Hot Topics Webinar Series

September 27, 2018

Influenza vaccination: a shot against frailty in older adults

Stefan Gravenstein, Brown University

Melissa Andrew, Dalhousie University

Richard Baydack, Manitoba Health

Canadian Frailty Network | Réseau canadien des soins aux personnes fragilisées

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Welcome

- **Today's webinar will be hosted by CFN's Partnerships Manager: Peter Aitken**
- **Q&As: Please submit your Qs online during presentation**
- **We will answer as many Qs as time permits**

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Agenda

- **Speaker order:**

  Stefan Gravenstein, Brown University

  Melissa Andrew, Dalhousie University

  Richard Baydack, Manitoba Health

- **Each speaker will present for 20 minutes w/ 5 min Q&A**
- **Wrap up with open Q&A session for the panel**

Partners for future Hot Topic Webinars:

- **CFN is working with and seeking partners, experts to develop more Hot Topics Webinars on key issues in the care of older adults living with frailty and all involved with their care**
- **Contact:**
- **Perry Kim CFN Assistant Scientific Director – perry@cfn-nce.ca**

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Reminder:
Upcoming CFN Webinars

Register at:

http://www.cfn-nce.ca/news-and-events-overview/webinars/

- **Wednesday, November 7, 2018 at 12 noon ET**

  FRAMING-LTC: Frailty and Recognizing Appropriate Medications IN Geriatrics and Long-Term Care – CFN-funded Strategic Impact Grant Program – Andrew Morris, Sinai Health System, Susan Bronskill, Institute for Clinical Evaluative Sciences and Lianne Jeffs, St. Michael's Hospital

- **Wednesday, November 21, 2018 at 12 noon ET**

  A National Comparison of Intensity of End-of-Life Care in Canada: Defining Changing Patterns, Risk Factors and Targets for Intervention – CFN-funded Core Research Grant Program – Robert Fowler and Andrea Hill, Sunnybrook Research Institute

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Presenter

- **Professor of Medicine, Professor of Health Services, Policy and Practice, Schools of Medicine and Public Health at Brown University**
- **Clinical Director at Healthcentric Advisors, Medicare's Quality Improvement Organization for New England**
- **Long-standing interest in immunity, inflammation and aging especially in the context of vaccines and the long-term care setting**
- **Specific nterest in quality improvement in health care, the culture of care, antimicrobial stewardship, and how to improve care across care transitions**

Stefan Gravenstein

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Influenza Vaccines: A Geriatrician's Perspective

Stefan Gravenstein, MD, MPH

Professor of Medicine and
Health Services Policy and Practice

Brown University

Providence, RI USA

Disclosures

Advisory Board/Honoraria: Merck & Co; Novavax, Inc; Sanofi-Aventis; Seqirus; Janssen

Consultant/Speaker/Honoraria: Gerontological Society of America; GlaxoSmithKline; Healthcentric Advisors; Janssen Pharmaceuticals, Inc; Novartis; Pfizer Inc; Seqirus

Research funding support: Centers for Disease Control and Prevention; National Institutes of Health; Sanofi-Aventis; Seqirus

Objectives

- Why: Influenza vaccine- who cares?
  - Why didn't we know?
- What
  - Understand the importance of immunizing patients and staff
  - Recognize the broader and often unmeasured benefits of vaccines and the case for annual influenza vaccination
- How

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Who cares?

- Influenza isn't "just a cold" in frail elderly, and often isn't given it's due for the misery and debility it creates
- How come we didn't know?
  - We think of flu as something "we have overcome and here we are, just fine"
  - We often think of flu like a "cold"'
  - No one has told us it does many other things we would reasonably not want

Immune Senescence: Who Cares?

- As we age, more likely to get infection, pneumonia[1]
  - More severe and can result in hospitalization
- As we age, vaccines work less well[1,2]
  - Need better vaccines to overcome declining response
  - Smaller response, doesn't last as long[3,4]
- As we age, we recover more slowly
- As we age, we have different symptoms

References:
1. Zheng B, et al. *J Immunol*. 2007;179(9):6153-6159. 2. Doria G, et al. Mech Ageing Dev. 1997;96(1-3):1-13. 3. Siegrist CA. Vaccine immunology. In: Plotkin SA, et al, eds. *Vaccines*. Sixth edition. Philadelphia, PA: Saunders Elsevier; 2012:17-36. 4.Goronzy JJ, Weyand CM. *Nature Immunol.* 2013;14(5):428-436.

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Immune Senescence: Lowers Response with Age

- Reduced response to influenza vaccine
- Reduced response to shingles vaccine
- Reduced response to pneumococcal vaccine
- … and all other vaccines

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Immune Senescence: Changes How Sick We Look

- Symptoms less severe with more severe infections
  - Less fever
  - Less muscle aches
- Symptoms tick up more slowly
  - Present later clinically
- Symptoms resolve more slowly
  - Takes longer to recover mild even mild symptoms
    - Anorexia
    - Malaise
    - Fatigue
- Greater consequences
  - Functional loss, vascular outcomes

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Immune Senescence: Changes How Sick We Look

- So what?
- Aging (and frailty) changes what happens when we get sick
- When we get infected, age changes our appetite, energy, functional independence, and risk for disability

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Infection and Inflammation: How These Conflate Risk for Vascular Complications in the Older Adult

Age-Adjusted Incidence Ratios of First MI and First CVA After Vaccination or Infection

Event (Count) Before First MI	Days 1-14 (IR, n)	Days 15-28 IR, n	Days 29-91 IR, n
Flu vaccine (20,486)	~ 0.72, 357	0.87, 417	~ 1, 2154
Td (7966)	~ 1, 54	~ 1, 46	~ 1, 253
PPSV23 (5925)	~ 1, 39	~ 1, 43	~ 1, 177
SRTI (20,921)	~ 3.8, 1020	1.95, 576	1.4, 1658
UTI (10,448)	~ 1.6, 233	1.32, 217	1.23, 820
Event (Count) Before First CVA	Days 1-14	Days 15-28	Days 29-91
Flu vaccine (19,063)	~ 0.77, 365	0.88, 409	~ 1, 2051
Td (6155)	~ 1, 41	~ 1, 40	~ 1, 209
PPSV23 (4416)	~ 1, 38	~ 1, 29	~ 1, 160
SRTI (22,400)	~ 2.4, 849	1.68, 561	1.33, 1650
UTI (14,603)	~ 2.2, 555	1.71, 445	1.22, 1250

Reference:
1. Smeeth L et al. *N Engl J Med*. 2004;351:2611-2618.

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Pneumonia and Cardiac Events

- Review of this by Corrales-Medina et al 2013 with pneumonia followed by cardiovascular events
  - **“a quarter of adults hospitalised with pneumonia develop a major acute cardiac complication during their stay, and these are 60% more likely to die.”**
- Prospective study 2017 in 1182 pneumonia admissions
  - **Over the next 30 days:**
    - **32% cardiovascular event in <30 days** (24% HF, 9% afib, 8% AMI)
    - 17.6% vs 4.5% mortality with vs w/o CVE (p<.001)

References: Corrales-Medina VG et al, Lancet 2013, Violi F et al, Clin Infec Dis, 2017

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Shingles and Vascular Event: Increased Heart Attack and Stroke

Kim et al (2017) report hazard ratios

- Heart attack after shingles is 1.59 overall, and increases with age

Erskine et al (2017) meta-analysis of 12 studies

- Stroke increases after shingles of the eye
  - Risk is up 1.39-4.42 for the 1st 3 months after shingles
- Stroke risk increases by 1.22-1.34 for the year after shingles
- Heart attack risk increases after shingles for a year (OR 1.19)

References:
1. Kim et al, *Letters*, J A C C 2017, 7 0(2):293–300. 2. Erskine et al, *PLoS One*. 2017; 12(7): e0181565.

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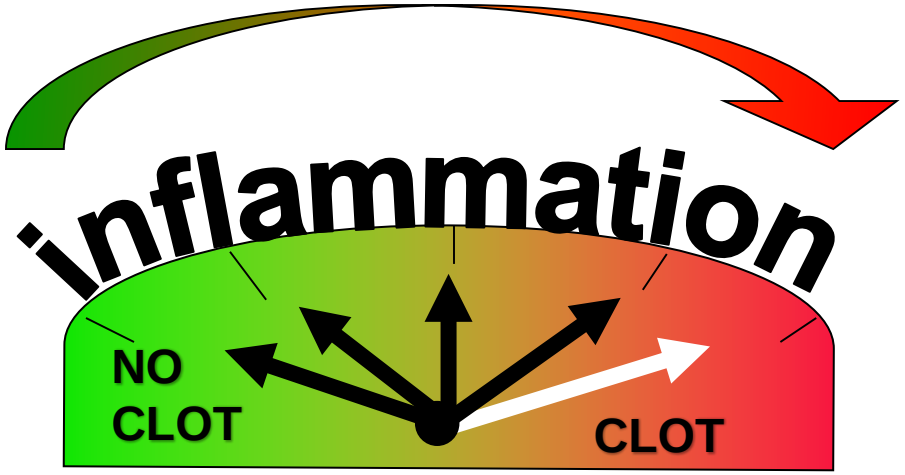
"Thrombometer"
The Propensity to Clot



LOW	**HIGH**
CRP	DVT
IL-1, 6	Stroke
TNF-alpha	MI
Serum Amyloid A	Delirium
Fibrinogen activation	Dementia

Increases with age
- Inflammatory markers of age
- IL-6, IL-8, C-reactive protein

Increases with disease
- Obesity
- Diabetes
- Arthritis, vascular disease
- Dementia
- COPD

Increases following infection
- Influenza
- Community acquired pneumonia
- Shingles
- Bladder infection
- Pressure sores

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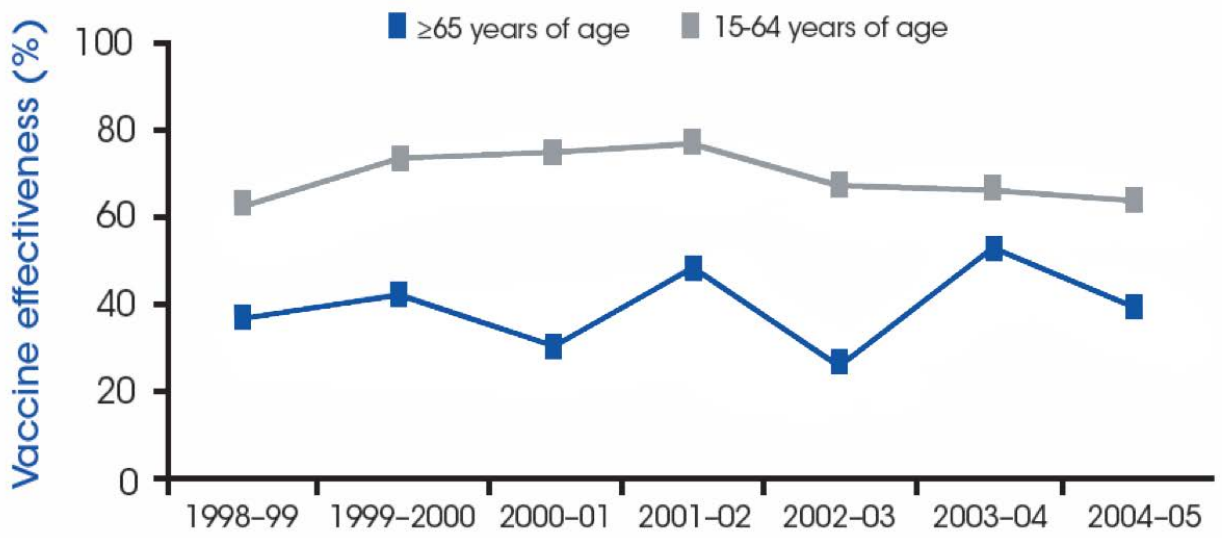
Effectiveness by Age of Influenza Vaccines Against Influenza-like Illness (ILI)[1,2]



During the 7 influenza seasons shown, the range of vaccine effectiveness was 26%-52% in persons ≥65 years of age and 62%-76% in those 15-64 years of age

References:
1. Monto AS, et al. *Vaccine.* 2009;27(37):5043-5053. 2. Legrand J, et al. *Vaccine.* 2006;24(44-46):6605-6611.

The Range of Efficacy of Coronary Interventions Compared With Influenza Vaccination

Table 1 Efficacy of accepted coronary interventions and influenza vaccine in the prevention of myocardial infarction

Coronary intervention	Prevention	Intervention efficacy/effectiveness against acute myocardial infarction (%)
Smoking cessation[4 23–25]	Secondary	32–43
Statins[38]	Secondary	19–30
Antihypertensive drugs[26–29 32]	Secondary	17–25
Influenza vaccine[5 9 18]	Secondary	15–45

MacIntyre CR et al. *Heart*. 2016;102:1953-1956.

We Need Better Vaccines Specific for Older Adults

- Pneumonia vaccine
  - Pneumococcal polysaccharide vaccine (Pneumovax®)
  - Conjugated pneumococcal vaccine (Prevnar®)
- Enhanced influenza vaccines
  - High dose influenza vaccine (Fluzone High Dose®)
  - Adjuvanted influenza vaccine (Fluad®)
- Shingles vaccine
  - Recombinant shingles subunit vaccine (Shingrix®)
  - Live shingles vaccine (Zostavax®)

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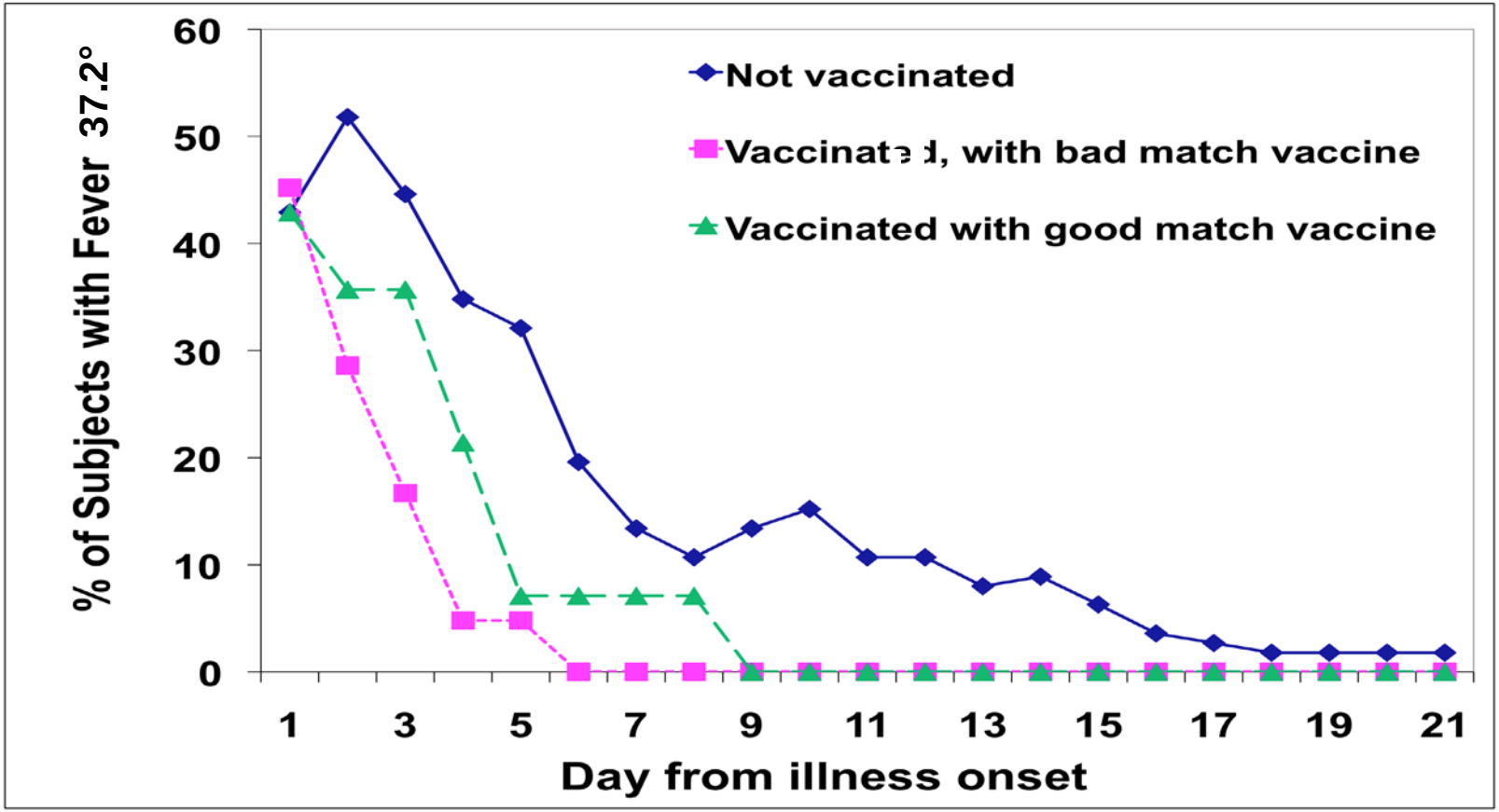
Focus on LTC Facilities and Influenza: Does Vaccine Match Matter?

In LTC, Residents' Fever From Flu Is Less, and Is Attenuated More If Vaccinated[1]



Reference:
1. Gravenstein S, et al. *Med Health R I.* 2010;93(12):382-384. 2. Ambrozaitis A, et al. *J Am Med Dir Assoc* 2005;6:367-374.

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Influenza Vaccination and Cardiovascular Impact

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Even so, even regular influenza vaccines protect

- Even when there is a bad match
- Even in ways that don't sound at all like influenza

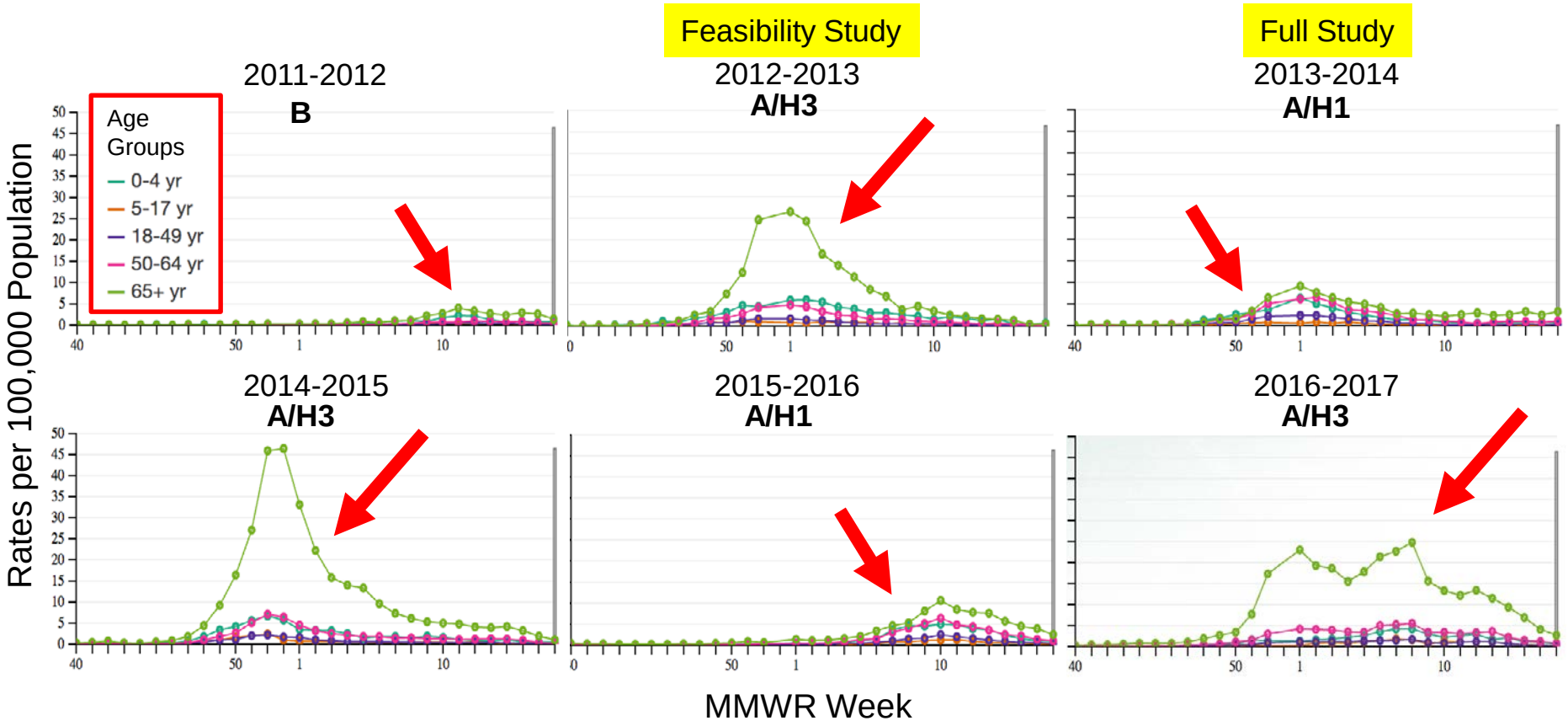
New influenza vaccines specific for 65 and older

- High dose influenza vaccine (Fluzone High Dose®)
  - Four times more influenza antigen than in regular vaccines
  - More antibody produced than with regular vaccine
  - It prevents influenza better than regular vaccine
    - 20% -24% less influenza based on RCT in outpatient elderly
    - 6-30% less likely to be hospitalized (from outpatient and nursing home)
    - Recognized as superior over regular vaccines in elderly
- Adjuvanted infuenza vaccine (Fluad®)
  - MF59 adjuvant with regular dose of infuenza antigen
  - More antibody than regular vaccine
  - Awaiting high quality evidence for clinical superiority in elderly
    - Retrospective/observational evidence suggests clinical superiority

We did two studies with high dose vaccine in nursing home elderly

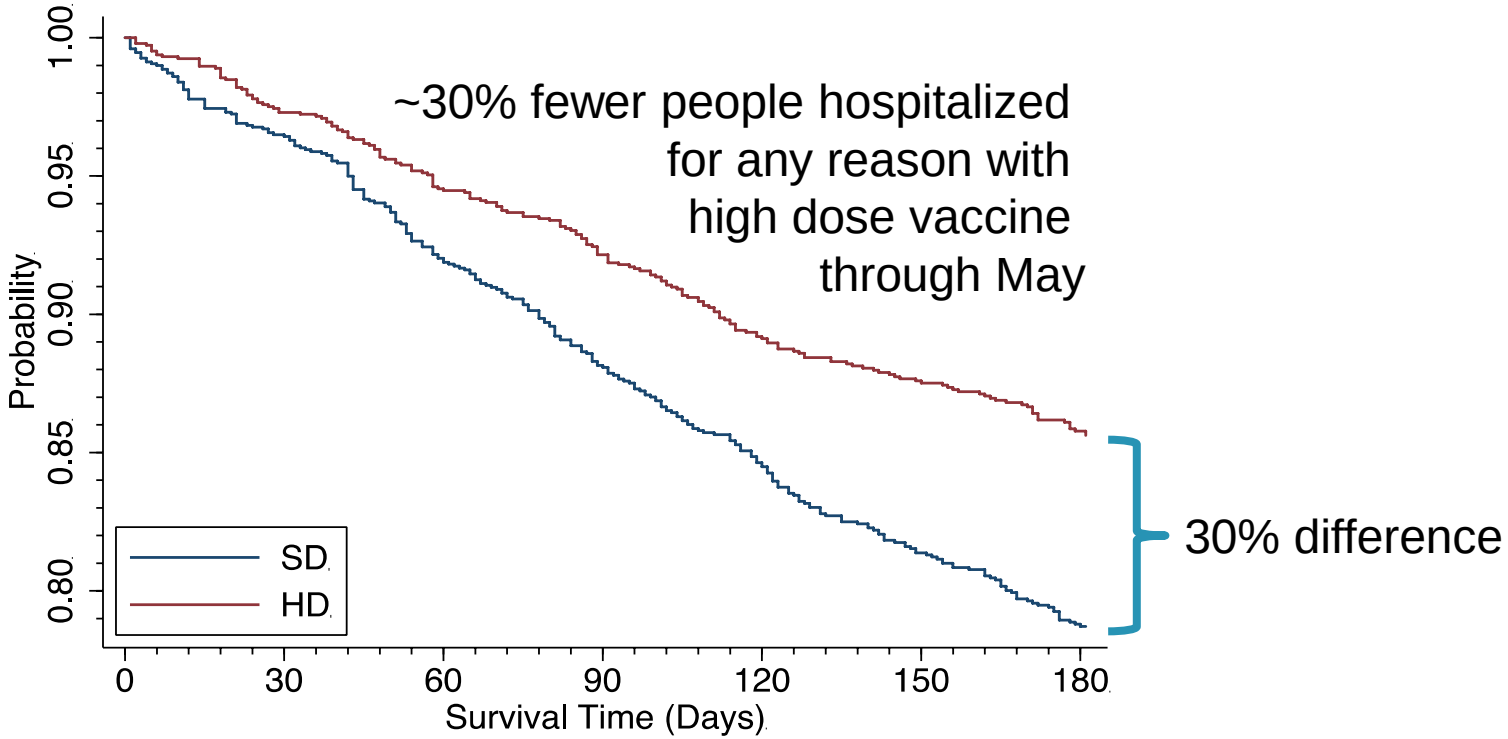
- 2012-2013, a predominant A/H3N2 year: small study
- 2012-2014, a predominant A/H1N1 year: big study

Weekly CDC Influenza Hospitalizations by Age and Season 2011-2017



https://gis.cdc.gov/GRASP/Fluview/FluHospRates.html; Downloaded 20 JUN 2017

Feasibility (small study)
Ever Hospitalized



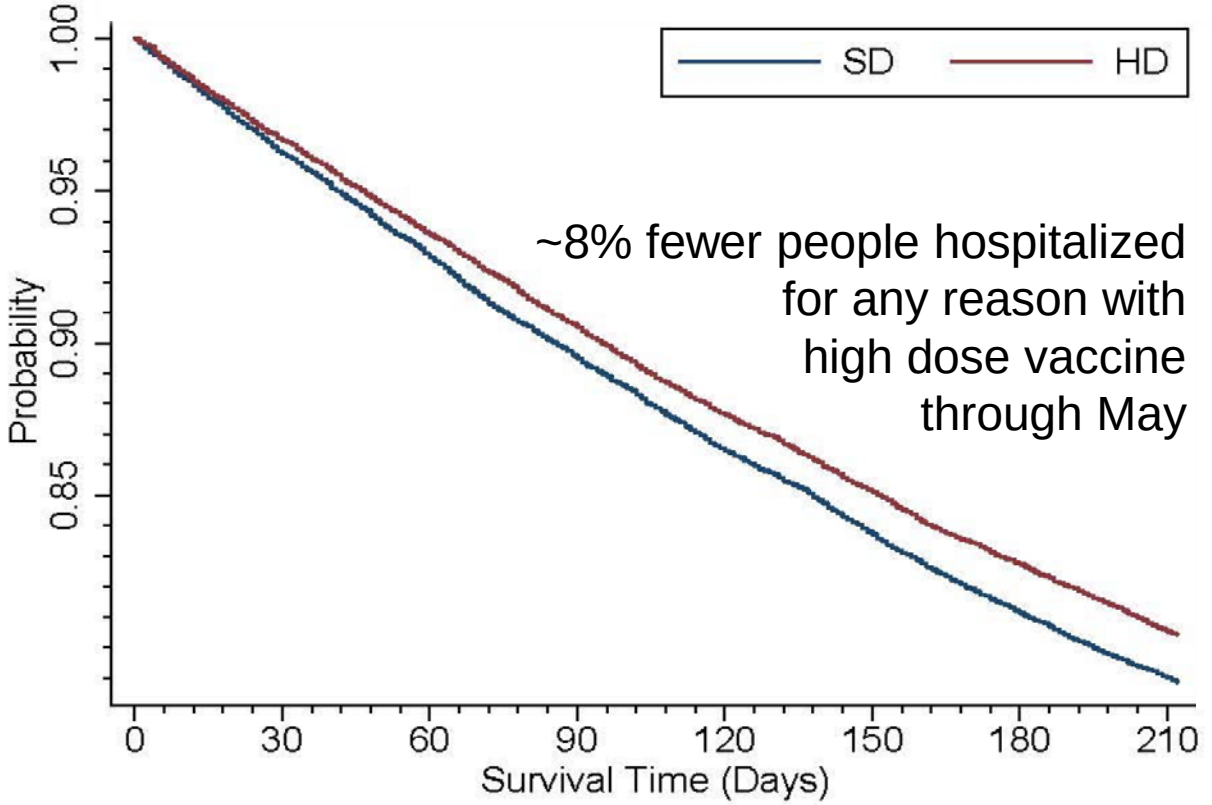
Number at risk

SD	1494	1418	1322	1241	1159	1082	1028
HD	1460	1395	1323	1264	1184	1129	1080

Time to All-Cause Index Hospitalization

Gravenstein S et al, *Hum Vaccin Immunother* 2017

Large Study
Ever Hospitalized



~8% fewer people hospitalized for any reason with high dose vaccine through May

~ 8% difference

Number at risk

Group: SD Vaccine	19129	18226	17410	16471	15600	14834	14125	13535
Group: HD Vaccine	19127	18301	17511	16612	15790	15053	14368	13768

Time to All-Cause Index Hospitalization

Gravenstein et al, *Lancet Respir Med* 2017

Number Needed to Vaccinate (for All Causes, Ever Hospitalized)

NNT = 1/ARR where ARR = CER – EER [a]

69, FFS sample

To prevent 1 person to be hospitalized need to give 69 a high-dose instead of a standard-dose vaccine

[a] NNT (or NNV) = number needed to treat; ARR = absolute risk reduction; CER = control event rate (i.e., probability of hospitalization for the SD group); EER = experimental event rate (i.e., probability of hospitalization for the HD group)

Gravenstein et al, *Lancet Respir Med* 2017

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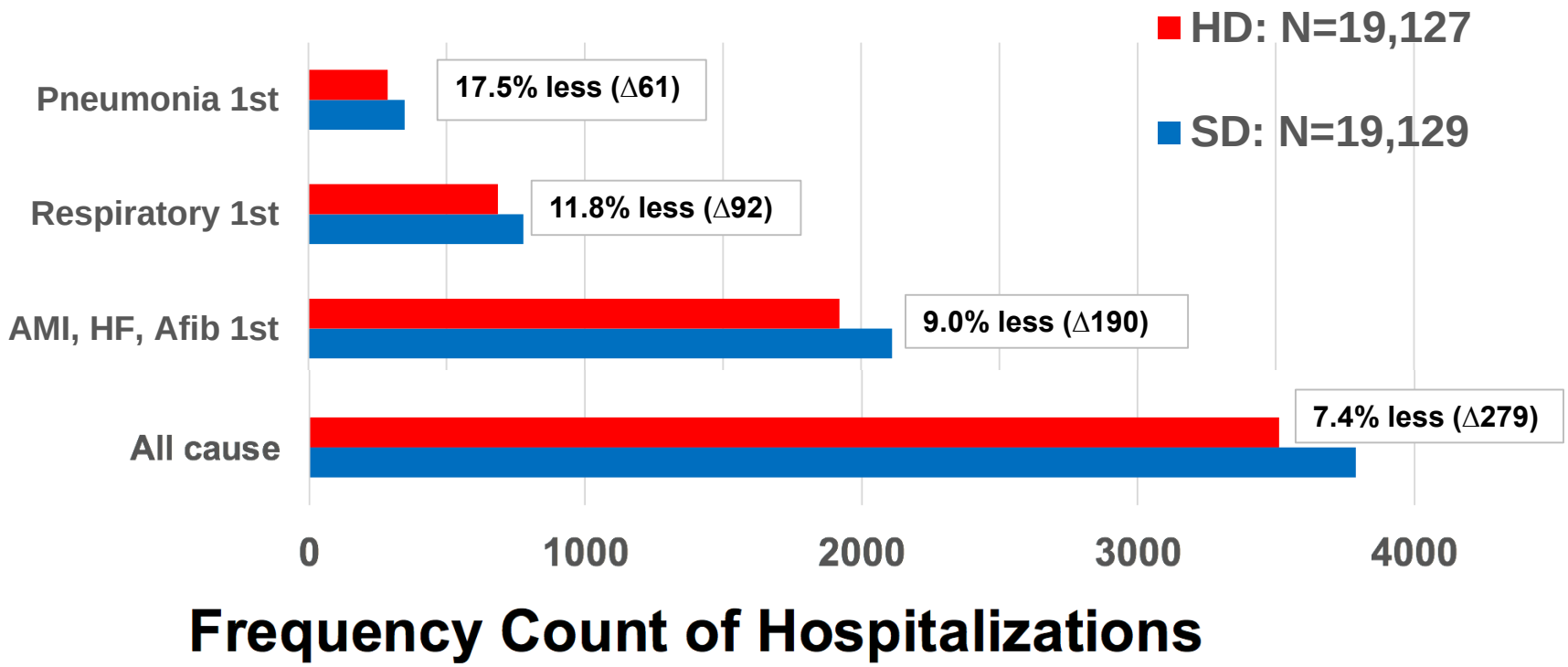
Medicare FFS Diagnosis-Related Hospitalizations 2013-2014 (Unadjusted)



1st = most important reason for hospitalization
AMI = heart attack
HF = heart failure
Afib = Atrial fibrillation

Why?

- For you: prevent influenza and heart attacks
- For employees
  - Prevent contagious disease to those they provide healthcare to
  - Protect from occupational exposure
  - Protect from exposure outside of work
- For nursing home residents
  - Prevent disease or serious complications of disease
  - Cheaper than treatment
  - Added risk for acquiring disease because of declining immunity and other changes of aging

What they need to do to get it done:

- Standing order generated at time of admission
  - Annual influenza vaccine
  - Up-to-date on other vaccines as needed
    - Goal to be up-to-date according to ACIP guidelines within a year of admission
- Offer vaccine as if it's an expectation, not an option
  - It is an option, but a strong recommendation gets the job done
    - "I'm giving you your scheduled influenza vaccine…"
      - **NOT**: "Would you like your influenza this year?"
      - "I get it. My family gets it. Everyone who works here gets it."
      - "It doesn't cause flu"
      - "Did you know, it's as effective as quitting smoking in preventing heart attacks?"
  - It benefits the people who get it, and they benefit the ones around them

Overall Summary

- **Aging** and frailty increases the risk for infectious complications
- Influenza and other infections are more than “just infections” in older adults
  - The impact on heart and brain as we age and an important (uncounted) consequence
- Vaccinate, vaccinate, vaccinate
  - With influenza vaccine, good match or not, every year
- More immunogenic vaccines can offer better protection

Resources

ACIP Recommendations

https://www.cdc.gov/mmwr/volumes/67/wr/mm6703a5.htm?s_cid=mm6703a5_w

Provider Newsletter

file:///C:/Users/rcooney/Downloads/SFTH_Provider_Newsletter_Fall2018.pdf

Patient Newsletter

file:///C:/Users/rcooney/Downloads/SFTH_Patient_Newsletter_080818-final.pdf

Presenter

- **Associate Professor of Medicine at Dalhousie University and a consultant in Geriatric Medicine at the QEII Health Sciences Centre in Halifax**
- **Principal Investigator of the Public Health Agency of Canada/CIHR Serious Outcomes Surveillance (SOS) Network, where she studies how frailty impacts vaccine effectiveness, burden of disease and clinical outcomes of infectious diseases in older adults**
- **CFN funded researcher on numerous studies**

Melissa Andrew

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Frailty and ‘flu:
Vaccination supports healthy aging across the spectrum of frailty

Melissa K. Andrew

Associate Professor of Medicine (Geriatrics) and Community Health & Epidemiology, Dalhousie University, Halifax, Canada

CFN Webinar

October 27, 2018

Disclosures

- Grant funding
  - Collaborative Research Agreements with GSK, Pfizer, Sanofi with the Canadian Institutes of Health Research, Public Health Agency of Canada and the Canadian Frailty Network
- No personal financial conflicts of interest
- Travel and honorarium funding from Immunize.ca and Canadian Frailty Network

Key Points

1) Frail older adults are at increased risk for influenza and its complications, BUT vaccine effectiveness is lower.
   - If we do not consider frailty in studies of influenza vaccine effectiveness, we underestimate vaccine effectiveness: “frailty bias”
2) The burden of influenza is usually considered over acute time horizons. We need to consider longer term impact of influenza illness and its complications, e.g. persistent functional decline.
3) Older adults may not present with classic symptoms of “influenza like illness”. This has implications for clinical care and surveillance.

So what does frailty have to do with influenza?

Figure credit: Janet McElhaney

Key Points

1) Frail older adults are at increased risk for influenza and its complications, BUT vaccine effectiveness is lower.
   - If we do not consider frailty in studies of influenza vaccine effectiveness, we underestimate vaccine effectiveness: “frailty bias”
2) The burden of influenza is usually considered over acute time horizons. We need to consider longer term impact of influenza illness and its complications, e.g. persistent functional decline.
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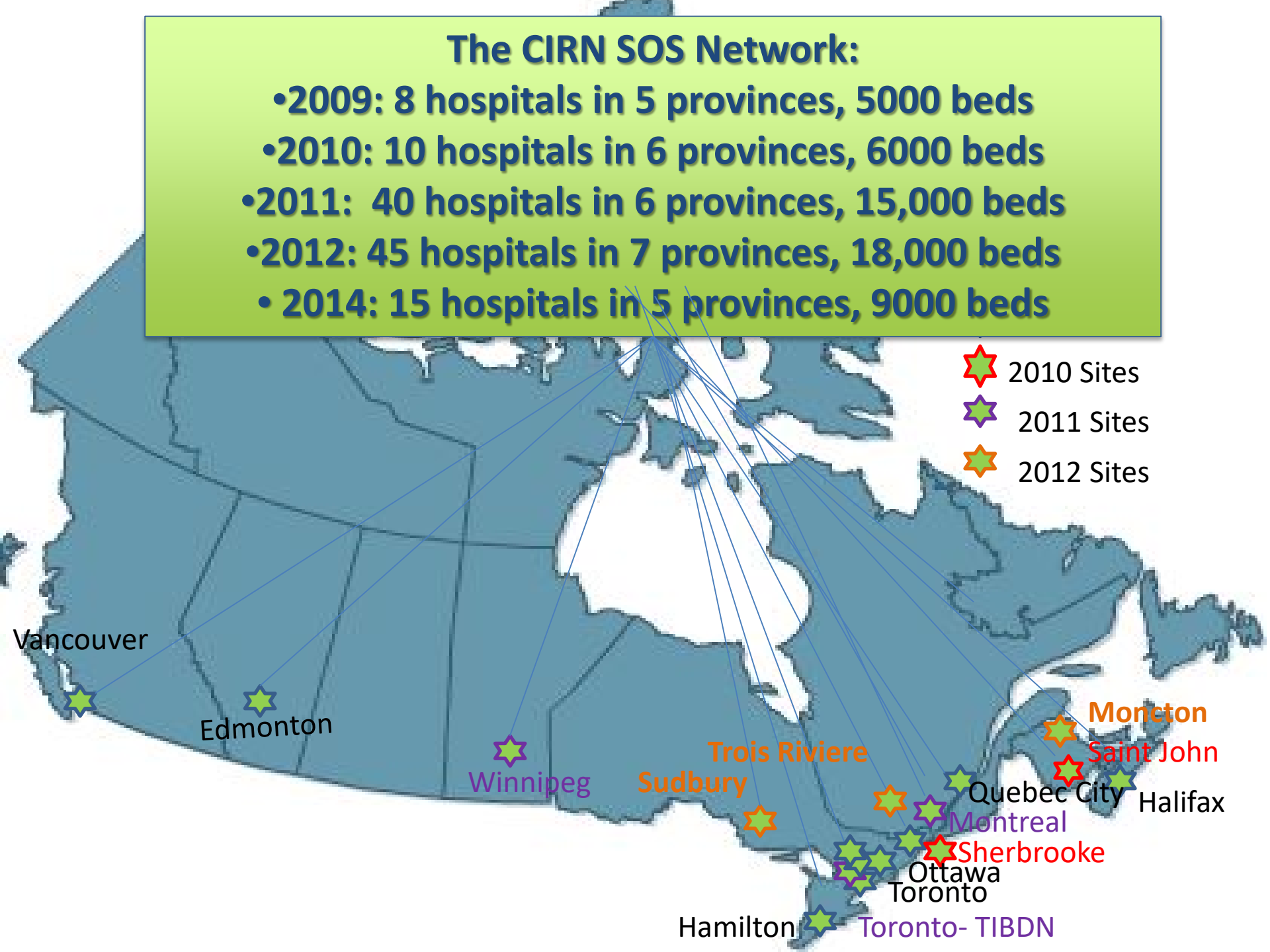

The CIRN SOS Network:
•2009: 8 hospitals in 5 provinces, 5000 beds
•2010: 10 hospitals in 6 provinces, 6000 beds
•2011: 40 hospitals in 6 provinces, 15,000 beds
•2012: 45 hospitals in 7 provinces, 18,000 beds
• 2014: 15 hospitals in 5 provinces, 9000 beds
2010 Sites
2011 Sites
2012 Sites
Vancouver
Edmonton
Winnipeg
Trois Riviere
Sudbury
Moncton
Saint John
Quebec City
Halifax
Montreal
Sherbrooke
Ottawa
Toronto
Hamilton
Toronto- TIBDN

SOS Methods

- Up to 45 sentinel teaching hospitals across Canada
- active surveillance for influenza infection in adults (≥ 16 years of age)
  - NP swab obtained from all patients with an admitting diagnosis of CAP, exacerbation of COPD/asthma, unexplained sepsis, any respiratory diagnosis or symptom OR acute coronary syndrome, stroke or any other cardiac diagnosis with fever (≥37.5˚C)
  - All NP swabs tested for influenza A & B by PCR

Vaccine Effectiveness calculation in a test-negative case control design

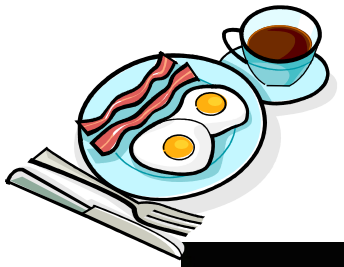
- VE estimated as:

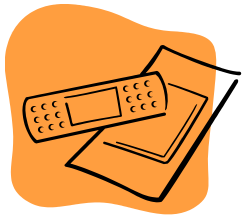
(1-OR of vaccination in cases vs controls)*100

  - Assuming protection from vaccine from 14 days post vaccination
  - Unadjusted & Adjusted (conditional logistic regression with backward stepwise selection; $p \leq 0.1$)
  - Overall VE and VE in age subgroups (16-49y, 50-64y, 65-75y, and >75y)
  - VE by influenza type/subtype
  - Consider health measures and outcomes important for older adults (frailty, function, mobility)

CIRN
CANADIAN IMMUNIZATION RESEARCH NETWORK

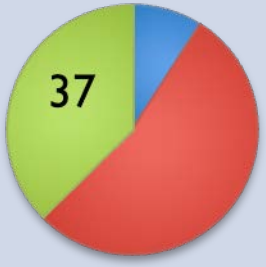
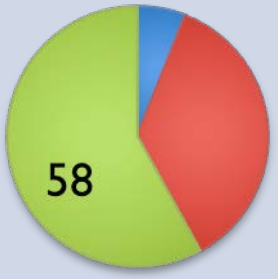
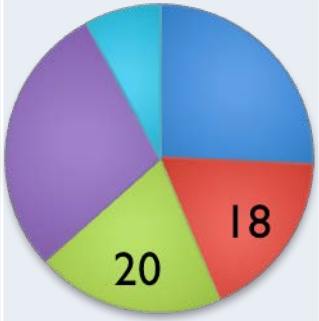
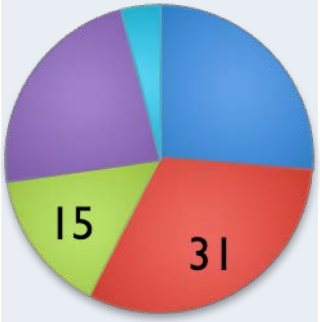
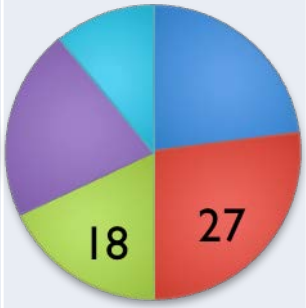
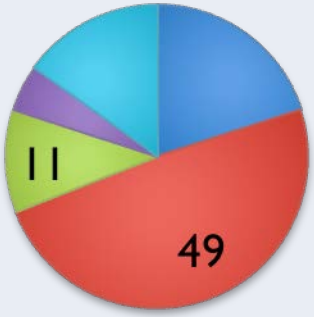
APPENDIX 6: Frailty Index and Frail Scale



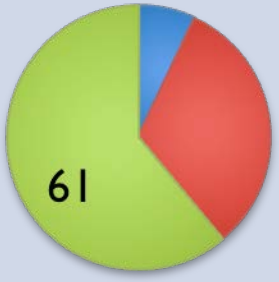
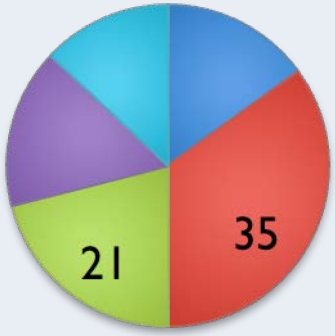
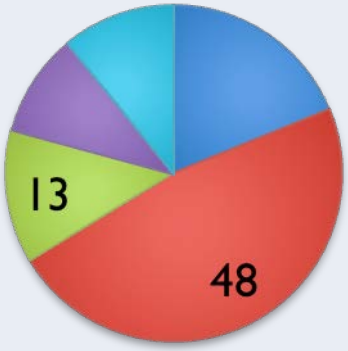
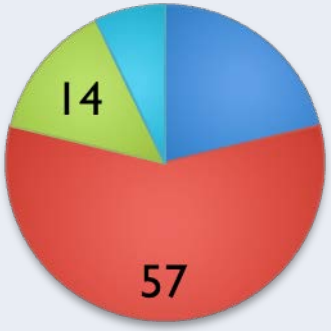


Frailty Index (for patients 65 years and older)		Check if Frailty Index was not done: ☐
	Two Weeks Prior to Admission	**On Admission**
A. Cognition	☐ WNL ☐ CIND ☐ Dementia ☐ Delirium due to illness? ☐ unk If dementia, type _____	☐ WNL ☐ CIND ☐ Dementia ☐ Delirium due to illness? ☐ unk If dementia, type _____
C. Mood	☐ WNL ☐ Low mood ☐Depression ☐ Anxiety ☐ unk	☐ WNL ☐ Low mood ☐Depression ☐ Anxiety ☐ unk
D. Sensory	Hearing ☐ WNL ☐ Impaired ☐ unk Vision ☐ WNL ☐ Impaired ☐ unk Speech ☐ WNL ☐ Impaired ☐ unk	Hearing ☐ WNL ☐ Impaired ☐ unk Vision ☐ WNL ☐ Impaired ☐ unk Speech ☐ WNL ☐ Impaired ☐ unk
E. Mobility	Transfers ☐ I ☐ A ☐ D ☐ unk Ambulates ☐ I ☐ A ☐ Non-amb ☐ unk Aid ☐ Y ☐ N ☐ unk If yes, aid type: ☐ Cane ☐ 2ww ☐ 4ww ☐ unk Balance ☐ WNL ☐ Impaired ☐ unk Falls ☐ Y ☐ N ☐ unk	Transfers ☐ I ☐ A ☐ D ☐ unk Ambulates ☐ I ☐ A ☐ Non-amb ☐ unk Aid ☐ Y ☐ N ☐ unk If yes, aid type: ☐ Cane ☐ 2ww ☐ 4ww ☐ unk Balance ☐ WNL ☐ Impaired ☐ unk Falls ☐ Y ☐ N ☐ unk
F. Nutrition	Weight ☐ Stable ☐ Loss ☐ Gain ☐ unk	Weight ☐ Stable ☐ Loss ☐ Gain ☐ unk
G. Function	Bathing ☐ I ☐ A ☐ D ☐ unk Toileting ☐ I ☐ A ☐ D ☐ unk Meds ☐ I ☐ A ☐ D ☐ unk Dressing ☐ I ☐ A ☐ D ☐ unk Eating ☐ I ☐ A ☐ D ☐ unk Finances ☐ I ☐ A ☐ D ☐ unk I =Independent, A=Assisted, D =Dependent	Bathing ☐ I ☐ A ☐ D ☐ unk Toileting ☐ I ☐ A ☐ D ☐ unk Meds ☐ I ☐ A ☐ D ☐ unk Dressing ☐ I ☐ A ☐ D ☐ unk Eating ☐ I ☐ A ☐ D ☐ unk Finances ☐ I ☐ A ☐ D ☐ unk I =Independent, A=Assisted, D =Dependent
H. Skin	Ulcers ☐ Y ☐ N ☐ unk Edema ☐ Y ☐ N ☐ unk	Ulcers ☐ Y ☐ N ☐ unk Edema ☐ Y ☐ N ☐ unk
I. Continence (ostomy managed by patient = continent)	Bladder : ☐ Continent ☐ Incontinent ☐ unk Bowel : ☐ Continent ☐ Incontinent ☐ unk	Bladder: ☐ Continent ☐ Incontinent ☐ unk Bowel : ☐ Continent ☐ Incontinent ☐ unk
J. Frailty Scale	1 to 9: _____	1 to 9: _____

Age and Burden of Disease

	Age 16 – 49 N = 128	Age 50-64 N = 118	Age 65-75 N = 109	Age >75 N = 237
% vaccinated				
BOD by strain				
Death	1 (0.8%)	3 (2.5%)	6 (5.5%)	36 (15.2%)
ICU	16 (12.5%)	20 (16.9%)	17 (15.6%)	22 (9.3%)

Frailty and Burden of Disease

	Low Frailty (FI < 0.2) N = 92	Med Frailty (FI 0.2-0.45) N = 84	High Frailty (FI <0.45) N = 14
% vaccinated			
BOD by strain			
Death	5 (5.4%)	11 (13.1%)	5 (35.7%)
ICU	7 (7.6%)	11 (13.1%)	1 (7.1%)

Frailty impacts Vaccine Effectiveness

(2011/2012) Andrew et al. JID 2017

	Unadjusted (95% CI)	Adjusted (95% CI)
Overall	41.8 (26.0-54.3)	42.8 (23.8-57.0)*
Age < 65y	35.8 (4.5-56.8)	33.2 (-6.7-58.2) †
Age ≥ 65y	45.0 (25.7-59.3)	58.0 (34.2-73.2) ‡

*Stepwise logistic regression – adjusted for, age, vaccine status, admit from LTCF

Adjusting for frailty alone very closely approximates the final fully adjusted model. Frailty is the most important confounder to take into account in adults 65+.

to admission, children <5y in house , medication prior to admission.

Vaccine Effectiveness decreases as frailty increases*

*Post-Hoc Analysis

Most older adults are not frail (prevalence ~24% in community-dwellers)

BUT the most frail are likely to be at highest risk from influenza and its complications

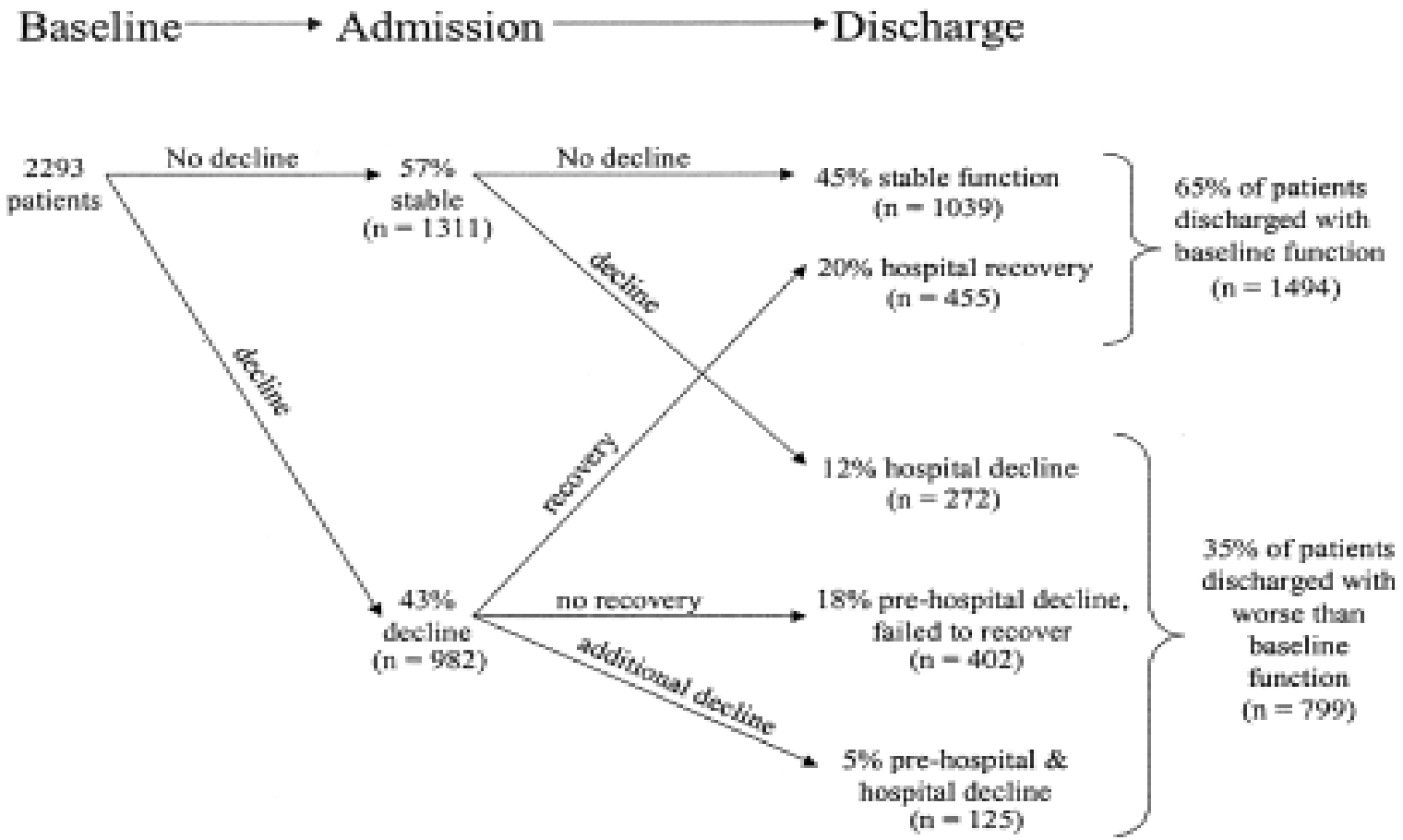
The problem of BIAS: how do vaccinated and unvaccinated people differ?

- **Bias** is any factor independently associated with risk of disease and vaccination status
  - Healthy user bias- persons more likely to be vaccinated are less likely to develop disease-
    - OVER-estimates VE
  - Indication (frailty) bias- persons more likely to be vaccinated (e.g. frail elderly people) are more likely to have suboptimal vaccine response and experience adverse more influenza outcomes
    - UNDER-estimates VE

Key Points

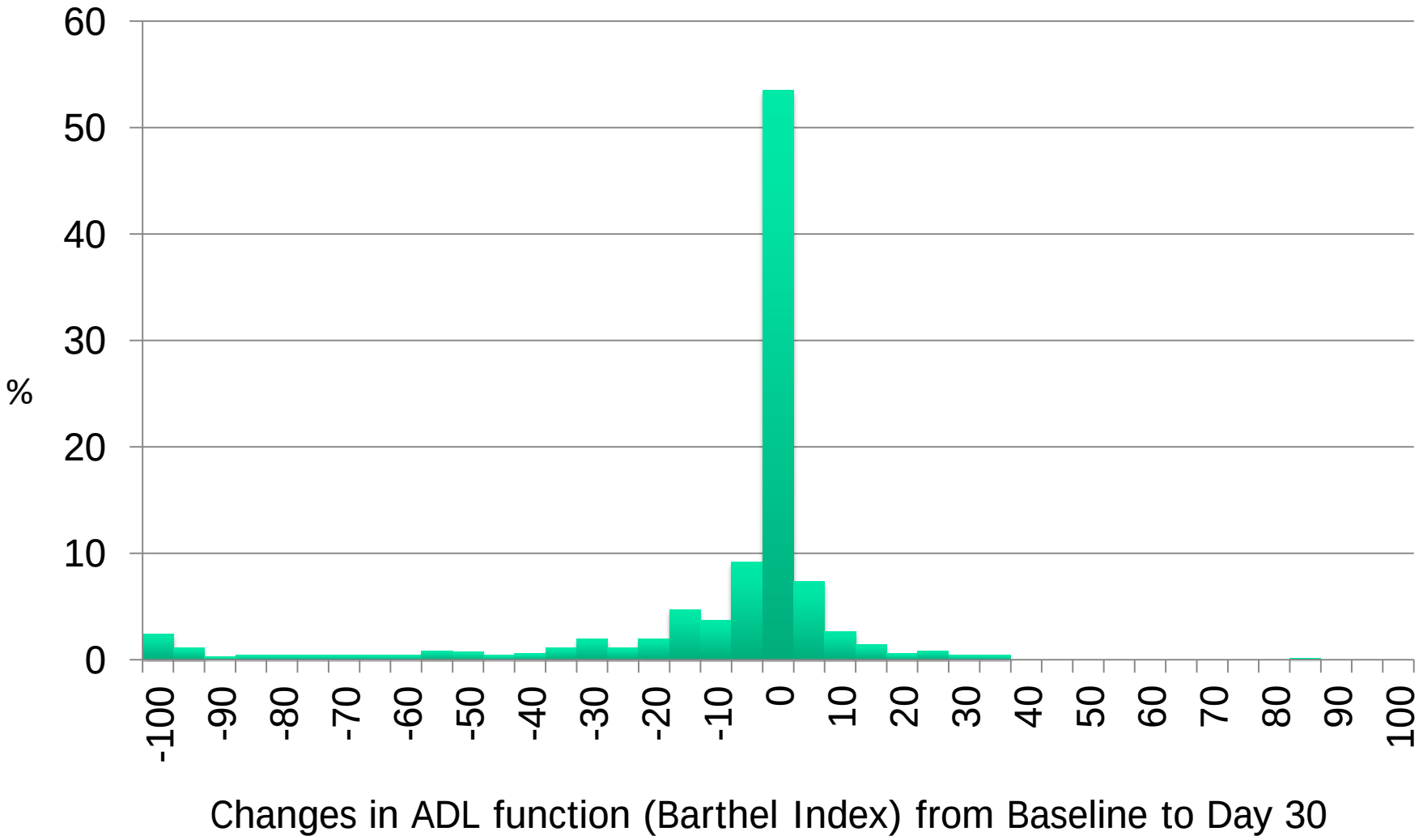
1) Frail older adults are at increased risk for influenza and its complications, BUT vaccine effectiveness is lower.
   - If we do not consider frailty in studies of influenza vaccine effectiveness, we underestimate vaccine effectiveness: “frailty bias”
2) The burden of influenza is usually considered over acute time horizons. We need to consider longer term impact of influenza illness and its complications, e.g. persistent functional decline.
3) Older adults may not present with classic symptoms of “influenza like illness”. This has implications for clinical care and surveillance.

Functional loss is common when older people are in hospital



Covinsky JAGS 2003

Older adults hospitalized with influenza suffer a significant burden of functional decline, which can be persistent



EXACT survey

- 5014 Canadian older adults completed our online survey (March-April 2017) about influenza, vaccine and complications
- Mean age 71.3 ± 5.17 years, 50% were female, and 42.6% had one or more chronic conditions.
- Clinical Frailty Scale: 7.8% were vulnerable and 1.8% frail
- 68% reported receiving the 2016/17 influenza vaccine
- 21.5% reported having influenza last season
- 20% of these were unable to conduct certain daily activities during the acute illness
- 40% took longer than two weeks to recover
- 3.1% “never fully recovered”
- Older age, memory loss, and having influenza/ILI were among the independent predictors of persistent declines in health and function.

Andrew M, Gilca V, Waite N, Pereira J. *Ms* submitted 2018

Key Points

1) Frail older adults are at increased risk for influenza and its complications, BUT vaccine effectiveness is lower.
   - If we do not consider frailty in studies of influenza vaccine effectiveness, we underestimate vaccine effectiveness: “frailty bias”
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3) Older adults may not present with classic symptoms of “influenza like illness”. This has implications for clinical care and surveillance.

How well do ILI and SARI criteria perform?

- Influenza-Like Illness
- An acute respiratory Infection with:
  - Measured fever >=38.0 ^{o}C
  - And cough
  - With onset within the last 10 days

Sensitivity
65+:
44.6 (43.5-45.8)
No High Risk:
57.0 (52.7-61.4)

- Severe Acute Respiratory Illness
- An acute respiratory infection with:
  - History of fever or measured fever >=38.0 ^{o}C
  - And cough
  - With onset within the last 10 days
  - And requires hospitalization

65+:
57.1 (55.9-58.2)
No High Risk:
70.7 (66.8-74.7)

Key Points

1) Frail older adults are at increased risk for influenza and its complications, BUT vaccine effectiveness is lower.
   - If we do not consider frailty in studies of influenza vaccine effectiveness, we underestimate vaccine effectiveness: “frailty bias”
2) The burden of influenza is usually considered over acute time horizons. We need to consider longer term impact of influenza illness and its complications, e.g. persistent functional decline.
3) Older adults may not present with classic symptoms of “influenza like illness”. This has implications for clinical care and surveillance.

So what does frailty have to do with influenza?

Figure credit: Janet McElhaney

Understanding frailty is important in identifying influenza illness and measuring influenza vaccine effectiveness

Understanding the impact of influenza on frailty and function is critical to understanding its true burden

NOT Adding Life to Years

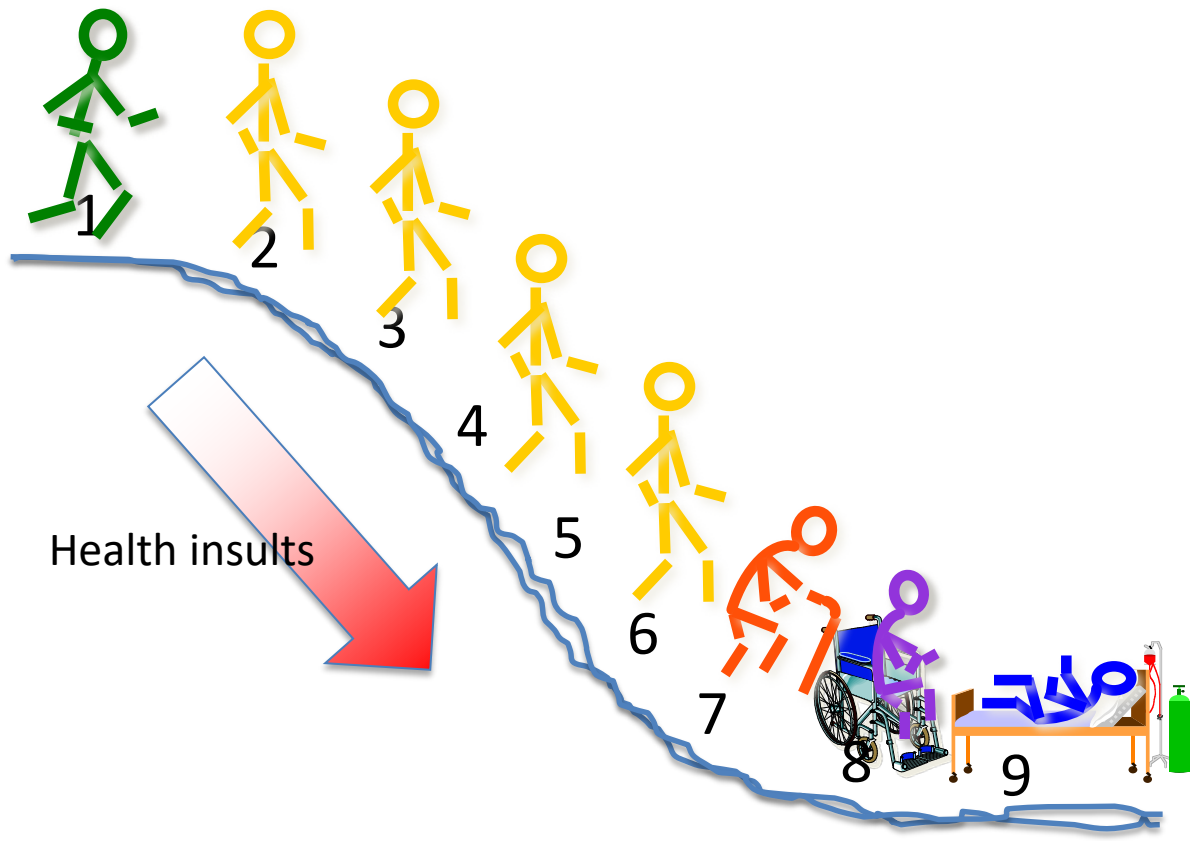


Figure credit: Janet McElhaney

Adding Life to Years: Can frailty and disability be prevented?

Candidates:

- Exercise
- Social integration
- Physiological interventions: nutrition, inflammation, immune, drugs?
- Good care?
  - * At least we can prevent some consequences and complications of frailty!
    - Avoidable illness & hospitalizations
    - Vaccine preventable illness and disability!

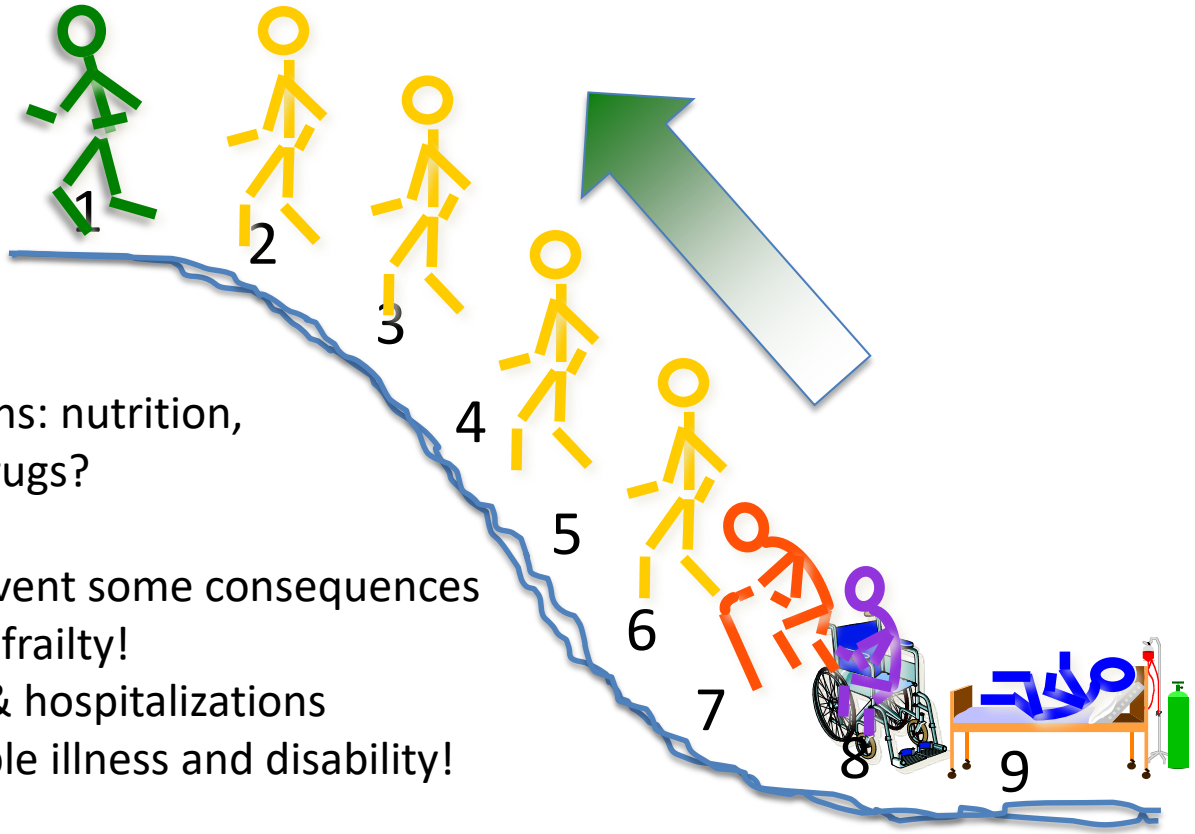
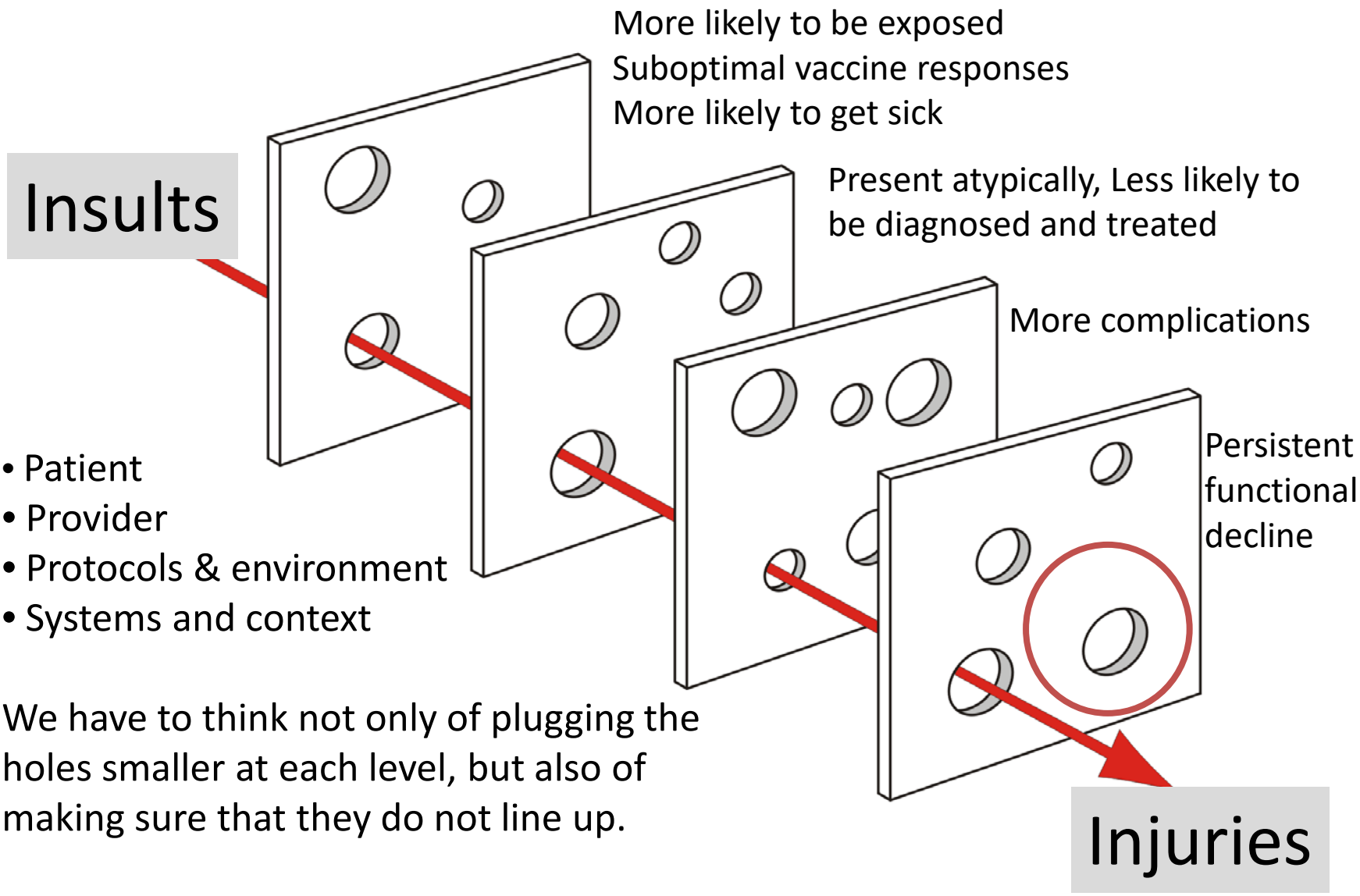


Figure credit: Janet McElhaney

How should this impact practice?

- Actively recommend vaccination for older adults across grades of frailty, establish protocols
- Consider different vaccine products, depending on setting
- Prevent influenza in those around them too
  - Vaccinate family, caregivers, health care professionals
  - Hand hygiene, self-isolate when ill…
- Broaden surveillance and clinical diagnosis and management
  - If we do not look for ‘flu, we will often miss it
- Consider frailty and function in research and clinical practice

Putting it all together – improving influenza prevention and care for older adults



Thank you for your interest!

Acknowledgements

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SOS trainees Sarah MacDonald, Caitlin Lees
Review paper collaborators: Susan Bowles, Graham Pawelec, Laura Haynes, George Kuchel, Shelly McNeil, Jan McElhaney

Presenter

- **Manitoba Health's director of communicable disease control**
- **Leadership in promoting and support the prevention and control of communicable diseases in Manitoba**
- **Provides leadership and strategic direction through the development of user-friendly policies and guidelines; promoting healthy behaviours and cultivating effective partnerships with stakeholders; identifying risk factors and detect communicable diseases early to inform public health**

Richard Baydeck

Canadian Frailty Network | Réseau canadien des soins aux personnes fragilisées

www.cfn-nce.ca

Presented in partnership with

SANOFI PASTEUR

Manitoba's High Dose Influenza Vaccine Program

Richard Baydack, PhD

September 26, 2018

Manitoba

Disclosure Statement

Richard Baydack, PhD
Canadian Frailty Network

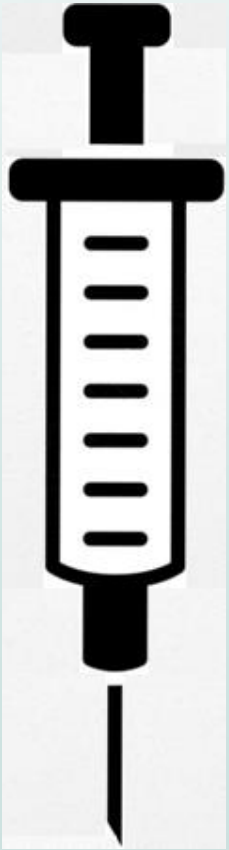
Type of relationship	**Modest (less than 10K)** *Please specify organization name*	**Significant (greater than $10K)** *Please specify organization name*
A - Consulting Fees/Honoraria		
B - Speaker's Bureau		
C - Equity Interests/Stock Options/Royalty Income/Non Royalty Payments		
D - Officer, Director, Or In Any Other Fiduciary Role		
E - Ownership/Partnership/Principal		
F- Research Grants/Educational Grants		
G- Fellowship Support		
H – Salary		
I - Intellectual Property Rights		
J - Other Financial Benefit		

There are no relationships to disclose X

Objectives

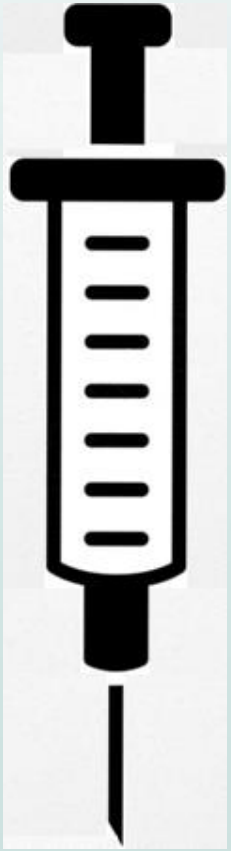
- Review the History of Influenza Vaccine in MB
- Understand the Essential Elements of the 2017-18 High Dose Influenza Vaccine Program for Residents Aged 65+ in Long Term Care (LTC)
- Compare and Contrast Influenza Epidemiology: 2017/18 vs 2014/15
- Describe MB's High-Dose Influenza Immunization Program Evaluation
  - Evaluation plan outline
  - Preliminary survey results
  - Preliminary descriptive data results

History of Influenza Vaccine Introduction in MB to Seniors & Residents of Long Term Care (LTC)



- 1999: Targeted Seasonal Influenza Program (NACI High Risk including 65+ and LTC residents).
- 2009: Seasonal influenza vaccine for all Manitobans.
- 2015: Transitioned from TIV to QIV
- 2017: High-Dose Influenza Vaccine 65+ in LTC

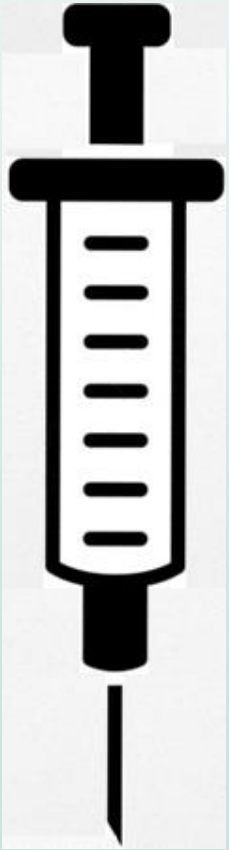
Manitoba's Influenza Vaccine Eligibility Criteria



An annual flu vaccine is **especially important for those at increased risk of serious illness from the flu**, their caregivers and close contacts. This includes:

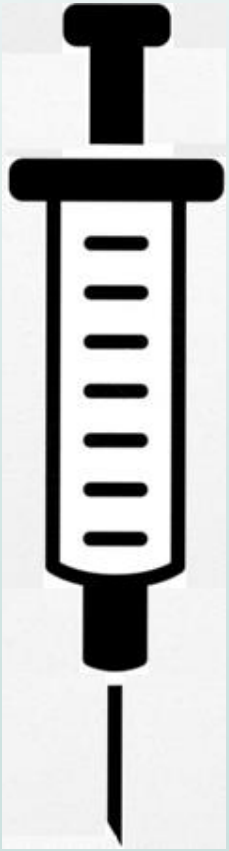
- **people 65 years of age and older**
- **residents of personal care homes or long-term care facilities**
- children six to 59 months of age
- individuals with the following chronic health conditions:
  - an immune system weakened by disease or medical treatment (ex: cancer)
  - cardiac or pulmonary disorders (ex: cystic fibrosis, asthma)
  - long-term acetylsalicylic acid (Aspirin®) therapy (for those between six months and 18 years of age *only*)
  - neurologic or neurodevelopmental conditions
  - diabetes and other metabolic diseases
  - renal disease
  - anemia or hemoglobinopathy
  - obesity (body mass index = 40)
- pregnant women
- health care workers and first responders
- regular caregivers of children up to five years of age
- household contacts of anyone at increased risk of serious illness from the flu including those with infants under six months of age and/or expecting a newborn
- Indigenous peoples

A Very Brief Summary of Process



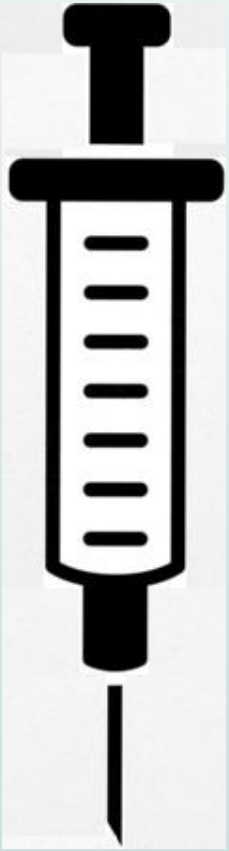
- Since 2013, PVAC discussion/consideration given to introducing senior-specific influenza vaccine for 65+ LTC
- Fall 2015: BGTD approves High-Dose Influenza Vaccine
- January 2016: NACI releases lit review on High-Dose Influenza Vaccine
- February 2016: PVAC recommends review
- October 2016: PVAC recommends High-Dose Influenza Vaccine
- 2016/17 NACI Statement recommending High-Dose Influenza Vaccine
- August 2017: Central Government Approval

2017/18 NACI Statement



- The National Advisory Committee on Immunization's Statement on Seasonal Influenza Vaccine for 2017-2018 stated that it is **expected that high dose influenza vaccine should provide superior protection compared with the standard dose vaccine to those who are 65 years of age and older**, given the burden of Influenza A(H3N2) disease and evidence of better efficacy in this age group.

The Case for High Dose



- The NACI Statement
- Higher dose in Fluzone HD is shown to provide better protection against those strains included in the vaccine.
- Highest number of cases and incidence of influenza A and B in Manitoba occurs in the senior population.
- Seniors in long-term care facilities are known to be very susceptible to complications from influenza, including pneumonia and bronchitis. In fact, lower respiratory tract infections are a leading cause of hospital admission in adults aged 65 years or older, especially in frail older adults such as those living in long-term care facilities.
- Fluzone® HD is expected to provide **superior protection against influenza A(H3N2)** disease. This strain has historically produced a disproportionate burden of illness (morbidity and mortality) in those over 65 years of age.

Determining Target Population Size

- Based on the Department's bed map of 125 licensed long-term care facilities (LTCFs), there were just over 9,000 residents eligible for high-dose influenza vaccine.
  - MB initially ordered 9,000 doses of high-dose influenza vaccine.
  - Based on subsequent demand, an additional 455 doses were ordered for a total of 9,455 doses.
- Electronically available information resources (factsheets) were created and made available to inform staff, residents and their families.
- Residents were offered high-dose influenza vaccine based on the province's recommendation that it provided superior protection. If refused, they were offered the standard-dose, quadrivalent product.

Manitoba

Seasonal Influenza Vaccine for Residents of Long-Term Care Facilities

Questions & Answers for Health Care Providers

The following is a set of commonly asked questions and answers to help guide health care providers in the implementation of Fluzone® High-Dose for residents of long-term care facilities as part of Manitoba's Seasonal Influenza Immunization Program.

1. What is Fluzone® High-Dose?

This year, a new seasonal influenza vaccine, known as Fluzone® High-Dose, is being offered to people 65 years of age or older who are living in long-term care facilities (LTCF) in Manitoba. This vaccine is a trivalent inactivated vaccine (TIV) and protects against three (2A + 1B) of the influenza strains predicted to be circulating in North America during the 2017-18 influenza season. Fluzone® High-Dose contains four times the amount of influenza virus antigen per strain compared to the standard-dose influenza vaccine, and is expected to provide better protection against seasonal influenza compared to the standard-dose vaccine.

2. How was Fluzone® High-Dose eligibility determined?

Manitoba Health, Seniors and Active Living (MHSAL), in consultation with provincial vaccine experts, is offering Fluzone® High-Dose to senior residents of LTCFs who are known to be very susceptible to complications from influenza.

Lower respiratory tract infections including pneumonia, bronchitis and tracheobronchitis are a leading cause of admission to hospital in adults aged 65 years of older, especially in frail older adults, such as those who reside in nursing homes. The number of nursing home residents admitted to hospital varies considerably between facilities, but is more frequent during the 16 weeks of peak influenza activity each year.

B, although an important cause of illness, produces less morbidity and mortality in this age group.

4. If there was a B strain mismatch this year, should I immunize my LTCF patients with the four-strain, standard-dose influenza vaccine later in the season?

No. See question above.

5. How is "long-term care facility (LTCF)" defined for the purposes of Fluzone® High-Dose eligibility?

For the purposes of Fluzone® High-Dose eligibility in the 2017-18 season, LTCFs are defined as residential facilities for predominantly older persons with chronic illness or disability, also known as personal care homes or nursing homes.

Respite care clients admitted to LTCF on a temporary basis are those for whom care is provided for on weekends or extended periods (e.g. vacation). Such care may be provided through temporary placement in an LTCF. So long as these clients are at least 65 years of age, they are also eligible to receive Fluzone® High-Dose while in the LTCF.

Clients in transitional beds, even though being assessed for LTCF eligibility, would NOT be eligible for publicly-funded Fluzone® High-Dose.

Clients living in the following community-based housing "alternatives" are not a part of the provincial personal care home bed map and should

Manitoba

Seasonal Influenza Vaccine for Residents of Long-Term Care Facilities

Public Health - Factsheet

Immunization has saved more lives in Canada in the last 50 years than any other medical intervention.[1] Vaccines help the immune system to recognize and fight bacteria and viruses that cause disease.

What is seasonal influenza?

Seasonal influenza (the flu) is a respiratory infection caused by a virus. Not everyone who gets the flu develops symptoms, but they can still spread it to others, especially if they cough or sneeze. The flu can seem similar to the common cold, but the signs and symptoms of the flu are usually more severe. Sudden high fever, body aches, extreme tiredness and dry cough are more common with the flu than the common cold. Other common symptoms include headache, chills, loss of appetite and sore throat. Nausea and upset stomach may also occur, especially in young children. The flu can lead to more serious problems like pneumonia and bacterial infections, sometimes resulting in hospitalization.

The flu can spread easily from person to person through coughing, sneezing or sharing food or drinks. You can also get the flu by touching objects contaminated with flu virus and then touching your mouth, eyes or nose. For this reason, it's important to cover your nose and mouth with your forearm when you cough or sneeze and wash your hands often with soap and water (or hand sanitizer if soap and water are unavailable), especially after coughing and sneezing.

The flu season in Manitoba usually begins in the fall and lasts into the spring. For your protection, you should get immunized early in the fall before the flu provided by the vaccine decreases over time, it's important to get the flu vaccine every fall.

The flu vaccine cannot offer protection against other viruses or bacteria that cause the common cold or stomach flu.

This year, a new flu vaccine is being offered to people 65 years of age or older who are living in long-term care facilities in Manitoba. This vaccine, known as Fluzone® High-Dose, is safe, effective, and will not cause the flu because it does not contain any live viruses. Fluzone® High-Dose is a trivalent inactivated vaccine (TIV) and protects against three (2A + 1B) of the influenza strains predicted to be circulating in North America during the 2017-18 seasonal influenza season. Fluzone® High-Dose is given by injection (needle) and is expected to provide better protection against seasonal influenza, compared to the standard inactivated influenza vaccine.

Why should people get the flu vaccine?

Immunization is the best way to protect yourself against the flu, which can often be serious and sometimes fatal.

Vaccines help prepare your body to fight potential future exposure to the flu by getting your immune system ready

Flu Vaccine Distribution in MB

- MB prioritizes distribution of flu vaccine to locations that have populations at greatest risk of influenza and its complications: hospitals, LTCFs and First Nations communities.
- All subsequent orders by health care providers are processed after priority orders to hospitals, LTCFs and First Nations communities have been shipped.
- For the 2017/18 flu season, high-dose influenza vaccine was delivered to MB after the initial standard-dose influenza vaccine supply arrived, creating high-dose influenza vaccine distribution delays.
- Total doses shipped for all flu vaccine types from Sept. 2017 to April 2018 was 422,185 to 827 different provider locations.

High-Dose Influenza Vaccine Distribution

- Health care providers ordering on behalf of a LTCF were asked to complete a special order form.
- Warehouse staff entered the orders into the inventory system and included info about facility name and # of licensed beds in the comments section of the special order form.
- All orders were reviewed by Inventory Management at MHSAL to cross-reference the # of beds with the licensed bed map as well as the number of doses ordered.
- Once product arrived at the warehouse, orders were processed and product was shipped to 112 different locations along with standard-dose vaccine that was used for staff as well as residents under 65 years of age.
- Product was redistributed later in the season by public health staff to minimize wastage of any unused high-dose influenza vaccine.

Manitoba

2017-18 Influenza and Pneumococcal Vaccine Order Form for Long Term Care Facilities

Manitoba

Fax or E-Mail the completed form to: Provincial Vaccine Warehouse
Fax: 204-942-6212 Ph: 204-948-1333 Toll Free: 855-683-3306 E-Mail: vacmda@gov.mb.ca

Date: mm / dd / yyyy			
Holding Point (Client) ID # (Req'd):		**Contact Person:**	
Holding Point Name:		**LTC Facility Name (If Different from Holding Point Name):**	
Address:		**City/Town:**	**Postal Code:**
Telephone:	**Ext.**	**Fax:**	**P.O #:**
Special Delivery Instructions:			
Open for Saturday Delivieries:	**Circle:** yes / no		

Given the burden of influenza A(H3N2) disease and evidence of better efficacy in adults aged 65 years and older, it is expected that Fluzone® High-Dose will provide superior protection compared with the standard dose influenza vaccine.
MHSAL recommends that dosing schedules be verified with the current *Canadian Immunization Guide* and product monographs.

Please fill in the following information regarding your facility. Influenza products will be assigned based on availability and eligibility criteria.

# of licensed beds	
# of influenza doses for residents 65 years of age and older	
# of influenza doses for residents under the age of 65 and staff/visitors	
# of Pneu-P-23 (Pneumovax 23) doses	

Product must be stored in a temperature monitored refrigerator that is kept between 2-8ºC. For more information see the Manitoba Health, Seniors and Active Living Cold Chain Resources Website at www.gov.mb.ca/health/publichealth/cdc/coldchain.html.

MHSAL' Seasonal Influenza Supply and Distribution website (www.gov.mb.ca/health/flu/distribution.html) will be updated accordingly to indicate an approximate date of when health care providers may expect to receive their shipment.

The Manitoba Immunization Registry

Immunizations are recorded on a client's electronic public health record through Manitoba's Immunization Registry (a module of the Public Health Information Management System – PHIMS) in one of three ways:

1. Direct data entry by users with access to PHIMS.
   - Health care providers who have access to PHIMS can enter immunization data directly into PHIMS (if their permissions allow for data entry).
   - For those who do not have access to PHIMS and in instances where a health care provider is unable to enter information directly into PHIMS (i.e. Private Flu Clinic), as well as for instances where the individual does not have a Personal Health Identification Number (PHIN) or the PHIN is unknown, health care providers are to complete a form and submit it to their local Public Health office where it will be entered manually into PHIMS by regional staff.
2. Uploaded into PHIMS from the Drug Program Information Network (DPIN) system when administered by pharmacists.
3. Uploaded into PHIMS from the Physician Billing System when administered by fee-for-service physicians and other health care providers that shadow bill (ex: regional nurse practitioners).

Flu Vaccine Inventory Management

- Introduction of the Inventory Module of Panorama increased the Department's command and control of all influenza vaccine inventory.
- There were considerable efficiencies realized as a result of MB's Inventory Management Specialist working directly with health care providers to match flu vaccine supply with demand.

Flu Epidemiology in Review: After H3N2 Peak, week 2, 2017/18 vs 2014/15

Data extracted Jan. 19th, 2018 @ 11:00am:

- Lab-confirmed flu cases since Sept. 1st 2017:
  - Flu A cases: **761**
  - Flu B cases: **58**
- Severe outcomes since Sept. 1st 2017:
  - Hospitalizations: **213**
  - ICU admissions: **16**
  - Deaths: **21**
- Lab-confirmed flu outbreaks since Sept. 1st 2017:
  - Flu A outbreaks: **43**
  - Flu B outbreaks: **2**
- As of January 12th, 2018, **20.2%** of MB residents immunized against seasonal influenza.

Data extracted Jan. 23rd, 2015 @ 11:00am:

- Lab-confirmed flu cases since Sept. 1st 2014:
  - Flu A cases: **863**
  - Flu B cases: **16**
- Severe outcomes since Sept. 1st 2014:
  - Hospitalizations: **228**
  - ICU admissions: **35**
  - Deaths: **22**
- Lab-confirmed flu outbreaks since Sept. 1st 2014:
  - Flu A outbreaks: **75**
  - Flu B outbreaks: **0**
- As of January 2nd, 2015, **16.8%** of MB residents immunized against seasonal influenza.

Flu Epidemiology in Review: End of Season, 2017/18 vs 2014/15

Data extracted May 4th, 2018 @ 11:00am:

- Lab-confirmed flu cases since Sept. 1st 2017:
  - Flu A cases: **1,073**
  - Flu B cases: **593**
- Severe outcomes since Sept. 1st 2017:
  - Hospitalizations: **505**
  - ICU admissions: **34**
  - Deaths: **46**
- Lab-confirmed flu outbreaks since Sept. 1st 2017:
  - Flu A outbreaks: **71**
  - Flu B outbreaks: **28**
- As of March 31st 2018, **22.5%** of MB residents immunized against seasonal influenza.

Data extracted May 8th, 2015 @ 11:00am:

- Lab-confirmed flu cases since Sept. 1st 2014:
  - Flu A cases: **1,072**
  - Flu B cases: **180**
- Severe outcomes since Sept. 1st 2014:
  - Hospitalizations: **353**
  - ICU admissions: **63**
  - Deaths: **45**
- Lab-confirmed flu outbreaks since Sept. 1st 2014:
  - Flu A outbreaks: **94**
  - Flu B outbreaks: **9**
- As of April 15th, 2015, **21.8%** of MB residents immunized against seasonal influenza.

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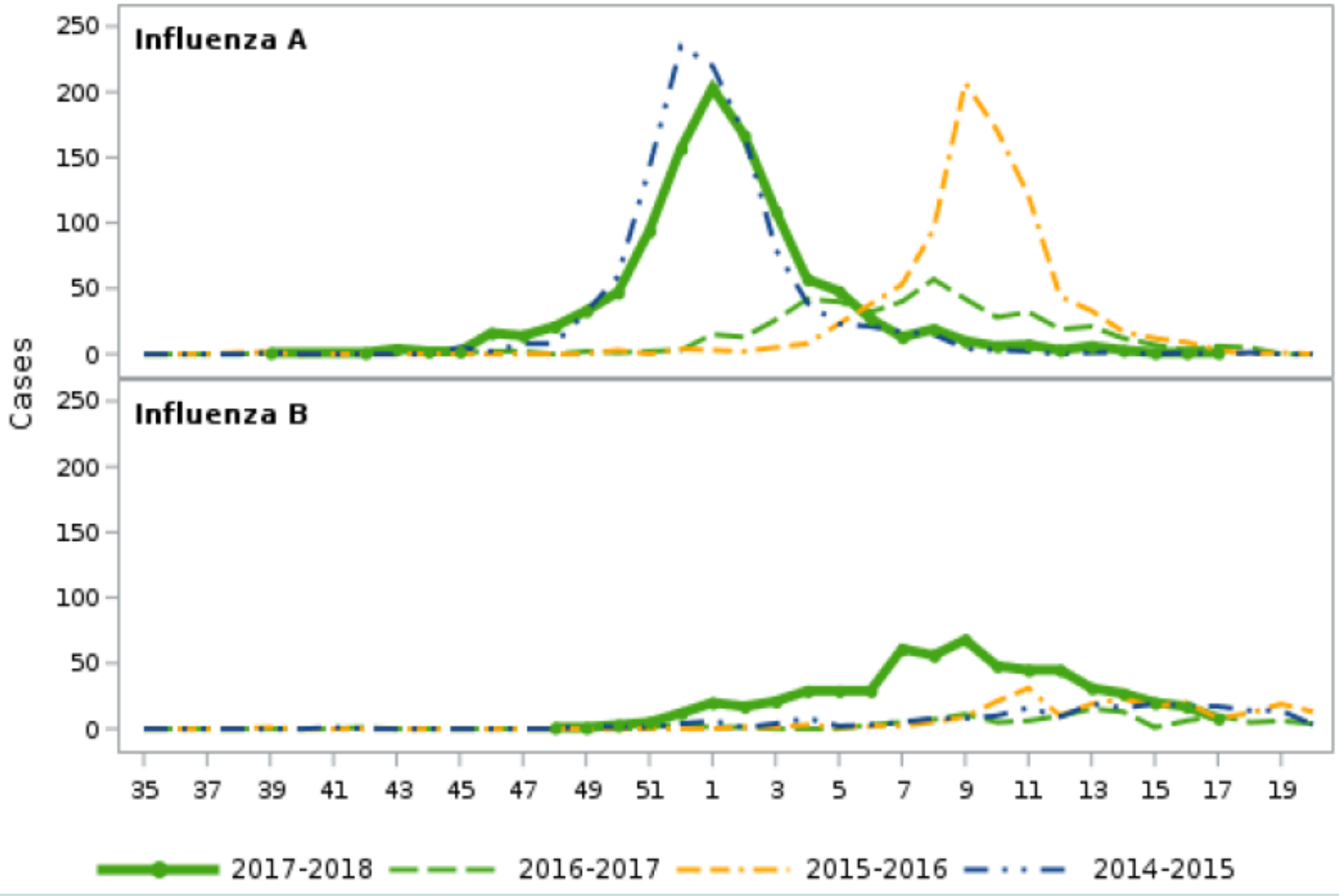
Weekly Cases of Laboratory-Confirmed Influenza, Manitoba



High-Dose Influenza Vaccine Program Evaluation Plan

Qualitative:

- 11 Question Survey

Quantitative:

- Laboratory-confirmed cases in LTC by season, by age
- Vaccine safety
  - Rate of AEFIs among 65+, by year: standard-dose vs. high-dose
- Vaccine coverage by season, by age

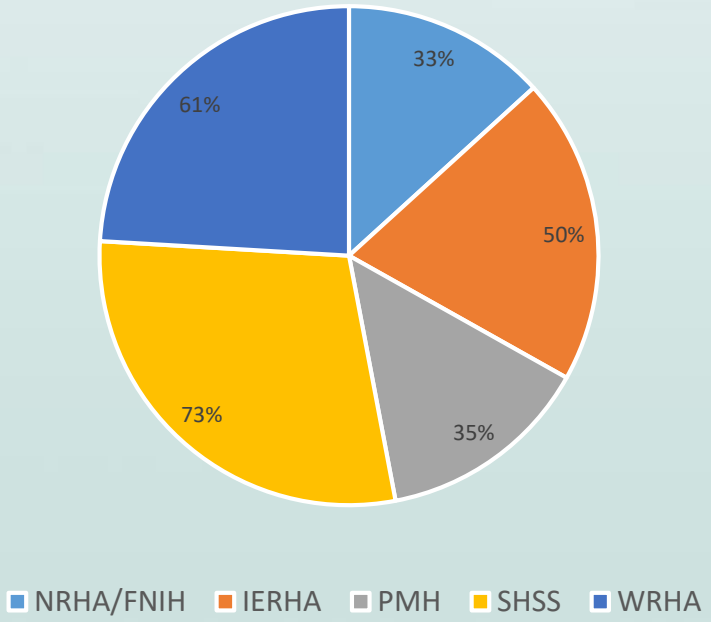
High-Dose Influenza Vaccine Program Evaluation Plan

Quantitative (cont'd):

- Respiratory outbreaks in LTCFs, by season
  - Respiratory vs. influenza A/B outbreaks
- Attack rate in LTCFs, by season
  - Duration of outbreaks
  - Symptomatic cases/rate
  - Confirmed cases/rate
  - Hospitalized cases/rate
  - Deceased cases/rate

Survey to Long-Term Care Facilities

- The Department distributed a questionnaire through Survey Monkey to all LTCFs within the province to obtain health care provider feedback on the launch of high-dose influenza vaccine.
- Based on the Department's bed map as of March 31st, 2017, there were 125 licensed LTCFs in MB.
  - A total of 66 surveys were completed and submitted resulting in a response rate of approx. 52.8%
  - There was representation from each health region.

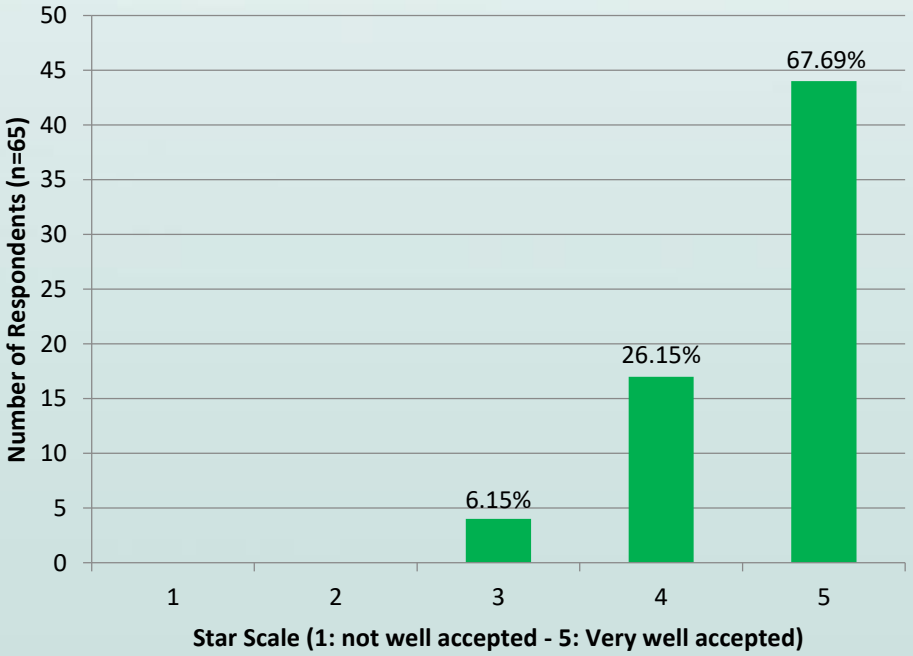


Offering High-Dose Influenza Vaccine in their Facility

- 65 of the 66 respondents (98.5%) offered high-dose influenza vaccine their residents.
- The one respondent that did not offer high-dose influenza vaccine advised that the facility opted to offer the standard-dose influenza vaccine in lieu of the high-dose influenza vaccine.

Acceptability of High-Dose Influenza Vaccine, by residents

- Majority of respondents identified that residents had no issues with the new product.
- Feedback received advised that any concerns were addressed by facility staff.



Safety concerns from staff &/or residents/family

- Majority of respondents (85%) identified no concerns with potential adverse events.
- The 15% that identified concerns reported the following: concerns with potential additional side-effects; concerns with additional benefits/efficacy of the new vaccine compared to standard-dose vaccine; and, concerns with being “guinea pigs.”
- Staff were reportedly able to address the concerns raised with the resources that were provided by the Department.

Usefulness of the resources created by the Department

- On a scale of 1-5 (5 being the most useful), the overall usefulness of the resources was rated as 4.3 for staff and 4.22 for residents.
- Suggestions to improve the resources:
  - Create a brochure comparing the available vaccines
  - Use more concise, simpler language
  - Use larger font
  - Earlier availability of the information/resources

Accessing High-Dose Influenza Vaccine from the Provincial Distribution Warehouse

- 58 respondents (89%) had no issues with accessing/ordering high-dose influenza vaccine for their facility.
- Suggestions to improve access:
  - Clear description of product format (i.e. pre-filled syringes)
  - Arrival with other flu vaccines to facility
  - Order based on consents received vs LTCF population count in order to reduce wastage

Would the facility like to see High-Dose Influenza Vaccine offered in the future?

- 91% (n=59) of respondents said yes, they would like MB to continue offering high-dose influenza vaccine in LTCFs.
- Feedback from those who said yes:
  - Although there were still outbreaks, the illness was not as severe
  - Continue as long as the efficacy shows that it helps this population
  - Format of pre-filled syringes made it much more efficient
- Feedback from the 9% who said no, they did NOT want MB to continue offering high-dose influenza vaccine in LTCFs:
  - Increases confusion with multiple products
  - Unsure of the increased effectiveness and the corresponding increased cost
  - Regular vaccine and handwashing is sufficient

Survey Conclusions

- Based on the responses to the survey, the addition of high-dose influenza vaccine was well received in LTCFs in MB for the 2017/18 flu season.
- The majority of LTCF residents accepted the vaccine, and the resources developed were useful for staff as well as the residents and their families.
- Manually recorded facility uptake of high-dose influenza vaccine appeared to be consistent with previous' years uptake of standard-dose flu vaccine.
- Concerns with the potential of additional adverse events were reportedly minimized through education.
- The majority of LTCFs that responded reported that offering high-dose influenza vaccine to residents of LTCFs should continue for future flu seasons in order to protect this vulnerable population.

Survey Recommendations

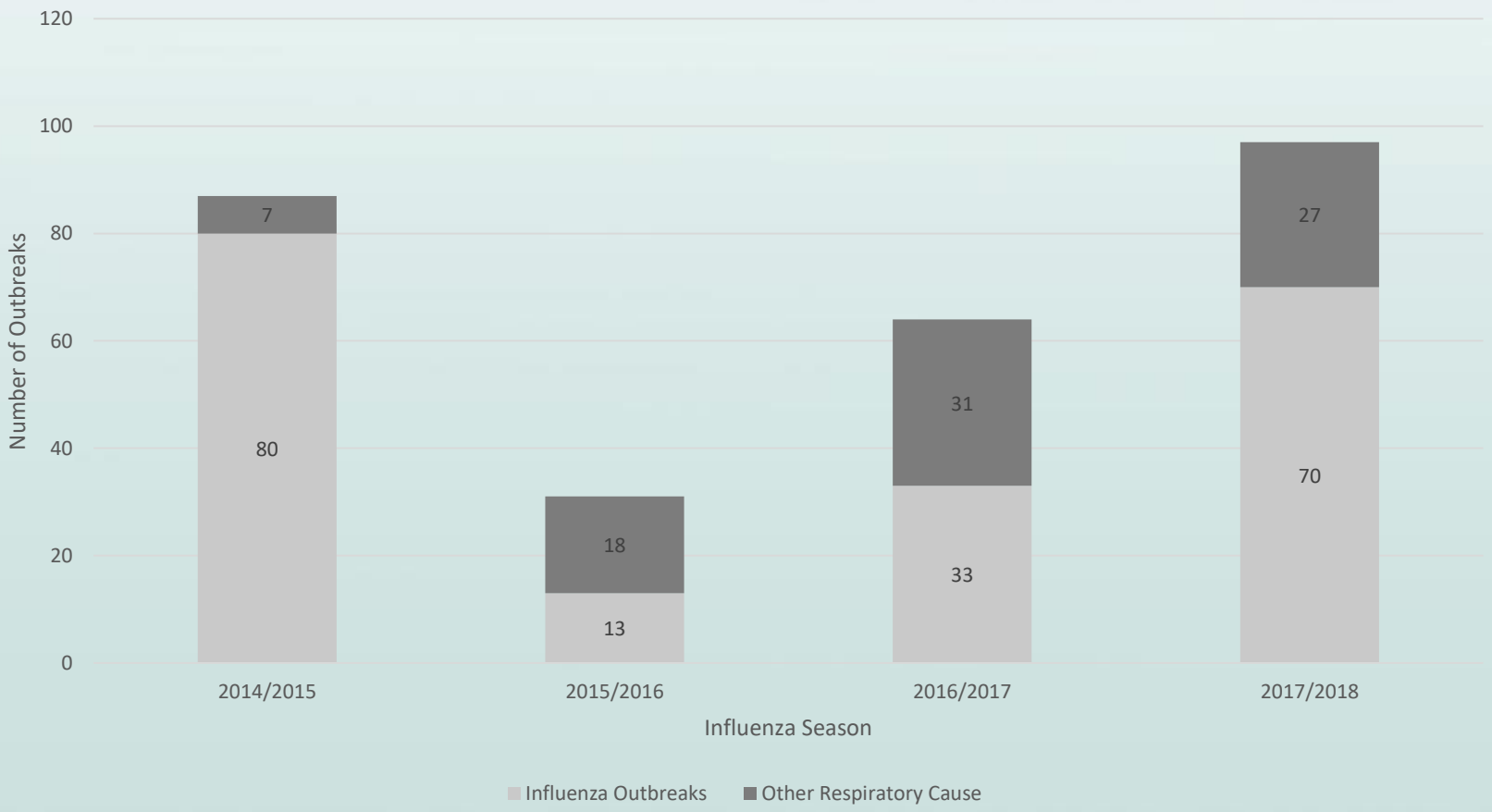
Survey feedback will assist MB with continuously improving its Program. Based on survey respondent feedback, the following will be considered for upcoming influenza seasons:

1. Earlier communication of the program plan: The roll out high-dose influenza vaccine was late in the planning process for the 2017/18 season as a result of the decision being made in August to add the product to MB's Program. Planning and communicating about MB's Seasonal Influenza Immunization Program is routinely done throughout the spring of each year. High-dose influenza vaccine information will be included in annual spring communications.
2. Development of a brochure comparing flu vaccines: Based on timing, the development of a brochure has not occurred for the 2018/19 influenza season. Rather, MB has updated its **Seasonal Influenza Vaccine for Residents of Long-Term Care Facilities Public Health Factsheet** to include the information that would have been included in the brochure (e.g. comparing the high-dose to standard-dose flu vaccine).

Survey Recommendations (cont'd)

3. Direct communication with LTCFs: MB is going to look at targeting its communications to LTCFs more directly.
4. Health care provider factsheet: flu vaccine uptake among health care workers is reportedly low relative to national targets and based on some of the responses. Additionally, there appears to be misinformation and inaccuracies about the use of flu vaccine among health care workers. As uptake can be influenced by health care provider recommendation, MB will review the suggestion of developing a factsheet directed to health care workers on the importance of being immunized against the flu, how the vaccines work at protecting themselves and those around them as well addressing the "myths".
5. Ordering High-Dose Influenza Vaccine: The process in which LTCFs order high-dose influenza vaccine has been reviewed and modified based on feedback provided to reduce wastage and clarify that ordering of the vaccines should be based on anticipated uptake, not the number of beds in the facility.

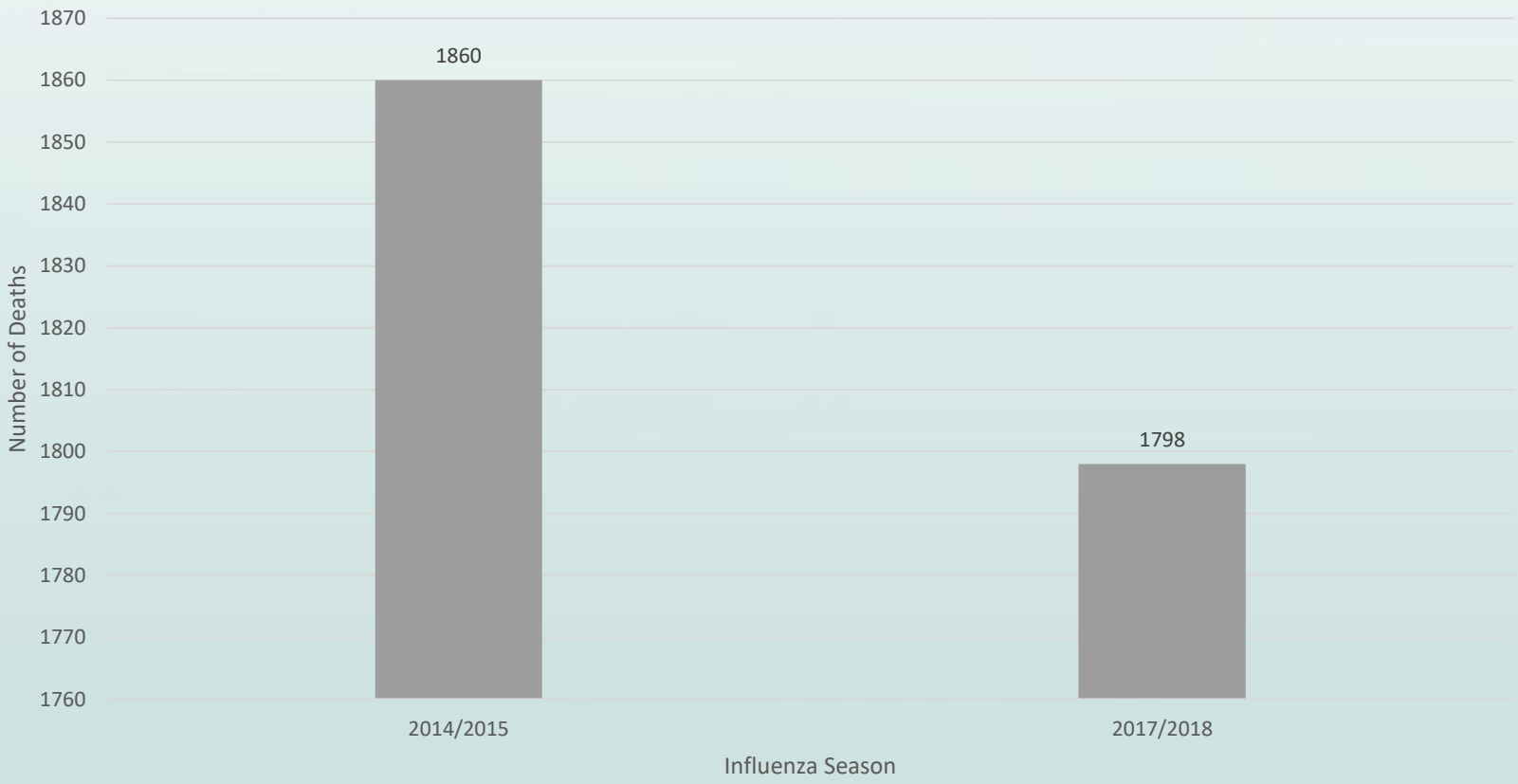
Respiratory Outbreaks in LTCFs, by Season



Respiratory Outbreaks in LTCFs, by Season

All-Cause Mortality Residents, Aged 65+

Number of All-Cause Deaths in those aged 65+ in LTCFs



Vaccine Safety

- No safety signal was detected through Manitoba's passive surveillance system.

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Post-webinar survey

Survey will pop up on your screen after webinar

- **Feedback on how to improve webinar series**

Presenters

Melissa Andrew: Melissa.Andrew@nshealth.ca

Richard Baydack: Richard.Baydack@gov.mb.ca

Stefan Gravenstein: stefan_gravenstein@brown.edu

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