



IMPACT

Canadian Immunization Monitoring Program, ACTive
Programme canadien de surveillance active de l'immunisation

Varicella (breakthrough) cases in previously vaccinated children in the Canadian IMPACT centres, 2000-15

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Public Health
Agency of Canada

Agence de santé
publique du Canada

Canada

Disclosure statement:

- ▶ I have no affiliation (financial or otherwise) with a pharmaceutical, medical device or communications organization.

IMPACT is a national surveillance initiative managed by the Canadian Paediatric Society (CPS) and conducted by the IMPACT network of pediatric investigators.

CPS receives ongoing funding from the Public Health Agency of Canada's Centre for Immunization and Respiratory Infectious Diseases for IMPACT.

Background

- ▶ Currently unknown as to how many varicella (var) hospitalizations in Canada occur in previously vaccinated children (“breakthrough disease”).
- ▶ IMPACT conducts surveillance for var-hospitalizations since 1999.
 - One-dose var vaccination programs began in Canadian P/T in **2000-06**, and 2-dose programs (Var &/or MMRV) in **2011-16**.
 - At CPS meeting, Quebec City, May 2018 we showed an **85% decline** in hospitalizations from baseline (no vaccination) to 2-dose vaccine eras in 8 provinces with IMPACT centers.

Study purpose:

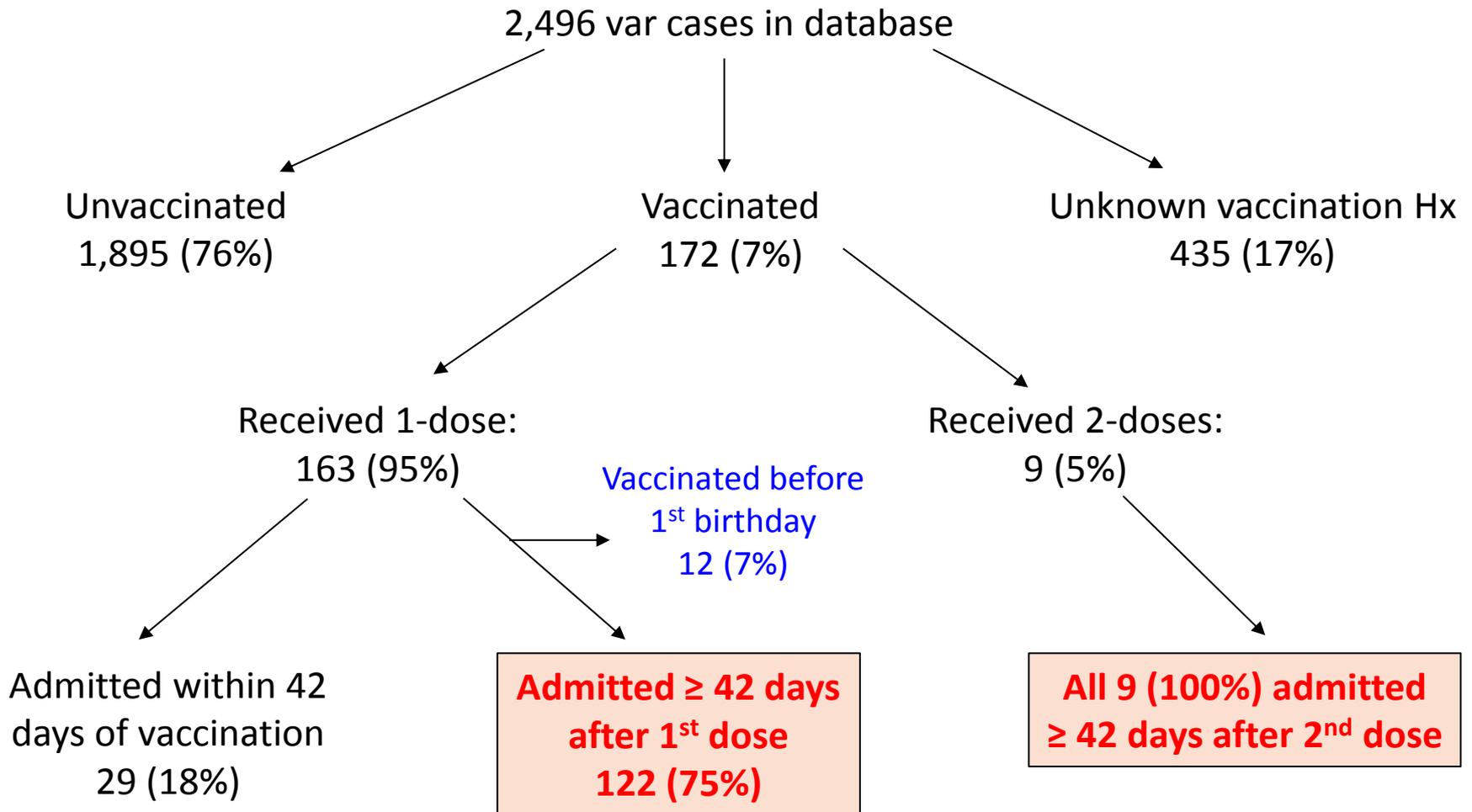
- ▶ To determine the proportion, clinical characteristics and outcome of previously vaccinated children hospitalized with breakthrough var in IMPACT centers from 2000 to 2015.

Methods

- ▶ Reviewed vaccination histories of var cases (not zoster) from 12 IMPACT centers in 8 provinces in 2000-15:
 - Breakthrough = illness-onset \geq 42 days after the last vaccine dose.
- ▶ We analyzed: admission age, time from vaccination, diagnostic method, immunocompromised or not-immunocompromised, var complications, need for intensive care, duration of hospital stay, and mortality outcome.
- ▶ Determining # vesicular lesions, var antibody levels and differentiating between vaccine or wild-type virus was not performed (not in protocol).

Results

Varicella vaccination history of cases at IMPACT centres 2000-15



Confirmation of var infection

- ▶ Diagnostic tests:
 - Lesion swab for PCR/viral culture.
 - Less commonly, var IgM + or IgG seroconversion.
- ▶ Amongst the vaccinated:
 - **1-dose – 76 tested (62%), +ve in 61 (80%).**
 - **2-doses – 4 tested (44%), +ve in all 4 (100%).**
- ▶ In contrast, only 25-30% of the unvaccinated or unknown vaccine history cases were tested (of which 78-82% were +ve).

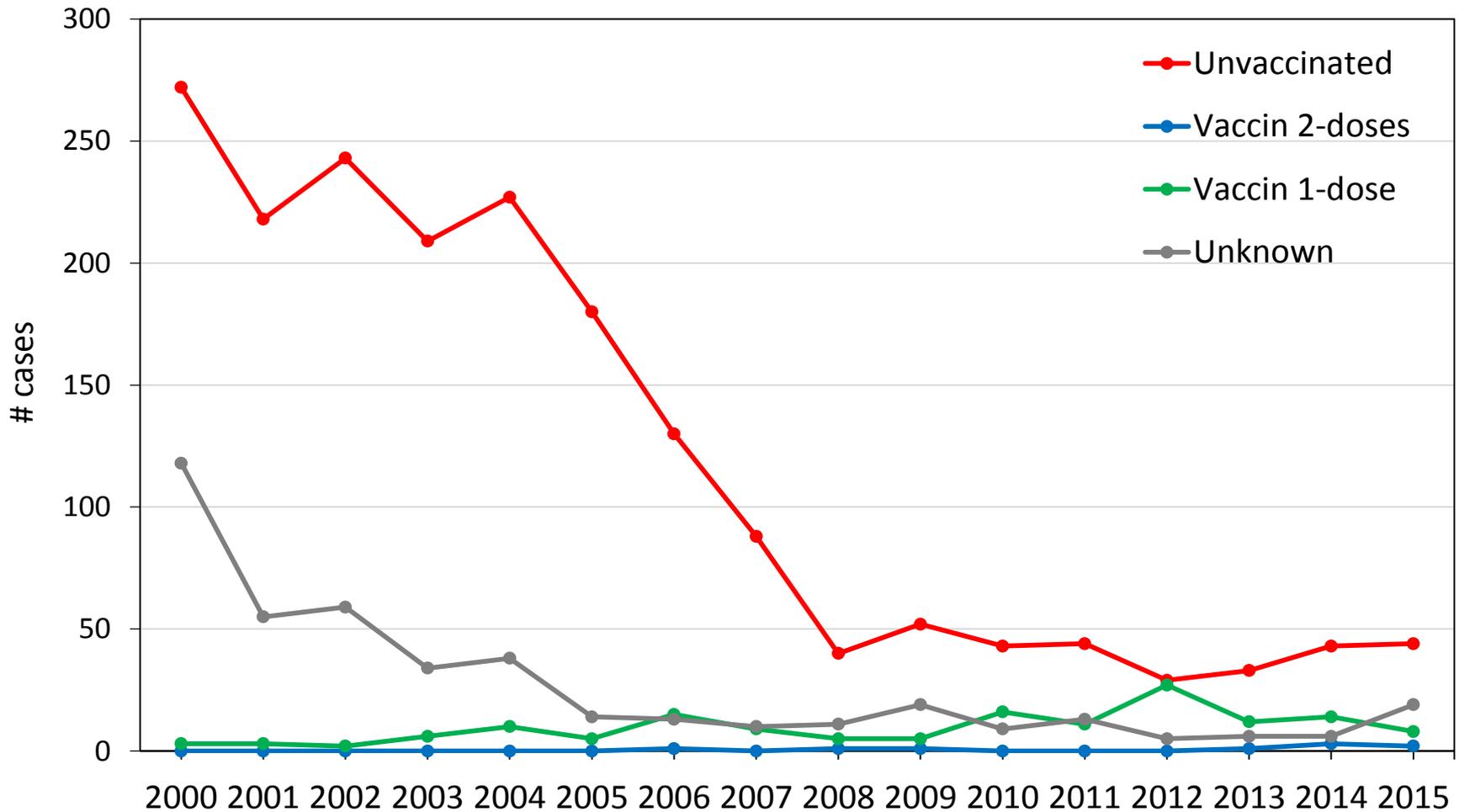
Breakthrough cases with onset ≥ 42 days after 1-dose var vaccination at ≥ 12 mos-of-age, 2000-15

- ▶ 122 cases (6% of those with known vaccination history):
 - Non-immunocompromised – 27 (22%).
 - Immunocompromised – 95 (78%).
- ▶ Mean \pm SD – no difference between imm/non-imm groups.
 - **Age at admission = 6.8 ± 3.2 years** (range 1.1 – 16.7 years).
 - Mean age at vaccination = 2.2 ± 2.2 years (range 1.0 – 11.2 years).
 - **Mean interval from vaccination to admission = 4.5 ± 2.8 years** (range 0.14 – 12.5 years).
- ▶ **No deaths.**

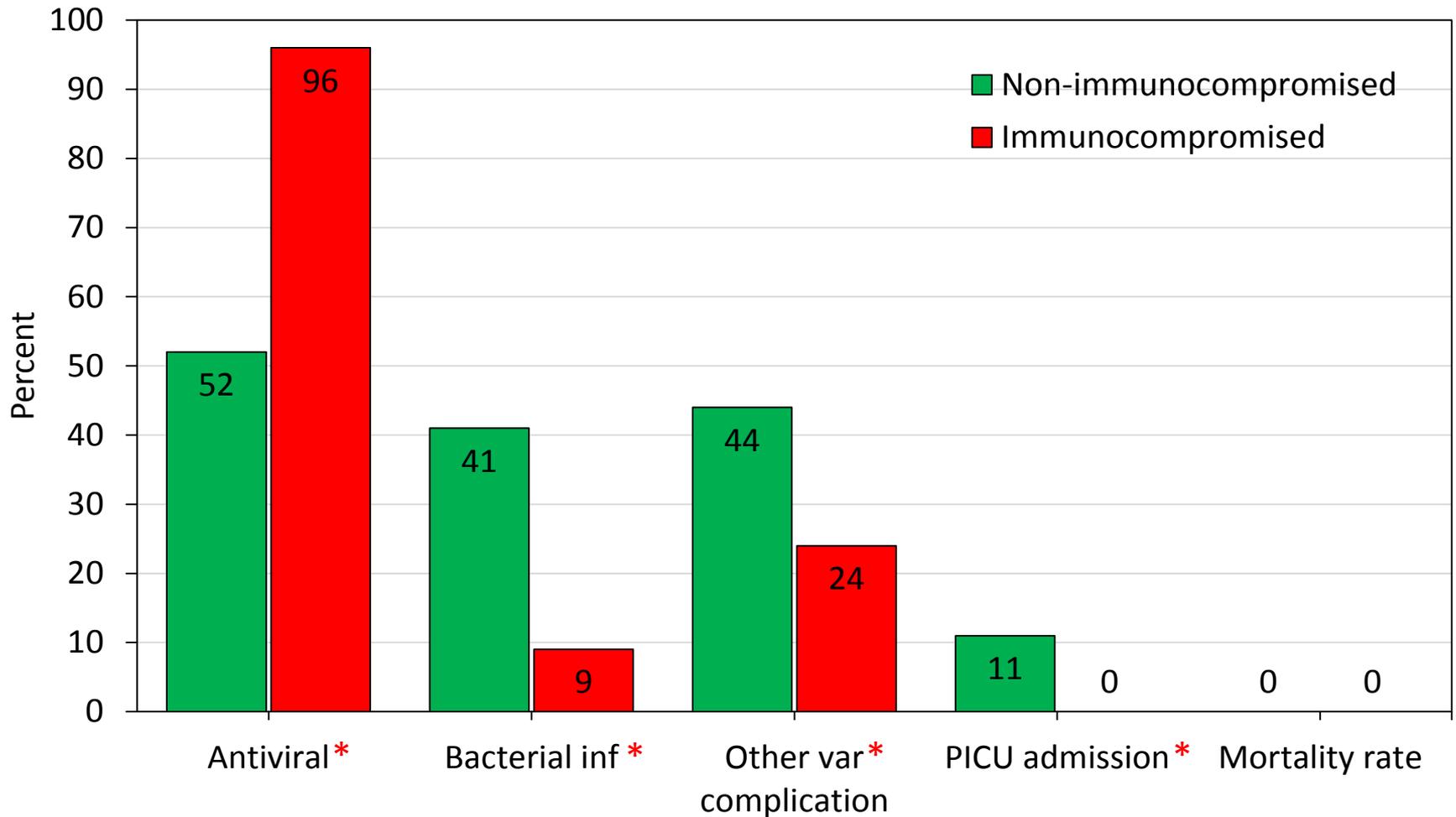
Breakthrough cases with onset ≥ 42 days after 2-doses var vaccination at ≥ 12 mos-of-age, 2000-15

- ▶ 9 cases (0.4% of cases with known vaccination history):
 - 4 non-immunocompromised, 5 immunocompromised.
- ▶ Mean \pm SD - no difference between imm/non-imm groups
 - **Age at admission = 8.2 ± 3.9 years** (range 2.7 – 14.6 years).
 - Mean age at second vaccination = 3.8 ± 3.1 years (range 1.5 – 11.4 years).
 - **Mean interval from vaccination to admission = 4.4 ± 3.2 years** (range 0.8 – 10.5 years).
- ▶ **No deaths.**

Var vaccination status of cases in IMPACT centres, 2000-15

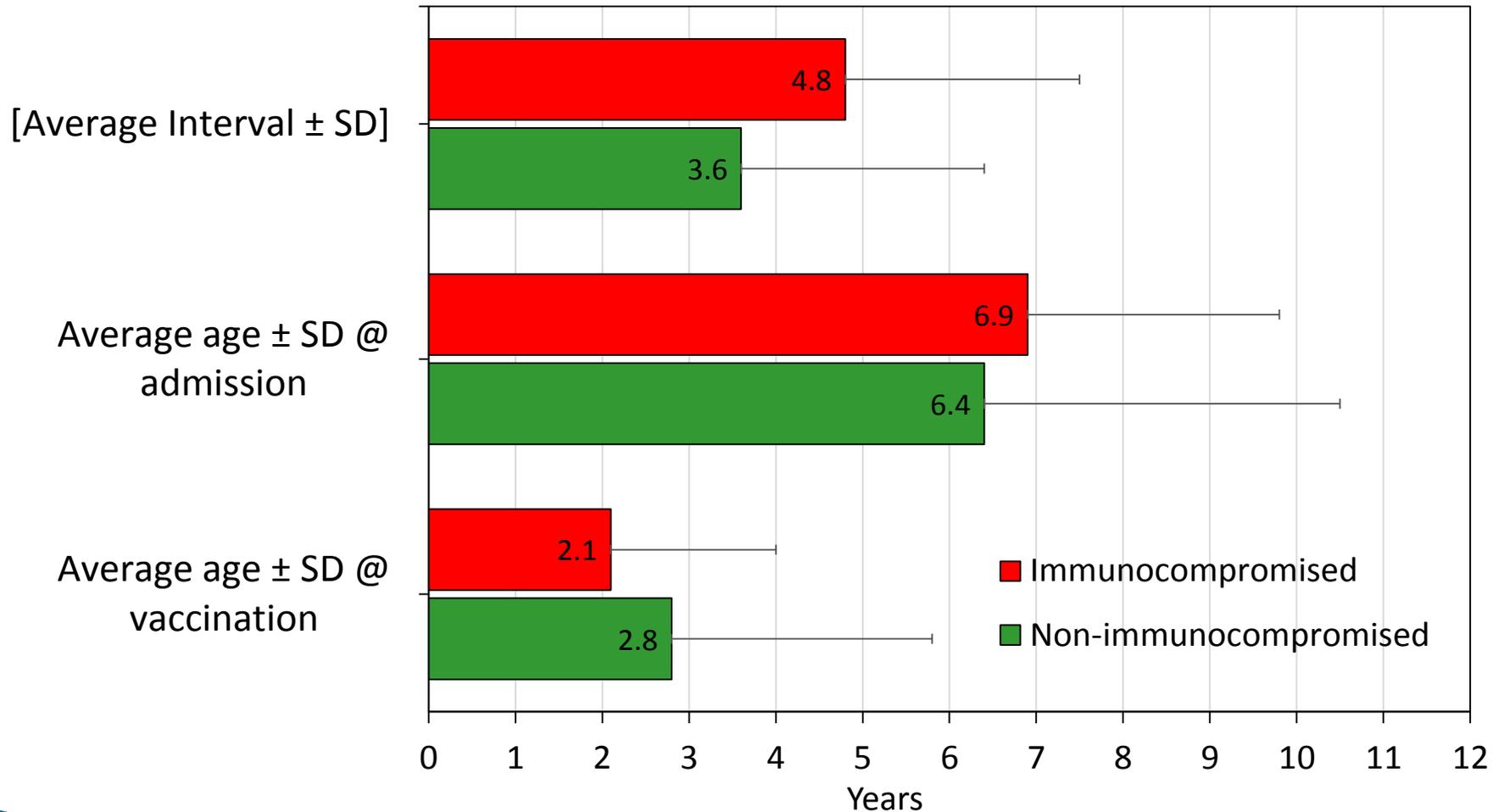


Comparing immunocompromised (n=95) vs non-immunocompromised (n=27) cases, 1-dose vaccination



• $P < 0.05$

Comparing immunocompromised (n=95) vs non-immunocompromised (n=27) cases, 1-dose vaccination



Comparing the unvaccinated, unknown hx, 1-dose and 2-dose var vaccine recipients, IMPACT 2000-15

Variables	Unvaccinated	Unknown vaccin Hx	1-dose recip	2-dose recip
# cases	1,895	435	122	9
Immunocompromised	482 (25%)	172 (40%)	95 (78%) *	5 (56%) *
Antiviral Rx	44%	56%	86% *	78%
Secondary bact infection	54%	43%	16% *	22%
Other var complication	48%	41%	29% *	56%
PICU adm	6%	6%	2.5% *	22%
Mean hosp stay \pm SD (d)	6.9 \pm 8.7	7.1 \pm 6.2	5.6 \pm 4.3 *	5.0 \pm 1.3

* P < 0.05 vs unvaccinated or unknown

Discussion

- ▶ Breakthrough reported in ~10-30% after 1-dose, and < 5% after 2-doses, mostly mild (80%).
 - A Turkish study on hospitalized breakthrough had similar interval of ~5 years after 1-dose vaccination (Dinleyici et al. Vaccine 2015;33:3983)
- ▶ Definite trend for improved determination of vaccination status as well as a reduction of unvaccinated cases over the 16 years.
- ▶ Limitations:
 - We capture tertiary care cases only.
 - Unknown vaccination Hx in 17% (no registry).
 - Relatively short 2-dose era, as compared with 1-dose era.
 - Description and severity of rash illness not ascertained.
 - Inability to differentiate wild-type or reactivation of vaccine strain.

Conclusions

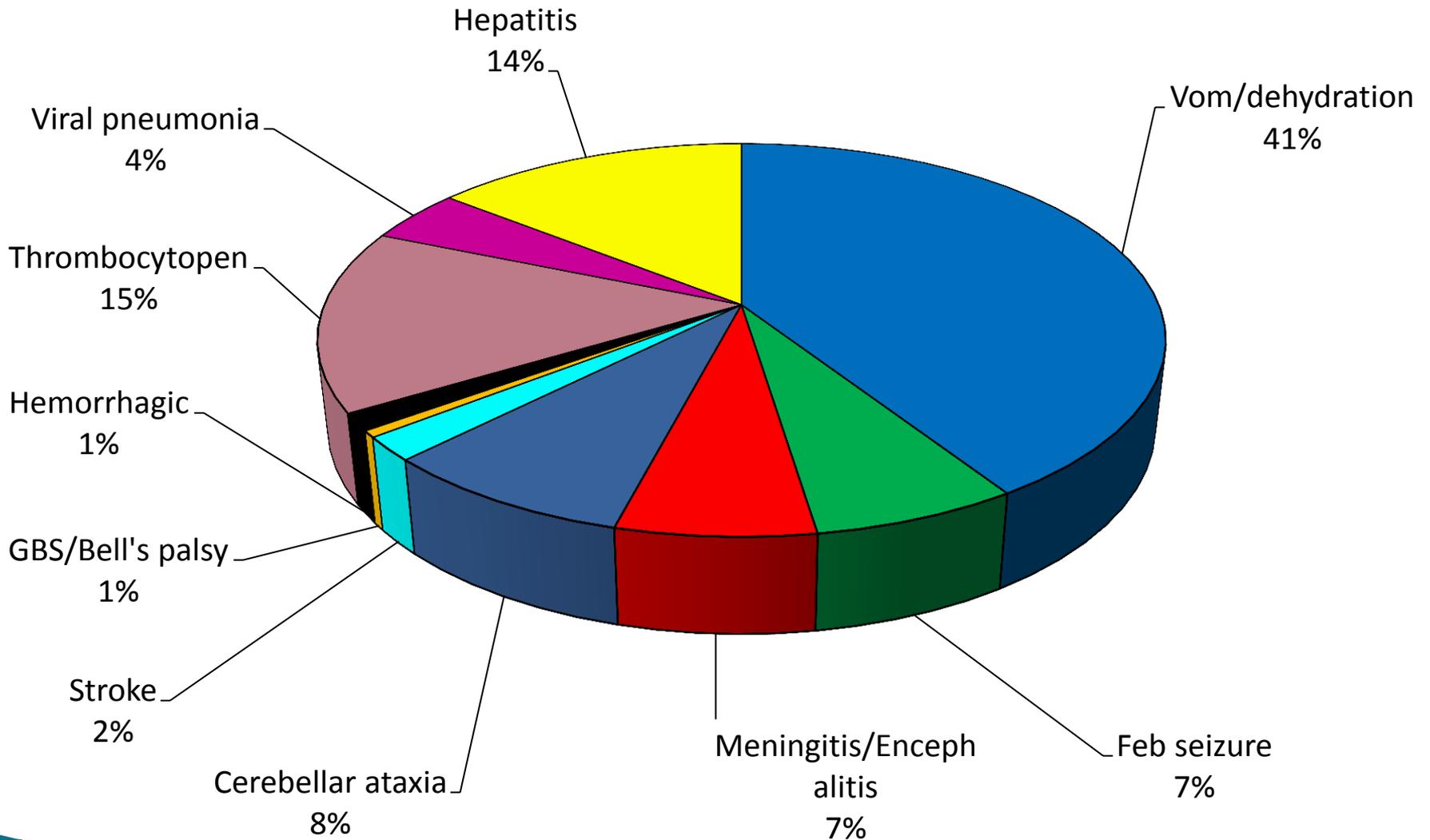
- ▶ Breakthrough disease accounted for approx. 6% of varicella admissions, with no deaths and rare PICU admission.
- ▶ The majority of breakthrough cases were immunocompromised (> 75%), and admitted for antiviral Rx, with fewer var-complications as compared with healthy, non-immunocompromised cases.

Acknowledgments

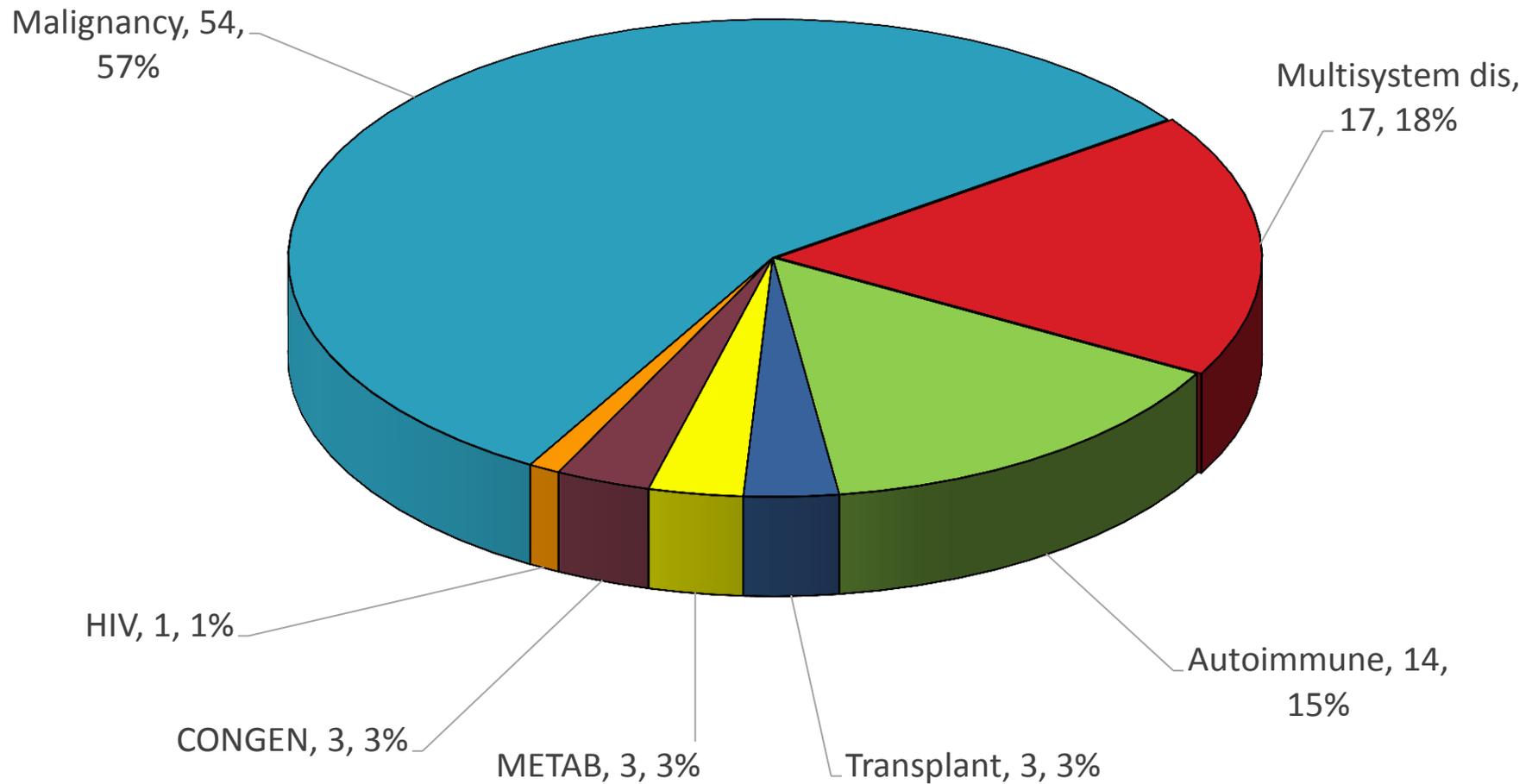
- ▶ Thank you to our dedicated:
 - IMPACT nurse-monitors.
 - Staff at the Vaccine Evaluation Centre (VEC), Vancouver.

- ▶ QUESTIONS?

Var complications, n = 1,271



1-dose recipients, immunocompromised conditions



Children in eight provinces admitted to IMPACT centres with varicella from 2000 to 2015 (St. John's, Halifax, Quebec City, Montreal [two centres], Ottawa, Toronto, Winnipeg, Saskatoon, Calgary, Edmonton and Vancouver). Cases from PEI, New Brunswick and the three territories are not included, as each had an average of < 2 cases/year in all eras).

Prov	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	Subtot
AB	39	39	30	13	12	8	6	8	4	7	8	10	11	3	5	2	206
BC	26	18	19	21	24	17	13	13	2	2	7	5	5	8	1	1	182
MB	38	24	29	38	29	13	15	9	2	9	6	4	4	8	4	6	238
NL	5	11	11	14	5	5	2	2	0	1	2	2	0	1	4	1	66
NS	19	16	13	6	2	5	2	0	1	4	0	3	1	4	2	1	78
ON	102	48	65	54	81	36	31	36	18	30	18	27	20	10	15	12	603
QC	154	106	120	91	114	101	87	35	28	20	21	16	19	19	37	51	1019
SK	10	14	18	12	8	14	5	5	2	4	6	3	1	1	1	0	104
Subtot	393	276	305	249	275	199	161	108	57	77	68	70	61	54	69	74	2496



Baseline (pre-vaccine program) era



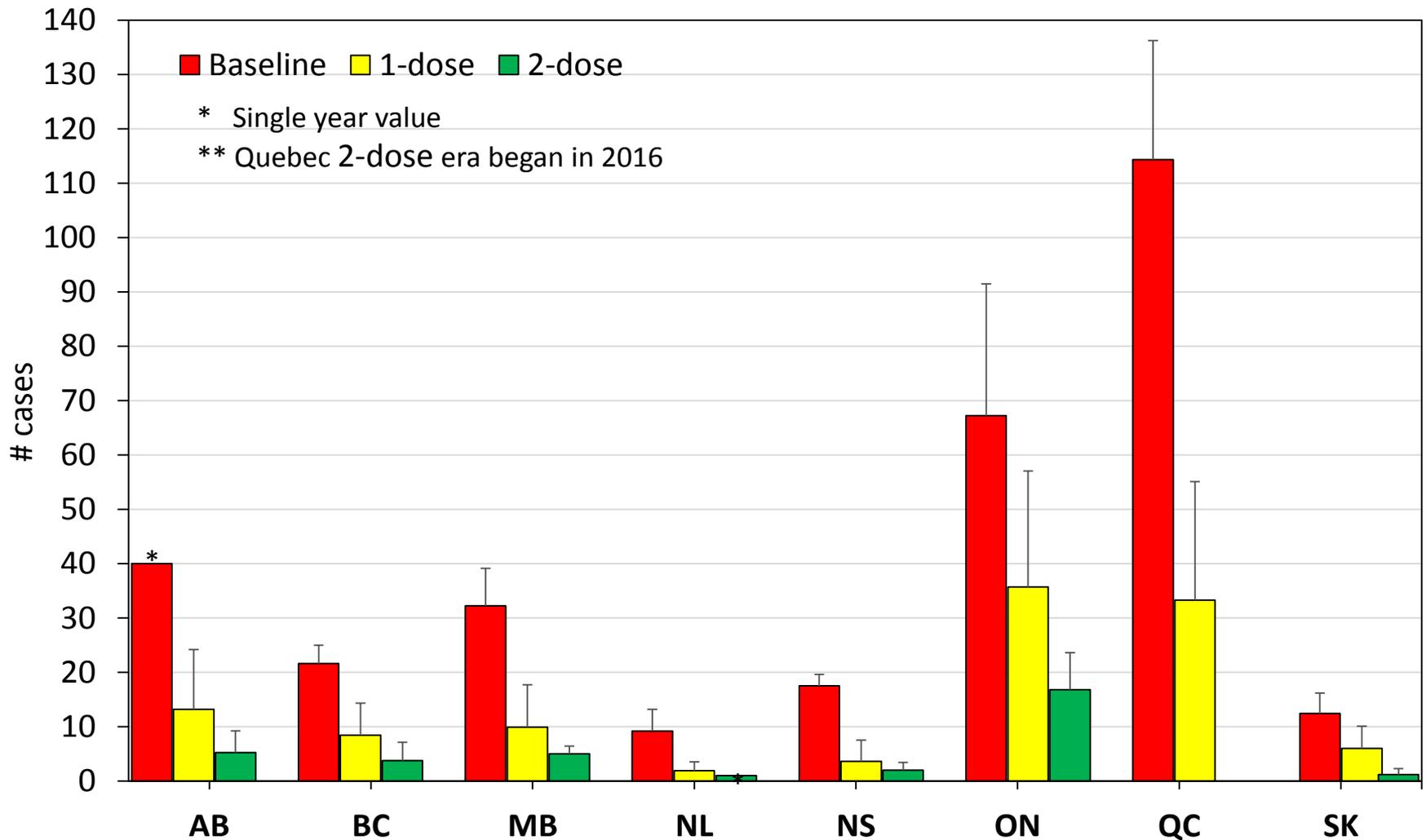
1-dose program era



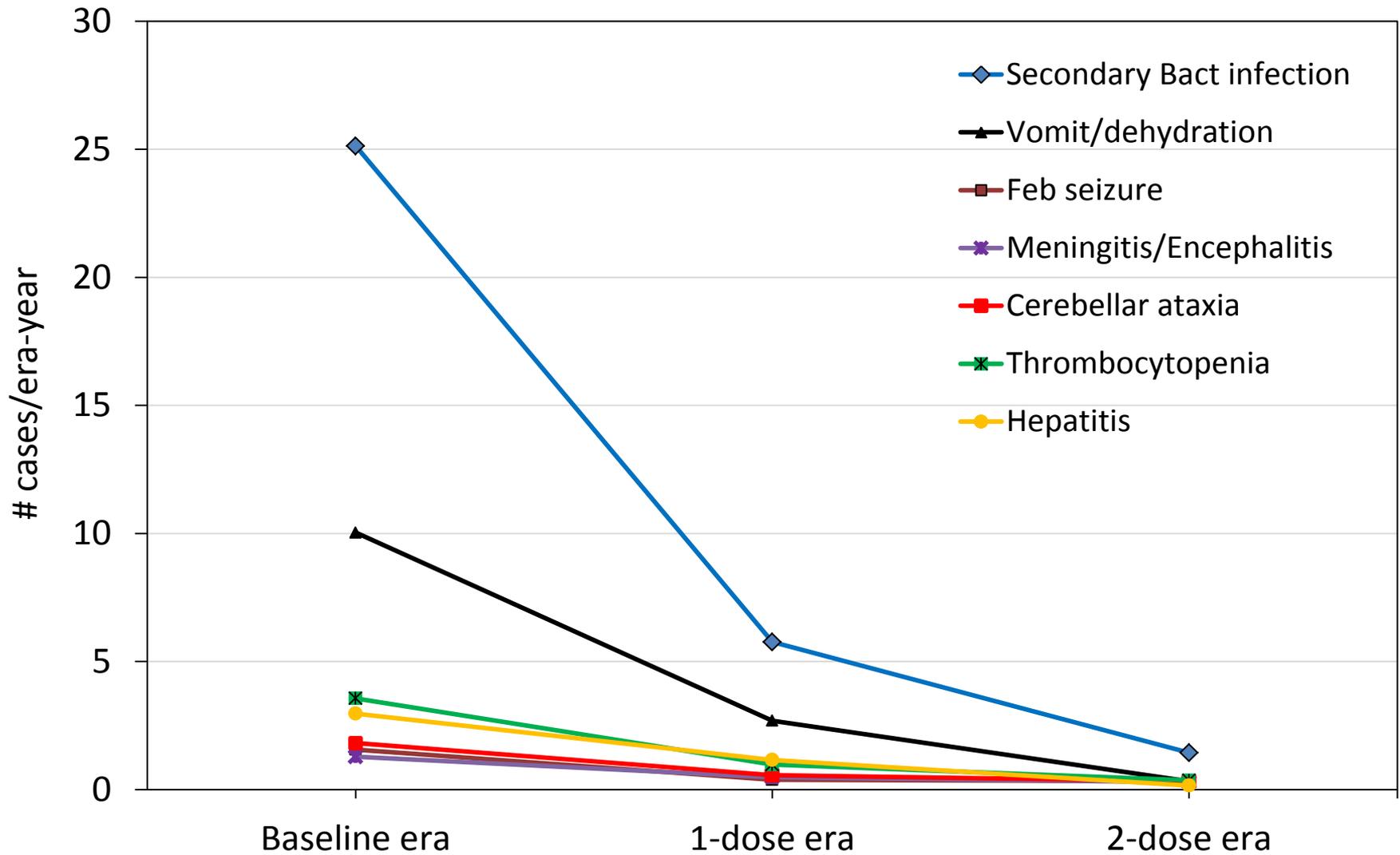
2-dose program era

Quebec's 2-dose program was initiated in Jan 2016, just outside our study period.

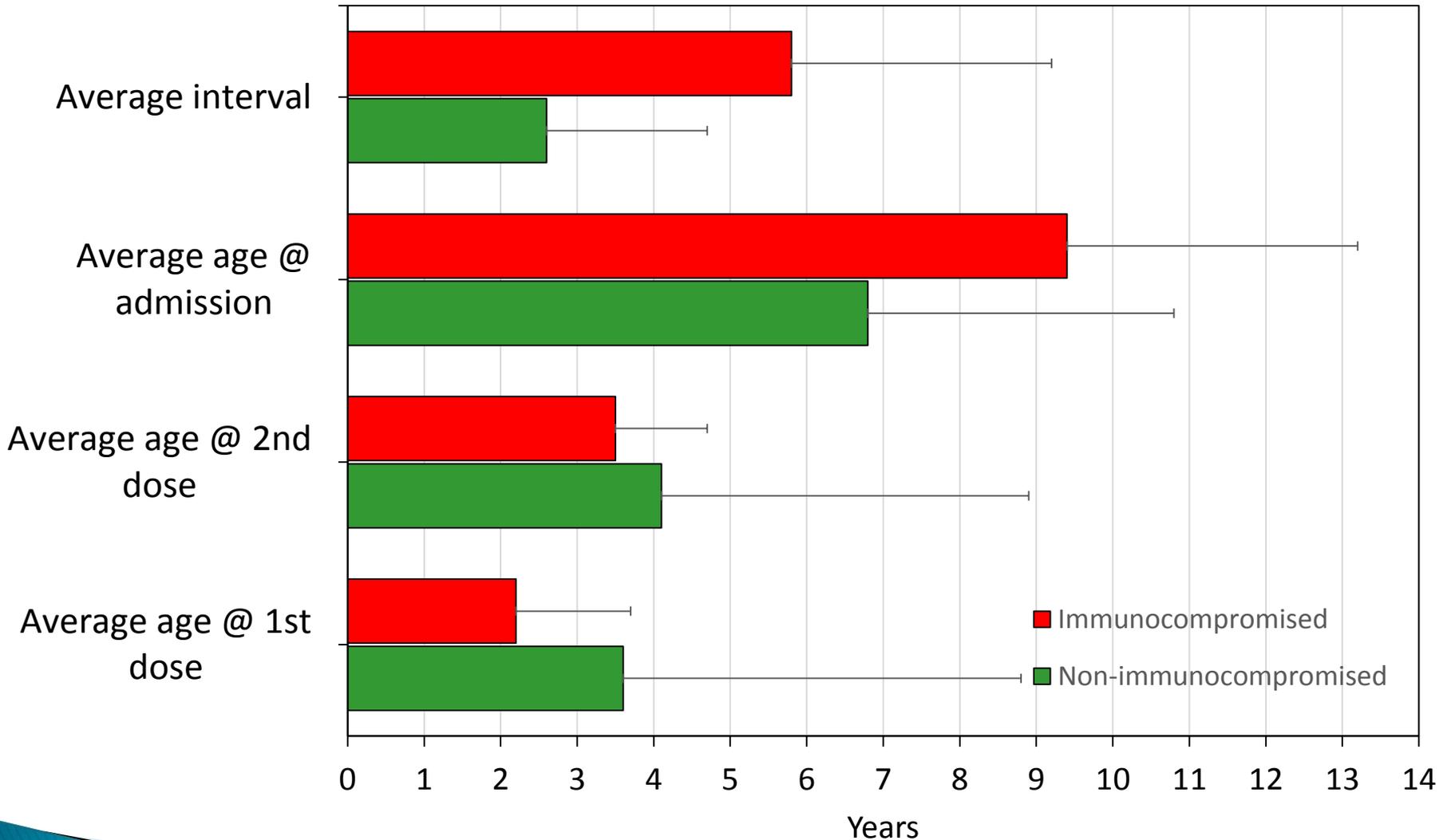
Mean (\pm SD) # cases from eight provinces admitted to IMPACT centres with varicella from 2000 to 2015



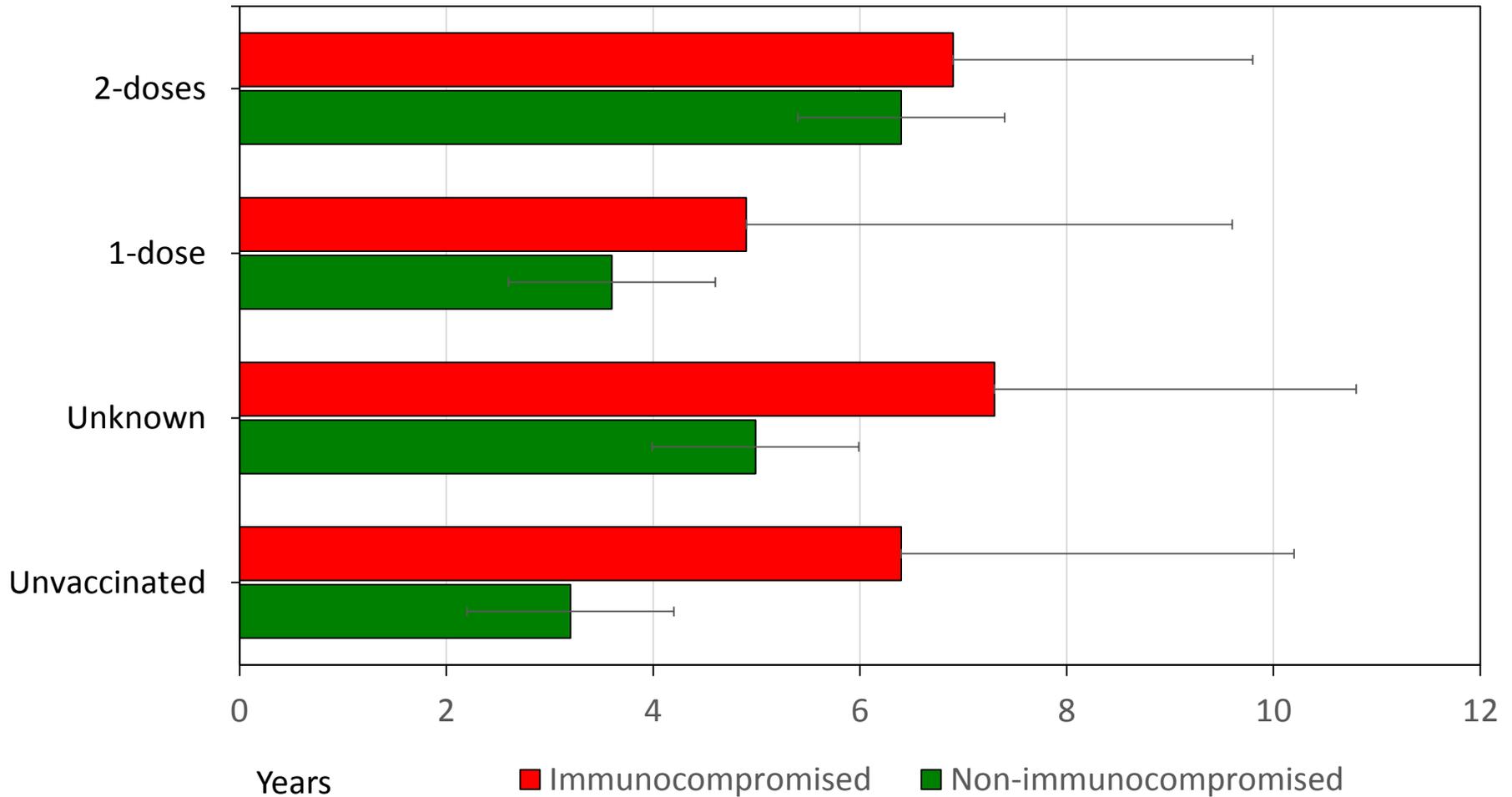
Varicella complication rate (per era-year)



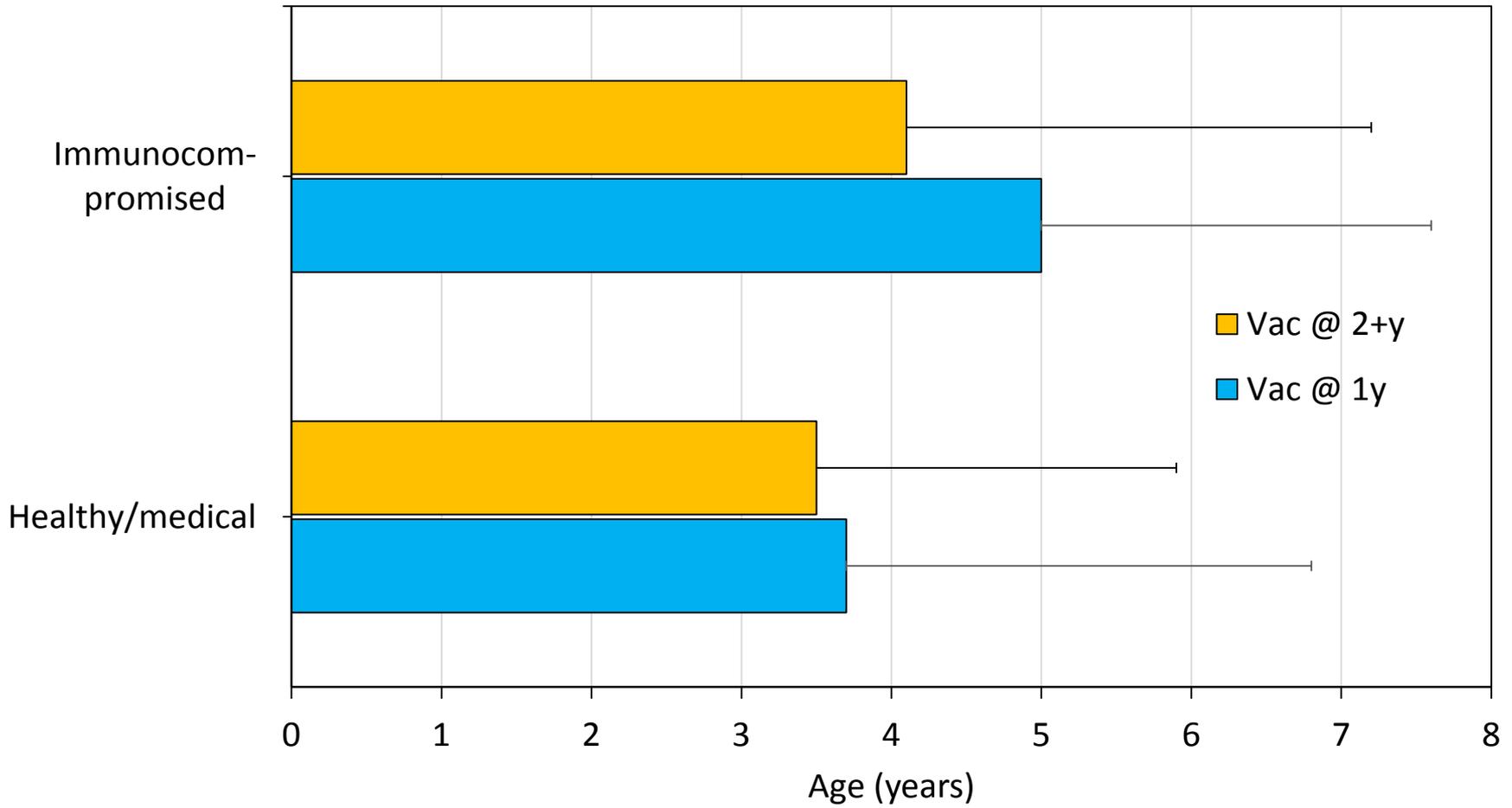
Immunocompromised (n=5) and non-immunocompromised (n=4) 2-dose recipients, ages at vaccination and interval to admission



Age at admission \pm SD for unvaccinated, unknown vaccine status, 1-dose & 2-dose recipients



Interval from vaccination to admission, 1-dose @ 12-23 mos, compared with ≥ 24 mos of age



END