Cost effectiveness of cervical cancer screening strategies after availability of HPV vaccine

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Agenda

- Background
- Data sources
- The model
- Results
- Discussion and conclusion

Background - Epidemiology

- Cervical cancer is the third most common cancer in women worldwide and is the 11th most common cancer in women in Canada.
- In 2011 there were about 500 and 1,300 incident cases of cervical cancer in Ontario and Canada, with 140 and 350 estimated cervical cancer related deaths.
- Cervical cancer screening program (Pap smear test) has reduced incidence and mortality significantly over the 20th century.

Background – HPV and cervical cancer

- Cervical cancer is caused by persistent infection with human papillomavirus (HPV).
- There are nearly 100 types of HPV, high-risk HPV types 16 and 18 cause 70% of cervical cancers
- The availability of HPV vaccination has the promise to prevent cervical cancer in most of women who receive it before becoming sexually active
- Two vaccines approved in Canada
  - Gardasil® – protects against HPV types 16, 18, 6 and 11. (6 and 11 cause 90% of genital warts)
  - Cervarix ® – protects against HPV types 16 and 18.

Background – programs in Ontario

- Cervical cancer screening program:
  - Screening is recommended every three years for all women starting at age 21 who are or ever have been sexually active
  - Between 2006 and 2008, 72.4% of women 20–69 years of age had at least one Pap test
- HPV vaccination program:
  - Ontario began a voluntary, publically funded, school-based vaccination program (Gardasil) that targeted grade eight girls in the fall of 2007.
  - Provincial cohort vaccination rates are estimated at 51%, 58% and 59% in years one, two and three respectively.

Background – vaccine efficacy

- The FUTURE (Females United to Unilaterally Reduce Endo/ectocervical disease) I and II trials evaluated the efficacy of Gardasil
- Used a composite outcome of CIN2, CIN3 and AIS related to HPV type 16 or 18. The outcome of interest, prevention of cervical cancer, was not suitable because trial size and duration would have been too great.
- 98% efficacy for individuals with no evidence of infection with HPV types 16 and/or 18 at enrollment; 44% in the intention-to-treat (ITT) population (women aged 16 – 26)
- Vaccination reduced incidence of infection with several oncogenic non-vaccine HPV types (31/33/45/52/58) by 25% in a sexually naïve population and by 17.7% in a population with sexually naïve and active women.

The question

- What is the most cost effective screening strategy for women who received HPV vaccination before becoming sexually active in Ontario?
  - The girls who were vaccinated in 2007 will turn 21 soon, if not already, thus eligible to participate in the screening program
  - Given their reduced risk, their screening strategy should be different from the general population, yet there is no current guidelines on the starting age and frequency of screening for them

Methods

- Seven alternatives evaluated:
  - No screening
  - Current practice (starting at 21, every 3 years)
  - Starting at 21, every 5 years
  - Starting at 21, every 7 years
  - Starting at 25, every 3 years
  - Starting at 25, every 5 years
  - Starting at 25, every 7 years
- There could be many other combinations of starting age and frequency;

The model

- Markov model representing the progression of cervical cancer in patients' lifetime
- Different probabilities and costs for different strategies
- Cost and QALY discounted 3% per year
- Follow a hypothetical cohort of 100,000 vaccinated women over their lifetime

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Mathematical Model for the Natural History of Human Papillomavirus Infection and Cervical Carcinogenesis

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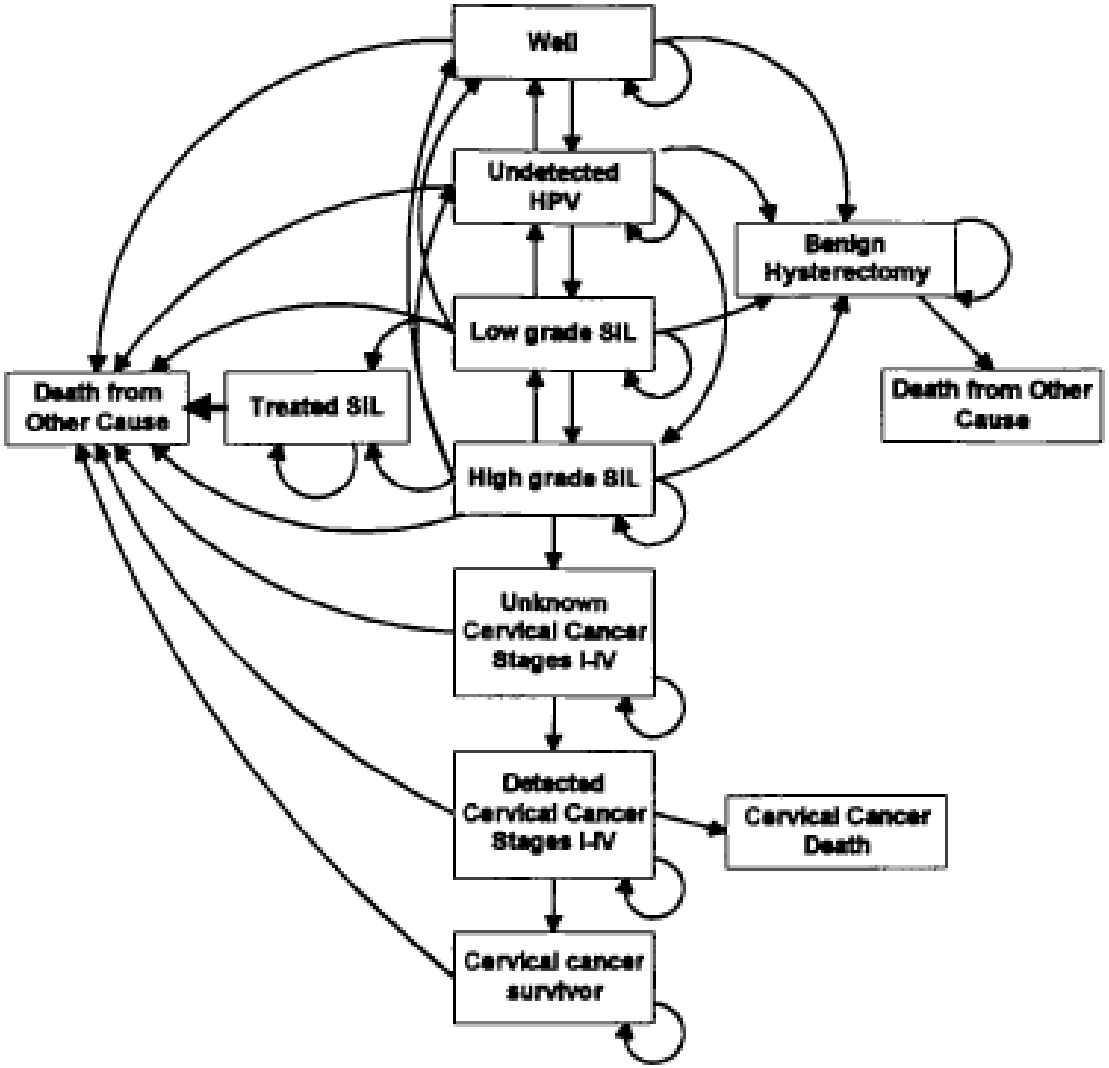

Input data - costs

Input Variable	**Base Case**
Cost Variables	2013 $CAD
Cytology	$65.90
Colposcopy & biopsy	$171.11
CIN1 treatment	$985.05
CIN2,3 treatment	$1,365.43
Stage I cancer treatment	$11,560.46
Stages II & III cancer treatment	$18,289.32
Stage IV cancer treatment	$24,991.59

Input data - probabilities

Input Variable	Base Case	Low	High
CIN Treatment Variables			
CIN1 treatment effectiveness, %			
Initial	97	93	100
Retreatment	99.5	99	100
CIN2,3 treatment effectiveness, %			
Initial	94	88	97
Retreatment	99.5	99	100
	10	0	25
Cervical Cancer Variables			
	43.7	40	45
	53.5	50	55
	68.3	65	70
Probability of symptoms with undiagnosed cancer			
Stage I	15	12	18
Stage II	22.5	20	25
Stage III	60	67	73
Stage IV	90	87	93
Stage I survival after diagnosis			
Year 1	96.88		
Year 2	95.25		
Year 3	95.44		
Year 4	97.96		
Year 5	97.61		
Stage II survival after diagnosis			
Year 1	90.66		
Year 2	87.6		
Year 3	92.25		
Year 4	93.32		
Year 5	96.04		
Stage III survival after diagnosis			
Year 1	70.64		
Year 2	73.78		
Year 3	86.1		
Year 4	92.31		
Year 5	91.42		
Stage IV survival after diagnosis			
Year 1	39.86		
Year 2	49.82		
Year 3	76.38		
Year 4	86.52		
Year 5	85.92		
Time to remission, years			

Input data - Utilities

Input Variable	Base Case	Low	High
State	QALY		
Healthy	1.00		
HPV infection	1.00	0.8	1
Diagnosed CIN1	0.91	0.91	1
Diagnosed CIN2,3	0.87	0.87	1
Diagnosed stage I cancer	0.68	0.49	0.81
Diagnosed stages II & III cancer	0.57	0.42	0.7
Diagnosed stage IV cancer	0.51	0.36	0.62
Cancer survivor	0.90	0.25	1

Primary results - costs

Strategy	Cost per patient (2013, CAD)	Incremental cost
No screening	$1,853.98	
25, 7-year	$3,189.02	$1335.04
21, 7-year	$3,734.76	$545.74
25, 5-year	$4,157.8	$423.04
21, 5-year	$4,748.23	$590.43
25, 3-year	$5,453.23	$705
21, 3-year	$5,976.4	$523.17

Primary results - QALY

Strategy	QALY	Incremental QALY
No screening	39.28	
25, 7-year	39.4	0.12
21, 7-year	39.41	0.01
25, 5-year	39.55	0.14
21, 5-year	39.56	0.01
25, 3-year	39.57	0.01
21, 3-year	39.58	0.01

Primary results - ICER

Strategy	ICER (cost/QALY)
No screening	
25, 7-year	11125.33
21, 7-year	54574.00
25, 5-year	3021.71
21, 5-year	59043.00
25, 3-year	70500.00
21, 3-year	52317.00

Primary results – sensitivity analysis

- Results very sensitive to:
- Vaccine efficacy
  - As efficacy gets higher, screening less frequently becoming more attractive
- Cost of screening
  - As cost of screening gets lower, starting early and screening more frequently becoming more attractive

Conclusions

- Women who received vaccination before becoming sexually active should use a different screening regime than those who did not
- Starting at 25 years, and screening every 5 years is the most cost effective strategy
- Compared to current guideline for the general public, using this strategy results in significant cost savings with only minor reduction in case prevented or QALY

Discussion

- It is important to provide clear guideline for this group as they become eligible for cervical cancer screening
- Long term and reliable data on vaccine efficacy and effectiveness should be used to update the analysis