CERVICAL CANCER SCREENING SCENARIOS for pan-Canadian Cervical Screening Initiative

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Objectives

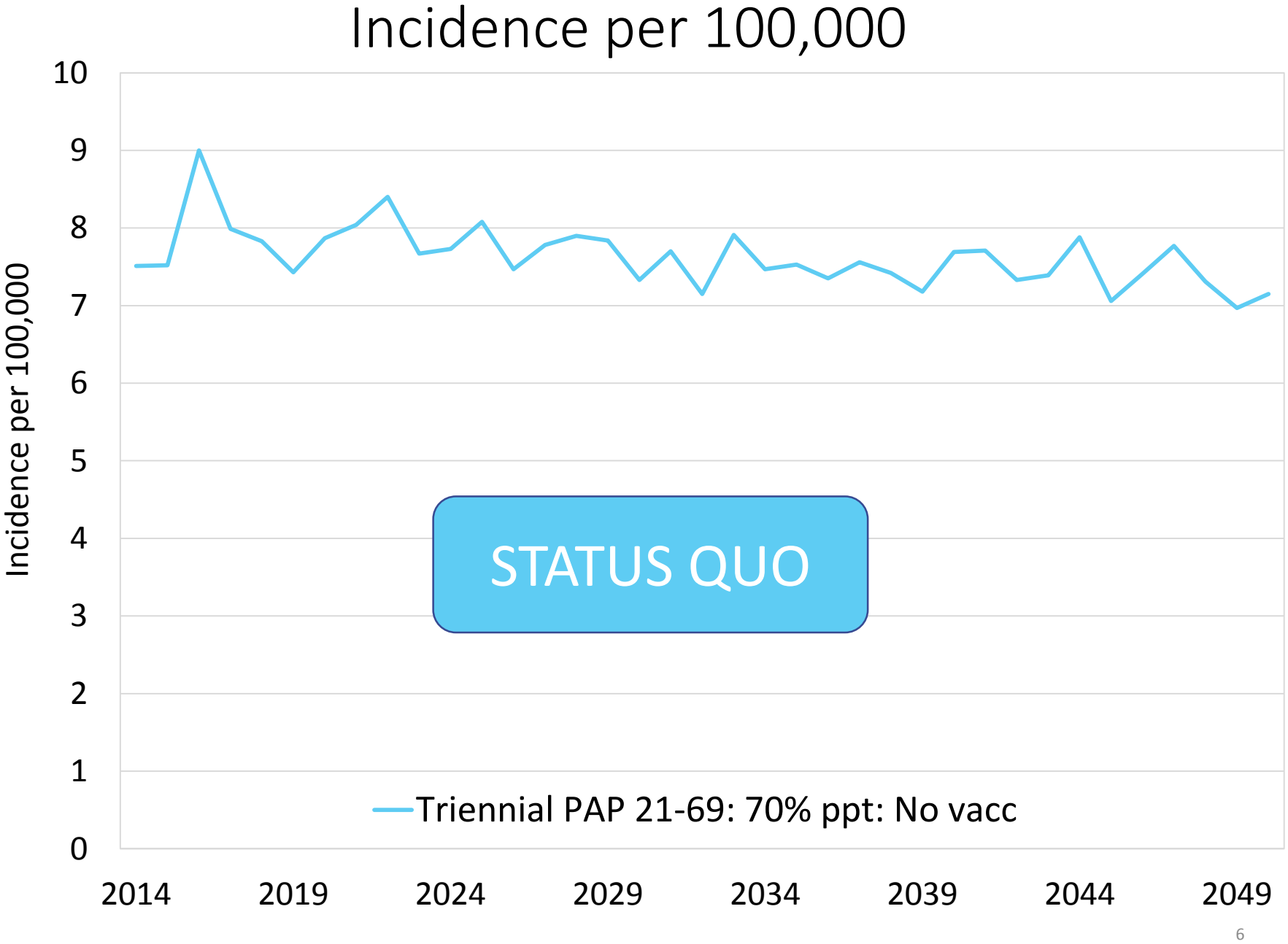
- Target setting: incidence rate
  - What will the incidence rate be in the future if we continue with the status quo?
  - What would the incidence rate be if we increased screening participation to 80%? Altered our screening programs? Introduced primary HPV DNA testing?
- If we switch to primary HPV DNA testing:
  - What are the health outcomes?
  - How much will it cost?
  - Is it cost-effective in Canada compared to cytology?

CRMM

Assumptions

Screening Inputs	Baseline assumptions
Recruitment period	2015 onward
Recruitment age for PAP screening	21-69 years old (25, 30-69)
Interval years between initial rescreen	3 (5, 10)
Screening participation	70%
Screening modalities	Pap or HPV DNA test

Vaccination Inputs	Baseline assumptions
Age	12
Sex	Female
Vaccine deployment year	2007
Vaccine type	Quadrivalent
Vaccination coverage	70% (50%, 90%)
Proportion protected	100%
Degree of protection	100%



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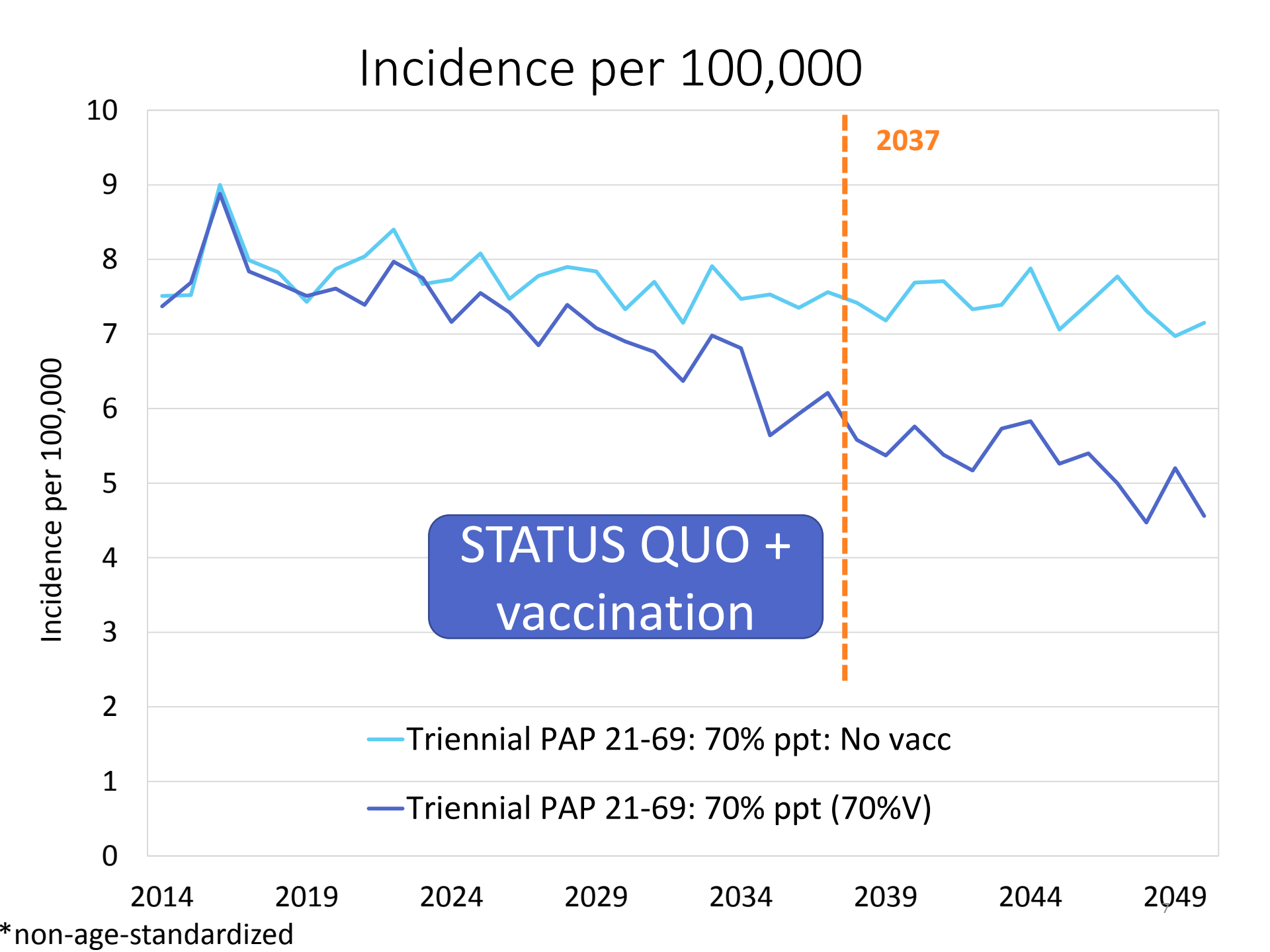

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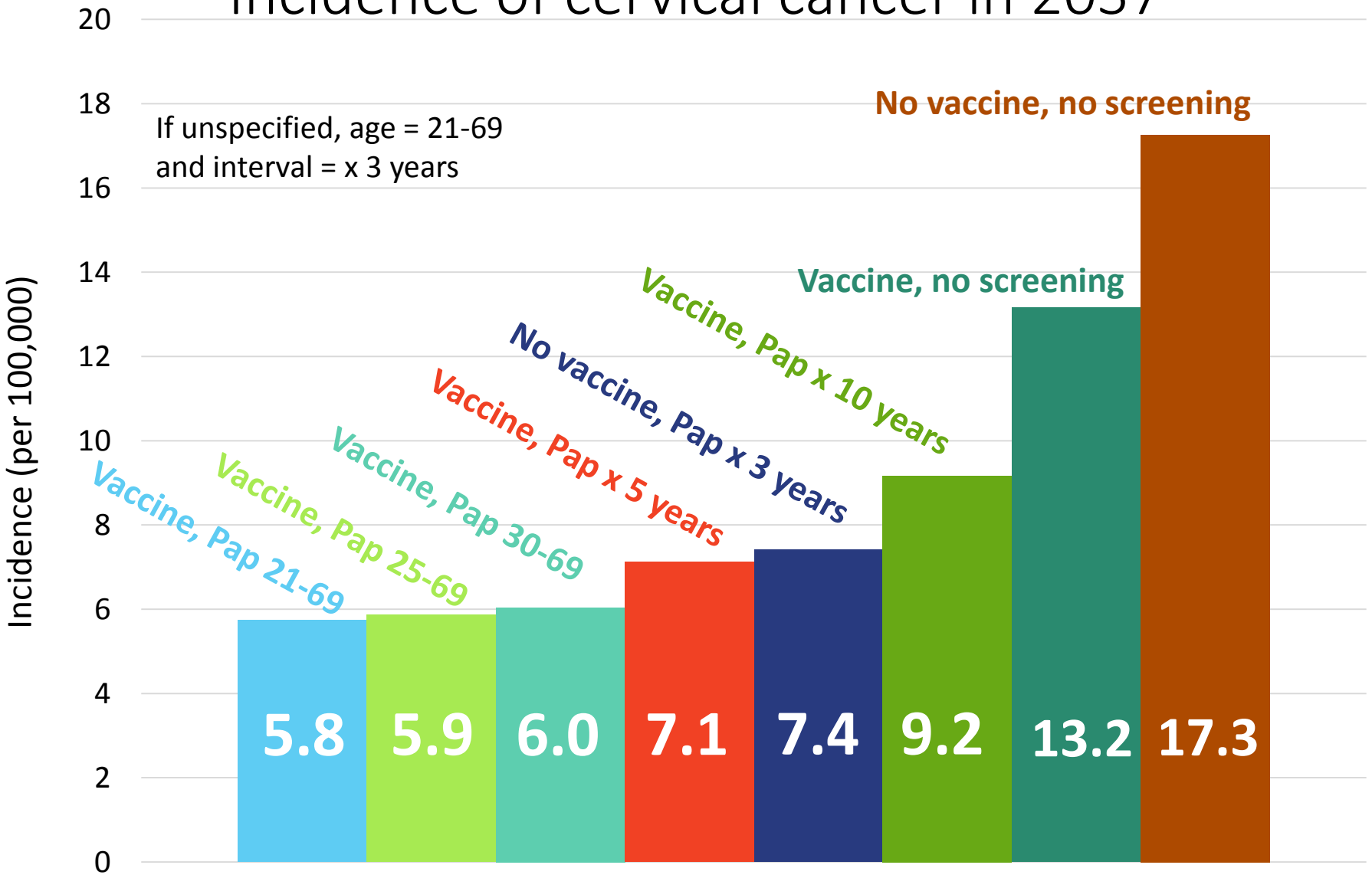
Incidence of cervical cancer in 2037



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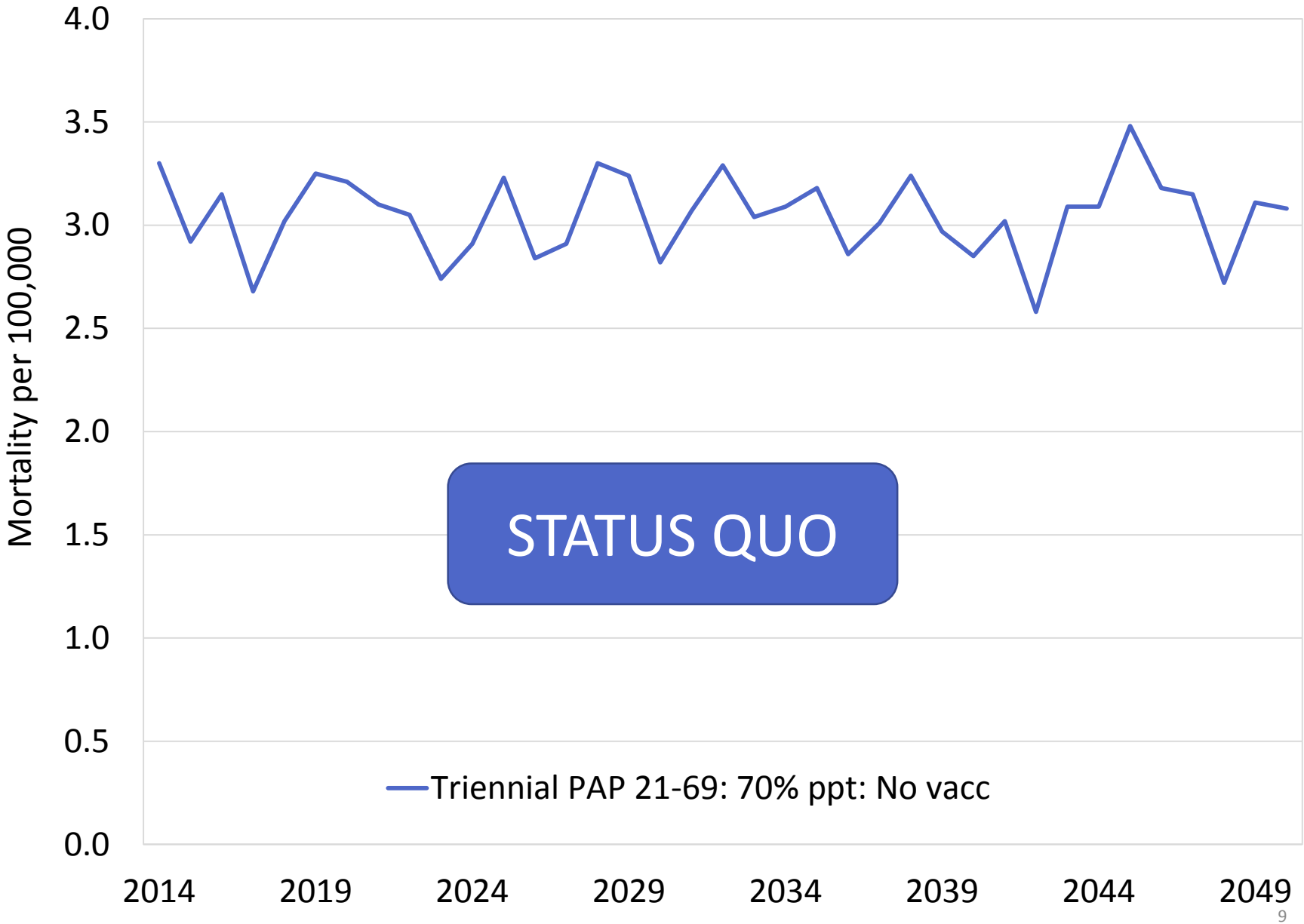
Mortality per 100,000



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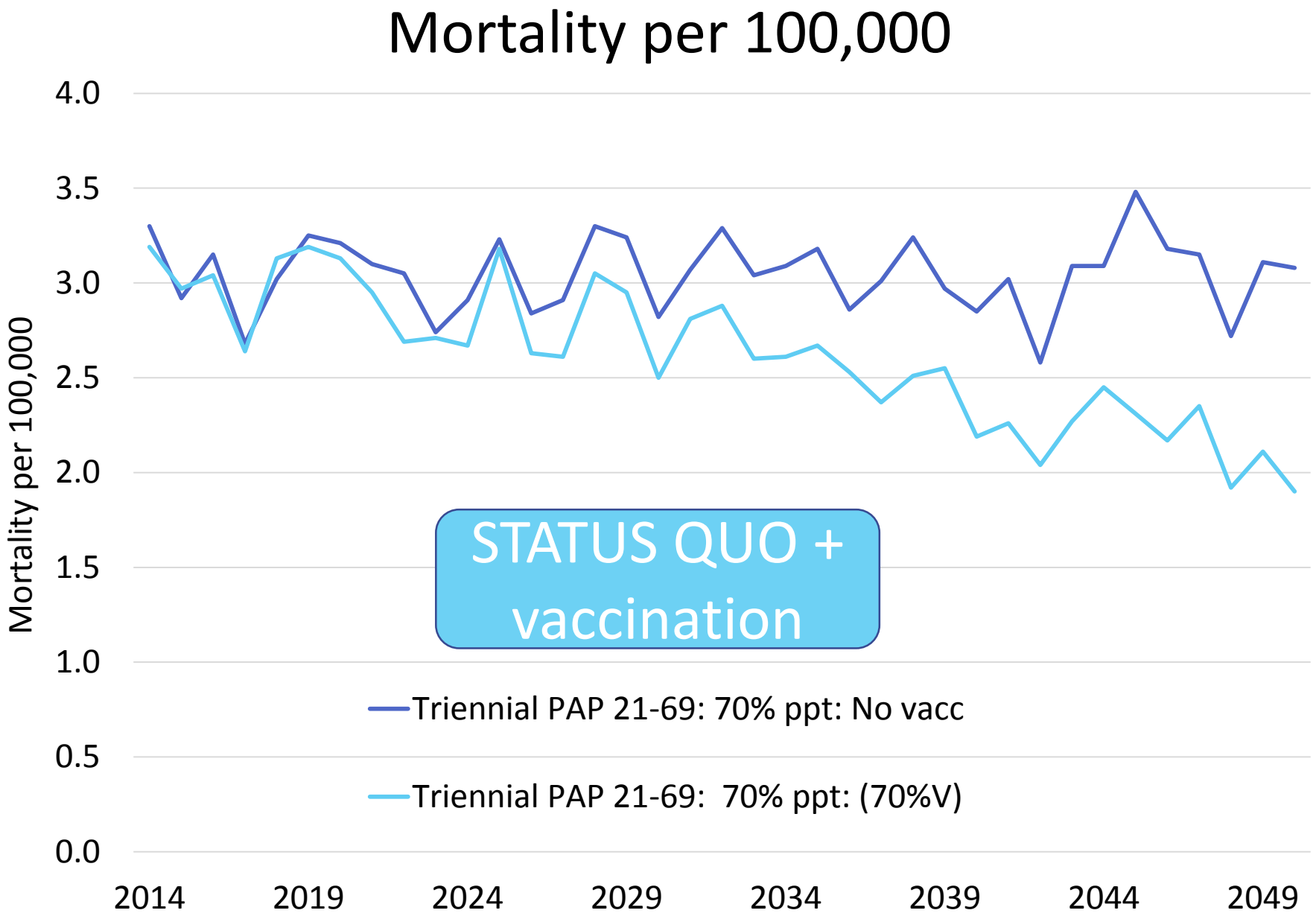

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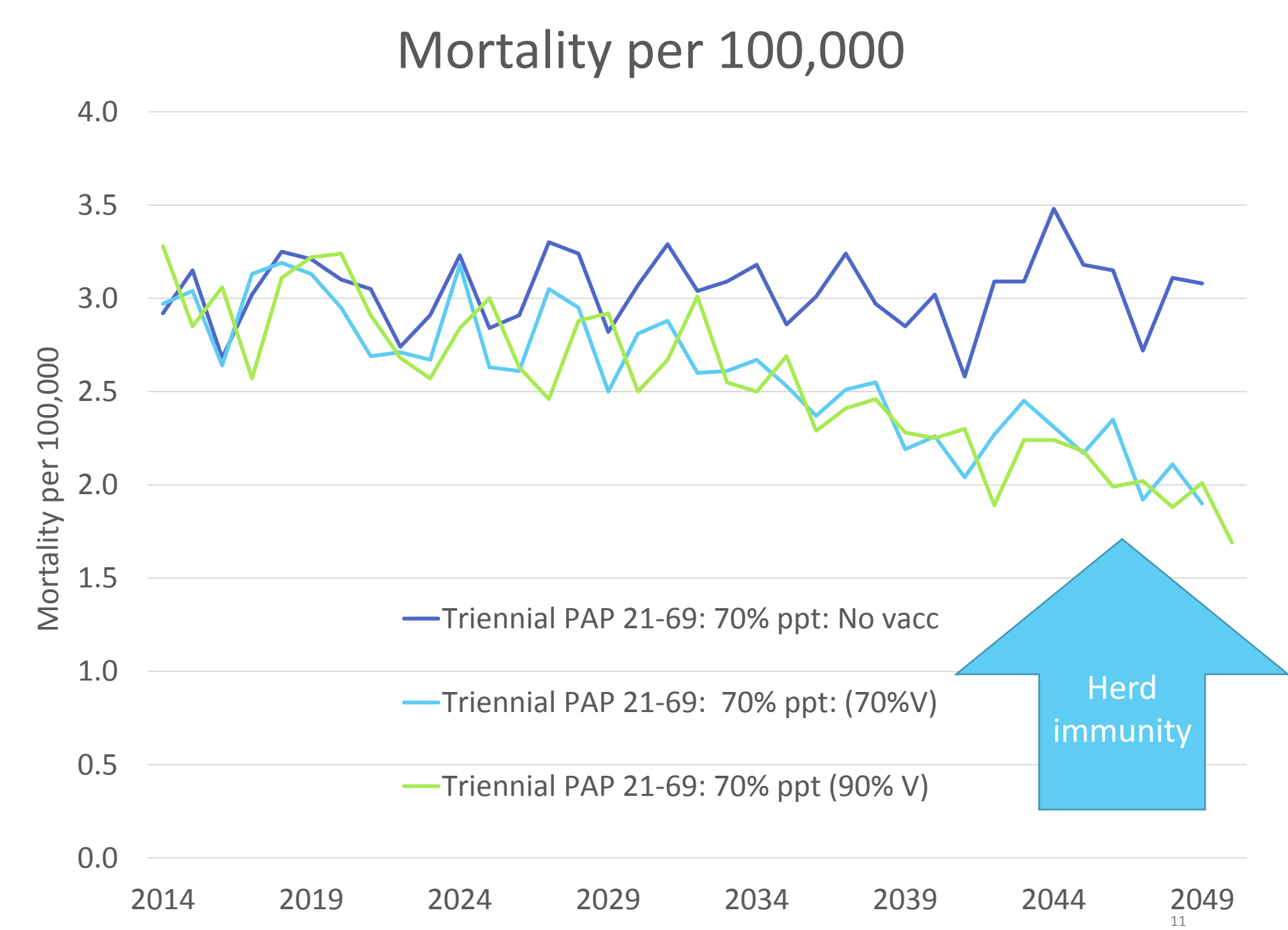

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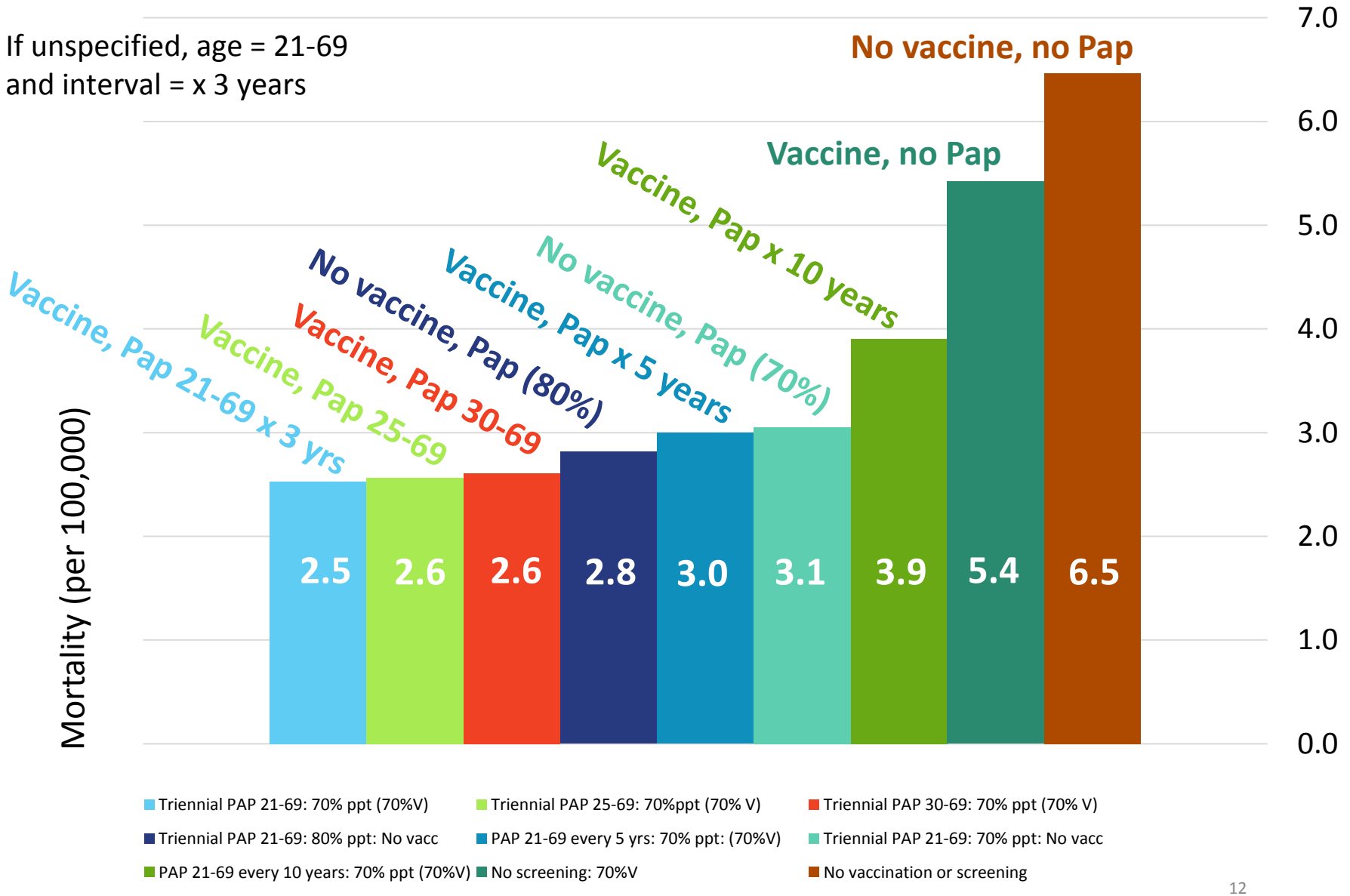
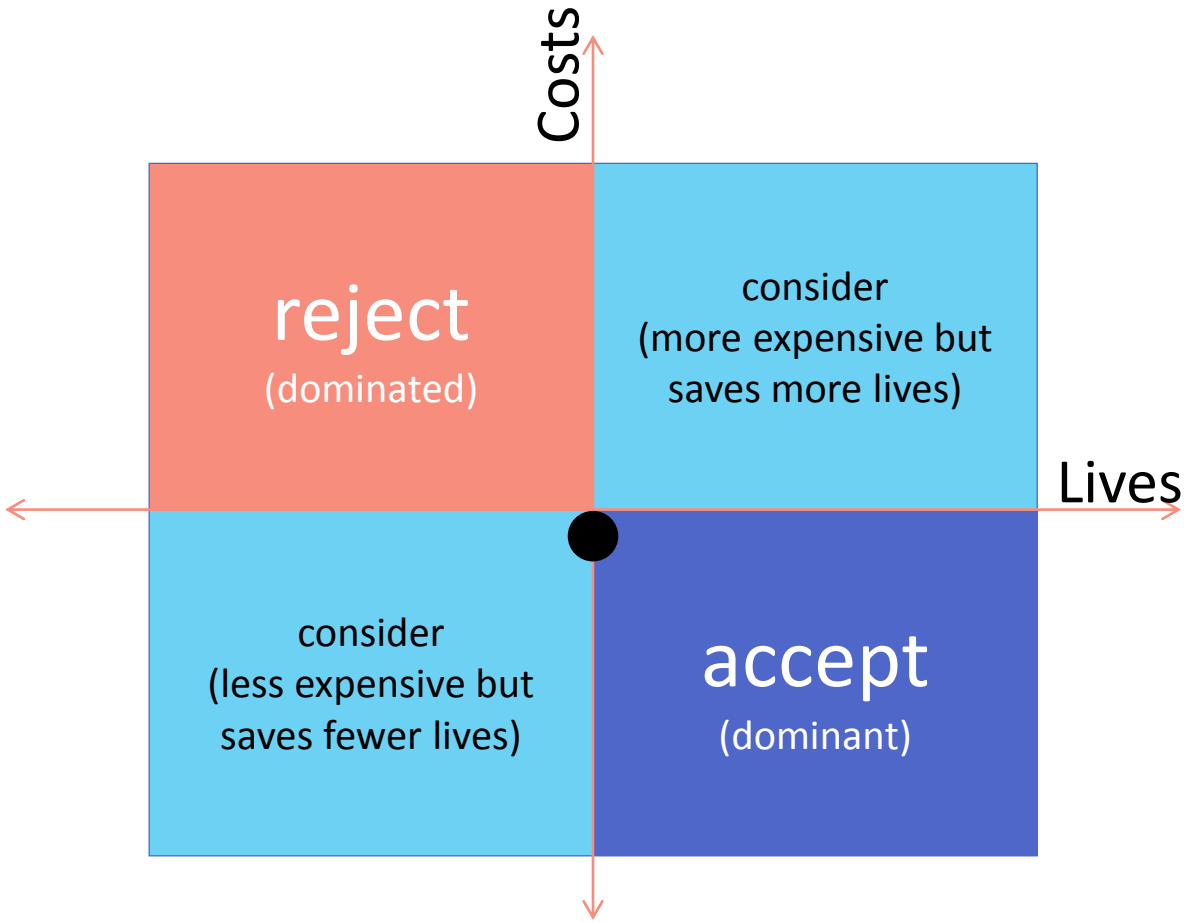
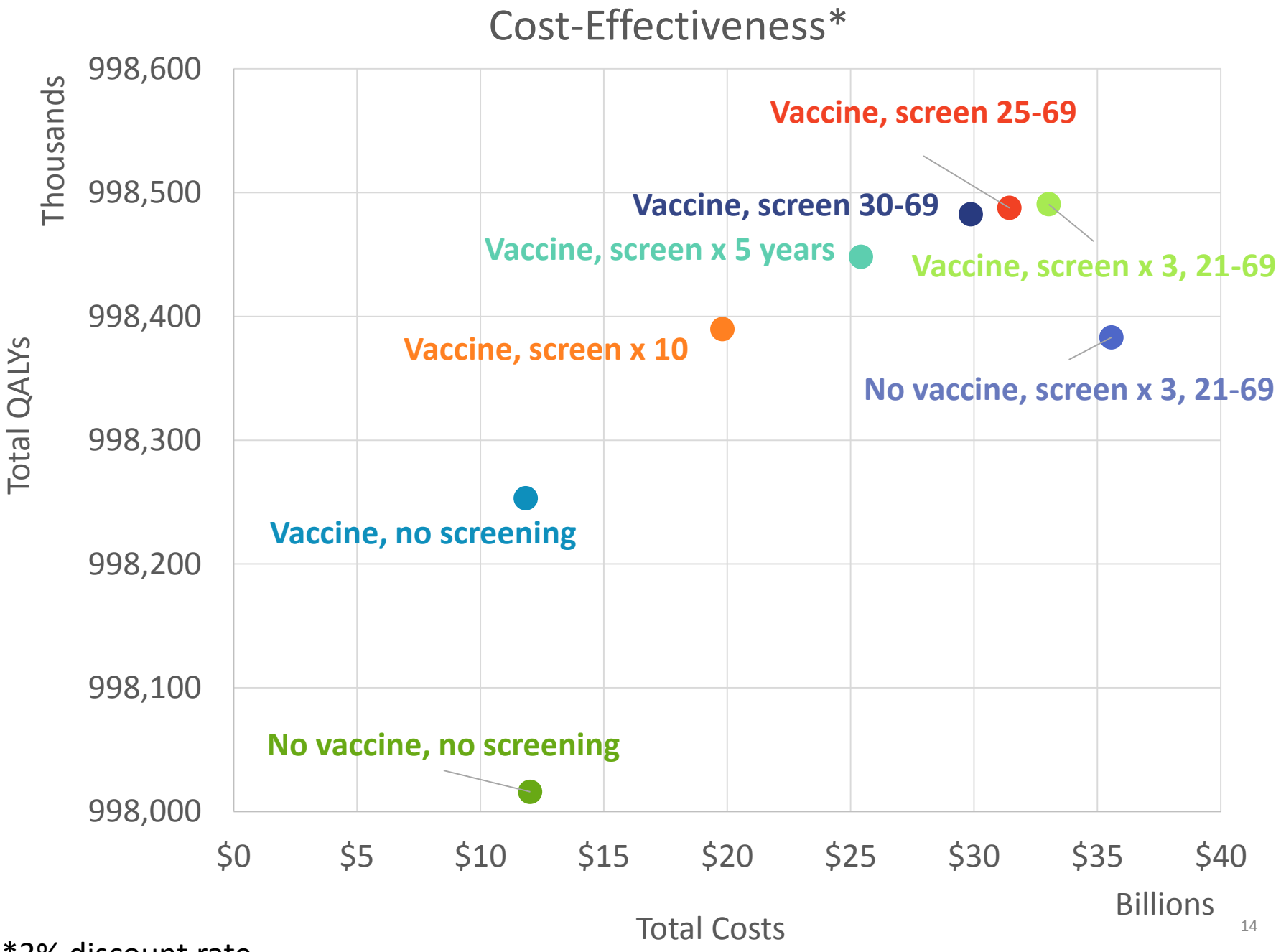
Mortality per 100,000 in 2037

If unspecified, age = 21-69
and interval = x 3 years



Incremental Cost-Effectiveness Ratios (ICERs)





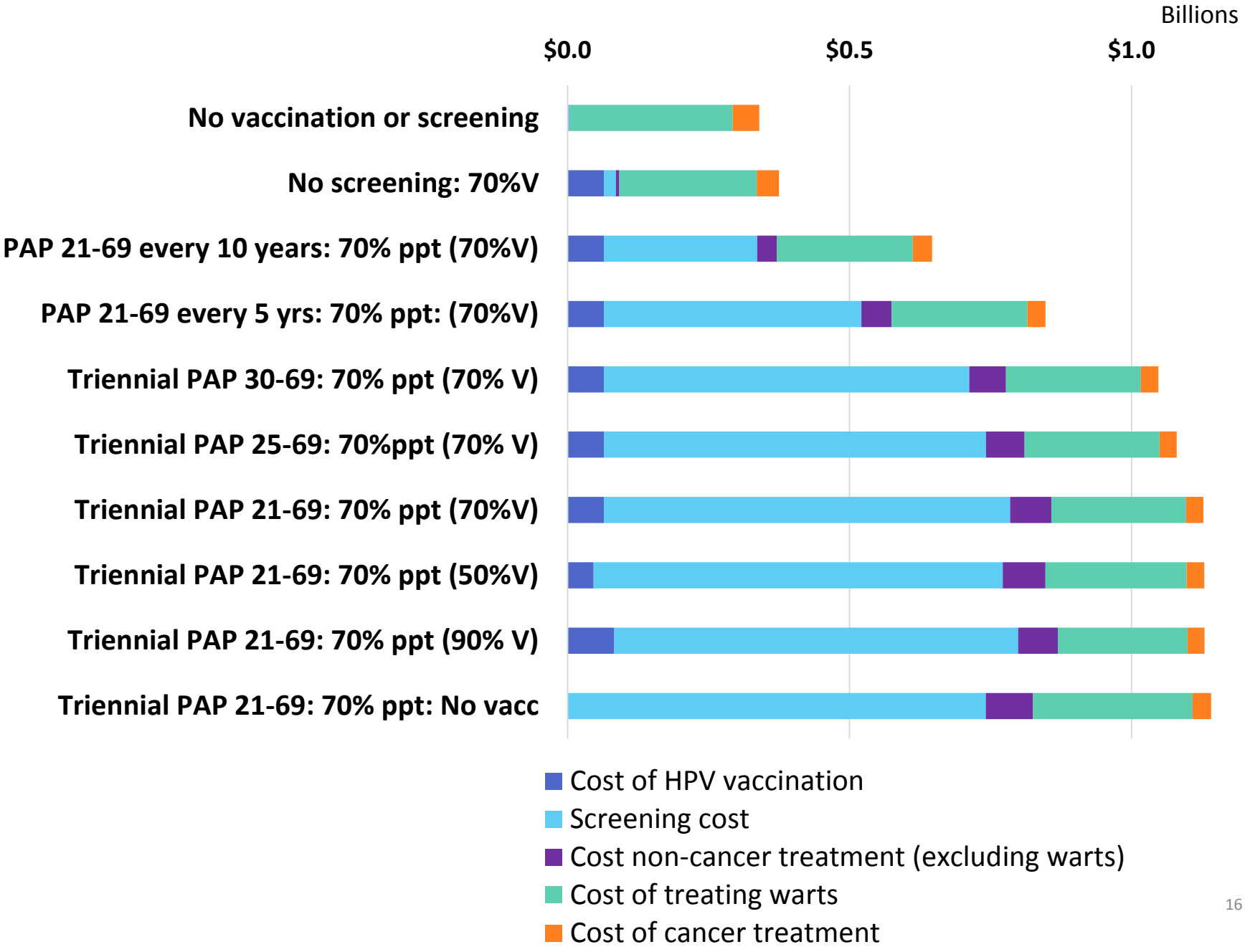
*3% discount rate

Cost-effectiveness ratios*

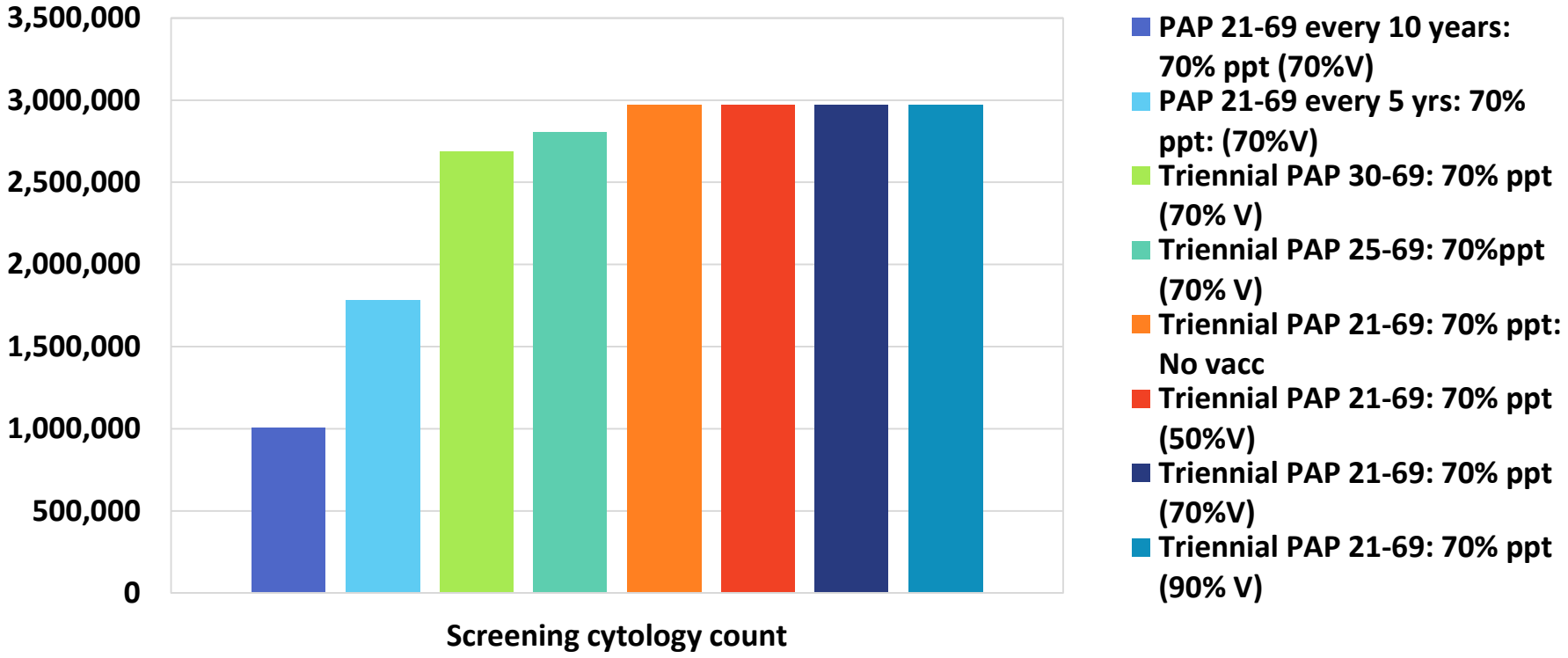
	Total Cost (in '000,000's)	Total QALYs (in '000's)	ICER
No vaccine, no screening	$12,016	998,016	-
Vaccine, no screening	$11,840	998,253	DOMINANT
Vaccine, cytology 21-69 x 10 years	$19,811	998,390	$ 21,000
Vaccine, cytology 21-69 x 5 years	$25,421	998,448	$ 31,000
Vaccine, cytology 30-69 x 3 years	$29,867	998,482	$ 38,000
Vaccine, cytology 25-69 x 3 years	$31,438	998,488	$ 41,000
Vaccine, cytology 21-69 x 3 years	$33,027	998,491	$ 44,000
No vaccine, cytology 21-69 x 3 years	$35,572	998,383	$ 64,000

*3% discount rate applied

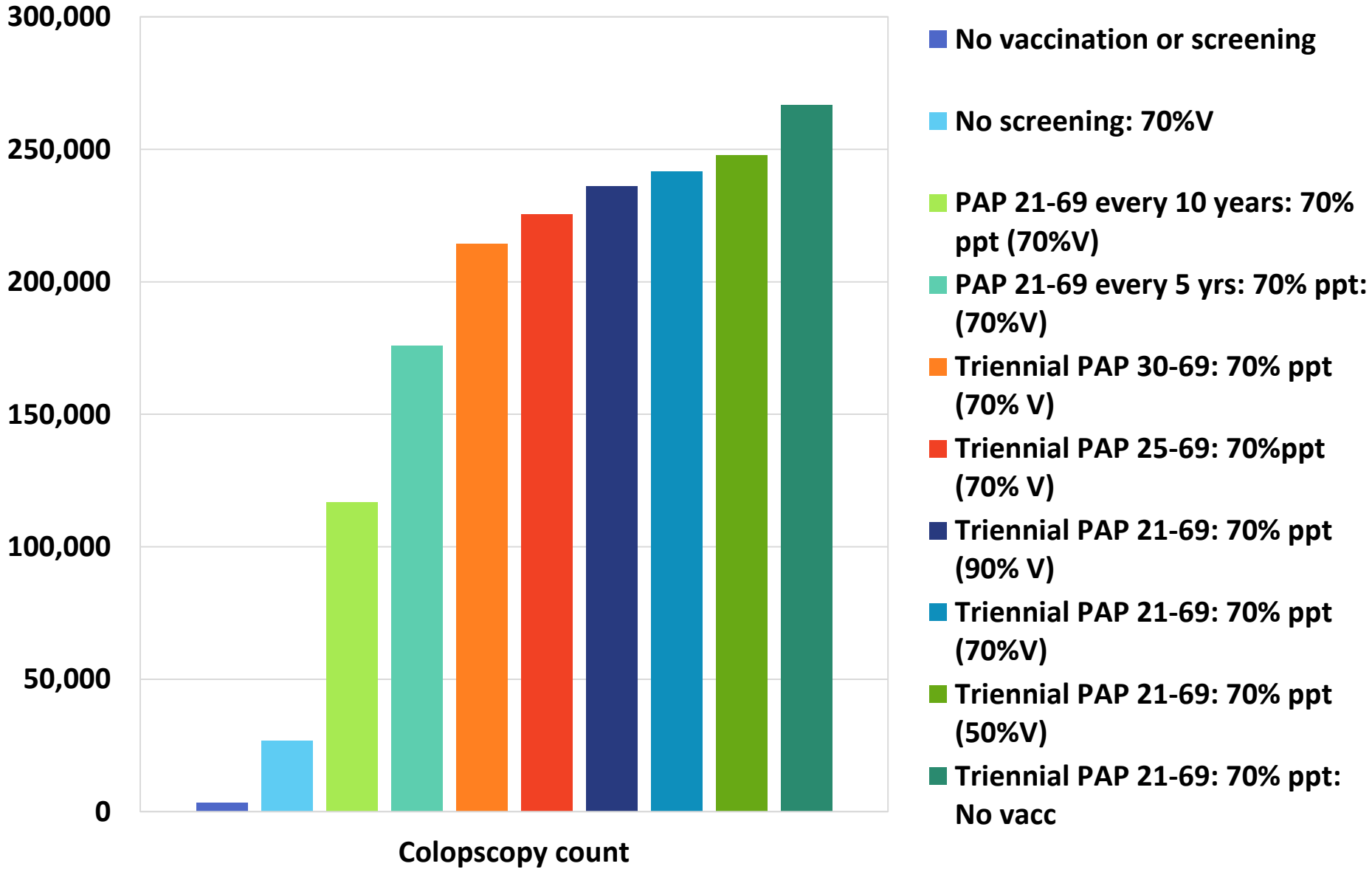
Average annual cost (2015-2025)



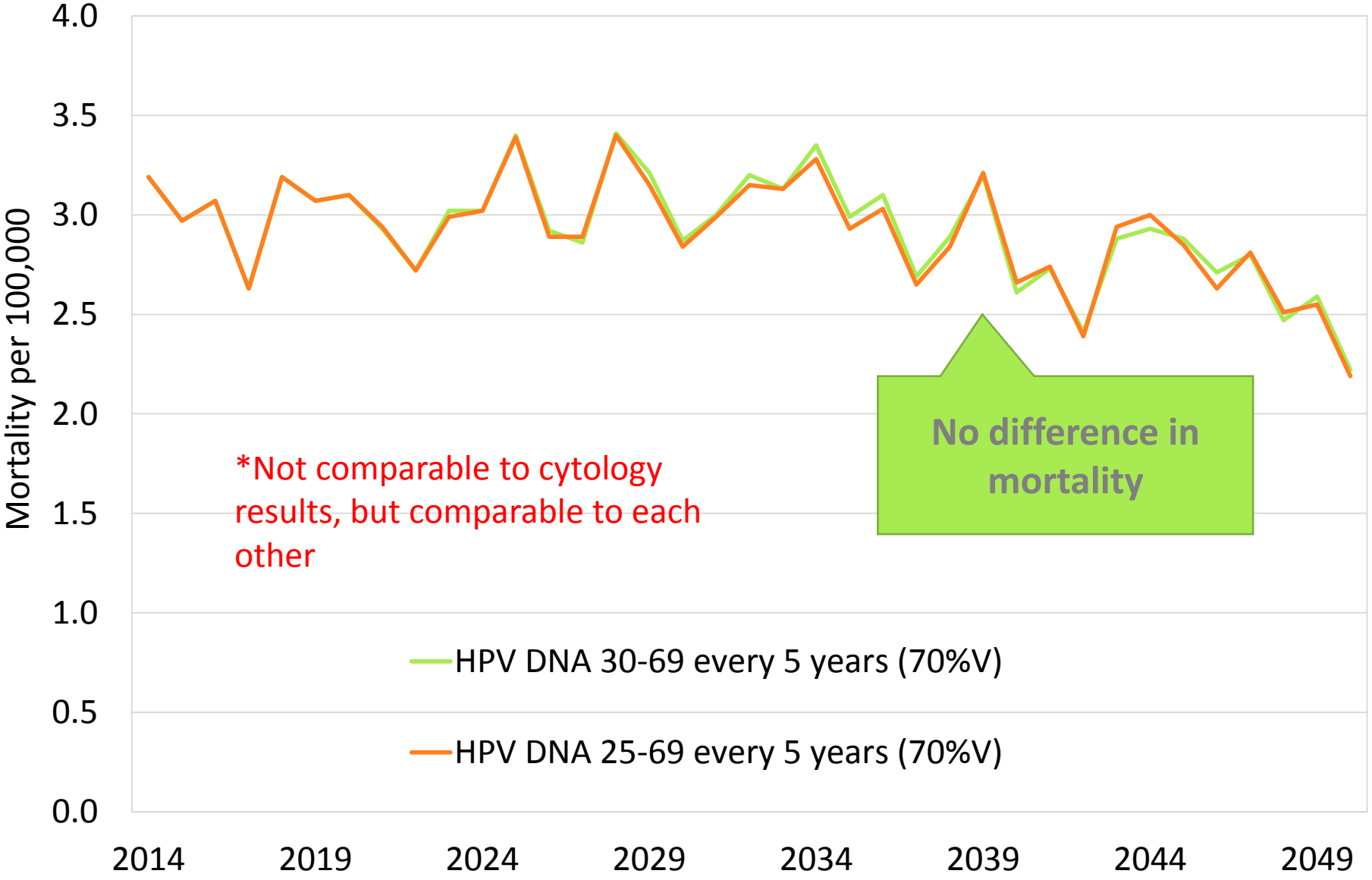
Average annual screening cytology count (2015-2025)



Average annual colopscopy count (2015-2025)



Mortality per 100,000



*non-age-standardized

Considerations

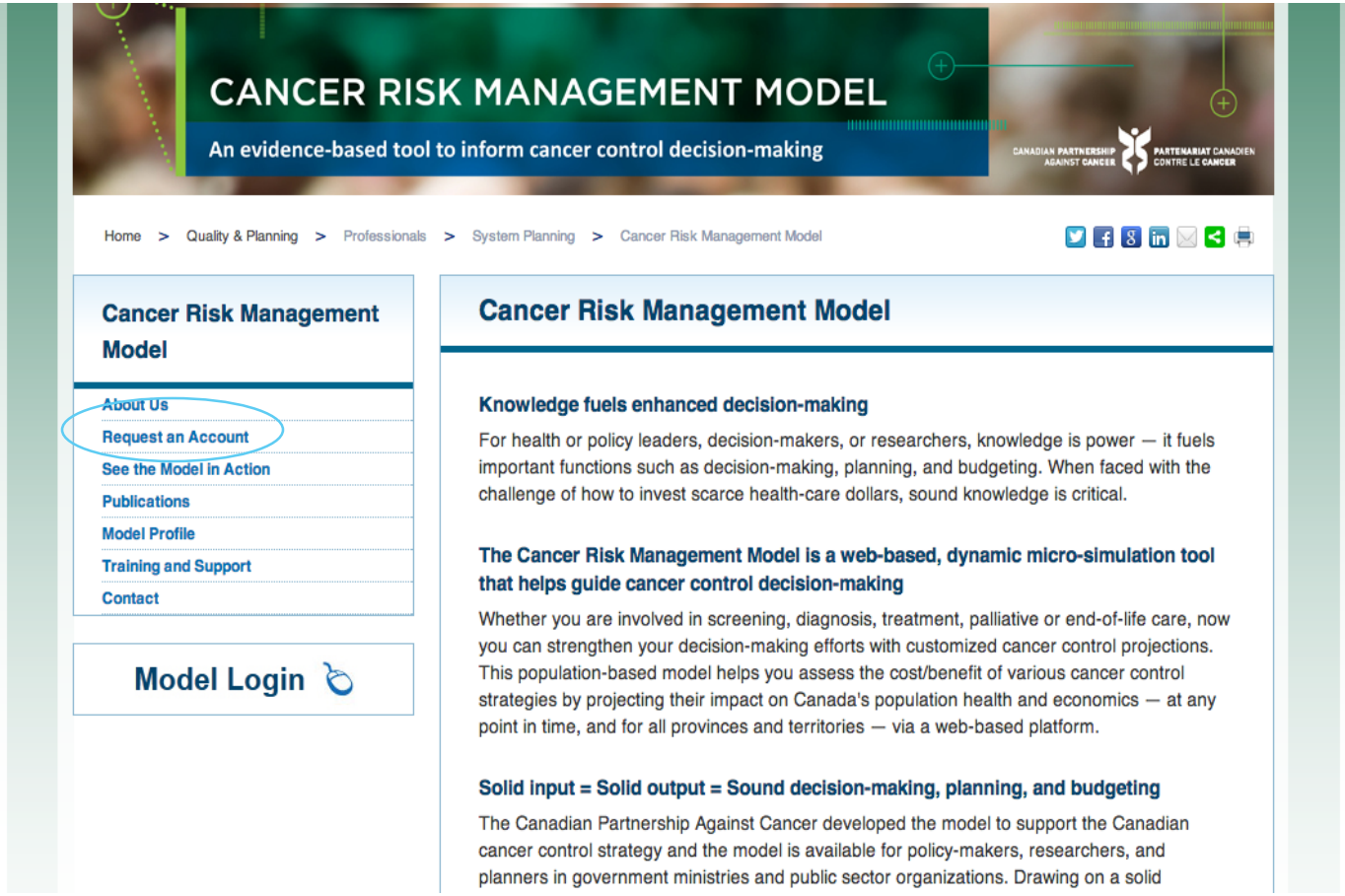
- Due to little empirical data on sexual behaviour, long-term data on vaccine efficacy, and existing questions around the development and progression of lesions and HPV-related cancers, higher degree of parameter uncertainty
- Uncertainty around future performance of cytology due to reduced prevalence
- Due to very low prevalence of cervical cancer, estimates are subject to higher degree of Monte Carlo uncertainty

Conclusions

- By 2037, an incidence of 6 per 100,000 is projected, assuming that screening programs remains unchanged (70% cytology x 3 years in 21-69).
- Increasing the start age of screening to 25 or 30 has little impact on cervical cancer incidence or mortality and generates cost-savings.
- Increasing the screening interval to every 5 or 10 years is more cost-effective, however is associated with increased mortality.

Next Steps

- Primary HPV DNA testing
  - 21-29 :cytology, 30-69 HPV
  - 21-34: cytology, 35-69 HPV
  - HPV only with cytology triage
- Different screening strategies in vaccinated vs unvaccinated cohorts
- Vaccinating boys
- Oropharyngeal, vulvar, vaginal and anal cancers
- Vaccine effectiveness or longevity



https://cancerview.ca/cancerriskmanagement

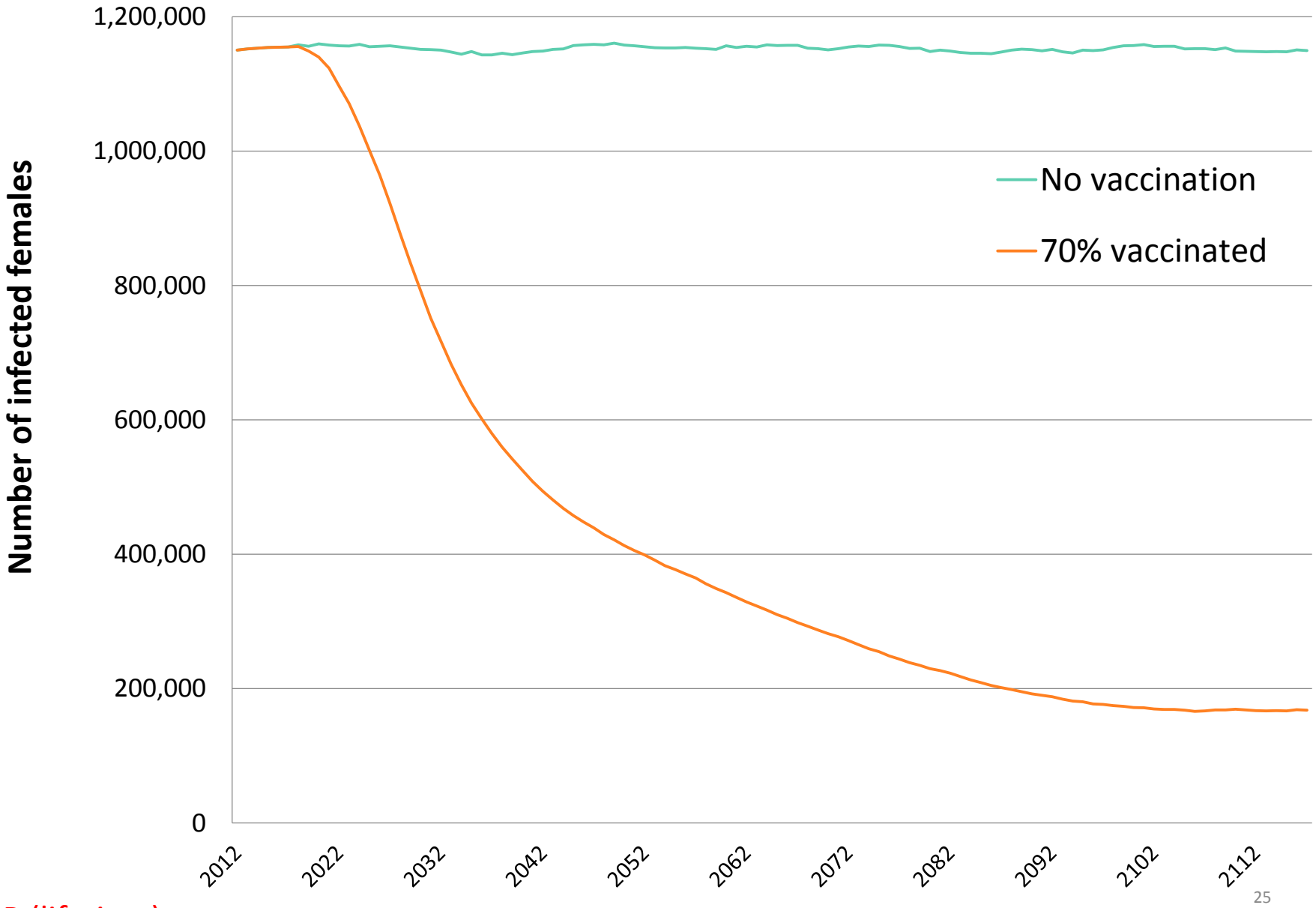
Natalie Fitzgerald, Program Manager, Economics, Cancer Risk Management Platform

natalie.fitzgerald@partnershipagainstcancer.ca

416-619-5780

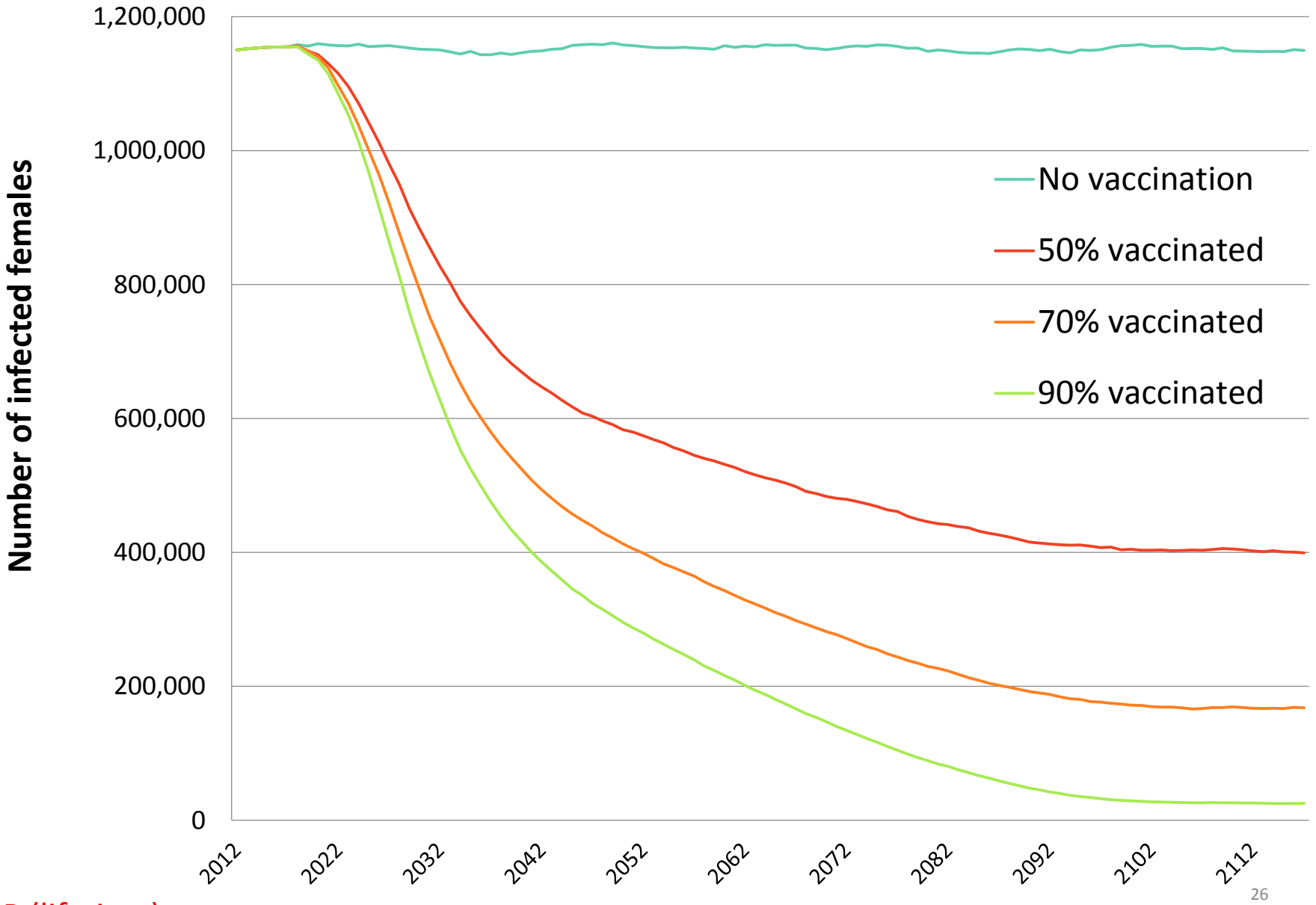
Appendix

Prevalence of HPV 16/18



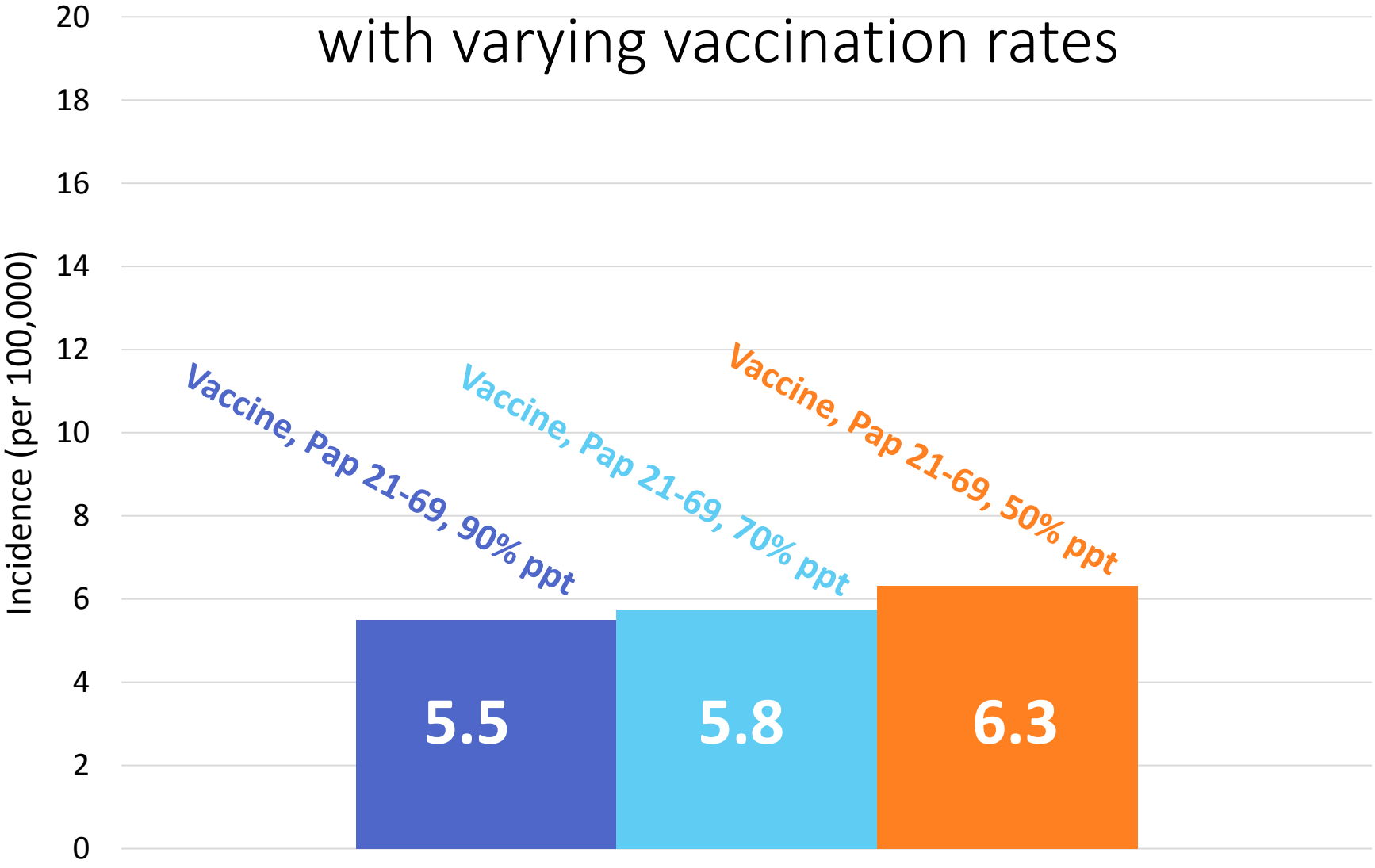
POP (lifetime)

Prevalence of HPV 16/18

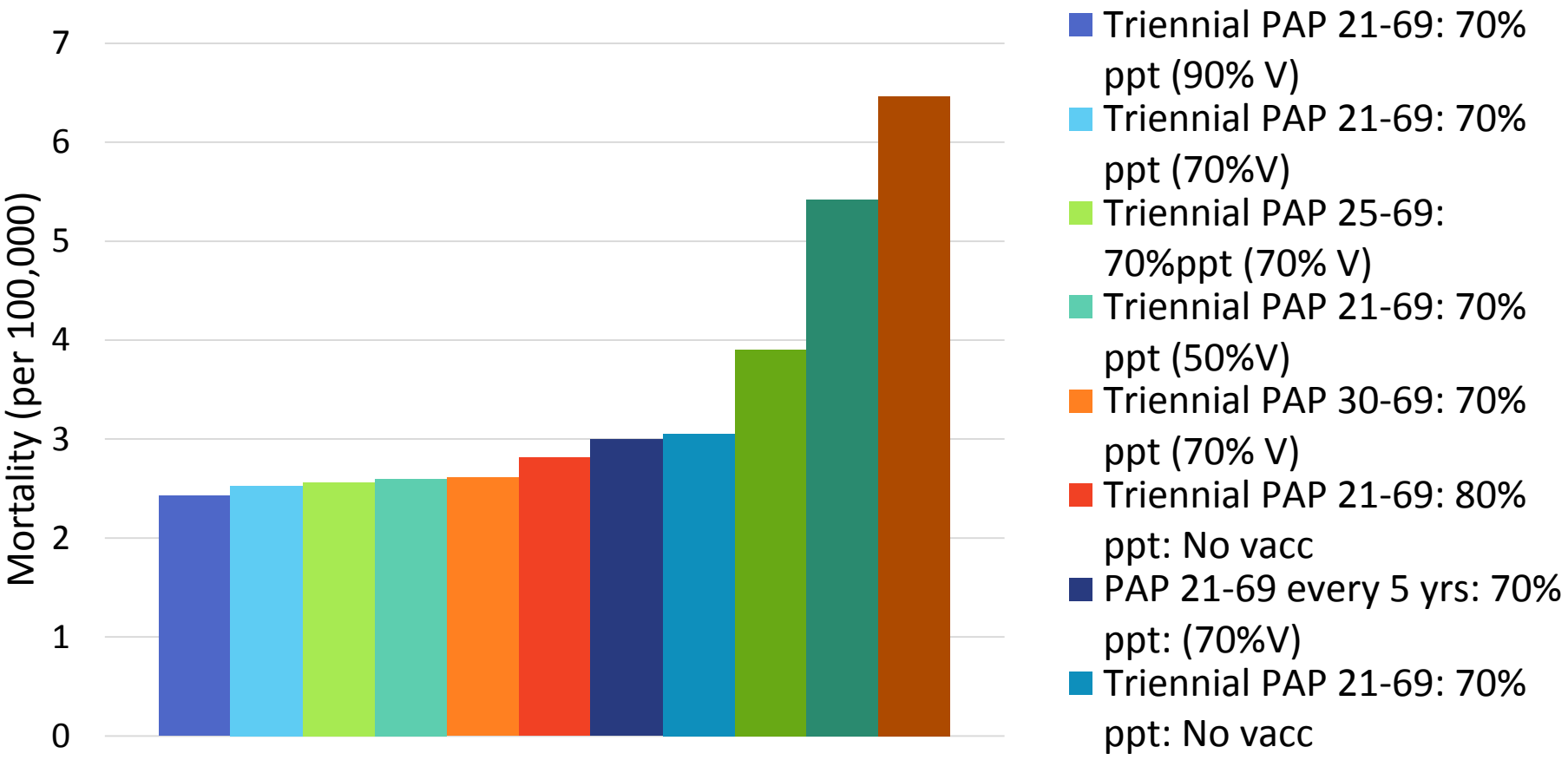


POP (lifetime)

Incidence of cervical cancer in 2037 with varying vaccination rates



2037 PAP Mortality Rate



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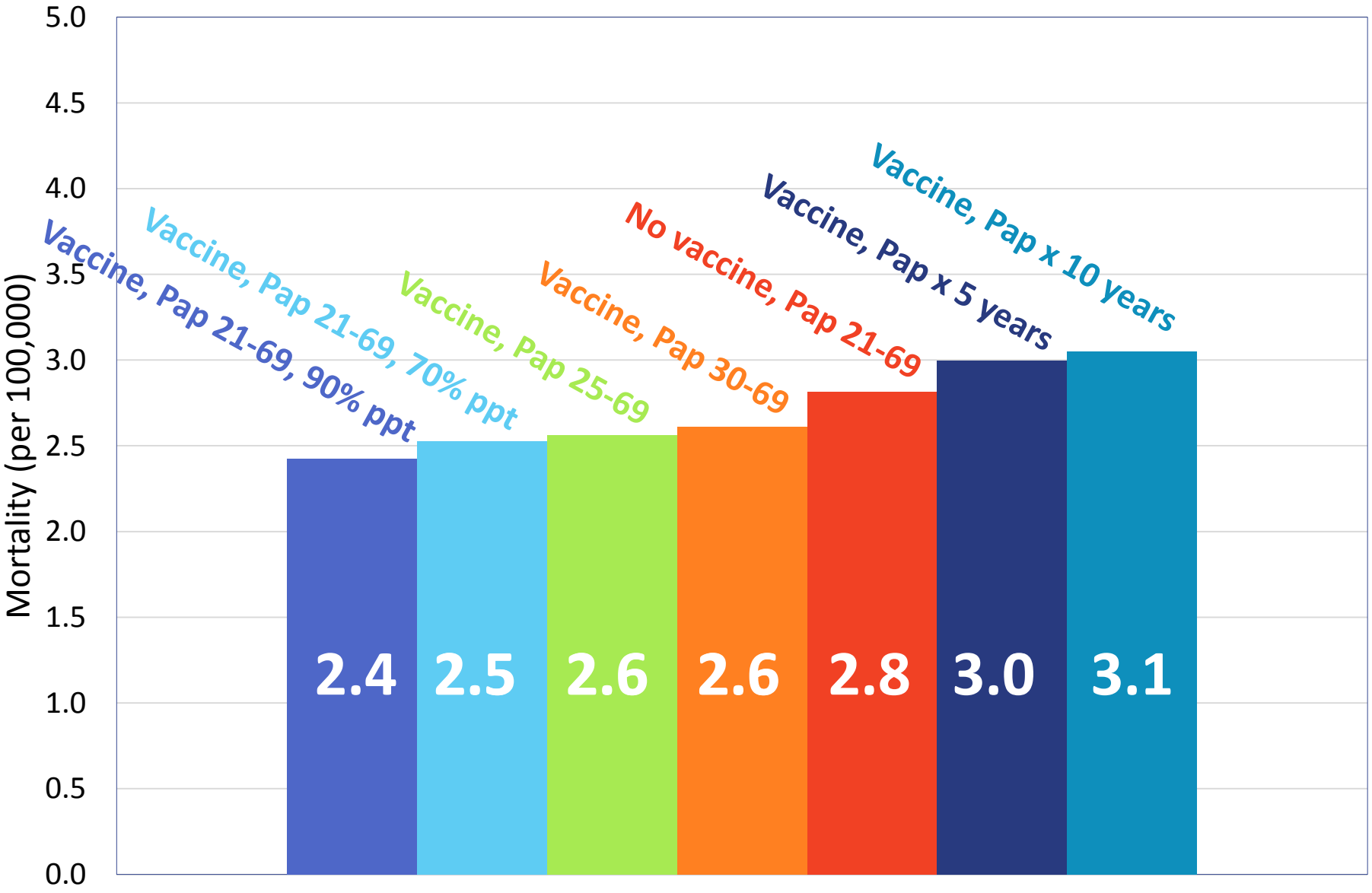
Mortality per 100,000 in 2037



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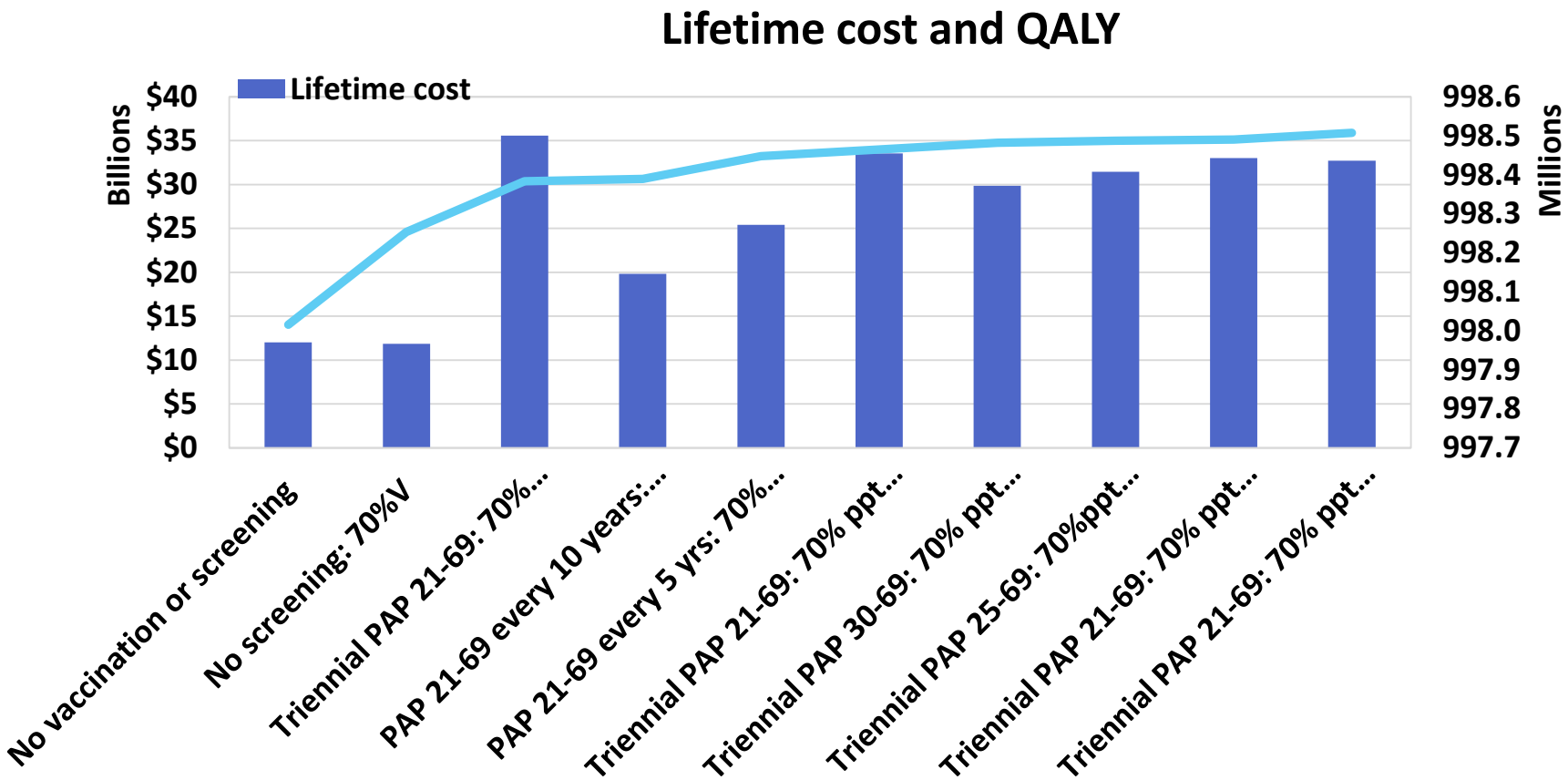
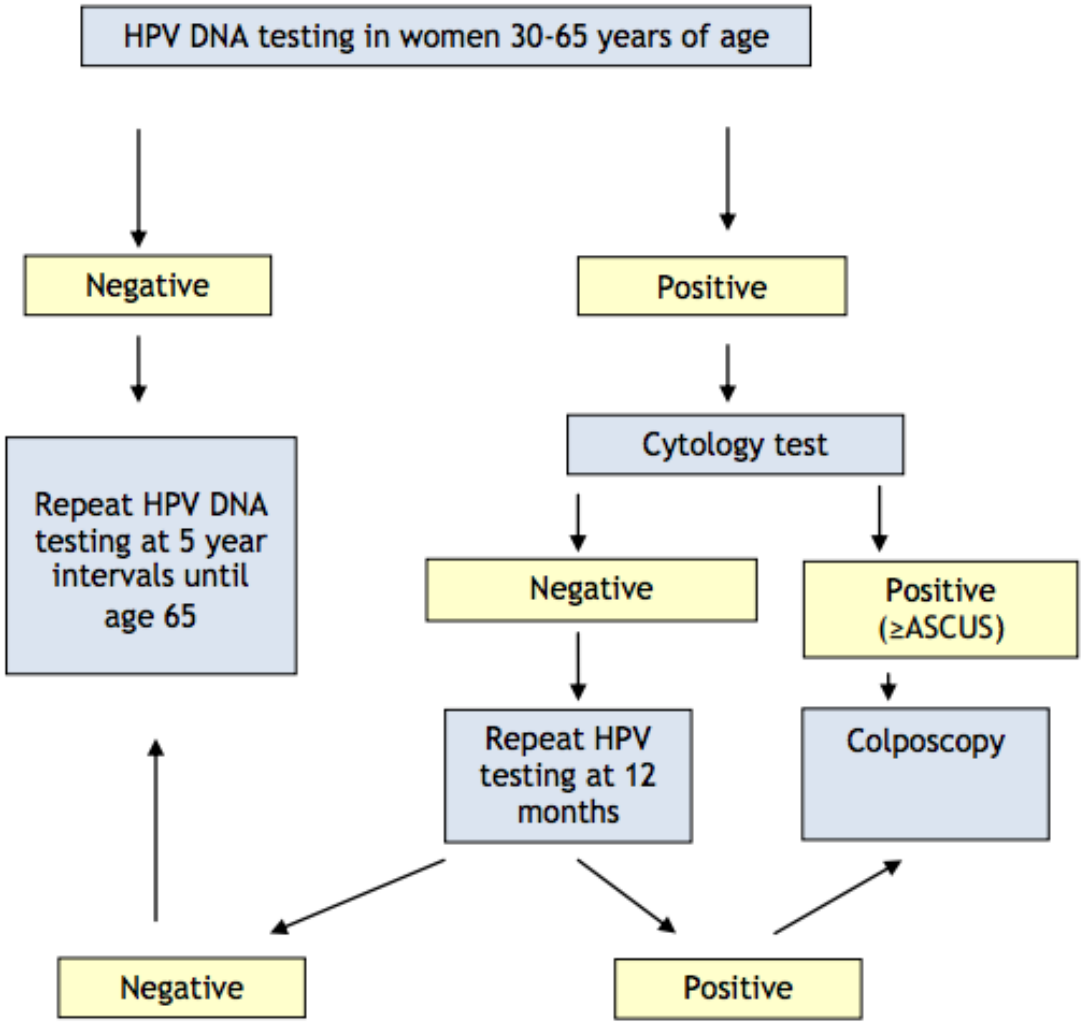

Lifetime cost and QALY
Lifetime cost
Billions
$40
$35
$30
$25
$20
$15
$10
$5
$0
998.6
998.5
998.4
998.3
998.2
998.1
998.0
997.9
997.8
997.7
Millions
No vaccination or screening
No screening: 70%V
Triennial PAP 21-69: 70%...
PAP 21-69 every 10 years:...
PAP 21-69 every 5 yrs: 70%...
Triennial PAP 21-69: 70% ppt...
Triennial PAP 30-69: 70% ppt...
Triennial PAP 25-69: 70%ppt...
Triennial PAP 21-69: 70% ppt...
Triennial PAP 21-69: 70% ppt...

* 3% discount

Figure 1: Primary cervical screening with HPV testing (women 30-65)[2] (adapted from Cuzick et al. 2008 (13)).



Murphy et al., Cervical screening: a guideline for clinical practice in Ontario. J Obstet Gynaecol Can, 2012 May; 34(5): 453-8.

Cost of screening test

	Cytology	HPV DNA test
Family physician visit	$67.82	$67.82
Tray fee	$10.99	$10.99
Lab cost - tech	$3.12	$3.12
Lab cost - pathologist	$93.24	$93.24
Test	n/a	$85.67
Total	$175.17	$260.85

Parameter: Cervical cancer screening and pre-cancer treatment costs															
Types of test and treatment in HPV cervical cancer screening	Cytology (PAP) screen	Cytology (PAP) re-assessment	Initial colposcopy (without biopsy)	Re-assessment colposcopy within 6 months (without biopsy)	Re-assessment colposcopy not within 6 months (without biopsy)	Biopsy	HPV test when recent (<=6 months) liquid sample already exists	HPV test when recent (<=6 months) liquid sample does not exist	Observation (do nothing)	Cold knife	Leep	Cryo	Laser	Hysterectomy	Warts removal
Base case scenario (default)	175.17	141.05	955.71	724	656.23	102.71	260.85	260.85	0	1851.23	1887.19	1887.19	1887.19	3068.01	190

View as: **Data** Chart

Parameter: HPV vaccination costs

Vaccine types	Quadrivalent vaccination
Scenario	
Base case scenario (default)	500

Parameter: Sensitivity and specificity of cytology

Cytology type - Conventional cytology	Scenario - Base case scenario (default)							
Cytology result / Progression status	All cells normal	Atypical squamous cells of undetermined significance (ASC-US)	Atypical squamous cells, maybe high grade lesion (ASC-H)	Low grade squamous intra-epithelial lesion (CIN1)	High grade squamous intra-epithelial lesion (CIN2 or CIN3)	Atypical glandular cells (AGC)	Adenocarcinoma in situ (AIS)	Has cervical cancer
No infection and no lesion	97	1.5	0.2	1	0.25	0	0	0.05
Infected but no lesion	97	1.5	0.28	1	0.17	0	0	0.05
Warts	97	1.5	0.28	1	0.17	0	0	0.05
CIN1	41	12	2.83	29	15.17	0	0	0
CIN2	20	5	4.14	20	48.86	0	0	2
CIN3	20	5	2.65	20	50.35	0	0	2
Adenocarcinoma in situ (AIS)	131.86	9.74	2.26	9	84	26.4756	58.5244	5
Cervical cancer	0	6	0.44	9	53.56	0	0	31

Parameter: Sensitivity and specificity of colposcopy

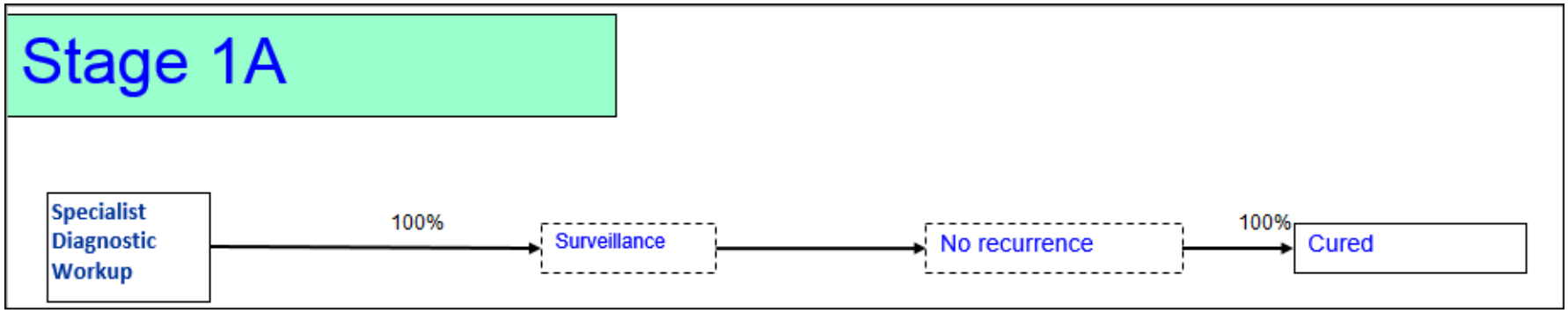
Scenario - Base case scenario (default)

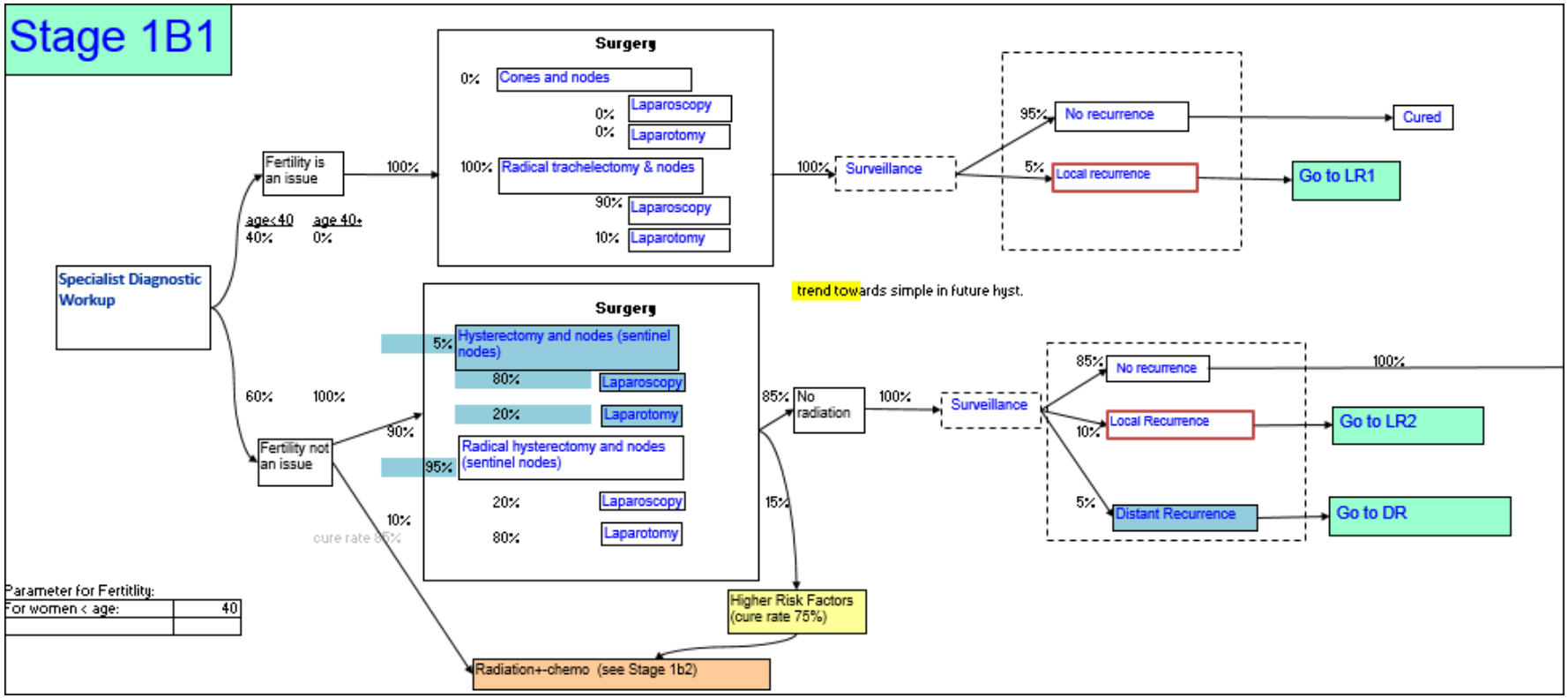
Colposcopy results / Progression status	Less than LSIL	LSIL	CIN2 or CIN3: lesion satisfactory and visible	CIN2 or CIN3: lesion not satisfactory	AIS	Cervical Cancer
No infection and no lesion	88	7	3	2	0	0
Infected but no lesion	88	7	3	2	0	0
Warts	88	7	3	2	0	0
CIN1	22	62	15	1	0	0
CIN2	8	10	47	35	0	0
CIN3	8	10	18	64	0	0
Adenocarcinoma in situ (AIS)	0	0	0	0	1	0
Cervical cancer	0	0	0	0	0	1

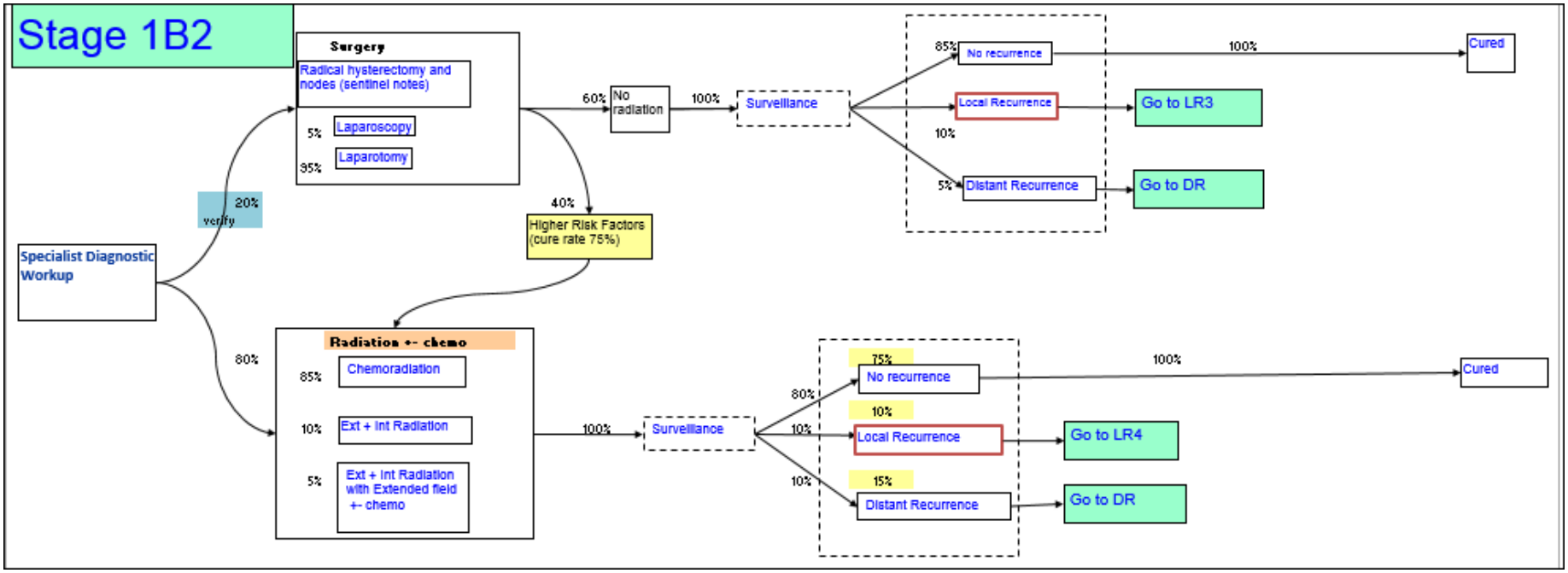
Parameter: Sensitivity and specificity of HPV DNA test

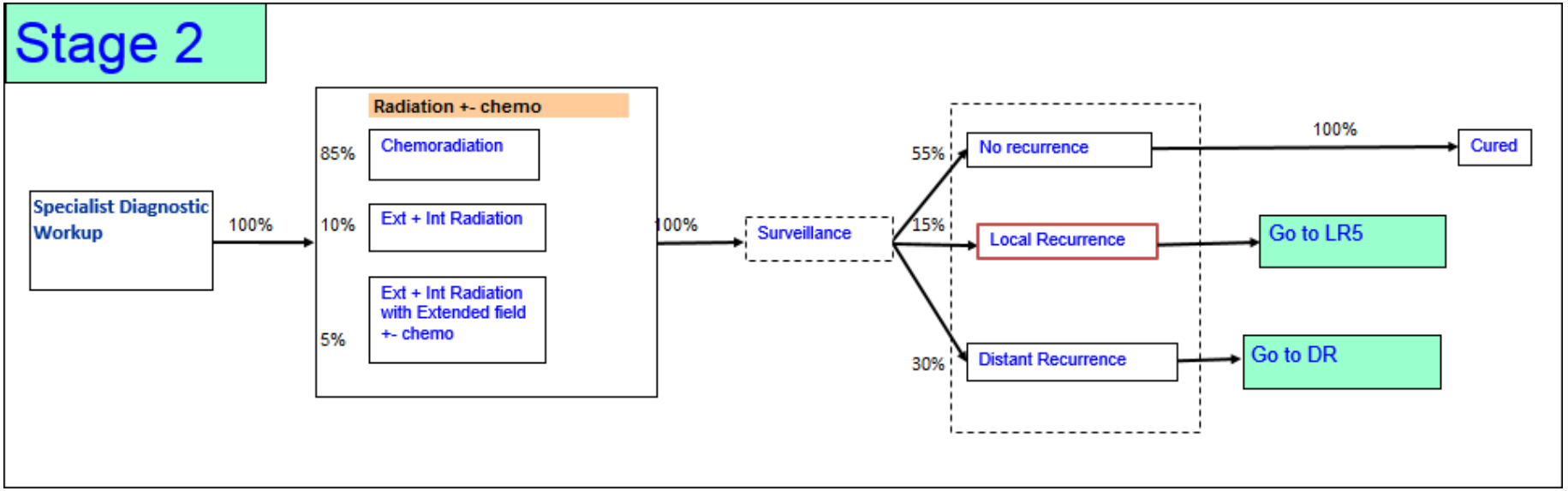
Scenario - Base case scenario (default)								
Progression status / HPV_INFECTION	No infection and no lesion	Infected but no lesion	Warts	CIN1	CIN2	CIN3	Adenocarcinoma in situ (AIS)	Cervical cancer
Not infected with HPV	0	0	0	0	0	0	0	0
Infected with HPV	1	1	1	1	1	1	1	1

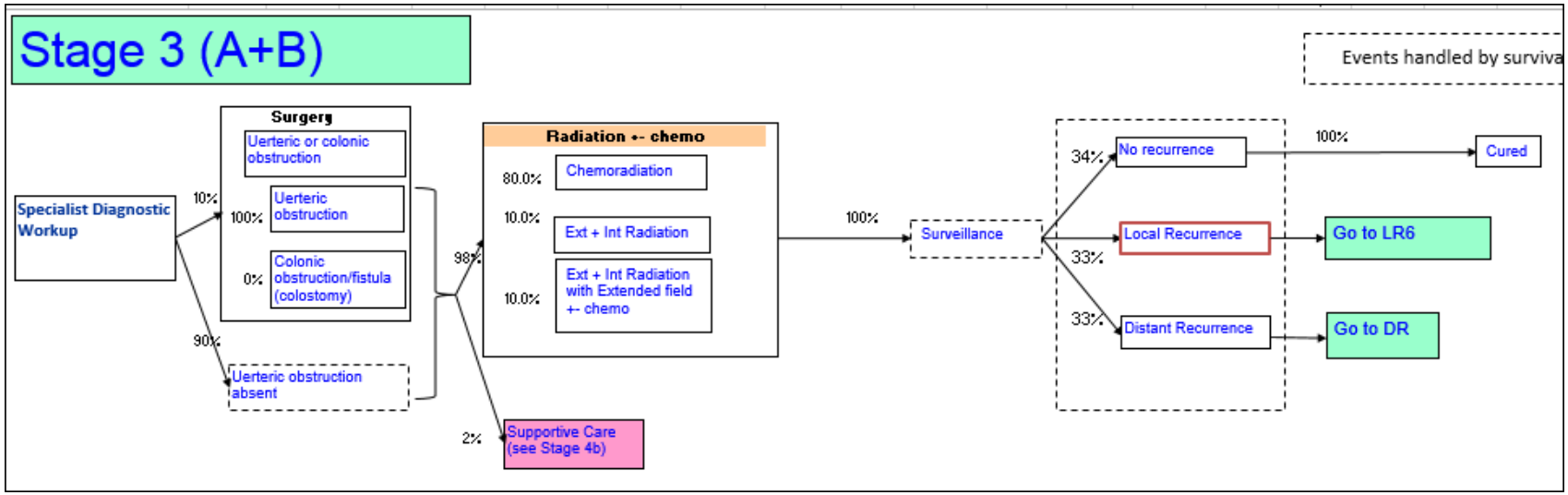
TREATMENT PATHWAYS

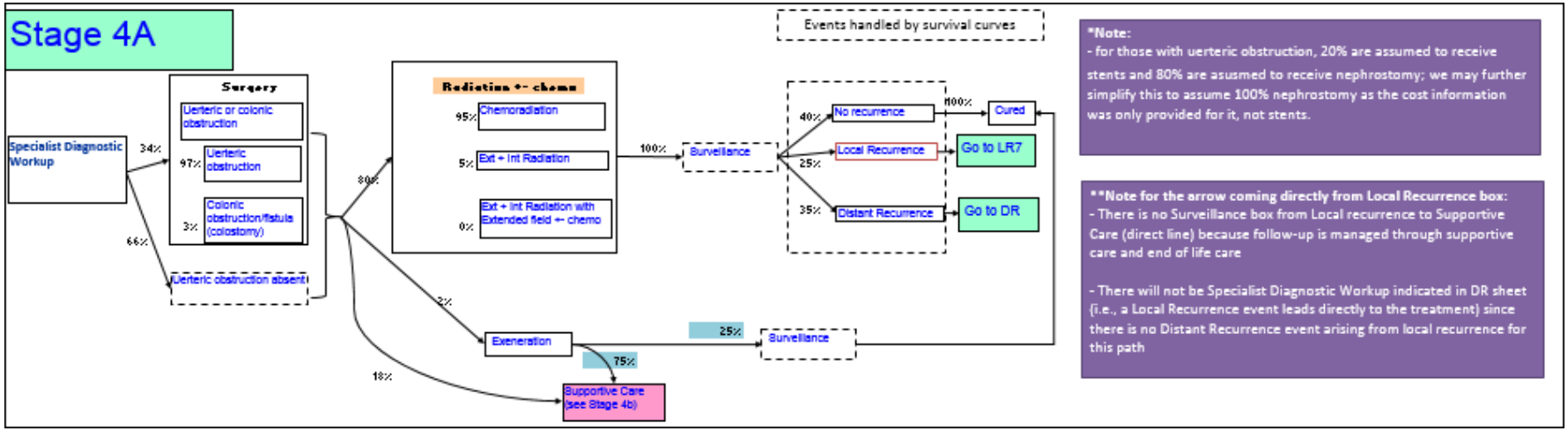

Stage 1A
Specialist Diagnostic Workup
100%
Surveillance
No recurrence
100%
Cured

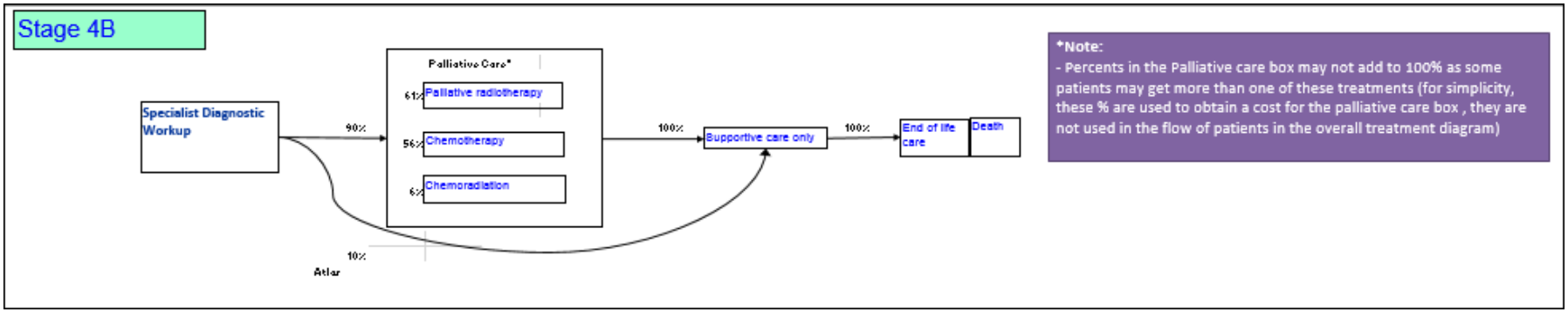

Stage 1B1
Specialist Diagnostic Workup
Fertility is an issue
100%
age<40
40%
age 40+
0%
Surgery
0% Cones and nodes
0% Laparoscopy
0% Laparotomy
100% Radical trachelectomy & nodes
90% Laparoscopy
10% Laparotomy
100% Surveillance
95% No recurrence
Cured
5% Local recurrence
Go to LR1
trend towards simple in future hyst.
60%
100%
Fertility not an issue
90%
10%
cure rate 85%
Surgery
5% Hysterectomy and nodes (sentinel nodes)
80% Laparoscopy
20% Laparotomy
95% Radical hysterectomy and nodes (sentinel nodes)
20% Laparoscopy
80% Laparotomy
85% No radiation
15%
100% Surveillance
85% No recurrence
100%
10% Local Recurrence
Go to LR2
5% Distant Recurrence
Go to DR
Higher Risk Factors (cure rate 75%)
Radiation+-chemo (see Stage 1b2)
Parameter for Fertitlity:
For women < age: 40


Stage 1B2
Surgery
Radical hysterectomy and nodes (sentinel notes)
5%
Laparoscopy
95%
Laparotomy
20%
verify
Specialist Diagnostic Workup
60%
No radiation
100%
Surveillance
85%
No recurrence
100%
Cured
Local Recurrence
Go to LR3
10%
5%
Distant Recurrence
Go to DR
40%
Higher Risk Factors (cure rate 75%)
80%
Radiation +- chemo
85%
Chemoradiation
10%
Ext + Int Radiation
5%
Ext + Int Radiation with Extended field +- chemo
100%
Surveillance
75%
No recurrence
100%
Cured
80%
10%
Local Recurrence
Go to LR4
10%
15%
Distant Recurrence
Go to DR

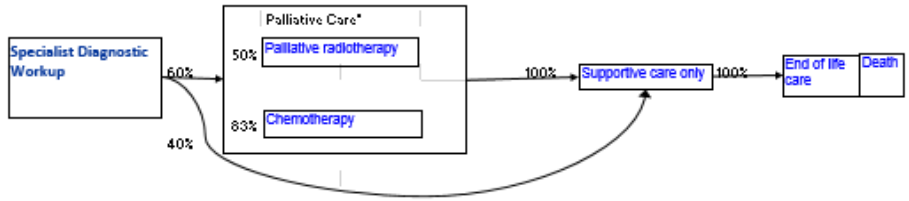

Stage 2
Specialist Diagnostic Workup
100%
Radiation +- chemo
85%
Chemoradiation
10%
Ext + Int Radiation
5%
Ext + Int Radiation with Extended field +- chemo
100%
Surveillance
55%
No recurrence
100%
Cured
15%
Local Recurrence
Go to LR5
30%
Distant Recurrence
Go to DR


Stage 3 (A+B)
Events handled by surviva
Specialist Diagnostic Workup
10%
90%
Surgery
100%
Uerteric or colonic obstruction
Uerteric obstruction
0%
Colonic obstruction/fistula (colostomy)
Uerteric obstruction absent
98%
2%
Supportive Care (see Stage 4b)
Radiation +- chemo
80.0%
Chemoradiation
10.0%
Ext + Int Radiation
10.0%
Ext + Int Radiation with Extended field +- chemo
100%
Surveillance
34%
No recurrence
100%
Cured
33%
Local Recurrence
Go to LR6
33%
Distant Recurrence
Go to DR


Stage 4A
Events handled by survival curves
Surgery
Specialist Diagnostic Workup
34%
97%
Ureteric or colonic obstruction
Ureteric obstruction
3%
Colonic obstruction/fistula (colostomy)
66%
Ureteric obstruction absent
80%
Radiation +- chemo
95%
Chemoradiation
5%
Ext + Int Radiation
0%
Ext + Int Radiation with Extended field +- chemo
100%
Surveillance
40%
No recurrence
100%
Cured
25%
Local Recurrence
Go to LR7
35%
Distant Recurrence
Go to DR
2%
Exenteration
25%
Surveillance
75%
18%
Supportive Care (see Stage 4b)
*Note:
- for those with uerteric obstruction, 20% are assumed to receive stents and 80% are asusmed to receive nephrostomy; we may further simplify this to assume 100% nephrostomy as the cost information was only provided for it, not stents.
**Note for the arrow coming directly from Local Recurrence box:
- There is no Surveillance box from Local recurrence to Supportive Care (direct line) because follow-up is managed through supportive care and end of life care
- There will not be Specialist Diagnostic Workup indicated in DR sheet (i.e., a Local Recurrence event leads directly to the treatment) since there is no Distant Recurrence event arising from local recurrence for this path


Stage 4B
Specialist Diagnostic Workup
90%
Palliative Care*
61%
Palliative radiotherapy
56%
Chemotherapy
6%
Chemoradiation
10%
Atlar
100%
Supportive care only
100%
End of life care
Death
*Note:
- Percents in the Palliative care box may not add to 100% as some patients may get more than one of these treatments (for simplicity, these % are used to obtain a cost for the palliative care box , they are not used in the flow of patients in the overall treatment diagram)

Distant recurrence



***Note:**
- Percents in the Palliative care box may not add to 100% as some patients may get both treatments (for simplicity, these % are used to obtain a cost for the palliative care box , they are not used in the flow of patients in the overall treatment diagram)