Vaccine for 'Older Individuals'

McGill Refresher Course 2020

https://www.youtube.com/watch?v=fQ8hGMt7IZk

Brian J Ward
McGill Division of Infectious Diseases
Research Institute - McGill University Health Center

LEARNING OBJECTIVES

After attending this session, participants will be able to:

1) Make better use of the vaccines routinely used to protect older adults

2) Explain the strengths and weaknesses of routine vaccines to their older patients

3) Answer the most common questions about vaccines routinely used in older people

Conflict of Interest Statement (Last 5 Years)

Position in Pharma	Medical Officer for Medicago Inc. (Oct 2011 - present)
Consulting	Pfizer, Merck, Novartis, GSK, Sanofi Pasteur MSSS, US Dept of Justice (Vaccine Compensation Programs)
Contracts	Vaccine trials for virtually all companies
Shared Awards	Shared CIHR Team grant (Laval U, GSK) CIHR-Industry grant (Medicago) Shared CQDM grant (Medicago, Laval U, SNC Lavalin)
Occasional Speakers Honoraria	Pfizer, Sanofi Pasteur,Novartis
Investments	None

One Tried & True Approach to Staying Alive

25 years

tps://www.pinterest.ca/pin/322429654562572305/

19 years

https://www.datingadvice.com/for-men/the-curse-of-the-older-man-and-the-younger-woman

Another …

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3499891/

al. Five-Day Whole-Body Cryostimulation, Blood Inflammatory Markers, and Performance in High-Ranking Professional


We’re here
to talk about
VACCINES
www.urbandojo.com

Vaccine 34 (2016) 6681–6690

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Review

Vaccination of special populations: Protecting the

Mark Doherty [a,*], Ruprecht Schmidt-Ott [a], Jose Ignacio Santos
Annika M. Hofstetter [e,f], Susan L. Rosenthal [c], Anthony L. Cu

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[b] Universidad Nacional Autónoma de México (UNAM), Mexico City, Mexico
[c] Columbia University College of Physicians and Surgeons, New York, NY, USA
[d] New York-Presbyterian/Morgan Stanley Children's Hospital, New York, NY, USA
[e] Department of Pediatrics, University of Washington, Seattle, WA, USA
[f] Center for Clinical and Translational Research, Seattle Children's Research Institute, Seattle, WA, USA
[g] Westmead Institute, The Centre for Virus Research, 176 Hawkesbury Road, NSW 2145, Australia

Influenza
Pneumonia
Shingles
Tetanus
Diphtheria
Pertussis

Box 3
Vaccination of older adults.

Population	• Older adults
Reasons for increased risk of disease	• Decline in innate and adaptive (antibody and T-cell) immune responses (immunosenescence)
Diseases most commonly targeted by vaccination	• Influenza • Community-acquired pneumonia • Shingles (herpes zoster) • Tetanus • Diphtheria • Pertussis
Reported vaccine uptake rates[a]	• 50–70% for influenza, tetanus, pneumococcus • <25% for herpes zoster
Common barriers to vaccination	• Attitudes and beliefs regarding vaccination (especially negative attitudes) • Failure of healthcare provider to recommend vaccination • Lack of knowledge of vaccine safety and effectiveness • Perceived susceptibility to disease • Lack of awareness of national recommendations
Unmet vaccination needs	• Vaccines with improved immunogenicity, particularly influenza and pneumococcal vaccines • Vaccines against other leading causes of infection in older adults, such as *Staphylococcus aureus*, *Clostridium difficile* • Among active older adults, better consideration should be given to immunity to and risk of travel-associated diseases

[a] In US.

Doherty M et al Vaccination of special populations: Protecting the vulnerable. Vaccine. 2016 Dec 20;34(52):6681-6690.

Vaccine Coverage in Older Individuals is Sub-Optimal

USA (≥ 65years of age)

- 67% for influenza vaccine
- 55-60% for tetanus and pneumococcal vaccines
- 24% for herpes zoster vaccine

Canada

- ~60% for influenza vaccine (varies by year!)
- 38% for tetanus (2004) and 40% for pneumococcus (2018)
- ~8% for herpes zoster vaccine (2014)

Doherty M et al Vaccination of special populations: Protecting the vulnerable. Vaccine. 2016 Dec 20;34(52):6681-6690.
Trends in influenza **vaccine coverage** and **vaccine** hesitancy in **Canada**, 2006/07 to 2013/14: results from cross-sectional survey data. Buchan SA, Kwong JC. CMAJ Open. 2016 Aug 19;4(3):E455-E462.
Herpes zoster **vaccine** (HZV): utilization and **coverage** 2009 - 2013, Alberta, **Canada**. Liu XC, Simmonds KA, Russell ML, Svenson LW. BMC Public Health. 2014 Oct 23;14:1098.
Coverage of anti-**tetanus vaccinations** in adults in **Canada**-year 2002.]. Coulibaly N, De Serres G. Can J Public Health. 2004 Nov-Dec;95(6):456-9.

Adult Vaccines Save Money

Published in final edited form as:
Vaccine. 2019 January 07; 37(2): 226–234. doi:10.1016/j.vaccine.2018.11.056.

Cost-effectiveness of adult vaccinations: A systematic review

Andrew J. Leidner[a,*], **Neil Murthy**[b,c], **Harrell W. Chesson**[d], **Matthew Biggerstaff**[b], **Charles Stoecker**[e], **Aaron M. Harris**[d], **Anna Acosta**[b], **Kathleen Dooling**[b], and **Carolyn B. Bridges**[a]

[a]Berry Technology Solutions, USA

[b]National Center for Immunization and Respiratory Diseases, CDC, USA

[c]Epidemic Intelligence Service, CDC, USA

[d]National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, CDC, USA

[e]School of Public Health and Tropical Medicine, Tulane University, USA

- 1688 publications: 78 publications retained
- Cost savings by disease
  - 56% for influenza
  - 31% for pneumococcal
  - 23% for tetanus-diphtheria-pertussis •
- Cost per QALY of ≤$100,000
  - 100% for influenza
  - 100% for pneumococcal
  - 71% for herpes zoster
  - 50% for tetanus-diphtheria-pertussis

Cost-effectiveness of adult vaccinations: A systematic review.
Leidner AJ, Murthy N, Chesson HW, Biggerstaff M, Stoecker C, Harris AM, Acosta A, Dooling K, Bridges Cbet al

https://www.dreamstime.com/photos-images/old-man-gardening-rose-bush.html

Tetanus

Clostridium tetani

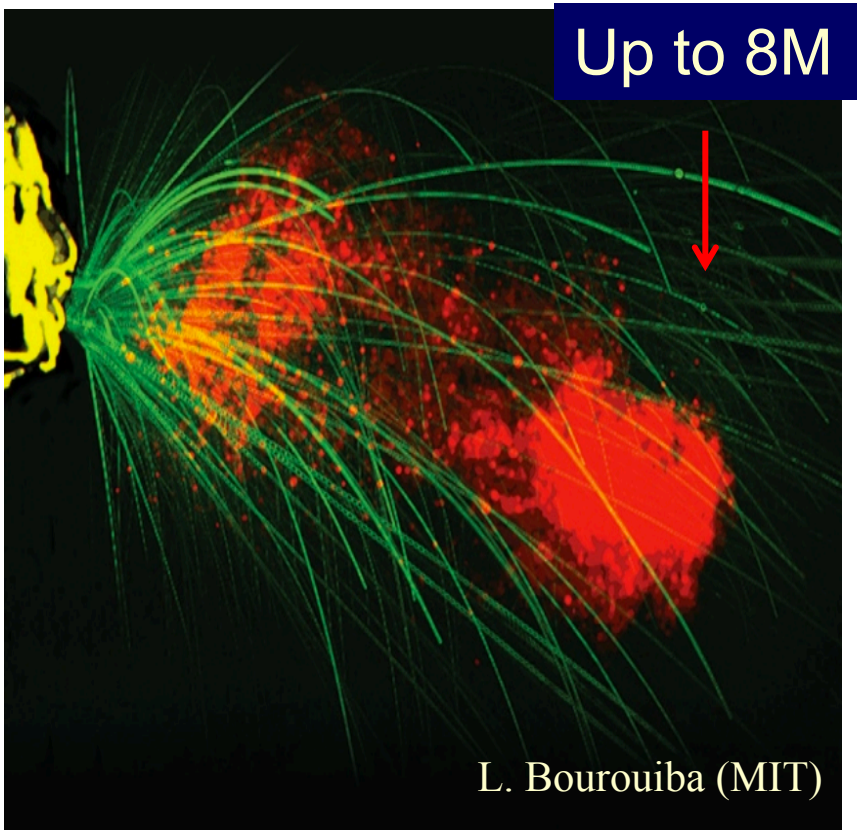
chemgapedia.de

immunizebc.ca

- Tetanospasmin
- Second most potent toxin (after Botulinum D toxin)
- LD50 in 1ng/Kg range

Amount needed to kill is less than amount needed for immune response

Pertussis and Chronic Cough



164 adults with chronic cough and 164 matched controls

- 4 culture-positive B. pertussis
- 11 PCR-positive
- 33 with evidence of recent infection

Bordetella **pertussis** and **chronic cough** in adults. Birkebaek NH, Kristiansen M, Seefeldt T, Degn J, Moller A, Heron I, Andersen PL, Moller JK, Ostergård L. Clin Infect Dis. 1999 Nov;29(5):1239-42.

Vaccine 37 (2019) 7240–7247

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

The health and economic burden of pertussis in Canada: A microsimulation study

Ashleigh McGirr [a], David N. Fisman [a,b,*], Ashleigh R. Tuite [a]

[a] Dalla Lana School of Public Health, University of Toronto, Toronto, Canada
[b] Division of Infectious Diseases, Department of Medicine, Faculty of Medicine, University of Toronto, Toronto, Canada

	Ontario		Canada	
Age Group	2012	2013	2012	2013
<6 mo	799	293	2528	951
6 mo to 4 y	997	282	3693	1013
5 to 17 y	2342	529	12,504	2967
18 to 64 y	1605	372	5782	1909
65+ y	113	45	1025	332
Total	5855	1520	25,532	7173

. McGirr A et al. The health and economic **burden** of **pertussis** in Canada: A microsimulation studyVaccine. 2019 Nov 20;37(49):7240-7247.

HUMAN VACCINES & IMMUNOTHERAPEUTICS
2020, AHEAD-OF-PRINT, 1-9
https://doi.org/10.1080/21645515.2020.1738168

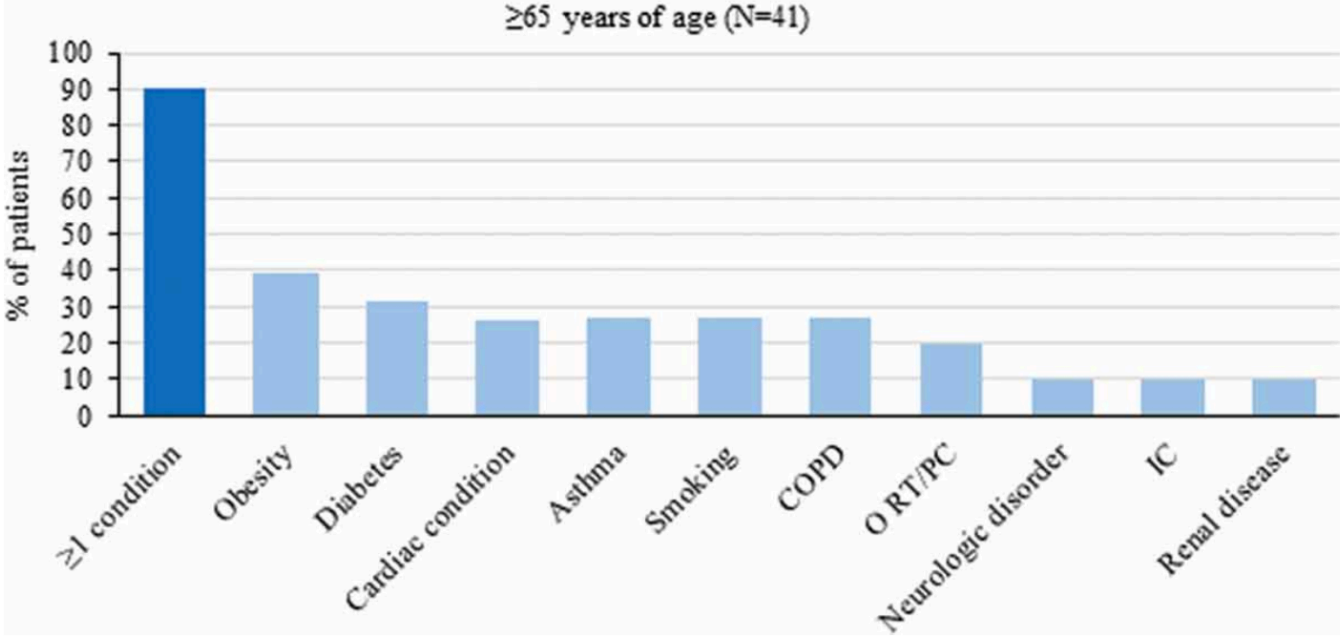
Taylor & Francis
Taylor & Francis Group

Pertussis in high-risk groups: an overview of the past quarter-century

Victoria A Jenkins , Miloje Savic , and Walid Kandeil *

Vaccines, GSK, Wavre, Belgium

- USA data between 2011 and 2015 → 15,942 cases (20.3 per 100,000)
- 3.2% required hospitalization
  - 29.6% of cases and 4.5% of hospitalizations in 12–20-year-olds
  - 18% of cases and 14.8% of hospitalizations in 21–64-year-olds
  - 2.1% of cases and 8.3% of hospitalizations in >65-year-olds.



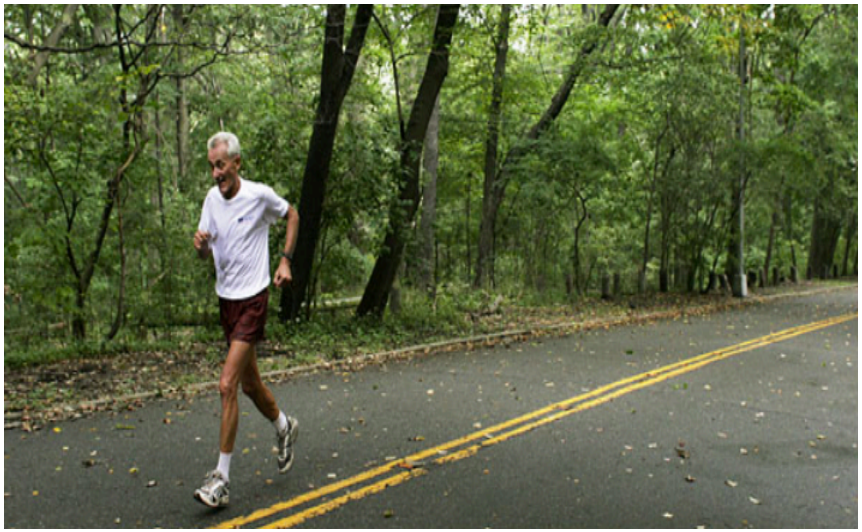
Jenkins VA, et al. **Pertussis** in high-risk groups: an overview of the past quarter-century. Hum Vaccin Immunother. 2020 Apr 16:1-9.

Influenza

most NO cases of influenza (so far) in 2020

https://byrslf.co/silent-thoughts-about-the-silence-in-relationships-426d733dba3f

Influenza: Outcomes



Catastrophic disability

Loss of independence in ≥ 3 ADL

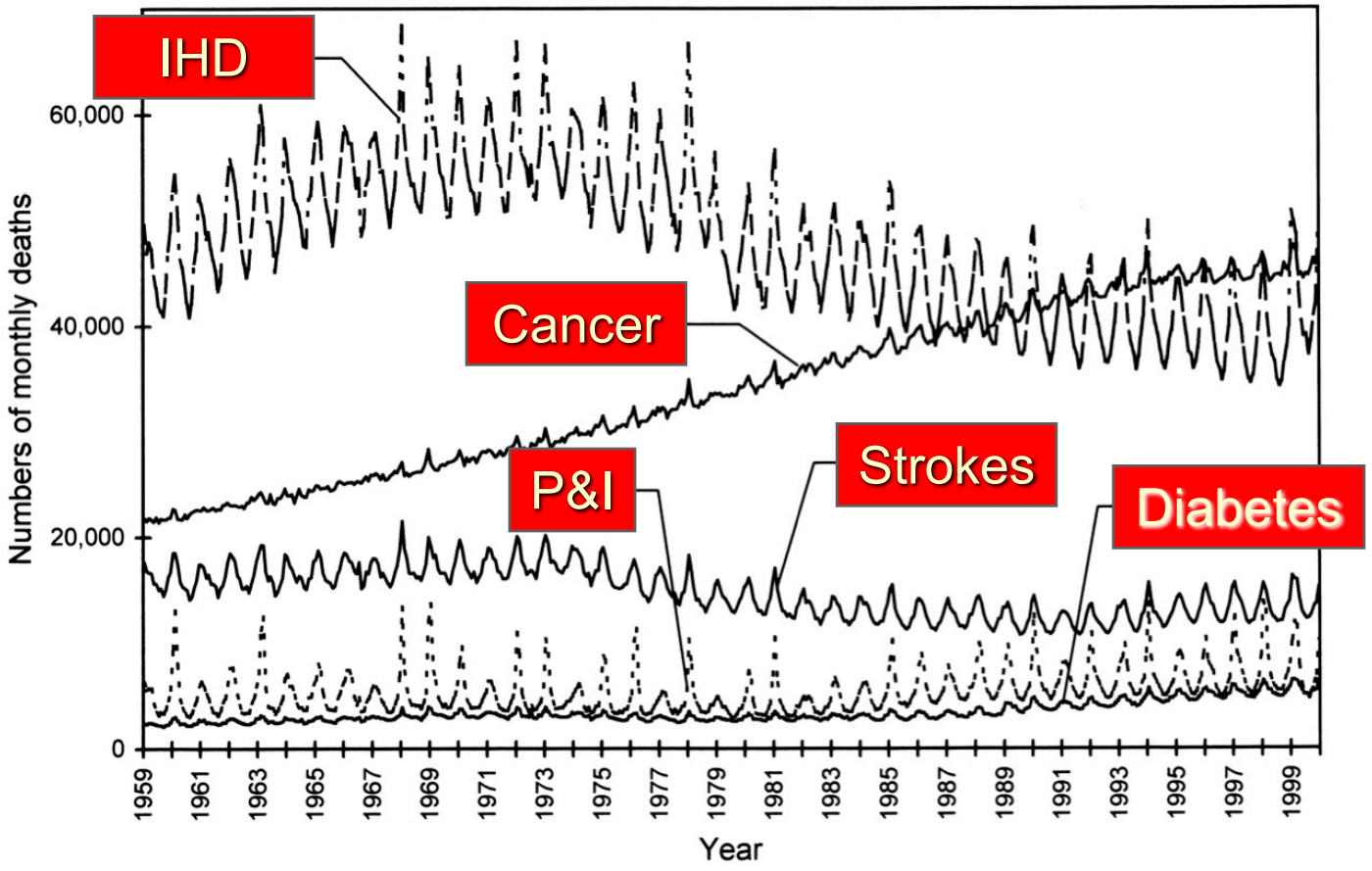
72% who experience catastrophic disability have been hospitalized

Leading causes of catastrophic disability

- Strokes
- CHF
- **Pneumonia and influenza**
- Ischemic heart disease
- Cancer
- Hip fracture

Ferrucci et al. JAMA 277:728, 1997
Barker et al. Arch Int Med 158:645, 1998
Falsey et al. *N Engl J Med*. 2005;352:1749
McElhaney JE, et al Vaccine. 2012 Mar 9;30(12):2060-7.

Influenza: Predictor of Excess Mortality



Reichert TA, et al. Am J Epidemiol 160:492, 2004

Meta-Analyzed to Death

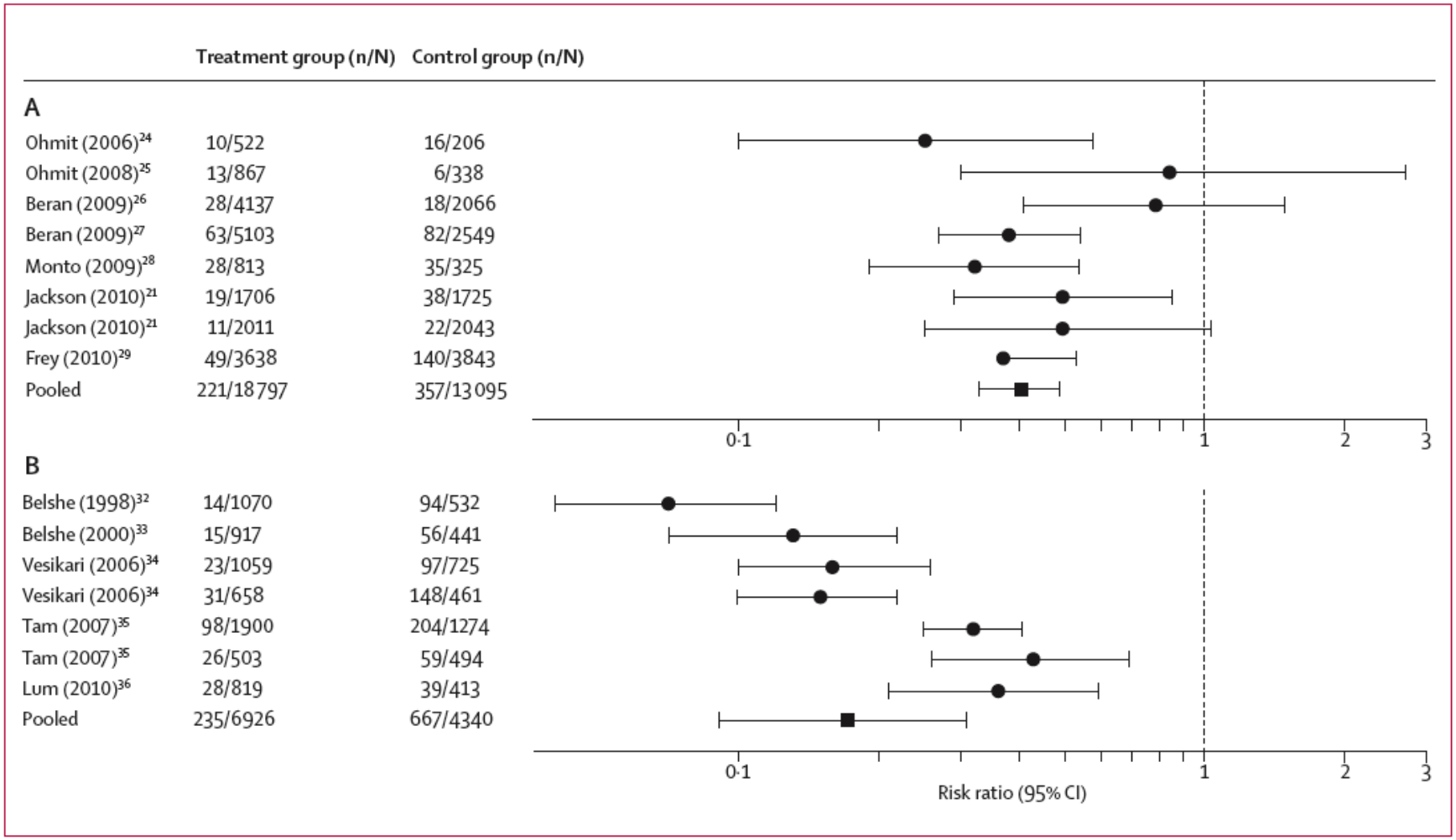


Figure 2: **Vaccine efficacy compared with placebo (Mantel-Haenszel random-effects model)**
(A) Trivalent inactivated influenza vaccine in adults aged 18–64 years. (B) Live attenuated influenza vaccine in children aged 6 months to 7 years. Studies were prospective (risk ratio) which are equivalent to case-control (odds ratio). n=cases of influenza. N=group size.

“Even at 38% Efficacy …”

Episodes of Illness	715,073
Medical Visits	400,441
Hospitalizations	65,007
Deaths	6,796

Effects of Influenza Vaccination in the United States During the 2017-2018 Influenza Season.
Rolfes MA, Flannery B, Chung JR, O'Halloran A, Garg S, Belongia EA, Gaglani M, Zimmerman RK, Jackson ML, Monto AS, Alden NB, Anderson E, Bennett NM, Billing L, Eckel S, Kirley PD, Lynfield R, Monroe ML, Spencer M, Spina N, Talbot HK, Thomas A, Torres SM, Yousey-Hindes K, Singleton JA, Patel M, Reed C, Fry AM; US Influenza Vaccine Effectiveness (Flu VE) Network, the Influenza Hospitalization Surveillance Network, and the Assessment Branch, Immunization Services Division, Centers for Disease Control and Prevention. Clin Infect Dis. 2019 Nov 13;69(11):1845-1853.

Recombinant Influenza Vaccines

- Insect Cell-derived vaccine (HA)
  - FluBlok™
  - 45µg of each strain with no adjuvant
  - more effective in subjects >50 years old
  - bought by Sanofi not sure what they will do with it yet
  - being tried with an adjuvant
  - not available in Canada (yet)

Protein Sciences CORPORATION
Makers of Flublok® Influenza vaccine

- Plant-derived recombinant (HA)
  - Fluforza™
  - 15µg of each strain in a virus-like particle
  - produced in *Nicotiana benthamiana* plants
  - Currently before regulators in Canada, USA and elsewhere
  - being tried with an adjuvant (AS03) in the elderly

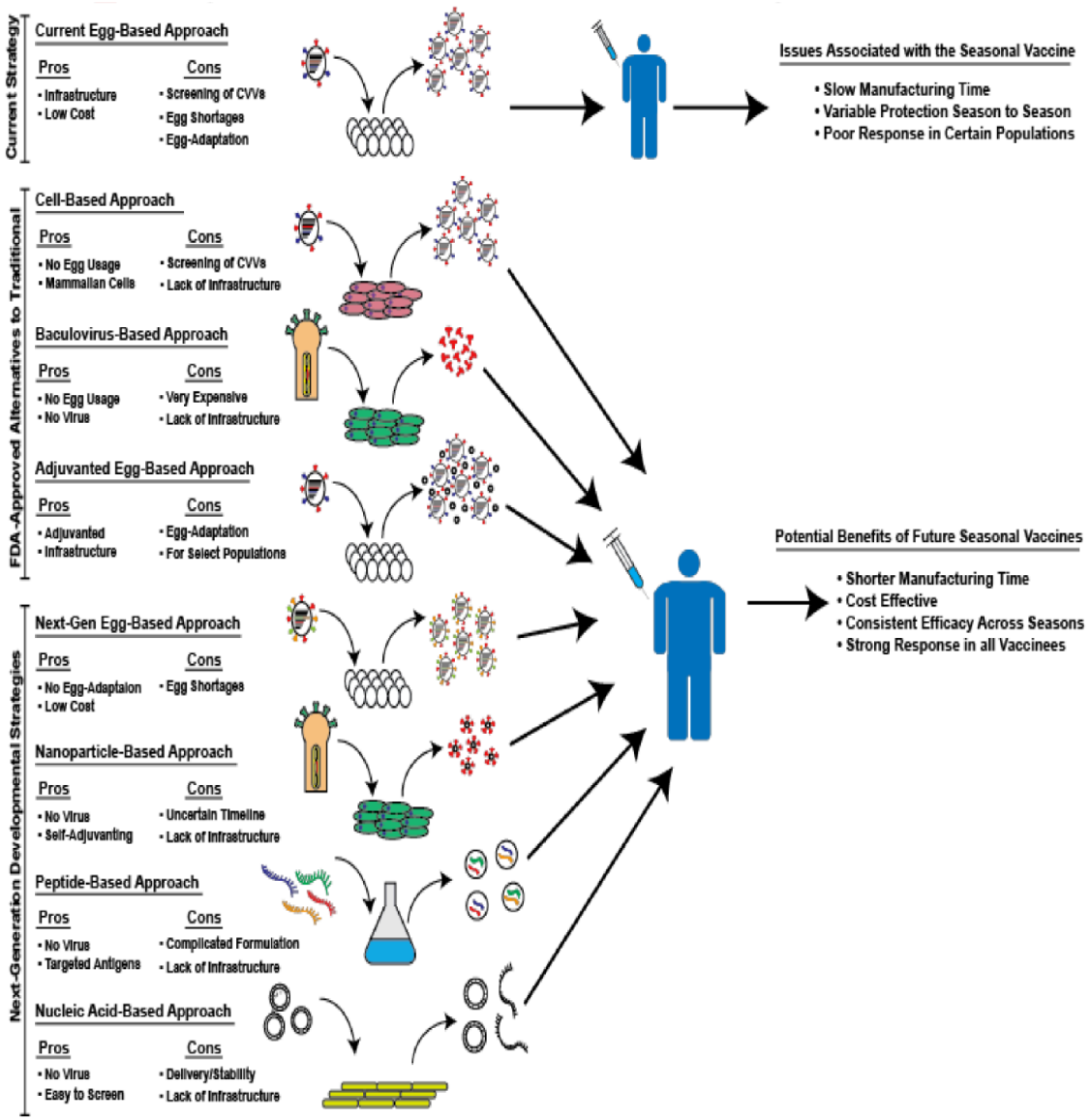
medicago

- Insect Cell recombinant (HA)
  - No name yet
  - uses proprietary adjuvant Matrix M

NOVAVAX

Zost SJ, et al. Contemporary H3N2 influenza viruses have a glycosylation site that alters binding of antibodies elicited by egg-adapted vaccine strains.Proc Natl Acad Sci U S A. 2017 Nov 21;114(47):12578-12583.
Ward BJ et al. Efficacy, immunogenicity, and safety of a plant-derived, quadrivalent, virus-like particle influenza vaccine in adults (18-64 years) and older adults (≥65 years): two multicentre, randomised phase 3 trials . Lancet. 2020 Nov 7;396(10261):1491-1503

Expanding Technologies for Seasonal Influenza Vaccines



Harding AT, Heaton NS. Efforts to Improve the Seasonal Influenza Vaccine. Vaccines (Basel). 2018 Mar 30;6(2). pii: E19. doi: 10.3390/vaccines6020019.

Influenza Vaccines for the Elderly

MIT Mathematics

1) High-Dose Inactivated (Fluzone)
   Tri-Valent
   Quadrivalent

2) Re

3) M

4) Any inactivated quadrivalent
   Cell-based (Flucelvax) better than egg-based
   Not available in Canada yet

Real World Data for the Elderly

Little-to-No benefit from quadrivalent

Benefit to cell-based & recombinant in mismatch years

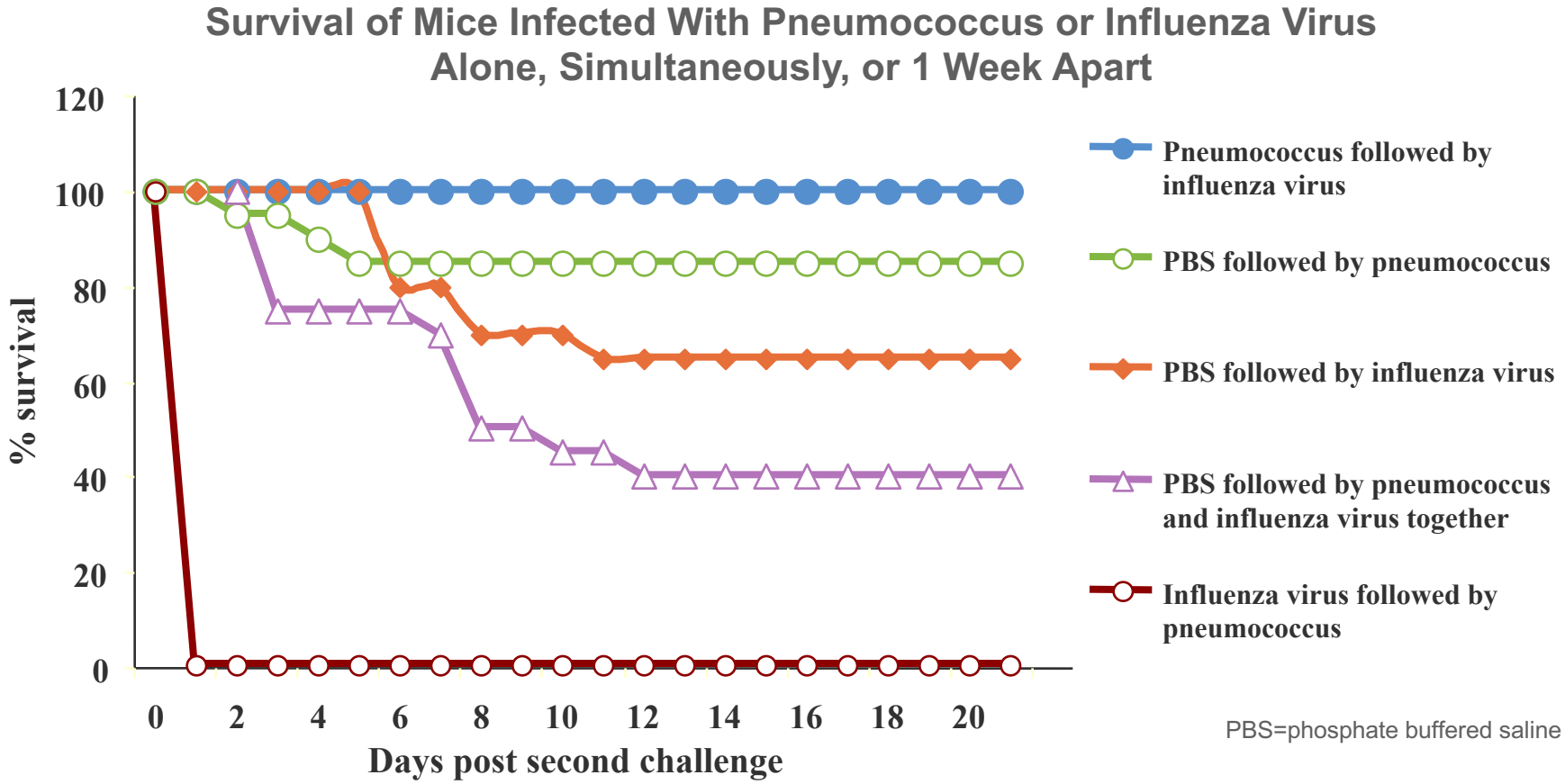
Small (5-10%) benefit from adjuvant

Modest (10-15%) benefit from HD/Recombinant

Advantages generally greatest for serious outcomes


CEMETERY
Elderly
people

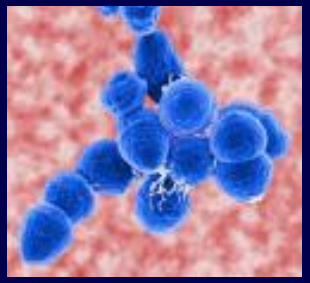
Influenza & S. pneumoniae
Synergistic Effect on Mortality (Animals)

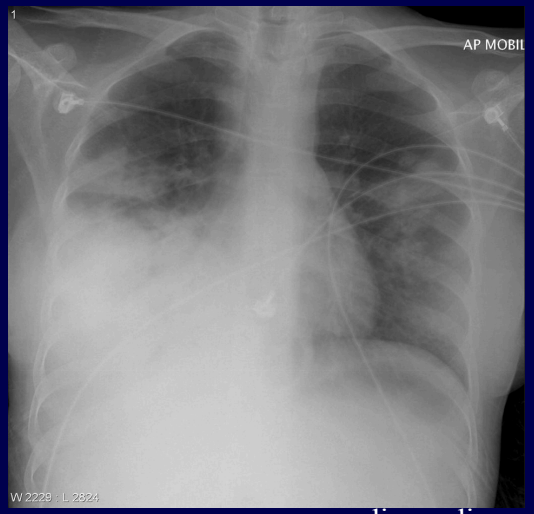


Mortality was 100% in mice challenged with *S. pneumoniae* after influenza

Adapted from McCullers JA, Rehg JE. *J Infect Dis*. 2002;186:341-350. Slide courtesy of Dr. Keith Klugman.

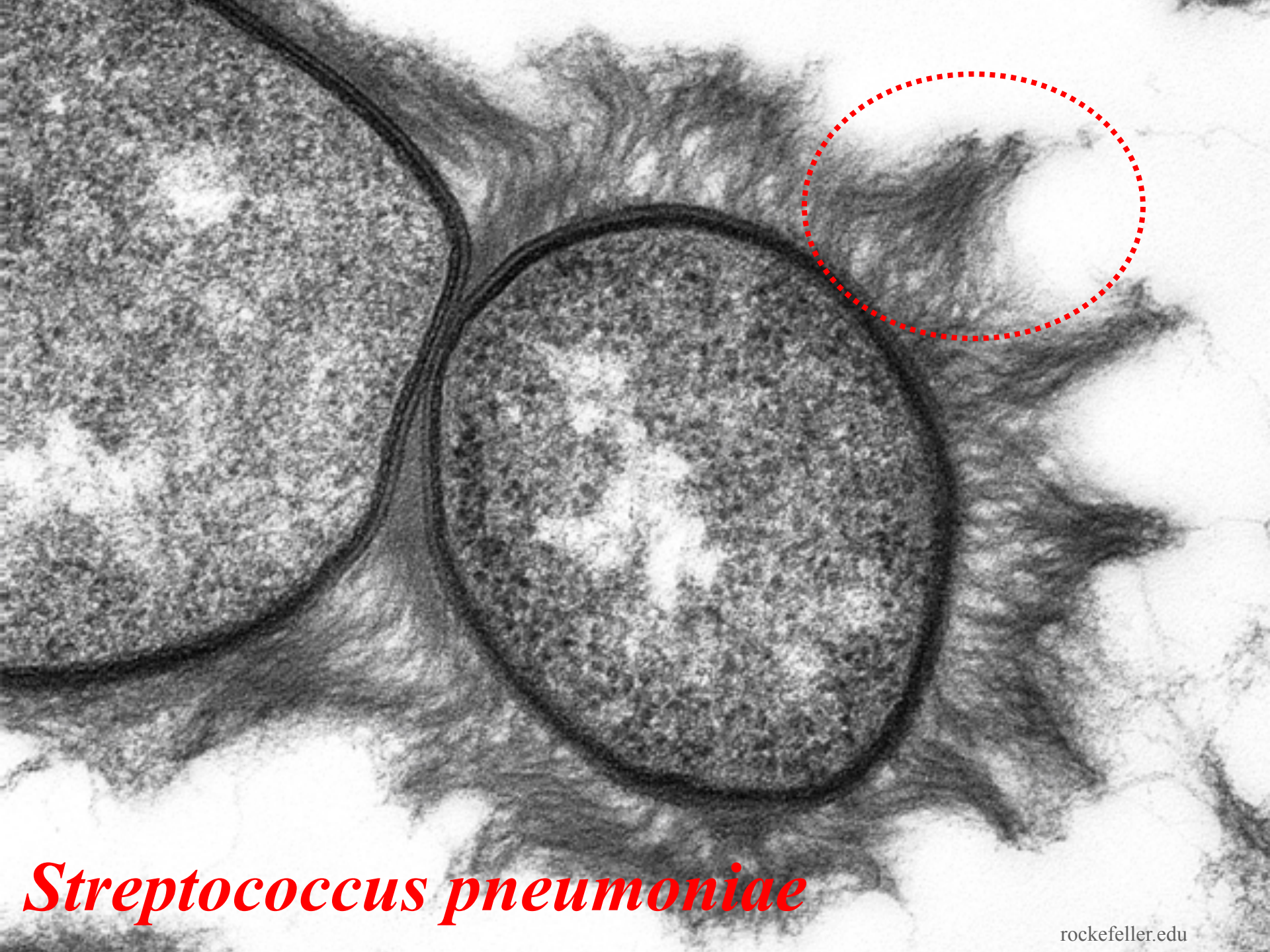
Streptococcus pneumoniae





radiopaedia.org

- World-wide distribution
- Encapsulated bacterium (polysaccharide)
- More than 90 different serotypes
- Predominant serotypes vary by region
- **Antibodies (opsinization & phagocytosis) essential**
- Babies make very poor responses to polysaccharides
- Mortality highest in infants and elderly


Streptococcus pneumoniae
rockefeller.edu

Pneumococcal Conjugate Vaccines

Wyeth (Licensed)	Pfizer (13-Valent)	GSK (10-Valent)	South African (9-Valent)	Who's Next (15 Valent)
4	1	1	1	1
6b	3	4	4	3
9v	4	5	5	4
14	5	6b	6b	5
19f	6a	7f	9v	6a
18c	6b	9v	14	6b
23f	7f	14	19f	7f
	9v	19f	18c	9v
	14	18c	23f	14
	19a	23f		18c
	19f			19a
	18c			19f
	23f			22f
				23f
				33f

PPV (23 Valent)	
1	17f
2	18c
3	19a
4	19f
5	20
6b	22f
7f	23f
8	33f
9n	
9v	
10a	
11a	
12f	
14	
15b	

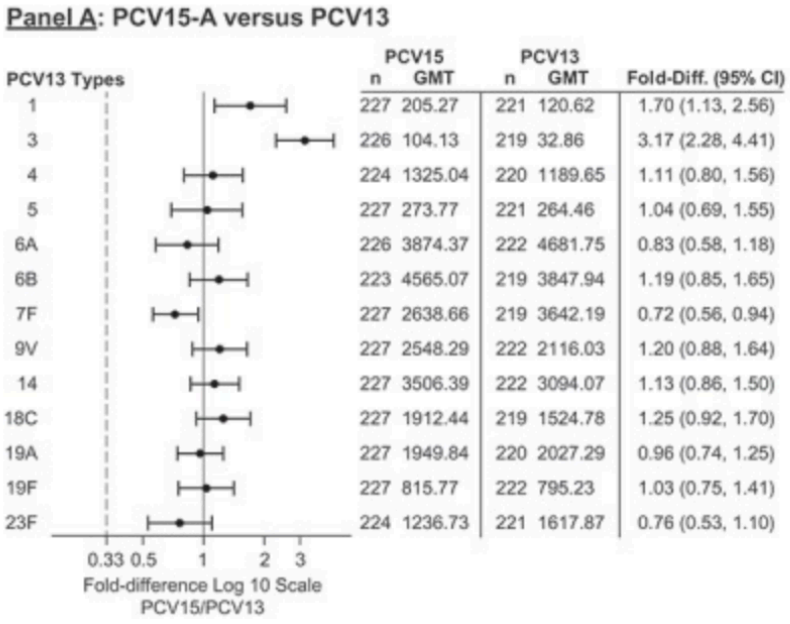
human VACCINES & IMMUNOTHERAPEUTICS

Hum Vaccin Immunother. 2019; 15(3): 530–539.
Published online 2019 Jan 16.
doi: 10.1080/21645515.2018.1532249

PMCID: PMC6605726
PMID: 30648919

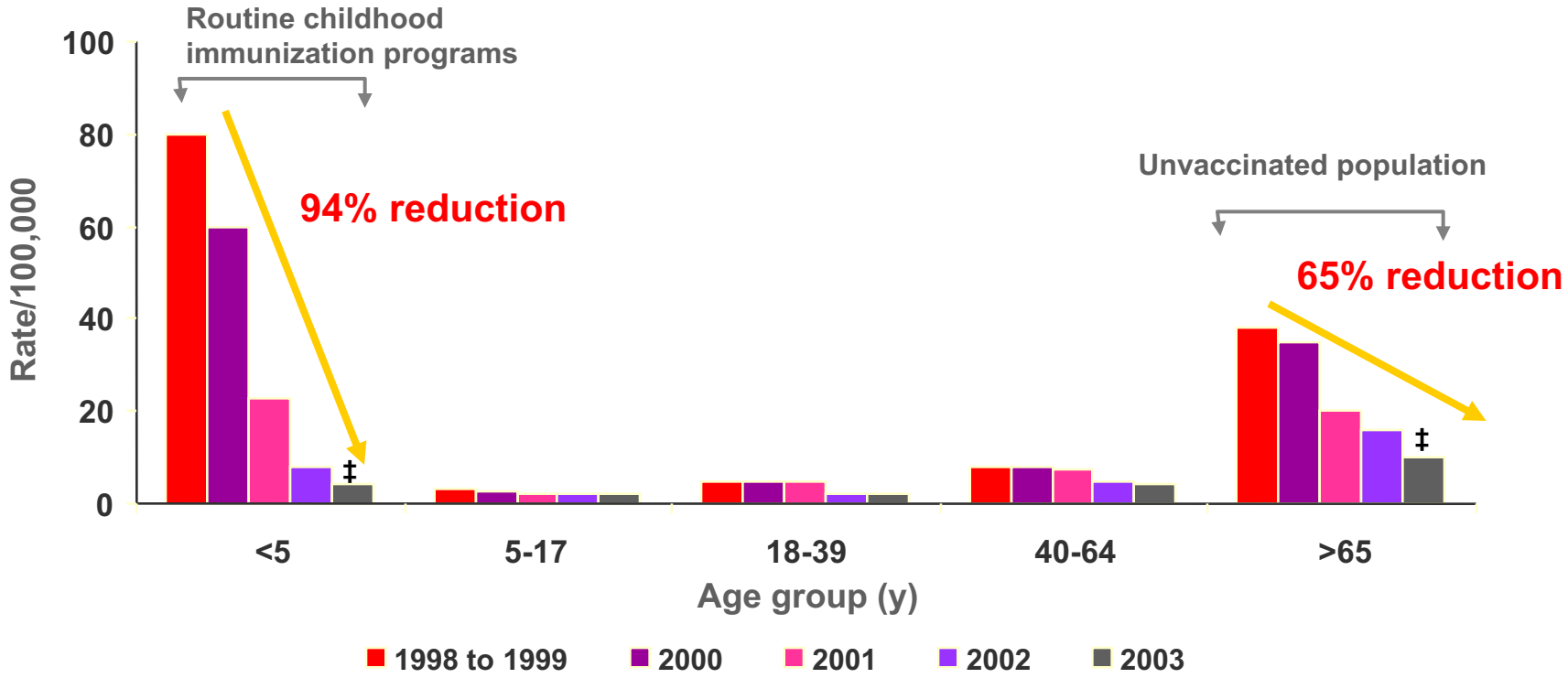
Safety and immunogenicity of 15-valent pneumococcal conjugate vaccine (PCV-15) compared to PCV-13 in healthy older adults

Helen L. Stacey,[a] Jeffrey Rosen,[b] James T. Peterson,[c] Angela Williams-Diaz,[d] Vanita Gakhar,[d] Tina M. Sterling,[d] Camilo J. Acosta,[d] Katrina M. Nolan,[d] Jianing Li,[d] Alison Pedley,[d] Patrice Benner,[d] Chitrananda Abeygunawardana,[d] Michael Kosinski,[d] William J. Smith,[d] Hari Pujar,[d] and Luwy K. Musey[d]



Conjugate (7): Indirect Effect—IPD (U.S.)

Rate of Vaccine-type (VT) IPD Before and After Introduction of PREVNAR, by Age Group and Year†



†Active Bacterial Core surveillance, United States, 1998 to 2003
‡$p<0.05$, 2003 vs 1998-1999

PREVNAR vaccination was associated with a reduction in IPD in vaccinated and unvaccinated populations

Adapted from CDC. *Morb Mortal Wkly Rep*. 2005;54:893-897.

'Best' Strategy for Adults

Identify high risk (≥ 65yo, co-morbidities)

Start with conjugate vaccine

- Highest valency available
- Prevnar 13™ for the moment

8-12 months later – polysaccharide vaccine

- Pneumo23™ for the moment
- minimum of 8 weeks if urgent

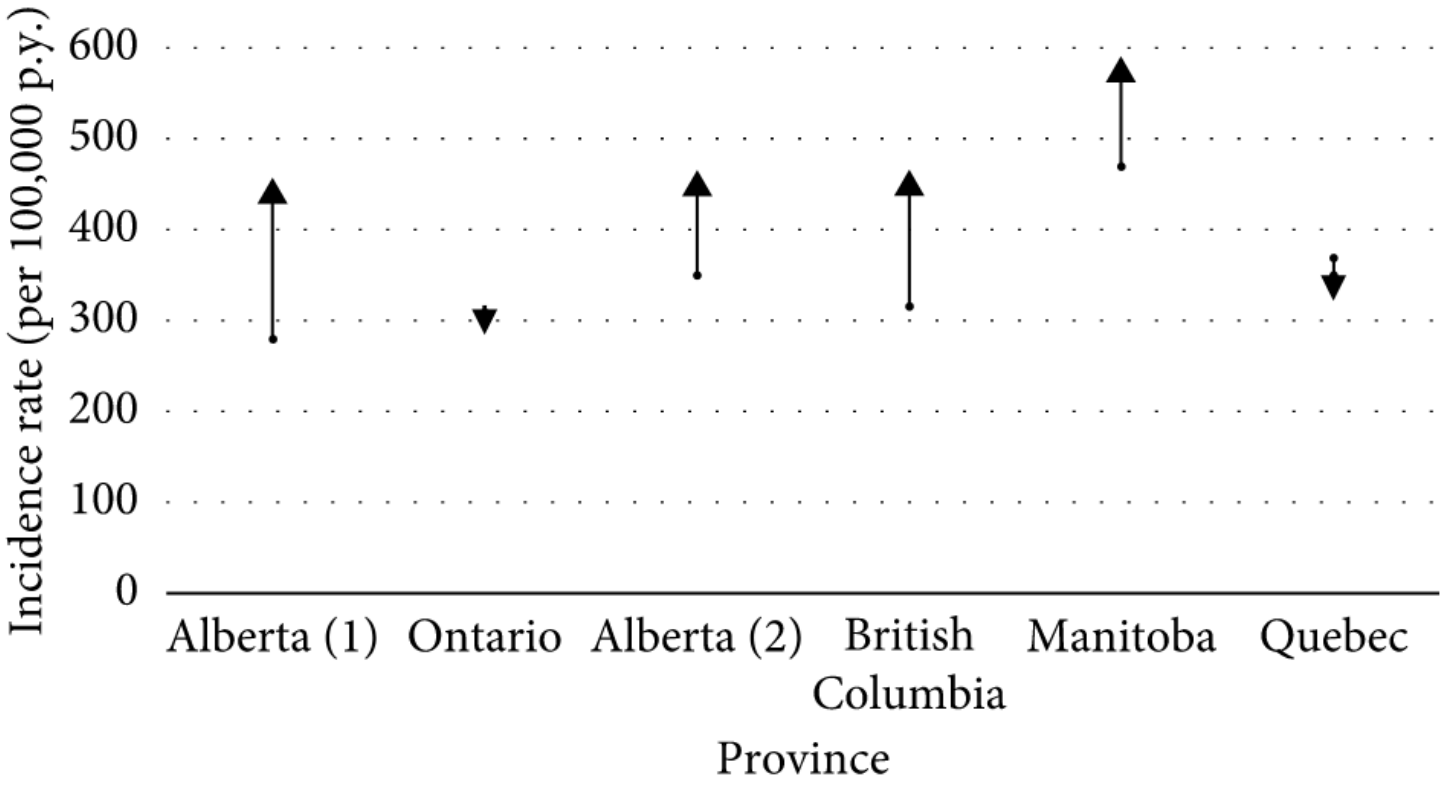
Boosters?

- Not yet known for conjugate vaccines
- Up to every 5-10 years for Pneumo23

VZV & Shingles

hardinmd.lib.uiowa.edu

Hospitalizations & Consultations for Herpes Zoster in Canadian Provinces

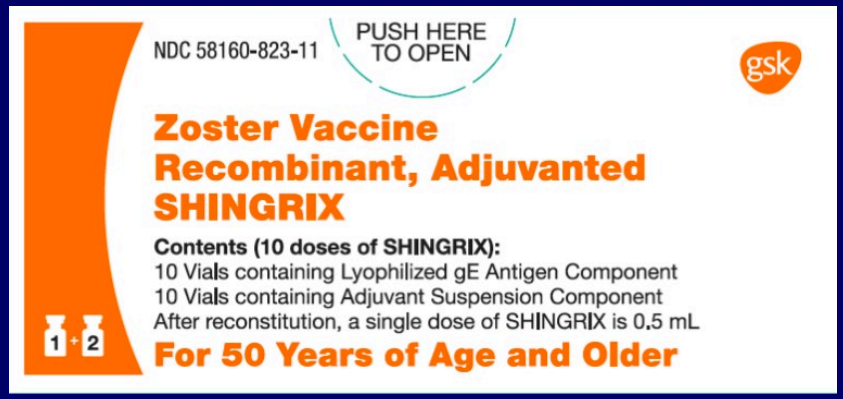


Herpes Zoster Burden in Canadian Provinces: A Narrative Review and Comparison with Quebec Provincial Data. Letellier MC, Amini R, Gilca V, Trudeau G, Sauvageau C. Can J Infect Dis Med Microbiol. 2018 Oct 21;2018:3285327.

Shingrix™ is a Good Vaccine

- **Vaccine that targets VZV glycoprotein E (gE) and $ASO1_B$ adjuvant**
- **Adjuvant MPL + QS21 (oil-in-water + TLR4 agonist)**
- **Need 2 doses 2-6 months apart (need for boosters not known but likely)**
- **Works in very old and the immunocomprimised (lower efficacy predicted but at least you can use it)**
- **Recommended for >50 yo and can give to those who have had Zostavax™**

When are we going to have to give a booster?



>90% efficacy

Safe

Replaces Zostavax

What's Next for the Elderly?

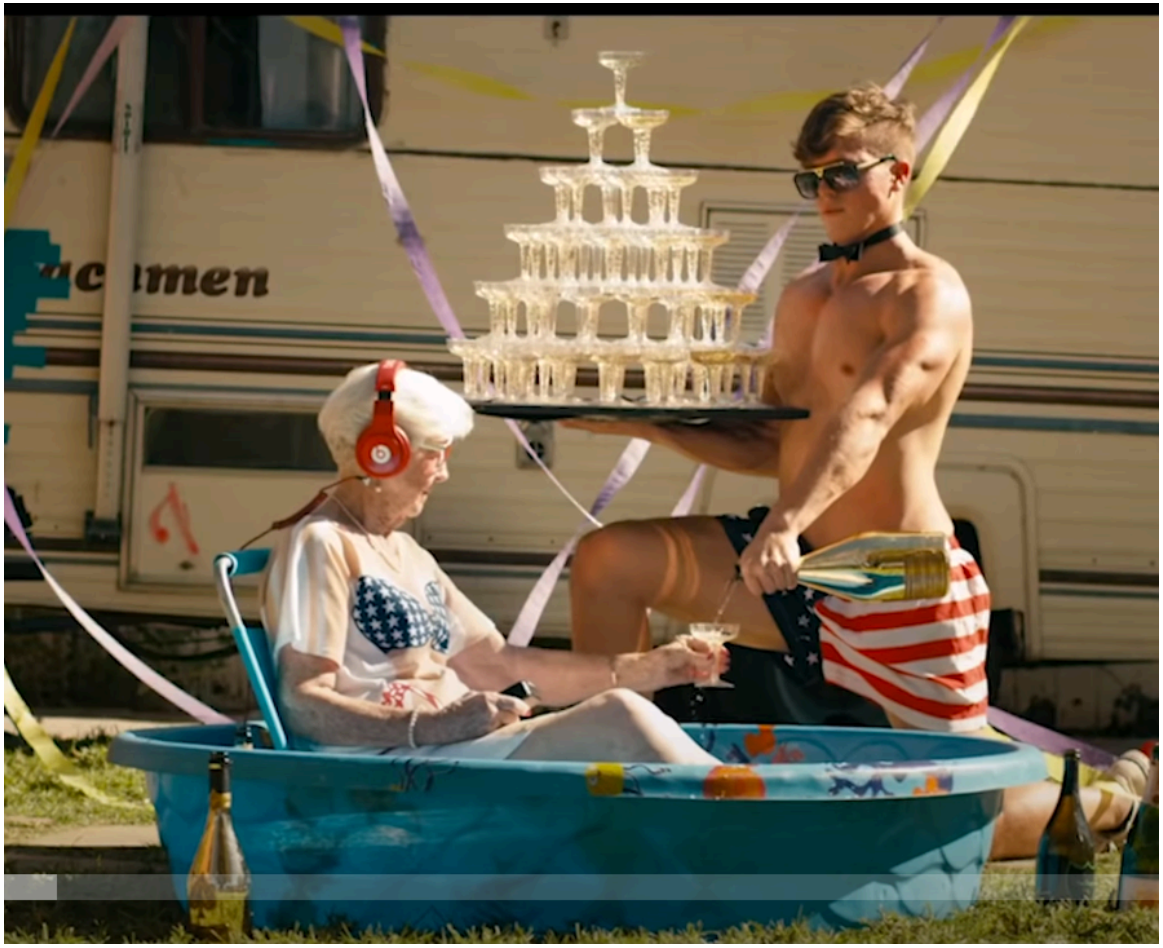
RSV vaccine

Better influenza vaccines

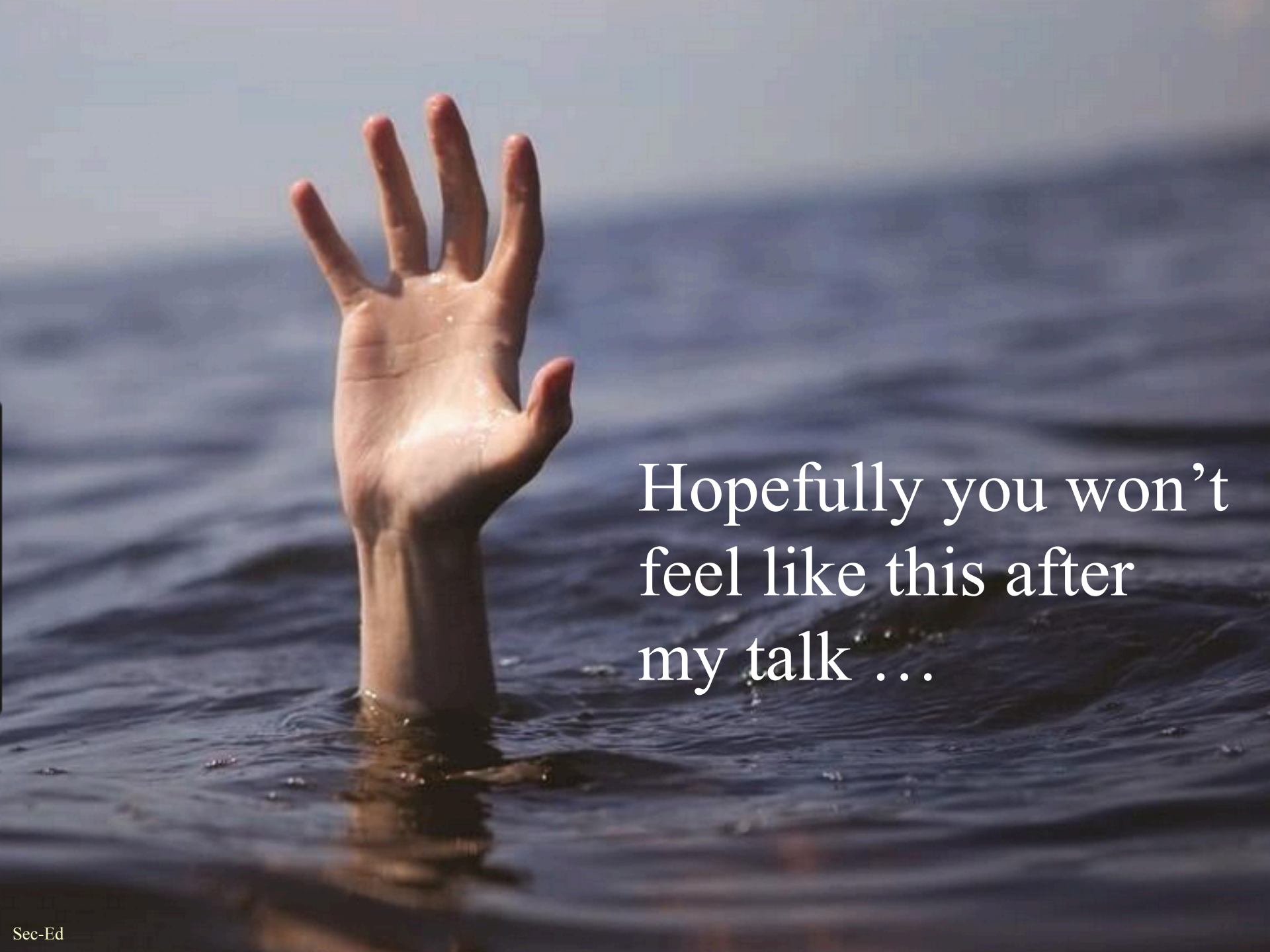
Cancer vaccines

C. difficile vaccine

We (me included) are Going to Stay Healthy and Active Longer



Appropriate use of vaccines will have an ever larger role to play ….


Hopefully you won’t feel like this after my talk …