

New Cervical Screening Guidelines

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Faculty/Presenter Disclosure

- **Speaker:** Dr. James Dickinson
- **Relationships with commercial interests:**
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- Dr. James Dickinson is presenting at this Program on a voluntary basis.
- **Potential for conflict(s) of interest: None**

Conflict of interest

- No funding for research on cervical cancer
- No commercial funding
- Previously member of Canadian Task Force on Preventive Health Care
- Have been supported to attend meetings by College of Family Physicians of Canada as their representative.
- Have wife and daughters. So it is indirectly personal.

Learning objectives

1. To understand the biology and epidemiology of cancer that informs screening recommendations
2. To balance the value of cervical screening against the harms of excess or inappropriate screening.
3. To use the changes in distribution of screening behaviours to choose how to focus screening in practice.
4. Identify personal screening behaviour that should change, to provide maximum benefit to patients.

Questions

Why should cervical screening:

Be repeated around every 3 years?

Start around age 25?

Stop around age 70?

How can we provide greatest benefit and least harm?

How can we change doctor and patient behaviour?

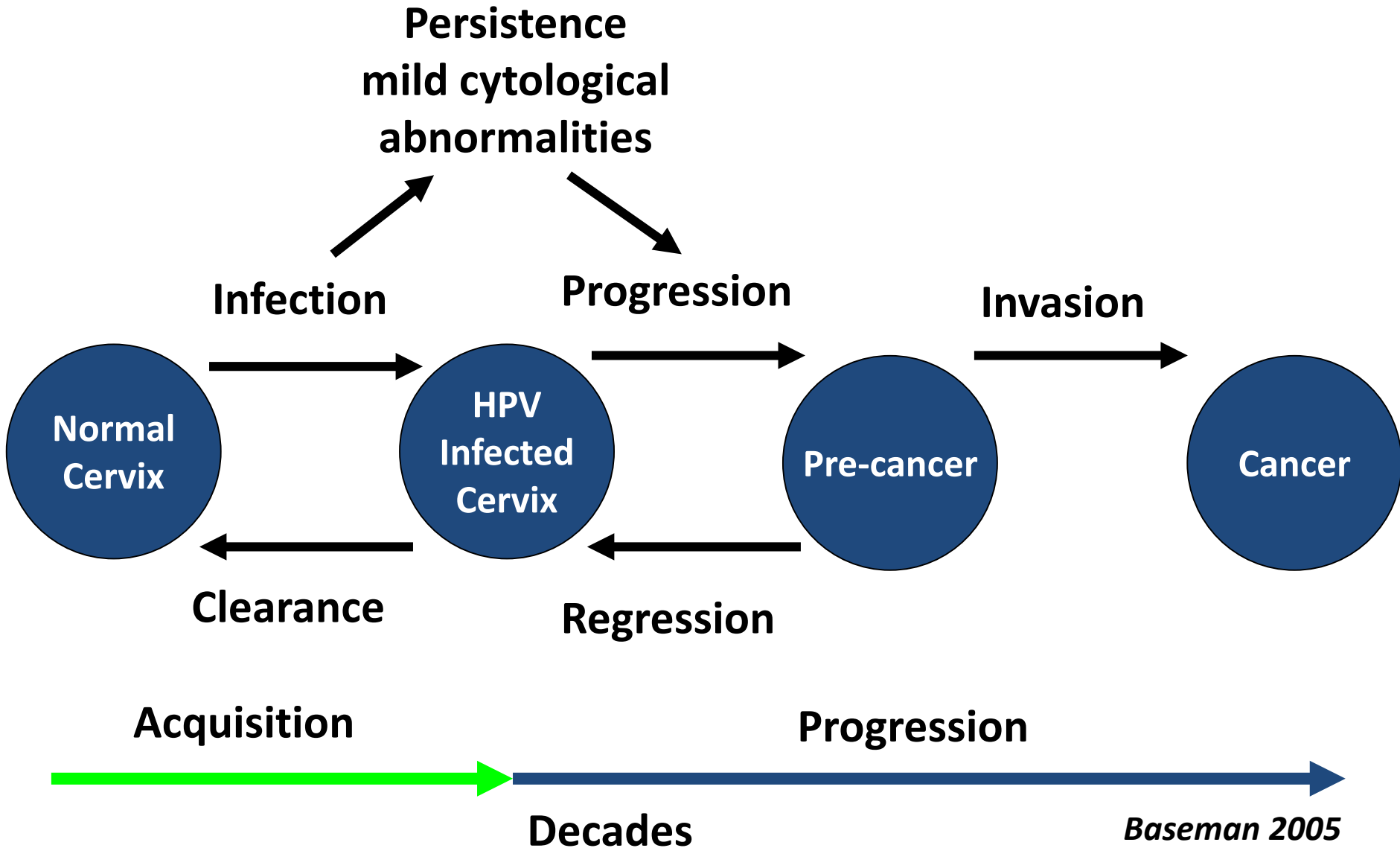
Biology

- Papilloma virus infection (HPV).
 - Condyloma, Warts
- Natural history: resolution
- **Some** may go on to cause cancer

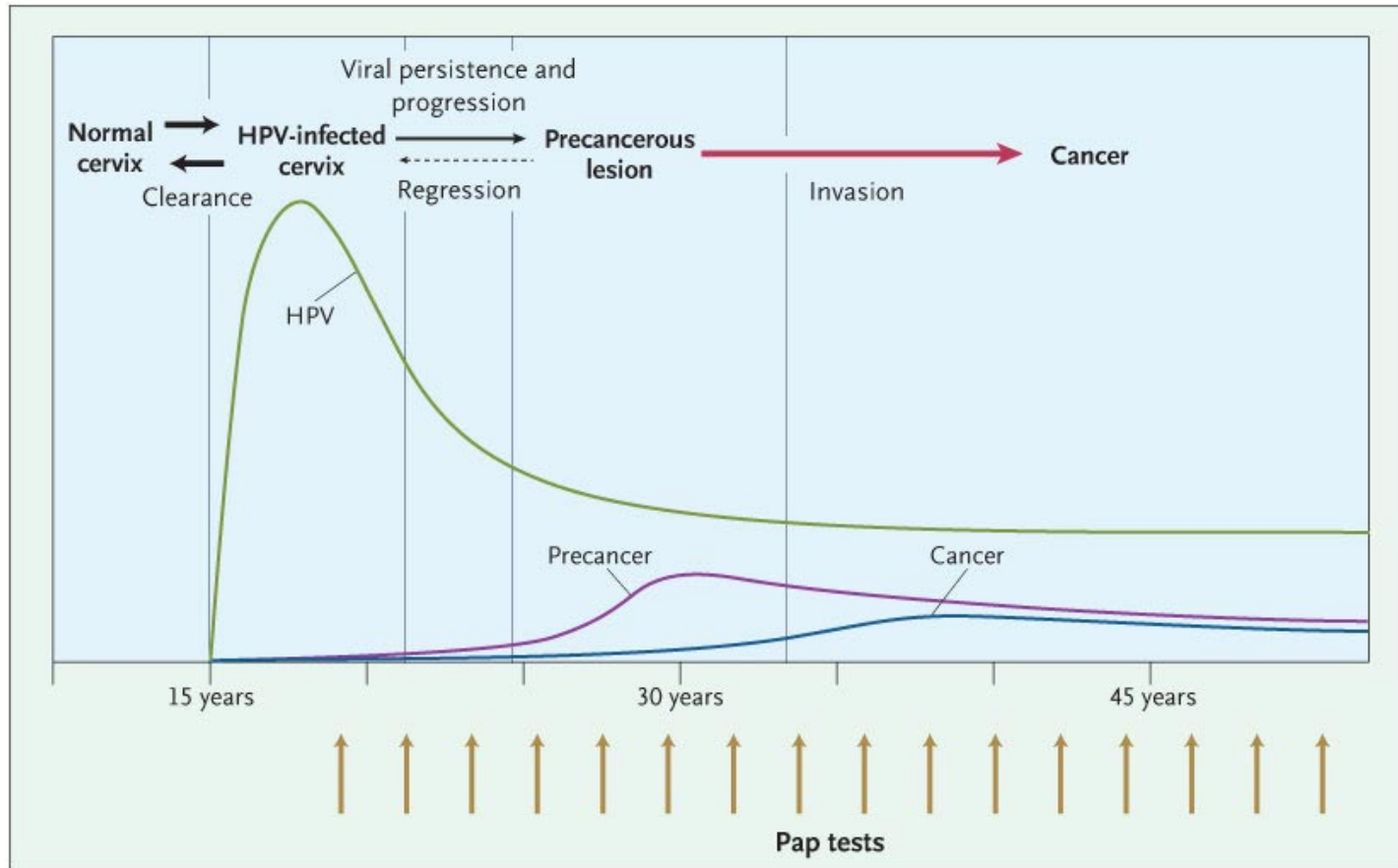
- HPV testing: using virus as marker for lab tests
 - Instead of human cytology by microscopy

- HPV immunization: to prevent infection

Cervical Cancer Natural History



Natural history of cervical cancer



Adapted from: Schiffman M. Castle PE. The promise of global cervical-cancer prevention. NEJM. 2005. 353(20):2101-4.

Interval
1 vs 3

Evidence re Interval

- Case control studies Multi-centre Europe
- % protection after normal pap test

Interval Months	IARC 1986	Van den Akke 2003
0-12	93	94
13-24	92	92
25-36	87	85
37-48	81	
49-60	64	80

Screening policy interval

Began with annual smears

- Walton report 1976: 3 yearly
 - Stop after hysterectomy, or age 60
- Canadian Task Force: 1991
 - 3 yearly from sexually active
 - 18 to 69
- Sabotaged immediately

Annual Screening

“The screening interval of every 3 years after satisfactory results from two Pap....can only be justified if a mechanism is in place to ensure strict patient compliance and optimal laboratory services.

Until such facilities are in place, routine screening at annual intervals should be a continued standard of practice in all women who have been sexually active.”

When should pap tests start?

Sunnybrook and Women's Health Sciences Centre

<http://www.womenshealthmatters.ca/index.cfm>

All women should have regular Pap smears starting at the age of 18 or when they become sexually active. Many physicians believe that even virginal women should begin regular Pap tests at the age of 18. Women who have had a hysterectomy (surgical removal of the uterus) and those past menopause still need to have regular Pap tests. Women who have had four normal Pap tests in the previous ten years may discontinue Pap tests at the age of 70.

Risk after First Sexual Activity

- Combined 20 studies different countries
- Odds ratio proportional to square of time since first intercourse to age 45.
 - Then flattens out.
- *Lower* infection rate if first intercourse close to menarche

Plummer M, Peto J, Francheschi S. Time since first intercourse and the risk of cervical cancer. *Int J cancer* 130, 2638-2644 (2012)

How long does it take from first sexual experience to invasive cancer?

Puget Sound area: all cases of invasive SCC.

63% participation rate.

N= 165: age range 22-35yrs, 168: range 36-53 yrs.

Interval age first intercourse to invasive cancer: 4 to 35 years.

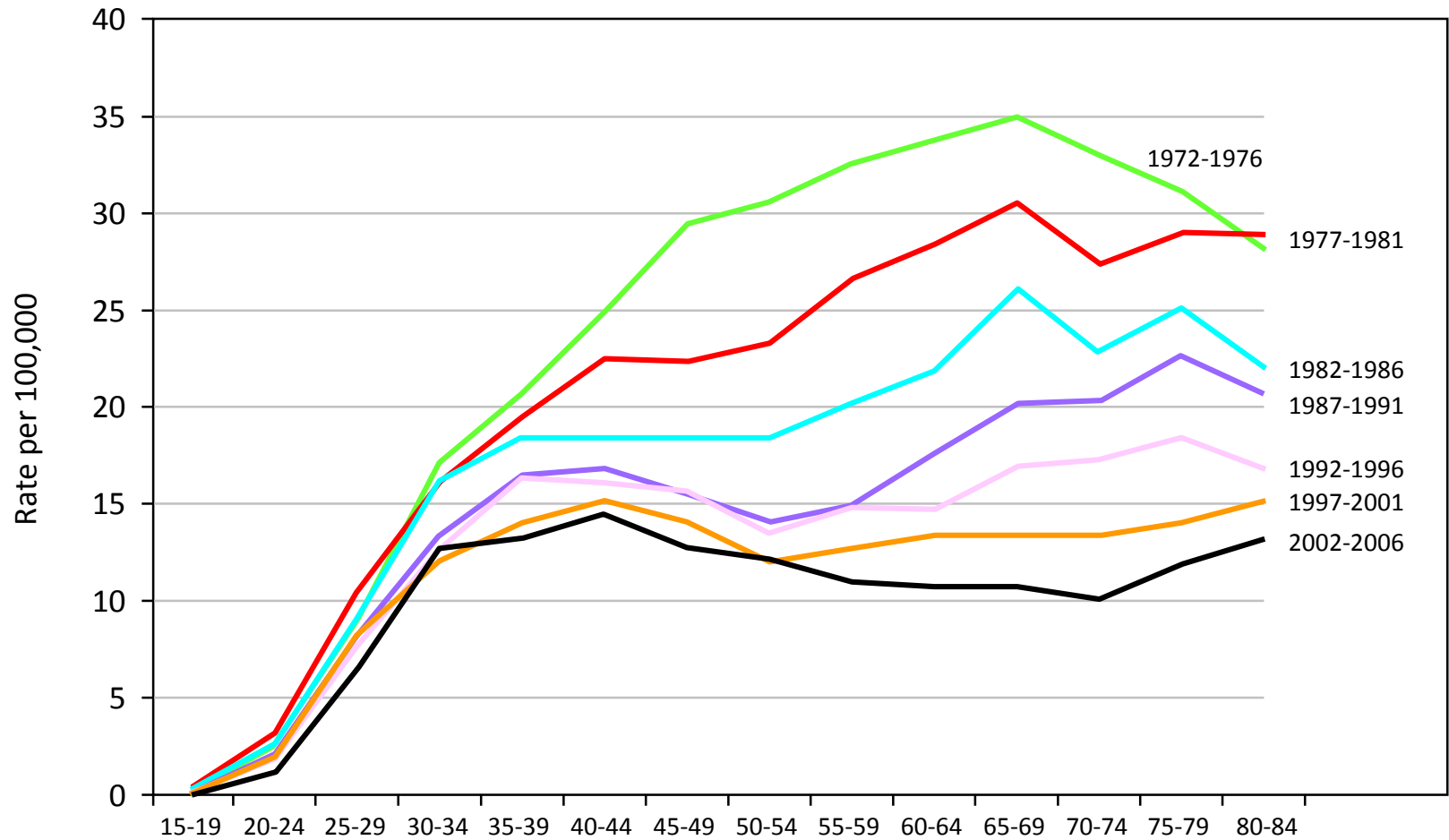
Young group: 20 (12%) 4-10 yrs.

Edelstein ZR, Madeleine MM, Hughes JP et al

Age of diagnosis of squamous cell cervical carcinoma and early sexual experience.

Cancer Epidemiol Biomarkers Prev 2009;18(4) 1070-6

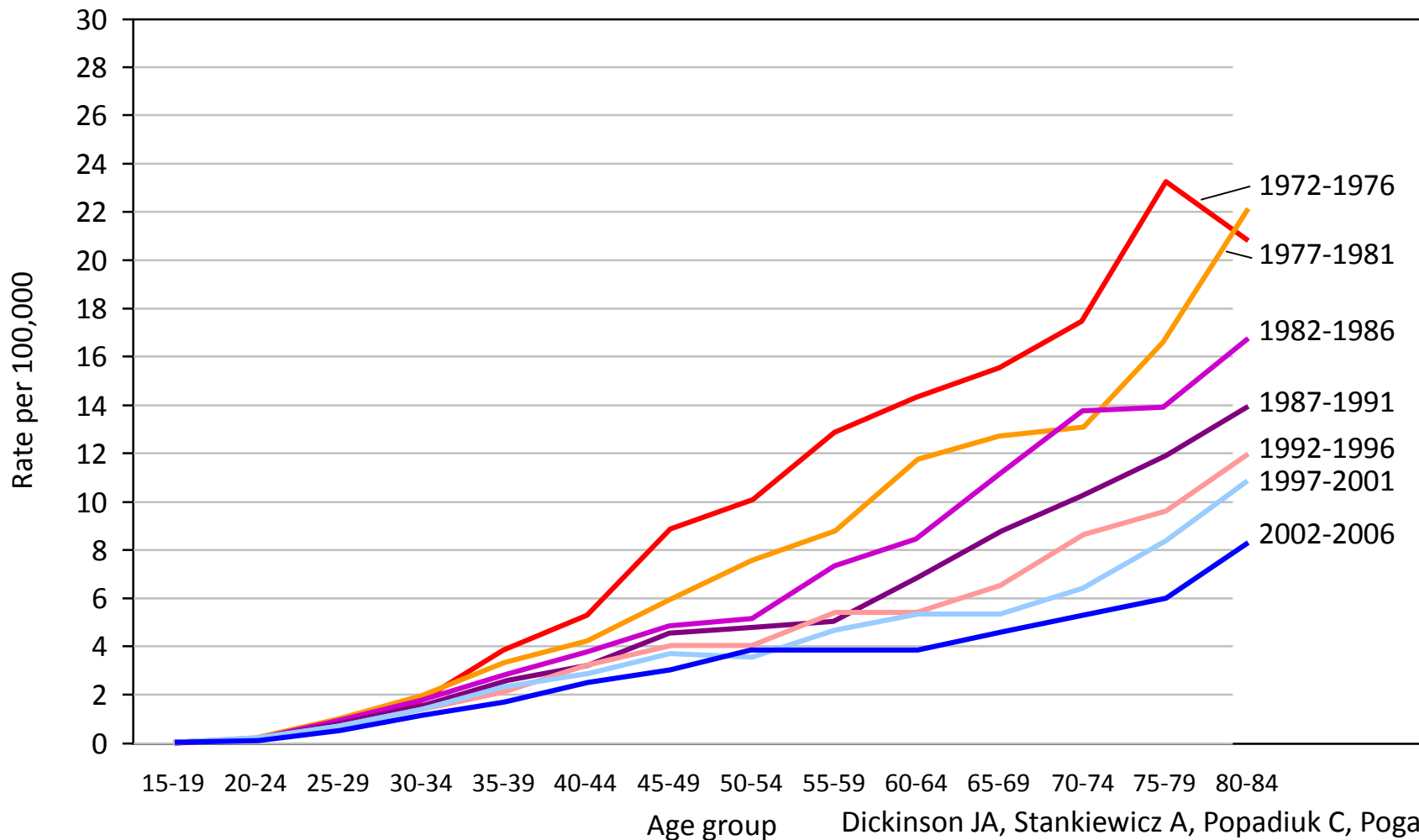
Age-Specific Incidence of Invasive Cervical Cancer in Canada, 1972-2006



Age of group (years)

Dickinson JA, Stankiewicz A, Popadiuk C, Pogany L, Onysko J Miller AB. BMC Public Health 2012 12:992

Mortality from Invasive Cervical Cancer in Canada in Periods from 1972 to 2006



Effectiveness in the young

Incidence

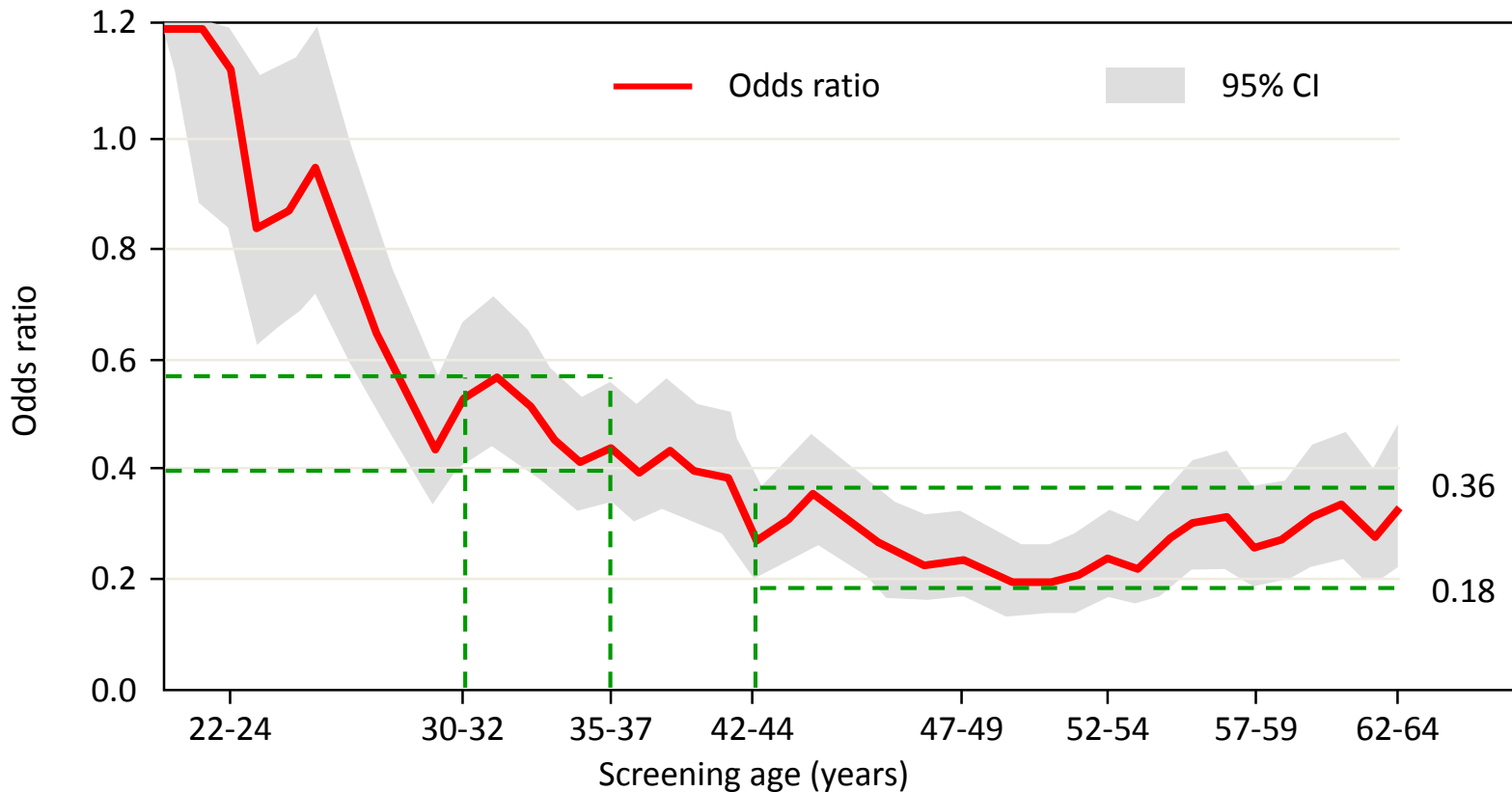
	1972-1976		2002-2006		Change	
	N	Rate/10 ⁵	N	Rate/10 ⁵	%	Absolute
15-19	9	0.3	9	0.2	35	0.1
20-24	143	2.7	70	1.3	52	1.4
25-29	629	9.1	355	6.7	26	2.4
30-34	643	17.1	689	12.7	26	4.4

Effectiveness in the young

Mortality

	1972-1976		2002-2006		Change	
	N	Rate/10 ⁵	N	Rate/10 ⁵	%	Absolute
15-19	*	*	0	0	+	+
20-24	5	0.1	9	0.2	+	+
25-29	30	0.6	31	0.6	+	+
30-34	66	1.8	65	1.2	32	0.6

Value of Smears by Age



Odds ratio for developing invasive cervical cancer stage IA or worse (in the next five year interval) in those screened in a given (three year) age band compared with those not screened in that age band (or in two previous years). Odds ratios plotted for overlapping age bands. Broken lines indicate risk of developing cervical cancer at ages 33-40 and 43-65. Odds ratios and CIs are truncated at 1.2. Based on 4012 cases (including 437 in women under age 30) and 7889 controls

Effect in young women

- Minimal reduction in disease or death.
- BUT: What is the harm: its just a test!

Presentation of Harms

- Guidelines do not tell us much about harms
- Physicians do not like to think about harms
- We do not measure them
- Trial publications do not require them
- So reviews/guidelines cannot include them

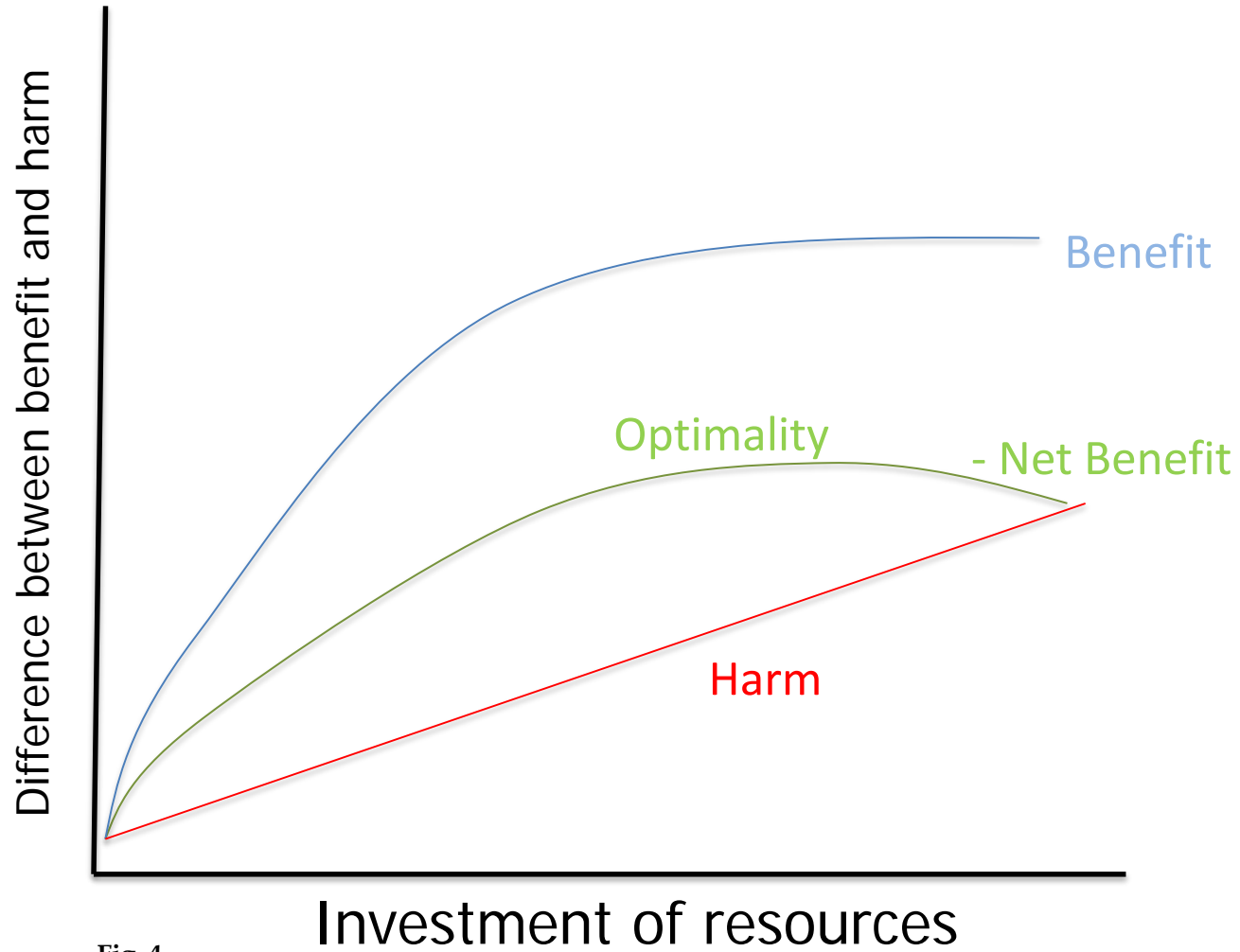
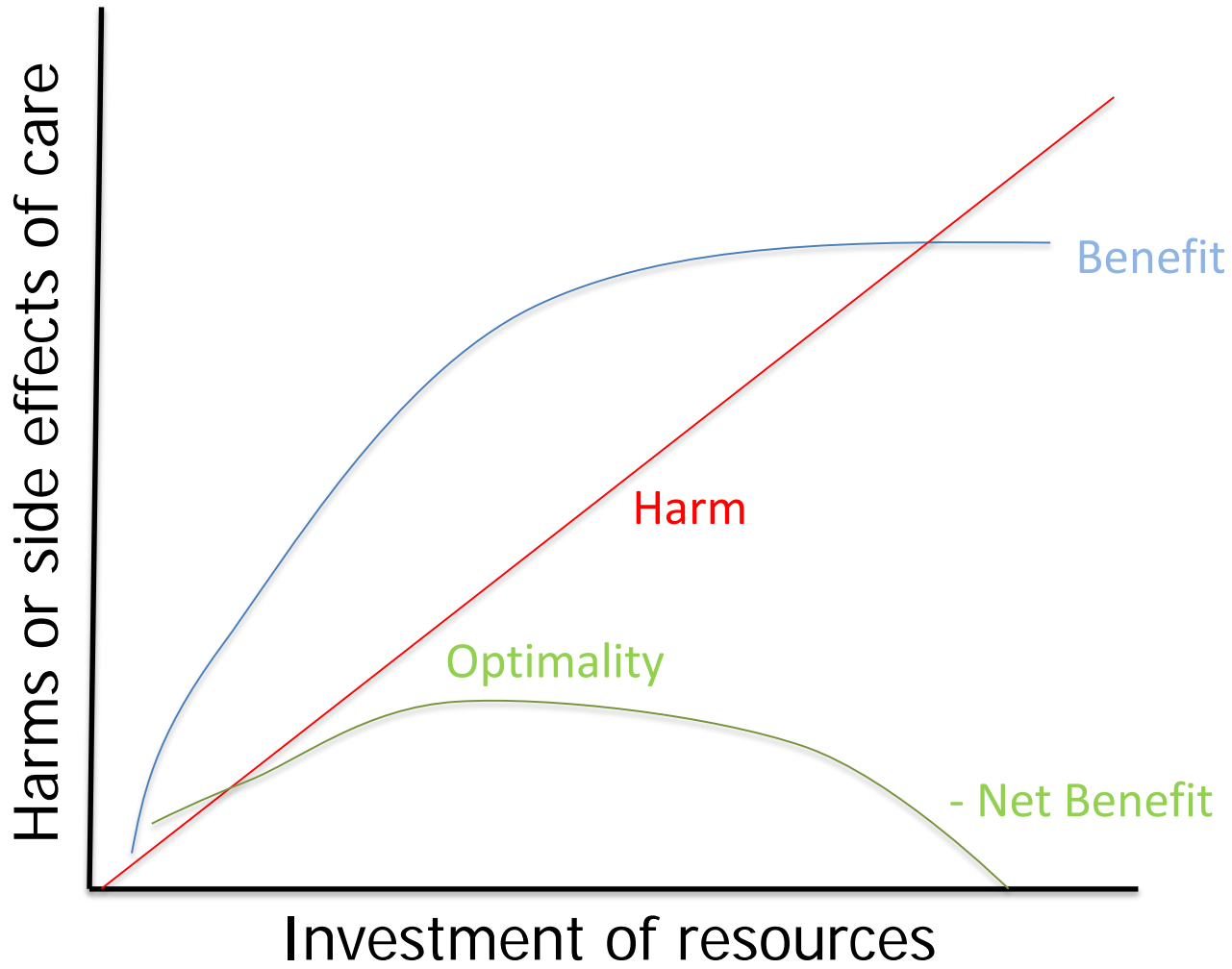


Fig. 4

The relationship between the beneficial and adverse effects of screening- after a certain level of investment, the health gain may start to decline.



Presentation of Harms

- Guidelines do not tell us much about harms
- Physicians do not like to think about harms
- We do not measure them
- Trial publications do not require them
- So reviews/guidelines cannot include them
- Physicians do not notice and recall them

Harm: pelvic exam

- Pelvic exam: no benefit found
- Purported to find ovarian and uterine cancer
- Both are diseases of women >40yrs.
- No evidence that screening works:
 - Uterine: causes bleeding before increased bulk
 - Ovarian: screening trial with ultrasound reduces mortality minimally (many false positives)

Don't do routine pelvic exams!

The most unpleasant component.

<http://canadiantaskforce.ca/guidelines/published-guidelines/pelvic-exam/>

Sawaya, George. Screening Pelvic Examinations: The Emperor's New Clothes, Now in 3 Sizes? doi:10.1001/jamainternmed.2017.0271

Colposcopy Referrals by Age Group in Alberta Cervical Cancer Screening Program (ACCSP) 2008-2013

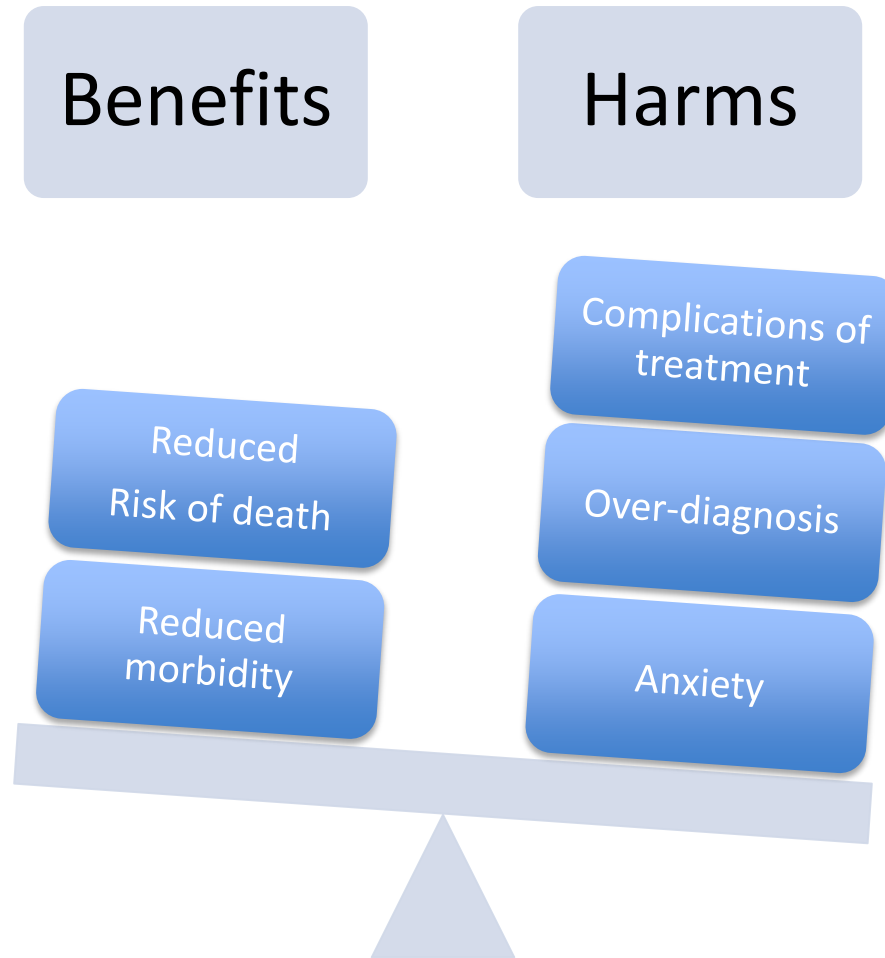
Age group (Years)	Number screened	Number referred for colposcopy	% referred
18 - 20	24,985	497	2.0%
21 - 29	194,499	10655	5.5%
30 - 39	210,833	7671	3.6%
40 - 49	173,359	3624	2.1%
50 - 59	154,986	2412	1.6%
60 - 69	80,344	806	1.0%
>= 70	13,705	166	1.2%
Total	852,711	25831	3.0%

What are the harms?

1. Labelling abnormal
2. Process of diagnosis: colposcopy & biopsy
Discomfort, bleeding and discharge
3. Treatment: LEEP
More bleeding and discharge
4. Cervical incompetence 1.2% ↑
Early Preg Loss
Premature labour: NICU etc
5. Difficult to get insurance

*Affect young, pre-family >>
those with completed family*

Decision balance

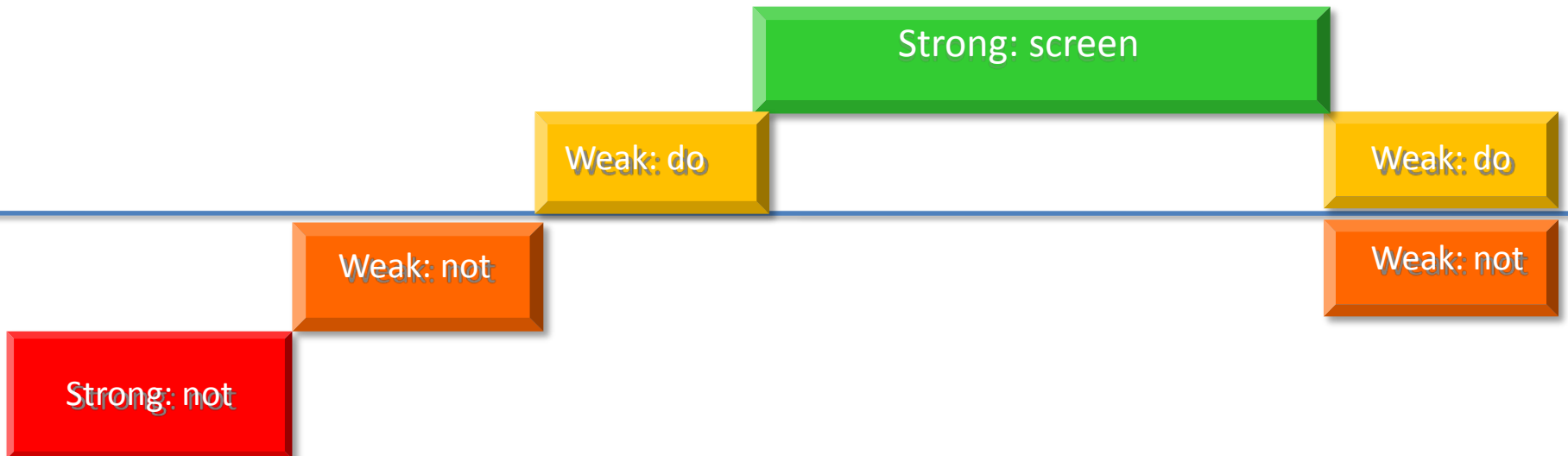


Policy changes

- Alberta 2009: start age 21, q 3 years
 - Other provinces followed: except Man, PEI q2yrs
- Canadian Task Force 2013, q 3 years
 - Strong against under 20
 - Weak against 20-24
 - Weak for 25-29
 - Strong for 30-69
 - Negative for over 70 (unless unscreened)

Canadian Task Force 2013

- GRADE approach: strong/weak
- Decisions reflect continuous change in evidence with age



How is evidence assessed? GRADE

Grading of **R**ecommendations, **A**ssessment, **D**evelopment & **E**valuation

- **High** confidence that the true effect lies close to the estimate of effect
- **Moderate** confidence that the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
- **Low** confidence that the true effect is close to the estimate of the effect. The true effect may be substantially different from the estimate of the effect

GRADE: How is the strength of recommendations determined?

strong or *weak*: Based on four factors:

1. quality of supporting evidence
2. certainty about the **balance between desirable and undesirable** effects
3. certainty / variability in **values and preferences** of individuals
4. certainty about whether the intervention represents a **wise use of resources**

Interpretations of the recommendations

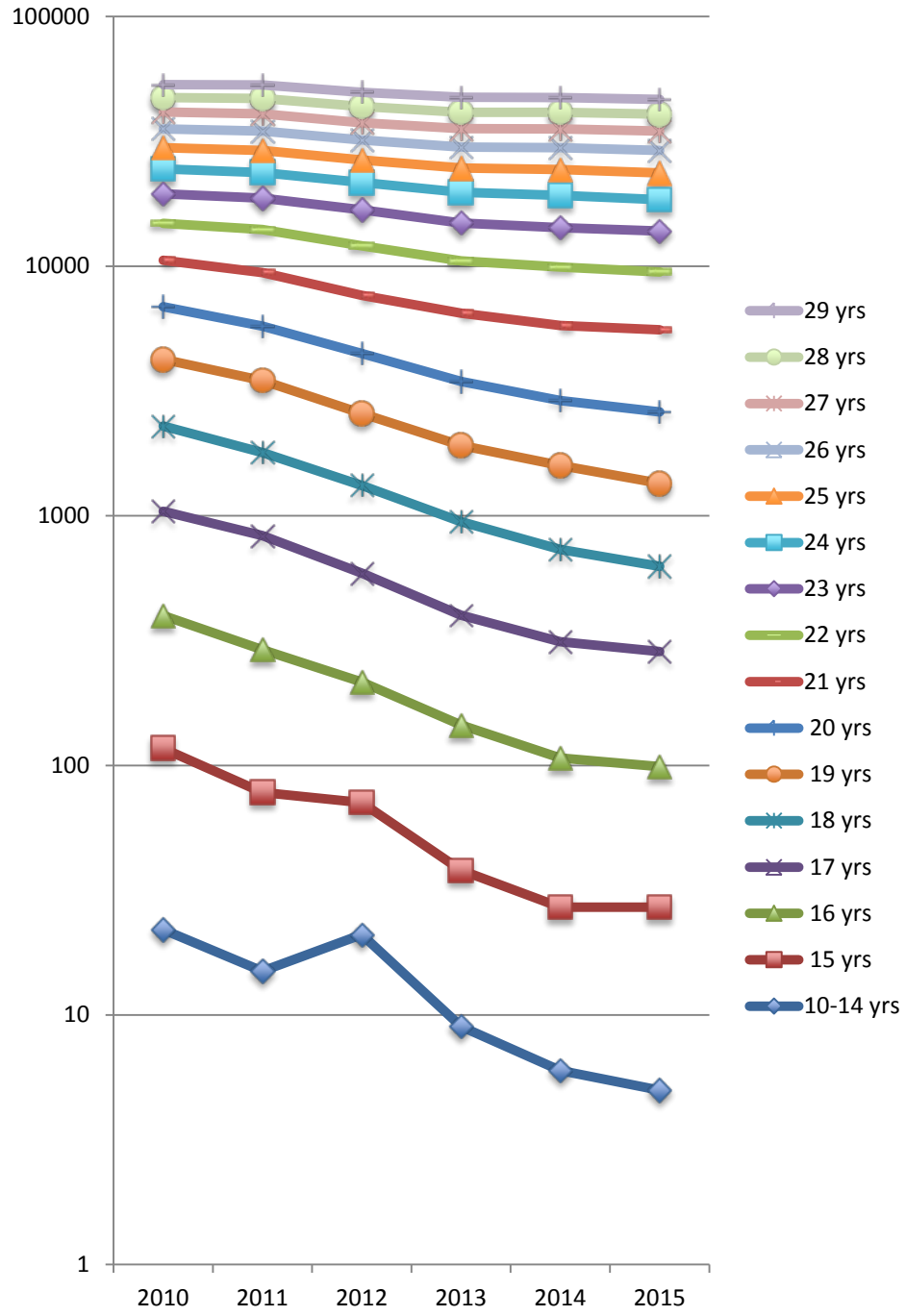
Implications	Strong Recommendation	Weak Recommendations
For patients	<ul style="list-style-type: none">• Most individuals would want the recommended course of action;• only a small proportion would not.	<ul style="list-style-type: none">• The majority of individuals in this situation would want the suggested course of action• but many would not.
For clinicians	<ul style="list-style-type: none">• Most individuals should receive the intervention.	<ul style="list-style-type: none">• Recognize that different choices will be appropriate for individual patients; clinicians must help patients make management decisions consistent with values and preferences.
For policy makers	<ul style="list-style-type: none">• The recommendation can be adapted as policy in most situations.	<ul style="list-style-type: none">• Policy making will require substantial debate and involvement of various stakeholders.

Aftermath of Task Force 2013

- CMAJ Editorial: lukewarm agreement
- Press: mostly positive, some very concerned about cases of invasive cancer among young
- SOGC, GOC, SCColposcopists
 - Reject findings. Recommend age 21
 - No reasoning
- Cancer Care Ontario: Letter to CMAJ: reject, recommend HPV testing, start age 21.
- Provincial guideline groups: to decide

Changes in Pap tests by age: Calgary area 2010-2015

SA Sayed, C Naugler, J Dickinson.
Work in progress

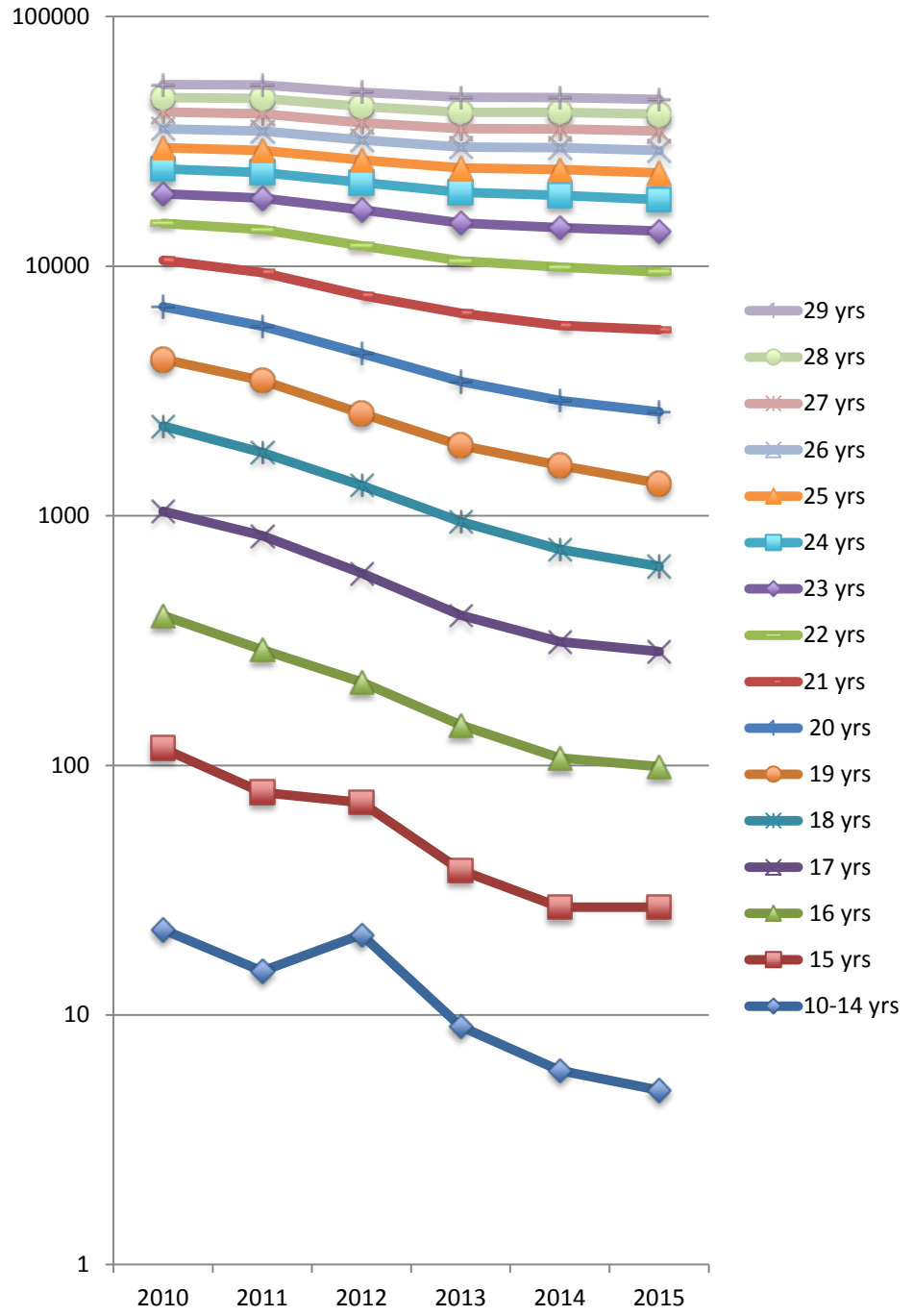


Changes in Pap tests by age: Calgary area 2010-2015

SA Sayed, C Naugler, J Dickinson.
Work in progress

>21: Minimal change in
frequency of testing.

No change in 2013



New Policy Changes

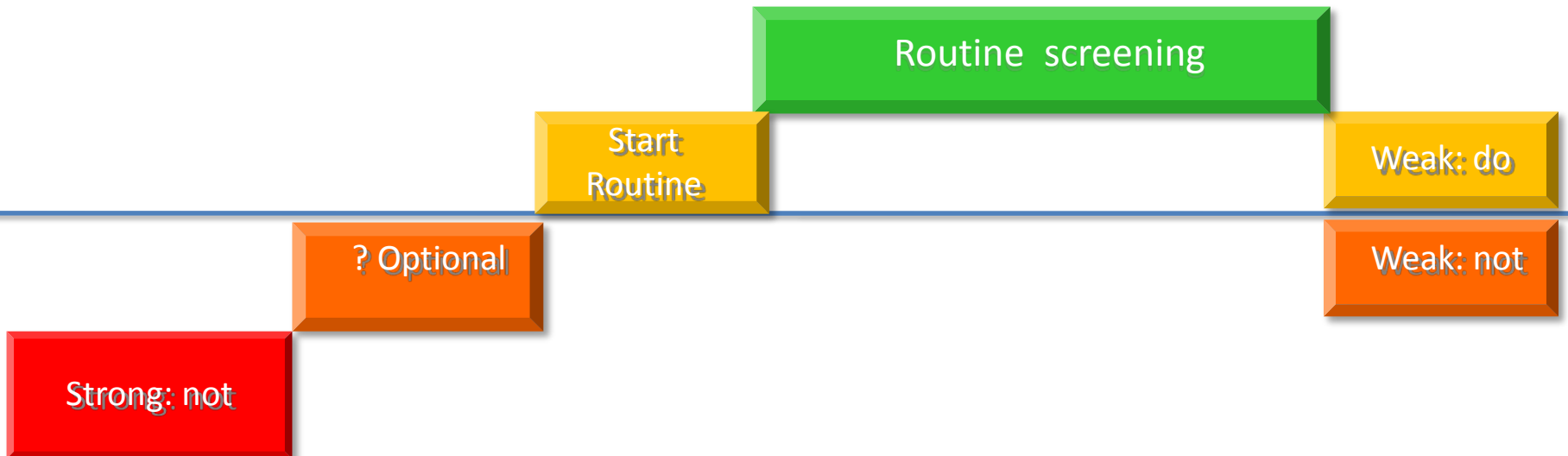
- Alberta Guidelines 2016
 - Start age 25, 3 yrly to 69
- BC Guidelines 2016
 - Start age 25, 3 yrly to 69
- CMAJ Commentary

James A. Dickinson, Gina Ogilvie, Dirk Van Niekerk, and Cathy Popadiuk. Evidence that supports policies to delay cervical screening until after age 25 years

CMAJ March 13, 2017 189:E380-E381; doi:10.1503/cmaj.160636

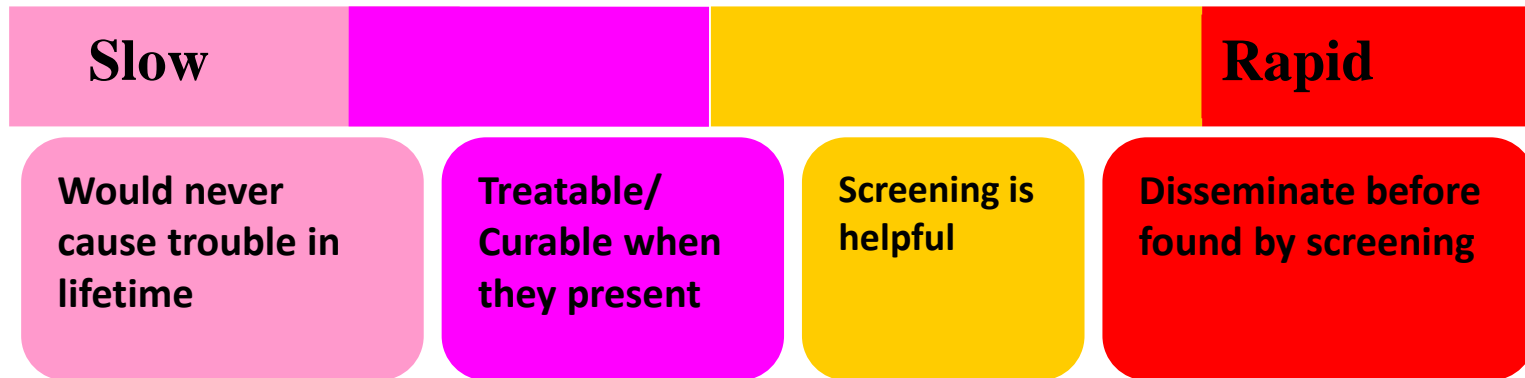
Alberta TOP 2016

- Yes/No
- Simple communication of evidence/policy



Who Does Screening Help?

Spectrum of Disease



Why is it so?

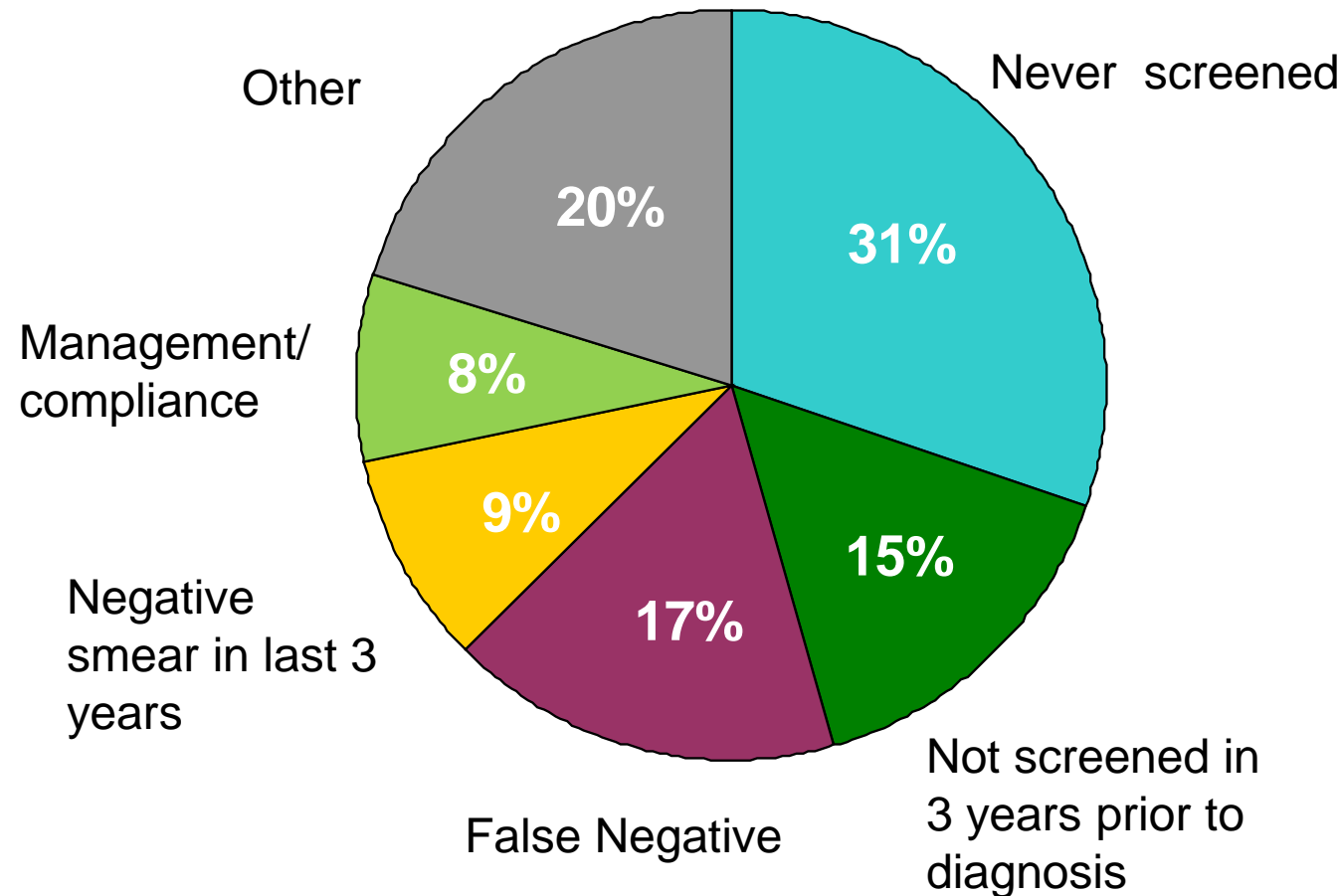
- Screening works for *common chronic* disease
- Range of growth rates
- Cannot work for rapidly developing disease
 - Disseminated before surgery
- No point for very slow disease
 - Still treatable at late stage
 - May never kill
- If too rare, not worthwhile

Ethics of prevention

- When a patient comes to us clinically with symptoms, we must do our best to relieve them and help.
- When we tell someone that they should have a preventive action, we are offering a small chance of future gain against an immediate cost, and measurable small chance of danger.

How Effective is Screening?

Alberta Women with Invasive Cervical Cancer

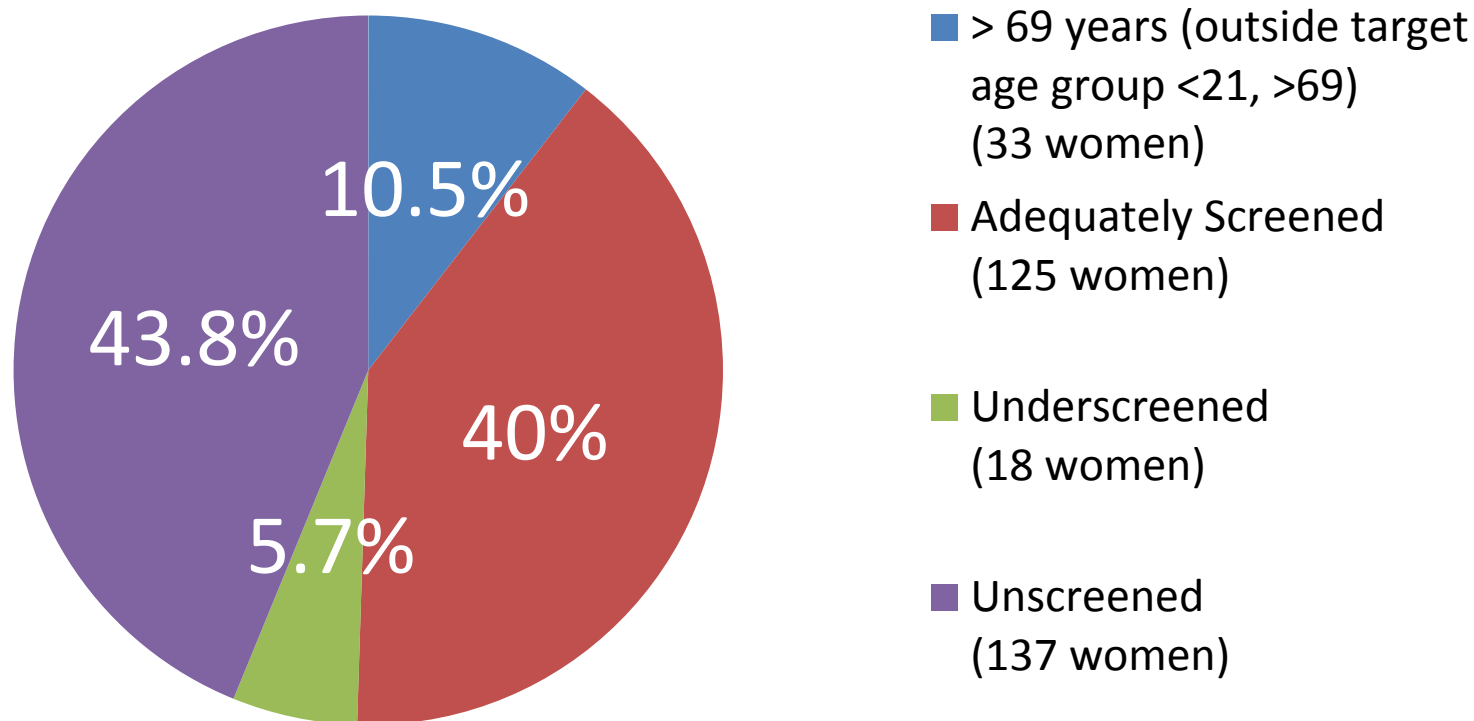


Underscreened:

- Older women
- Rural women
- Aboriginal women
- Recent immigrants
- Lower education
- Lower income

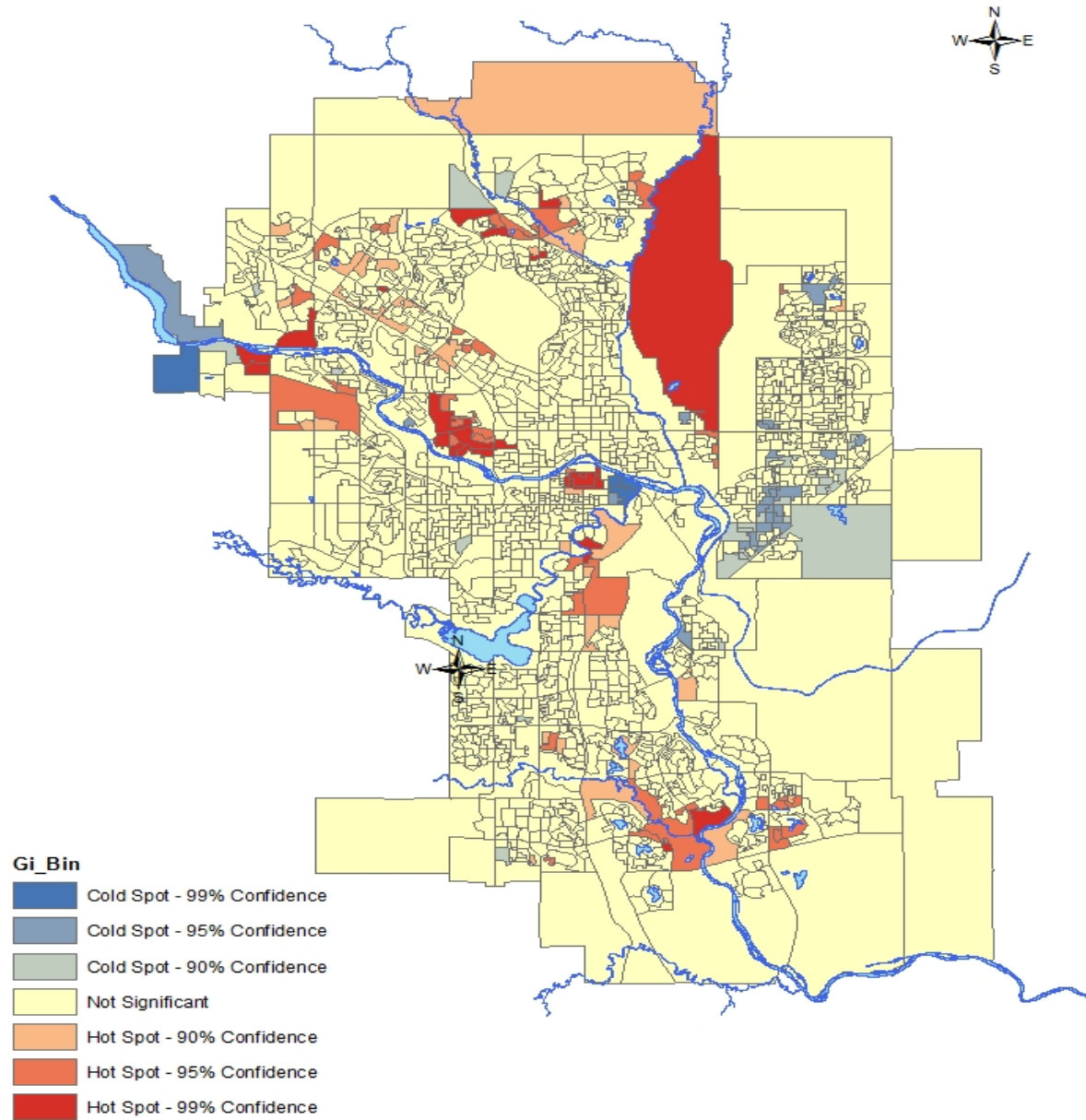
Screening History of 313 cases of invasive cancer in Southern Alberta 2009-2012

Screened / Unscreened



Mema SC, Nation J, Yang H, Waghray R, Sun MC, Xu L, et al. Screening History in 313 Cases of Invasive Cancer: A Retrospective Review of Cervical Cancer Screening in Alberta, Canada. J Low Genit Tract Dis. 2016 Nov 7;

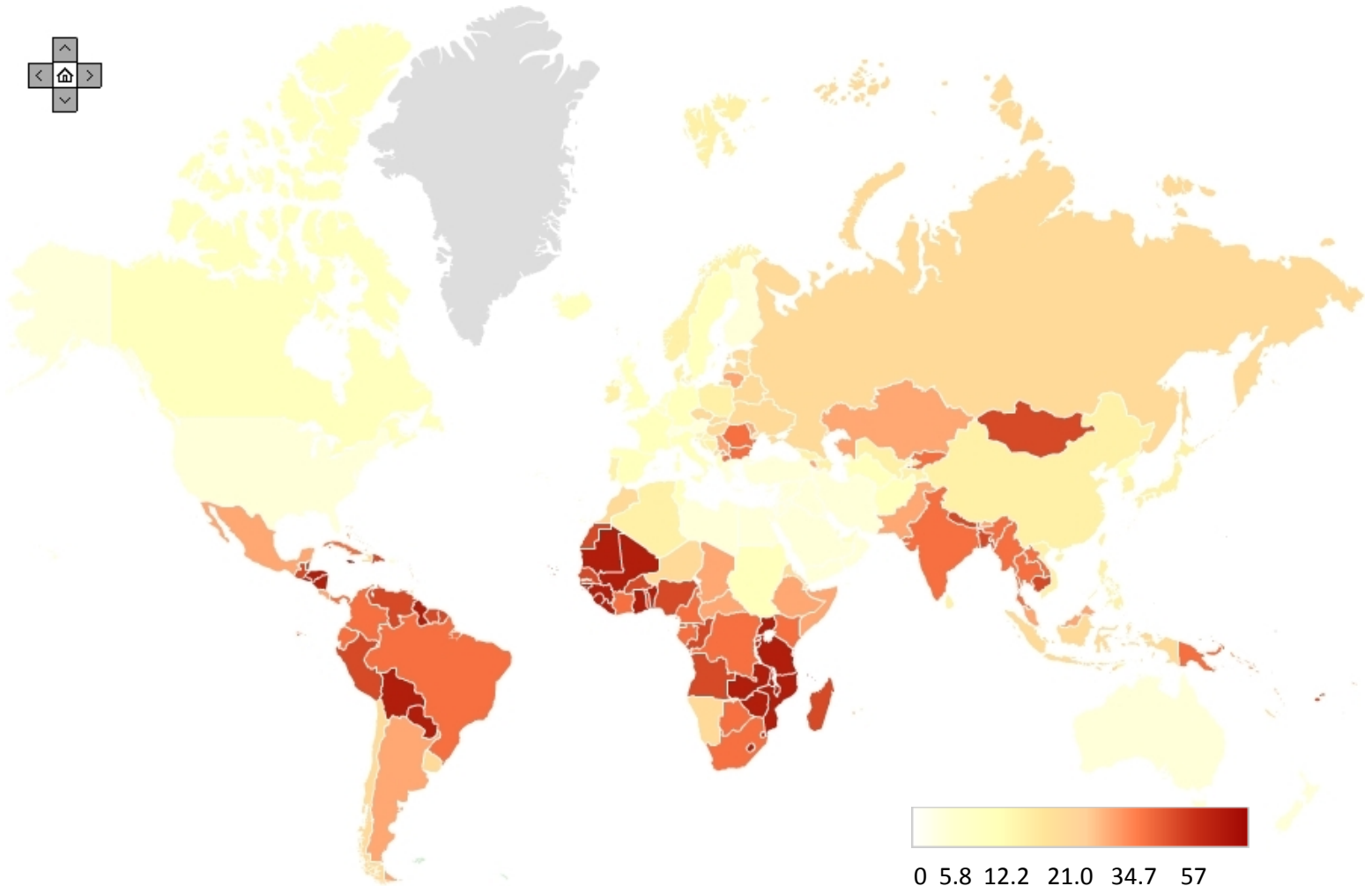
PAP TEST RATE YEAR 25 TO 69



Underscreening

- Lower social status
- North East
- Immigrant: esp. South Asia, Middle East, Africa
- Note not Chinese

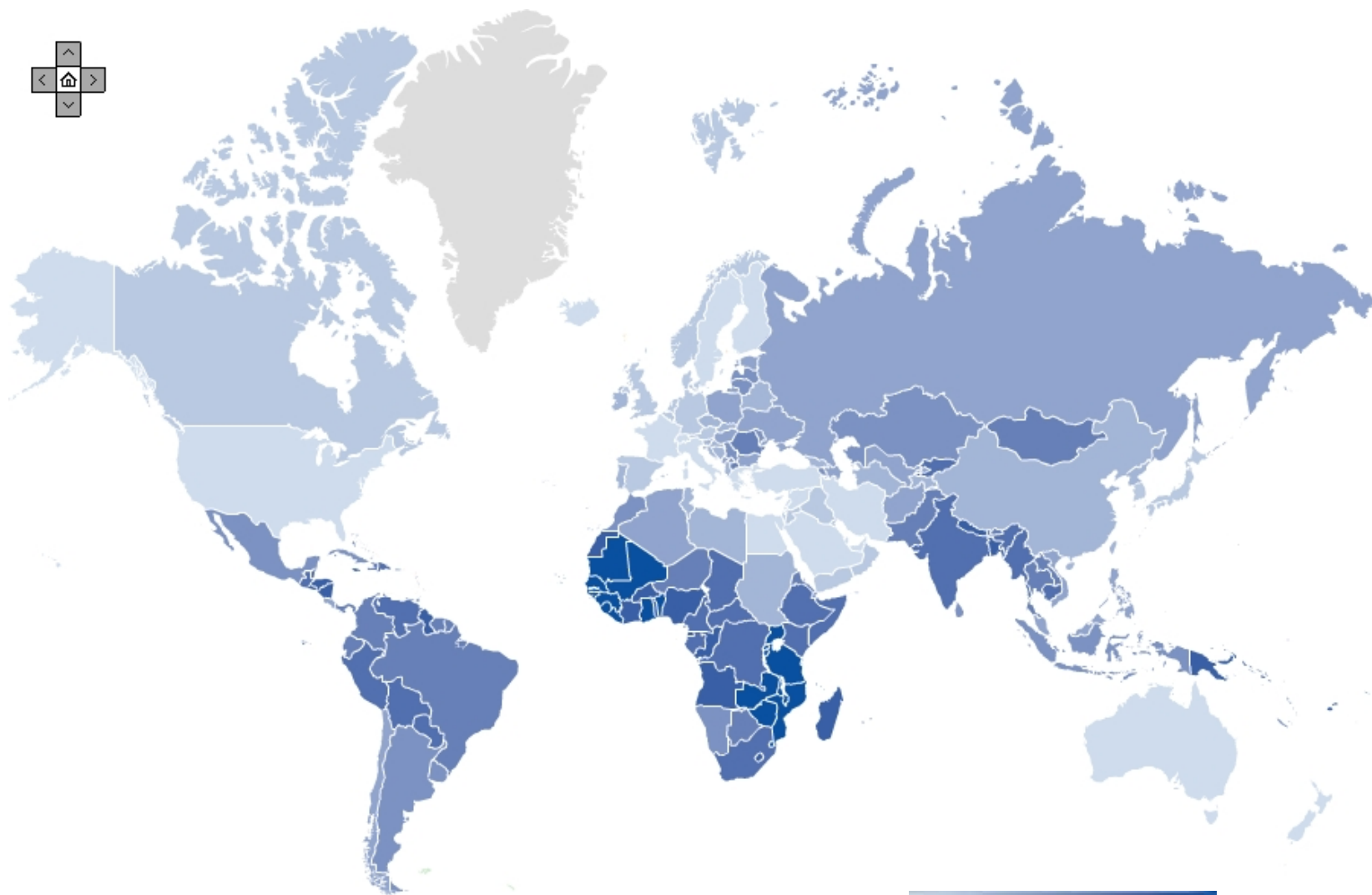
Estimated Cervical Cancer **Incidence** Worldwide in 2008



0 5.8 12.2 21.0 34.7 57

Age-standardised incidence rates per 100,000

Estimated Cervical Cancer **Mortality** Worldwide in 2008



0 1.9 4.9 9.7 17.3 42

Age-standardised mortality rates per 100,000

Overscreening: Who is leading who?

- Do women want annual testing?
- Do doctors teach women to want annual testing?
- Do doctors insist on annual testing and force it on reluctant women?
- How can doctors and patients unlearn?

Special risk groups?

Many suggested high risk groups

- Start sexual activity young
- Multiple partners
- Aboriginal
- Attending STI clinics

Minimal evidence: no specific recommendations

Women sex with women

- Limited evidence that they are at risk

Comprehensive Cervical Cancer Control

A guide to essential practice

Second edition



World Health
Organization

Cervical screening should not start before 30 years of age.

How do we change?

- Physicians?
- Patients?

James A. Dickinson, Gina Ogilvie, Dirk Van Niekerk, and Cathy Popadiuk. Evidence that supports policies to delay cervical screening until after age 25 years

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HPV testing

- More sensitive, less specific
- Therefore more recalls
- Unsuitable when HPV prevalence is high
- Better >30yrs.
- More expensive
- Not yet clear whether reduces testing overall
- US moved to recommend 5 year intervals
- But many still doing annual: harm and cost

HPV immunization

- Cohort started in 2008: females only, types 16, 18.
- Only 65% of girls cohort participated
- Boys from 2015 80% participation
- First group reaching 21 in 2017, 25 in 2021

Therefore:

- Need to continue screening older women
- This group is only partially protected
- Males may still be carriers
- Do not know how long protection will last.

What bothers me!

- Focus of gynecological literature
 - Effects of HPV immunization
 - Changing to HPV testing
- No cancer left un-diagnosed

Almost nothing on *harms*

overscreening/overtreatment