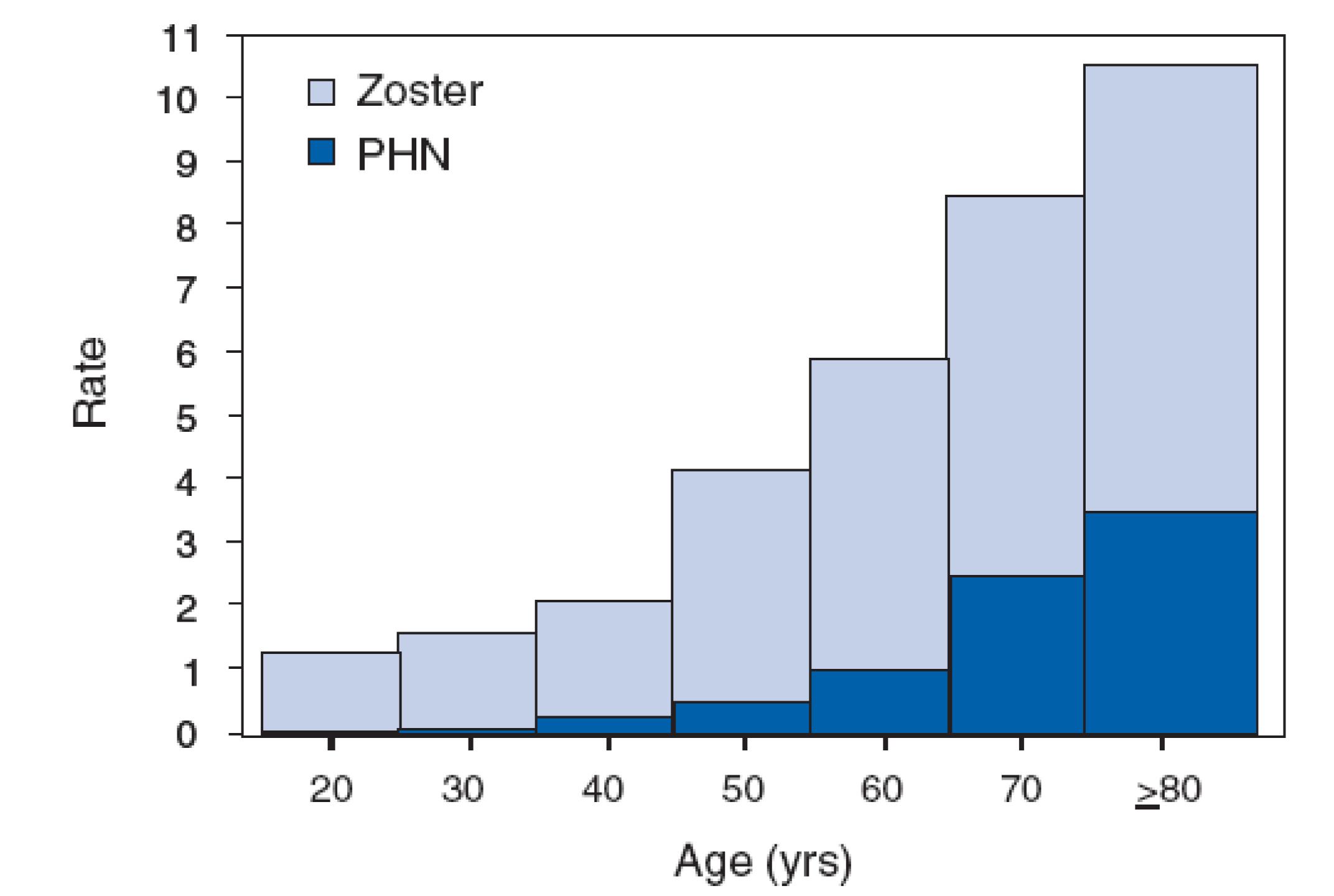


# Herpes-Zoster = Varicella-Zoster

- Almost 1 out of 3 people in the United States will develop shingles in their lifetime. Most people will have it only once. However, you can get the disease more than once.
- Your risk of getting shingles increases as you get older. The most common complication of shingles is postherpetic neuralgia (10-18%).

Approximately 1-4% of people are hospitalized for complications.





# Herpes-Zoster = Varicella-Zoster

Herpes zoster vaccination is indicated for individuals ≥50 years of age to reduce the risk of developing zoster and postherpetic neuralgia. Vaccination is **not** indicated for the treatment of zoster or postherpetic neuralgia.

### Currently 2 vaccines:

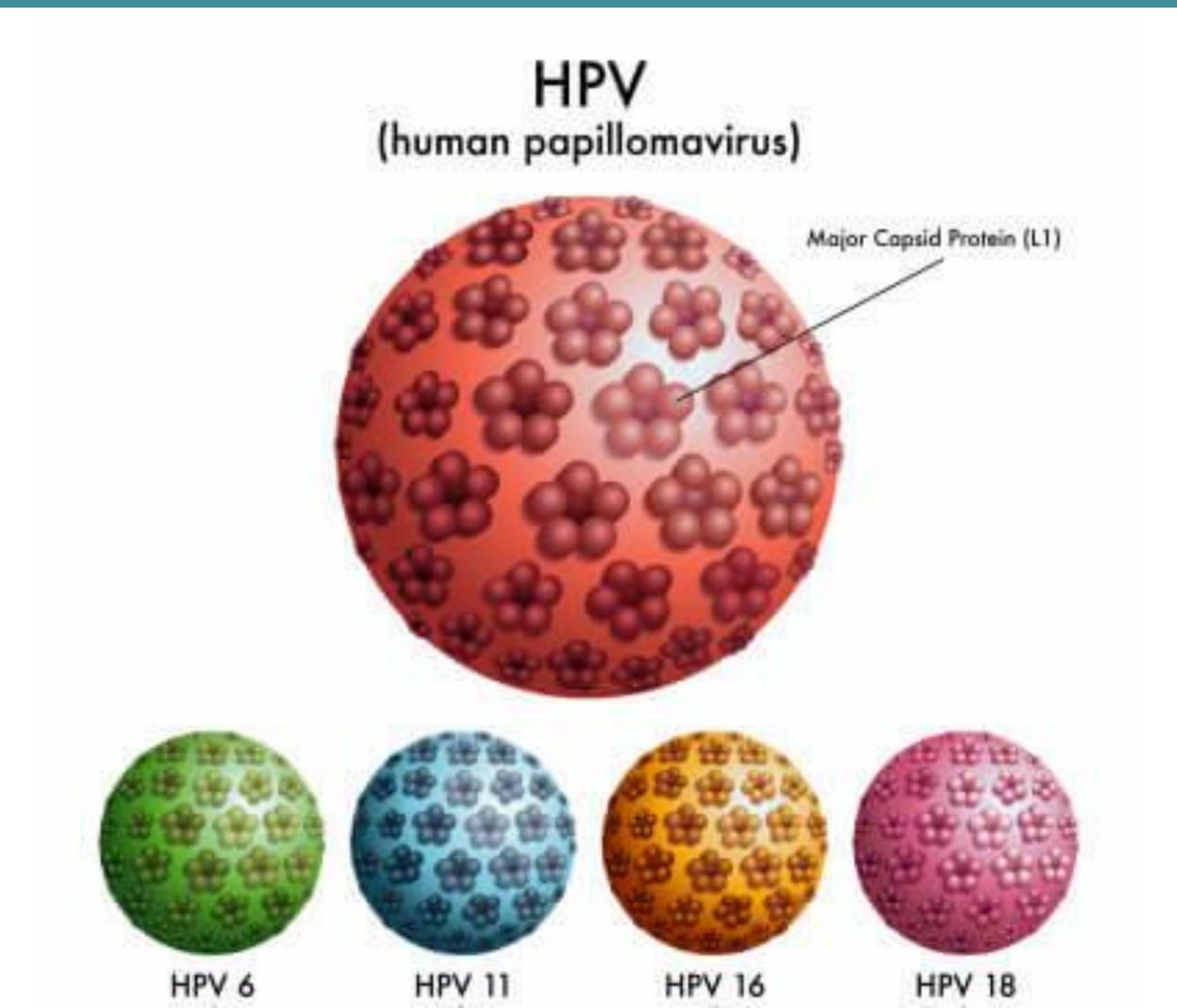
- ✓ A live attenuated vaccine (Zostavax)

  Recommended at 60, 1 dose needed
- ✓ A non-live recombinant glycoprotein E vaccine. Sold as Shingrix. Recommended at 50, 2 dosis needed

#### Comparison of zoster vaccine live (ZVL) and recombinant zoster vaccine (RZV)

| Vaccine                             | Efficacy (incidence HZ)  | Systemic side effects that prevented normal everyday activities (vaccine versus placebo) | Follow-up |
|-------------------------------------|--|--|-----------|
| ZVL (single dose)                   | Population ≥60 <sup>[1]</sup> :<br>51% reduction in risk of HZ<br>compared with placebo (95% CI<br>44.2-57.6%; 11.12 versus 5.42<br>per 1000 person-years) | <1% reported in post-hoc analysis [5]  | 3.1 years |
|                                     | Population 50 to 59 <sup>[2]</sup> : 70% reduction in risk of HZ compared with placebo (95% CI 54.1-80.6%; 6.57 versus 1.99 per 1000 person-years)         |  | 1.3 years |
| RZV (2 doses separated by 2 months) | Population ≥70 <sup>[3]</sup> : 89% reduction in risk of HZ compared with placebo (95% CI 84.2-93.7%; 9.2 versus 0.9 per 1000 person-years)                | 6 versus 2%  | 3.7 years |
|                                     | Population ≥50 <sup>[4]</sup> : 96.2% reduction in risk of HZ compared with placebo (95% CI 92.7-98.3%; 9.1 versus 0.3 per 1000 person-years)              | 11.4 versus 2.4%   | 3.2 years |

# Human papilloma virus

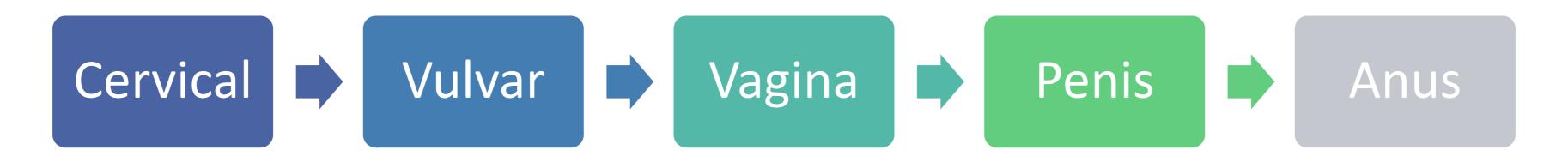


# Human papilloma virus

HPV is the most common sexually transmitted infection (STI). 79 million Americans are infected. About 14 million people become newly infected each year.

In most cases, HPV goes away on its own and does not cause any health problems. But when HPV does not go away, it can cause health problems like genital warts and cancer.

HPV can cause <u>cancers</u> including:



It can also cause cancer in the back of the throat, including the base of the tongue and tonsils

# Human papilloma virus

- Genital warts: Before HPV vaccines:
  - 340,000 360,000 women and men were affected by genital warts yearly.
  - About 1/100 sexually active adults in the U.S. has genital warts at any given time.

#### Cervical cancer:

- Every year, nearly 12,000 women living in the U.S. will be diagnosed with cervical cancer
- More than 4,000 women die from cervical cancer—even with screening and treatment.

## Human papilloma virus

#### RATIONALE

**Females** — Vaccination provides a direct benefit to female recipients by safely protecting against cancers that result from HPV infection. This preventive effect is most notable and best studied with cervical cancer. HPV types 16 and 18 cause approximately 70% of all cervical cancers worldwide, and HPV types 31, 33, 45, 52, cause an additional 20%.

HPV types 16 and 18 also cause nearly 90% of anal cancers and a substantial proportion of vaginal, vulvar, and oropharyngeal cancers. Vaccination also protects against anogenital warts.

## Adult vaccinations - HPV

- Every year in the US 33,700 women and men are diagnosed with a cancer caused by HPV infection. HPV vaccination could prevent more than 90% of these cancers.
- HPV vaccination prevents more than just cervical cancer.
   Vaccination can prevent uncomfortable testing and treatment, even for cervical pre-cancers.
- Every year in the US, nearly 300,000 women are diagnosed with high grade cervical lesions. Testing and treatment for these precancers can have lasting effects.

## Subsequent vaccinations - HPV

#### HPV also causes cancers of:

- √The penis in men
- ✓ Cancers of the vagina and vulva in women
- ✓ Cancers of the anus
- ✓ Cancers of the orohpharynx in men and women.

While doctors routinely screen for cervical cancer, there are no recommended cancer screening tests for the other types of cancers caused by HPV infections.

These cancers may not be detected until they cause health problems.

## Human papilloma virus

- The potential benefits of HPV vaccination appear to be cost effective for the recommended age range. One study suggested that vaccination of the entire United States population of 12-year-old girls would:
  - Annually prevent more than 200,000 HPV infections
  - 100,000 abnormal cervical cytology examinations
  - 3,300 cases of cervical cancer

## Human papilloma virus

#### **RATIONALE**

Males — HPV vaccination provides a direct benefit to male recipients by safely protecting against cancers that can result from HPV infection.

HPV types 16 and 18 cause nearly 90% of anal cancers and substantial proportion of oropharyngeal and penile cancers. Vaccination also protects against anogenital warts (90% HPV types 6 and 11).

The overall burden of HPV-associated cancers/precancers among males is less than the burden of cervical cancer in females. Nevertheless, despite a smaller direct absolute benefit of HPV vaccination in males compared with females, the overall benefit of vaccinating males outweighs its potential risks (population benefits from herd immunity and the documented safety of HPV vaccines).

| Characteristic | Bivalent (2vHPV)*  | Quadrivalent (4vHPV) <sup>†</sup>                       | 9-valent (9vHPV) <sup>§</sup>                           |
|----------------|--|---|---|
| Brand name     | Cervarix   | Gardasil  | Gardasil 9  |
| VLPs           | 16, 18   | 6, 11, 16, 18   | 6, 11, 16, 18, 31, 33, 45, 52, 58                       |
| Manufacturer   | GlaxoSmithKline  | Merck and Co., Inc.                                     | Merck and Co., Inc.                                     |
| Manufacturing  | Trichoplusia ni insect cell line infected with L1 encoding recombinant baculovirus | Saccharomyces cerevisiae (Baker's yeast), expressing L1 | Saccharomyces cerevisiae (Baker's yeast), expressing L1 |
| Adjuvant       | 500 μg aluminum hydroxide,<br>50 μg 3-O-desacyl-4' monophosphoryl lipid A          | 225 µg amorphous aluminum<br>hydroxyphosphate sulfate   | 500 µg amorphous aluminum<br>hydroxyphosphate sulfate   |

## FDA approves expanded use of Gardasil 9 to include individuals 27 through 45 years old



For Immediate Release

October 5, 2018

## Tetanus vaccine

Tetanus +/- Pertusis

Recommended booster every 10 years, if no trauma!

If trauma in the first 5 years post vaccine, no further intervention needed. If trauma after 5 years of vaccine, booster advised.

#### Wound management and tetanus prophylaxis

| Previous doses        | Clean and minor wound                              |                                  | All other wounds¶                                  |                                   |
|-----------------------|--|----------------------------------|--|-----------------------------------|
| of tetanus<br>toxoid* | Tetanus toxoid-<br>containing vaccine <sup>△</sup> | Human tetanus<br>immune globulin | Tetanus toxoid-<br>containing vaccine <sup>∆</sup> | Human tetanus<br>immune globulin¢ |
| <3 doses or unknown   | Yes⁵   | No                               | Yes⁵   | Yes                               |
| ≥3 doses              | Only if last dose given<br>≥10 years ago           | No                               | Only if last dose given<br>≥5 years ago¥           | No                                |

## Tetanus Stats 2016-17

- The proportion of adults aged ≥19 years reporting having received any tetanus toxoid-containing vaccination during the past 10 years was 63.4%
- Among adults aged > 19 years for whom Tdap vaccination could be assessed, increased from 2016 to 2017 overall and by age group.
- Among adults aged ≥19 years, white adults had higher coverage

## Pregnancy vaccines

#### Pertussis

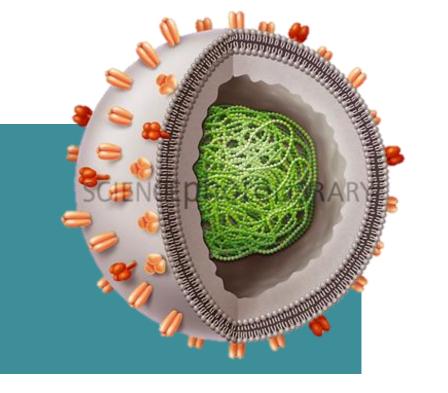
Recommended during each pregnancy! 27 to 36 week gestational age

Vaccination of household contacts

#### <u>Influenza</u>

Recommended during the influenza season Only inactivated vaccines





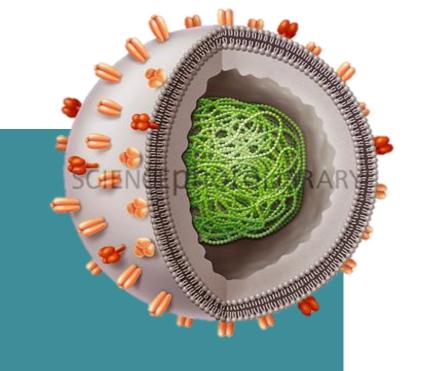
## Influenza

Influenza (flu) is a contagious respiratory illness caused by influenza viruses. There 3 types of Influenza:

Influenza A

Influenza B

Influenza C



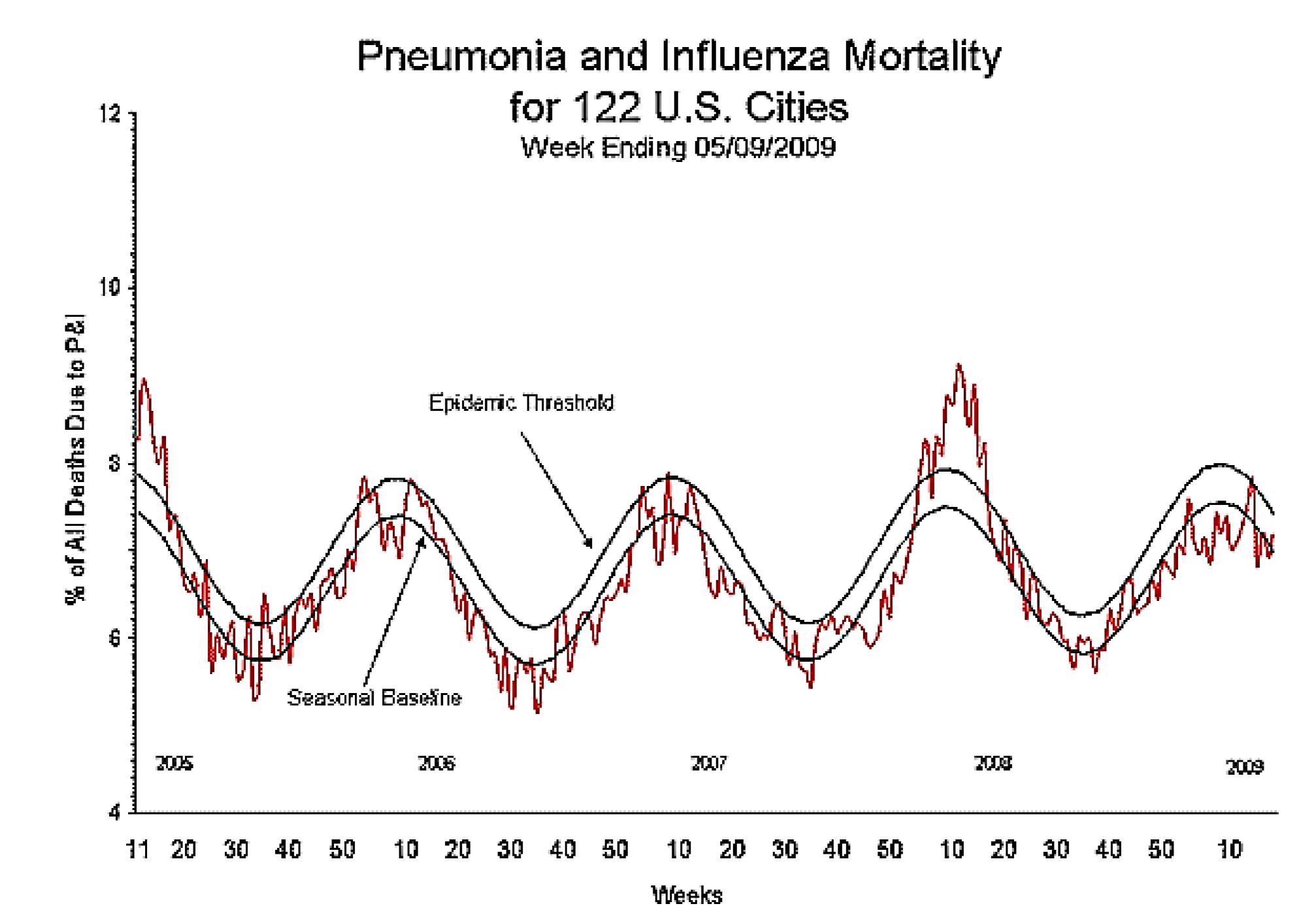
## Seasonal Influenza

Every year, millions of people get the flu. The good news is that the seasonal flu vaccine can lower the risk of getting the flu by about half.

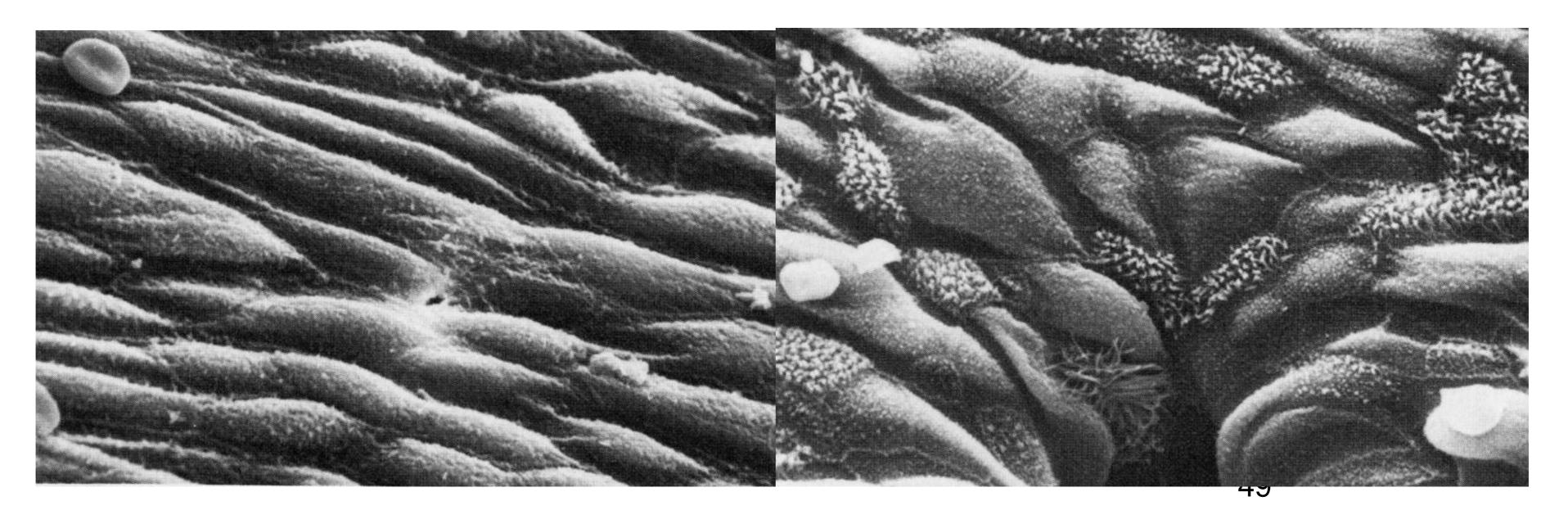
It mostly killed young adults with more than half of the deaths in people between 20-40 years old due to novel surface proteins on the virus.

The majority of deaths were from a secondary infection (bacterial pneumonia)

Spanish flu killed as many as 25 million in the first **25 weeks**, whereas HIV/AIDS has killed 25 million in the first 25 years. It killed 2-20 % of those infected; normal rate is 0.1 %

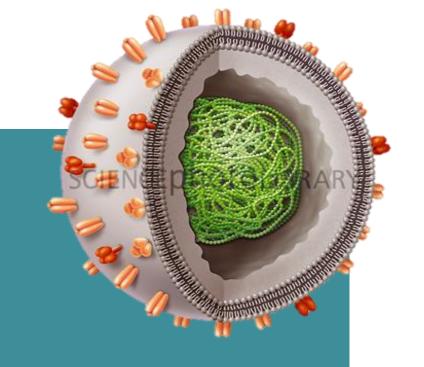






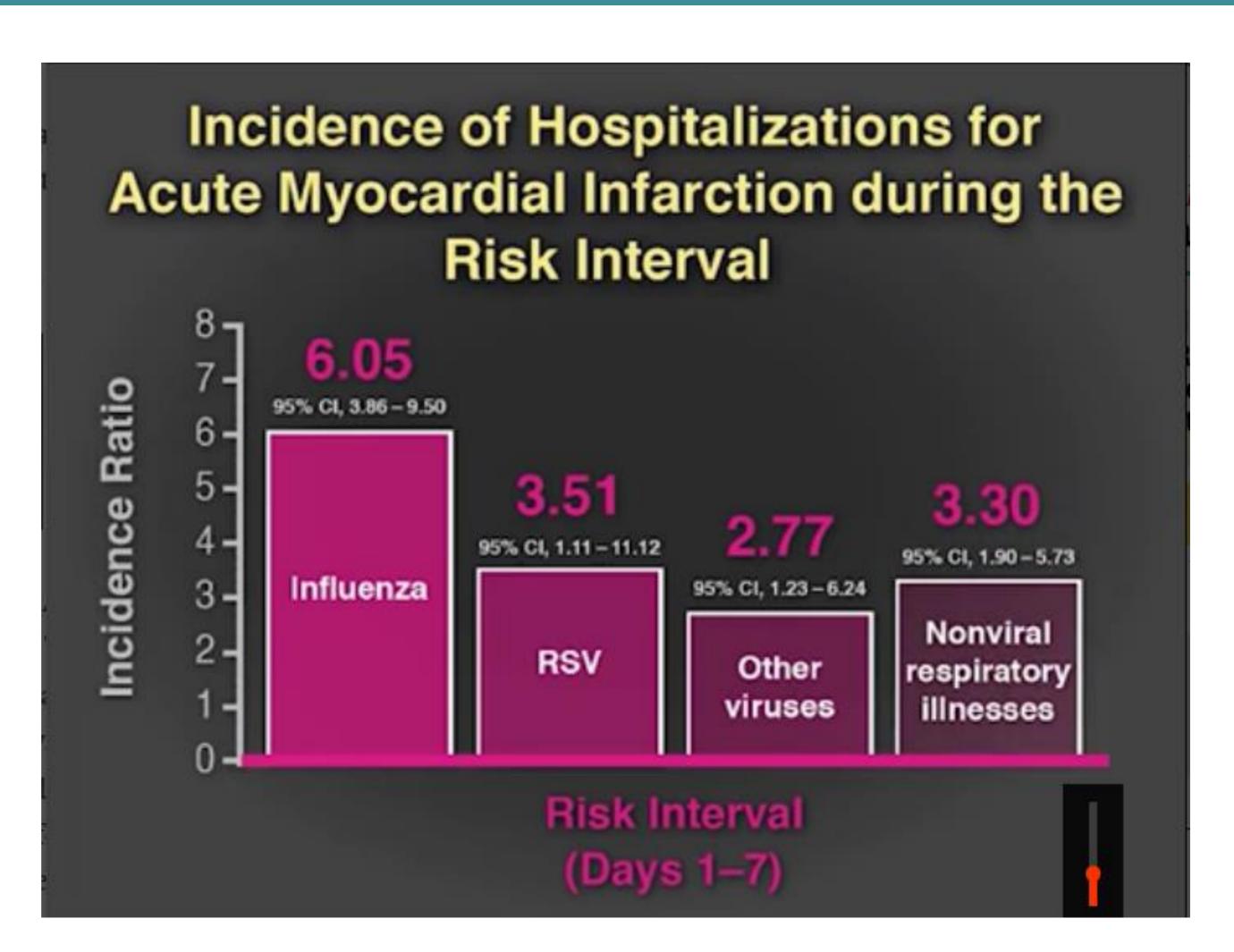
Lycke and Norrby Textbook of Medical Virology 1983

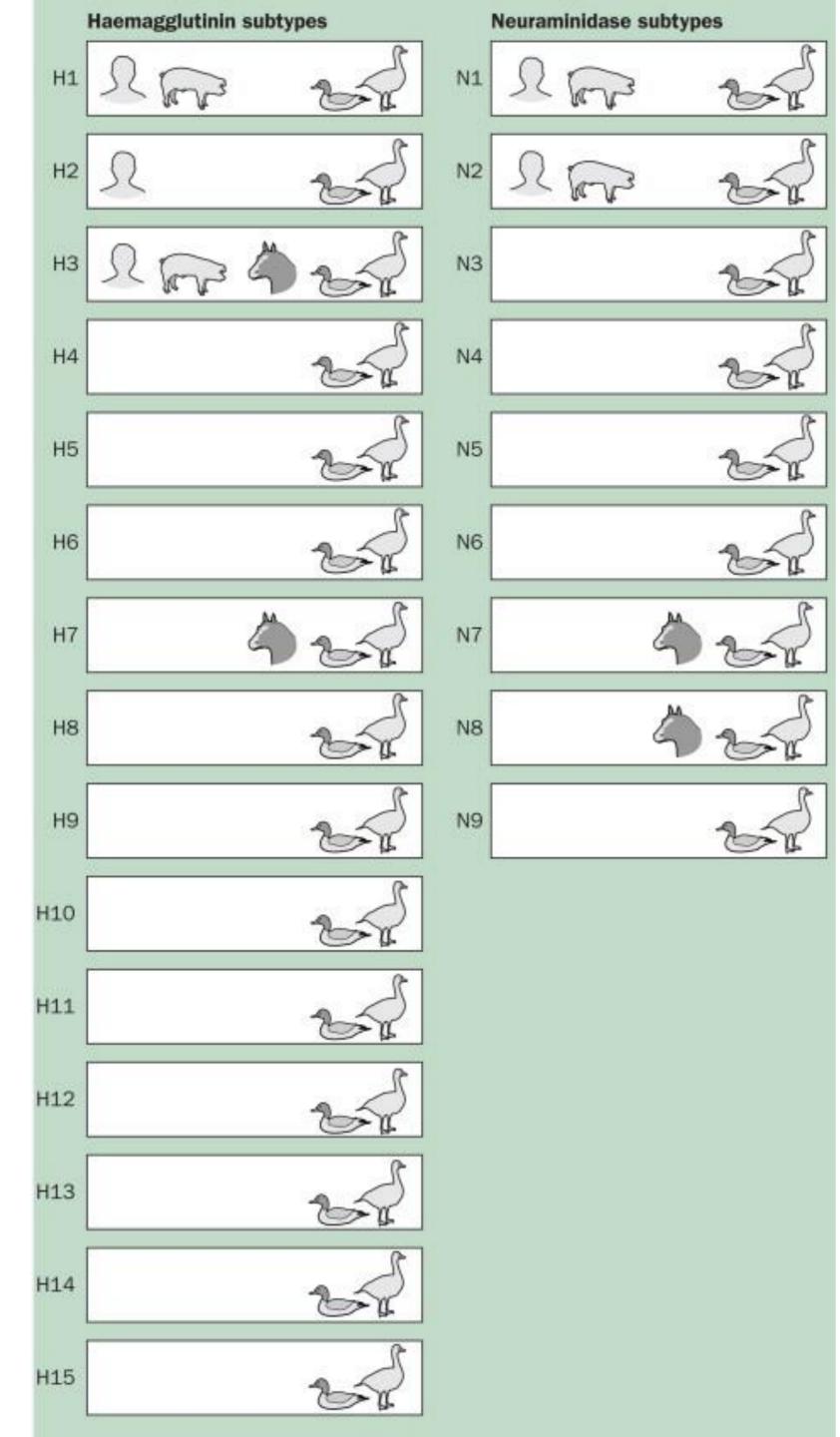




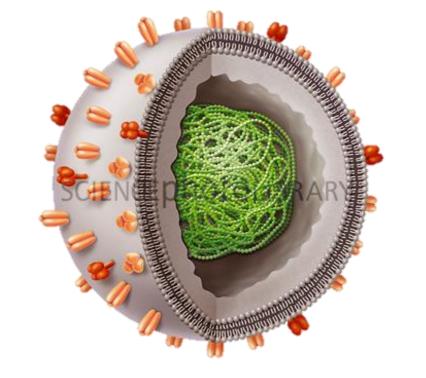
NEJM January 2018

Acute MI in the initial 6 days



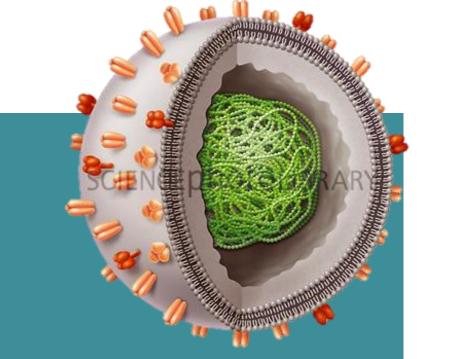


## Possible Strains



Reassortment between the RNA segments encoding haemagglutinin (HA) and neuraminidase (NA) produces virus with novel HA and NA subtype combinations, and this has preceded the emergence of pandemic strains.

 $15 \times 9 = 135$  possible strains



## People at increased risk for complications

It's especially important for people who are at high risk of developing complications from the flu to get the vaccine every year. People at high risk for complications from the flu include:

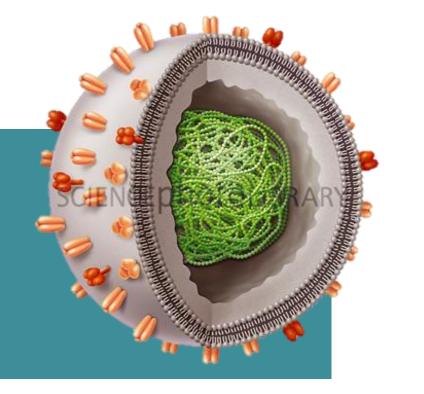
- ✓ Pregnant women including women up to 2 weeks after the end of pregnancy
- ✓ Adults age 65 years and older
- ✓ Children younger than 5 years and especially children younger than 2 years
- ✓ People with long-term health conditions like asthma, diabetes, or cancer
- ✓ People in long-term care or nursing homes

# SGEN AR AR

## Vaccine

The formula for the influenza vaccine is updated every year on the basis of worldwide surveillance by the collaborating centers of the World Heath Organization (WHO).

Advisory committees of the CDC and of the FDA review the information and select for inclusion those variants of the 3 prevalent viruses in the human population that are most likely to cause outbreaks in the upcoming season.



## Vaccine

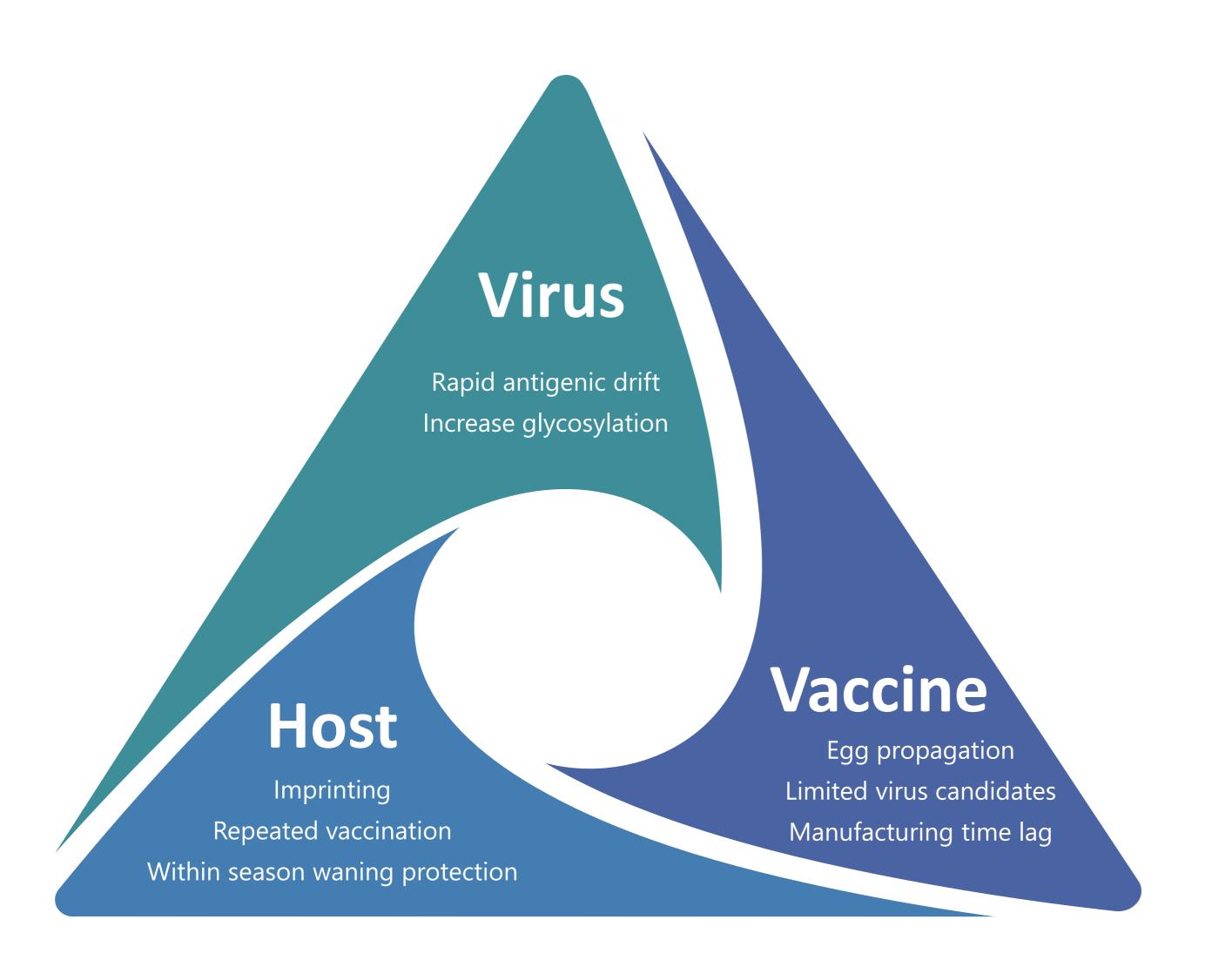
The current production system requires that the viruses used for vaccine production be selected in February-March of each year:

✓ It is not unusual for new variants to appear in the southern hemisphere after the vaccine formula for the northern hemisphere has been set and production has begun.

A new variant that was not contained in the vaccine has been the major virus involved in 80% of the epidemics.

#### Influenza Vaccine Effectiveness

Defining the problem



#### **Reduced protection**

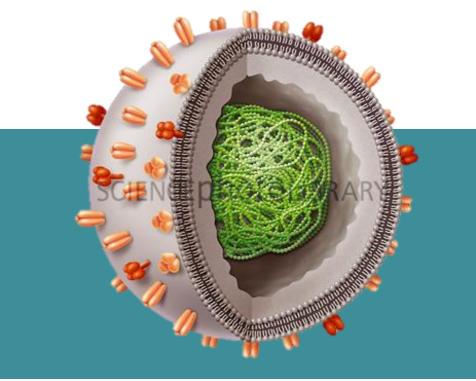
H3N2 – 33% H1N1 -- 62% Flu B – 54%

#### Age dependent

For H3N2: Pediatrics – 43% Age > 60 – 24%

#### Increase glycosylation

Original H3N2 (HK1968) had 2 glycosylation sites, but now has 6-7 sites in the HA site.



## Who Needs Vaccination

Everybody from 6 months old

All pregnant female should be assess for vaccination.

- ✓ Vaccine is safe in pregnancy
- ✓ Decreases disease in mother and baby

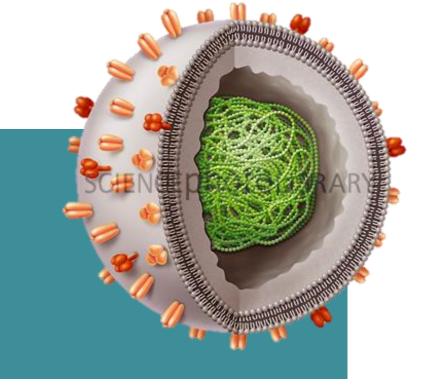
Vaccines DOSES NOT increase risk of Guillain-Barre

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### Vaccine

- •Healthcare workers vaccination is associated with:
  - ✓ Decrease in missing work
  - ✓ Decrease influenza death in patients

- •There is also strong correlation to decrease HCW-patient transmission:
  - ✓ Patient exposed to HCW RR 5.48
  - ✓ Patient exposed to contagious patient RR 17.96
  - ✓ Patient exposed to HCW and contagious patient 34.75
  - ✓ Always use PPE despite receiving vaccination.



## Vaccines 2019

Basics of influenza vaccine: not all vaccines are the same.

| Vaccine                       |                |                      |  |
|-------------------------------|----------------|----------------------|--|
| Trivalent SD                  | H3N2,H1N1, B   | 18-64 years old      |  |
| Trivalent HD                  | H3N2,H1N1, B   | 65 plus years old    |  |
| Recombinant Egg-free          | H3N2,H1N1, B   | 18 plus years old    |  |
| Trivalent w/ adjuvant         | H3N2,H1N1, B   | 65 plus years old    |  |
| Quadrivalent                  | H3N2,H1N1, Bx2 | Different age groups |  |
| Quadrivalent intradermal      | H3N2,H1N1, Bx2 | 18 plus years old    |  |
| Quadrivalent<br>Cell-cultured | H3N2,H1N1, Bx2 | 4 plus years old     |  |
| Quadrivalent<br>Nasal Spray   | H3N2,H1N1, Bx2 | AGAIN RECOMMENDED    |  |

## Influenza Vaccine Side Effects

| Symptom     | Vaccine (%) | Placebo (%) | P     |
|-------------|-------------|-------------|-------|
| Fever       | 5.7         | 4.2         | .68   |
| Cough       | 6.6         | 5.1         | .62   |
| Coryza      | 13.2        | 10.2        | .27   |
| Fatigue     | 8.0         | 7.7         | .82   |
| Malaise     | 7.2         | 6.3         | .83   |
| Myalgia     | 4.8         | 4.2         | .84   |
| Headache    | 6.9         | 7.6         | .99   |
| Any symptom | 27.7        | 22.9        | .21   |
| Sore arm    | 20.1        | 4.9         | <.001 |

#### Practice Standards for All Healthcare Professionals

1. ASSESS immunization status of all your patients at every clinical encounter.

Follow yearly updates at www.CDC.gov

2. Strongly RECOMMEND vaccines that patients need.

Share tailored reasons why vaccination is right for the patient.

Highlight positive experiences with vaccination.

Address patient questions and concerns.

Remind patients that vaccines protect them and their loved ones against a number of common and serious diseases.

Explain the potential costs of getting sick.

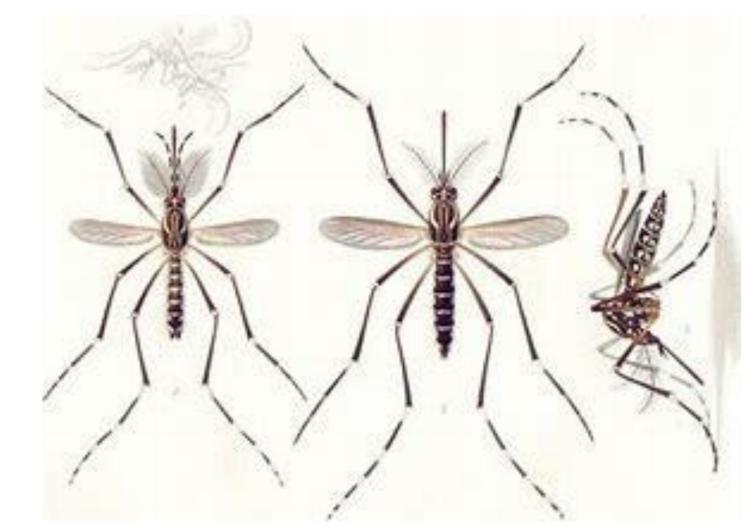
#### Practice Standards for All Healthcare Professionals

- 3. ADMINISTER or REFER your patients to a vaccination provider. **Offer the vaccines** you stock.
  - Refer patients to providers in the area that offer vaccines that you don't stock.
- 4. DOCUMENT vaccines received by your patients.
  - ✓ Participate in your state's immunization registry. Help your office, your patients, and your patients' other providers know which vaccines your patients have had.
  - ✓ **Follow up.** Confirm that patients received recommended vaccines that you referred them to get from other immunization providers.

## Dengue Vaccine

Dengvaxia (live attenuated tetravalent chimeric vaccine)

- \*3 dosis
- \*Recommended age 9-16 years
- \*only in persons with laboratory confirmed



#### Why? ADE

✓ ADE (antibody-dependent enhancement of infection) Phenomenon

#### DENGVAXIA

#### Limitations of use:

• Not approved for use in individuals not previously infected by any dengue virus serotype. Those not previously infected are at increased risk for severe dengue disease when vaccinated.

#### Warning:

• In persons not previously infected by dengue virus, an increased risk of severe dengue disease can occur following vaccination with DENGVAXIA.

• There is no FDA-cleared test available to determine a previous dengue infection.

## Dengue Vaccine in pipeline...

- TetraVax-DV Brasil
- TDENV PIV GSK with Walter Reed Army Institute of Research
- V180 MERCK

Should we vaccinate or wait further options?

## Covid vaccines (SARS-CoV-2)

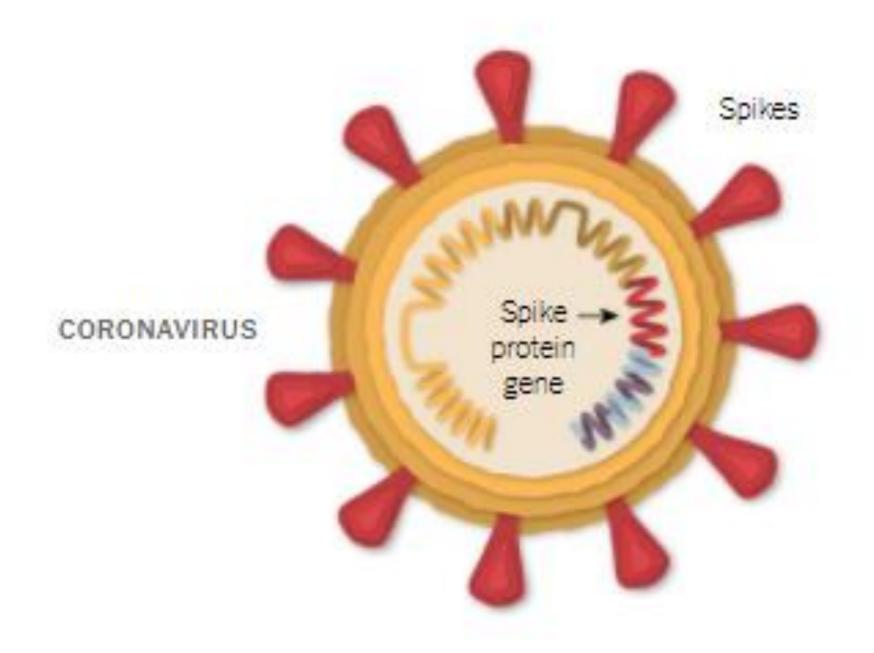
• The German company BioNTech partnered with Pfizer to develop and test a coronavirus vaccine known as **BNT162b2**, the generic name **tozinameran** or the brand name **Comirnaty**.

Vaccine based on mRNA.

• A clinical trial demonstrated that the vaccine has an <u>efficacy rate</u> of 95% in preventing Covid-19.

#### A Piece of the Coronavirus

The SARS-CoV-2 virus is <u>studded with proteins</u> that it uses to enter human cells. These so-called spike proteins make a tempting target for potential <u>vaccines</u> and <u>treatments</u>.



Like the Moderna vaccine, the Pfizer-BioNTech vaccine is based on the virus's genetic instructions for building the spike protein.

#### mRNA Inside an Oily Shell

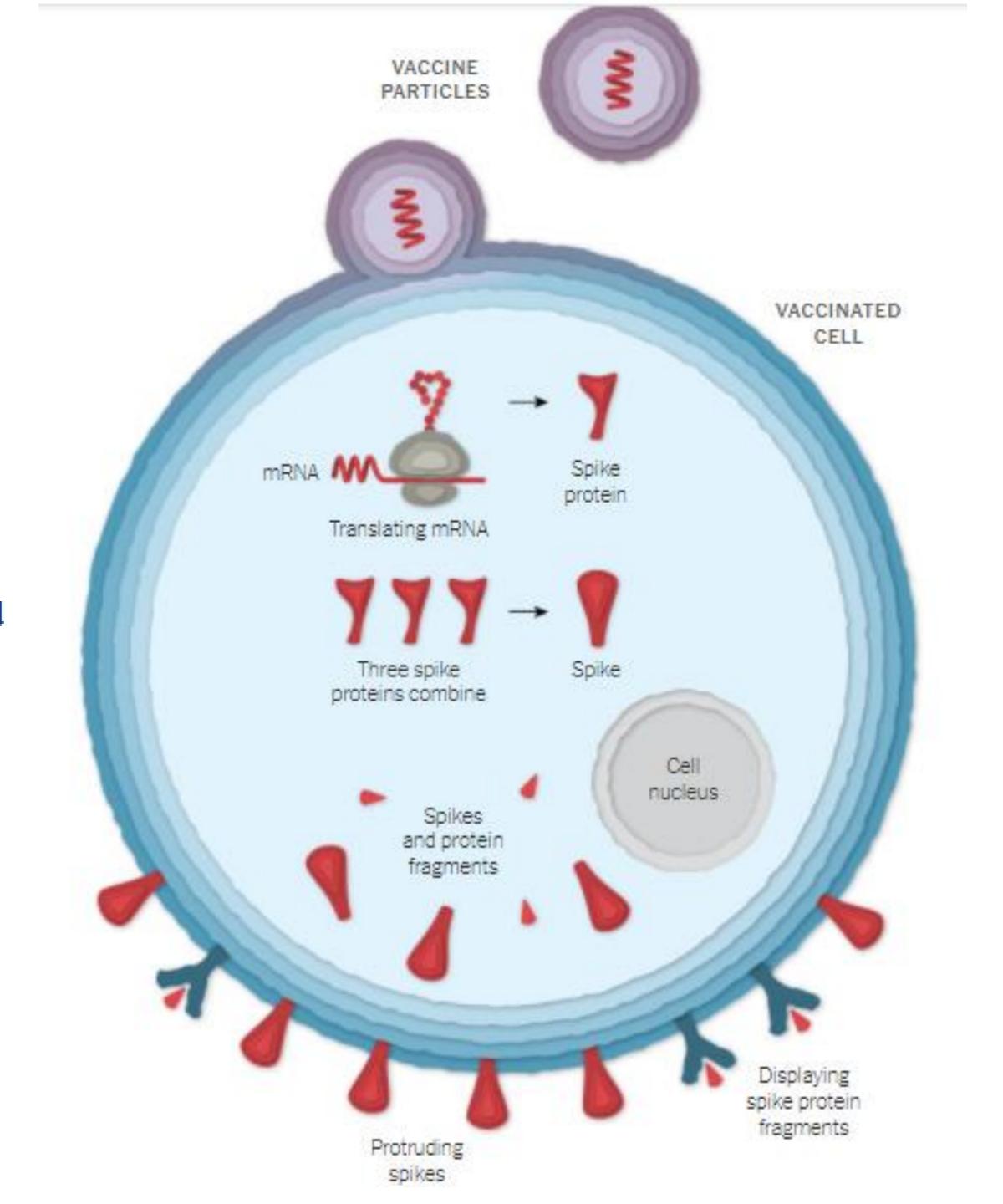
The vaccine uses messenger RNA, genetic material that our cells read to make proteins. The molecule — called mRNA for short — is fragile and would be chopped to pieces by our natural enzymes if it were injected directly into the body. To protect their vaccine, Pfizer and BioNTech wrap the mRNA in oily bubbles made of lipid nanoparticles.



Because of their fragility, the mRNA molecules will quickly fall apart at room temperature. Pfizer is building special containers with dry ice, thermal sensors and GPS trackers to ensure the vaccines can be transported at -94°F (-70°C) to stay viable.

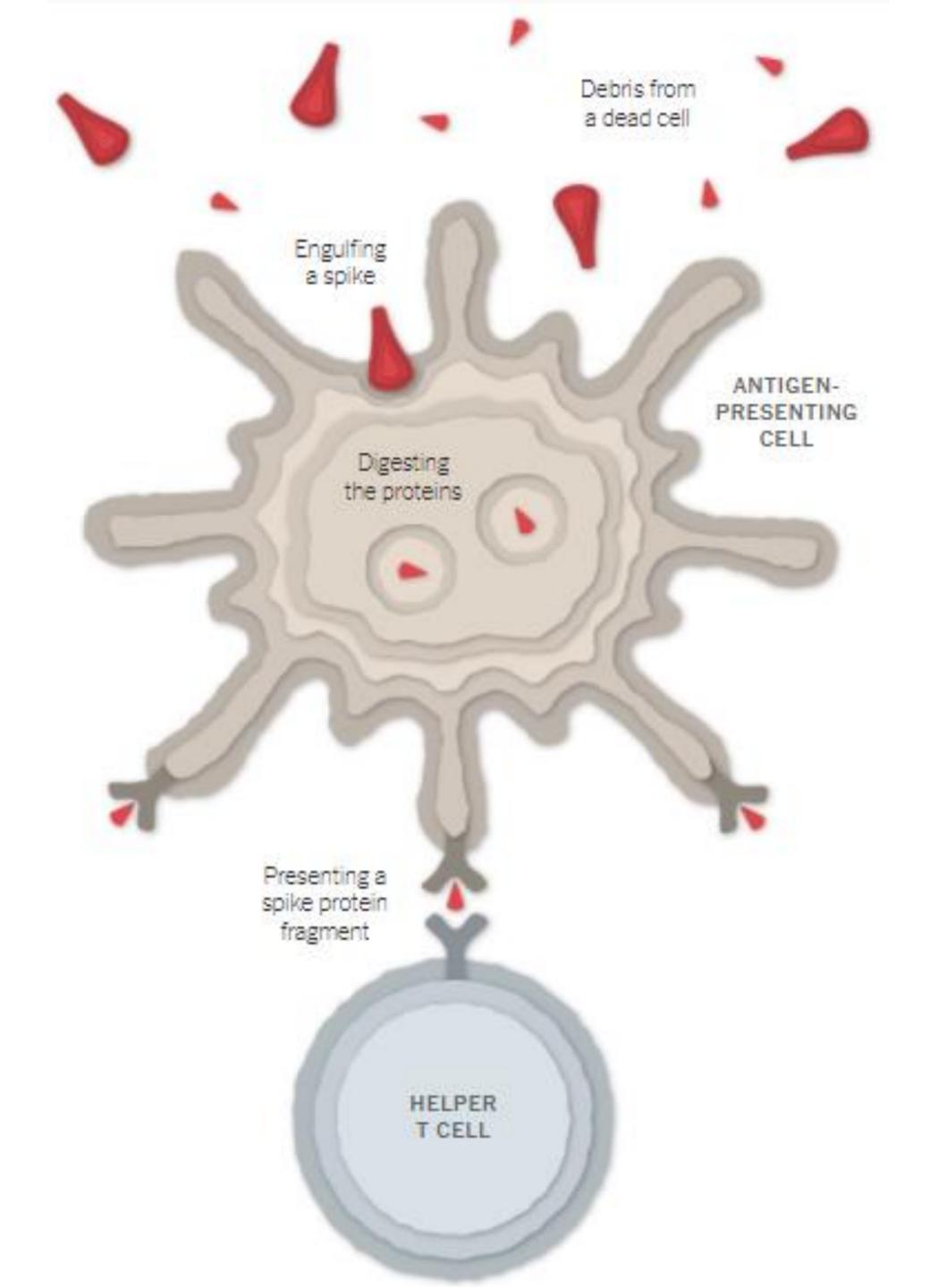
#### Entering a Cell

After injection, the vaccine particles bump into cells and fuse to them, releasing mRNA. The cell's molecules read its sequence and build spike proteins. The mRNA from the vaccine is eventually destroyed by the cell, leaving no permanent trace.



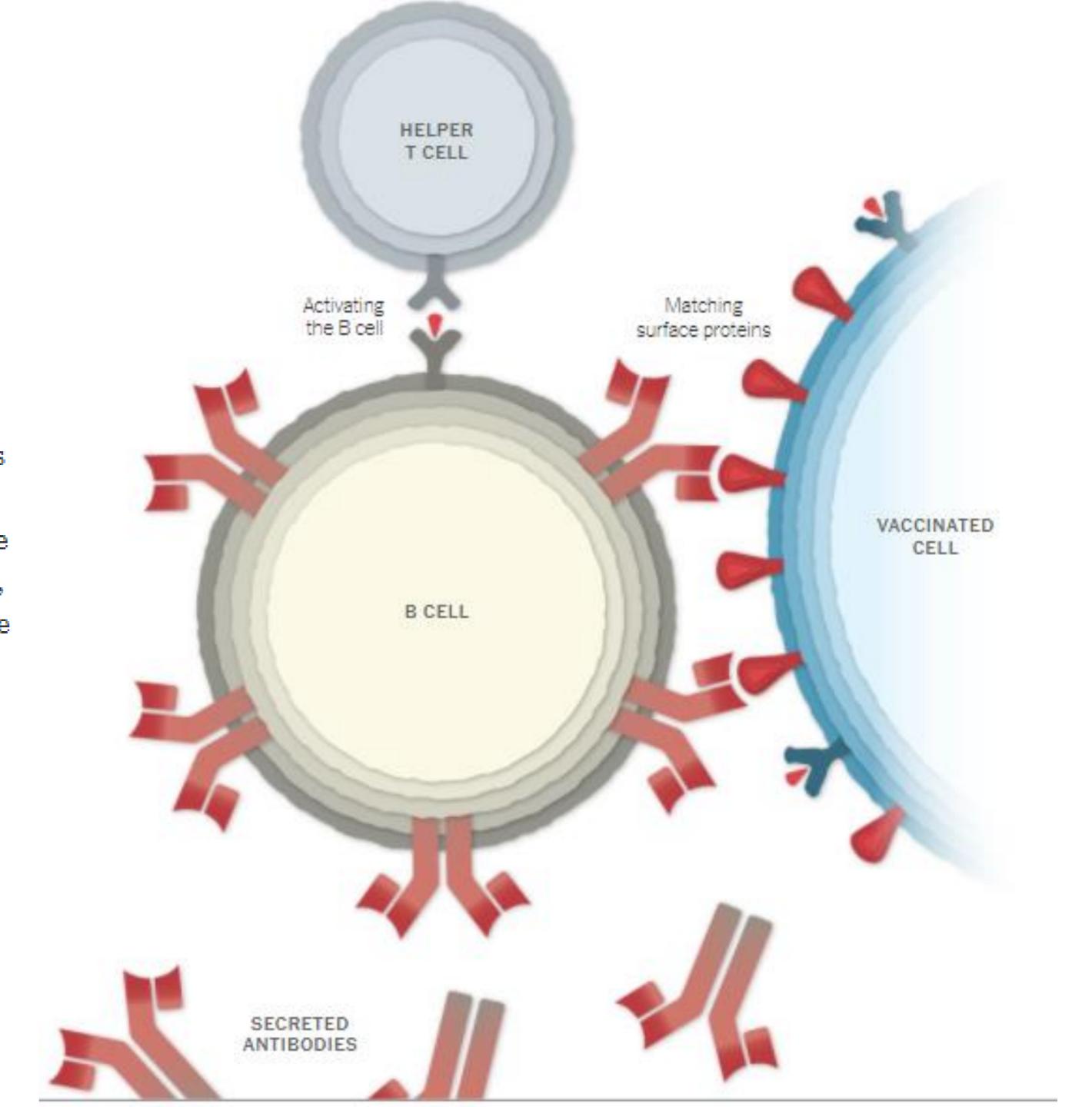
#### Spotting the Intruder

When a vaccinated cell dies, the debris will contain many spike proteins and protein fragments, which can then be taken up by a type of immune cell called an antigen-presenting cell.



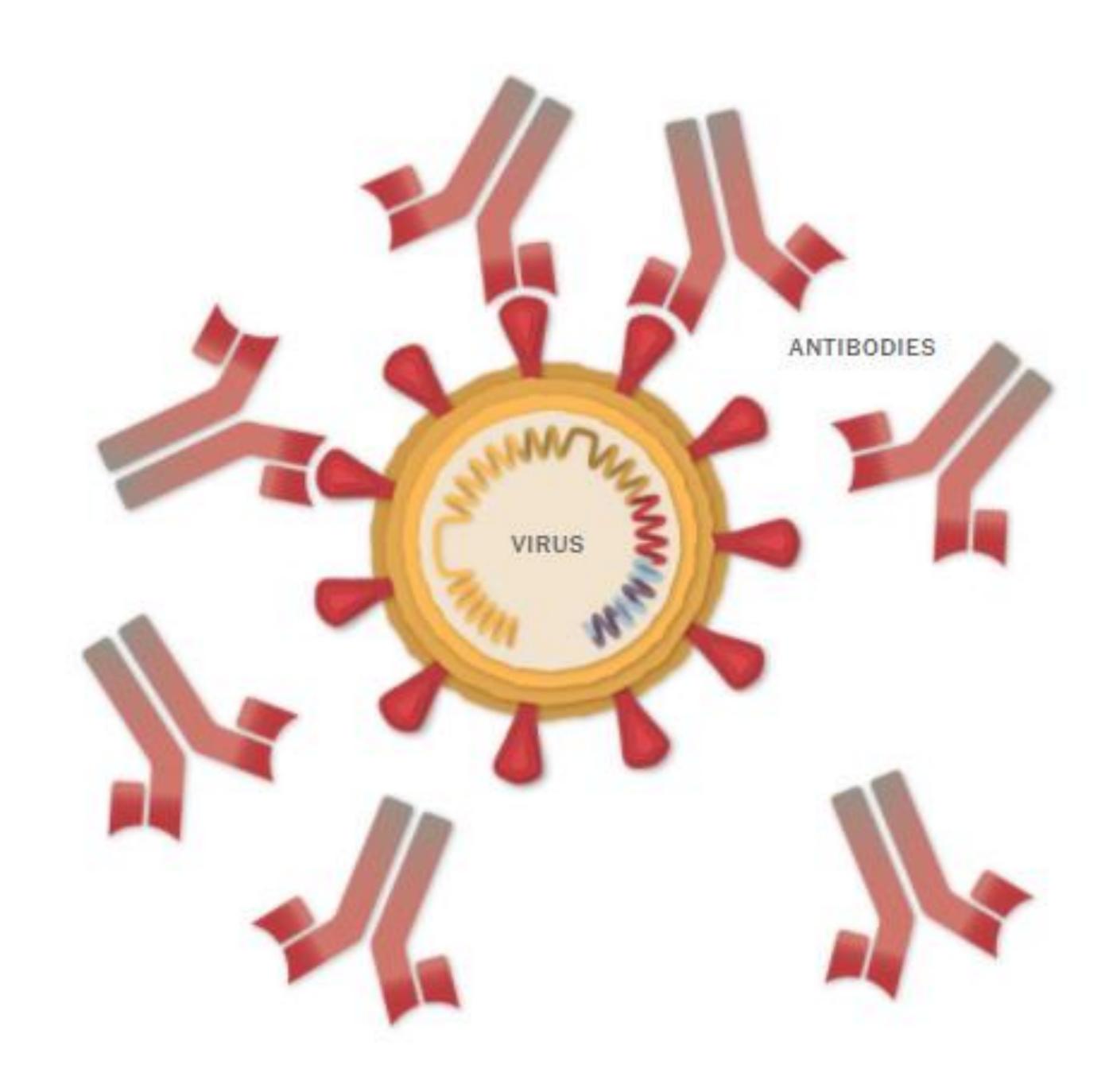
#### Making Antibodies

Other immune cells, called B cells, may bump into the coronavirus spikes on the surface of vaccinated cells, or free-floating spike protein fragments. A few of the B cells may be able to lock onto the spike proteins. If these B cells are then activated by helper T cells, they will start to proliferate and pour out antibodies that target the spike protein.



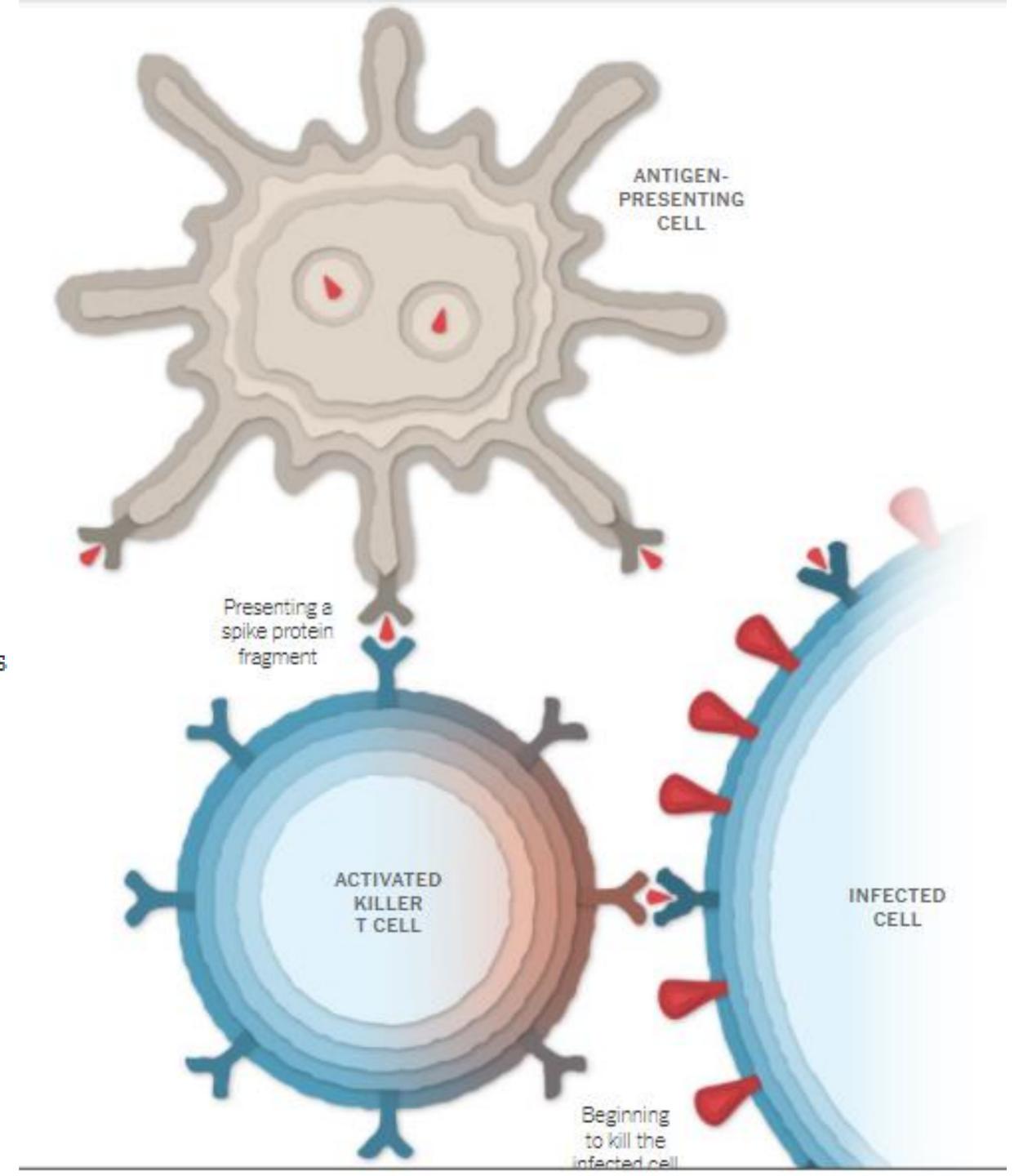
#### Stopping the Virus

The antibodies can latch onto coronavirus spikes, mark the virus for destruction and prevent infection by blocking the spikes from attaching to other cells.



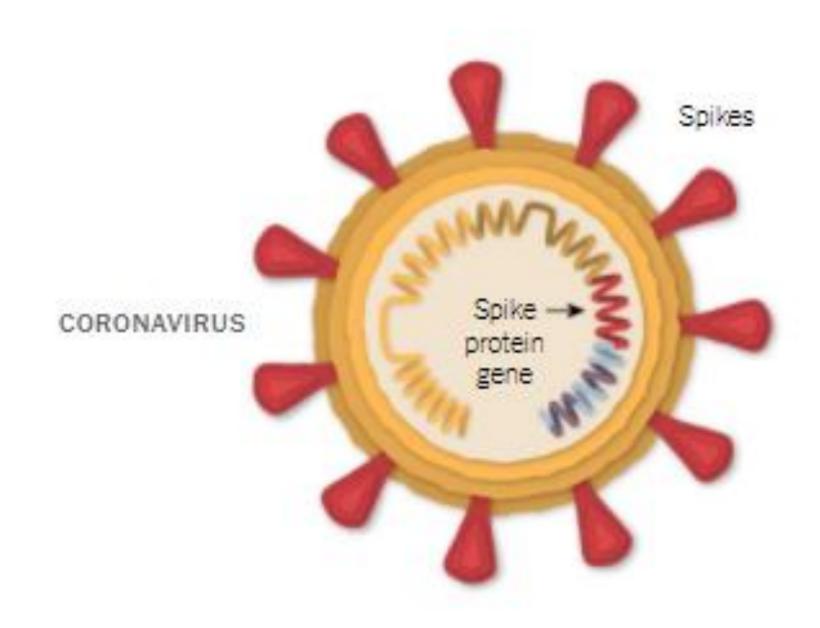
#### Killing Infected Cells

The antigen-presenting cells can also activate another type of immune cell called a killer T cell to seek out and destroy any coronavirus-infected cells that display the spike protein fragments on their surfaces.



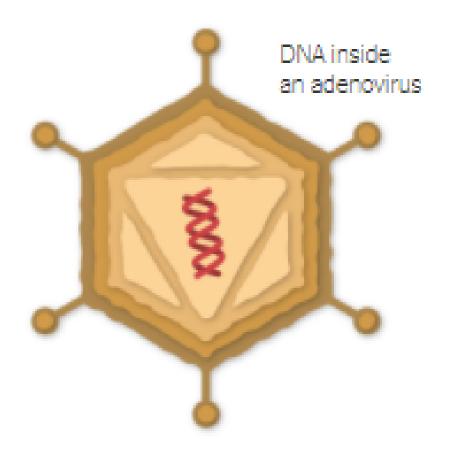
#### A Piece of the Coronavirus

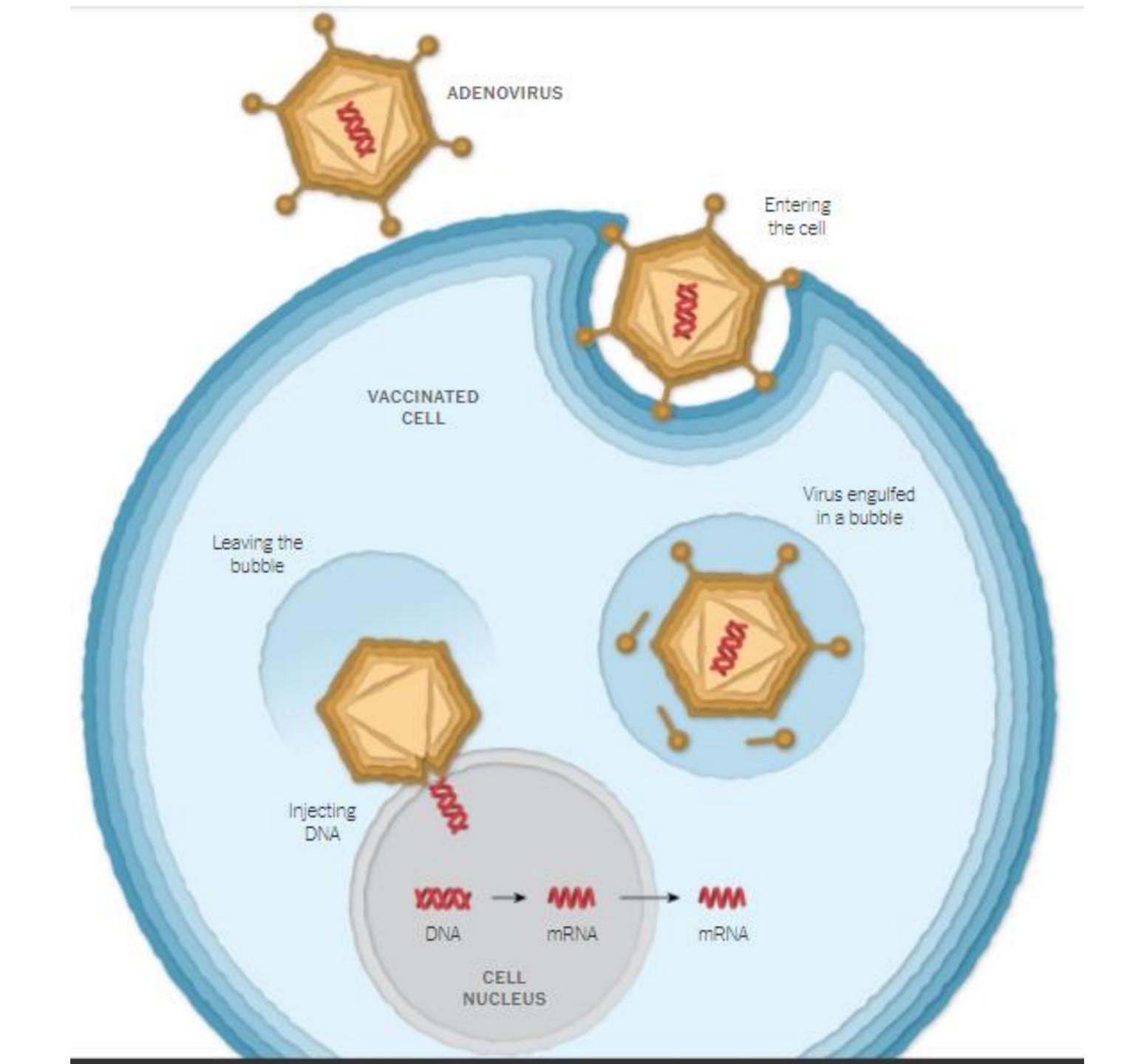
The SARS-CoV-2 virus is <u>studded with proteins</u> that it uses to enter human cells. These so-called spike proteins make a tempting target for potential <u>vaccines</u> and <u>treatments</u>.



#### DNA Inside an Adenovirus

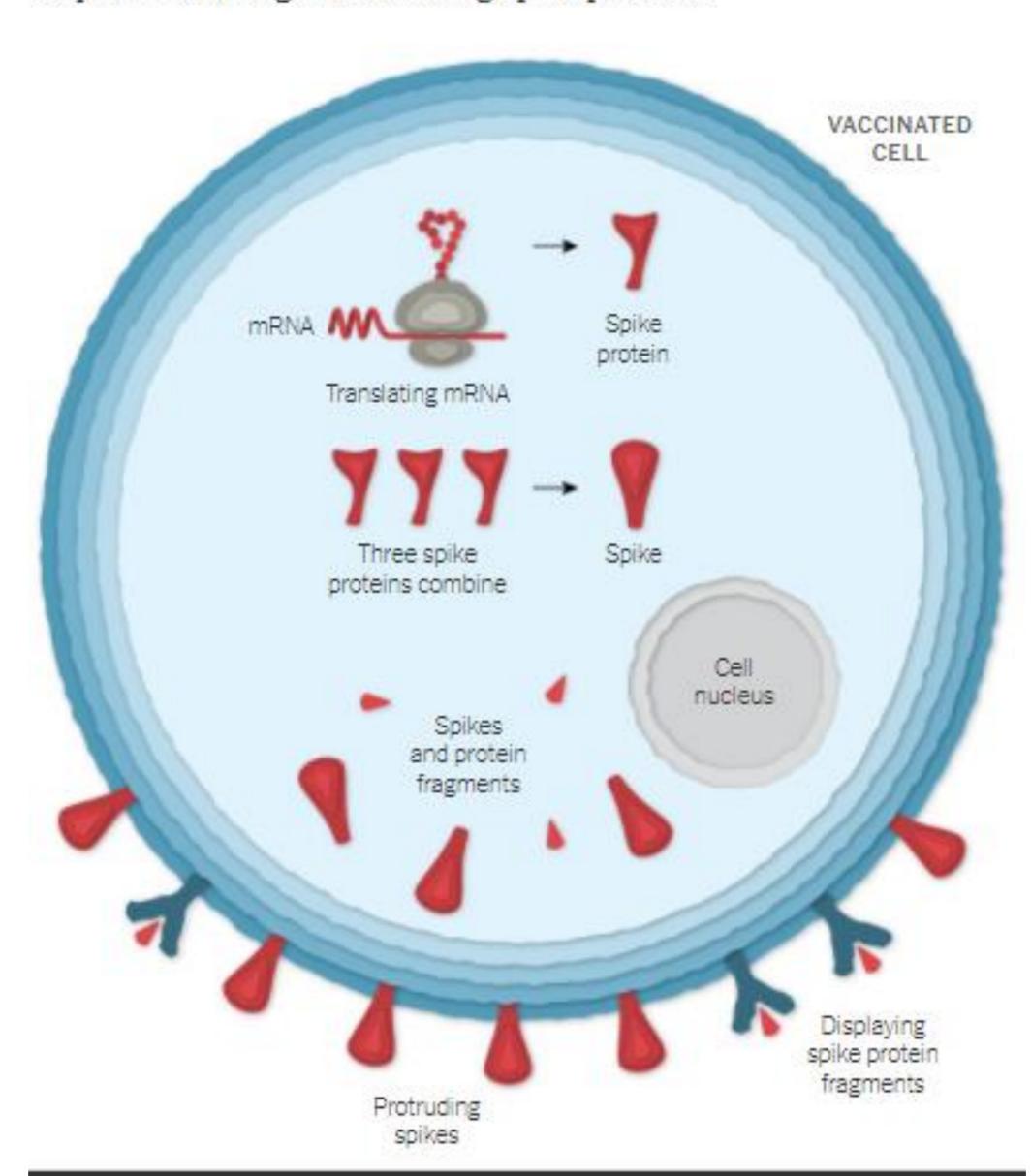
The researchers added the gene for the coronavirus spike protein to another virus called <u>Adenovirus 26</u>. Adenoviruses are common viruses that typically cause colds or flu-like symptoms. The Johnson & Johnson team used a modified adenovirus that can enter cells but can't replicate inside them or cause illness.



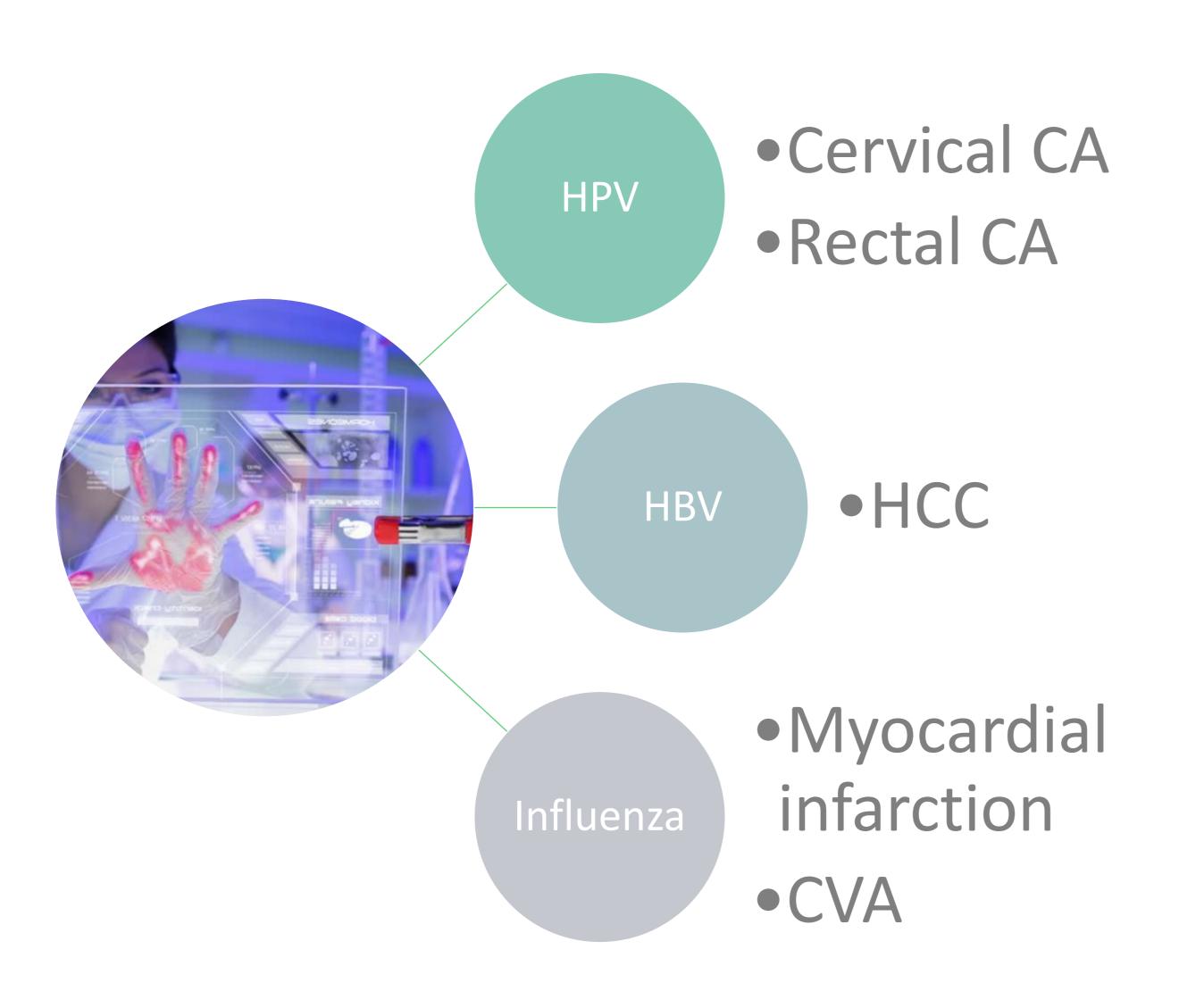


#### **Building Spike Proteins**

The mRNA leaves the nucleus, and the cell's molecules read its sequence and begin assembling spike proteins.



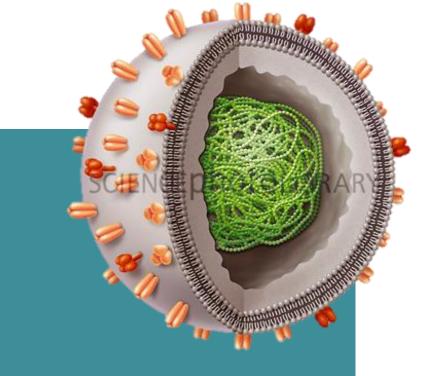
## The present is bright, and the future even brighter





Dengue

- Zika
- Malaria
- HCV
- CMV
- HIV
- Universal influenza



## Contraindication for live-attenuated

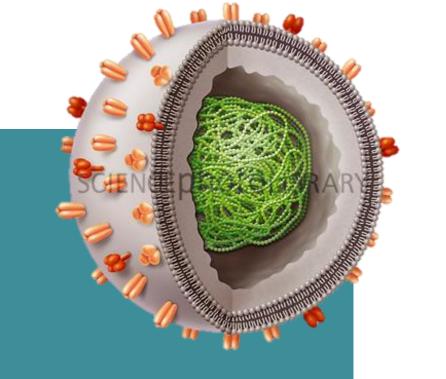
Live, attenuated influenza vaccine (LAIV) is an option for adults through age 49 years, except those who:

- Immunosuppressed (including HIV)
- Have anatomical or functional asplenia
- Are pregnant
- Have close contact with or are caregivers of severely immunocompromised persons in a protected environment
- Have received influenza antiviral medications in the previous 48 hours
- Have a cerebrospinal fluid leak or a cochlear implant

#### Live vaccines

- Adenovirus vaccine
- Bacille Calmette-Guérin (BCG)
- Live attenuated influenza vaccine (intranasal)\*
- Live attenuated oral poliovirus vaccine\*
- Measles, mumps, and rubella vaccine
- Measles, mumps, rubella, and varicella vaccine
- Measles vaccine
- Mumps vaccine
- Oral typhoid vaccine\*
- Rotavirus vaccine
- Rubella vaccine
- Smallpox vaccine
- Varicella vaccine
- Yellow fever vaccine
- Zoster vaccine

In the United States, live virus vaccines are routinely recommended for protection against rotavirus, measles, mumps, rubella, varicella, and herpes zoster. Either inactivated or live attenuated influenza vaccine may be used for people 2 through 49 years of age. Oral poliovirus vaccine is not available in the United States. Routinely recommended vaccines for other countries are available through the World Health Organization. Refer to the relevant UpToDate topic reviews for specific vaccine recommendations.



## Vaccine Contraindication

Moderate to severe illness with or without fever

History of Guillain-Barré syndrome within 6 weeks of receipt of influenza vaccine

History of severe allergic reaction (e.g., anaphylaxis) to egg is a labeled contraindication to the use of IIV and LAIV.

ACIP recommends that any licensed, recommended, and appropriate IIV or RIV may be administered to persons with egg allergy of any severity