




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

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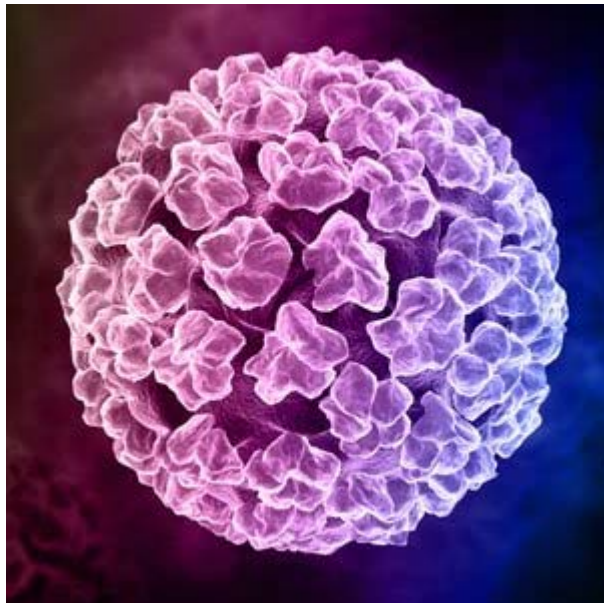
April 2019



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

Co-factors for HPV Infection

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

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*

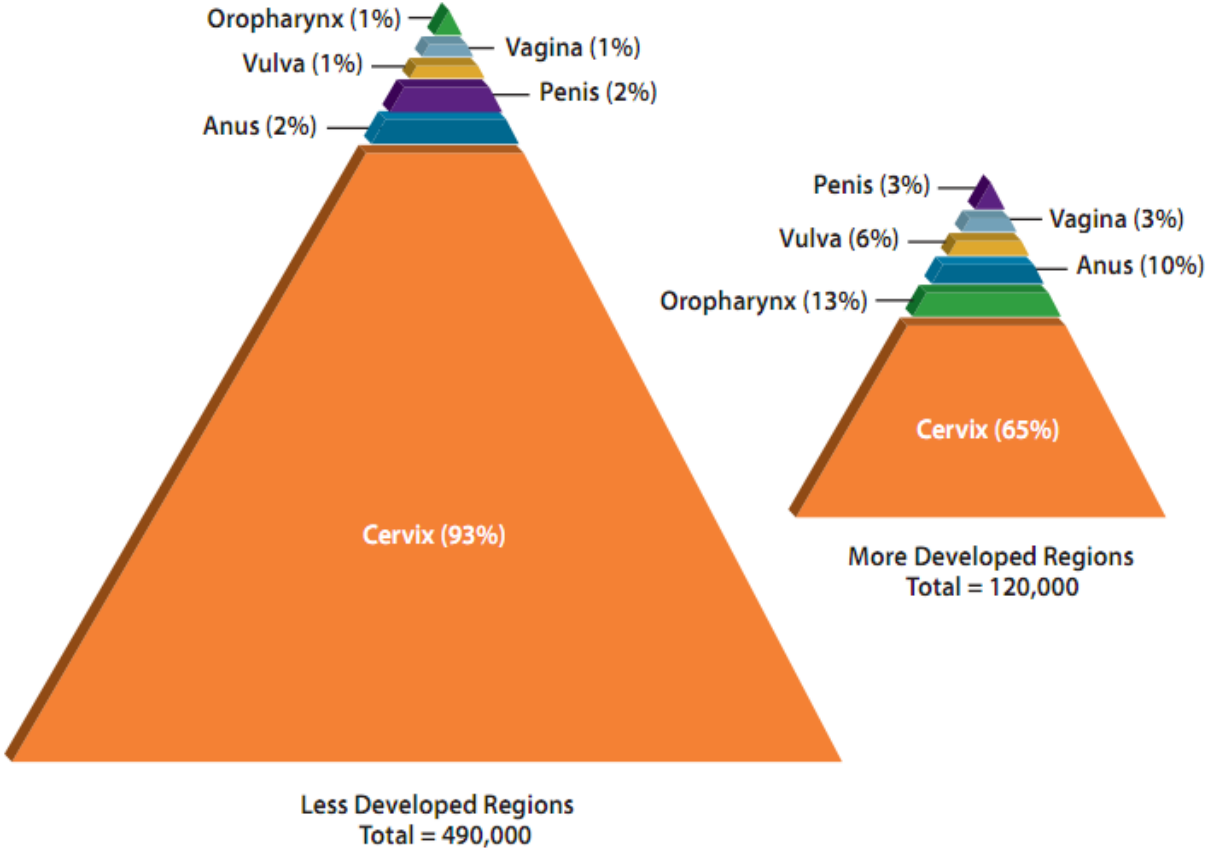


Table 1. Number of cancer cases attributable to HPV and corresponding attributable fraction (AF) by cancer site, sex and age; World, 2012

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

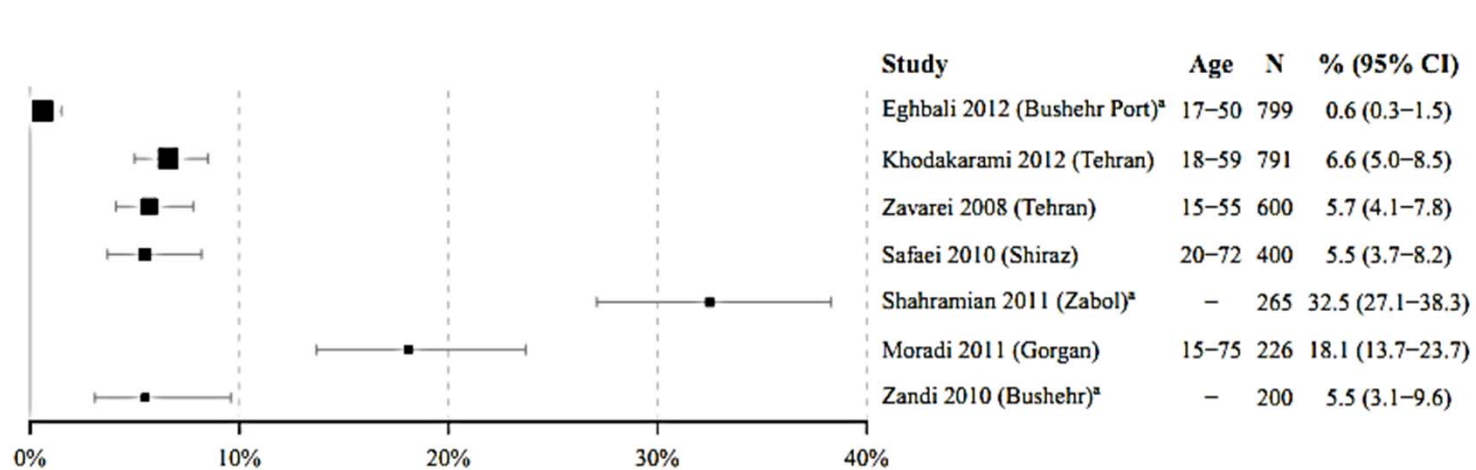


Table 2. Number of all cancer cases attributable to HPV and corresponding attributable fraction (AF) for all cancers, by region, cancer site(s) and sex; World, 2012

Region	Cervix uteri ¹	Anus		Penis		Vulva/vagina		Head and neck		All cancer Attributable to HPV Both sexes	AF (%)		
	F	M	F	M	F	M	F	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		

¹Numbers 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



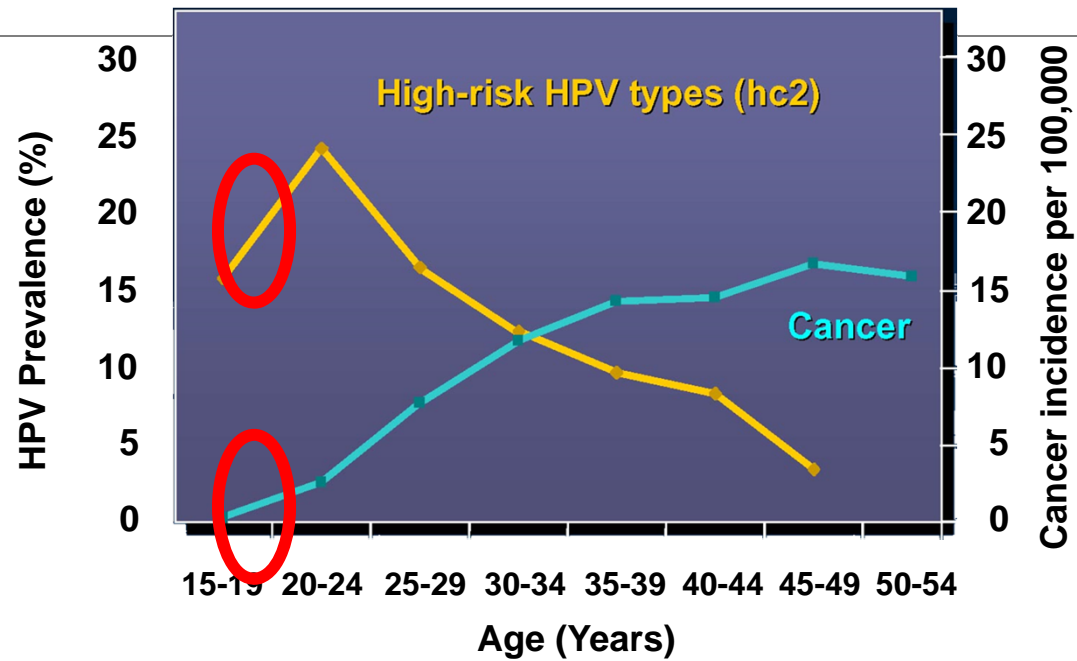
Prevalence of HPV 16, 18 by cytology in Iran

	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



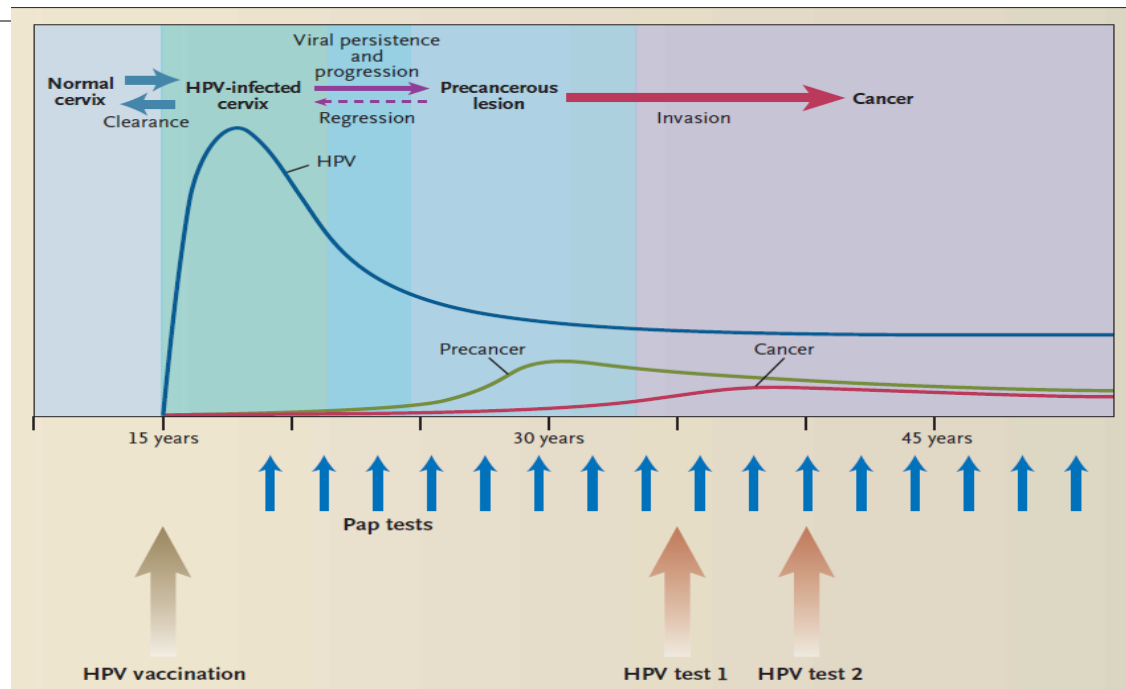
HPV and Cervical Cancer Rates by Age



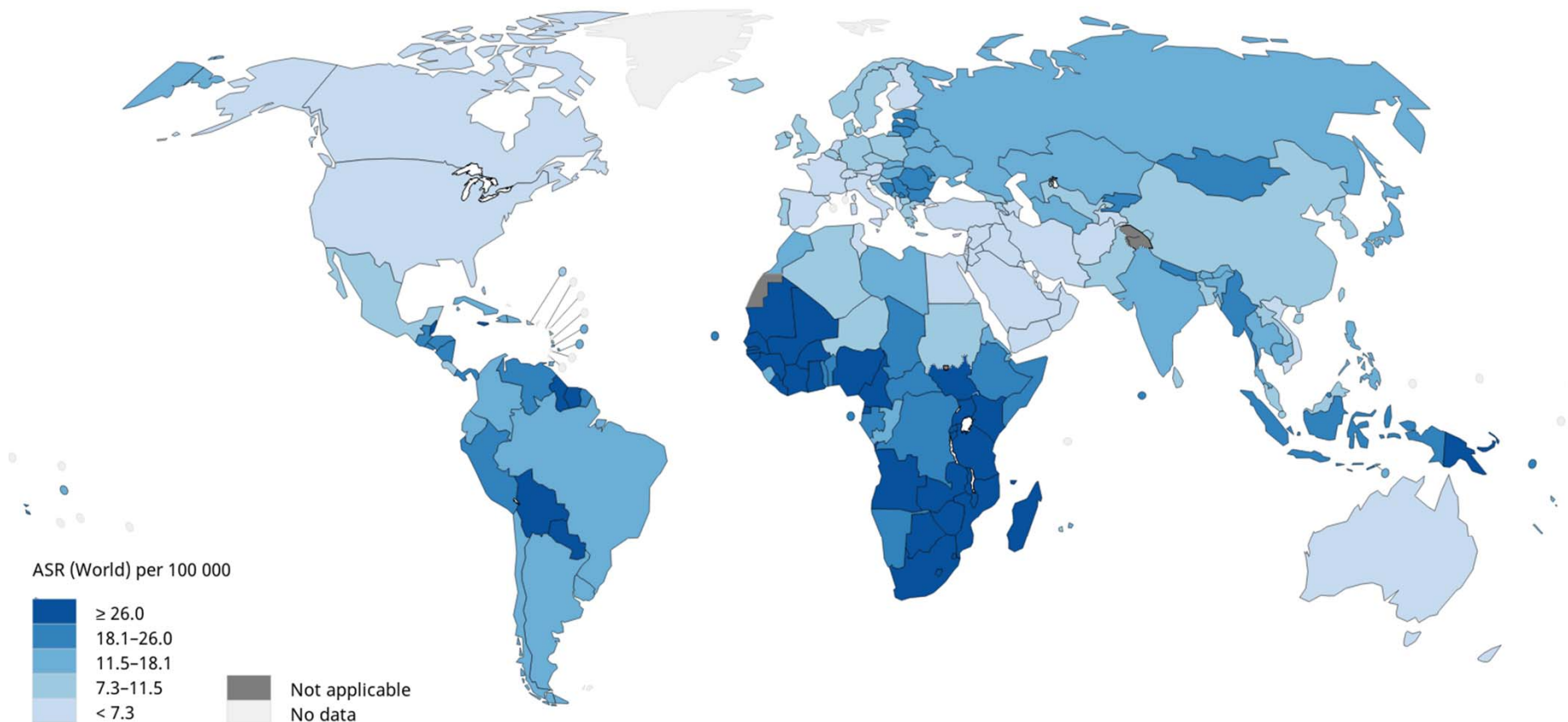
1. Sellors et al. *CMAJ*. 2000;163:503.

2. Ries et al. *Surveillance, Epidemiology and End Results (SEER) Cancer Stats NCI, 1973-1997*. 2000.

Natural History



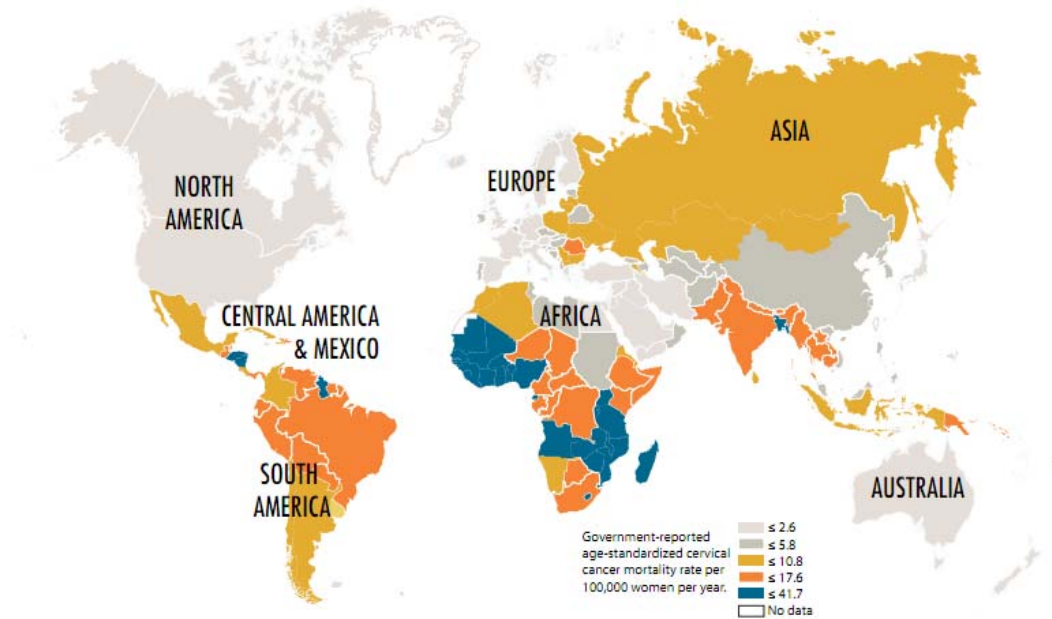
Estimated age-standardized incidence rates (World) in 2018, cervix uteri, all ages



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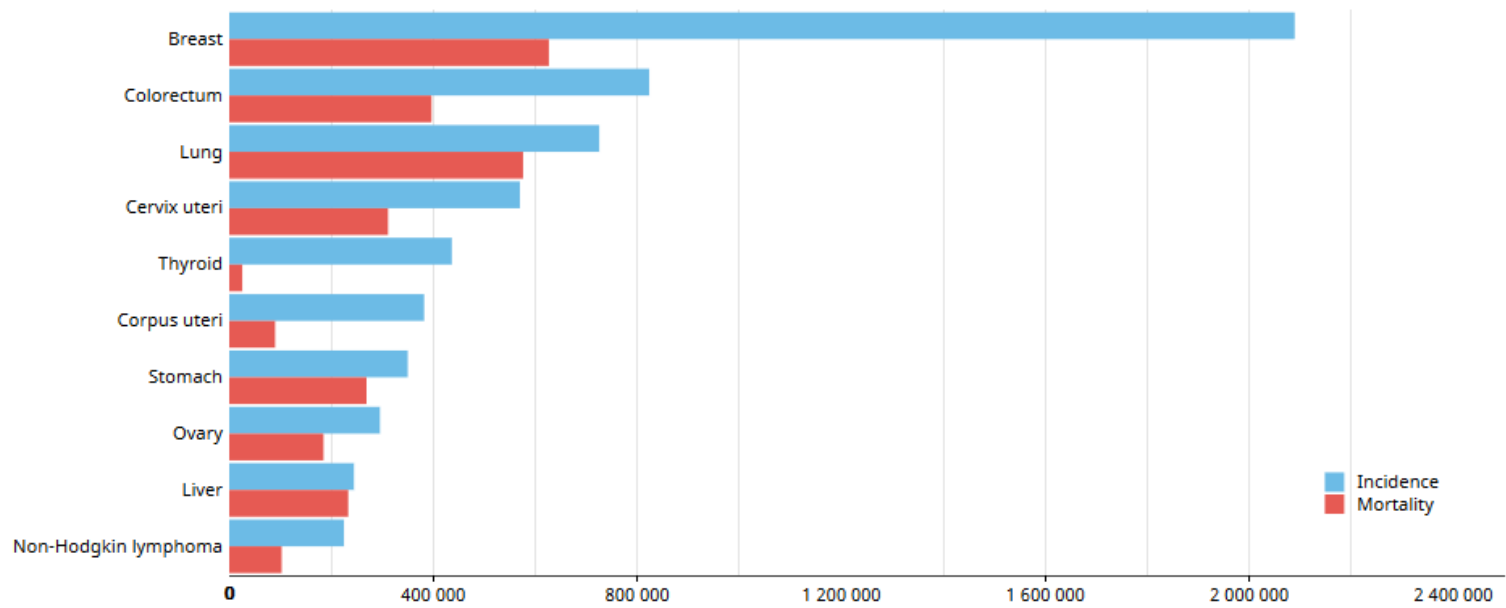
Data source: GLOBOCAN 2018
Graph production: IARC
(<http://gco.iarc.fr/today>)
World Health Organization

Mortality of Cervical Cancer in the World American Cancer Society 2014



Modified from: Crow, JM. HPV: the global burden. *Nature*. 2012;488:52-3. Data from: World Health Organization, Institut Catala d'Oncologia. Human papillomavirus and related cancers: summary report update. Barcelona (ES): WHO/ICO; 2010 Nov 15.

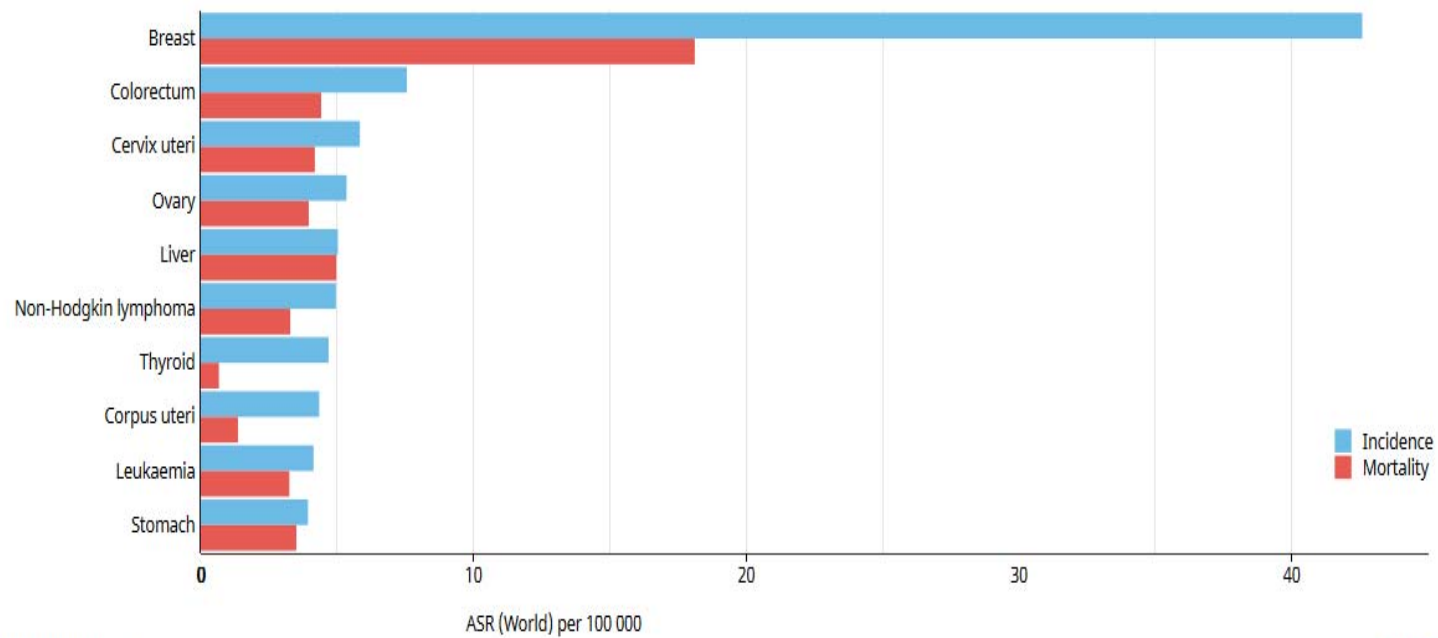
Estimated number of incident cases and deaths worldwide, females, all ages



Source: GLOBOCAN 2018
Production: Global Cancer Observatory (<http://gco.iarc.fr/>)
International Agency for Research on Cancer 2019



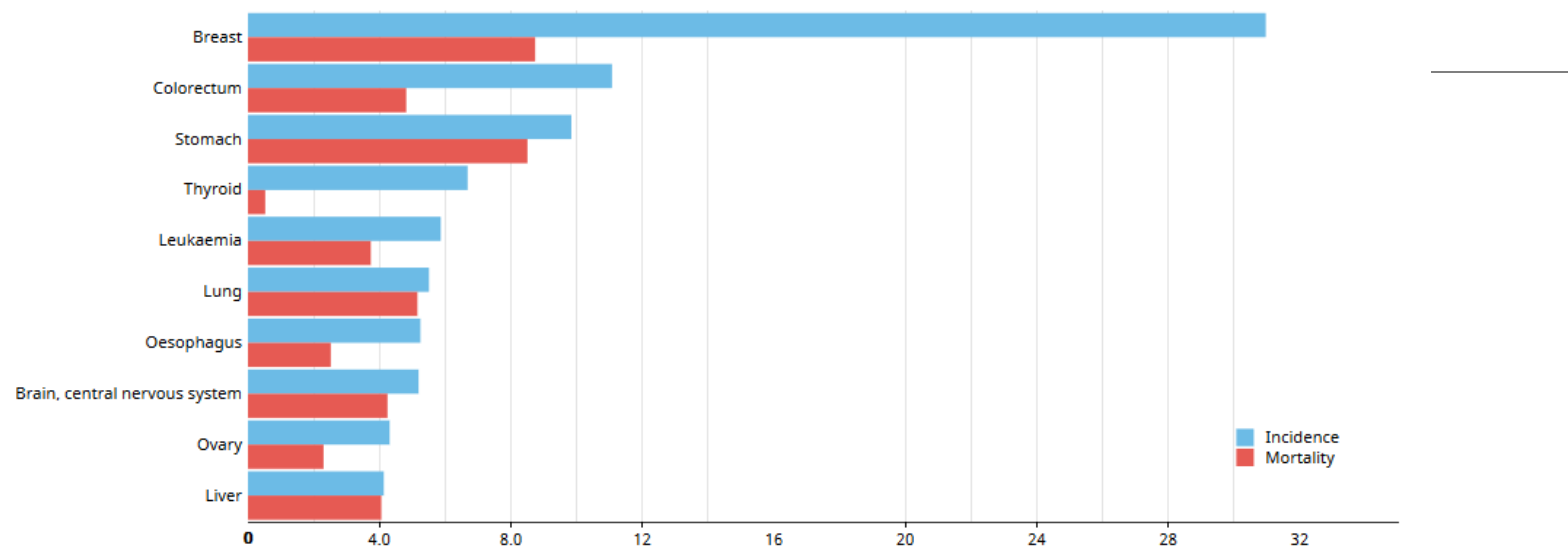
Estimated age-standardized incidence and mortality rates (World) in 2018, WHO East Mediterranean region (EMRO), females, all ages



Data source: GLOBOCAN 2018
Graph production: Global Cancer Observatory (<http://gco.iarc.fr/>)
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Estimated age-standardized incidence and mortality rates (World) in 2018, Iran, Islamic Republic of, females, all ages

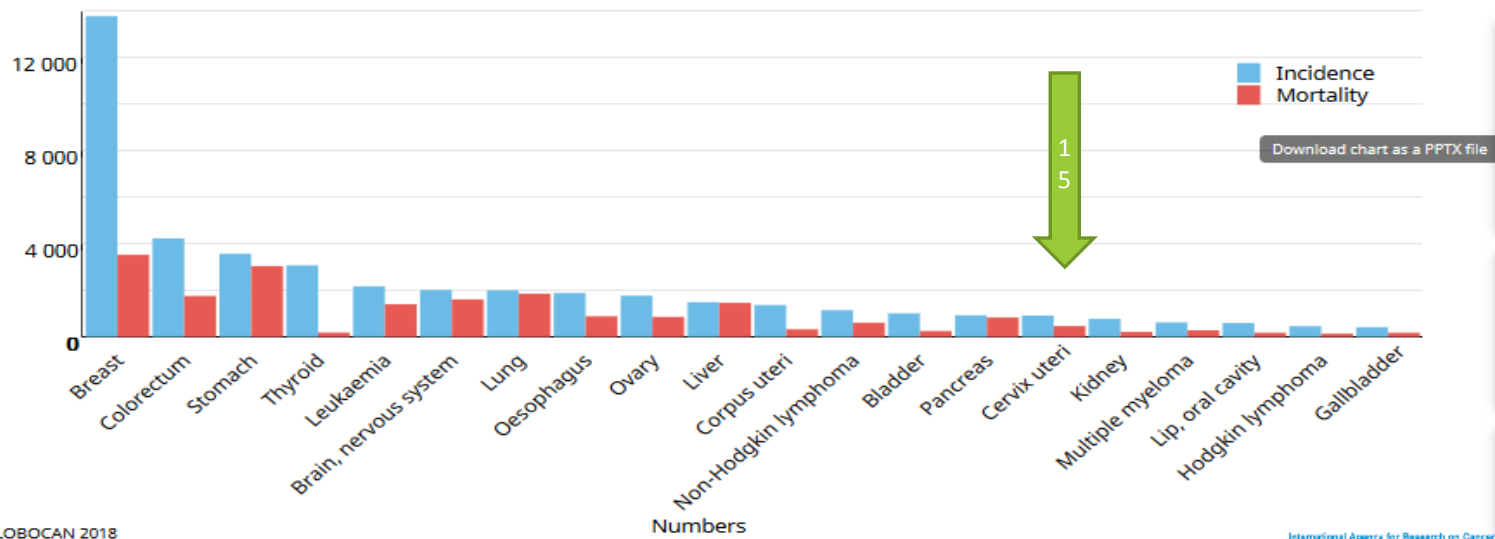


Data source: GLOBOCAN 2018
Graph production: Global Cancer Observatory (<http://gco.iarc.fr/>)
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Estimated number of incident cases and deaths Iran, Islamic Republic of, females, all ages



Data source: GLOBOCAN 2018
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Golestan Province

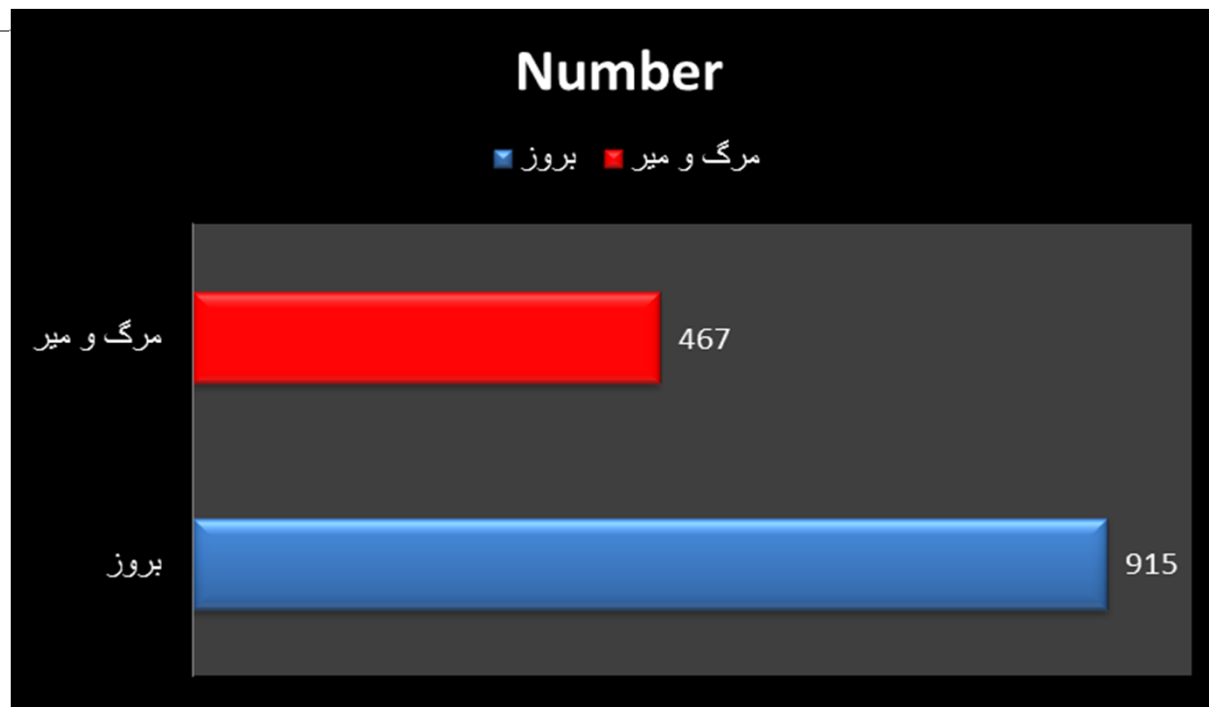
CI5 vol X

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	7.2	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



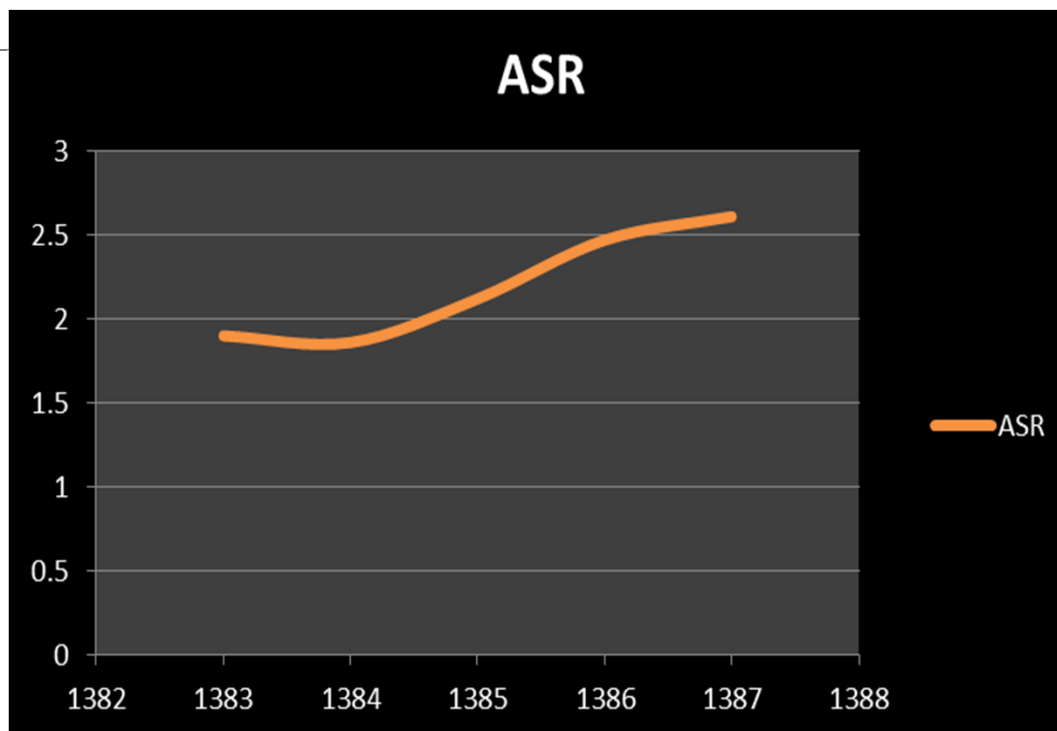
**Incidence & Mortality of Cervical Cancer :Iran
Cancer Office MOHME (1393)**



Provinces with cervical cancer in the 12 common cancers

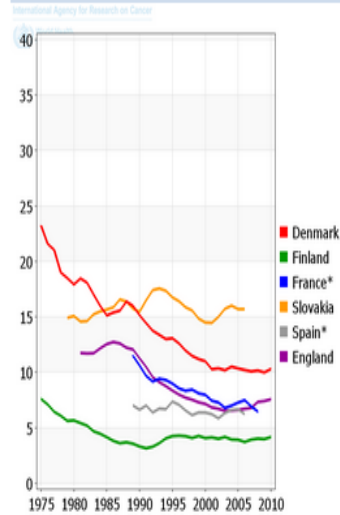
Province	Number	ASR	Rank
Golestan	37	4.24	8
Mazandaran	41	2.28	12

Cervical cancer trend in Iran

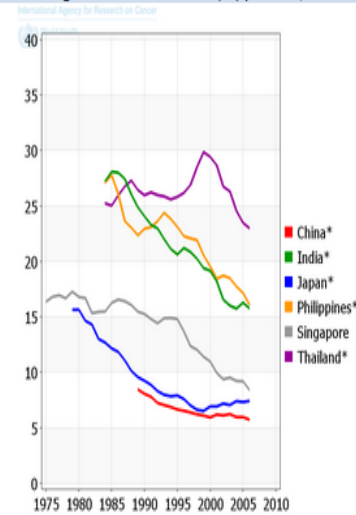


Time series of Cervical Cancer

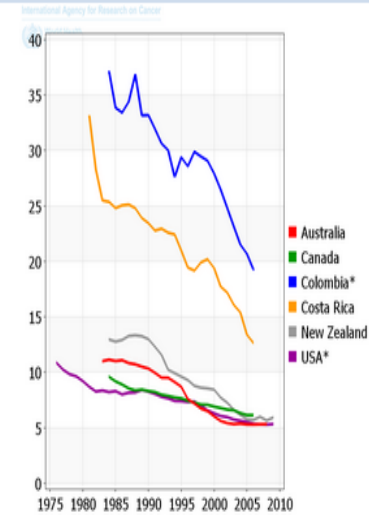
Trends in incidence of cervical cancer in selected countries: age-standardised rate (W) per 100,000



*Regional data
 NORCCAN (www.ncr.nu)
 ECO (eco.iarc.fr)
 England: www.ons.gov.uk



*Regional data
 CI5.iarc.fr

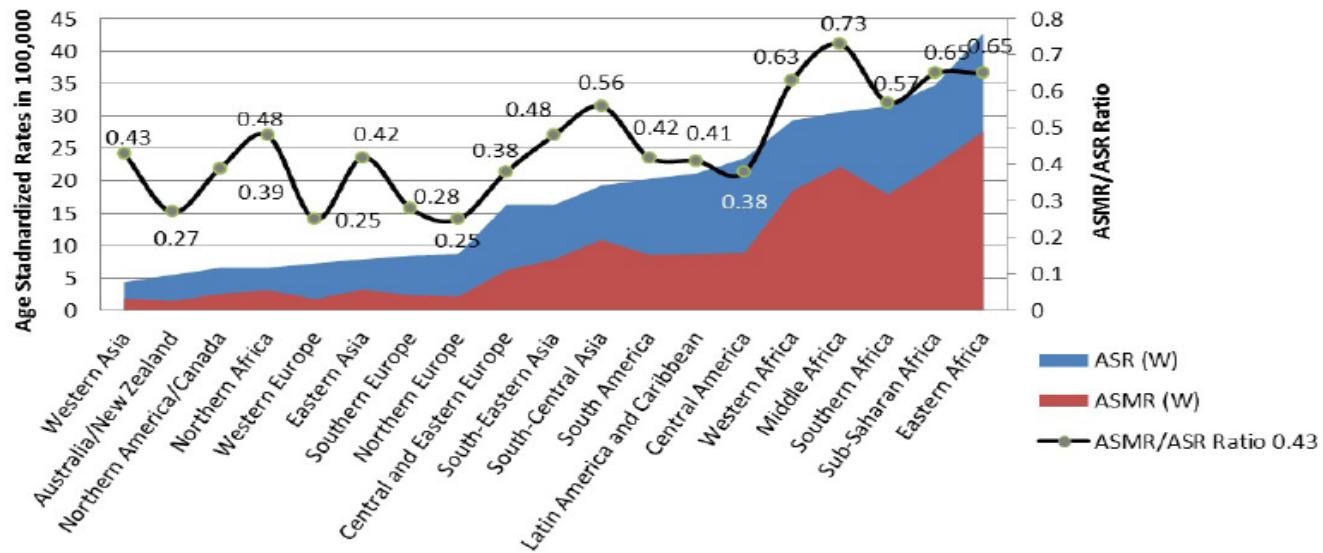


*Regional data
 CI5.iarc.fr
 Australia: www.aihw.gov.au
 New Zealand: www.health.govt.nz
 USA: seer.cancer.gov

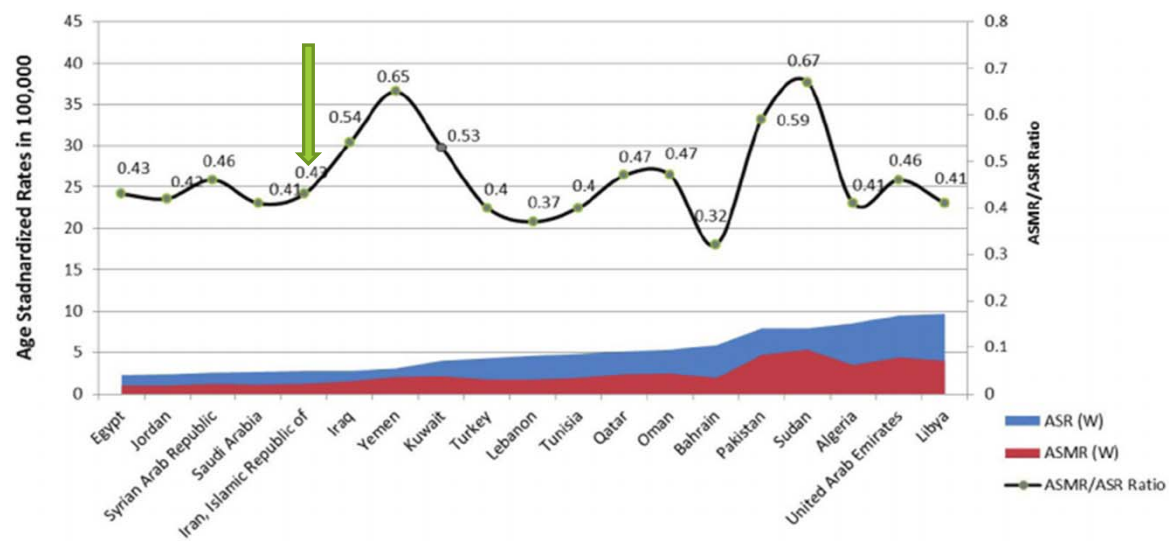
Time series of Cervical Cancer High Income Countries



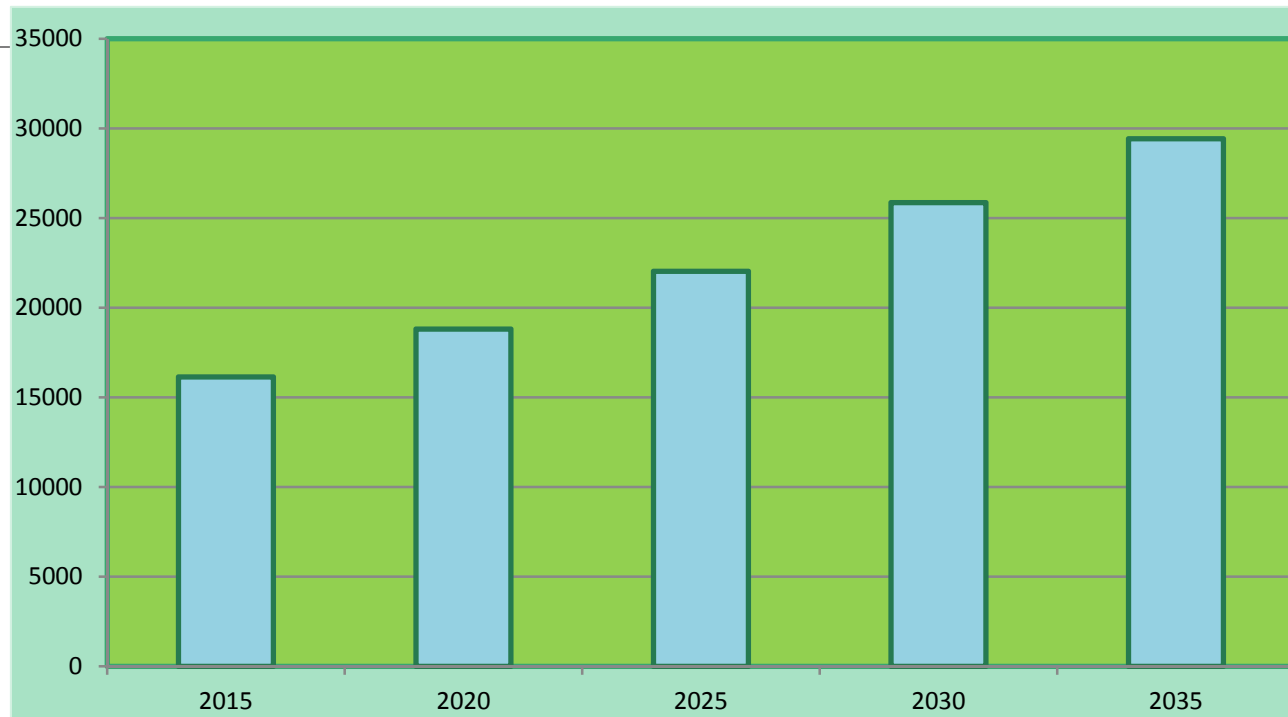
ASR/ASMR in the World Globocan 2012



ASR/ASMR in the Muslim Countries GLOBOCAN 2012



Cervical Cancer prediction of cervical cancer 2015-2035 EMRO region

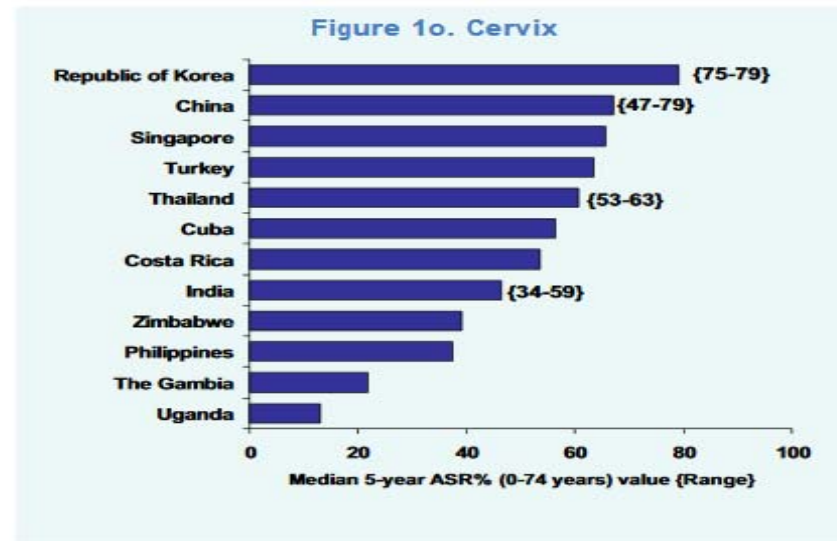


Preventing Cervical Cancer

Screening for precancerous changes (and treatment if problems found)

Vaccination against HPV

Survival of Cervical Cancer



Economic studies on Cervical Screening

RESEARCH ARTICLE

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

Aziz Nohviziou^{1*}, Ali Akbari Sari², Kazem Zandehdel³, Ahmad Barati Marnani⁴

DOI: [10.7314/APJCP.2014.15.19.8229](https://doi.org/10.7314/APJCP.2014.15.19.8229)
Economic Aspects of Cervical Cancer Screening Strategies

Economic Aspects of Cervical Cancer Worldwide: Discrepancy between Policymaking

Ali Akbari Sari^{1*}, Fatemeh Tourang², Kazem Zandehdel³, Ahmad Barati Marnani⁴

Abstract
Burden of cancer is increasing worldwide, especially in the low and middle-income countries (LMICs), including Iran. Several reports have been published on cancer statistics in Iran, although they had shortcomings and provided inconsistent information. We reported the most valid cancer statistics data in Iran, based on the Global Cancer Database and reported age-standardized incidence rate (ASIR) and five-year prevalence of cancer in Iran in 2012, and compared the ASIR and five-year prevalence of cancer in Iran in 2012, with the results of 2008. We also provided the projection of cancer in 2035 and estimated the life-time cancer risk by age 75. For men, the ASIR was 114.7 for men and 120.1 for women. The most common cancer sites were breast (ASIR 28.1), colorectal (ASIR 10.5), stomach (ASIR 9.7) and stomach (ASIR 20.6), bladder (ASIR 13.2), prostate (ASIR 11.5) in men. The ASIR was about 19% higher in 2012 (112.7/100,000) compared with 2008 (107.3/100,000). ASIR of all cancer sites will increase about 2.17 times in 2035. ASIR was about 20% higher in men (90.4/100,000) than women (78.9) in 2012. The highest ASIRs were observed for breast cancer in women and stomach cancer (17.3/100,000) in men. Five-year prevalence was 79,184 for men and 90,521 for women in 2012. Lifetime risk of all cancer sites was 74% for men and 74% for women in 2035.

Keywords: Screening and cervical cancer prevention programs (Ries, 1999). Different screening tests including: conventional cytology (Pap smear), liquid-based cytology (LBC) and human papillomavirus (HPV) DNA testing. Direct Involvement (DVI) are used for cervical screening. However, a combination of these methods with different screening intervals and starting age creates a variety of strategies in a screening program. Regular screening with Pap smears has been the only screening strategy for many years (Wortkeller & Anderson, 2008).

in women worldwide, a precancerous cervical lesion tree. Materials and consultation with sectors were identified provided services (visits NA test. The number of lesions and HPV were DNA test. The total cost and 174 \$ respectively, it is to be included in the , it is suggested that we

V DNA test to be more using the disease (Malloy Five Continents book, age Golestan province of Iran et al., 2013). Gynecologic of total female cancers in Muslim countries like incidence cervical cancer (2014). The prevalence in Iran were 76% and rasmizadeh et al., 2013). program in Iran includes test is performed outside

REVIEW ARTICLE
Received June 2017
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Comparing Health Economic Models to Answer Public Health Problems: A Review

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Abstract
Nowadays, decision analysis models are extensively used in solving healthcare problems. Considering the limited resources, the results of these studies will greatly assist policymakers with resource allocation. The purpose of this study is to provide a review of different decision analysis models in healthcare systems and to compare the components used in developing these models in studies addressing cervical cancer prevention. In this comprehensive review on decision analysis models used for cervical cancer prevention, we determined that the major components of the models included costs, outcomes, cycle lengths, discount rate, and perspective. The most commonly used model found in our review was the Markov model; nevertheless, it appears that dynamic models are gaining popularity over recent years. Conclusion: Using decision analysis models and encouraging healthcare policymakers to apply the results of modeling studies will result in saving time and costs, and will facilitate decision making in healthcare issues.

<http://ijhpm.com>
Int J Health Policy Manag 2016, 5(4): 225-232

IJHPM
International Journal of Health Policy Management

Original Article



Priority Setting for Improvement of Cervical Cancer Prevention in Iran

Azam Majidi¹, Reza Ghiasvand², Maryam Hadji³, Aziz Nohviziou⁴, Azam-Sadat Mousavi⁵, Minoo Pakgohar⁶, Nahid Khatkhatani⁷, Mehroozeh Abadipour⁸, Farzad Amouzgar Hashemi⁹, Marjan Rahmani¹⁰, Farzad Jafari¹¹

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

Aziz Nohviziou¹, Rajabali Darouei², Mansour Tahmassebi³, Farzad Amouzgar Hashemi⁴, Mohsen Rezaei Hosseini⁵, Ali Akbari Sari⁶, Ahmad Barati Marnani⁷, Kazem Zandehdel⁸

Abstract
Invasive cervical cancer (ICC) is the fourth most common cancer among women worldwide. Cervical screening programs have reduced the incidence and mortality rates of ICC. We studied the cost-effectiveness of different cervical screening strategies in the Islamic Republic of Iran, a Muslim country with a low incidence rate of ICC.

Objective
We constructed an 11-state Markov model, in which the parameters included regression and progression probabilities, test characteristics, costs, and utilities; these were extracted from primary data and the literature. Our strategies included Pap smear screening and human papillomavirus (HPV) DNA testing plus Pap smear triaging with different starting ages and screening intervals. Model outcomes included lifetime costs, life years gained, quality-adjusted life years (QALY), and incremental cost-effectiveness ratios (ICERs). One-way sensitivity analysis was performed to examine the stability of the results.

Results
We found that the prevented mortalities for the 11 strategies compared with no screening varied from 26% to 64%. The most cost-effective strategy was HPV screening, starting at age 30 years and repeated every 10 years. The ICER of this strategy was \$8,875 per QALY compared with no screening. We found that screening at 5-year intervals was also cost-

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ICERs should contribute
to the development of
screening strategies
necessary for regular
screening for improvement of

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 1999 and 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), Stoczynski(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 Screening Intervals Stratified by the Economic Situation of the Countries

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*
Sroczyński(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 ^{3**}	30	30-69 ^{3**}	HPV-T	PC ^{3**}
Andres-Gamboa(2008)	Colombia	5	1-1-3 ^{3**}	30	21 ^{3**}	HPV-P	PC ^{3**}
Levin(2010)	China	5(3 times)	-	35	35*	HPV-P	PC, PLC, VILI/VIA*
Vijayaraghavan(2008)	South Africa	10(3 times)	10 ^{4**}	-	>30 ^{4**}	Co screening	PC ^{4**}
Mandelblatt(2002)	Thailand	5	3	35	-	VIA with immediate treatment	-
Goldie(2001)	South Africa	3	10 ^{4**}	35	>30 ^{4**}	HPV-P or DVI	PC ^{4**}
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 ^{4**}	35	>30 ^{4**}	HPV-P or DVI	PC ^{4**}
Low income country							
Goldie(2005)	Peru	10	2	35	25	HPV-P or DVI	-

*From International Cancer Screening Network⁵; **From articles; ***PLC=Liquid-based cytology; PC=Pap test; HPV-T=HPV test triage; HPV-P=HPV test primary screening; DVI=Direct

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

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Thank You!

