Epidemiology of HPV and Cervical Cancer & Health Economic Aspect of Cervical Screening in Iran

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HPV Statistics

Human Papillomavirus (HPV)

Over 100 types identified

Most benign, but 15-20 can cause cancers

Very common

- 80% of women have HPV by age 50
- 50% of college students are infected

HPV & Cervical Cancer

HPV recognized as the underlying cause of

cervical cancer since 1996

- NIH Consensus Conference on Cervical Cancer, 1996
- World Health Organization/European Research Organization on Genital Infection and Neoplasia, 1996

Natural History of HPV Infections

Sexually transmitted

- Usually no symptoms
- No treatment for HPV infection before symptoms
- Immune system clears most cases; some persist

HPV present in >99% of cervical cancers

- High risk types (16, 18) associated with cancer
- Low risk types (6, 11) are associated with genital warts
- All can cause abnormal Pap tests

Human Papillomavirus. ACOG Practice Bulletin No. 61. 2005; 105: 905-18.

Co-factors for HPV Infection

- Smoking
- HIV infection
- Other immune system defect
- Pregnancy
- Oral contraceptive use

Ferris et al. *Modern Colposcopy.* 2004.

Common HPV Types and their effects

	HPV Types	Lead to:
Low-Risk	HPV 6, 11, 40, 42, 43, 44, 54, 61, 70, 72, 81	Benign cervical changes Genital warts
High-Risk	HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, 82	Precancer cervical changes Cervical cancer Anal and other cancers

Numbers of HPV-Associated Cancers in Less Developed and More Developed Regions*

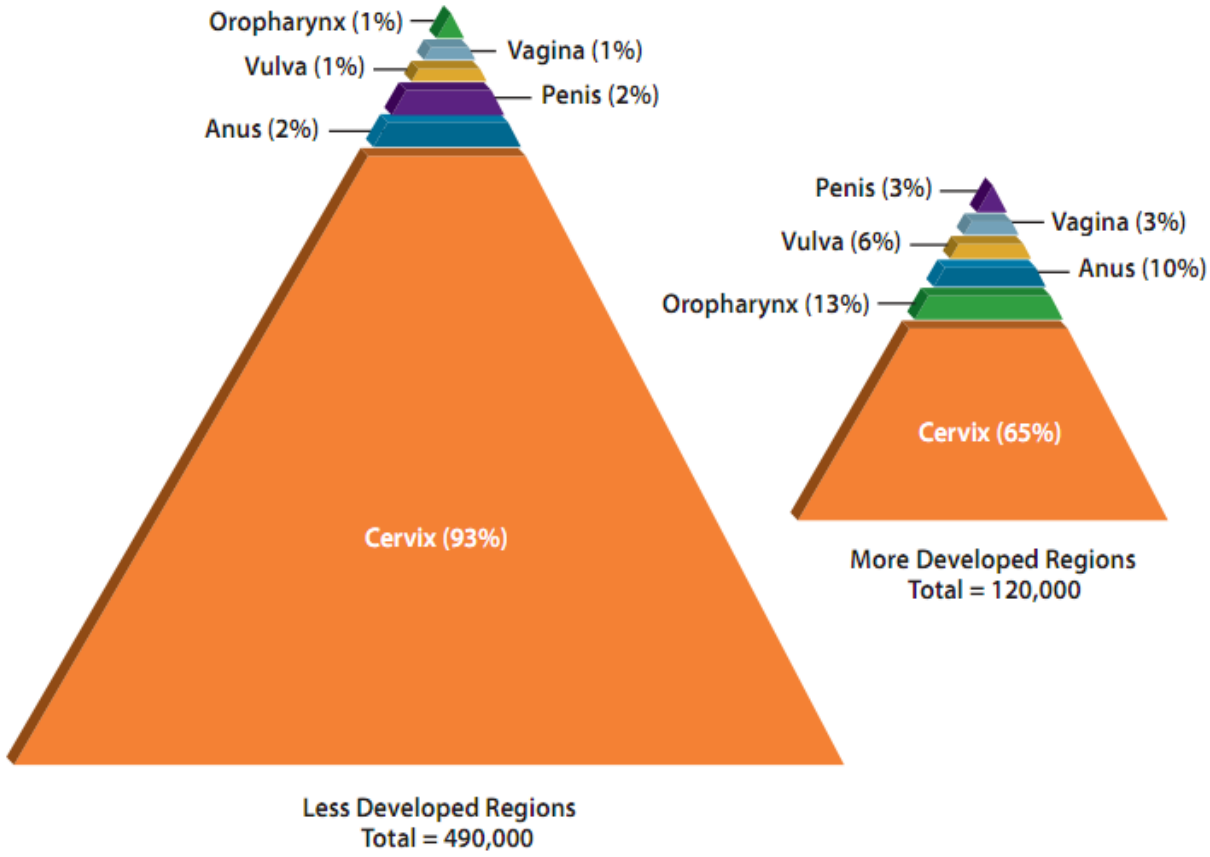


Table 1. Number of cancer cases attributable to HPV and corresponding attributable fraction (AF) by cancer site, sex and age; World, 2012

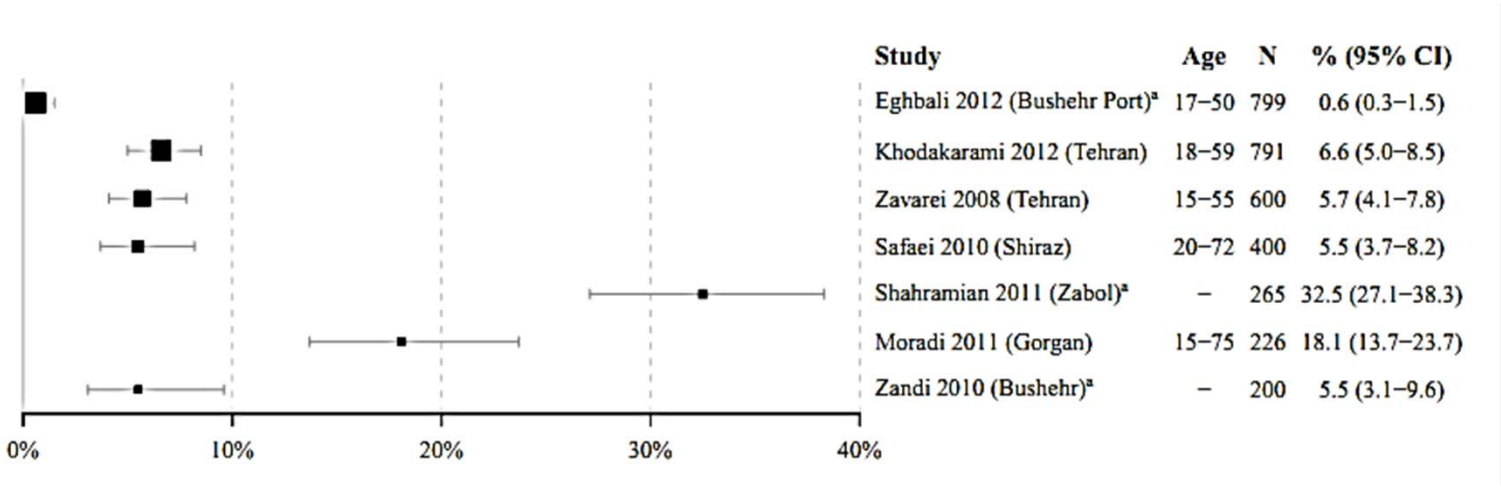
HPV-related cancer site (ICD-10 code)	Number of incident cases[1,2]	Number attributable to HPV	AF (%)	Number attributable to HPV by gender		Number attributable to HPV by age group		
				Males	Females	<50 years	50–69 years	70+ years
Cervix uteri (C53)	530,000	530,000	100.0	0	530,000	250,000	220,000	58,000
Anus[3] (C21)	40,000	35,000	88.0	17,000	18,000	6,600	17,000	12,000
Vulva[3] (C51)	34,000	8,500	24.9	0	8,500	2,600	3,400	2,500
Vagina[3] (C52)	15,000	12,000	78.0	0	12,000	2,500	5,200	3,900
Penis[3] (C60)	26,000	13,000	50.0	13,000	0	2,700	5,800	4,400
Oropharynx[3] (C01, C09–10)	96,000	29,000	30.8	24,000	5,500	5,400	18,000	6,000
Oral cavity[3] (C02–06)	200,000	4,400	2.2	2,900	1,500	890	2,300	1,200
Larynx (C32)	160,000	3,800	2.4	3,300	460	420	2,200	1,200
Other pharynx[3] (C12–C14)	78,000	0	0	–	–	–	–	–
Total HPV-related sites	1,200,000	630,000	54.0	60,000	570,000	270,000	270,000	88,000

Table 2. Number of all cancer cases attributable to HPV and corresponding attributable fraction (AF) for all cancers, by region, cancer site(s) and sex; World, 2012

Region	Cervix uteri[1]	Anus		Penis	Vulva/ vagina	Head and neck		All cancer Attributable to HPV	AF (%)		
	F	M	F	M	F	M	F	Both sexes	M	F	Both
Africa											
Sub-Saharan Africa	93,000	1,000	1,200	1,000	2,100	360	150	99,000	0.9	26.1	15.8
Northern Africa/ Western Asia	10,000	430	350	70	650	240	80	12,000	0.3	4.3	2.2
Asia											
India	120,000	2,600	1,900	3,200	2,800	5,600	1,000	140,000	2.4	23.9	13.8
Other Central Asia	29,000	490	410	30	460	760	300	31,000	0.5	11.4	6.3
China	62,000	5,900	3,600	1,300	1,600	950	270	75,000	0.5	5.4	2.5
Japan/Republic of Korea	13,000	600	560	250	460	1,500	350	16,000	0.5	3.5	1.8
Other Eastern Asia	54,000	550	530	1,100	1,000	1,000	280	59,000	0.6	11.7	6.2
America											
Latin America	69,000	1,000	1,900	2,000	2,500	980	280	78,000	0.8	13.0	7.1
Northern America	14,000	1,800	2,700	1,100	3,300	7,000	1,900	32,000	1.1	2.6	1.8
Europe											
Europe	58,000	2,700	4,200	2,700	5,100	11,000	2,800	87,000	0.9	4.4	2.5
Oceania											
Australia/New Zealand	940	150	190	50	150	290	80	1,900	0.6	2.2	1.3
Other Oceania	1,300	10	10	10	30	30	10	1,300	0.8	18.5	11.1
Less developed countries	370,000	10,000	7,600	6,800	8,300	8,600	2,100	410,000	0.8	13.2	6.7
More developed countries	160,000	6,800	10,000	6,100	12,000	22,000	5,500	220,000	0.8	5.0	2.8
World	530,000	17,000	18,000	13,000	20,000	30,000	7,500	630,000	0.8	8.6	4.5

[1]Numbers over 100 are rounded to two significant digits; numbers <100 are rounded to the closest ten.

Prevalence of HPV among women with normal cytology in Iran, By study



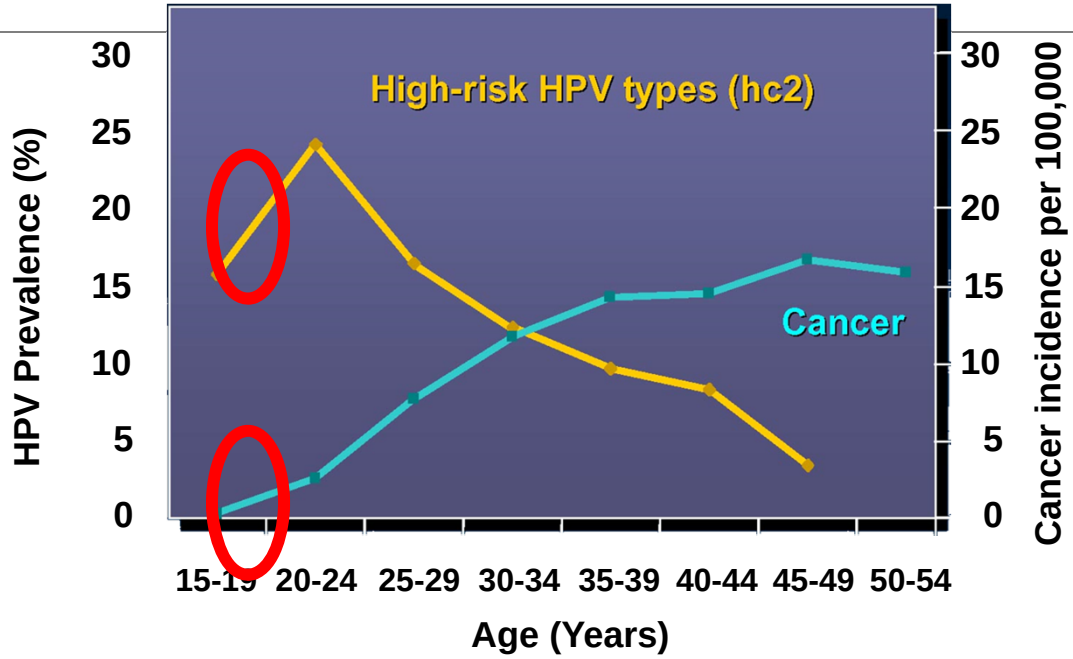
Study	Age	N	% (95% CI)
Eghbali 2012 (Bushehr Port)[a]	17–50	799	0.6 (0.3–1.5)
Khodakarami 2012 (Tehran)	18–59	791	6.6 (5.0–8.5)
Zavarei 2008 (Tehran)	15–55	600	5.7 (4.1–7.8)
Safaei 2010 (Shiraz)	20–72	400	5.5 (3.7–8.2)
Shahramian 2011 (Zabol)[a]	–	265	32.5 (27.1–38.3)
Moradi 2011 (Gorgan)	15–75	226	18.1 (13.7–23.7)
Zandi 2010 (Bushehr)[a]	–	200	5.5 (3.1–9.6)

Prevalence of HPV 16, 18 by cytology in Iran

	No. tested	HPV 16/18 Prevalence % (95% CI)
Normal cytology[1,2]	1,417	2.8 (2.1-3.8)
Low-grade lesions[3,4]	35	42.9 (28.0-59.1)
High-grade lesions[5,4]	34	67.6 (50.8-80.9)
Cervical cancer[6,7]	333	58.6 (53.2-63.7)

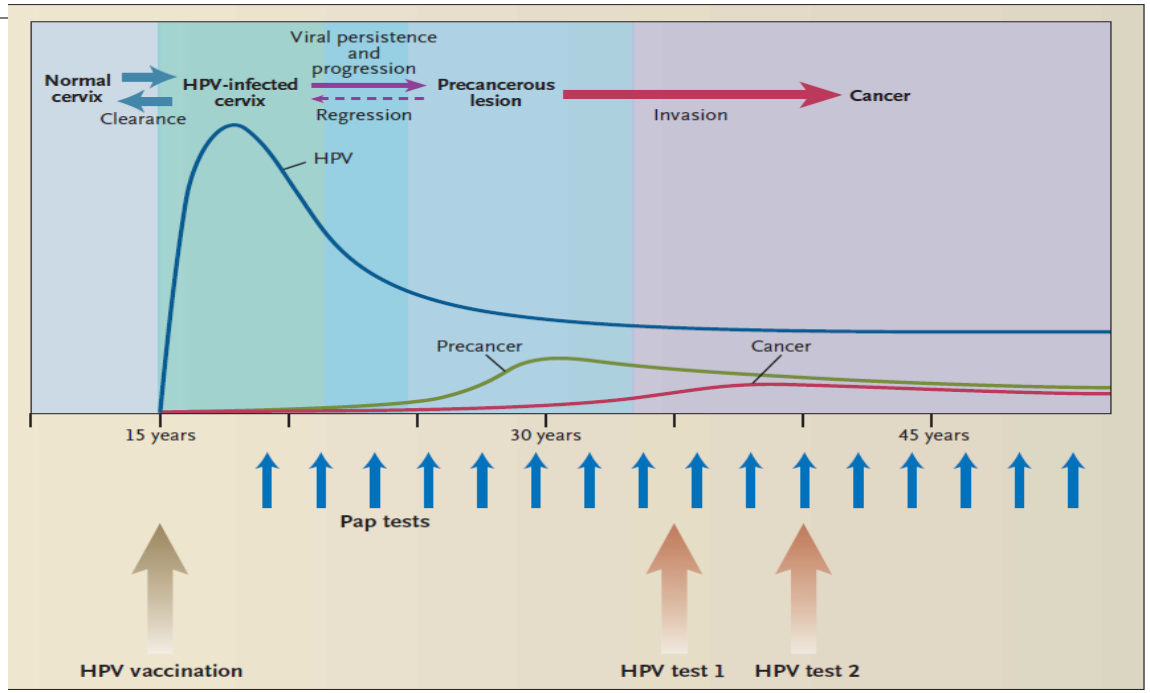
Cervical Cancer Statistics

HPV and Cervical Cancer Rates by Age

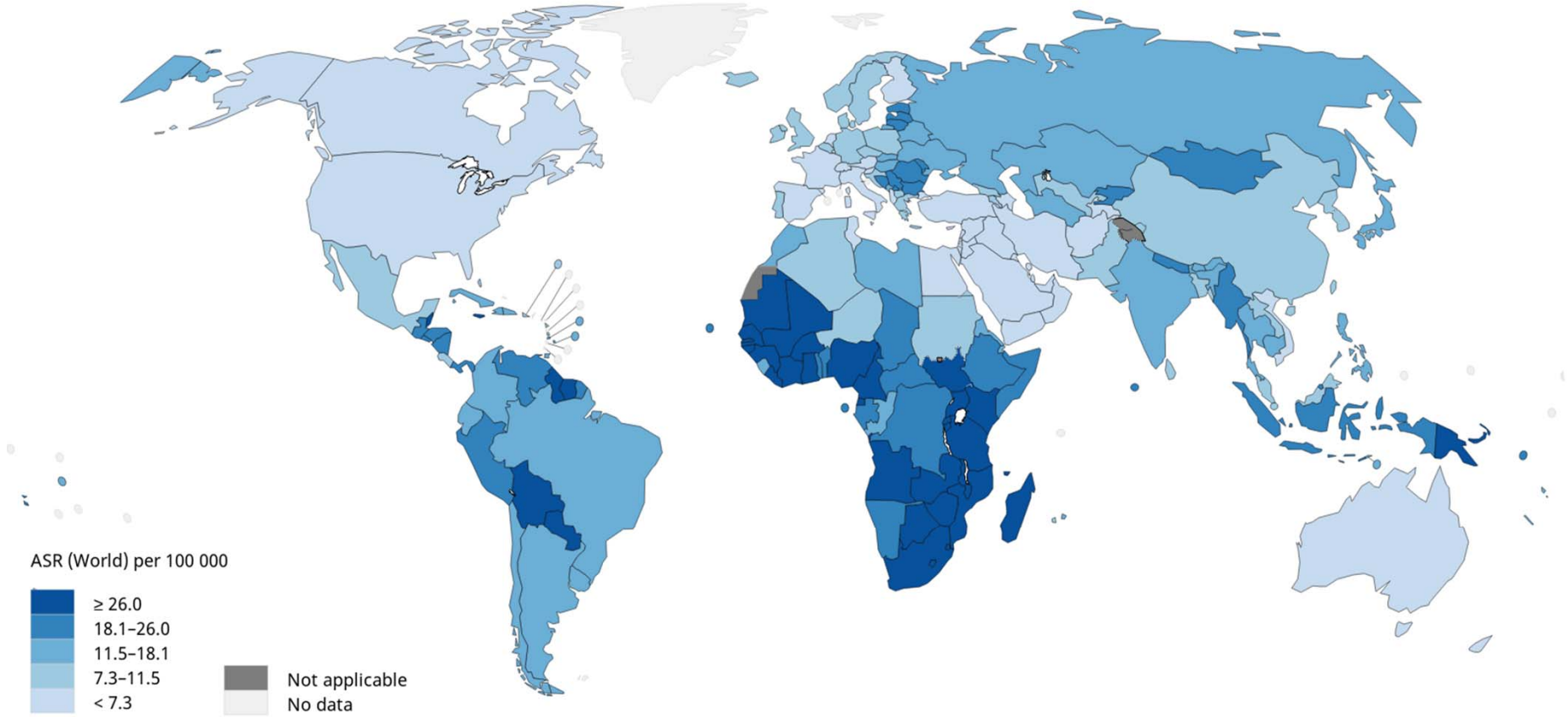


1. Sellors et al. *CMAJ.* 2000;163:503.
2. Ries et al. Surveillance, Epidemiology and End Results (SEER) Cancer Stats NCI, 1973-1997. 2000.

Natural History



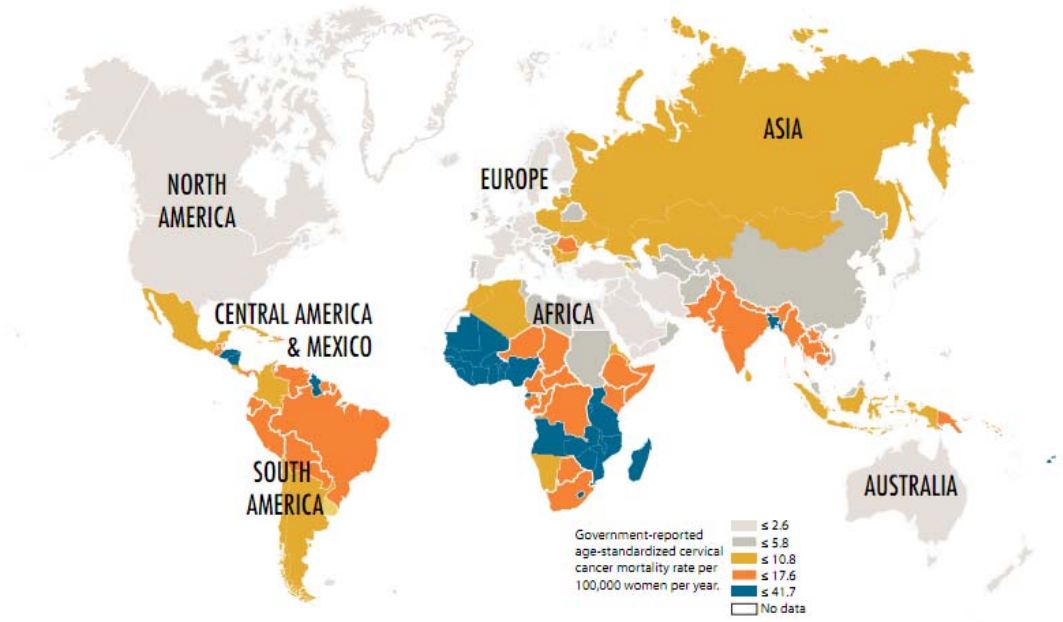
Estimated age-standardized incidence rates (World) in 2018, cervix uteri, all ages



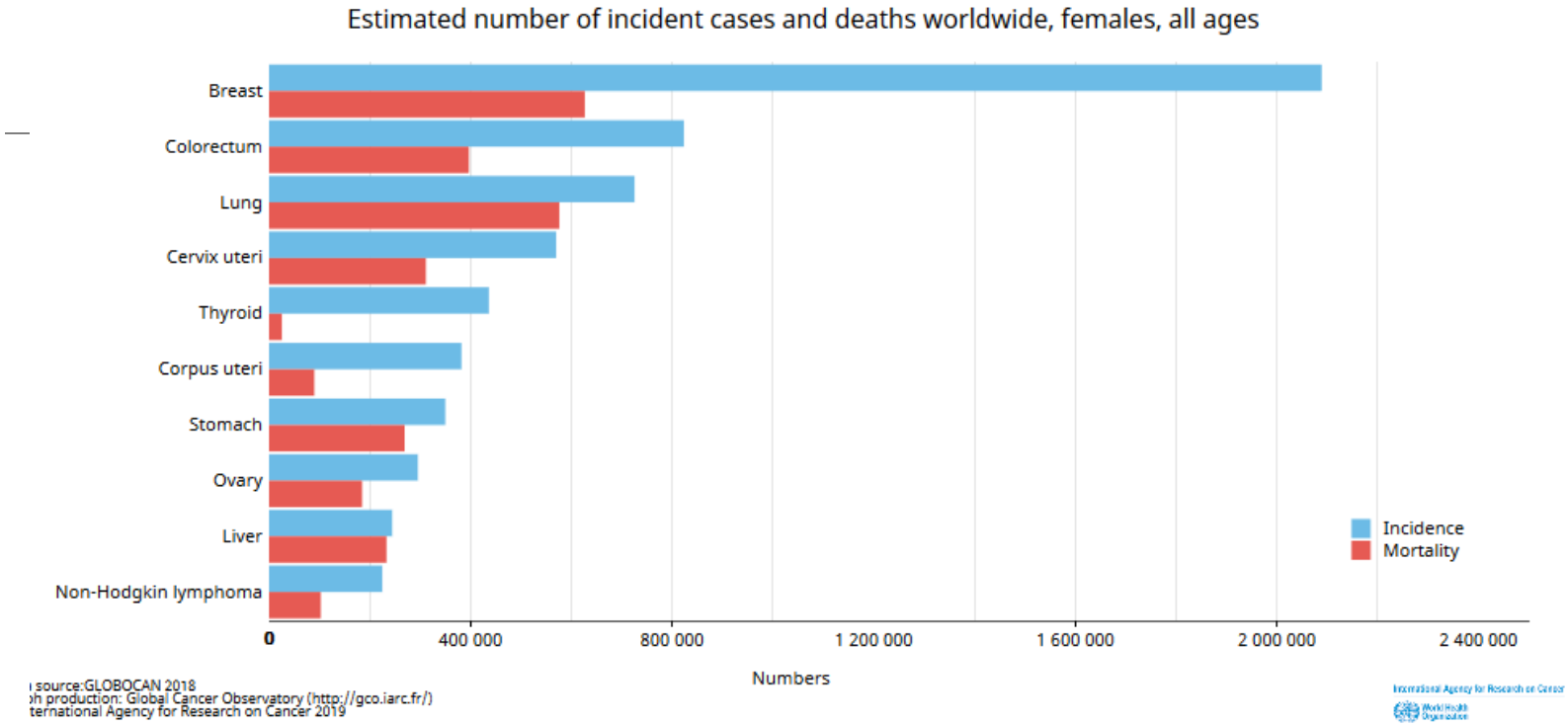
Data source: GLOBOCAN 2018
Graph production: IARC (http://gco.iarc.fr/today)
World Health Organization

World Health Organization

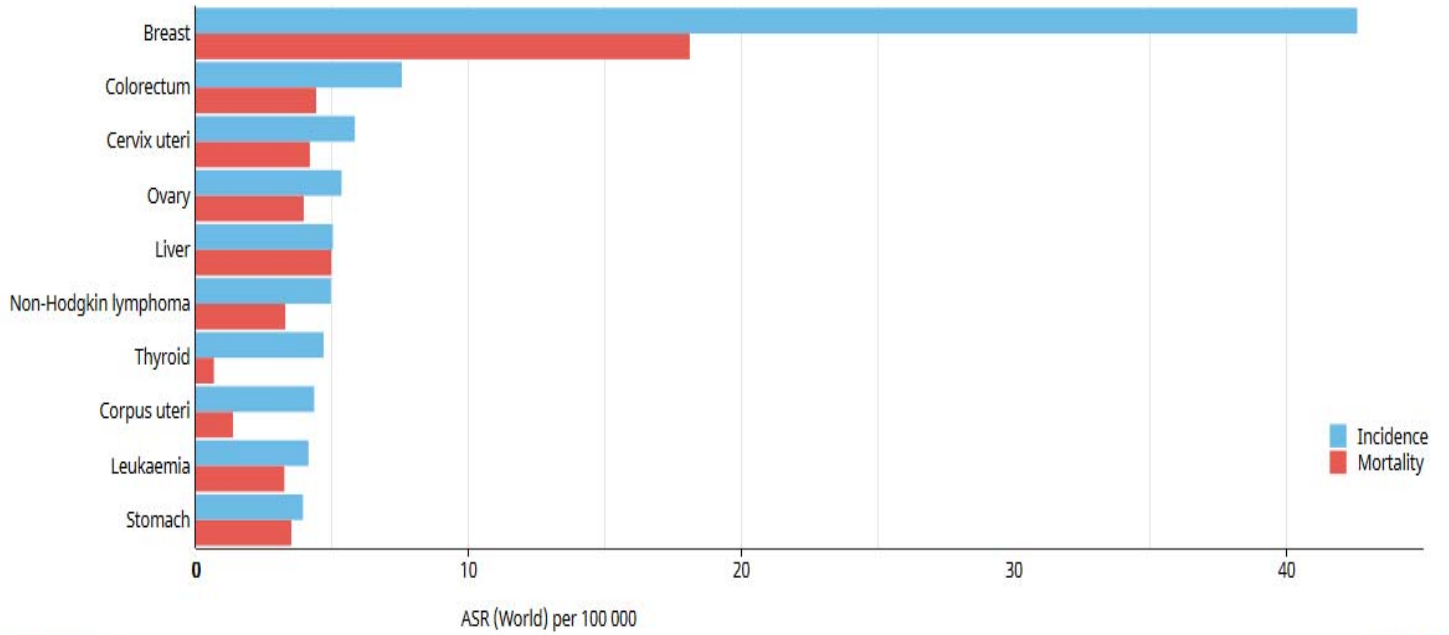
Mortality of Cervical Cancer in the World
American Cancer Society
2014



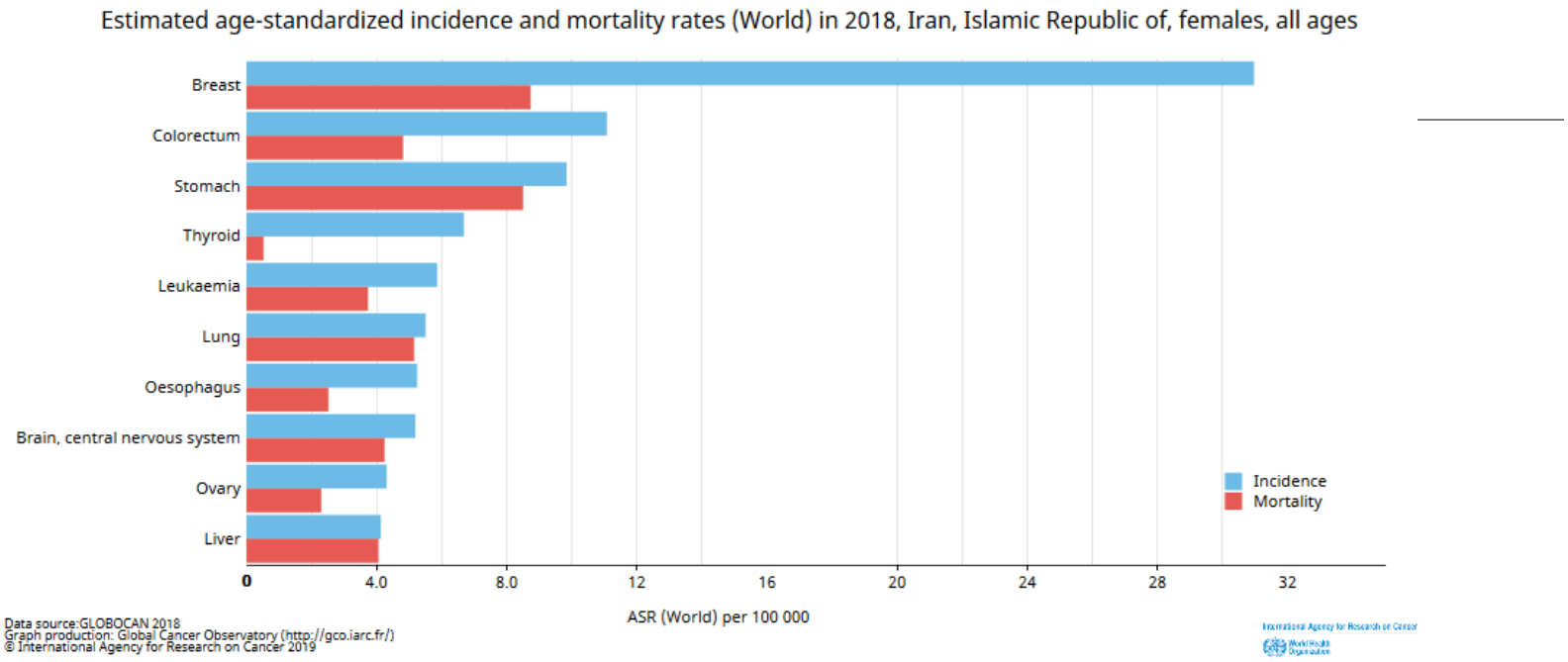
Modified from: Crow, JM. HPV: the global burden. Nature. 2012;488:S2-3. Data from: World Health Organization, Institut Catala d'Oncologia. Human papillomavirus and related cancers: summary report update. Barcelona (ES): WHO/ICO; 2010 Nov 15.

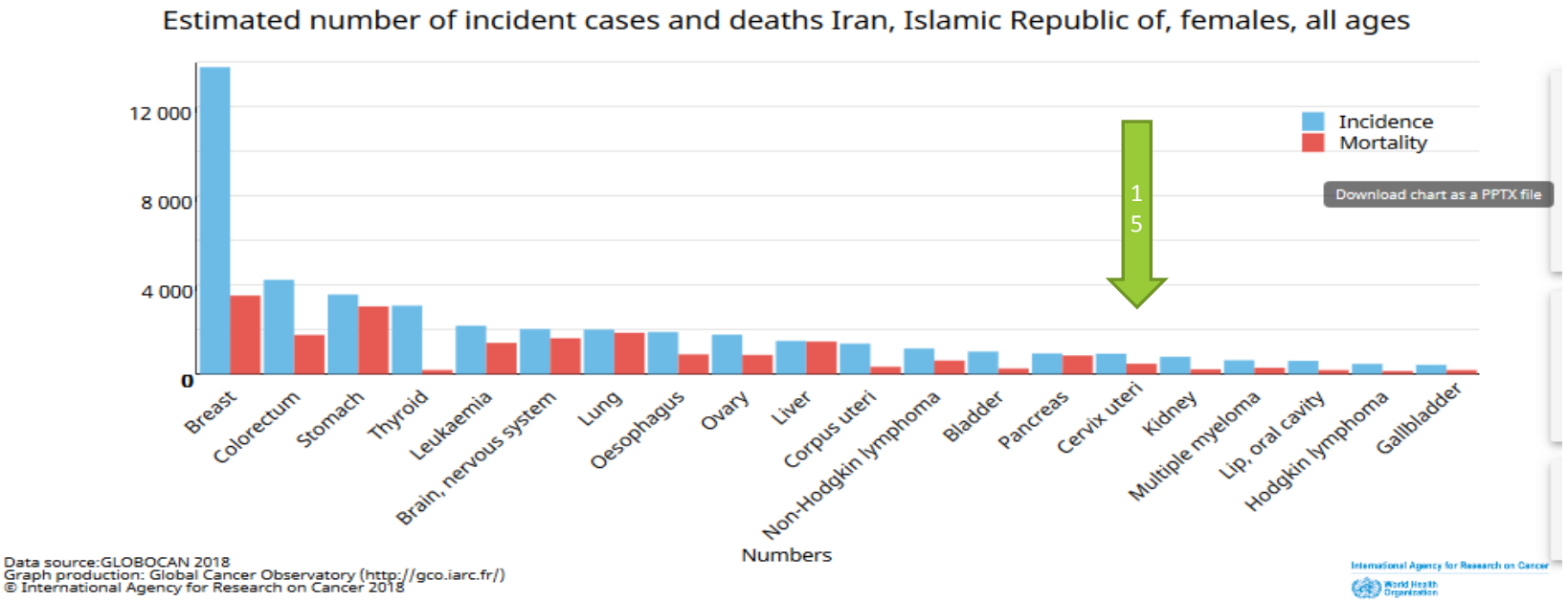

Estimated number of incident cases and deaths worldwide, females, all ages
Breast
Colorectum
Lung
Cervix uteri
Thyroid
Corpus uteri
Stomach
Ovary
Liver
Non-Hodgkin lymphoma
Incidence
Mortality
0
400 000
800 000
1 200 000
1 600 000
2 000 000
2 400 000
Numbers
source:GLOBOCAN 2018
h production: Global Cancer Observatory (http://gco.iarc.fr/)
ternational Agency for Research on Cancer 2019
International Agency for Research on Cancer
World Health Organization

Estimated age-standardized incidence and mortality rates (World) in 2018, WHO East Mediterranean region (EMRO), females, all ages



Data source:GLOBOCAN 2018
Graph production: Global Cancer Observatory (http://gco.iarc.fr/)


Estimated age-standardized incidence and mortality rates (World) in 2018, Iran, Islamic Republic of, females, all ages
Breast
Colorectum
Stomach
Thyroid
Leukaemia
Lung
Oesophagus
Brain, central nervous system
Ovary
Liver
Incidence
Mortality
0
4.0
8.0
12
16
20
24
28
32
ASR (World) per 100 000
Data source:GLOBOCAN 2018
Graph production: Global Cancer Observatory (http://gco.iarc.fr/)
© International Agency for Research on Cancer 2019

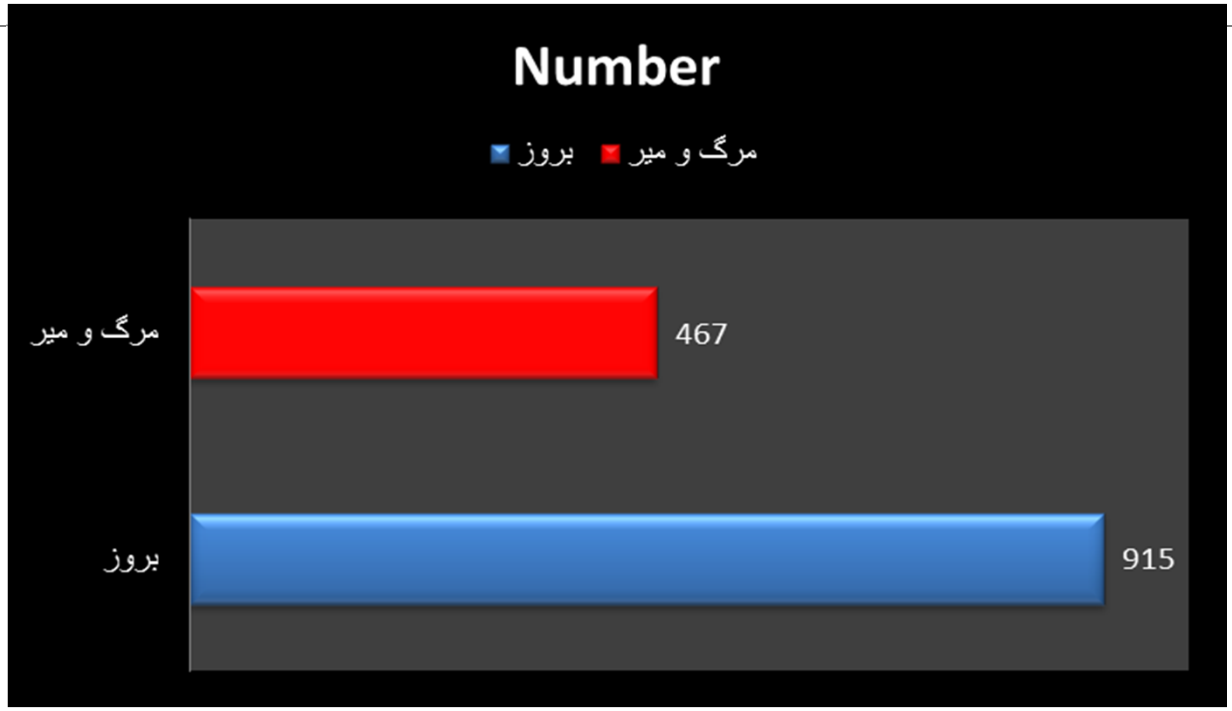

Estimated number of incident cases and deaths Iran, Islamic Republic of, females, all ages
12 000
8 000
4 000
0
Incidence
Mortality
Download chart as a PPTX file
15
Breast
Colorectum
Stomach
Thyroid
Leukaemia
Brain, nervous system
Lung
Oesophagus
Ovary
Liver
Corpus uteri
Non-Hodgkin lymphoma
Bladder
Pancreas
Cervix uteri
Kidney
Multiple myeloma
Lip, oral cavity
Hodgkin lymphoma
Gallbladder
Numbers
Data source:GLOBOCAN 2018
Graph production: Global Cancer Observatory (http://gco.iarc.fr/)
© International Agency for Research on Cancer 2018
International Agency for Research on Cancer
World Health Organization

Golestan Province
CI5 vol X

10 MAJOR CANCERS, ASR (WORLD) PER 100 000

Male		Female	
Stomach	30.4	Breast	28.0
Oesophagus	23.2	Oesophagus	18.8
Trachea, bronchus and lung	17.5	Stomach	12.6
Non-melanoma skin cancer	11.0	Colon	7.7
Prostate	10.6	Non-melanoma skin cancer	7.7
Colon	9.9	Ovary	6.1
Bladder	8.5	Trachea, bronchus and lung	5.6
Brain, nervous system	[illegible]	Cervix uteri	5.4
Non-Hodgkin lymphoma	7.2	Brain, nervous system	5.3
Lymphoid leukaemia	5.2	Non-Hodgkin lymphoma	3.3
All sites	176.3	All sites	142.0

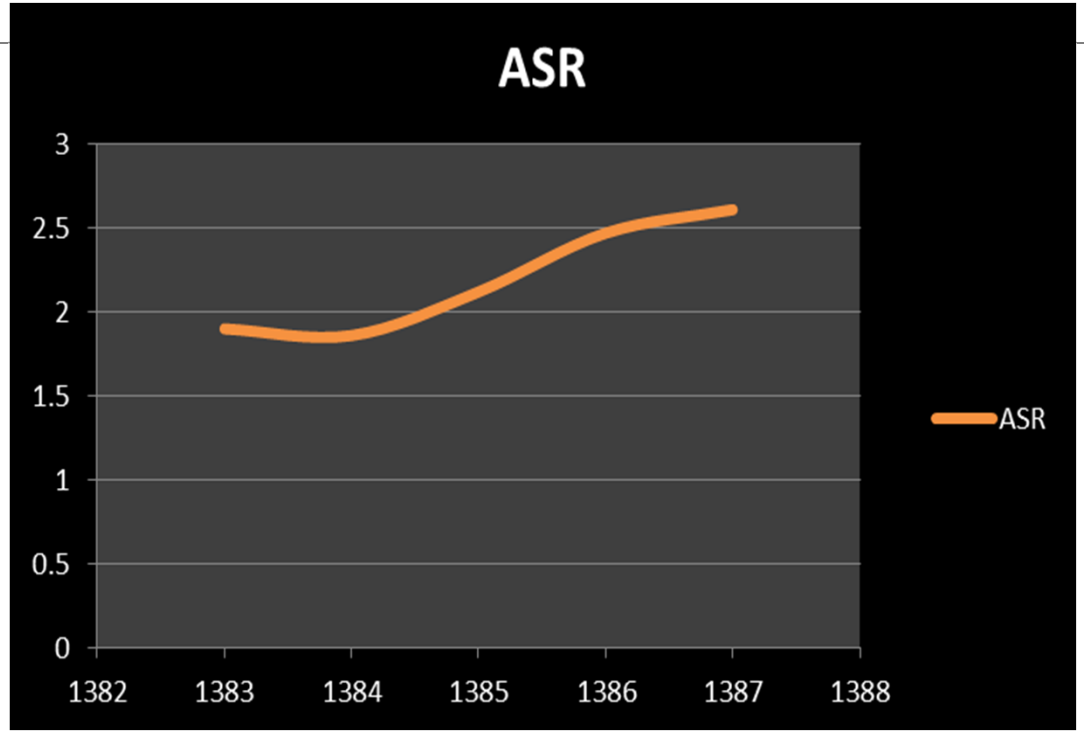
Incidence & Mortality of Cervical Cancer :Iran Cancer Office MOHME (1393)



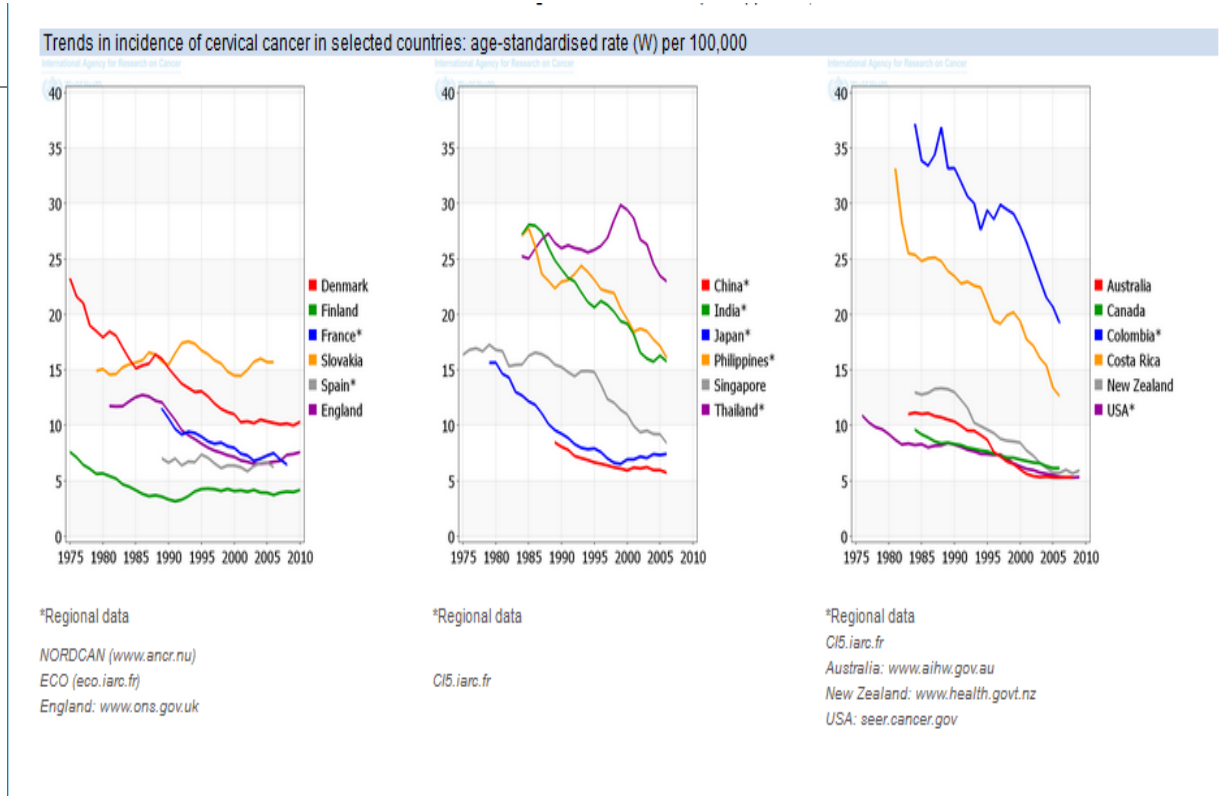
Provinces with cervical cancer in the 12 common cancers

Province	Number	ASR	Rank
Golestan	37	4.24	8
Mazandaran	41	2.28	12

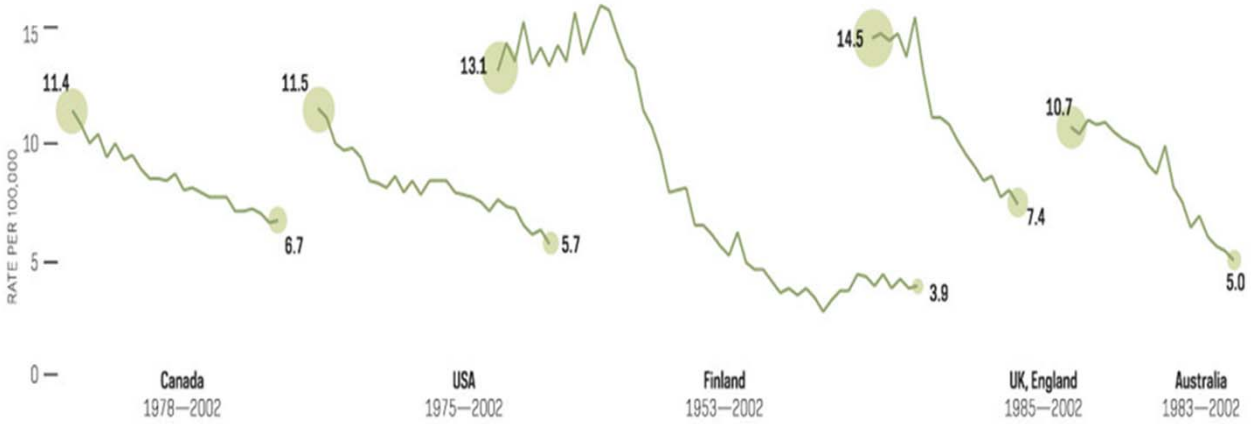
Cervical cancer trend in Iran



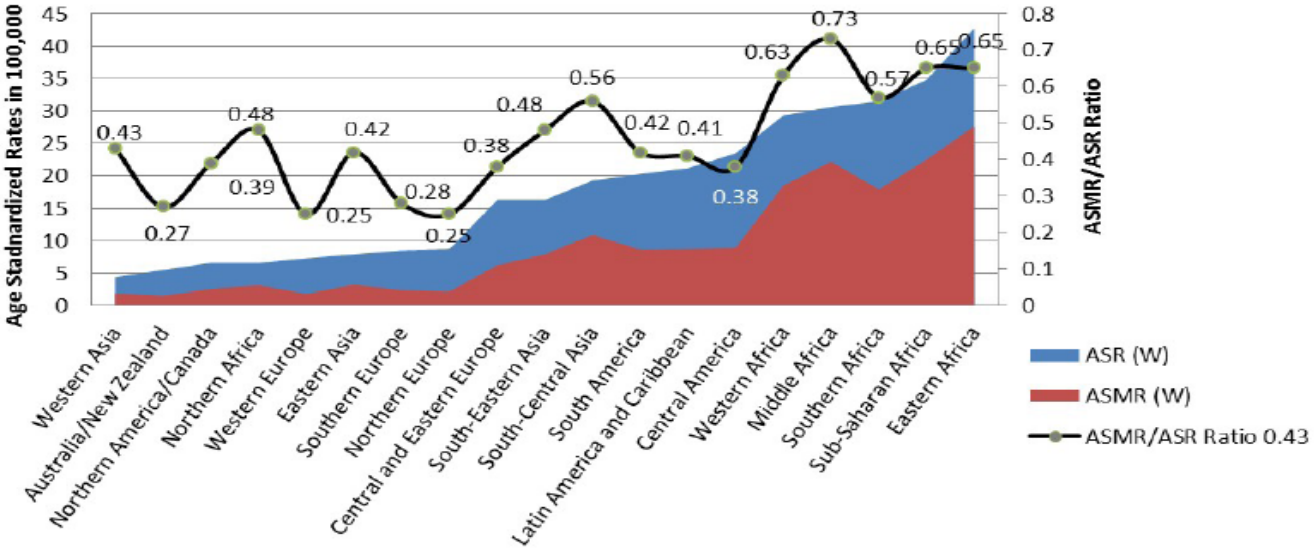
Time series of Cervical Cancer



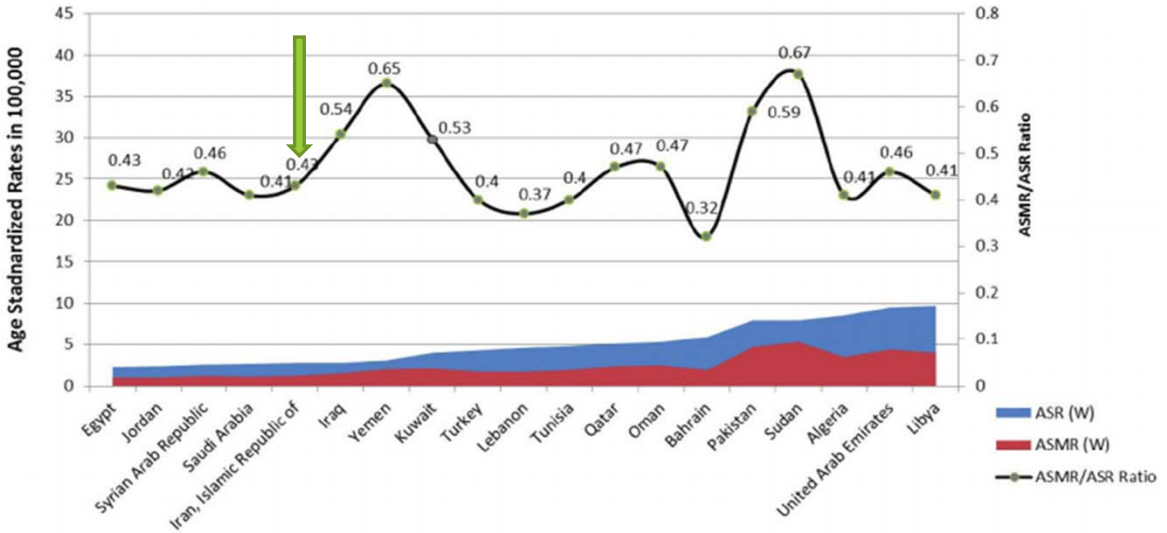
Time series of Cervical Cancer
High Income Countries



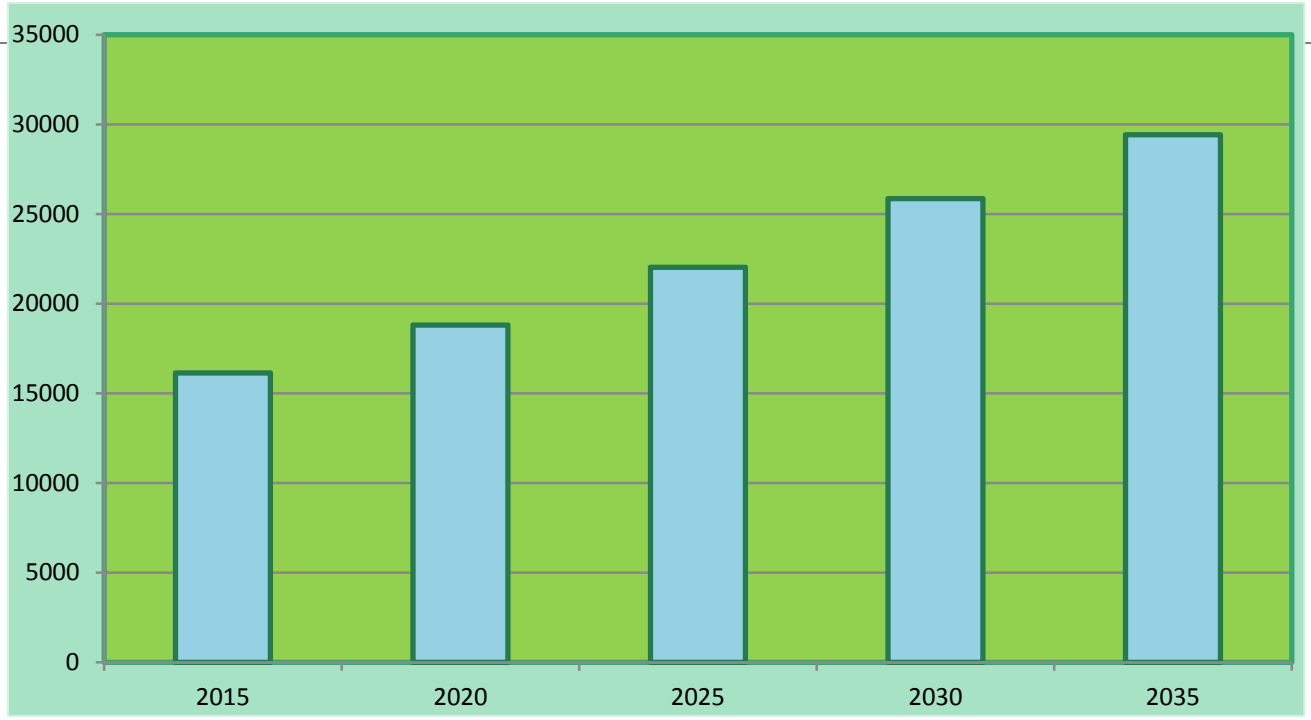
ASR/ASMR in the World
Globocan 2012



ASR/ASMR in the Muslim Countries
GLOBOCAN 2012



Cervical Cancer prediction of cervical cancer 2015-2035 EMRO region

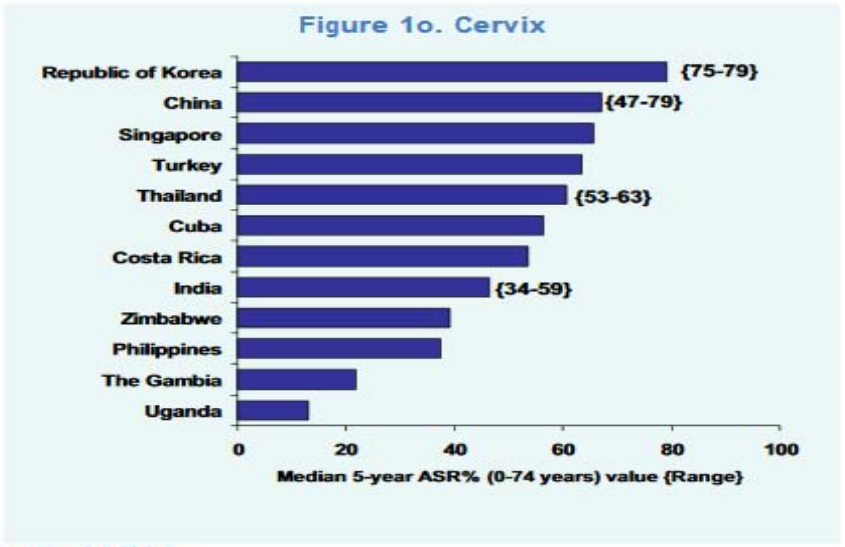


Preventing Cervical Cancer

Screening for precancerous changes (and treatment if problems found)

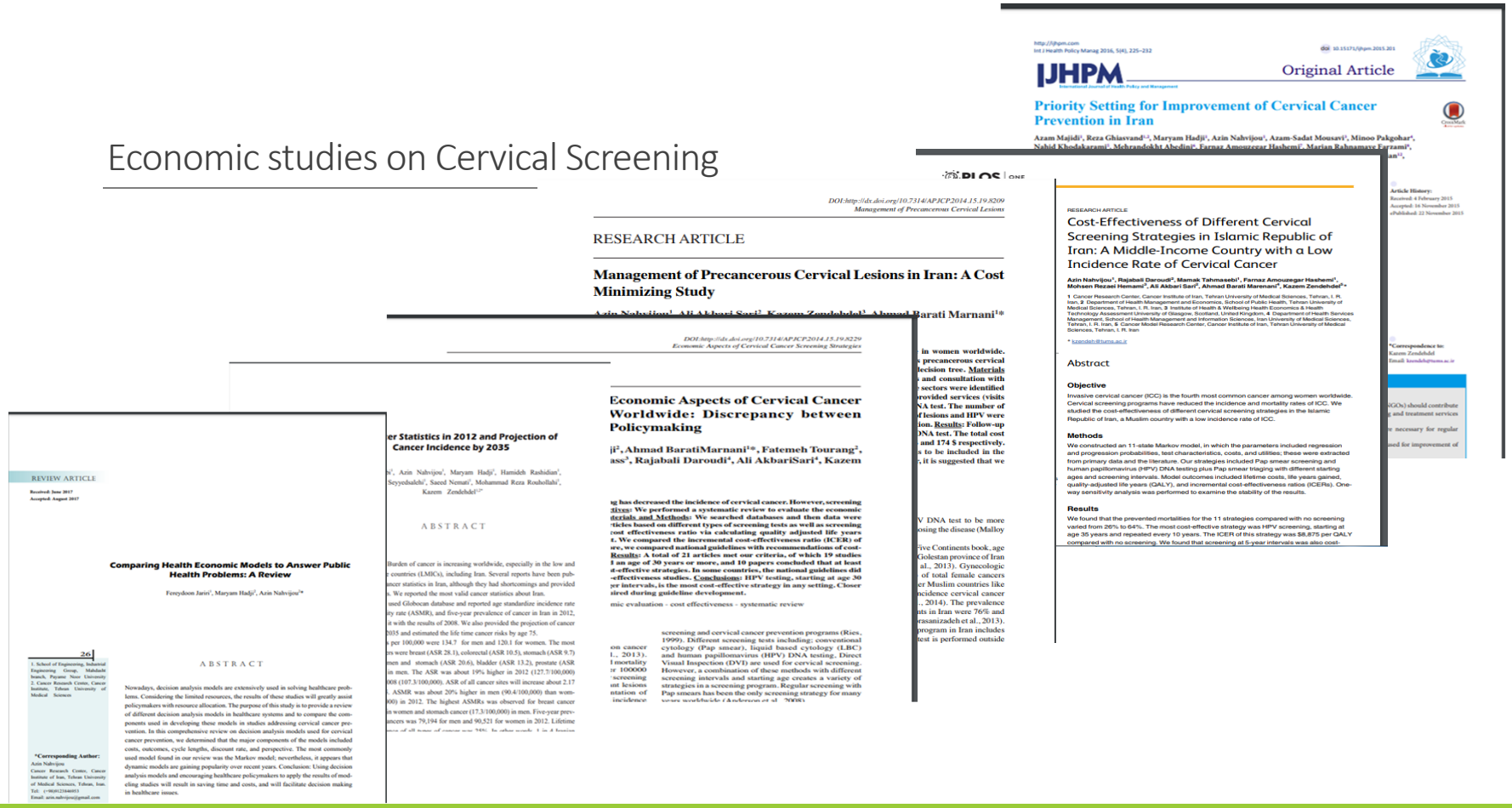
Vaccination against HPV

Survival of Cervical Cancer



Surv Can http://survcan.iarc.fr

Economic studies on Cervical Screening



IJHPM

Original Article

Priority Setting for Improvement of Cervical Cancer Prevention in Iran

RESEARCH ARTICLE

Cost-Effectiveness of Different Cervical Screening Strategies in Islamic Republic of Iran: A Middle-Income Country with a Low Incidence Rate of Cervical Cancer

Abstract

Objective

Methods

Results

RESEARCH ARTICLE

Management of Precancerous Cervical Lesions in Iran: A Cost Minimizing Study

RESEARCH ARTICLE

Economic Aspects of Cervical Cancer Worldwide: Discrepancy between Policymaking

REVIEW ARTICLE

Comparing Health Economic Models to Answer Public Health Problems: A Review

ABSTRACT

A Systematic Review of Economic Aspects of Cervical Cancer Screening Strategies Worldwide: Discrepancy between Economic Analysis and Policymaking

Table 2. The Most Cost Effective Cervical Screening Strategies Suggested by Different Research Groups Worldwide between 1999and 2012

Cost effective Strategies	High income countries	Middle Income Countries	Low income countries
HPV DNA triage	Kim(2005),Vijayaraghavan(2010), Berkhof(2010),Bidus(2006)	Chow(2010)	-
Cytology with HPV combination (co-screening)	Kim(2005),Mandelblatt(2002), Goldie(2004), Bistoletti(2008), Maxwell(2002)	vijayaraghavan(2008)	-
HPV DNA testing	De Kok(2012), Burger(2012), Kulasingam(2009), Sroczynski(2011)*	Goldie(2001), Andrés-Gamboa(2008), Levin(2010), Goldie(2005)	Goldie(2005)
3 year Pap+ HPV+ Pap age(Pap screening every 3 years for all women and HPV triage for women older than 30 with ASCUS)	Chuck(2010)	-	-
VIA with the immediate treatment	-	Mandelblatt (2002)	-
Pap smear with 10% rescreening with Pap net	Brown(1999)	-	-

*For age 25-29 cytology was cost effective

Table 1. Comparison of National Guidelines with Recommendations of Cost-Effectiveness Analyses in the Corresponding Countries about Cervical Screening Tests, Starting Age and Screenig Intervals Stratified by the Economic Situaiotn of the Countires

Authors(Year)/Country	Country	Screening Interval		Screening Interval		Screening test	
		Suggestion	National guideline	Suggestion	National guideline	Suggestion	National guideline[2]
High income country							
Berkhof(2010)/	Netherlands	5	5*	-	30*	HPV-T	PLC, PC*
Bistoletti(2008)	Sweden	9	3**	>30	25**	Co screening	PC, HPV-T**
Burger(2012)	Norway	4	3*	34	20*	Cytology for younger & HPV DNA after 34	PC, PLC*
Kim(2005)	UK	3-5	3(25-49)-5(50-64) *	-	25 and 50*	HPV-T	PLC*
Kim(2005)	Netherlands	3-5	5*	-	30*	HPV-T	PLC, PC*
Kim(2005)	France	3-5	1 and 3*	-	25 and 27*	HPV-T	PC, HPV-P*
Kim(2005)	Italy	3-5	3*	-	25*	HPV-T or co screening	PLC, PC, HPV-P*
Sroczynski(2011)	Germany	2	1**	25-29/30	20**	PC/ HPV-P	PC**
De Kok(2012)	Europe	5	-	>30	-	-	-
Vijayaraghavan(2010)	USA	3	3*	<30	21*	HPV-T	PLC, PC*
Mandelblatt(2002)	USA	2	3*	20	21*	Co screening	PLC, PC*
Goldie(2004)	USA	2-3	3*	>30	21*	Co screening	PLC, PC*
Bidus(2006)	USA	2	3	-	21	PLC, reflex HPV	PLC, PC*
Brown(1999)	USA	3	3	-	21	PC, 10% PLC	PLC, PC*
Maxwell(2002)	USA	3	3*	-	21*	Co Screening	PLC, PC*
Chuck(2010)	Canada	3	Varies by Prov. *	>30	21*	PC, HPV-P,PC	PLC, PC*
Kulasingam (2009)	Canada	5	Varies by Prov. *	25	21*	HPV-P	PLC, PC*
Middle income country							
Chow(2010)	Taiwan	5	1[a]**	30	30-69[a]**	HPV-T	PC[a]**
Andres-Gamboa(2008)	Colombia	5	1-1-3[a]**	30	21[a]**	HPV-P	PC[a]**
Levin(2010)	China)	5(3 times)	-	35	35*	HPV-P	PC, PLC, VILI/VIA*
Vijayaraghavan(2008)	South Africa	10(3 times)	10[a]**	-	>30[a]**	Co screening	PC[a]**
Mandelblatt(2002)	Thailand	5	3	35		VIA with immediate treatment	-
Goldie(2001)	South Africa	3	10[a]**	35	>30[a]**	HPV-P or DVI	PC[a]**
Goldie(2005)	India	10	-	35	-	HPV-P or DVI	-
Goldie(2005)	Thailand	10		35		HPV-P or DVI	-
Goldie(2005)	Kenya	10	-	35	-	HPV-P or DVI	-
Goldie(2005)	South Africa	10	10[a]**	35	>30[a]**	HPV-P or DVI	PC[a]**
Low income country							
Goldie(2005)	Peru	10	2	35	25	HPV-P or DVI	-

*From International Cancer Screening Network67; **From articles; ***PLC=Liquid-based cytology; PC=Pap test; HPV-T=HPV test triage; HPV-P=HPV test primary screening; DVI=Direct visual inspection

Table 2. Incidence, mortality, cost, effectiveness, ICER, and undiscounted ICER of 11 strategies compared with no screening strategy.

Strategies	Incidence(No of cases)	Mortality(No of cases)	Cost($)	QALY	ICER(US $/QALY)	Undiscounted ICER
No screening	1321	509	13.93	24.406	0	0
HPV 35–10	940	363	42.89	24.409	8,875	2,472
Pap smear35-10	591	229	45.39	24.409	9,080	2,589
HPV 35–5	727	281	63.69	24.411	9,087	2,554
Pap smear 35–5	779	300	66.24	24.411	9,650	2,747
HPV 30–5	674	259	76.94	24.412	10,248	2,978
HPV 30 10	933	359	50.20	24.409	10,695	3,069
Pap smear 30–5	731	281	81.03	24.412	11,189	3,276
Pap smear 30–10	974	375	53.75	24.409	11,193	3,261
Pap smear 35–3	611	236	94.70	24.413	11,362	3,251
Pap smear 30–3	543	208	119.30	24.413	13,342	3,920
Pap smear 21–3	483	184	192.04	24.414	20,492	6,234

doi:10.1371/journal.pone.0156705.t002


Thank You!