Influenza in the time of COVID: Hoping for the best, planning for the worst

Allison McGeer, MSc, MD, FRCPC, FSHEA, FAMMI

Sinai Health System, University of Toronto

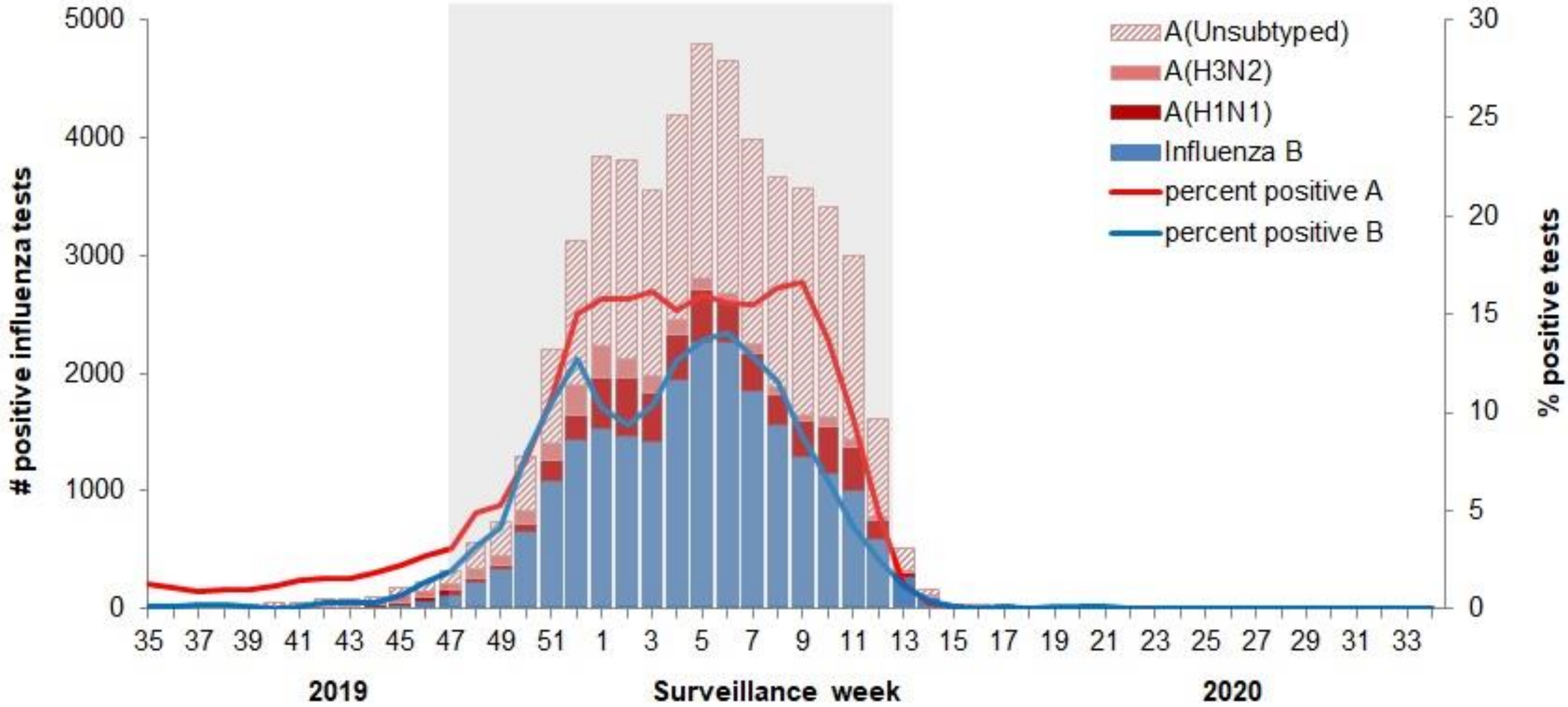
Disclosures

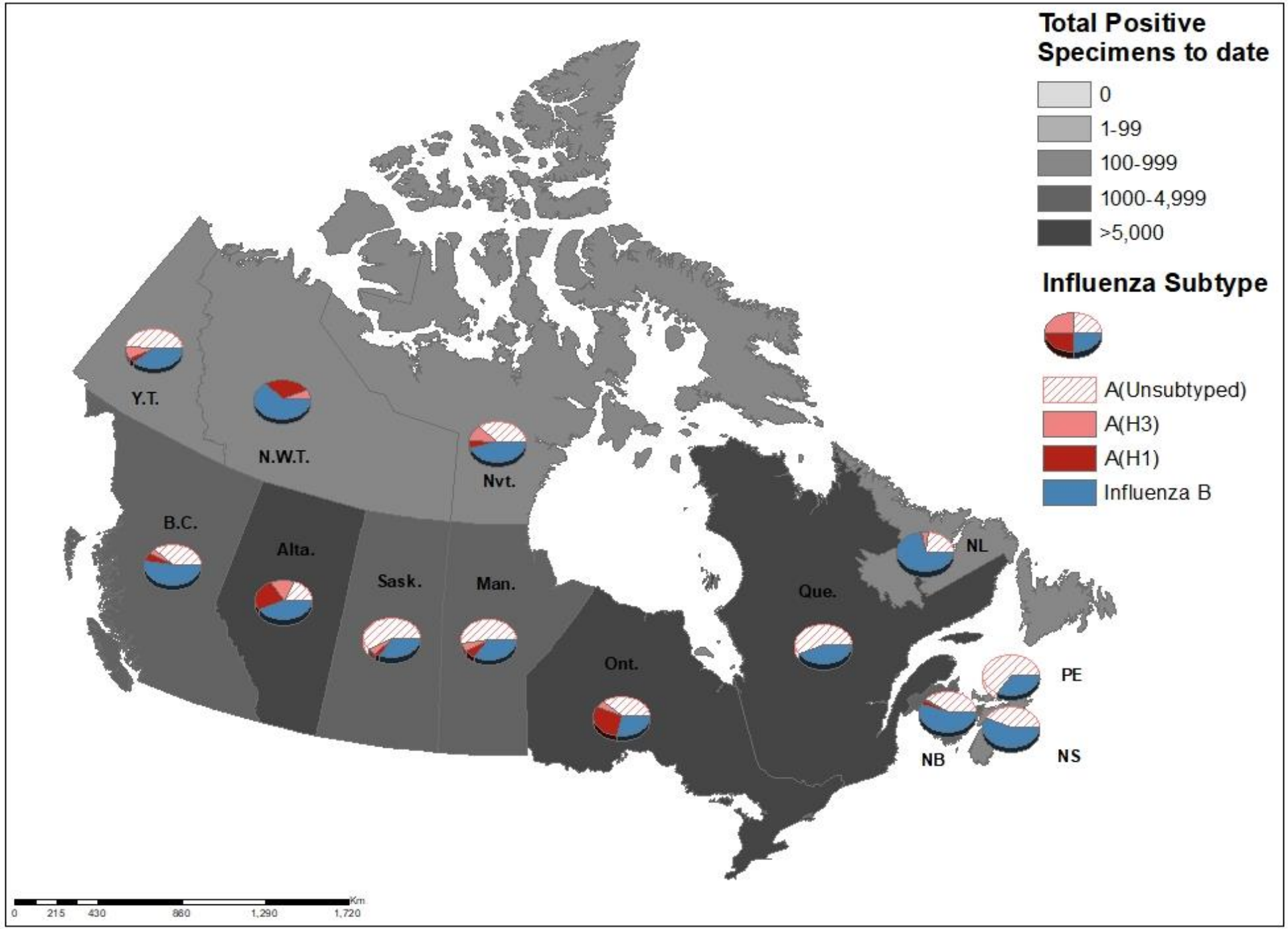
- I hold research funding (paid to my institution) from influenza vaccine manufacturers:
  - GlaxoSmithKline, Sanofi Pasteur, Seqirus

- I have been paid honoraria for advisory boards, DMSB membership, and other consultation
  - GlaxoSmithKline, Medicago, Sanofi Pasteur, Seqirus, Cidara

Objectives

- To describe the 2019/20 influenza season in Canada, and the 2020 southern hemisphere season
- To assess the potential impact of the pandemic and public health control measures on influenza incidence
- To review NACI updates to influenza statements over the last year, and current vaccination recommendations
- To discuss approaches and priorities for managing the 2020/2021 influenza season

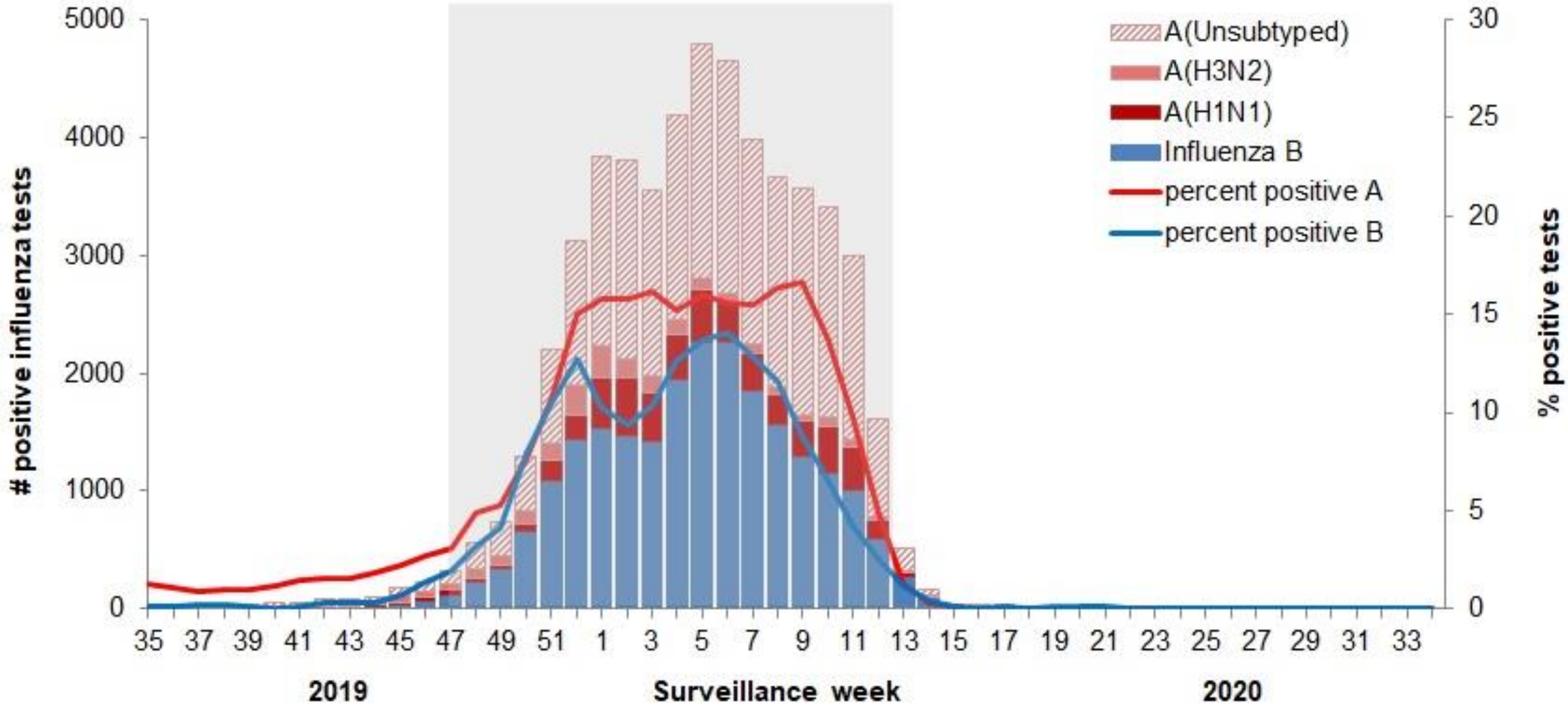

5000
4000
3000
2000
1000
0
positive influenza tests
30
25
20
15
10
5
0
% positive tests
A(Unsubtyped)
A(H3N2)
A(H1N1)
Influenza B
percent positive A
percent positive B
35 37 39 41 43 45 47 49 51 1 3 5 7 9 11 13 15 17 19 21 23 25 27 29 31 33
2019
Surveillance week
2020


Total Positive Specimens to date
0
1-99
100-999
1000-4,999
>5,000
Influenza Subtype
A(Unsubtyped)
A(H3)
A(H1)
Influenza B
Y.T.
N.W.T.
Nvt.
B.C.
Alta.
Sask.
Man.
Ont.
Que.
NL
PE
NB
NS
0
215
430
860
1,290
1,720
Km

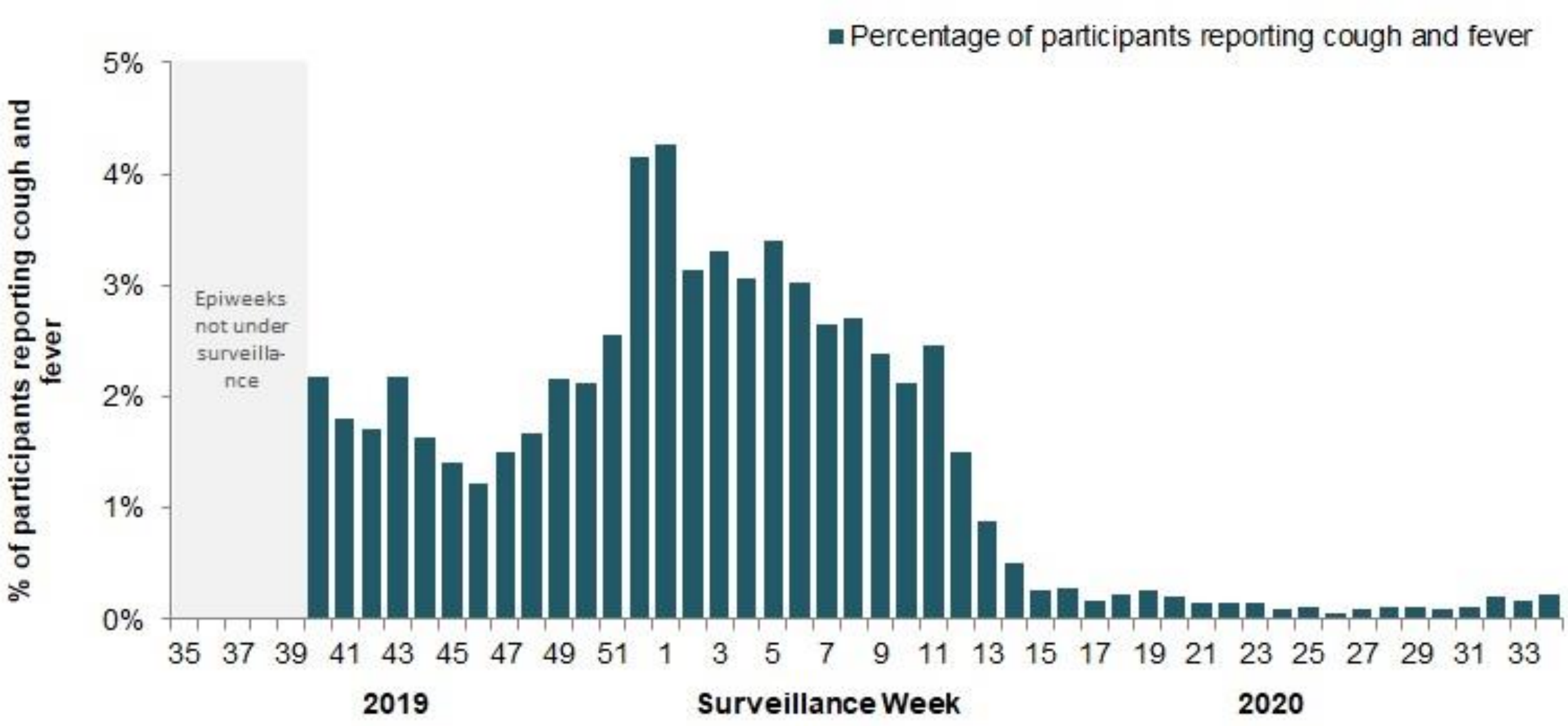
Vaccine Effectiveness Estimates, Canada

Season	Any Flu	A	A/H1N1	A/H3N2	B	Dominant A (ON)	Circulating / TIV B (ON)
2014/15	9 (-14,27)	-13 (-45,12)	NA	-17 (-50,9)	45 (18,64)	H3N2	Yamagata / Yamagata
2015/16	46 (32,57)	44 (27,57)	43 (25,57)	NA	50 (31,63)	H1N1	Victoria (66%)/ Yamagata
2016/17	45 (31,56)	37 (20,51)	NA	37 (20,51)	73 (52,84)	H3N2	Yamagata/ Victoria
2017/18	38 (27,47)	24 (7,38)	58 (30,75)	15 (-6,32)	46 (34,56)	H3N2	Yamagata/ Victoria
2018/19	61 (53,69)	61 (52,68)	69 (60,76)	23 (-9,46)	-	H1N1/ H3N2	Victoria/ Victoria
2019/20	**58 (47,66)**	**49 (36,60)**	**44 (26,58)**	**62 (37,77)**	**69 (57,77)**	**H1N1**	**Victoria/ Victoria**

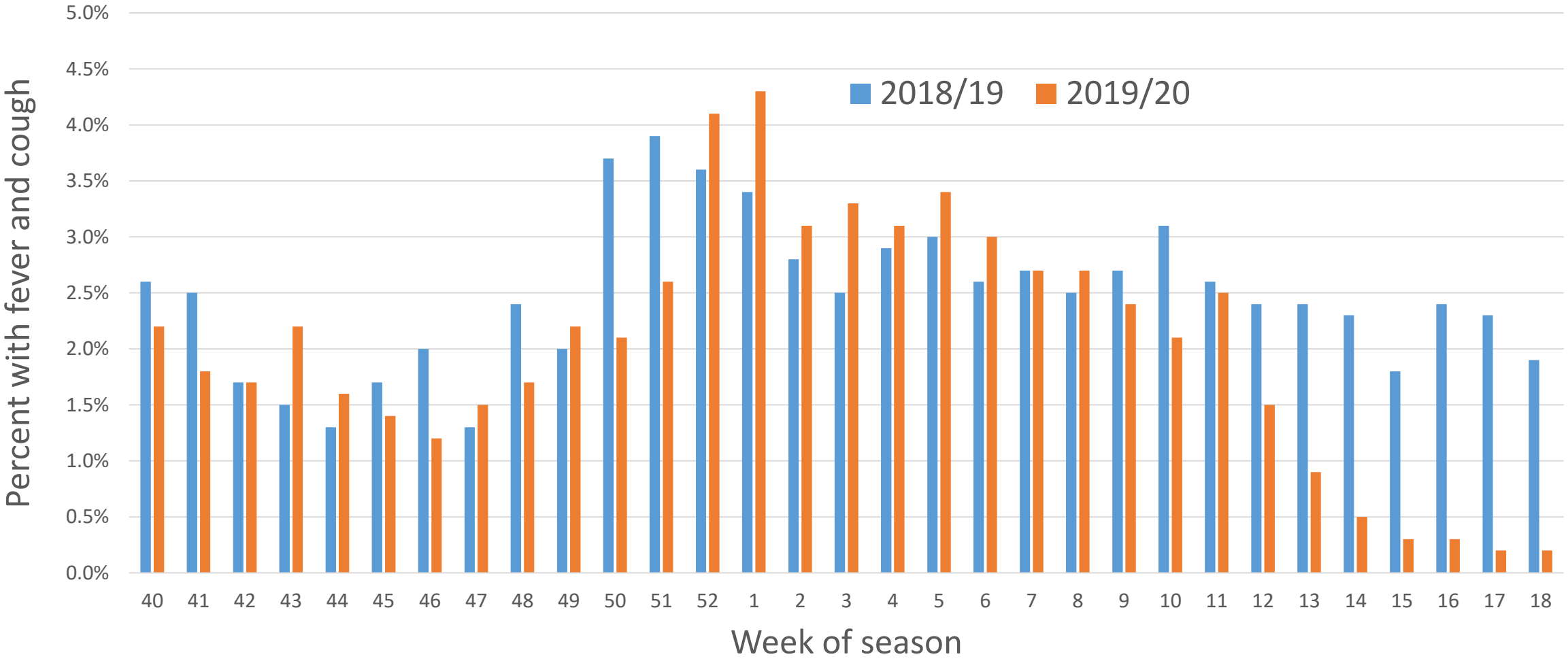
Adapted from: BC Centre for Disease Control. Canadian Sentinel Practitioner Surveillance Network (SPSN) influenza vaccine effectiveness estimates % (95% CI), 2004-05 to 2019-20 seasons [Internet]. Vancouver, BC: British Columbia Provincial Health Services Authority; 2020 [modified 2020 Feb 20; cited 2020 Aug 26]. Available from: http://www.bccdc.ca/resource-gallery/Documents/Statistics%20and%20Research/Publications/Epid/Influenza%20and%20Respiratory/SPSN_VE_By_Year_Table.pdf


5000
4000
3000
2000
1000
0
positive influenza tests
30
25
20
15
10
5
0
% positive tests
A(Unsubtyped)
A(H3N2)
A(H1N1)
Influenza B
percent positive A
percent positive B
35 37 39 41 43 45 47 49 51 1 3 5 7 9 11 13 15 17 19 21 23 25 27 29 31 33
2019
Surveillance week
2020

Participatory syndromic surveillance



Participatory syndromic surveillance 2019/20 compared to 2018/19



Influenza in Australia

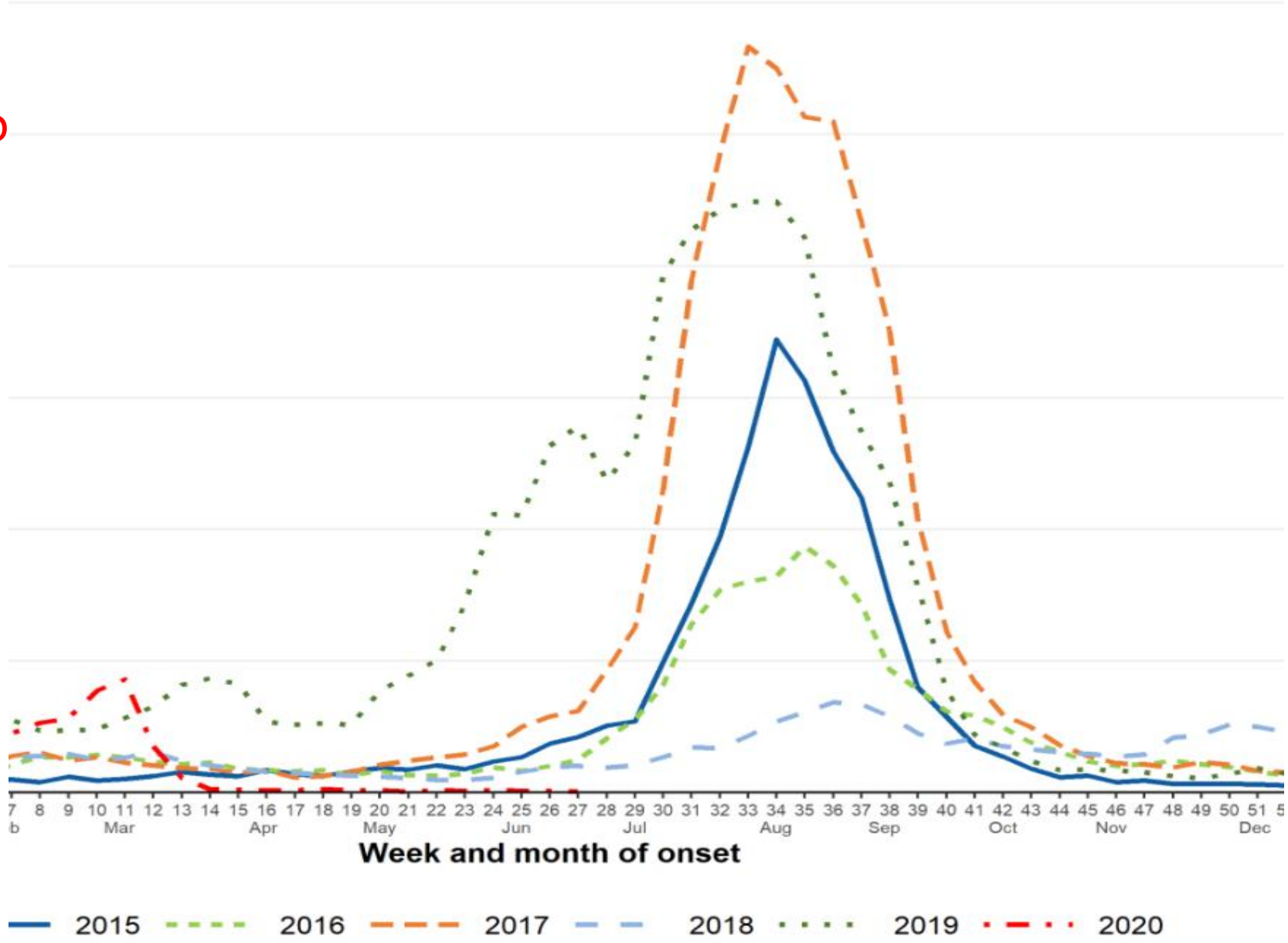
- 3 major inputs this year
  1. International border closures by end of February
  2. Restrictions on social gatherings and the way people live which continue in varying forms across the country
     - Mass cancellations of gatherings, sports, theatre attendances, …
     - Mask use,
     - Perspex screens in supermarkets, banks, many shops,
     - alcohol hand rub everywhere
     - Registration on entering facilities
  3. Record flu vaccine doses and adjuvanted vaccine

Influenza Vaccination 2020

- Marketed as avoiding the “twindemic”
- *Not a lot of data on what happens when you get both COVID-19 and influenza together but it will be bad .. Get a flu shot*
- Remarkably effective. Over 17 million doses distributed, shortages throughout campaign, almost 70% of population
- Early distribution of adjuvanted vaccine to elderly in March
- 2019 record flu year in Oz, >300,000 notifications but elderly hospitalisations only 40% of previous big year in 2017 .. Thought that adj vacc protected against severe disease

Impact of the three control mechanisms?

- 21,000 cases in Australia year to date compared to over 300,000 in 2019
- Only 7% of previous BUT
- High inter-seasonal numbers in January to March caused all of this



Eg Queensland..1 case in last week..
Winter cases less than 1% of mean

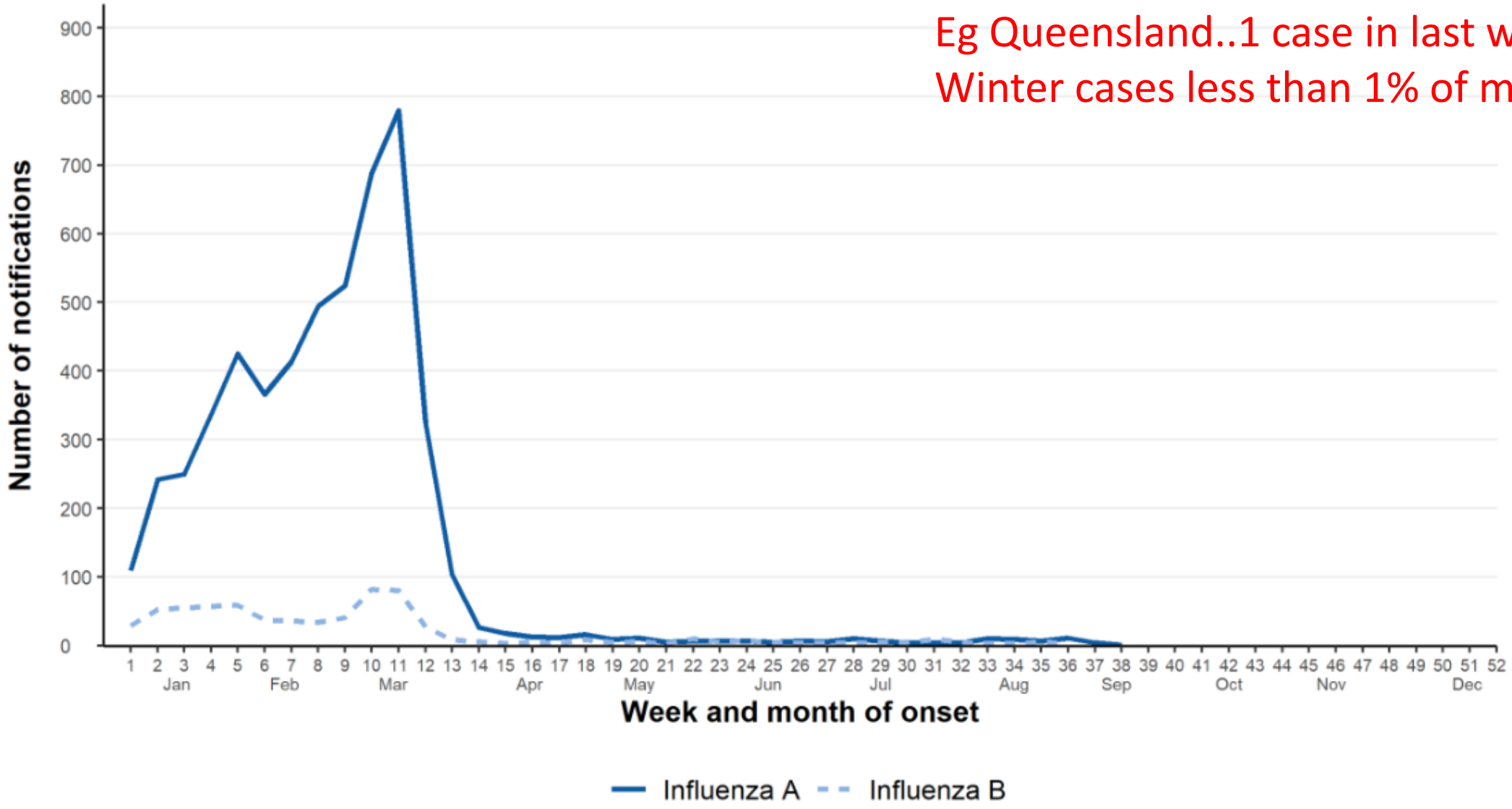
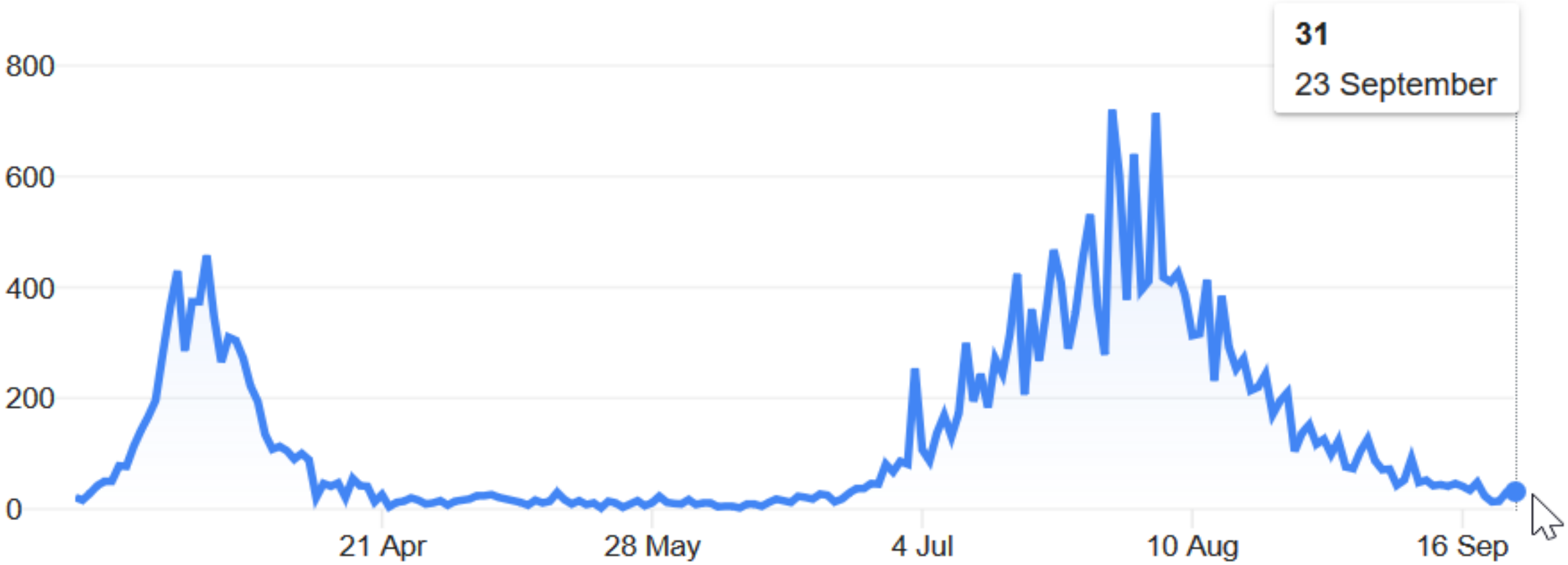


Figure 2: Queensland weekly influenza notifications by type, week and month of onset, 1 Jan to 20 Sep 2020.

Daily change

Control of second wave achieved by use of emergency powers .. 12 cases only 25 Sept



What are we expecting for 2020?

- We hope that travel restrictions and physical distancing measures (?and maybe masks?) will substantially reduce influenza transmission

- BUT, we are not on an island, and our travel restrictions and quarantine are not as draconian as Australia/New Zealand

- The very low activity means that predicting evolution of strains is impossible

NACI influenza statements

- New reviews for 2019/2020
  - Vaccination of HCWs
  - Live attenuated vaccine for HIV-infected individuals
  - Flucelvax (first cell culture based vaccine available in Canada)

- COVID-19 related statements
  - *Recommendations on the Duration of the Post-vaccination Observation Period for Influenza Vaccination during the COVID-19 Pandemic*.

- To be expected for 2020/2021
  - Quadrivalent high dose vaccine
  - Influvac Tetra

Vaccination of health care workers and other care providers

Based on their reassessment of the evidence in the context of ethics and acceptability, NACI continues to recommend that, in the absence of contraindications, HCWs and other care providers in facilities and community settings should be vaccinated annually against influenza…….. NACI recommends the inclusion of this group among those particularly recommended to receive the influenza vaccine. **NACI considers the receipt of influenza vaccination to be an essential component of the standard of care for all HCWs and other care providers for their own protection and that of their patients. This group should consider annual influenza vaccination as part of their responsibilities to provide the highest standard of care.**

Use of live attenuated influenza vaccine in HIV-infected individuals

NACI concluded that LAIV is immunogenic in children with stable HIV infection on highly active antiretroviral therapy (HAART) and with adequate immune function.

NACI concluded that the quantity of evidence available on the immunogenicity and safety of LAIV in adults with HIV is insufficient to justify a recommendation for the use of LAIV in this age group. Based on their assessment of the evidence, NACI has made the following recommendation:

NACI recommends that LAIV may be considered as an option for children 2–17 years of age with stable HIV infection on HAART and with adequate immune function* *LAIV should only be considered in children with HIV who meet the following criteria:

- receiving HAART for ≥4 months
- CD4 count ≥500/µL if 2–5 years of age, or ≥200/µL if 6–17 years of age
- HIV plasma RNA <10,000 copies/mL

While IM influenza vaccination is still considered the standard for children living with HIV, LAIV would be reasonable for children meeting the criteria outlined above, if IM vaccination is not accepted by the patient or substitute decision-maker.

NACI recommends that Flucelvax® Quad may be considered among the IIV4 offered to adults and children ≥9 years of age (Discretionary NACI Recommendation)

- NACI concludes that there is fair evidence to recommend vaccination of adults and children ≥9 years of age with Flucelvax® Quad (Grade B Evidence).

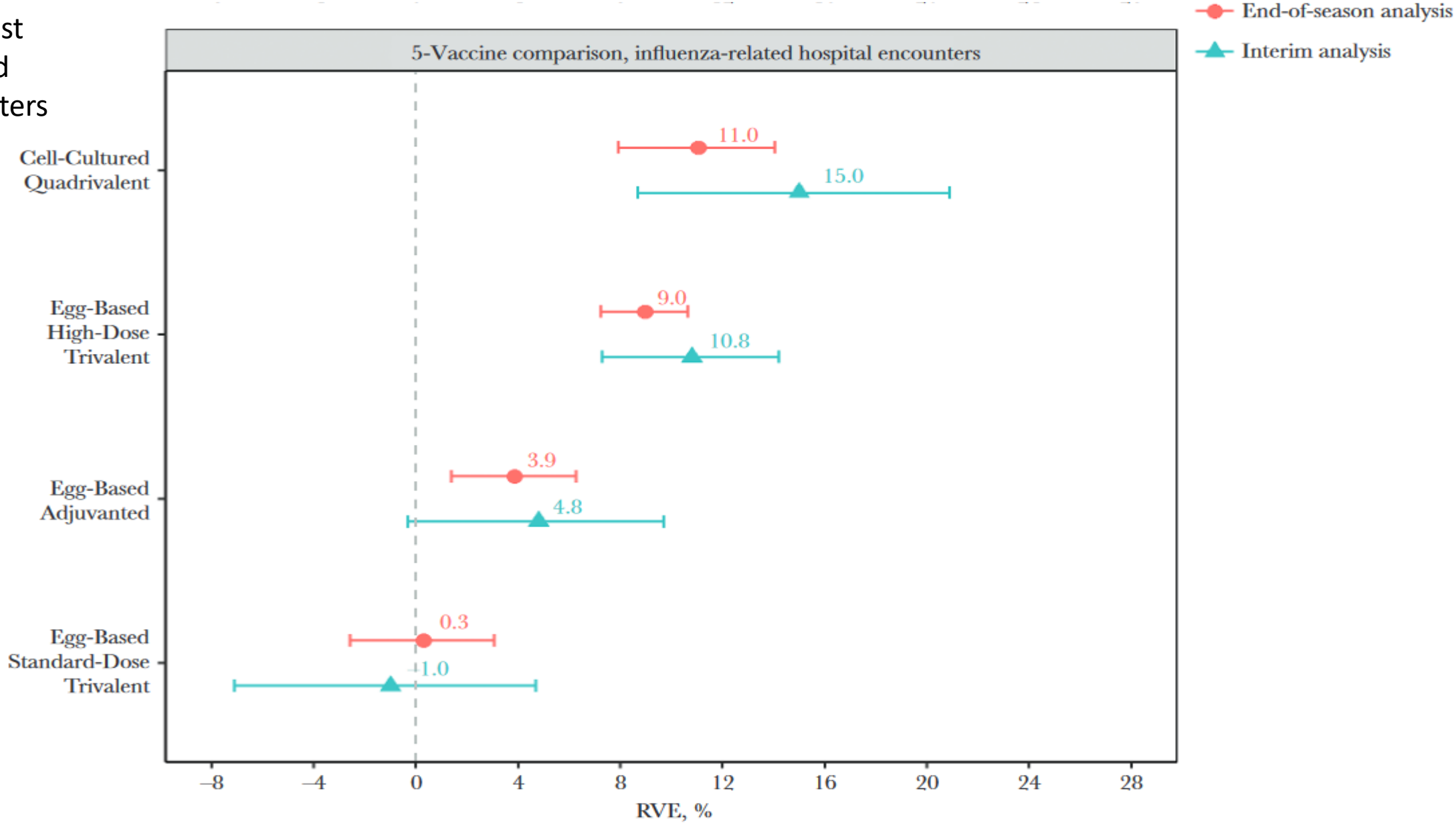
https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/mammalian-cell-culture-based-influenza-vaccines.html

Cell-based vaccines

- Authorized in Europe since 2007 and the US since 2012

- Potential advantages
  - Does not require egg supply
  - Avoids egg adaptation
  - (theoretically) reduces time for vaccine production in pandemics, increases scalability

Protection against
Influenza-related
Hospital encounters
Adults ≥65y



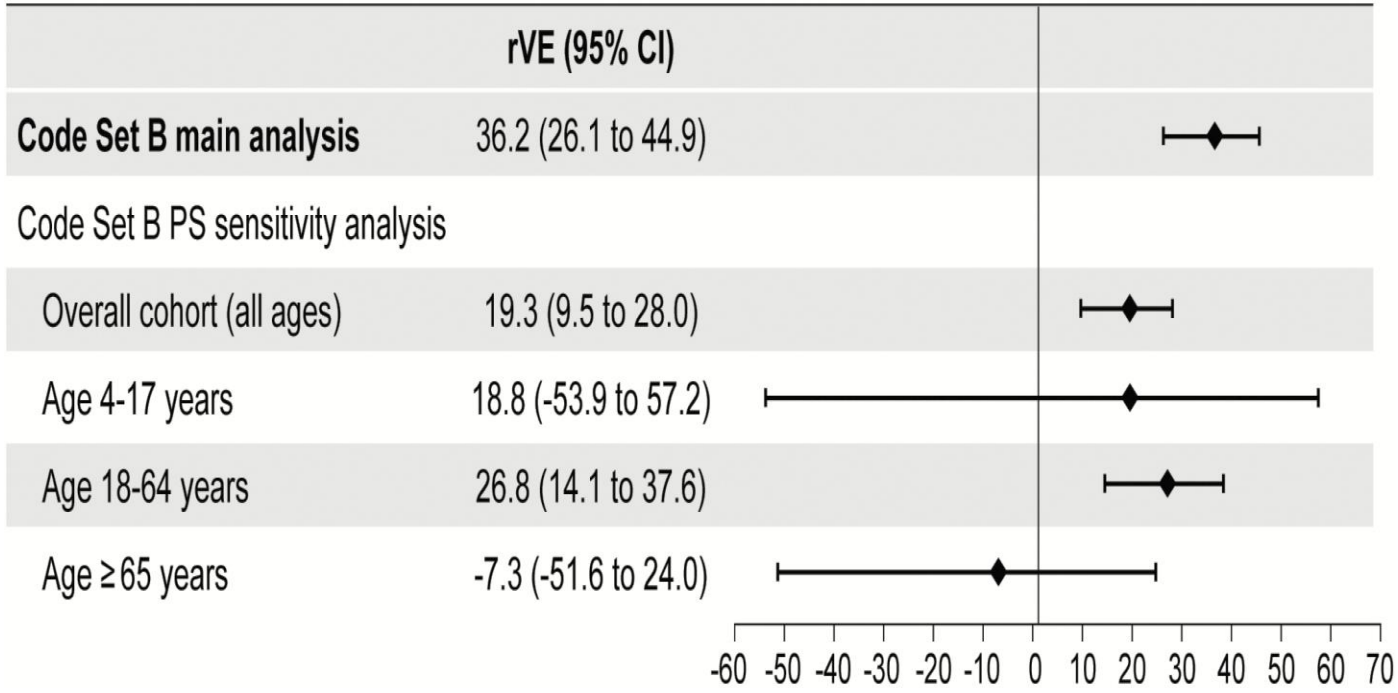
Izurieta HS. J Infect Dis. 2019 Sep 13;220(8):1255-1264. doi: 10.1093/infdis/jiy716.

Relative Effectiveness of the Cell-Cultured Quadrivalent Influenza Vaccine Compared to Standard, Egg-derived Quadrivalent Influenza Vaccines in Preventing Influenza-like Illness in 2017–2018

Constantina Boikos,[1] Gregg C. Sylvester,[2] John S. Sampalis,[3] and James A. Mansi[1]

[1]Seqirus Inc, Montreal, Quebec, Canada, [2]Seqirus USA Inc, Summit, New Jersey, USA, and [3]Department of Experimental Surgery, McGill University, Montreal, Quebec, Canada

Figure 1. Results from the propensity score (PS)–matched and adjusted models. Main analyses are multivariable logistic; PS sensitivity analyses are conditional logistic based on match pairs



Clin Infect Dis, ciaa371, https://doi.org/10.1093/cid/ciaa371

age group	Vaccine types authorized for use	Recommendations on choice of influenza vaccine
6–23 months	•IIV3-SD •IIV3-Adj •IIV4-SD	Quadrivalent preferred; if a quadrivalent vaccine is not available, any of the available trivalent vaccines should be used
2–17 years	•IIV3-SD •IIV4-SD •LAIV4	•Either IIV4-SD or LAIV4 should be used in children without contraindications •If IIV4-SD or LAIV4 is not available, IIV3-SD should be used •IIV4-SD should be used for children for whom LAIV is contraindicated, such as in children with: • Severe asthma • Medically attended wheezing in the seven days prior to vaccination • Current receipt of aspirin or aspirin-containing therapy • Immune compromising conditions, with the exception of stable HIV infection, if the child is currently being treated with HAART and has adequate immune function

Age Group	Vaccines authorized for use	Recommendations on choice of vaccine
8–59 years	•IIV3-SD •IIV4-SD •LAIV4 •IIV4-cc	•Any of the available influenza vaccines should be used in adults without contraindications •IIV should be used for adults for whom LAIV is contraindicated or not recommended, such as in: • Pregnant women • Adults with any of the chronic health conditions identified in Table 2, including immune compromising conditions • HCWs
60–64 years	•IIV3-SD •IIV4-SD •IIV4-cc	•Any of the available influenza vaccines should be used in those without contraindications

Age group	Vaccines authorized for use	Recommendations on choice of vaccine
65 years and older	•IIV3-SD •IIV3-Adj •IIV3-HD •IIV4-SD •IIV4-cc	•IIV3-HD should be used over IIV3-SD, given the burden of influenza A(H3N2) disease and the good evidence of better protection compared to IIV3-SD in adults 65 years of age and older • NACI does not make comparative individual-level recommendations on the use of IIV3-Adj or IIV4-SD over IIV3-SD, or among IIV3-Adj, IIV3-HD, and IIV4-SD • In the absence of any specific product, any of the available influenza vaccines should be used

Influenza Vaccine Composition for Northern Hemisphere

2019-20 Northern Hemisphere	2020-21 Northern Hemisphere Egg-based vaccines	2020-21 Northern Hemisphere Cell-based vaccines
A/Brisbane/02/2018 (H1N1)pdm09-like virus	A/Guangdong-Maonan/SWL1536/2019 (H1N1)pdm09-like virus	A/Hawaii/70/2019 (H1N1)pdm09-like virus
A/Kansas/14/2017 (H3N2)-like virus	A/Hong Kong/2671/2019 (H3N2)-like virus	A/Hong Kong/45/2019 (H3N2)-like virus
B/Colorado/06/2017 (B/Victoria/2/87 lineage)-like virus	B/Washington/02/2019 (B/Victoria lineage)-like virus	B/Washington/02/2019 (B/Victoria lineage)-like virus
B/Phuket/3073/2013 (B/Yamagata/16/88 lineage) -like virus	B/Phuket/3073/2013 (B/Yamagata lineage)-like virus	B/Phuket/3073/2013 (B/Yamagata lineage)-like virus

Adapted from: World Health Organization. Influenza laboratory surveillance information by the Global Influenza Surveillance and Response System (GISRS) [Internet]. Geneva: World Health Organization; 2020 [cited 2020 Aug 26]. Available from: https://www.who.int/influenza/vaccines/virus/recommendations/en/

Vaccines in the context of COVID-19

- Consider space and timing of clinics to avoid crowding
- Screening patients, volunteers, staff
- Physical distancing, masks, hand hygiene
- Physical barriers
- Increased environmental cleaning
- Reduce contact
  - On-line appointment systems, on-line consent, timed appointments

https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/guidance-influenza-vaccine-delivery-covid-19.html#a3

APPROACHES FOR INFLUENZA VACCINE CLINICS

- holding multiple smaller public clinics instead of large clinics with many attendees
- considering extended clinic hours to avoid crowding
- providing immunization opportunistically to patients and their accompanying persons when they are discharged from hospital or are seen for other reasons
- in primary care settings, designating specific times for immunization clinics to ensure that only well persons are in the area at the time
    - for example, at the start or end of the day
- cooperation between several medical practices to operate a joint influenza vaccine clinic in a dedicated space with dedicated staff
- providing influenza vaccine during senior shopping hours at pharmacies in grocery stores, or creating special hours for seniors and other vulnerable persons at pharmacies and other venues
- administering vaccines outdoors (weather permitting)
- establishing mobile clinics in vans or buses to visit neighbourhoods
- developing an outreach strategy to administer influenza vaccine to vulnerable persons, housebound persons, and seniors who are sheltering in place
- providing immunization during home care visits
- administering influenza vaccine at congregate living centres (eg. Dorms, shelters, retirement homes
- having health care organizations, including long-term care facilities provide their own immunization for staff, volunteers and patients/clients (usual practice)
- encouraging workplaces to organize their own on-site immunization programs

Observation period post-vaccination

- Australia: 15 mins (immediate adverse reactions)
- US: 15 mins (syncope; clients should be sitting or lying)
  - 80% of syncope occurs within 15 mins
  - 76% of syncope occurs in adolescents
  - SAE largely related to falls (one MVA)
- Canada: 15 mins (anaphylaxis)
- UK: no additional time beyond that required to complete documentation etc.

https://www.health.gov.au/sites/default/files/documents/2020/04/atagi-clinical-statement-on-vaccination-observation-time.pdf
CDC. Syncope after vaccination—United States, January 2005-July 2007. *MMWR Morb Mortal Wkly Rep.* 2008;57(17):457-460.

Risks of SAE post-vaccination

- Anaphylaxis
  - 0.8-1.3 per million doses
  - 80% of anaphylaxis is reported to meet criteria for SAE
  - 50% of reactions occur in the first 15 minutes

- Syncope
  - 7-8 per 100,000 doses
  - Most common in adolescents (62%), more common in women
    - 7% of reports in adults >50 years of age
  - 70-80% of episodes reported in first 15 minutes
  - 7% of episodes reported to VAERS/NVIC severe
    - 40-50% of these associated with injury

NACI Recommendations

- NACI recommends that the current post-vaccination observation period, as specified in the Canadian Immunization Guide, should be maintained for influenza vaccination settings that can adhere to appropriate public health and infection prevention and control measures to reduce SARS-CoV-2 transmission, particularly physical distancing. (Strong NACI recommendation).
- NACI concludes that there is fair evidence to maintain a 15-minute post-vaccination observation period during the COVID-19 pandemic for individuals with no known history of severe allergic reactions (including anaphylaxis) to any component of the influenza vaccine being considered for administration or any history of other immediate post-vaccination reactions (e.g., syncope with or without seizure) (Grade B Evidence).

A shorter observation period may be considered only if the vaccine recipient meets the following conditions:

- Past history of receipt of influenza vaccine and no history of allergic reactions to any component of the influenza vaccine being offered
- No history of immediate post-vaccination reaction (e.g., syncope)
- The vaccine recipient is accompanied by responsible adult who will act as a chaperone. Two responsible adults may monitor each other.
- The vaccine recipient will not be operating a motorized vehicle or other wheeled transportation (e.g., bicycle)
- The vaccine recipient and responsible adult chaperone are aware of when and how to seek post-vaccination advice
- The vaccine recipient and responsible adult agree to remain in the post-vaccination waiting area for the post-vaccination observation period

Testing for the fall/winter in Ontario

- By November, multiplex COVID19/influenza PCR testing should be available and validated
- Plan
  - COVID+flu: outbreaks, hospital admissions
    - If both negative: outbreaks & ICU admissions will be tested for other viruses
    - ?Add other viruses for remote communities
  - COVID19 alone
    - Assessment centers
    - Out-patient settings; EDs (patient not being admitted)
    - Surveillance screening for LTC (in Ontario): COVID 19 alone

Antiviral recommendations

- AMMI guidelines generally recommend treatment of laboratory confirmed disease
- US guidelines are more liberal

- Because we MAY not have much influenza activity, it is particularly important this year to get information on influenza activity to prescribers

https://www.publichealthontario.ca/-/media/documents/q/2019/qa-antiviral-medication-influenza.pdf?la=en
https://jammi.utpjournals.press/doi/10.3138/jammi.2019.02.08


Thank
You
Merci
Gracias
TapadhLeat
Köszönöm
Murakoze
aDank
Grazzi
Grazie
Buznyg
WaadMahadsantahay
Takk
ThintKo
Mèsi
Chokrane
Kiitos
Blagodaram
Rahmat
BarakAllahuFiik
Xièxie
Dziakuju
Mauruuru
Matondo
Aabhar
Barkal
GratiasAgimus
Mercé
TerimaKasih
Taiku
Tanemirt
Tenki
Ačiū
Dankie
Tak
Motashakkeram
Dakujem
Spacibo
Danke
Chnorakaloutioun
TänanVaga
Sagolun
GratiasAgo
Grandmercé
Gràcies
Hvala
Arigatô
KamSahHamnida
Gracie
KopKhunKha
Faleminderit
NajisTuke
CámOn
Efharisto
Nirringrazzjak
Bayarlalaa
Obrigado
Salamat
Saha
Multumesc
Gratzias
Dhanyavaad
Mamnun

Resources

- Immunize Canada: https://www.immunize.ca/resources/flu-influenza
- IPAC Canada: https://ipac-canada.org/influenza-resources.php

- BC seasonal update course: http://www.bccdc.ca/health-professionals/education-development/immunization-courses/seasonal-influenza-update

- CDC: https://www.cdc.gov/flu/resource-center/index.htm
- ECDC: https://www.ecdc.europa.eu/en/seasonal-influenza