

# MATION CENTRE ON HPV AND **Human Papillomavirus** and **Related Diseases Report**



JIVARC IN

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# **Executive summary**

Human papillomavirus (HPV) infection is now a well-established cause of cervical cancer and there is growing evidence of HPV being a relevant factor in other anogenital cancers (anus, vulva, vagina and penis) and head and neck cancers. HPV types 16 and 18 are responsible for about 70% of all cervical cancer cases worldwide. HPV vaccines that prevent against HPV 16 and 18 infection are now available and have the potential to reduce the incidence of cervical and other anogenital cancers.

This report provides key information for Bulgaria on cervical cancer, other anogenital cancers and head and neck cancers, HPV-related statistics, factors contributing to cervical cancer, cervical cancer screening practices, and HPV vaccine introduction. The report is intended to strengthen the guidance for health policy implementation of primary and secondary cervical cancer prevention strategies in the country.

# Table 1: Key Statistics

	10,510 1, 1109 , 50001,50105		
Population	colonomylation and a 15 rms)		3.06 million
Women at risk for cervical cancer (Fen Burden of cervical cancer and oth			3.06 million
Annual number of cervical cancer case			1009
Annual number of cervical cancer deat			503
Crude incidence rates per 100,000 pop		Male	Female
Crude incidence rates per 100,000 pop		Male	
	Cervical cancer	-	28.2
	Anal cancer	0.68	0.84
	Vulva cancer	-	3.30
	Vaginal cancer	-	0.92
	Penile cancer	1.57	
	Oropharyngeal cancer	3.38	0.64
	Oral cavity cancer	9.40	3.86
	Laryngeal cancer	14.8	1.15
Burden of cervical HPV infection			
Prevalence (%) of HPV 16 and/or HPV	18 among women with:		
		Normal cytology	3.8
	Low-grade cervical les		27.1
	High-grade cervical lesions (HSIL		54.5
		Cervical cancer	80.3
Other factors contributing to cerv			
Smoking prevalence (%) [95% UI], wor			23.8 [16.8-31.2]
Total fertility rate (live births per won	nen)		1.6
Oral contraceptive use (%)			6.23
HIV prevalence (%) [95% UI], women	(15-49 years)		<0.1 [<0.1 -<0.1]
Sexual behaviour			
Percentage of 15-year-old who have ha			40.0/21.0
Range of median age at first sexual in			_/-
Cervical screening practices and p			
Existence of official national recomme			Yes
Starting year of current recommendat	ions		Unk
Active invitation to screening			No
Screening ages (years), primary screen	ning test used, and screening interval or fr	equency of screen-	30-40 (cytology, 3
ings			years
HPV vaccine in females			
HPV vaccination programme			Introduced
Year of introduction			2012
Year of estimation of HPV vaccination	coverage		2021
HPV coverage – first dose (%)			8
HPV coverage – last dose (%)			ç

 $\ast\,$  Please see the specific sections for more information.

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# **1** Introduction

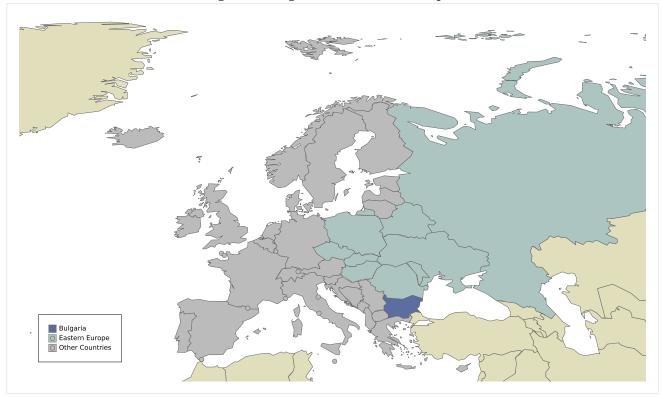


Figure 1: Bulgaria and Eastern Europe

Information Centre aims to compile and centralise updated data and statistics on human papillomavirus (HPV) and related cancers. This report aims to summarise the data available to fully evaluate the burden of disease in Bulgaria and to facilitate stakeholders and relevant bodies of decision makers to formulate recommendations on the prevention of cervical cancer and other HPV-related cancers. Data include relevant cancer statistic estimates, epidemiological determinants of cervical cancer such as demographics, socioeconomic factors, risk factors, burden of HPV infection in women and men, cervical screening and immunization practices. The report is structured into the following sections:

**Section 2, Demographic and socioeconomic factors**. This section summarises the socio-demographic profile of Bulgaria. For analytical purposes, Bulgaria is classified in the geographical region of Eastern Europe (Figure 1, lighter blue), which is composed of the following countries: Czechia, Hungary, Republic of Moldova, Poland, Romania, Russian Federation, Slovakia, and Ukraine. Throughout the report, Bulgaria estimates will be complemented with corresponding regional estimates.

**Section 3, Burden of HPV related cancers**. This section describes the current burden of invasive cervical cancer and other HPV-related cancers in Bulgaria ith estimates of prevalence, incidence, and mortality rates. Information in other HPV-related cancers includes other anogenital cancers (anus, vulva, vagina, and penis) and head and neck cancers (oral cavity, oropharyngeal, and larynx).

**Section 4, HPV related statistics**. This section reports on prevalence of HPV and HPV type-specific distribution in Bulgaria, in women with normal cytology, precancerous lesions and invasive cervical cancer. In addition, the burden of HPV in other anogenital cancers (anus, vulva, vagina, and penis), head and neck cancers (oral cavity, oropharynx, and larynx) and men are presented.

**Section 5, Factors contributing to cervical cancer**. This section describes factors that can modify the natural history of HPV and cervical carcinogenesis such as smoking, parity, oral contraceptive use, and co-infection with HIV.

**Section 6, Sexual and reproductive health behaviour indicators**. This section presents sexual and reproductive behaviour indicators that may be used as proxy measures of risk for HPV infection and anogenital cancers, such as age at first sexual intercourse, average number of sexual partners, and anal intercourse among others.

**Section 7, HPV preventive strategies**. This section presents preventive strategies that include basic characteristics and performance of cervical cancer screening status, status of HPV vaccine licensure introduction, and recommendations in national immunisation programmes.

**Section 8, Protective factors for cervical cancer**. This section presents male circumcision and the use of condoms.

#### 2 **Demographic and socioeconomic factors**

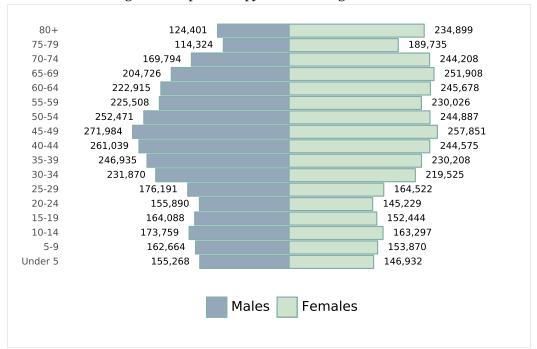
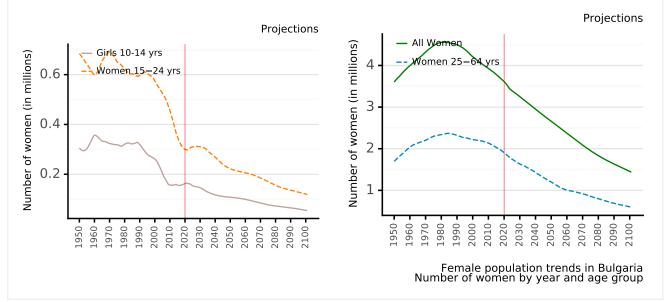


Figure 2: Population pyramid of Bulgaria for 2022

#### Data accessed on 30 Jul 2022

Please refer to original source for methods of estimation. Year of estimate: 2022

Data Sources: United Nations, Department of Economic and Social Affairs, Population Division (2022). World Population Prospects 2022, Online Edition. [Accessed on July 30, 2022].



#### Figure 3: Population trends in four selected age groups in Bulgaria

Data accessed on 30 Jul 2022

Please refer to original source for methods of estimation. Year of estimate: 2022

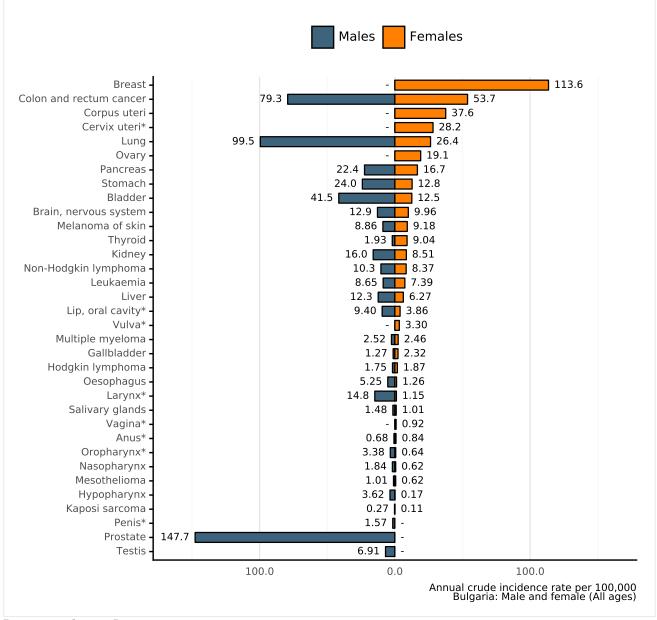
Data Sources: United Nations, Department of Economic and Social Affairs, Population Division (2022). World Population Prospects 2022, Online Edition. [Accessed on July 30, 2022].

#### 3 **Burden of HPV related cancers**

HPV is the cause of almost all cervical cancer cases and is responsible for an important fraction of other anogenital and head and neck cancer. Here, we present the most recent estimations on the burden of HPV-associated cancer.

# 3.1 HPV related cancers incidence

Figure 4: Comparison of HPV related cancers incidence to other cancers in men and women of all ages in Bulgaria (estimates for 2020)

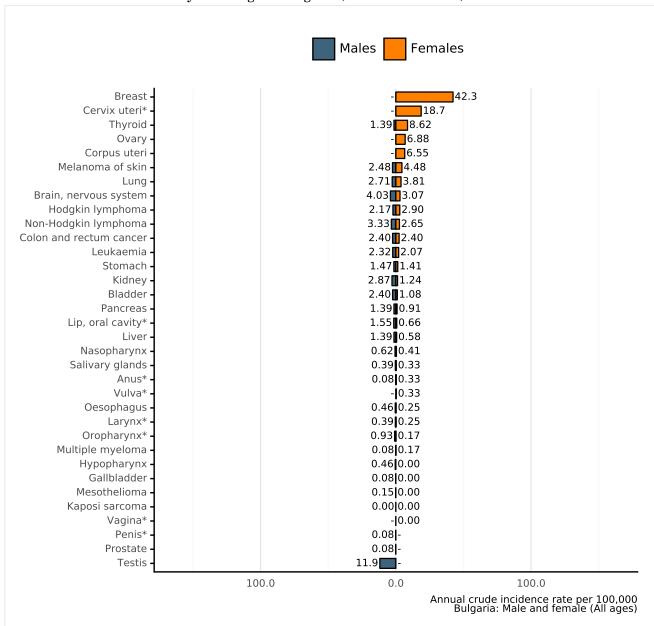


#### Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods Non-melanoma skin cancer is not included

Rates per 100,000 men per year.

Rates per 100,000 women per year.



#### Figure 5: Comparison of HPV related cancers incidence to other cancers among men and women 15-44 years of age in Bulgaria (estimates for 2020)

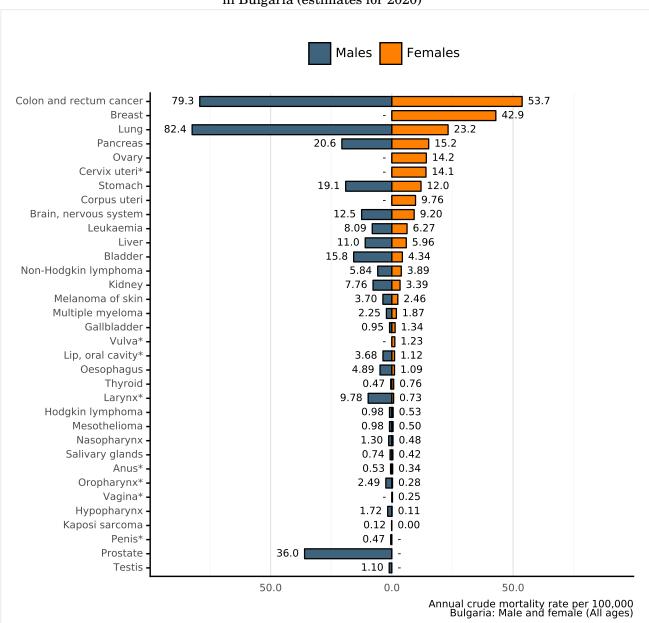
#### Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods

Non-melanoma skin cancer is not included

Rates per 100,000 men per year. Rates per 100,000 women per year.

# 3.2 HPV related cancers mortality

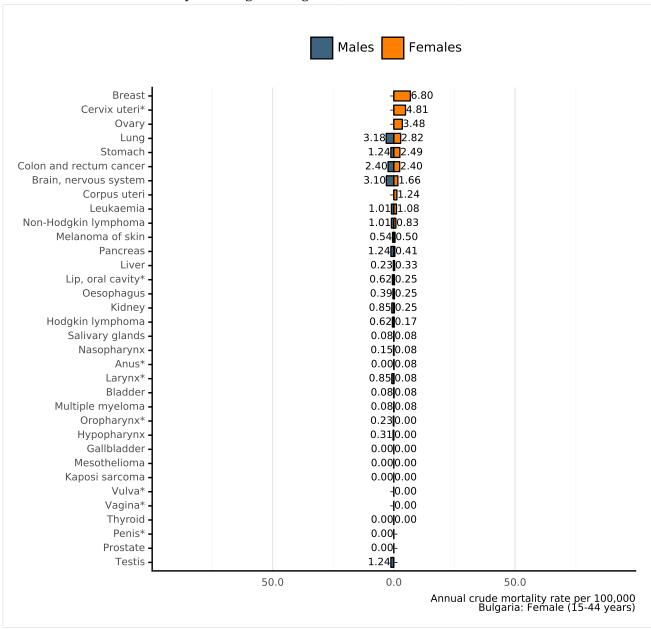


# Figure 6: Comparison of HPV related cancers mortality to other cancers in men and women of all ages in Bulgaria (estimates for 2020)

#### Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods Non-melanoma skin cancer is not included

Rates per 100,000 men per year. Rates per 100,000 women per year.



#### Figure 7: Comparison of HPV related cancers mortality to other cancers among men and women 15-44 years of age in Bulgaria (estimates for 2020)

#### Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods Non-melanoma skin cancer is not included

Rates per 100,000 men per year. Rates per 100,000 women per year.

#### 3.3 Cervical cancer

Cancer of the cervix uteri is the  $4^{th}$  most common cancer among women worldwide, with an estimated 604,127 new cases and 341,831 deaths in 2020. Worldwide, mortality rates of cervical cancer are substantially lower than incidence with a ratio of mortality to incidence to 57% (GLOBOCAN 2020). The majority of cases are squamous cell carcinoma followed by adenocarcinomas. (Vaccine 2006, Vol. 24, Suppl 3; Vaccine 2008, Vol. 26, Suppl 10; Vaccine 2012, Vol. 30, Suppl 5; IARC Monographs 2007, Vol. 90)

This section describes the current burden of invasive cervical cancer in Bulgaria and in comparison to geographic region, including estimates of the annual number of new cases, deaths, incidence, and mortality rates.

#### 3.3.1 Cervical cancer incidence in Bulgaria

Key Stats.
------------

About 1,009 new cervical cancer cases are diagnosed annually in Bulgaria (estimations for 2020).

Cervical cancer ranks\* as the 4<sup>th</sup> leading cause of female cancer in Bulgaria.

Cervical cancer is the 2<sup>nd</sup> most common female cancer in women aged 15 to 44 years in Bulgaria.

\* Ranking of cervical cancer incidence to other cancers among all women according to highest incidence rates (ranking 1st) excluding non-melanoma skin cancer. Ranking is based on crude incidence rates (actual number of cervical cancer cases). Ranking using age-standardized rate (ASR) may differ.

Indicator	Bulgaria	Eastern Europe	World
Annual number of new cancer cases	1,009	32,348	604,127
Uncertainty intervals of new cancer cases [95% UI]	[864-1,179]	[31,584-33,131]	[582,031-627,062]
Crude incidence rate <sup>b</sup>	28.2	20.8	15.6
Age-standardized incidence rate <sup>b</sup>	18.0	14.5	13.3
Cumulative risk (%) at 75 years old <sup>a</sup>	1.86	1.42	1.39

# Table 2: Cervical cancer incidence in Bulgaria (estimates for 2020)

Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods
<sup>a</sup> Cumulative risk (incidence) is the probability or risk of individuals getting from the disease during ages 0-74 years. For cancer, it is expressed as the % of new born children who would be expected to develop from a particular cancer before the age of 75 if they had the rates of cancer observed in the period in the absence of competing cause

<sup>b</sup> Rates per 100,000 women per year.

Table 3: Cervical cancer incidence in Bulgaria by cancer registry

Cancer registry <sup>1</sup>	Period	N cases <sup>a</sup>	Crude rate <sup>b</sup>	<b>ASR</b> <sup>b</sup>
National	2008-2012	5557	28.9	19.6

Data accessed on 5 Oct 2018

Please refer to original source (available at http://ci5.iarc.fr/CI5-XI/Default.aspx) ASR: Age-standardized rate, Standardized rates have been estimated using the direct method and the World population as the reference. <sup>a</sup> Accumulated number of cases during the period in the population covered by the corresponding registry.

<sup>a</sup> Accumulated number of cases ouring the period in the p

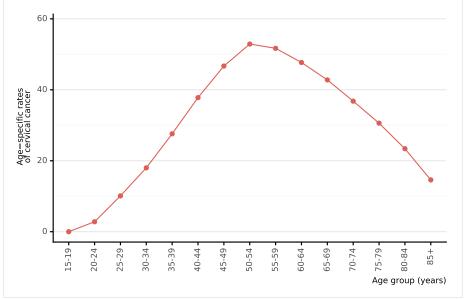


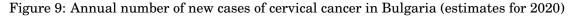
Figure 8: Age-specific incidence rates of cervical cancer in Bulgaria (estimates for 2020)

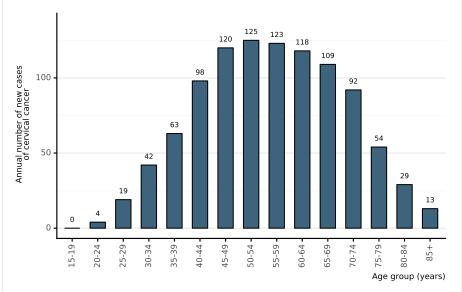
#### Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 women per year.

Data Sources

Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2020). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer. Available from: https://gco.iarc.fr/today, accessed [27 January 2021].





Data accessed on 27 Jan 2021

For more detailed methods of estimation plea e refer to http://gco.iarc.fr/today/data-sources-methods Data Sources

- For age-standardised incidence rates of cervical cancer of Bulgaria (estimates for 2020) please refer to Figure 73
- For annual number of new cases of cervical cancer by age group in Bulgaria (estimates for 2020) please refer to Figure 74
- For comparison of age-specific cervical cancer incidence rates in Bulgaria, within the region, and • the rest of world please refer to Figure 75

# 3.3.2 Cervical cancer incidence by histology in Bulgaria

Table 4: Age-standardised incidence rates of cervical cancer in Bulgaria by histological type and cancer registry

	registry				
Cancer registry <sup>1</sup>	Period	Squamo	Adeno	Other	Unspec.
National	2008-2012	17.1	1.4	0.7	0.2

Data accessed on 5 Oct 2018

Rates per 100,000 women per year. Standarized rates have been estimated using the direct method and the World population as the references.

Adeno: adeno: adenocarcinoma; Other: Other carcinoma; Squamous: Squamous cell carcinoma; Unspec: Unspecified carcinoma; <u>Data Sources:</u> <sup>1</sup> Bray F, Colombet M, Mery L, Piñeros M, Znaor A, Zanetti R and Ferlay J, editors (2017). Cancer Incidence in Five Continents, Vol. XI (electronic version). Lyon: International Agency for Research on Cancer. Available from: http://ci5.iarc.fr, accessed [05 October 2018].

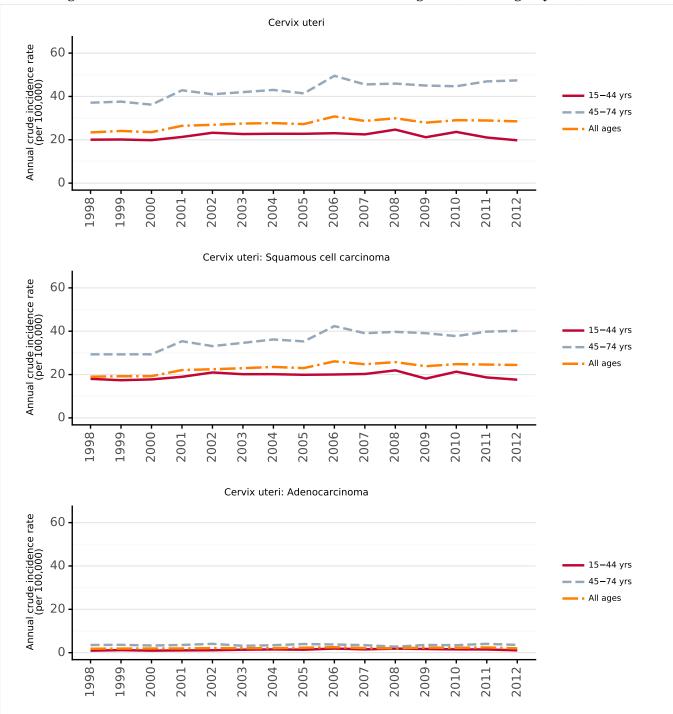


Figure 10: Time trends in cervical cancer incidence in Bulgaria (cancer registry data)

Data accessed on 28 Aug 2018 <sup>a</sup> Estimated annual percentage change based on the trend variable from the net drift for 15 years, from 1994-2008.

Data Sources:

Ferlay J. Colombet M and Bray F. Cancer Incidence in Five Continents, CI5plus: IARC CancerBase No. 9 [Internet]. Lyon, France: International Agency for Research on Cancer; 2018. Available from: http://ci5.iarc.fr

Vaccarella S, Lortet-Tieulent J, Plummer M, Franceschi S, Bray F. Worldwide trends in cervical cancer incidence: Impact of screening against changes in disease risk factors. eur J Cancer 2013;49:3262-73.

#### 3.3.3 Cervical cancer mortality in Bulgaria

# Key Stats. About 503 cervical cancer deaths occur annually in Bulgaria are diagnosed annually (estimations for 2020). Cervical cancer ranks\* as the 6<sup>th</sup> leading cause of cancer deaths of female cancer deaths in Bulgaria. Cervical cancer is the 2<sup>nd</sup> leading cause of cancer deaths in women aged 15 to 44 years in Bulgaria.

\* Ranking of cervical cancer incidence to other cancers among all women according to highest incidence rates (ranking 1st) excluding non-melanoma skin cancer. Ranking is based on crude incidence rates (actual number of cervical cancer cases). Ranking using age-standardized rate (ASR) may differ.

Indicator	Bulgaria	Eastern Europe	World
Annual number of deaths	503	15,854	341,831
Uncertainty intervals of mortal- ity cancer cases [95% UI]	[409-619]	[15,373-16,350]	[324,231-360,386]
Crude mortality rate <sup>b</sup>	14.1	10.2	8.84
Age-standardized mortality rate <sup>b</sup>	7.13	6.06	7.25
Cumulative risk (%) at 75 years old <sup>a</sup>	0.77	0.65	0.82

### Table 5: Cervical cancer mortality in Bulgaria (estimates for 2020)

Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods
<sup>a</sup> Cumulative risk (mortality) is the probability or risk of individuals dying from the disease during ages 0-74 years. For cancer, it is expressed as the % of new born children who would be Expected to die from a particular cancer before the age of 75 if they had the rates of cancer observed in the period in the absence of competing causes b Rates per 100,000 women per year.

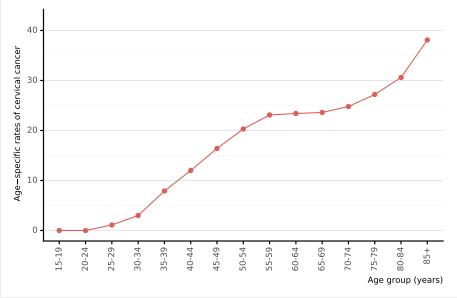
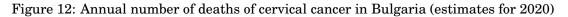


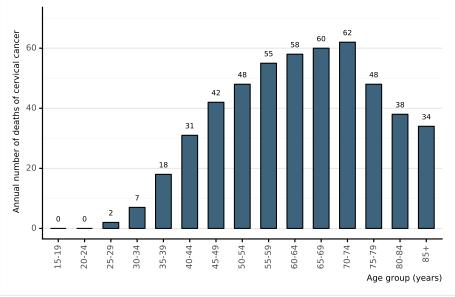
Figure 11: Age-specific mortality rates of cervical cancer in Bulgaria (estimates for 2020)

#### Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 women per year.

Data So Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2020). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer. Available from: https://gco.iarc.fr/today, accessed [27 January 2021].





Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods

- For age-standardised mortality rates of cervical cancer of Bulgaria (estimates for 2020) please refer to Figure 105
- For annual number of deaths of cervical cancer by age group in Bulgaria (estimates for 2020) please refer to Figure 106
- For comparison of age-specific cervical cancer mortality rates in Bulgaria, within the region, and the rest of world please refer to Figure 107

#### 3.3.4 Cervical cancer incidence and mortality comparison in Bulgaria

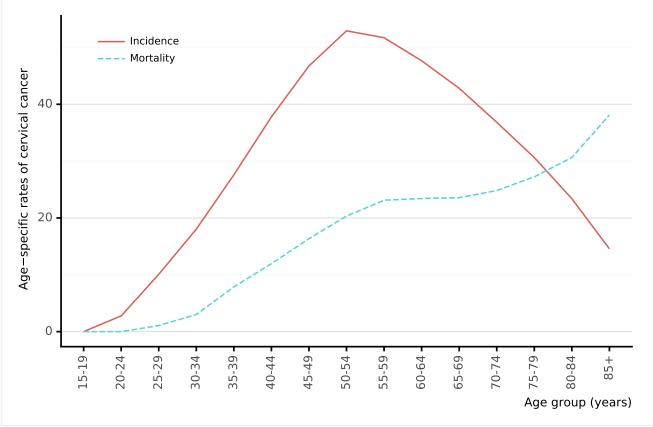


Figure 13: Comparison of age-specific cervical cancer incidence and mortality rates in Bulgaria (estimates for 2020)

Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 women per year.

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Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2020). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer. Available from: https://gco.iarc.fr/today, accessed [27 January 2021].

#### Table 6: Premature deaths and disability from cervical cancer in Bulgaria, Europe and the rest of the world (estimates for 2019)

	Bulgaria		Europe		World		
Indicator	Number	Rate	Number	Rate	Number	Rate	
DALYs (95% UI) <sup>a</sup>	15,434	433	824,336	189	8,955,013	232	
	(10,558-20,191)	(296-566)	(726, 198-913, 992)	(166-209)	(7,547,733-9,978,462)	(196-259)	
YLLs (95% UI) <sup>b</sup>	14,914	418	793,756	182	8,712,962	226	
1 LLS (95% UI)~	(10, 217 - 19, 603)	(286-549)	(703,004-877,841)	(161-201)	(7, 365, 279 - 9, 728, 886)	(191-252)	
YLDs (95% UI) <sup>c</sup>	520 (289-781)	15 (8-22)	30,580	7 (5-10)	242,051	6 (4-8)	
1LDS (95 // 01)	520 (265-761)	15 (0-22)	(21,266-42,064)	1,266-42,064)	(171,644-326,024)	0 (4-0)	

Data accessed on 29 Apr 2021

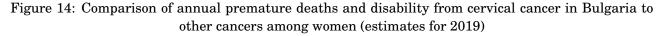
<sup>a</sup> DALYs (95% UI): estimated disability adjusted life years (95% uncertainty interval)

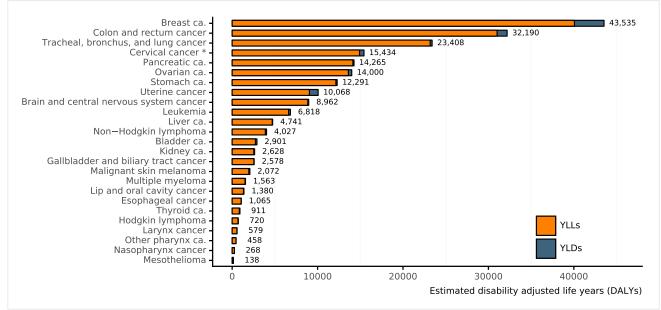
 $^b$  YLLs (95% UI): years of life lost (95% uncertainty interval)

 $^{c}$  YLDs (95% UI): estimated years lived with disability (95% uncertainty interval)

Data Sources:

GBD 2019 Diseases and Injuries Collaborators. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet. 2020 Oct 17;396(10258):1204-1222





#### Data accessed on 29 Apr 2021

YLLs: years of life lost YLDs: years lived with disability

Data Sources: GBD 2019 Diseases and Injuries Collaborators. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet. 2020 Oct 17;396(10258):1204-1222

#### 3.4 Anogenital cancers other than the cervix

Data on HPV role in anogenital cancers other than cervix are limited, but there is an increasing body of evidence strongly linking HPV DNA with cancers of anus, vulva, vagina, and penis. Although these cancers are much less frequent compared to cervical cancer, their association with HPV make them potentially preventable and subject to similar preventative strategies as those for cervical cancer. (Vaccine 2006, Vol. 24, Suppl 3; Vaccine 2008, Vol. 26, Suppl 10; Vaccine 2012, Vol. 30, Suppl 5; IARC Monographs 2007, Vol. 90).

#### 3.4.1 Anal cancer

Anal cancer is rare in the general population with an average worldwide incidence of 1 per 100,000, but is reported to be increasing in more developed regions. Globally, there are an estimated 29,000 new cases in 2018 every year (de Martel C et al. Lancet Glob Health 2020;8(2):e180-e190). Women have higher incidences of anal cancer than men. Incidence is particularly high among populations of men who have sex with men (MSM), women with history of cervical or vulvar cancer, and immunosuppressed populations, including those who are HIV-infected and patients with a history of organ transplantation. These cancers are predominantly squamous cell carcinoma, adenocarcinomas, or basaloid and cloacogenic carcinomas.

#### 3.4.1.1 Anal cancer incidence in Bulgaria

Table 7: Anal cancer incidence in Bulgaria (estimates for 2020)				
Indicator	Bulgaria	Eastern Europe	World	
MEN				
Annual number of new cancer cases	23	900	21,706	
Uncertainty intervals of new cancer cases [95% UI]	[15-36]	[648-1,250]	[18,432-25,561]	
Crude incidence rate <sup>b</sup>	0.68	0.65	0.55	
Age-standardized incidence rate <sup>b</sup>	0.35	0.41	0.49	
Cumulative risk (%) at 75 years old <sup>a</sup>	0.04	0.05	0.06	
WOMEN				
Annual number of new cancer cases	30	1,558	29,159	
Uncertainty intervals of new cancer cases [95% UI]	[20-45]	[1,228-1,977]	[25,656-33,140]	
Crude incidence rate <sup>c</sup>	0.84	1.00	0.75	
Age-standardized incidence rate <sup>c</sup>	0.41	0.50	0.58	
Cumulative risk (%) at 75 years $old^a$	0.05	0.06	0.07	

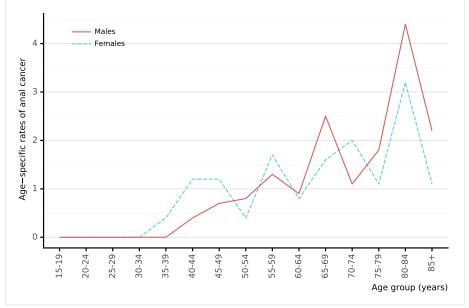
Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods
<sup>a</sup> Cumulative risk (incidence) is the probability or risk of individuals getting from the disease during ages 0-74 years. For cancer, it is expressed as the % of new born children who would be expected to develop from a particular cancer before the age of 75 if they had the rates of cancer observed in the period in the absence of competing causes

<sup>b</sup> Rates per 100,000 men per year.

<sup>c</sup> Rates per 100,000 women per year.

Data Sources:

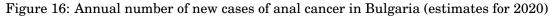


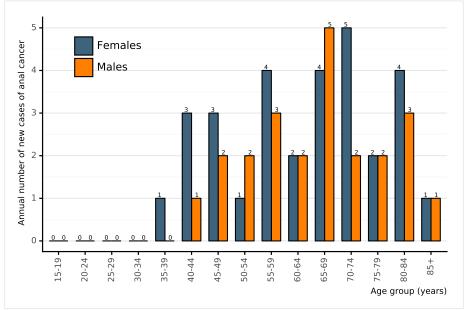
Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods a Rates per 100,000 men per year.

<sup>b</sup> Rates per 100,000 women per year.

Data Sources: Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2020). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for  $Research \ on \ Cancer. \ Available \ from: \ \texttt{https://gco.iarc.fr/today} \ , \ accessed \ [27 \ January \ 2021].$ 





Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods

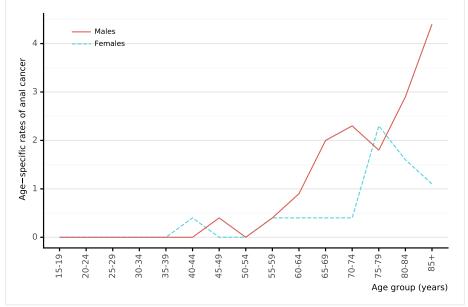
#### 3.4.1.2 Anal cancer mortality in Bulgaria

|--|

Indicator	Bulgaria	Eastern Europe	World
MEN			
Annual number of new cancer cases	18	523	9,416
Uncertainty intervals of new cancer cases [95% UI]	[11-30]	[356-769]	[7,282-12,175]
Crude incidence rate <sup>b</sup>	0.53	0.38	0.24
Age-standardized incidence rate <sup>b</sup>	0.24	0.23	0.21
Cumulative risk (%) at 75 years old <sup>a</sup>	0.03	0.03	0.02
WOMEN			
Annual number of new cancer cases	12	715	9,877
Uncertainty intervals of new cancer cases [95% UI]	[6-23]	[515-993]	[7,795-12,516]
Crude incidence rate <sup>c</sup>	0.34	0.46	0.26
Age-standardized incidence rate <sup>c</sup>	0.11	0.20	0.19
Cumulative risk (%) at 75 years $old^a$	0.01	0.02	0.02

Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Cumulative risk (mortality) is the probability or risk of individuals dying from the disease during ages 0-74 years. For cancer, it is expressed as the % of new born children who would be expected to die from a particular cancer before the age of 75 if they had the rates of cancer observed in the period in the absence of competing causes. <sup>b</sup> Rates per 100,000 men per year. <sup>c</sup> Rates per 100,000 women per year.

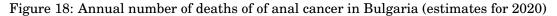


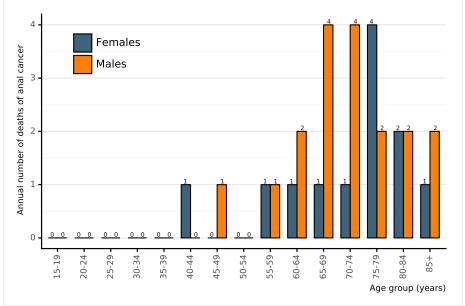
Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods a Rates per 100,000 men per year.

<sup>b</sup> Rates per 100,000 women per year.

Data Sources: Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2020). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for  $Research \ on \ Cancer. \ Available \ from: \ \texttt{https://gco.iarc.fr/today} \ , \ accessed \ [27 \ January \ 2021].$ 





Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods

#### 3.4.1.3 Anal cancer incidence and mortality comparison in Bulgaria

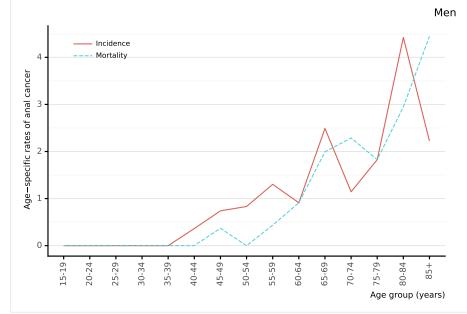


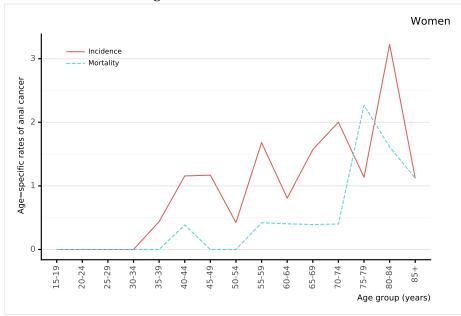
Figure 19: Comparison of age-specific anal cancer incidence and mortality rates among men in Bulgaria (estimates for 2020)

Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods  $^a$  Rates per 100,000 men per year.

Data Sources: Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2020). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer. Available from: https://gco.iarc.fr/today, accessed [27 January 2021].

Figure 20: Comparison of age-specific anal cancer incidence and mortality rates among women in Bulgaria (estimates for 2020)



#### Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods a Rates per 100,000 women per year.

Data Sources:

#### 3.4.2 Vulva cancer

Cancer of the vulva is rare among women worldwide, with an estimated 44,000 new cases in 2018, representing 6% of all gynaecologic cancers (de Martel C et al. Lancet Glob Health 2020;8(2):e180e190). Worldwide, about 60% of all vulvar cancer cases occur in more developed countries. Vulvar cancer has two distinct histological patterns with two different risk factor profiles: (1) basaloid/warty types (2) keratinising types. Basaloid/warty lesions are more common in young women, are very often associated with HPV DNA detection (75-100%), and have a similar risk factor profile as cervical cancer. Keratinising vulvar carcinomas represent the majority of the vulvar lesions (>60%), they occur more often in older women and are more rarely associated with HPV (IARC Monograph Vol 100B).

#### 3.4.2.1 Vulva cancer incidence in Bulgaria

Table 9: Vulva cancer incidence in Bulgaria (estimates for 2020)				
Indicator	Bulgaria	Eastern Europe	World	
Annual number of new cancer cases	118	5,012	45,240	
Uncertainty intervals [95% UI]	[92-152]	[4,689-5,357]	[40,656-50,342]	
Crude incidence rate <sup>b</sup>	3.30	3.23	1.17	
Age-standardized incidence rate <sup>b</sup>	1.21	1.30	0.85	
Cumulative risk (%) at 75 years old <sup>a</sup>	0.14	0.15	0.09	

Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods

<sup>a</sup> Cumulative risk (incidence) is the probability or risk of individuals getting from the disease during ages 0-74 years. For cancer, it is expressed as the % of new born children who would be expected to develop from a particular cancer before the age of 75 if they had the rates of cancer observed in the period in the absence of competing causes.

<sup>b</sup> Rates per 100,000 women per year. <u>Data Sources</u>:

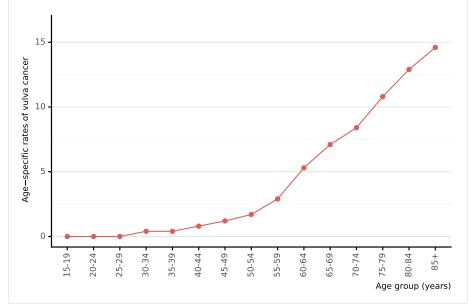
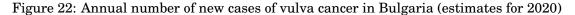


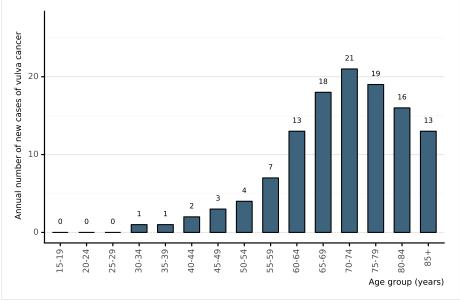
Figure 21: Age-specific incidence rates of vulva cancer in Bulgaria (estimates for 2020)

#### Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 women per year.

Data Sources: Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2020). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer. Available from: https://gco.iarc.fr/today, accessed [27 January 2021].





Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods

#### 3.4.2.2 Vulva cancer mortality in Bulgaria

Indicator	Bulgaria	Eastern Europe	World
Annual number of deaths	44	$2,\!561$	$17,\!427$
Uncertainty intervals [95% UI]	[31-63]	[2,144-3,059]	[14, 497 - 20, 950]
Crude mortality rate <sup>b</sup>	1.23	1.65	0.45
Age-standardized mortality rate <sup>b</sup>	0.36	0.59	0.30
Cumulative risk (%) at 75 years old <sup>a</sup>	0.04	0.06	0.03

Table 10: Vulve concer mortality in Bulgaria (estimates for 2020)

Data accessed on 27 Jan 2021

Data accessed on 2/Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods a Cumulative risk (mortality) is the probability or risk of individuals dying from the disease during ages 0-74 years. For cancer, it is expressed as the % of new born children who would be expected to die from a particular cancer before the age of 75 if they had the rates of cancer observed in the period in the absence of competing causes. b Rates per 100,000 women per year.

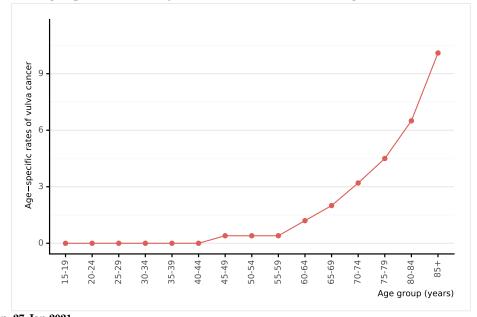
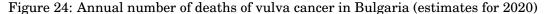
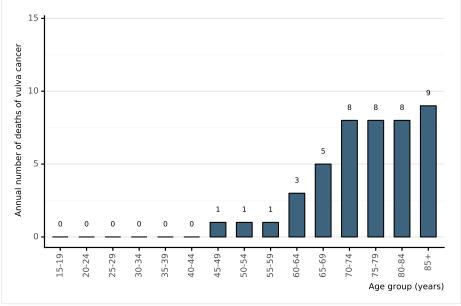


Figure 23: Age-specific mortality rates of vulva cancer in Bulgaria (estimates for 2020)

Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 women per year.

Data Sources: Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2020). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for  $Research \ on \ Cancer. \ Available \ from: \ \texttt{https://gco.iarc.fr/today} \ , \ accessed \ [27 \ January \ 2021].$ 





Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 women per year.

Data Sources:

#### 3.4.2.3 Vulva cancer incidence and mortality comparison in Bulgaria

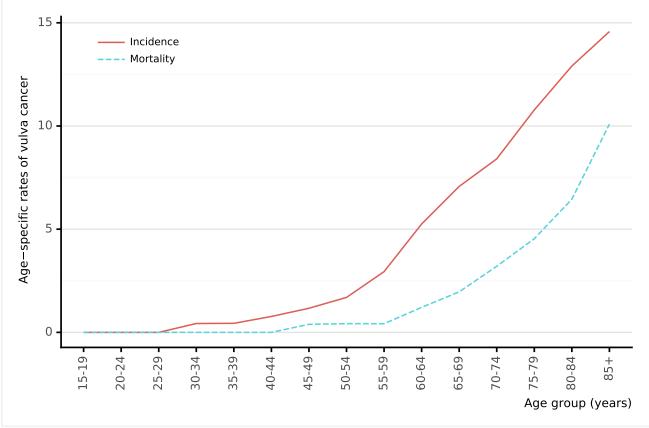


Figure 25: Comparison of age-specific vulva cancer incidence and mortality rates in Bulgaria (estimates for 2020)

#### Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 women per year.

### 3.4.3 Vaginal cancer

Cancer of the vagina is a rare cancer, with an estimated 18,000 new cases in 2018, representing 3% of all gynaecologic cancers (de Martel C et al. Lancet Glob Health 2020;8(2):e180-e190). Similar to cervical cancer, the majority of vaginal cancer cases (68%) occur in less developed countries. Most vaginal cancers are squamous cell carcinoma (90%) generally attributable to HPV, followed by clear cell adenocarcinomas and melanoma. Vaginal cancers are primarily reported in developed countries. Metastatic cervical cancer can be misclassified as cancer of the vagina. Invasive vaginal cancer is diagnosed primarily in old women (>= 65 years) and the diagnosis is rare in women under 45 years whereas the peak incidence of carcinoma in situ is observed between ages 55 and 70 (Vaccine 2008, Vol. 26, Suppl 10).

### 3.4.3.1 Vaginal cancer incidence in Bulgaria

Indicator	Bulgaria	Eastern Europe	World
Annual number of new cancer cases	33	1,005	17,908
Uncertainty intervals [95% UI]	[23-48]	[877-1,152]	[14,678-21,848]
Crude incidence rate <sup>b</sup>	0.92	0.65	0.46
Age-standardized incidence rate <sup>b</sup>	0.37	0.31	0.36
Cumulative risk (%) at 75 years old <sup>a</sup>	0.05	0.04	0.04

Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Cumulative risk (incidence) is the probability or risk of individuals getting from the disease during ages 0-74 years. For cancer, it is expressed as the % of new born children who would be expected to develop from a particular cancer before the age of 75 if they had the rates of cancer observed in the period in the absence of competing causes.

 $^{b}$  Rates per 100,000 women per year. Data Sources

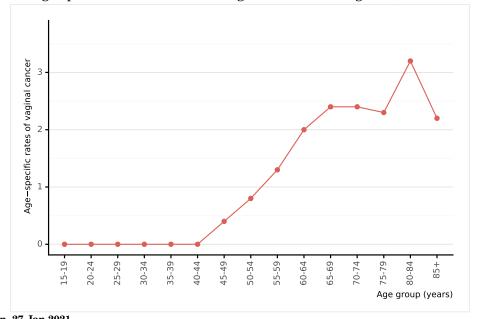
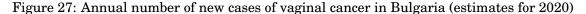
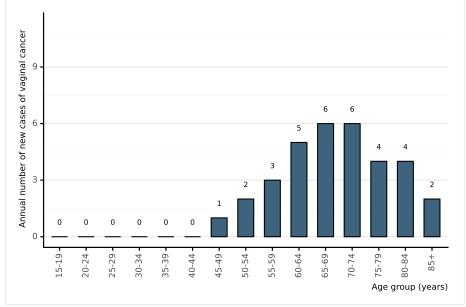


Figure 26: Age-specific incidence rates of vaginal cancer in Bulgaria (estimates for 2020)

Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 women per year.

Data Sources: Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2020). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for  $Research \ on \ Cancer. \ Available \ from: \ \texttt{https://gco.iarc.fr/today} \ , \ accessed \ [27 \ January \ 2021].$ 





Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods

# 3.4.3.2 Vaginal cancer mortality in Bulgaria

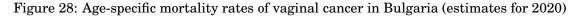
Indicator	Bulgaria	Eastern Europe	World
Annual number of deaths	9	485	7,995
Uncertainty intervals [95% UI]	[4-19]	[322-730]	[5,983-10,684]
Crude mortality rate <sup>b</sup>	0.25	0.31	0.21
Age-standardized mortality rate <sup>b</sup>	0.09	0.13	0.16
Cumulative risk (%) at 75 years old <sup>a</sup>	0.01	0.01	0.02

Table 12: Vaginal cancer mortality in Bulgaria (estimates for 2020)

Data accessed on 27 Jan 2021

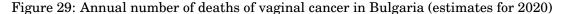
Data accessed on 2/Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods a Cumulative risk (mortality) is the probability or risk of individuals dying from the disease during ages 0-74 years. For cancer, it is expressed as the % of new born children who would be expected to die from a particular cancer before the age of 75 if they had the rates of cancer observed in the period in the absence of competing causes. b Rates per 100,000 women per year.

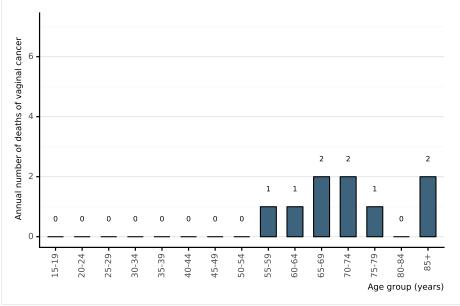
Age-specific rates of vaginal cancer 2 1 0 15-19 20-24 25-29 30-34 35-39 40-44 45-49 50-54 55-59 60-64 62-69 70-74 75-79 80-84 85+ Age group (years)



Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 women per year.

Data Sources: Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2020). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for  $Research \ on \ Cancer. \ Available \ from: \ \texttt{https://gco.iarc.fr/today} \ , \ accessed \ [27 \ January \ 2021].$ 





Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods

# 3.4.3.3 Vaginal cancer incidence and mortality comparison in Bulgaria

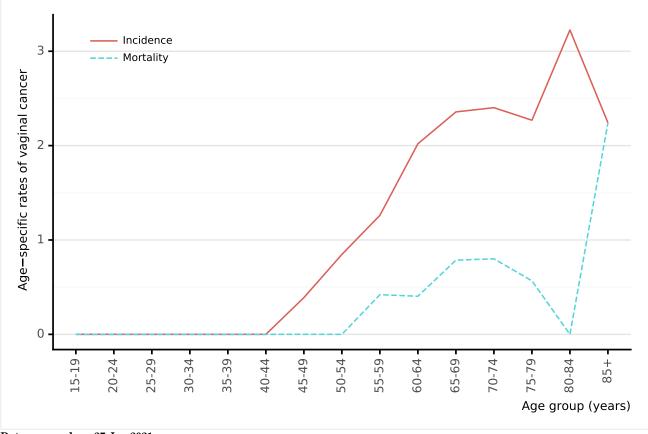


Figure 30: Comparison of age-specific vaginal cancer incidence and mortality rates in Bulgaria (estimates for 2020)

Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 women per year.

### 3.4.4 Penile cancer

The annual burden of penile cancer has been estimated to be 34,000 cases in 2018 worldwide with incidence rates strongly correlating with those of cervical cancer (de Martel C et al. Lancet Glob Health 2020;8(2):e180-e190). Penile cancer is rare and most commonly affects men aged 50-70 years. Incidence rates are higher in less developed countries than in more developed countries, accounting for up to 10% of male cancers in some parts of Africa, South America and Asia. Precursor cancerous penile lesions (PeIN) are rare.

Cancers of the penis are primarily of squamous cell carcinomas (SCC) (95%) and the most common penile SCC histologic sub-types are keratinising (49%), mixed warty-basaloid (17%), verrucous (8%) warty (6%), and basaloid (4%). HPV is most commonly detected in basaloid and warty tumours but is less common in keratinising and verrucous tumours. Approximately 60-100% of PeIN lesions are HPV DNA positive.

### 3.4.4.1 Penile cancer incidence in Bulgaria

Table 13: Penile cancer incidence in Bulgaria (estimates for 2020)			
Indicator	Bulgaria	Eastern Europe	World
Annual number of new cancer cases	53	2,038	36,068
Uncertainty intervals [95% UI]	[40-70]	[1,828-2,272]	[30,963-42,015]
Crude incidence rate <sup>b</sup>	1.57	1.48	0.92
Age-standardized incidence rate <sup>b</sup>	0.77	0.91	0.80
Cumulative risk (%) at 75 years old <sup>a</sup>	0.10	0.11	0.09

#### Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Cumulative risk (incidence) is the probability or risk of individuals getting from the disease during ages 0-74 years. For cancer, it is expressed as the % of new born children who would be expected to develop from a particular cancer before the age of 75 if they had the rates of cancer observed in the period in the absence of competing causes.

<sup>b</sup> Rates per 100,000 men per year. Data Sources

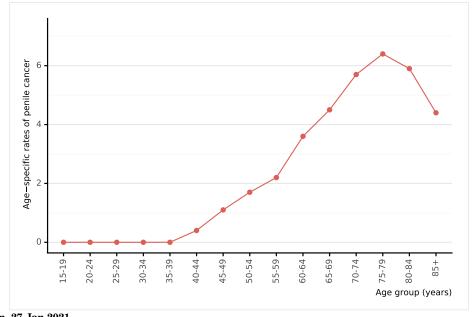
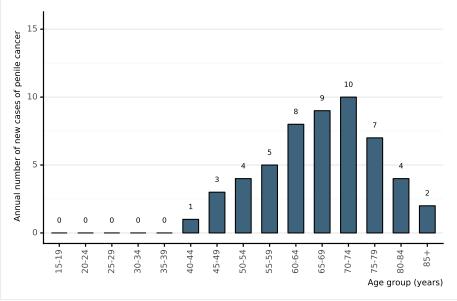


Figure 31: Age-specific incidence rates of penile cancer in Bulgaria (estimates for 2020)

Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 men per year.

Data Sources: Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2020). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for  $Research \ on \ Cancer. \ Available \ from: \ \texttt{https://gco.iarc.fr/today} \ , \ accessed \ [27 \ January \ 2021].$ 





Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods

# 3.4.4.2 Penile cancer mortality in Bulgaria

Indicator	Bulgaria	Eastern Europe	World
Annual number of deaths	16	762	13,211
Uncertainty intervals [95% UI]	[9-27]	[551-1,055]	[10,687-16,332]
Crude mortality rate <sup>b</sup>	0.47	0.55	0.34
Age-standardized mortality rate <sup>b</sup>	0.22	0.33	0.29
Cumulative risk (%) at 75 years old <sup>a</sup>	0.02	0.04	0.03

Table 14: Penile cancer mortality in Bulgaria (estimates for 2020)

Data accessed on 27 Jan 2021

Data accessed on 2/Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods a Cumulative risk (mortality) is the probability or risk of individuals dying from the disease during ages 0-74 years. For cancer, it is expressed as the % of new born children who would be expected to die from a particular cancer before the age of 75 if they had the rates of cancer observed in the period in the absence of competing causes. b Rates per 100,000 men per year.

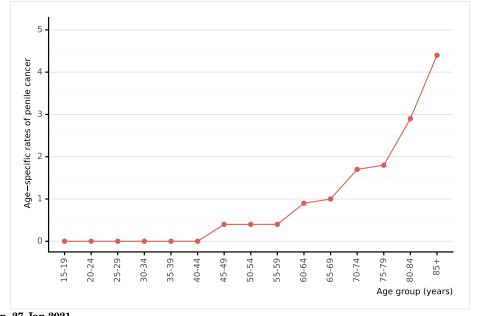
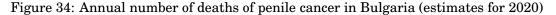
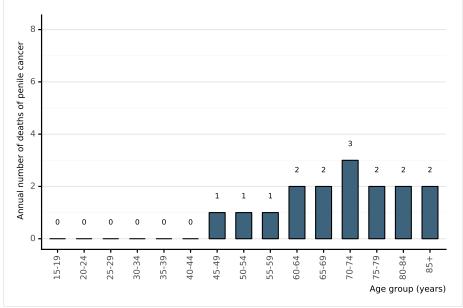


Figure 33: Age-specific mortality rates of penile cancer in Bulgaria (estimates for 2020)

Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 men per year.

Data Sources: Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2020). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for  $Research \ on \ Cancer. \ Available \ from: \ \texttt{https://gco.iarc.fr/today} \ , \ accessed \ [27 \ January \ 2021].$ 





Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods

# 3.4.4.3 Penile cancer incidence and mortality comparison in Bulgaria

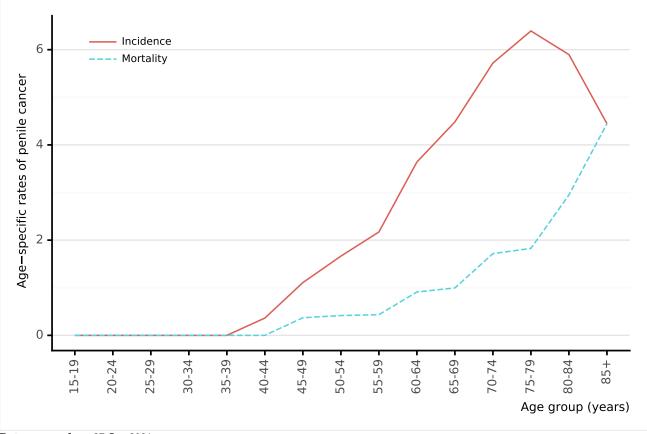


Figure 35: Comparison of age-specific penile cancer incidence and mortality rates in Bulgaria (estimates for 2020)

Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 men per year.

# 3.5 Head and neck cancers

The majority of head and neck cancers are associated with high tobacco and alcohol consumption. However, increasing trends in the incidence at specific sites suggest that other aetiological factors are involved, and infection by certain high-risk types of HPV (i.e. HPV16) have been reported to be associated with head and neck cancers, in particular with oropharyngeal cancer. Current evidence suggests that HPV16 is associated with tonsil cancer (including Waldeyer ring cancer), base of tongue cancer and other oropharyngeal cancer sites. Associations with other head and neck cancer sites such as oral cancer are neither strong nor consistent when compared to molecular-epidemiological data on HPV and oropharyngeal cancer. Association with laryngeal cancer is still unclear (IARC Monograph Vol 100B)

### 3.5.1 Oropharyngeal cancer

#### 3.5.1.1 Oropharyngeal cancer incidence in Bulgaria

Table 15: Oropharyngeal cancer incidence in Bulgaria (estimates for 2020)			
Indicator	Bulgaria	Eastern Europe	World
MEN			
Annual number of new cancer cases	114	9,200	79,045
Uncertainty intervals of new cancer cases [95% UI]	[88-149]	[8,757-9,665]	[72,769-85,862]
Crude incidence rate sa <sup>b</sup>	3.38	6.67	2.01
Age-standardized incidence rate sa <sup>b</sup>	1.93	4.36	1.79
Cumulative risk (%) at 75 years old <sup>a</sup>	0.23	0.54	0.22
WOMEN			
Annual number of new cancer cases	23	1,891	19,367
Uncertainty intervals of new cancer cases [95% UI]	[14-36]	[1,696-2,108]	[16,279-23,041]
Crude incidence rate sa <sup>c</sup>	0.64	1.22	0.50
Age-standardized incidence rate sa <sup>c</sup>	0.31	0.68	0.40
Cumulative risk (%) at 75 years old <sup>a</sup>	0.03	0.08	0.05

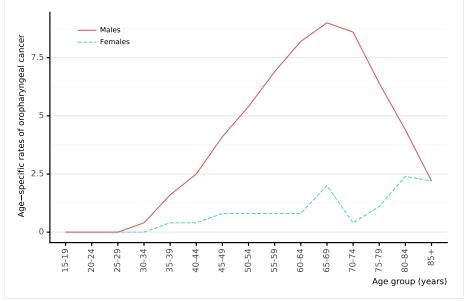
Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods
<sup>a</sup> Cumulative risk (incidence) is the probability or risk of individuals getting from the disease during ages 0-74 years. For cancer, it is expressed as the % of new born children who would be expected to develop from a particular cancer before the age of 75 if they had the rates of cancer observed in the period in the absence of competing causes.

<sup>b</sup> Rates per 100,000 men per year.

<sup>c</sup> Rates per 100,000 women per year.

Data Sources



#### Figure 36: Age-specific incidence rates of oropharyngeal cancer in Bulgaria (estimates for 2020)

#### Data accessed on 27 Jan 2021

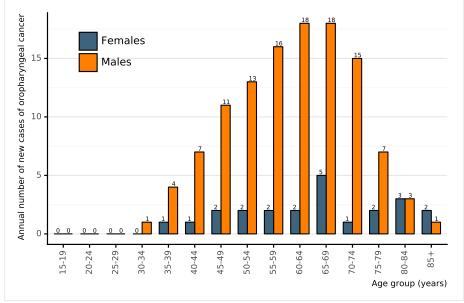
For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods a Rates per 100,000 men per year.

<sup>b</sup> Rates per 100,000 women per year

Data Sources

Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2020). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer. Available from: https://gco.iarc.fr/today, accessed [27 January 2021].

#### Figure 37: Annual number of new cases of oropharyngeal cancer in Bulgaria (estimates for 2020)



Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods Data Sources:

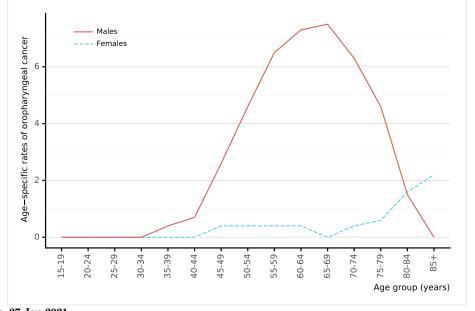
# 3.5.1.2 Oropharyngeal cancer mortality in Bulgaria

Table 16: Oropharyngeal cancer mortality in Bulgaria (estimates for 2020)			
Indicator	Bulgaria	Eastern Europe	World
MEN			
Annual number of deaths	84	4,925	39,590
Uncertainty intervals of mortality cancer cases [95% UI]	[54-130]	[4,331-5,601]	[35,255-44,458]
Crude mortality rate sa <sup>b</sup>	2.49	3.57	1.01
Age-standardized mortality rate sa <sup>b</sup>	1.41	2.31	0.89
Cumulative risk (%) at 75 years old <sup>a</sup>	0.18	0.29	0.11
WOMEN			
Annual number of deaths	10	710	8,553
Uncertainty intervals of mortality cancer cases [95% UI]	[4-23]	[506-996]	[6,684-10,945]
Crude mortality rate sa <sup>c</sup>	0.28	0.46	0.22
Age-standardized mortality rate sa <sup>c</sup>	0.11	0.23	0.17
Cumulative risk (%) at 75 years old <sup>a</sup>	0.01	0.03	0.02

Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Cumulative risk (mortality) is the probability or risk of individuals dying from the disease during ages 0-74 years. For cancer, it is expressed as the % of new born children who would be expected to die from a particular cancer before the age of 75 if they had the rates of cancer observed in the period in the absence of competing causes.

<sup>b</sup> Rates per 100,000 men per year. <sup>c</sup> Rates per 100,000 women per year.



#### Figure 38: Age-specific mortality rates of oropharyngeal cancer in Bulgaria (estimates for 2020)

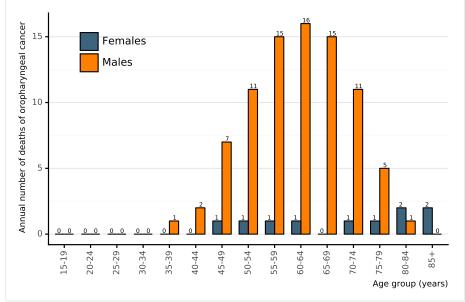
Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods a Rates per 100,000 men per year.

<sup>b</sup> Rates per 100,000 women per year.

Data Sources: Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2020). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for  $Research \ on \ Cancer. \ Available \ from: \ \texttt{https://gco.iarc.fr/today} \ , \ accessed \ [27 \ January \ 2021].$ 

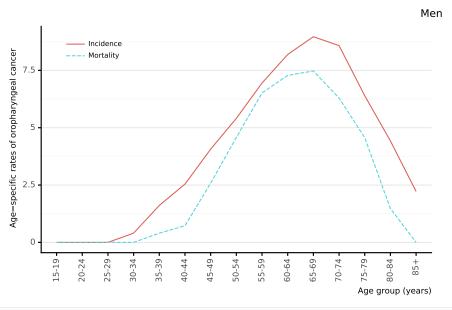
# Figure 39: Annual number of deaths of oropharyngeal cancer in Bulgaria (estimates for 2020)



Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods Data Sources

# 3.5.1.3 Oropharyngeal cancer incidence and mortality comparison in Bulgaria

Figure 40: Comparison of age-specific oropharyngeal cancer incidence and mortality rates among men in Bulgaria (estimates for 2020)

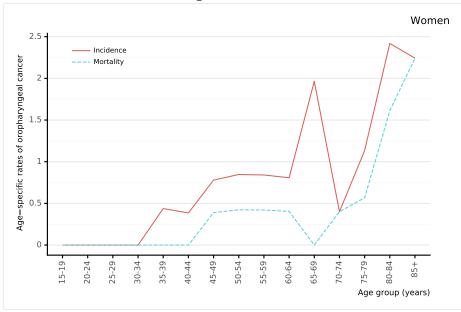


Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 men per year.

Data Sources: Ferlay J. Ervik M, Lam F, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2020). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer. Available from: https://gco.iarc.fr/today, accessed [27 January 2021].

# Figure 41: Comparison of age-specific oropharyngeal cancer incidence and mortality rates among women in Bulgaria (estimates for 2020)



#### Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 women per year.

### 3.5.2 Oral cavity cancer

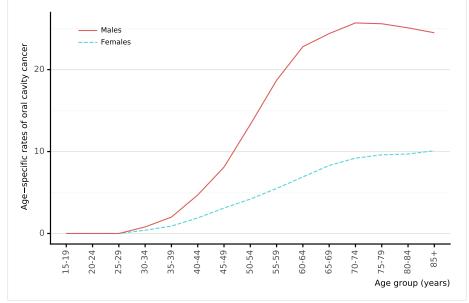
# 3.5.2.1 Oral cavity cancer incidence in Bulgaria

Indicator	Bulgaria	Eastern Europe	World
MEN			
Annual number of new cancer cases	317	19,884	264,211
Uncertainty intervals of new cancer cases [95% UI]	[264-381]	[19,288-20,498]	[251,153- 277,948]
Crude incidence rate sa <sup>b</sup>	9.40	14.4	6.72
$\begin{array}{llllllllllllllllllllllllllllllllllll$	5.01	9.22	5.96
Cumulative risk (%) at 75 years $old^a$	0.60	1.12	0.68
WOMEN			
Annual number of new cancer cases	138	6,199	113,502
Uncertainty intervals of new cancer cases [95% UI]	[101-189]	[5,864-6,553]	[105,599- 121,997]
Crude incidence rate sa <sup>c</sup>	3.86	3.99	2.94
Age-standardized incidence rate sa <sup>c</sup>	1.71	1.87	2.28
Cumulative risk (%) at 75 years $old^a$	0.20	0.21	0.26

#### incid in Bulgaria (actimates for 2020) Table 17. Oral ovitv o

Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Cumulative risk (incidence) is the probability or risk of individuals getting from the disease during ages 0-74 years. For cancer, it is expressed as the % of new born children who would be expected to develop from a particular cancer before the age of 75 if they had the rates of cancer observed in the period in the absence of competing causes. <sup>b</sup> Rates per 100,000 men per year. <sup>c</sup> Rates per 100,000 women per year.



#### Figure 42: Age-specific incidence rates of oral cavity cancer in Bulgaria (estimates for 2020)

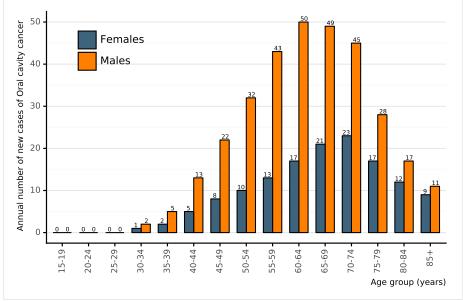
#### Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 men per year.

<sup>b</sup> Rates per 100,000 women per year.

Data Sources: Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2020). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for  $Research \ on \ Cancer. \ Available \ from: \ \texttt{https://gco.iarc.fr/today} \ , \ accessed \ [27 \ January \ 2021].$ 

#### Figure 43: Annual number of new cases of oral cavity cancer in Bulgaria (estimates for 2020)



Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods

# 3.5.2.2 Oral cavity cancer incidence and mortality comparison in Bulgaria

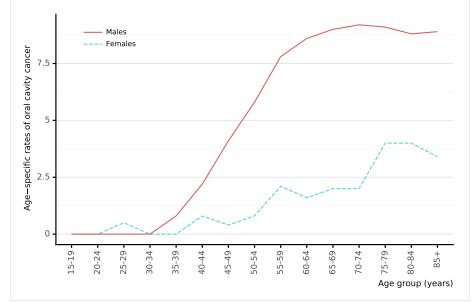
Table 18: Oral cavity cancer mortality in Bulgaria (estimates for 2020)			
Indicator	Bulgaria	Eastern Europe	World
MEN			
Annual number of deaths	124	9,761	125,022
Uncertainty intervals of mortality	[92-167]	[8,901-10,704]	[116,573-
cancer cases [95% UI]	[32-107]	[0,301-10,704]	134,084]
Crude mortality rate sa <sup>b</sup>	3.68	7.08	3.18
Age-standardized mortality rate sa <sup>b</sup>	2.00	4.54	2.82
Cumulative risk (%) at 75 years $old^a$	0.24	0.56	0.32
WOMEN			
Annual number of deaths	40	2,729	52,735
Uncertainty intervals of mortality	[28-57]	[2,286-3,258]	[47,690-58,313]
cancer cases [95% UI]			_ , , _
Crude mortality rate sa <sup>c</sup>	1.12	1.76	1.36
Age-standardized mortality rate sa <sup>c</sup>	0.48	0.82	1.04
Cumulative risk (%) at 75 years $old^a$	0.05	0.09	0.12

. .....

Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods
<sup>a</sup> Cumulative risk (mortality) is the probability or risk of individuals dying from the disease during ages 0-74 years. For cancer, it is expressed as the % of new born children who would be
expected to die from a particular cancer before the age of 75 if they had the rates of cancer observed in the period in the absence of competing causes.

<sup>b</sup> Rates per 100,000 men per year. <sup>c</sup> Rates per 100,000 women per year.



#### Figure 44: Age-specific mortality rates of oral cavity cancer in Bulgaria (estimates for 2020)

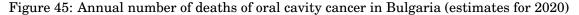
#### Data accessed on 27 Jan 2021

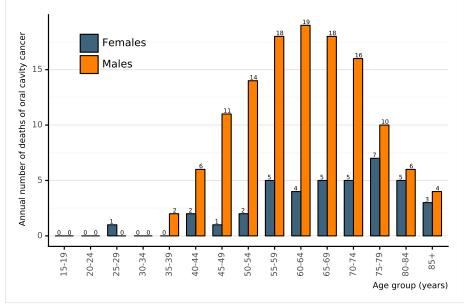
For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods a Rates per 100,000 men per year.

<sup>b</sup> Rates per 100,000 women per year

Data Sources

Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2020). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer. Available from: https://gco.iarc.fr/today, accessed [27 January 2021].

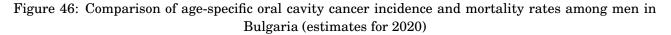


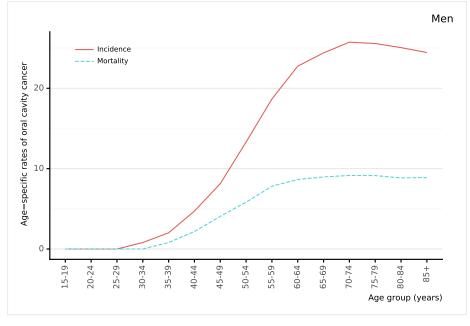


Data accessed on 27 Jan 2021

 $For more detailed methods of estimation please refer to {\tt http://gco.iarc.fr/today/data-sources-methods} and the set of the set o$ 

#### 3.5.2.3Oral cavity cancer incidence and mortality comparison in Bulgaria

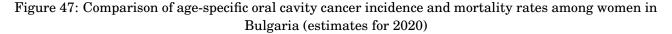


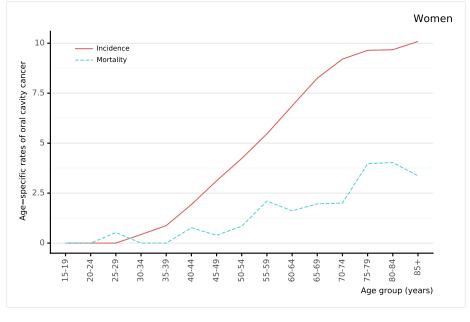


#### Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods a Rates per 100,000 men per year.

Data Sources: Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2020). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer. Available from: https://gco.iarc.fr/today, accessed [27 January 2021].





#### Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods a Rates per 100,000 women per year.

### 3.5.3 Laryngeal cancer

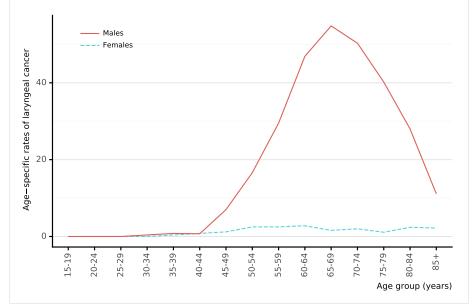
# 3.5.3.1 Laryngeal cancer incidence in Bulgaria

Table 19: Laryngeal cancer incidence in Bulgaria (estimates for 2020)			
Indicator	Bulgaria	Eastern Europe	World
MEN			
Annual number of new cancer cases	501	16,580	160,265
Uncertainty intervals of new cancer cases [95% UI]	[429-585]	[16,000-17,181]	[150,633- 170,513]
Crude incidence rate sa <sup>b</sup>	14.8	12.0	4.08
$\begin{array}{c} Age-standardized  incidence  rate \\ sa^b \end{array}$	7.67	7.58	3.59
Cumulative risk (%) at 75 years $old^a$	1.03	0.97	0.45
WOMEN			
Annual number of new cancer cases	41	1,550	24,350
Uncertainty intervals of new cancer cases [95% UI]	[29-58]	[1,367-1,757]	[20,845-28,444]
Crude incidence rate sa <sup>c</sup>	1.15	1.00	0.63
Age-standardized incidence rate sa <sup>c</sup>	0.61	0.53	0.49
Cumulative risk (%) at 75 years $old^a$	0.07	0.07	0.06

#### Table 10. I .1 incid o in Bula amia (antim $a_{1}$

Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Cumulative risk (incidence) is the probability or risk of individuals getting from the disease during ages 0-74 years. For cancer, it is expressed as the % of new born children who would be expected to develop from a particular cancer before the age of 75 if they had the rates of cancer observed in the period in the absence of competing causes. <sup>b</sup> Rates per 100,000 men per year. <sup>c</sup> Rates per 100,000 women per year.



#### Figure 48: Age-specific incidence rates of laryngeal cancer in Bulgaria (estimates for 2020)

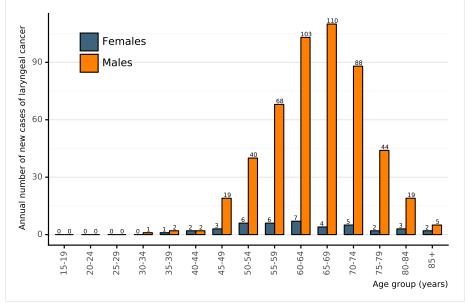
#### Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 men per year.

<sup>b</sup> Rates per 100,000 women per year.

Data Sources: Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2020). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for  $Research \ on \ Cancer. \ Available \ from: \ \texttt{https://gco.iarc.fr/today} \ , \ accessed \ [27 \ January \ 2021].$ 

#### Figure 49: Annual number of new cases of laryngeal cancer in Bulgaria (estimates for 2020)



Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods

# 3.5.3.2 Laryngeal cancer incidence and mortality comparison in Bulgaria

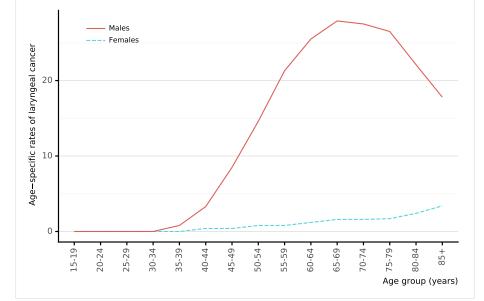
Table 20: Laryngeal cancer mortality in Bulgaria (estimates for 2020)			
Indicator	Bulgaria	Eastern Europe	World
MEN			
Annual number of deaths	330	9,518	85,351
Uncertainty intervals of mortality cancer cases [95% UI]	[279-391]	[9,130-9,923]	[78,895-92,335]
Crude mortality rate sa <sup>b</sup>	9.78	6.91	2.17
Age-standardized mortality rate sa <sup>b</sup>	5.20	4.26	1.89
Cumulative risk (%) at 75 years $old^a$	0.64	0.55	0.23
WOMEN			
Annual number of deaths	26	741	14,489
Uncertainty intervals of mortality cancer cases [95% UI]	[16-41]	[633-868]	[11,902-17,639]
Crude mortality rate sa <sup>c</sup>	0.73	0.48	0.37
Age-standardized mortality rate sa <sup>c</sup>	0.30	0.24	0.28
Cumulative risk (%) at 75 years $old^a$	0.03	0.03	0.03

**T** 11 00 T . ( 0000)

Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods
<sup>a</sup> Cumulative risk (mortality) is the probability or risk of individuals dying from the disease during ages 0-74 years. For cancer, it is expressed as the % of new born children who would be
expected to die from a particular cancer before the age of 75 if they had the rates of cancer observed in the period in the absence of competing causes.

<sup>b</sup> Rates per 100,000 men per year. <sup>c</sup> Rates per 100,000 women per year.



#### Figure 50: Age-specific mortality rates of laryngeal cancer in Bulgaria (estimates for 2020)

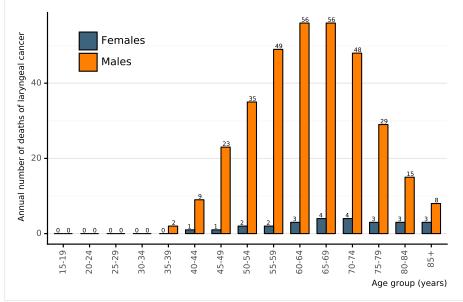
#### Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 men per year.

<sup>b</sup> Rates per 100,000 women per year.

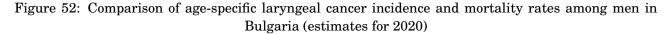
Data Sources: Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2020). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for  $Research \ on \ Cancer. \ Available \ from: \ \texttt{https://gco.iarc.fr/today} \ , \ accessed \ [27 \ January \ 2021].$ 

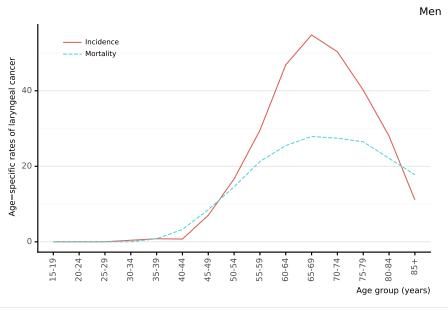
#### Figure 51: Annual number of deaths of of laryngeal cancer in Bulgaria (estimates for 2020)



Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods

# 3.5.3.3 Laryngeal cancer incidence and mortality comparison in Bulgaria

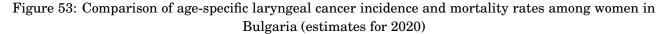


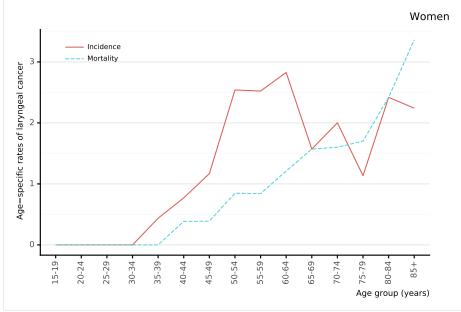


Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods a Rates per 100,000 men per year. Data Sources

Farlay J. Ervik M, Lam F, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2020). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer. Available from: https://gco.iarc.fr/today, accessed [27 January 2021].





#### Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods a Rates per 100,000 women per year.

Data Sources

# 4 HPV related statistics

HPV infection is commonly found in the anogenital tract of men and women with and without clinical lesions. The aetiological role of HPV infection among women with cervical cancer is well-established, and there is growing evidence of its central role in other anogenital sites. HPV is also responsible for other diseases such as recurrent juvenile respiratory papillomatosis and genital warts, both mainly caused by HPV types 6 and 11 (Lacey CJ, Vaccine 2006; 24(S3):35). For this section, the methodologies used to compile the information on HPV burden are derived from systematic reviews and meta-analyses of the literature. Due to the limitations of HPV DNA detection methods and study designs used, these data should be interpreted with caution and used only as a guide to assess the burden of HPV infection within the population. (Vaccine 2006, Vol. 24, Suppl 3; Vaccine 2008, Vol. 26, Suppl 10; Vaccine 2012,Vol. 30, Suppl 5; IARC Monographs 2007, Vol. 90).

# 4.1 HPV burden in women with normal cervical cytology, cervical precancerous lesions or invasive cervical cancer

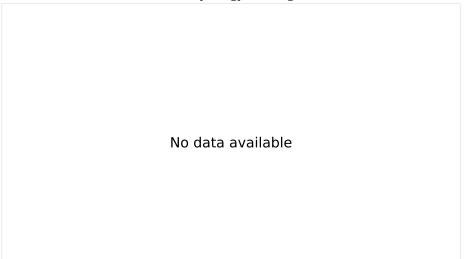
The statistics shown in this section focus on HPV infection in the cervix uteri. HPV cervical infection results in cervical morphological lesions ranging from normalcy (cytologically normal women) to different stages of precancerous lesions (CIN-1, CIN-2, CIN-3/CIS) and invasive cervical cancer. HPV infection is measured by HPV DNA detection in cervical cells (fresh tissue, paraffin embedded or exfoliated cells). The prevalence of HPV increases with lesion severity. HPV causes virtually 100% of cervical cancer cases, and an underestimation of HPV prevalence in cervical cancer is most likely due to the limitations of study methodologies. Worldwide, HPV16 and 18 (the two vaccine-preventable types) contribute to over 70% of all cervical cancer cases, between 41% and 67% of high-grade cervical lesions and 16-32% of low-grade cervical lesions. After HPV16/18, the six most common HPV types are the same in all world regions, namely 31, 33, 35, 45, 52 and 58; these account for an additional 20% of cervical cancers worldwide (Clifford G, Vaccine 2006;24(S3):26).

# Methods: Prevalence and type distribution of human papillomavirus in cervical carcinoma, low-grade cervical lesions, high-grade cervical lesions and normal cytology: systematic review and meta-analysis

A systematic review of the literature was conducted regarding the worldwide HPV-prevalence and type distribution for cervical carcinoma, low-grade cervical lesions, high-grade cervical lesions and normal cytology from 1990 to 'data as of' indicated in each section. The search terms for the review were 'HPV' AND cerv\* using Pubmed. There were no limits in publication language. References cited in selected articles were also investigated. Inclusion criteria were: HPV DNA detection by means of PCR or HC2, a minimum of 20 cases for cervical carcinoma, 20 cases for low-grade cervical lesions, 20 cases for highgrade cervical lesions and 100 cases for normal cytology and a detailed description of HPV DNA detection and genotyping techniques used. The number of cases tested and HPV positive extracted for each study were pooled to estimate the prevalence of HPV DNA and the HPV type distribution globally and by geographical region. Binomial 95% confidence intervals were calculated for each HPV prevalence. For more details refer to the methods document.

# 4.1.1 HPV prevalence in women with normal cervical cytology

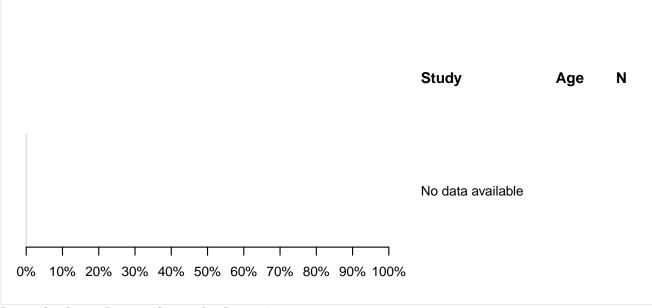
Figure 54: Crude age-specific HPV prevalence (%) and 95% confidence interval in women with normal cervical cytology in Bulgaria



Data updated on 30 Jun 2015 (data as of 30 Jun 2014)

Data Sources: Based on systematic reviews and meta-analysis performed by ICO. The ICO HPV Information Centre has updated data until June 2014. Reference publications: 1) Bruni L, J Infect Dis 2010; 202: 1789. 2) De Sanjosé S, Lancet Infect Dis 2007; 7: 453

#### Figure 55: HPV prevalence among women with normal cervical cytology in Bulgaria, by study



Data updated on 30 Jun 2015 (data as of 30 Jun 2014)

The samples for HPV testing come from cervical specimens (fresh/fixed biopsies or exfoliated cells)  $^a$  Number of women tested

Data Sources:

Based on systematic reviews and meta-analysis performed by ICO. The ICO HPV Information Centre has updated data until June 2014. Reference publications: 1) Bruni L, J Infect Dis 2010; 202: 1789. 2) De Sanjosé S, Lancet Infect Dis 2007; 7: 453

# 4.1.2 HPV type distribution among women with normal cervical cytology, precancerous cervical lesions and cervical cancer

No. tested	HPV 16/18 Prevalence % (95% CI)
-	
-	
-	
127	80.3 (72.6-86.3)

#### Table 21: Prevalence of HPV16 and HPV18 by cytology in Bulgaria

#### Data updated on 19 May 2017 (data as of 30 Jun 2015 / 30 Nov 2014)

The samples for HPV testing come from cervical specimens (fresh/fixed biopsies or exfoliated cells)

Number of women tested <sup>b</sup> 95% Confidence Interval

Data Sources:

<sup>1</sup> Based on systematic reviews and meta-analysis performed by ICO. The ICO HPV Information Centre has updated data until November 2014. Reference publications: 1) Bruni L, J Infect Dis 2010; 202: 1789. 2) De Sanjosé S, Lancet Infect Dis 2007; 7: 453

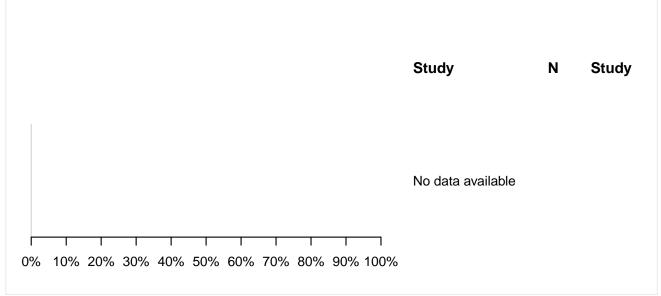
2 Based on meta-analysis performed by IARC's Infections and Cancer Epidemiology Group up to November 2011, the ICO HPV Information Centre has updated data until June 2015. Reference publications: 1) Guan P, Int J Cancer 2012;131:2349 2) Clifford GM, Cancer Epidemiol Biomarkers Prev 2005;14:1157

<sup>3</sup> Based on meta-analysis performed by IARC's Infections and Cancer Epidemiology Group up to November 2011, the ICO HPV Information Centre has updated data until June 2015. Reference publications: 1) Guan P, Int J Cancer 2012;131:2349 2) Smith JS, Int J Cancer 2007;121:621 3) Clifford GM, Br J Cancer 2003;89:101.

<sup>4</sup> Contributing studies: Todorova I, J Clin Pathol 2010; 63: 1121

<sup>5</sup> Based on meta-analysis performed by IARC's Infections and Cancer Epidemiology Group up to November 2011, the ICO HPV Information Centre has updated data until June 2015. Reference publications: 1) Guan P, Int J Cancer 2012;131:2349 2) Li N, Int J Cancer 2011;128:927 3) Smith JS, Int J Cancer 2007;121:621 4) Clifford GM, Br J Cancer 2003;88:63 5) Clifford GM, Br J Cancer 2003;89:101.

#### Figure 56: HPV 16 prevalence among women with normal cervical cytology in Bulgaria, by study

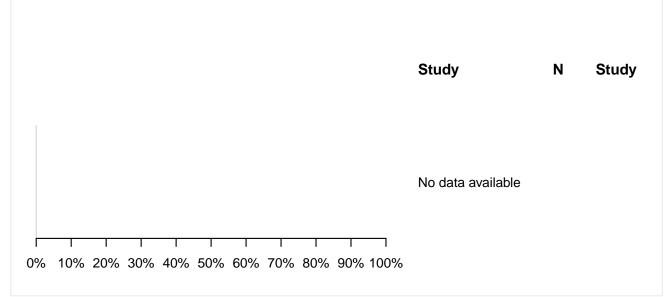


#### Data updated on 30 Jun 2015 (data as of 30 Jun 2014)

The samples for HPV testing come from cervical specimens (fresh/fixed biopsies or exfoliated cells) Number of women tested

Data Sources:

Based on systematic reviews and meta-analysis performed by ICO. The ICO HPV Information Centre has updated data until June 2014. Reference publications: 1) Bruni L, J Infect Dis 2010; 202: 1789. 2) De Sanjosé S, Lancet Infect Dis 2007; 7: 453



#### Figure 57: HPV 16 prevalence among women with low-grade cervical lesions in Bulgaria, by study

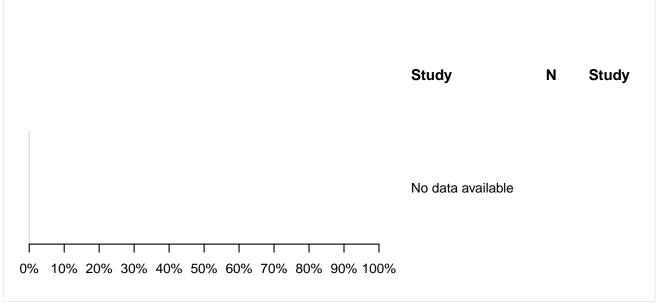
#### Data updated on 27 Jan 2017 (data as of 30 Jun 2015)

The samples for HPV testing come from cervical specimens (fresh/fixed biopsies or exfoliated cells)  $^a$  Number of women tested

Data Sources:

Based on meta-analysis performed by IARC's Infections and Cancer Epidemiology Group up to November 2011, the ICO HPV Information Centre has updated data until June 2015. Reference publications: 1) Guan P, Int J Cancer 2012;131:2349 2) Clifford GM, Cancer Epidemiol Biomarkers Prev 2005;14:1157

# Figure 58: HPV 16 prevalence among women with high-grade cervical lesions in Bulgaria, by study



Data updated on 27 Jan 2017 (data as of 30 Jun 2015)

The samples for HPV testing come from cervical specimens (fresh/fixed biopsies or exfoliated cells)  $^a$  Number of women tested

Data Sources:

Based on meta-analysis performed by IARC's Infections and Cancer Epidemiology Group up to November 2011, the ICO HPV Information Centre has updated data until June 2015. Reference publications: 1) Guan P, Int J Cancer 2012;131:2349 2) Smith JS, Int J Cancer 2007;121:621 3) Clifford GM, Br J Cancer 2003;89:101.

# Figure 59: HPV 16 prevalence among women with invasive cervical cancer in Bulgaria, by study

L		
Γ	Ι	
60%	70%	80%

#### Data updated on 19 May 2017 (data as of 30 Jun 2015)

The samples for HPV testing come from cervical specimens (fresh/fixed biopsies or exfoliated cells) <sup>a</sup> Number of women tested <u>Data Sources</u>: Todorova I, J Clin Pathol 2010; 63: 1121 Based on meta-analysis performed by IARC's Infections and Cancer Epidemiology Group up to November 2011, the ICO HPV Information Centre has updated data until June 2015. Refer-ence publications: 1) Guan P, Int J Cancer 2012;131:2349 2) Li N, Int J Cancer 2011;128:927 3) Smith JS, Int J Cancer 2007;121:621 4) Clifford GM, Br J Cancer 2003;88:63 5) Clifford GM, Br J Cancer 2003;89:101.

# Figure 60: Comparison of the ten most frequent HPV oncogenic types in Bulgaria among women with and without cervical lesions

No data available

Data updated on 30 Jun 2015 (data as of 30 Jun 2015)

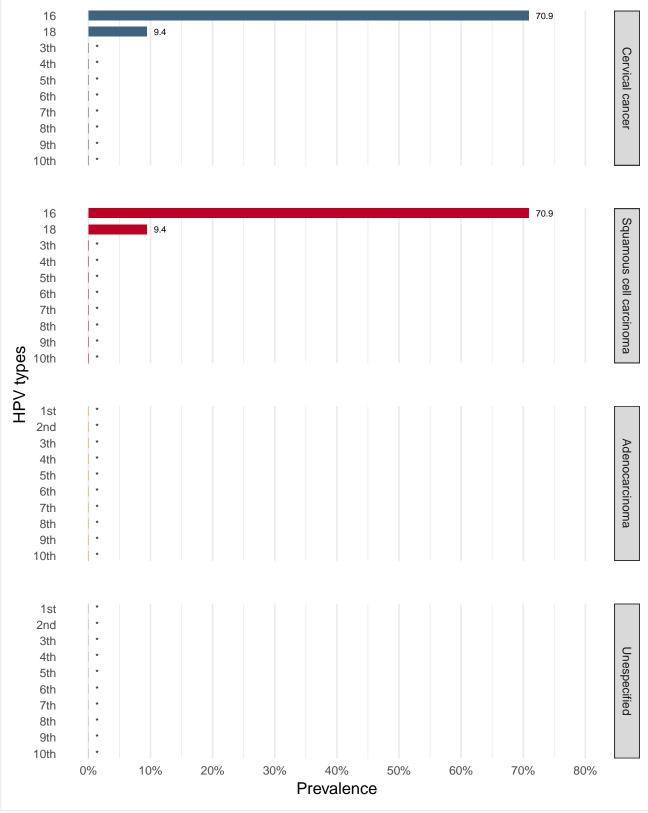
Data Sources:

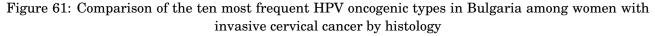
<sup>2</sup> Based on meta-analysis performed by IARC's Infections and Cancer Epidemiology Group up to November 2011, the ICO HPV Information Centre has updated data until June 2015. Reference publications: 1) Guan P, Int J Cancer 2012;131:2349 2) Li N, Int J Cancer 2011;128:927 3) Smith JS, Int J Cancer 2007;121:621 4) Clifford GM, Br J Cancer 2003;88:63 5) Clifford GM, Br J Cancer 2003;89:101.

GM, Br J Cancer 2003;89:101.
 <sup>3</sup> Based on meta-analysis performed by IARC's Infections and Cancer Epidemiology Group up to November 2011, the ICO HPV Information Centre has updated data until June 2015.
 Reference publications: 1) Guan P, Int J Cancer 2012;131:2349 2) Smith JS, Int J Cancer 2007;121:621 3) Clifford GM, Br J Cancer 2003;89:101.
 <sup>4</sup> Based on meta-analysis performed by IARC's Infections and Cancer Epidemiology Group up to November 2011, the ICO HPV Information Centre has updated data until June 2015.
 Reference publications: 1) Guan P, Int J Cancer 2012;131:2349 2) Clifford GM, Cancer Epidemiol Biomarkers Prev 2005;14:1157

Contributing studies: Todorova I, J Clin Pathol 2010; 63: 1121

<sup>5</sup> Based on systematic reviews and meta-analysis performed by ICO. The ICO HPV Information Centre has updated data until November 2014. Reference publications: 1) Bruni L, J Infect Dis 2010; 202: 1789. 2) De Sanjosé S, Lancet Infect Dis 2007; 7: 453





#### Data updated on 30 Jun 2015 (data as of 30 Jun 2015)

 $^{\ast}\,$  No data available. No more types than shown were tested or were positive

Data Sources:

<sup>1</sup>Contributing studies: Todorova I, J Clin Pathol 2010; 63: 1121

<sup>2</sup> Based on meta-analysis performed by IARC's Infections and Cancer Epidemiology Group up to November 2011, the ICO HPV Information Centre has updated data until June 2014. Reference publications: 1) Guan P, Int J Cancer 2012;131:2349 2) Li N, Int J Cancer 2011;128:927 3) Smith JS, Int J Cancer 2007;121:621 4) Clifford GM, Br J Cancer 2003;88:63 5) Clifford GM, Br J Cancer 2003;89:101.

<sup>3</sup> Based on meta-analysis performed by IARC's Infections and Cancer Epidemiology Group up to November 2011, the ICO HPV Information Centre has updated data until June 2015. Reference publications: 1) Guan P, Int J Cancer 2012;131:2349 2) Li N, Int J Cancer 2011;128:927 3) Smith JS, Int J Cancer 2007;121:621 4) Clifford GM, Br J Cancer 2003;88:63 5) Clifford GM, Br J Cancer 2003;89:101.

# Table 22: Type-specific HPV prevalence in women with normal cervical cytology, precancerous cervical lesions and invasive cervical cancer in Bulgaria

lesions and invasive cervical cancer in Bulgaria									
	Normal cytology <sup>1</sup>			Low-grade lesions $^2$		High-grade lesions <sup>3</sup>		Cervical cancer <sup>4,5</sup>	
HPV	No.	HPV Prev %	No.	HPV Prev %	No.	HPV Prev %	No.	HPV Prev %	
Туре	tested	(95% CI)	tested	(95% CI)	tested	(95% CI)	tested	(95% CI)	
	ENIC HPV	TYPES							
	isk HPV ty								
16		-	-	-	-	-	127	70.9 (62.4-78.1)	
18	-	-	-	-	-	-	127	9.4 (5.5-15.8)	
31	-	-	-	-	-	-	-	-	
33	-	-		-				-	
35	-	-							
			-	-	-	-		-	
39	-	-	-	-	-	-	-	-	
45	-	-	-	-	-	-	-	-	
51	-	-	-	-	-	-	-	-	
52	-	-	-	-	-	-	-	-	
56	-	-		-	-	-	-	-	
58	-	-	-	-	-	-	-	-	
59	-	-	-	-	-	-	-	-	
	ble/possibl	e carcinogen							
26	-	-	-	-	-	-	-	-	
30	-	-	-	-	-	-	-	-	
34	-	-	-	-	-	-	-	-	
53	-	-	-	-	-	-	-	-	
66	-	-	-	-	-	-	-	-	
67	-	-	-	-	-	-	-	-	
68	-	-	-	-	-	-	-	-	
69	-	-	-	-	-	-	-	-	
70	-	-	-	-	-	-	-	-	
73	-	-	-	-	-	-	-	-	
82	-	-	-	-	-	-	-	-	
85	-	-	-	-	-	-	-	-	
97	-	-	-	-	-	-	-	-	
LOW RIS	SK HPV TY	PES							
6	-		-	-	-	-	-	-	
11	-	-	-	-	-	-	-	-	
32	-	-	-	-	-	-	-	-	
40	-	-	-	-	-	-	-	-	
42	-	-	-	-	-	-	-	-	
43	-	-	-	-	-		-	-	
44	_	-	-	-		-	-	-	
54	-	-		-	-	-		-	
55	-	-		-	-	-		-	
57	-	-		-	-	-		-	
61	-	-	-	-	-	-		-	
61	-	-	-	-	-			-	
64									
	-	-	-	-	-	-		-	
71	-	-	-	-	-	-	-	-	
72	-	-	-	-	-	-	-	-	
74	-	-	-	-	-	-	-	-	
81	-	-	-	-	-	-	-	-	
83	-	-	-	-	-	-	-	-	
84	-	-	-	-	-	-	-	-	
86	-	-	-	-	-	-	-	-	
87	-	-	-	-	-	-	-	-	
89	-	-	-	-	-	-	-	-	
90	-	-	-	-	-	-	-	-	
91	-	-	-	-	-	-	-	-	

#### Data updated on 30 Jun 2015 (data as of 30 Jun 2015 / 30 Nov 2014)

The samples for HPV testing come from cervical specimens (fresh/fixed biopsies or exfoliated cells)

<sup>4</sup> Contributing studies: Todorova I, J Clin Pathol 2010; 63: 1121

5 Based on meta-analysis performed by IARC's Infections and Cancer Epidemiology Group up to November 2011, the ICO HPV Information Centre has updated data until June 2015. Reference publications: 1) Guan P, Int J Cancer 2012;131:2349 2) Li N, Int J Cancer 2011;128:927 3) Smith JS, Int J Cancer 2007;121:621 4) Clifford GM, Br J Cancer 2003;88:63 5) Clifford GM, Br J Cancer 2003;89:101.

The samples for HPV testing come from cervical specimens (freshmixed biopsies or extended cents) Data Sources: <sup>1</sup> Based on systematic reviews and meta-analysis performed by ICO. The ICO HPV Information Centre has updated data until November 2014. Reference publications: 1) Bruni L, J Infect Dis 2010; 202: 1789. 2) De Sanjosé S, Lancet Infect Dis 2007; 7: 453 <sup>2</sup> Based on meta-analysis performed by IARC's Infections and Cancer Epidemiology Group up to November 2011, the ICO HPV Information Centre has updated data until June 2015.

Reference publications: 1) Guan P, Int J Cancer 2012;131:2349 2) Clifford GM, Cancer Epidemiol Biomarkers Prev 2005;14:1157 <sup>3</sup> Based on meta-analysis performed by IARC's Infections and Cancer Epidemiology Group up to November 2011, the ICO HPV Information Centre has updated data until June 2015. Reference publications: 1) Guan P, Int J Cancer 2012;131:2349 2) Smith JS, Int J Cancer 2007;121:621 3) Clifford GM, Br J Cancer 2003;89:101.

Table 23: Type-specific HPV prevalence among invasive cervical cancer cases in Bulgaria by histology

	An	y Histology	Squamo	among invasiv us cell carcinoma	Ade	especified			
HPV	No.	HPV Prev %	No.	HPV Prev %	No.	HPV Prev %	No. HPV Prev %		
Туре	tested	(95% CI)	tested	(95% CI)	tested	(95% CI)	tested	(95% CI)	
	ENIC HPV		testeu		lested		testeu		
	risk HPV ty								
			107	F0.0 (C0.4 F0.1)					
16	127	70.9 (62.4-78.1)	127	70.9 (62.4-78.1)	-	-	-	-	
18	127	9.4 (5.5-15.8)	127	9.4 (5.5-15.8)	-	-	-	-	
31	-	-	-	-	-	-	-	-	
33	-	-	-	-	-	-	-	-	
35	-	-	-	-	-	-	-	-	
39	-	-	-	-	-	-	-	-	
45	-	-	-	-	-	-	-	-	
51	-	-	-	-	-	-	-	-	
52	-	-	-	-	-	-	-	-	
56		-	-	-	-	-	-	-	
58		-	-	-	-	-	-	-	
59				-		-			
	- 1.1/	-	-	-	-	-	-	-	
	ble/possible	e carcinogen							
26	-	-	-	-	-	-	-	-	
30	-	-	-	-	-	-	-	-	
34	-	-	-	-	-	-	-	-	
53	-	-	-	-	-	-	-	-	
66	-	-	-	-	-	-	-	-	
67	-	-	-	-	-	-	-	-	
68	-	-	-	-	-	-	-	-	
69	-	-	-	-	-	-	-	-	
70	-	-	-	-	-	-	-	-	
73	-	-	-	-	-	-	-	-	
82	-	_	-	_	-	-	-	-	
85									
	-	-	-	-	-	-		-	
97	-	-	-	-	-	-	-	-	
	SK HPV TY	PES							
6	-	-	-	-	-	-	-	-	
11	-	-	-	-	-	-	-	-	
32	-	-	-	-	-	-	-	-	
40	-	-	-	-	-	-	-	-	
42	-	-	-	-	-	-	-	-	
43	-	-	-	-	-	-	-	-	
44	-	-	-	-	-	-	-	-	
54	-	-	-	-	-	-	-	-	
55	-	-	-	_	-	-		-	
57	-					-			
								-	
61	-	-	-	-	-	-		-	
62	-	-	-	-	-	-		-	
64	-	-	-	-	-	-	-	-	
71	-	-	-	-	-	-	-	-	
	-	-	-	-	-	-	-	-	
72	-	-	-	-	-	-	-	-	
72 74			-	-	-	-	-	-	
	-	-				-			
74		-	-	-	-	-	-	-	
74 81 83	-		-	-	-	-	-	-	
74 81 83 84		-	-	-	-	-	-	-	
74 81 83 84 86	-	- - -	-	-	-	-	-	-	
74 81 83 84 86 87	- - - - -	- - -		-				- - -	
74 81 83 84 86	-	- - -	-	-	-	-	-	-	

# Data updated on 19 May 2017 (data as of 30 Jun 2015)

The samples for HPV testing come from cervical specimens (fresh/fixed biopsies or exfoliated cells)  $^a$  Number of women tested  $^b$  95% Confidence Interval

<sup>9</sup> 95% Contidence Interval <u>Data Sources</u>: Contributing studies: Todorova I, J Clin Pathol 2010; 63: 1121 Based on meta-analysis performed by IARC's Infections and Cancer Epidemiology Group up to November 2011, the ICO HPV Information Centre has updated data until June 2015. Refer-ence publications: 1) Guan P, Int J Cancer 2012;131:2349 2) Li N, Int J Cancer 2011;128:927 3) Smith JS, Int J Cancer 2007;121:621 4) Clifford GM, Br J Cancer 2003;88:63 5) Clifford GM, Br J Cancer 2003;89:101.

# 4.1.3 HPV type distribution among HIV+ women with normal cervical cytology

Table 24: Studies on HPV prevalence among HIV+ women with normal cytology in Bulgaria

HPV Prevalence							
	Study	HPV detection method and targeted HPV types	No. Tested <sup>a</sup>	%	(95% CI) <sup>b</sup>	Prevalence of 5 most frequent HPVs, HPV type (%)	
	-	-	-	-	-		

#### Data updated on 31 Dec 2011 (data as of 31 Dec 2011)

DBH: Dot Blot Hybridization; EIA: Enzyme ImmunoAssay; HC2: Hybrid Capture 2; PCR: Polymerase Chain Reaction; TS: Type Specific  ${}^a$  Number of women tested  ${}^b$  95% Confidence Interval

Data Sources:

Data Sources: Systematic review and meta-analysis were performed by the ICO HPV Information Centre up to December 2011. Selected studies had to include at least 20 HIV positive women who had both normal cervical cytology and HPV test results (PCR or HC2).

# 4.1.4 Terminology

# Cytologically normal women

No abnormal cells are observed on the surface of their cervix upon cytology.

# Cervical Intraepithelial Neoplasia (CIN) / Squamous Intraepithelial Lesions (SIL)

SIL and CIN are two commonly used terms to describe precancerous lesions or the abnormal growth of squamous cells observed in the cervix. SIL is an abnormal result derived from cervical cytological screening or Pap smear testing. CIN is a histological diagnosis made upon analysis of cervical tissue obtained by biopsy or surgical excision. The condition is graded as CIN 1, 2 or 3, according to the thickness of the abnormal epithelium (1/3, 2/3 or the entire thickness).

# Low-grade cervical lesions (LSIL/CIN-1)

Low-grade cervical lesions are defined by early changes in size, shape, and number of abnormal cells formed on the surface of the cervix and may be referred to as mild dysplasia, LSIL, or CIN-1.

# High-grade cervical lesions (HSIL/ CIN-2 / CIN-3 / CIS)

High-grade cervical lesions are defined by a large number of precancerous cells on the surface of the cervix that are distinctly different from normal cells. They have the potential to become cancerous cells and invade deeper tissues of the cervix. These lesions may be referred to as moderate or severe dysplasia, HSIL, CIN-2, CIN-3 or cervical carcinoma in situ (CIS).

# Carcinoma in situ (CIS)

Preinvasive malignancy limited to the epithelium without invasion of the basement membrane. CIN 3 encompasses the squamous carcinoma in situ.

# Invasive cervical cancer (ICC) / Cervical cancer

If the high-grade precancerous cells invade the basement membrane is called ICC. ICC stages range from stage I (cancer is in the cervix or uterus only) to stage IV (the cancer has spread to distant organs, such as the liver).

# Invasive squamous cell carcinoma

Invasive carcinoma composed of cells resembling those of squamous epithelium.

## Adenocarcinoma

Invasive tumour with glandular and squamous elements intermingled.

# Methods: Prevalence and type distribution of human papillomavirus in carcinoma of the vulva, vagina, anus and penis: systematic review and meta-analysis

A systematic review of the literature was conducted on the worldwide HPV-prevalence and type distribution for anogenital carcinomas other than cervix from January 1986 to 'data as of' indicated in each section. The search terms for the review were 'HPV' AND (anus OR anal) OR (penile) OR vagin\* OR vulv\* using Pubmed. There were no limits in publication language. References cited in selected articles were also investigated. Inclusion criteria were: HPV DNA detection by means of PCR, a minimum of 10 cases by lesion and a detailed description of HPV DNA detection and genotyping techniques used. The number of cases tested and HPV positive cases were extracted for each study to estimate the prevalence of HPV DNA and the HPV type distribution. Binomial 95% confidence intervals were calculated for each HPV prevalence.

# 4.2.1 Anal cancer and precancerous anal lesions

Anal cancer is similar to cervical cancer with respect to overall HPV DNA positivity, with approximately 100% of anal squamous cell carcinoma cases associated with HPV infection worldwide (de Martel C et al. Lancet Glob Health 2020;8(2):e180-e190). HPV16 is the most common type detected, representing 73% of all HPV-positive tumours. HPV18 is the second most common type detected and is found in approximately 5% of cases. HPV DNA is also detected in the majority of precancerous anal lesions (AIN) (91.5% in AIN1 and 93.9% in AIN2/3) (De Vuyst H et al. Int J Cancer 2009; 124: 1626-36). In this section, the burden of HPV among cases of anal cancers and precancerous anal lesions in Bulgaria are presented.

Table 25: Studies on HPV prevalence among anal cancer cases in Bulgaria (male and female)

	HPV Prevalence								
Study	HPV detection method and targeted HPV types	No. Tested	%	(95% CI) <sup>a</sup>	Prevalence of 5 most frequent HPVs, HPV type (%)				
No data available	-	-	-	-					

Data updated on 30 Jun 2015 (data as of 30 Jun 2015)

DBH: Dot Blot Hybridization; EIA: Enzyme ImmunoAssay; HC2: Hybrid Capture 2; ISH: In Situ Hybridization; LBA: Line-Blot Assay; LiPA: Line Probe Assay; PCR: Polymerase Chain Reaction; RFLP: Restriction Fragment Length Polymorphism; RLBH: Reverse Line Blot Hybridization; RT-PCR: Real Time Polymerase Chain Reaction; SBH: Southern Blot Hybridization; SPF: Short Primer Fragment; TS: Type Specific; a 95% Confidence Interval

Data Sources:

Based on systematic reviews (up to 2008) performed by ICO for the IARC Monograph on the Evaluation of Carcinogenic Risks to Humans volume 100B and IARC's Infections and Cancer Epidemiology Group. The ICO HPV Information Centre has updated data until June 2015. Reference publications: 1) Bouvard V, Lancet Oncol 2009;10:321 2) De Vuyst H, Int J Cancer 2009;124:1626

### Table 26: Studies on HPV prevalence among cases of AIN2/3 in Bulgaria

	HPV Prevalence								
Study	HPV detection method and targeted HPV types	No. Tested	%	(95% CI) <sup>a</sup>	Prevalence of 5 most frequent HPVs, HPV type (%)				
No data available	-	-	-	-					

#### Data updated on 30 Jun 2015 (data as of 30 Jun 2015)

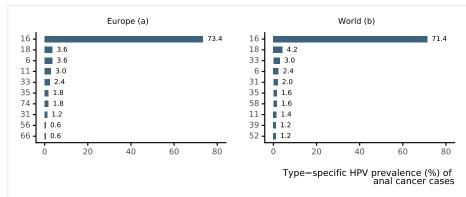
DBH: Dot Blot Hybridization; EIA: Enzyme ImmunoAssay; HC2: Hybrid Capture 2; ISH: In Situ Hybridization; LBA: Line-Blot Assay; LiPA: Line Probe Assay; PCR: Polymerase Chain Reaction; RFLP: Restriction Fragment Length Polymorphism; RLBH: Reverse Line Blot Hybridization; RT-PCR: Real Time Polymerase Chain Reaction; SBH: Southern Blot Hybridization; SPF: Short Primer Fragment; TS: Type Specific;

AIN 2/3: Anal intraepithelial neoplasia of grade 2/3  $^a$  95% Confidence Interval

Data <u>Sources</u>:

Eased on systematic reviews (up to 2008) performed by ICO for the IARC Monograph on the Evaluation of Carcinogenic Risks to Humans volume 100B and IARC's Infections and Cancer Epidemiology Group. The ICO HPV Information Centre has updated data until June 2015. Reference publications: 1) Bouvard V, Lancet Oncol 2009;10:321 2) De Vuyst H, Int J Cancer 2009;124:1626

# Figure 62: Comparison of the ten most frequent HPV types in anal cancer cases in Europe and the World



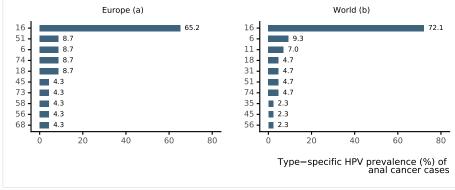
#### Data updated on 9 Feb 2017 (data as of 30 Jun 2014)

<sup>a</sup> Includes cases from Bosnia-Herzegovina, Czech Republic, France, Germany, Poland, Portugal, Slovenia, Spain and United Kingdom

<sup>b</sup> Includes cases from Europe (Bosnia-Herzegovina, Czech Republic, France, Germany, Poland, Portugal, Slovenia, Spain and United Kingdom); America (Chile, Colombia, Ecuador, Guatemala, Honduras, Mexico, Paraguay and United States); Africa (Mali, Nigeria and Senegal); Asia (Bangladesh, India and South Korea) Data Sources:

Data from Alemany L, Int J Cancer 2015; 136: 98. This study has gathered the largest international series of anal cancer cases and precancerous lesions worldwide using a standard protocol with a highly sensitive HPV DNA detection assay.

# Figure 63: Comparison of the ten most frequent HPV types in AIN 2/3 cases in Europe and the World



Data updated on 7 Feb 2017 (data as of 30 Jun 2014)

AIN 2/3: Anal intraepithelial neoplasia of grade 2/3

Includes cases from Bosnia-Herzegovina, Czech Republic, France, Germany, Poland, Portugal, Slovenia, Spain and United Kingdom

b Includes cases from Europe (Bosnia-Herzegovina, Czech Republic, France, Germany, Poland, Portugal, Slovenia, Spain and United Kingdom); America (Chile, Colombia, Ecuador, Guatemala, Honduras, Mexico, Paraguay)

Data Sources: Data from Alemany L, Int J Cancer 2015; 136: 98. This study has gathered the largest international series of anal cancer cases and precancerous lesions worldwide using a standard protocol with a highly sensitive HPV DNA detection assay

# 4.2.2 Vulvar cancer and precancerous vulvar lesions

HPV attribution for vulvar cancer is 48% among age 15-54 years, 28% among age 55-64 years, and 15% among age 65+ worldwide (de Martel C et al. Lancet Glob Health 2020;8(2):e180-e190). Vulvar cancer has two distinct histological patterns with two different risk factor profiles: (1) basaloid/warty types (2) keratinising types. Basaloid/warty lesions are more common in young women, are frequently found adjacent to VIN, are very often associated with HPV DNA detection (86%), and have a similar risk factor profile as cervical cancer. Keratinising vulvar carcinomas represent the majority of the vulvar lesions (>60%). These lesions develop from non HPV-related chronic vulvar dermatoses, especially lichen sclerosus and/or squamous hyperplasia, their immediate cancer precursor lesion is differentiated VIN, they occur more often in older women, and are rarely associated with HPV (6%) or with any of the other risk factors typical of cervical cancer. HPV prevalence is frequently detected among cases of high-grade VIN (VIN2/3) (85.3%). HPV 16 is the most common type detected followed by HPV 33 (De Vuyst H et al. Int J Cancer 2009; 124: 1626-36). In this section, the HPV burden among cases of vulvar cancer cases and precancerous vulvar lesions in Bulgaria are presented.

# Table 27: Studies on HPV prevalence among vulvar cancer cases in Bulgaria

	HPV Prevalence							
Study	HPV detection method and targeted HPV types	No. Tested	%	(95% CI) <sup>a</sup>	Prevalence of 5 most frequent HPVs, HPV type (%)			
No data available	-	-	-	-				
				-				

Data updated on 30 Jun 2015 (data as of 30 Jun 2015)

DBH: Dot Blot Hybridization; EIA: Enzyme ImmunoAssay; HC2: Hybrid Capture 2; ISH: In Situ Hybridization; LBA: Line-Blot Assay; LiPA: Line Probe Assay; PCR: Polymerase Chain Reaction; RFLP: Restriction Fragment Length Polymorphism; RLBH: Reverse Line Blot Hybridization; RT-PCR: Real Time Polymerase Chain Reaction; SBH: Southern Blot Hybridization; SPF: Short Primer Fragment; TS: Type Specific; <sup>a</sup> 95% Confidence Interval

Data Sources:

Eased on systematic reviews (up to 2008) performed by ICO for the IARC Monograph on the Evaluation of Carcinogenic Risks to Humans volume 100B and IARC's Infections and Cancer Epidemiology Group. The ICO HPV Information Centre has updated data until June 2015. Reference publications: 1) Bouvard V, Lancet Oncol 2009;10:321 2) De Vuyst H, Int J Cancer 2009;124:1626

### Table 28: Studies on HPV prevalence among VIN 2/3 cases in Bulgaria

HPV Prevalence						
Study	HPV detection method and targeted HPV types	No. Tested	%	(95% CI) <sup>a</sup>	Prevalence of 5 most frequent HPVs, HPV type (%)	
No data available	-	-	-	-		

#### Data updated on 30 Jun 2015 (data as of 30 Jun 2015)

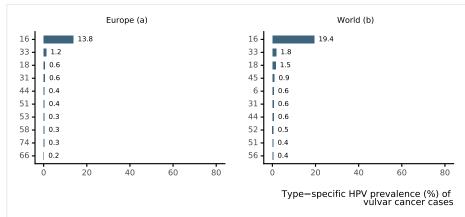
DBH: Dot Blot Hybridization; EIA: Enzyme ImmunoAssay; HC2: Hybrid Capture 2; ISH: In Situ Hybridization; LBA: Line-Blot Assay; LiPA: Line Probe Assay; PCR: Polymerase Chain Reaction; RFLP: Restriction Fragment Length Polymorphism; RLBH: Reverse Line Blot Hybridization; RT-PCR: Real Time Polymerase Chain Reaction; SBH: Southern Blot Hybridization; SPF: Short Primer Fragment; TS: Type Specific;

VIN 2/3: Vulvar intraepithelial neoplasia of grade 2/3 <sup>a</sup> 95% Confidence Interval

#### Data Sources:

Based on systematic reviews (up to 2008) performed by ICO for the IARC Monograph on the Evaluation of Carcinogenic Risks to Humans volume 100B and IARC's Infections and Cancer Epidemiology Group. The ICO HPV Information Centre has updated data until June 2015. Reference publications: 1) Bouvard V, Lancet Oncol 2009;10:321 2) De Vuyst H, Int J Cancer 2009;124:1626

# Figure 64: Comparison of the ten most frequent HPV types in cases of vulvar cancer in Europe and the World

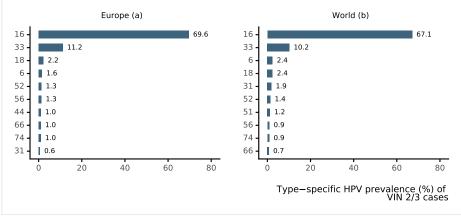


#### Data updated on 30 Jun 2015 (data as of 30 Jun 2015)

<sup>a</sup> Includes cases from Austria, Belarus, Bosnia-Herzegovina, Czech Republic, France, Germany, Greece, Italy, Poland, Portugal, Spain and United Kingdom.
 <sup>b</sup> Includes cases from America (Argentina, Brazil, Chile, Colombia, Ecuador, Guatemala, Honduras, Mexico, Paraguay, Uruguay, United States of America and Venezuela); Africa (Mali, Mozambique, Nigeria, and Senegal); Oceania (Australia and New Zealand); Europe (Austria, Belarus, Bosnia-Herzegovina, Czech Republic, France, Germany, Greece, Italy, Poland, Portugal, and United Kingdom); and in Asia (Bangladesh, India, Israel, South Korea, Kuwait, Lebanon, Philippines, Taiwan and Turkey)

Data Sources: Data from de Sanjosé S, Eur J Cancer 2013; 49: 3450. This study has gathered the largest international series of vulva cancer cases and precancerous lesions worldwide using a standard protocol with a highly sensitive HPV DNA detection assay.

# Figure 65: Comparison of the ten most frequent HPV types in VIN 2/3 cases in Europe and the World



#### Data updated on 30 Jun 2014 (data as of 30 Jun 2014)

VIN 2/3: Vulvar intraepithelial neoplasia of grade 2/3

<sup>a</sup> Includes cases from Austria, Belarus, Bosnia-Herzegovina, Czech Republic, France, Germany, Greece, Italy, Poland, Portugal, Spain and United Kingdom.

<sup>b</sup> Includes cases from America (Argentina, Brazil, Chile, Colombia, Ecuador, Guatemala, Honduras, Mexico, Paraguay, Uruguay and Venezuela); Oceania (Australia and New Zealand); Europe (Austria, Belarus, Bosnia-Herzegovina, Czech Republic, France, Germany, Greece, Italy, Poland, Portugal, Spain and United Kingdom); and in Asia (Bangladesh, India, Israel, South Korea, Kuwait, Lebanon, Philippines, Taiwan and Turkey) Data Sources:

Data from de Sanjosé S, Eur J Cancer 2013; 49: 3450. This study has gathered the largest international series of vulva cancer cases and precancerous lesions worldwide using a standard protocol with a highly sensitive HPV DNA detection assay.

# 4.2.3 Vaginal cancer and precancerous vaginal lesions

Vaginal and cervical cancers share similar risk factors and it is generally accepted that both carcinomas share the same aetiology of HPV infection although there is limited evidence available. Women with vaginal cancer are more likely to have a history of other ano-genital cancers, particularly of the cervix, and these two carcinomas are frequently diagnosed simultaneously. HPV DNA is detected among 78% of invasive vaginal carcinomas and 91% of high-grade vaginal neoplasias (VaIN2/3). HPV16 is the most common type in high-grade vaginal neoplasias and it is detected in at least 78% of HPV-positive carcinomas (de Martel C et al. Lancet Glob Health 2020;8(2):e180-e190; De Vuyst H et al. Int J Cancer 2009; 124:1626-36). In this section, the HPV burden among cases of vaginal cancer cases and precancerous vaginal lesions in Bulgaria are presented.

### Table 29: Studies on HPV prevalence among vaginal cancer cases in Bulgaria

		HPV Prevalence				
Study	HPV detection method and targeted HPV types	No. Tested	%	(95% CI) <sup>a</sup>	Prevalence of 5 most frequent HPVs, HPV type (%)	
No data available	-	-	-	-		

#### Data updated on 30 Jun 2015 (data as of 30 Jun 2015)

DBH: Dot Blot Hybridization; EIA: Enzyme ImmunoAssay; HC2: Hybrid Capture 2; ISH: In Situ Hybridization; LBA: Line-Blot Assay; LiPA: Line Probe Assay; PCR: Polymerase Chain Reaction; RFLP: Restriction Fragment Length Polymorphism; RLBH: Reverse Line Blot Hybridization; RT-PCR: Real Time Polymerase Chain Reaction; SBH: Southern Blot Hybridization; SPF: Short Primer Fragment; TS: Type Specific; a 95% Confidence Interval

Data Sources:

Based on systematic reviews (up to 2008) performed by ICO for the IARC Monograph on the Evaluation of Carcinogenic Risks to Humans volume 100B and IARC's Infections and Cancer Epidemiology Group. The ICO HPV Information Centre has updated data until June 2015. Reference publications: 1) Bouvard V, Lancet Oncol 2009;10:321 2) De Vuyst H, Int J Cancer 2009;124:1626

#### Table 30: Studies on HPV prevalence among VaIN 2/3 cases in Bulgaria

HPV Prevalence							
Study	HPV detection method and targeted HPV types	No. Tested	%	(95% CI) <sup>a</sup>	Prevalence of 5 most frequent HPVs, HPV type (%)		
No data available	-	-	-	-			

#### Data updated on 30 Jun 2015 (data as of 30 Jun 2015)

DBH: Dot Blot Hybridization; EIA: Enzyme ImmunoAssay; HC2: Hybrid Capture 2; ISH: In Situ Hybridization; LBA: Line-Blot Assay; LiPA: Line Probe Assay; PCR: Polymerase Chain Reaction; RFLP: Restriction Fragment Length Polymorphism; RLBH: Reverse Line Blot Hybridization; RT-PCR: Real Time Polymerase Chain Reaction; SBH: Southern Blot Hybridization; SPF: Short Primer Fragment; TS: Type Specific;

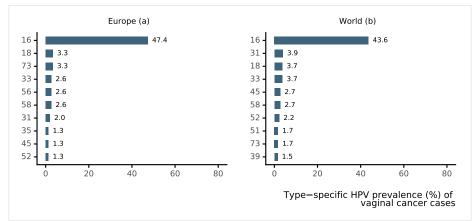
VAIN 2/3: Vaginal intraepithelial neoplasia of grade 2/3

a 95% Confidence Interval

Data Sources:

Based on systematic reviews (up to 2008) performed by ICO for the IARC Monograph on the Evaluation of Carcinogenic Risks to Humans volume 100B and IARC's Infections and Cancer Epidemiology Group. The ICO HPV Information Centre has updated data until June 2015. Reference publications: 1) Bouvard V, Lancet Oncol 2009;10:321 2) De Vuyst H, Int J Cancer 2009;124:1626

# Figure 66: Comparison of the ten most frequent HPV types in cases of vaginal cancer in Europe and the World



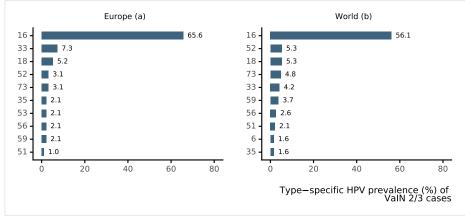
#### Data updated on 30 Jun 2015 (data as of 30 Jun 2015)

<sup>a</sup> Includes cases from Austria, Belarus, Czech Republic, France, Germany, Greece, Poland, Spain and United Kingdom.

<sup>b</sup> Includes cases from Europe (Austria, Belarus, Czech Republic, France, Germany, Greece, Poland, Spain and United Kingdom); America (Argentina, Brazil, Chile, Colombia, Ecuador, Guatemala, Mexico, Paraguay, Uruguay, United states of America and Venezuela); Africa (Mozambique, Nigeria); Asia (Bangladesh, India, Israel, South Korea, Kuwait, Philippines, Taiwan and Turkey); and Oceania (Australia)

Data Sources: Data from Alemany L, Eur J Cancer 2014; 50: 2846. This study has gathered the largest international series of vaginal cancer cases and precancerous lesions worldwide using a standard protocol with a highly sensitive HPV DNA detection assay.

# Figure 67: Comparison of the ten most frequent HPV types in VaIN 2/3 cases in Europe and the World



#### Data updated on 30 Jun 2014 (data as of 30 Jun 2014)

VAIN 2/3: Vaginal intraepithelial neoplasia of grade 2/3

<sup>a</sup> Includes cases from Austria, Belarus, Czech Republic, France, Germany, Greece, Poland, Spain and United Kingdom.

b Includes cases from Flaveria, Belarus, Status, Statu

Data from Alemany L, Eur J Cancer 2014; 50: 2846. This study has gathered the largest international series of vaginal cancer cases and precancerous lesions worldwide using a standard protocol with a highly sensitive HPV DNA detection assay.

# 4.2.4 Penile cancer and precancerous penile lesions

HPV DNA is detectable in approximately 51% of all penile cancers (de Martel C et al. Lancet Glob Health 2020;8(2):e180-e190). Among HPV-related penile tumours, HPV16 is the most common type detected, followed by HPV18 and HPV types 6/11 (Miralles C et al. J Clin Pathol 2009;62:870-8). Over 95% of invasive penile cancers are SCC and the most common penile SCC histologic sub-types are keratinising (49%), mixed warty-basaloid (17%), verrucous (8%), warty (6%), and basaloid (4%). HPV is commonly detected in basaloid and warty tumours but is less common in keratinising and verrucous tumours. In this section, the HPV burden among cases of penile cancer cases and precancerous penile lesions in Bulgaria are presented.

# Table 31: Studies on HPV prevalence among penile cancer cases in Bulgaria

		HPV Prevalence			
Study	HPV detection method and targeted HPV types	No. Tested	%	(95% CI) <sup>a</sup>	Prevalence of 5 most frequent HPVs, HPV type (%)
No data available	-	-	-	-	

#### Data updated on 5 Mar 2015 (data as of 30 Jun 2014)

DBH: Dot Blot Hybridization; EIA: Enzyme ImmunoAssay; HC2: Hybrid Capture 2; ISH: In Situ Hybridization; LBA: Line-Blot Assay; LiPA: Line Probe Assay; PCR: Polymerase Chain Reaction; RFLP: Restriction Fragment Length Polymorphism; RLBH: Reverse Line Blot Hybridization; RT-PCR: Real Time Polymerase Chain Reaction; SBH: Southern Blot Hybridization; SPF: Short Primer Fragment; TS: Type Specific; <sup>a</sup> 95% Confidence Interval

Data Sources:

The ICO HPV Information Centre has updated data until June 2014. Reference publications (up to 2008): 1) Bouvard V, Lancet Oncol 2009;10:321 2) Miralles-Guri C,J Clin Pathol 2009;62:870

# Table 32: Studies on HPV prevalence among PeIN 2/3 cases in Bulgaria

HPV Prevalence							
Study	HPV detection method and targeted HPV types	No. Tested	%	(95% CI) <sup>a</sup>	Prevalence of 5 most frequent HPVs, HPV type (%)		
No data available	-	-	-	-			

#### Data updated on 10 Feb 2015 (data as of 30 Jun 2014)

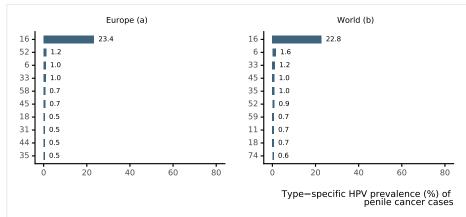
PeIN 2/3: Penile intraepithelial neoplasia of grade 2/3

DBH: Dot Blot Hybridization; EIA: Enzyme ImmunoAssay; HC2: Hybrid Capture 2; ISH: In Situ Hybridization; LBA: Line-Blot Assay; LiPA: Line Probe Assay; PCR: Polymerase Chain Reaction; RFLP: Restriction Fragment Length Polymorphism; RLBH: Reverse Line Blot Hybridization; RT-PCR: Real Time Polymerase Chain Reaction; SBH: Southern Blot Hybridization; SPF: Short Primer Fragment; TS: Type Specific;

a 95% Confidence Interval

Data Sources: The ICO HPV Information Centre has updated data until June 2014. Reference publication (up to 2008): Bouvard V, Lancet Oncol 2009;10:321

# Figure 68: Comparison of the ten most frequent HPV types in cases of penile cancer in Europe and the World



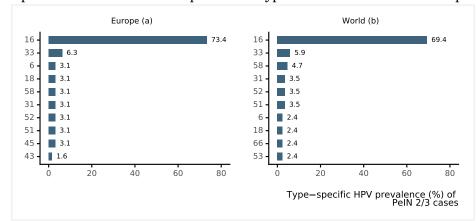
#### Data updated on 9 Feb 2017 (data as of 30 Jun 2015)

<sup>a</sup> Includes cases from Czech Republic, France, Greece, Poland, Portugal, Spain and United Kingdom

<sup>b</sup> Includes cases from Australia, Bangladesh, India, South Korea, Lebanon, Philippines, Chile, Colombia, Ecuador, Guatemala, Honduras, Mexico, Paraguay, Venezuela and United States, Mozambique, Nigeria, Senegal, Czech Republic, France, Greece, Poland, Portugal, Spain and United Kingdom.

Data Sources: Alemany L, Eur Urol 2016; 69: 953

# Figure 69: Comparison of the ten most frequent HPV types in PeIN 2/3 cases in Europe and the World



#### Data updated on 9 Feb 2017 (data as of 30 Jun 2015)

PeIN 2/3: Penile intraepithelial neoplasia of grade 2/3

<sup>a</sup> Includes cases from Czech Republic, France, Greece, Poland, Portugal, Spain and United Kingdom

<sup>b</sup> Includes cases from Australia, Bangladesh, India, South Korea, Lebanon, Philippines, Chile, Colombia, Ecuador, Guatemala, Honduras, Mexico, Paraguay, Venezuela, Mozambique, Nigeria, Senegal, Czech Republic, France, Greece, Poland, Portugal, Spain and United Kingdom. Data Sources:

Based on systematic reviews and meta-analysis performed by ICO. Reference publications: 1) Ndiaye C, Lancet Oncol 2014; 15: 1319 2) Kreimer AR, Cancer Epidemiol Biomarkers Prev 2005; 14: 467

# 4.3 HPV burden in men

The information to date regarding anogenital HPV infection is primarily derived from cross-sectional studies of selected populations such as general population, university students, military recruits, and studies that examined husbands of control women, as well as from prospective studies. Special subgroups include mainly studies that examined STD (sexually transmitted diseases) clinic attendees, MSM (men who have sex with men), HIV positive men, and partners of women with HPV lesions, CIN (cervical intraepithelial neoplasia), cervical cancer or cervical carcinoma in situ. Globally, prevalence of external genital HPV infection in men is higher than cervical HPV infection in women, but persistence is less likely. As with genital HPV prevalence, high numbers of sexual partners increase the acquisition of oncogenic HPV infections (Vaccine 2012, Vol. 30, Suppl 5). In this section, the HPV burden among men in Bulgaria is presented.

# Methods

HPV burden in men was based on published systematic reviews and meta-analyses (Dunne EF, J Infect Dis 2006; 194: 1044, Smith JS, J Adolesc Health 2011; 48: 540, Olesen TB, Sex Transm Infect 2014; 90: 455, and Hebnes JB, J Sex Med 2014; 11: 2630) up to October 31, 2015. The search terms for the review were human papillomavirus, men, polymerase chain reaction (PCR), hybrid capture (HC), and viral DNA. References cited in selected articles were also investigated. Inclusion criteria were: HPV DNA detection by means of PCR or HC (ISH if data are not available for the country), and a detailed description of HPV DNA detection and genotyping techniques used. The number of cases tested and HPV positive cases were extracted for each study to estimate the anogenital prevalence of HPV DNA. Binomial 95% confidence intervals were calculated for each anogenital HPV prevalence.

Study	Anatomic sites samples	HPV detection method	Population	Age (years)	No. Tested	%	(95% CI) <sup>a</sup>
-	-	-	-	-	-	-	-

Table 33: Studies on HPV prevalence among men in Bulgaria

### Data updated on 31 Oct 2015 (data as of 31 Oct 2015)

HC2: Hybrid Capture 2; ISH: In Situ Hybridization; PCR: Polymerase Chain Reaction; RT-PCR: Real Time Polymerase Chain Reaction; SPF: Short Primer Fragment; TS: Type Specific; MSM: Men who have sex with men; MSW:Men who have sex with women; STD: sexually transmitted diseases <sup>a</sup> 95% Confidence Interval

Data Sources:

Based on published systematic reviews, the ICO HPV Information Centre has updated data until October 2015. Reference publications: 1) Dunne EF, J Infect Dis 2006; 194: 1044 2) Smith JS, J Adolesc Health 2011; 48: 540 3) Olesen TB, Sex Transm Infect 2014; 90: 455 4) Hebnes JB, J Sex Med 2014; 11: 2630.

# Table 34: Studies on HPV prevalence among men from special subgroups in Bulgaria

						HPV	Prevalence
Study	Anatomic sites samples	HPV detection method	Population	Age (years)	No. Tested	%	(95% CI) <sup>a</sup>
-	-	-	-	-	-	-	

#### Data updated on 31 Oct 2015 (data as of 31 Oct 2015)

DBH: Dot Blot Hybridization; EIA: Enzyme ImmunoAssay; HC2: Hybrid Capture 2; LiPA: Line Probe Assay; PCR: Polymerase Chain Reaction; RFLP: Restriction Fragment Length Polymorphism; RLH: Reverse Line Hybridisation; RT-PCR: Real Time Polymerase Chain Reaction; SPF: Short Primer Fragment; TS: Type Specific; MSM: Men who have sex with men; MSW:Men who have sex with women; STD: sexually transmitted diseases <sup>a</sup> 95% Confidence Interval

Data Sources:

Based on published systematic reviews, the ICO HPV Information Centre has updated data until October 2015. Reference publications: 1) Dunne EF, J Infect Dis 2006; 194: 1044 2) Smith JS, J Adolesc Health 2011; 48: 540 3) Olesen TB, Sex Transm Infect 2014; 90: 455 4) Hebnes JB, J Sex Med 2014; 11: 2630.

# 4.4 HPV burden in the head and neck

The last evaluation of the International Agency for Research in Cancer (IARC) on the carcinogenicity of HPV in humans concluded that (a) there is enough evidence for the carcinogenicity of HPV type 16 in the oral cavity, oropharynx (including tonsil cancer, base of tongue cancer and other oropharyngeal cancer sites), and (b) limited evidence for laryngeal cancer (IARC Monograph Vol 100B). There is increasing evidence that HPV-related oropharyngeal cancers constitute an epidemiological, molecular and clinical distinct form as compared to non HPV-related ones. Some studies indicate that the most likely explanation for the origin of this distinct form of head and neck cancers associated with HPV is a sexually acquired oral HPV infection that is not cleared, persists and evolves into a neoplastic lesion. Around 30% of oropharyngeal cancers (which mainly comprises the tonsils and base of tongue sites) are caused by HPV with HPV16 being the most frequent type (de Martel C et al. Int J Cancer 2017;141(4):664-670). Attributable fraction varies greatly worldwide, being highest in more developed countries (60% in Republic of Korea, 51% in North America, 50% in Eastern Europe, 46% in Japan, 42% in North-Western Europe, 41% in Australia/New Zealand, 24% in South Europe, 23% in China, 22% in India, and 13% in elsewhere) (de Martel C et al. Lancet Glob Health 2020;8(2):e180-e190). In this section, the HPV burden in the head and neck in Bulgaria is presented.

# 4.4.1 Burden of oral HPV infection in healthy population

Study	Specimen collection method / anatomic site	HPV detec- tion method <sup>a</sup>	Population	% males	Age (years) <sup>b</sup>	No. tested <sup>c</sup>	HPV prevalence % (95% CI)	High-Risk HPV prevalence % (95% CI)	5 most frequent HPVs, HPV type (n) <sup>d</sup>
-	-	-	-	-	-	-	-	-	-

Table 35: Studies on oral HPV prevalence among healthy in Bulgaria

#### Data updated on 19 Oct 2021 (data as of 19 May 2015)

(95% CI): 95% Confidence Interval

<sup>a</sup> TS: type-specific; RT-PCR: real-time PCR; qPCR: quantitative PCR

 $^{b}$  NS: not specified

 $\stackrel{c}{d}$  number of cases tested for HPV DNA  $\stackrel{d}{d}$  number of cases positive for the specific HPV-type

Data Sources:

Systematic review and meta-analysis was performed by ICO HPV Information Centre until May 19, 2015. Reference publication: Mena M et al. J Infect Dis 2019;219(10):1574-1585.

# 4.4.2 HPV burden in head and neck cancers

HPV Prevalence									
Study	HPV detection method and targeted HPV types	No. Tested	%	(95% CI) <sup>a</sup>	Prevalence of 5 most frequent HPVs, HPV type (%)				
MEN									
No data available	-	-	-	-	-				
WOMEN									
No data available	-	-	-	-	-				
BOTH OR UNSPECIFIE	ED								
No data available	-	-	-	-	-				

#### Table 36: Studies on HPV prevalence among cases of oral cavity cancer in Bulgaria

#### Data updated on 9 May 2016 (data as of 31 Dec 2015)

DBH: Dot Blot Hybridization; EIA: Enzyme ImmunoAssay; HC2: Hybrid Capture 2; ISH: In Situ Hybridization; LBA: Line-Blot Assay; LiPA: Line Probe Assay; PCR: Polymerase Chain Reaction; RFLP: Restriction Fragment Length Polymorphism; RLBH: Reverse Line Blot Hybridization; RT-PCR: Real Time Polymerase Chain Reaction; SBH: Southern Blot Hybridization; SPF: Short Primer Fragment; TS: Type Specific;

Only for European countries <sup>a</sup> 95% Confidence Interval

Data Sources:

Based on systematic reviews and meta-analysis performed by ICO. Reference publications: 1) Ndiaye C, Lancet Oncol 2014; 15: 1319 2) Kreimer AR, Cancer Epidemiol Biomarkers Prev 2005; 14: 467

#### Table 37: Studies on HPV prevalence among cases of oropharyngeal cancer in Bulgaria

			HPV	Prevalence	
Study	HPV detection method and targeted HPV types	No. Tested	%	(95% CI) <sup>a</sup>	Prevalence of 5 most frequent HPVs, HPV type (%)
MEN					
No data available	-	-	-	-	-
WOMEN					
No data available	-	-	-	-	-
BOTH OR UNSPECIFIED					
No data available	-	-	-	-	-
				• • • • • • • • • • • • • • • • • • •	

#### Data updated on 9 May 2016 (data as of 31 Dec 2015)

DBH: Dot Blot Hybridization; EIA: Enzyme ImmunoAssay; HC2: Hybrid Capture 2; ISH: In Situ Hybridization; LBA: Line-Blot Assay; LiPA: Line Probe Assay; PCR: Polymerase Chain Reaction; RFLP: Restriction Fragment Length Polymorphism; RLBH: Reverse Line Blot Hybridization; RT-PCR: Real Time Polymerase Chain Reaction; SBH: Southern Blot Hybridization; SPF: Short Primer Fragment; TS: Type Specific

Only for European countries a 95% Confidence Interval

Data Sources:

Based on systematic reviews and meta-analysis performed by ICO. Reference publications: 1) Ndiaye C, Lancet Oncol 2014; 15: 1319 2) Kreimer AR, Cancer Epidemiol Biomarkers Prev 2005; 14: 467

## Table 38: Studies on HPV prevalence among cases of hypopharyngeal or laryngeal cancer in Bulgaria

			HPV Prevalence				
Study	HPV detection method and targeted HPV types	No. Tested	%	(95% CI) <sup>a</sup>	Prevalence of 5 most frequent HPVs, HPV type (%)		
MEN							
No data available	-	-	-	-	-		
WOMEN							
No data available	-	-	-	-	-		
BOTH OR UNSPECIFIE	D						
No data available	-	-	-	-	-		

#### Data updated on 9 May 2016 (data as of 31 Dec 2015)

DBH: Dot Blot Hybridization; EIA: Enzyme ImmunoAssay; HC2: Hybrid Capture 2; ISH: In Situ Hybridization; LBA: Line-Blot Assay; LiPA: Line Probe Assay; PCR: Polymerase Chain Reaction; RFLP: Restriction Fragment Length Polymorphism; RLBH: Reverse Line Blot Hybridization; RT-PCR: Real Time Polymerase Chain Reaction; SBH: Southern Blot Hybridization; SPF: Short Primer Fragment; TS: Type Specific

Only for European countries <sup>a</sup> 95% Confidence Interval

Data Sources:

Based on systematic reviews and meta-analysis performed by ICO. Reference publications: 1) Ndiaye C, Lancet Oncol 2014; 15: 1319 2) Kreimer AR, Cancer Epidemiol Biomarkers Prev 2005; 14: 467

#### 5 **Factors contributing to cervical cancer**

HPV is a necessary cause of cervical cancer, but it is not a sufficient cause. Other cofactors are necessary for progression from cervical HPV infection to cancer. Tobacco smoking, high parity, long-term hormonal contraceptive use, and co-infection with HIV have been identified as established cofactors. Co-infection with Chlamydia trachomatis and herpes simplex virus type-2, immunosuppression, and certain dietary deficiencies are other probable cofactors. Genetic and immunological host factors and viral factors other than type, such as variants of type, viral load and viral integration, are likely to be important but have not been clearly identified. (Muñoz N, Vaccine 2006; 24(S3): 1-10). In this section, the prevalence of smoking, parity (fertility), oral contraceptive use, and HIV in Bulgaria are presented.

INDICATOR		MALE	FEMALE	TOTAL
Smoking				
Smoking of any tobacco adjusted	Current <sup>a</sup>	42.2 [31.4-56]	23.8 [16.8-31.2]	32.7 [23.8-43.1]
prevalence (%) [95% UI]	Daily <sup>b</sup>	33.8 [23.3-44.9]	16.6 [11.2-22.4]	24.9 [17-33.2]
Cigarette smoking adjusted	Current <sup>c</sup>	42.2 [31.4-56]	23.8 [16.8-31.2]	32.7 [23.8-43.1]
prevalence (%) [95% UI]	Daily <sup>d</sup>	33.8 [23.3-44.9]	16.6 [11.2-22.4]	24.9 [17-33.2]
Parity				
Total fertility rate per woman		-	1.6	-
	15-19 yrs	-	38.2	-
	20-24 yrs	-	71.5	-
	25-29 yrs	-	88.6	-
Age-specific fertility rate (per 1000 women)	30-34 yrs	-	71.5	-
(per 1000 women)	35-39 yrs	-	32.7	-
	40-44 yrs	-	7.1	-
	45-49 yrs	-	0.8	-
Oral contraceptive use (%) among v married or in union		-	6.23	
Injectable contraception use (%)	among women	-	-	-
who are married or in union Implant contraceptive use (%) amo				
are married or in union	ng women who	-	-	-
HIV				
Estimated percent of adults aged living with HIV [95% UI]		0.1 [<0.1-0.2]	<0.1 [<0.1 -<0.1]	<0.1 [<0.1-0.1]
Estimated percent of young adults a are living with HIV [95% UI]	aged 15-24 who	<0.1 [<0.1 - <0.1]	<0.1 [<0.1-<0.1]	- [—]
HIV prevalence (%) among sex wor	kers	0	0.30000001	0.30000001
HIV prevalence (%) among men who men	o have sex with	3.7	-	3.7
Estimated number of people living UI]	with HIV [95%	-	-	3500 [3000-4100]
Estimated number of adults (15+ y HIV [95% UI]	vrs) living with	2800 [2300-3200]	<1000 [<1000-<1000]	3500 [3000-4000]
Estimated number of AIDS-relate	d deaths [050			<100 [<100-<100]

Table 39: Factors contributing to cervical carcinogenesis (cofactors) in Bulgaria

Crude adjusted prevalence (%) estimates of tabacco use among people aged >= 15 years by country, for the year 2016. <sup>a</sup> "Current" means smoking at the time of the survey, including both daily and non-daily or occasional smoking. "Tobacco smoking" means smoking any form of tobacco, including cigarettes, cigars, pipes, or any other smoked tobacco products and excluding smokeless products.

<sup>b</sup> "Daily" means smoking every day at the time of the survey. "Tobacco smoking" means smoking any form of tobacco, including cigarettes, cigars, pipes, or any other smoked tobacco products and excluding smokeless products <sup>c</sup> "Current" means smoking at the time of the survey, including both daily and non-daily or occasional smoking

 $d\,$  "Daily" means smoking every day at the time of the survey. Data pertain to women with co-resident male partner.

Year of estimate: 2016

Data Sources:

WHO global report on trends in prevalence of tobacco use 2000-2025, third edition. Geneva: World Health Organization; 2019. Available at https://www.who.int/publications/i/ item/who-global-reporttrends-in-prevalence-of-tobacco-use-2000-2025-third-edition Eurostat - Statistical office of the European Comission [web site]. Luxembourg: European Commission; 2017. Available at: https://ec.europa.eu/eurostat/web/products-datasets/

/demofrate. [Accessed on November 13, 2019]. United Nations, Department of Economic and Social Affairs, Population Division (2017). World Population Prospects: The 2017 Revision, DVD Edition. Available at: https://www.un.org/

en/development/desa/population/publications/dataset/fertility/wfd2017.asp. [Accessed on November 13, 2019]. United Nations, Department of Economic and Social Affairs, Population Division (2019). World Contraceptive Use 2019 (POP/DB/CP/Rev2019). https://www.un.org/en/development/ desa/population/publications/dataset/contraception/wcu2019.asp. Available at: [Accessed on November 18, 2019].

UNAIDS database [internet]. Available at: http://aidsinfo.unaids.org/ [Accessed on November 21, 2019]

ECDC 2017

<sup>2</sup> Behavioral surveillance

# 6 Sexual and reproductive health behaviour indicators

Sexual intercourse is the primary route of transmission of genital HPV infection. Information about sexual and reproductive health behaviours is essential to the design of effective preventive strategies against anogenital cancers. In this section, we describe sexual and reproductive health indicators that may be used as proxy measures of risk for HPV infection and anogenital cancers. Several studies have reported that earlier sexual debut is a risk factor for HPV infection, although the reason for this relationship is still unclear. In this section, information on sexual and reproductive health behaviour in Bulgaria are presented.

Table 40: Percentage of 15-year-olds who have had sexual intercourse in Bulgaria

8 7	8	
Indicator	Male	Female
Percentage of 15-year-old subjects who report sexual intercourse	40.0	21.0
Data accessed on 16 Mar 2017		
Please refer to original source for methods of estimation		

Fifteen-year-olds teenagers only were asked whether they had ever had sexual intercourse.

Indicates a significant gender difference (at p<0.05).

Year of estimation: 2013-2014

Data Sources:

Growing up unequal: gender and socioeconomic differences in young people's health and well-being. Health Behaviour in School-aged Children (HBSC) study: international report from the 2013/2014 survey. Inchley J, Currie D, Young T, et al. Copenhagen, WHO Regional Office for Europe, 2016 (Health Policy for Children and Adolescents, No. 7). Available at: http://www.euro.who.int/\_\_data/assets/pdf\_file/0003/303438/HSBC-No.7-Growing-up-unequal-Full-Report.pdf?ua=1

# Table 41: Median age at first sex in Bulgaria

				MALE		FEMALE		TOTAL
Study	Year/period	Birth cohort N	N	Median age at first sex	N	Median age at first sex	N	Median age at first sex

Data accessed on 16 Mar 2017

Please refer to original source for methods of estimation

	01 0		
Indicator		Male	Female
Average age at first marriage <sup>1</sup>		34.9	31.7
Age-specific % of ever married <sup>2</sup>	15-19 years	0.19	1.82
	20-24 years	3.86	11.67
	25-29 years	14.42	28.49
	30-34 years	29.66	45.97
	35-39 years	43.67	59.82
	40-44 years	57.33	72.27
	45-49 years	71.09	84.62
	50-54 years	82.56	90.94
	55-59 years	87.65	93.86
	60-64 years	90.91	95.76
	65-69 years	93.74	96.95
	70-74 years	95.72	97.58
	+75	97.55	98.09

# Table 42: Marriage patterns in Bulgaria

Data accessed on 20 Feb 2020 Please refer to original source for methods of estimation. <sup>a</sup> 2018 Estimate <sup>b</sup> UNSD

Data Sources: The world bank: health nutrition and population statistics. Updated 20-Dec-2019. Accessed on February 20 2020. Available at http://data.worldbank.org/data-catalog/ health-nutrition-and-population-statistics <sup>2</sup> United Nations, Department of Economic and Social Affairs, Population Division (2019). World Marriage Data 2019 (POP/DB/Marr/Rev2019). Available at: https://population.un.

org/MarriageData/Index.html#/home Accessed on February 24, 2020.

# Table 43: Average number of sexual partners in Bulgaria

Study	Period of estimate	Year/Period	Birth cohort	Male Mean(N)	Female Mean(N)	Total Mean(N)
-	-	-	-	-(-)	-(-)	-(-)

Data accessed on 8 Aug 2013 Please refer to original source for methods of estimation

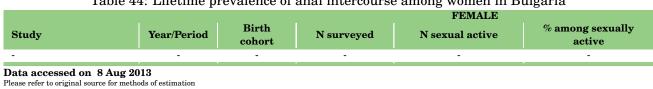


Table 44: Lifetime prevalence of anal intercourse among women in Bulgaria

# 7 HPV preventive strategies

It is established that well-organised cervical screening programmes or widespread good quality cytology can reduce cervical cancer incidence and mortality. The introduction of HPV vaccination could also effectively reduce the burden of cervical cancer in the coming decades. This section presents indicators on basic characteristics and performance of cervical cancer screening, status of HPV vaccine licensure and introduction in Bulgaria.

# 7.1 Cervical cancer screening practices

Screening strategies differ between countries. Some countries have population-based programmes, where in each round of screening women in the target population are individually identified and invited to attend screening. This type of programme can be implemented nationwide or only in specific regions of the country. In opportunistic screening, invitations depend on the individual's decision or on encounters with health-care providers. The most frequent method for cervical cancer screening is cytology, and there are alternative methods such as HPV DNA tests and visual inspection with acetic acid (VIA). VIA is an alternative to cytology-based screening in low-resource settings (the 'see and treat' approach). HPV DNA testing is being introduced into some countries as an adjunct to cytology screening ('co-testing') or as the primary screening test to be followed by a secondary, more specific test, such as cytology.

Tabl	e 45: Main	characteris	tics of	cervical	cancer	screening i	n Bul	garia	ι

Region	Existence of official national recommendations	Starting year of current recommendations	Active invitation to screening	Screening ages (years), primary screening test used, and screening interval or frequency of screenings
Bulgaria	Yes	Unk	No	30-40 (cytology, 3 years)

Data accessed on 31 Aug 2022

Data Sources: Bruni L, Serrano B, Roura E, Alemany L, Cowan M, Herrero R, et al. Cervical cancer screening programmes and age-specific coverage estimates for 202 countries and territories worldwide: a review and synthetic analysis. Lancet Glob Health. 2022;10(8):e1115.

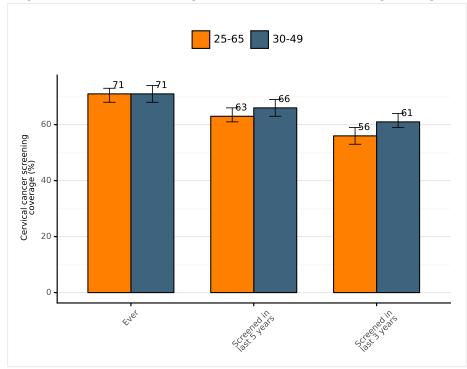


Figure 70: Estimated coverage\* of cervical cancer screening in Bulgaria

 Data accessed on 31 Aug 2022

 \* Estimated coverage and 95% confidence interval in 2019

 Data Sources:

 Bruni L, Serrano B, Roura E, Alemany L, Cowan M, Herrero R, et al. Cervical cancer screening programmes and age-specific coverage estimates for 202 countries and territories worldwide: a review and synthetic analysis. Lancet Glob Health. 2022;10(8):e1115.

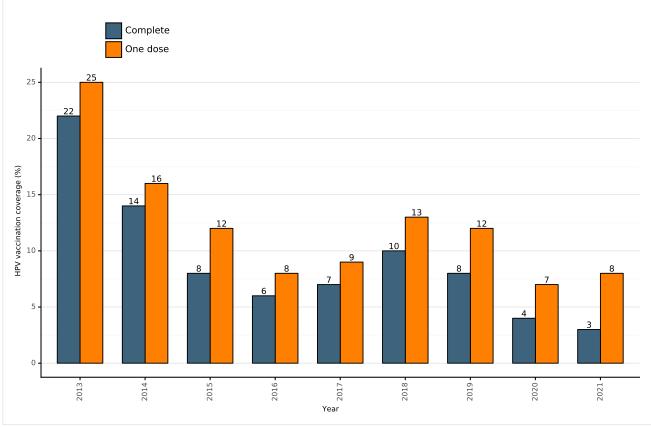
# 7.2 HPV vaccination

	Burna	
	Female	Male
HPV vaccination programme	Introduced	Not Available/Not Introduced
Year of introduction	2012	-
Year of estimation of HPV vaccination coverage	2021	-
HPV coverage – first dose (%)	8	-
HPV coverage – last dose (%)	3	-

# Table 46: National HPV Immunization programme in Bulgaria

Data accessed on 24 Oct 2022

Data Sources: Human papillomavirus (HPV) vaccination coverage. World Health Organization. 2022. Available from: https://immunizationdata.who.int/pages/coverage/hpv.html, accessed [24] Oct 2022] Bruni L, Saura-Lázaro A, Montoliu A, Brotons M, Alemany L, Diallo MS, et al. HPV vaccination introduction worldwide and WHO and UNICEF estimates of national HPV immunization coverage 2010-2019. Prev Med. 2021;144(106399):106399.



# Figure 71: HPV vaccination coverage in females by year in Bulgaria

Data accessed on 24 Oct 2022

Data Sources: Human papillomavirus (HPV) vaccination coverage. World Health Organization. 2022. Available from: https://immunizationdata.who.int/pages/coverage/hpv.html, accessed [24] Oct 2022]

Bruni L, Saura-Lázaro A, Montoliu A, Brotons M, Alemany L, Diallo MS, et al. HPV vaccination introduction worldwide and WHO and UNICEF estimates of national HPV immunization coverage 2010-2019. Prev Med. 2021;144(106399):106399.



# Figure 72: HPV vaccination coverage in males by year in Bulgaria

Data accessed on 24 Oct 2022

Data accessed on D4 Oct 2022 Data Sources: Human papillomavirus (HPV) vaccination coverage. World Health Organization. 2022. Available from: https://immunizationdata.who.int/pages/coverage/hpv.html, accessed [24 Oct 2022] Bruni L, Saura-Lázaro A, Montoliu A, Brotons M, Alemany L, Diallo MS, et al. HPV vaccination introduction worldwide and WHO and UNICEF estimates of national HPV immunization coverage 2010-2019. Prev Med. 2021;144(106399):106399.

#### **Protective factors for cervical cancer** 8

Male circumcision and the use of condoms have shown a significant protective effect against HPV transmission.

Table 47: Prevalence of male circumcision in Bulgaria				
Reference		Prevalence % (95% CI)	Methods	
Drain 2006		<20	Data from Demographic and Health Surveys (DHS) and other publications to categorize the country-wide prevalence of male circumcision as <20%, 20-80%, or >80%.	
WHO 2007		<20	Data from Demographic and Health Surveys (DHS) and other publications to categorize the country-wide prevalence of male circumcision as <20%, 20-80%, or >80%	

#### Data accessed on 31 Aug 2015

Please refer to country-specific reference(s) for full methodologies.

Data Sources: Drain PK, BMC Infect Dis 2006; 6: 172 | WHO 2007: Male circumcision: Global trends and determinants of prevalence, safety and acceptability Based on systematic reviews and meta-analysis performed by ICO. The ICO HPV Information Centre has updated data until August 2015. Reference publication: Albero G, Sex Transm Dis. 2012 Feb;39(2):104-13.

Table 48: Prevalence of condom use in Bulgaria

Indicator	Age range	Year of estimate	Prevalence % <sup>a</sup>
Condom use	20-49	2007	22.3260869565217
	•	•	•

# Data accessed on 18 Nov 2019

Please refer to original source for methods of estimation. Data pertain to women with co-resident male partner. <sup>a</sup> Condom use: Proportion of male partners who are using condoms with their female partners of reproductive age to whom they are married or in union by country.

Data Sources:

2007 GGS United Nations, Department of Economic and Social Affairs, Population Division (2019). World Contraceptive Use 2019 (POP/DB/CP/Rev2019). https://www.un.org/en/development/  $\texttt{desa/population/publications/dataset/contraception/wcu2019.asp.}\ Available\ at:\ [Accessed\ on\ November\ 18,\ 2019].$ 

#### 9 Annex

# 9.1 Incidence

# 9.1.1 Cervical cancer incidence in Bulgaria across Eastern Europe

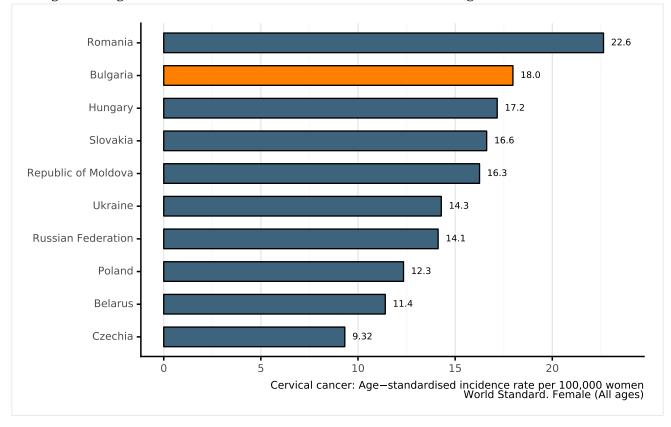
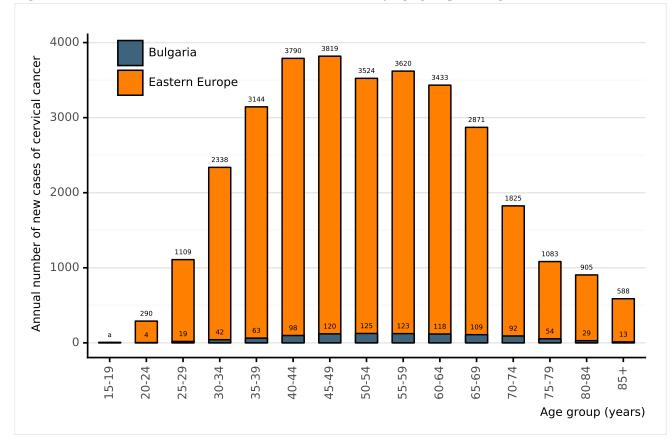


Figure 73: Age-standardised incidence rates of cervical cancer of Bulgaria (estimates for 2020)

#### Data accessed on 27 Jan 2021

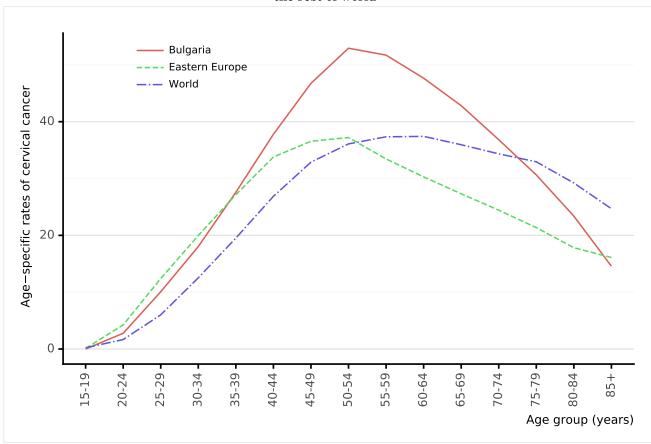
For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 women per year.



# Figure 74: Annual number of new cases of cervical cancer by age group in Bulgaria (estimates for 2020)

#### Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods a 0 cases for Bulgaria and 7 cases for Eastern Europe in the 15-19 age group.

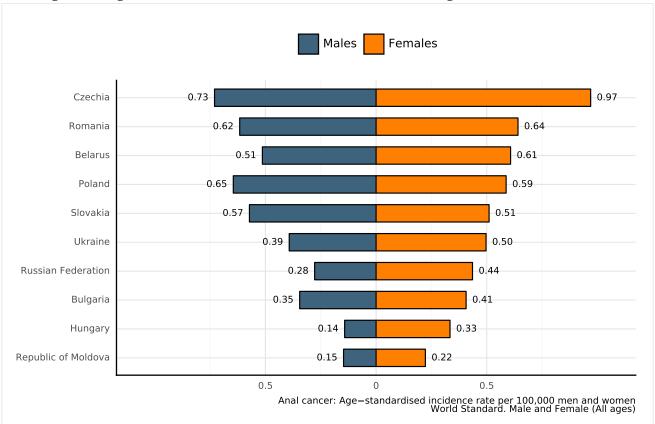


# Figure 75: Comparison of age-specific cervical cancer incidence rates in Bulgaria, within the region, and the rest of world

#### Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 women per year.

# 9.1.2 Anal cancer incidence in Bulgaria across Eastern Europe

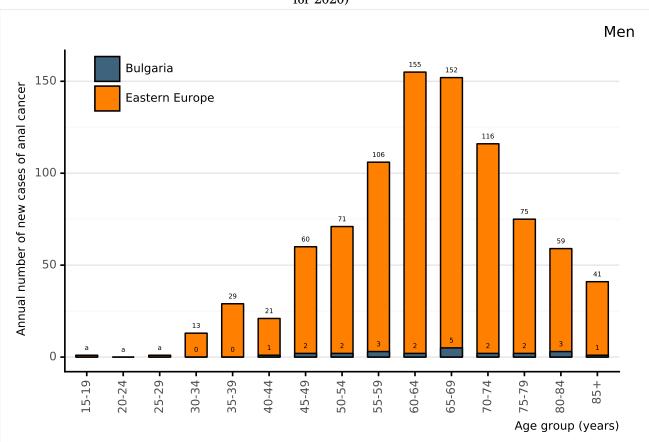


# Figure 76: Age-standardised incidence rates of anal cancer of Bulgaria (estimates for 2020)

Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 men per year.

<sup>b</sup> Rates per 100,000 women per year.

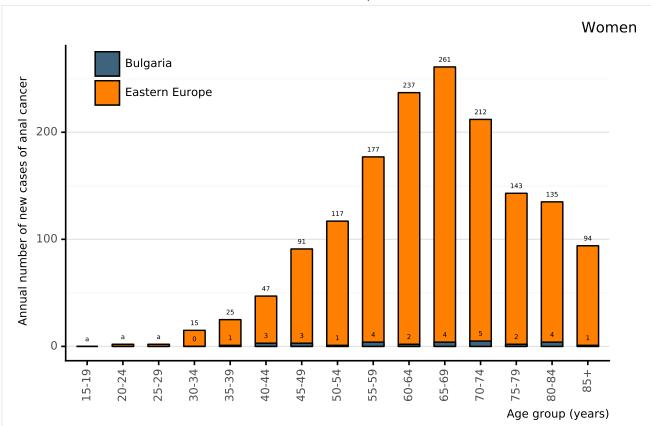


# Figure 77: Annual number of new cases of anal cancer among men by age group in Bulgaria (estimates for 2020)

#### Data accessed on 27 Jan 2021

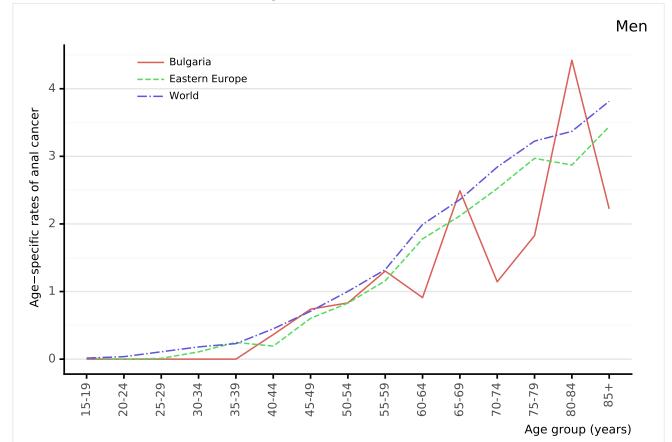
For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods
<sup>a</sup> 0 cases for Bulgaria and 1 cases for Eastern Europe in the 15-19 age group. 0 cases for Bulgaria and 0 cases for Eastern Europe in the 20-24 age group. 0 cases for Bulgaria and 1 cases

For Cases for Bulgaria and 1 cases for Eastern Europe in the 15-15 age group. O cases for Bulgaria and 0 cases for Eastern Europe in the 25-24 age group. O cases for Bulgaria and 1 cases for Eastern Europe in the 25-24 age group. O cases for Bulgaria and 1 cases for Eastern Europe in the 25-24 age group. O cases for Bulgaria and 1 cases for Eastern Europe in the 25-24 age group. O cases for Bulgaria and 1 cases for Eastern Europe in the 25-24 age group. O cases for Bulgaria and 1 cases for Eastern Europe in the 25-24 age group. O cases for Bulgaria and 1 cases for Eastern Europe in the 25-24 age group. O cases for Bulgaria and 1 cases for Eastern Europe in the 25-24 age group. O cases for Bulgaria and 1 cases for Eastern Europe in the 25-24 age group. O cases for Bulgaria and 1 cases for Eastern Europe in the 25-24 age group. O cases for Bulgaria and 1 cases for Eastern Europe in the 25-24 age group. O cases for Bulgaria and 1 cases for Eastern Europe in the 25-24 age group. O cases for Eastern Europe in the 25



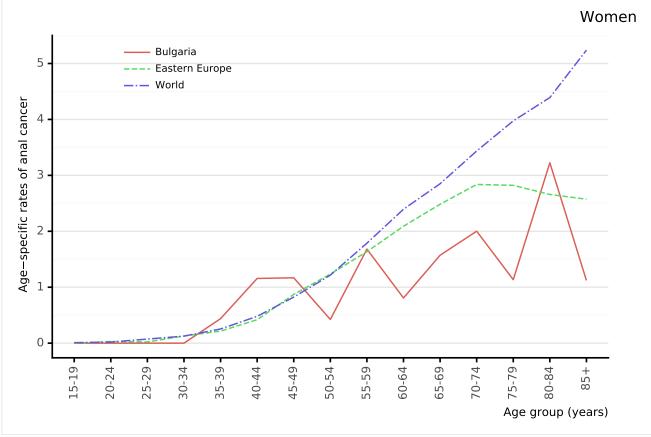
# Figure 78: Annual number of new cases of anal cancer among women by age group in Bulgaria (estimates for 2020)

Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> 0 cases for Bulgaria and 0 cases for Eastern Europe in the 15-19 age group. 0 cases for Bulgaria and 2 cases for Eastern Europe in the 20-24 age group. 0 cases for Bulgaria and 2 cases for Eastern Europe in the 25-29 age group.



# Figure 79: Comparison of age-specific anal cancer incidence rates among men by age in Bulgaria, within the region, and the rest of world

Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 men per year. <u>Data Sources:</u> Ferlay J. Ervik M, Lam F, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2020). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer. Available from: https://gco.iarc.fr/today, accessed [27 January 2021].



# Figure 80: Comparison of age-specific anal cancer incidence rates among women by age in Bulgaria, within the region, and the rest of world

#### Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 women per year.

# 9.1.3 Vulva cancer incidence in Bulgaria across Eastern Europe

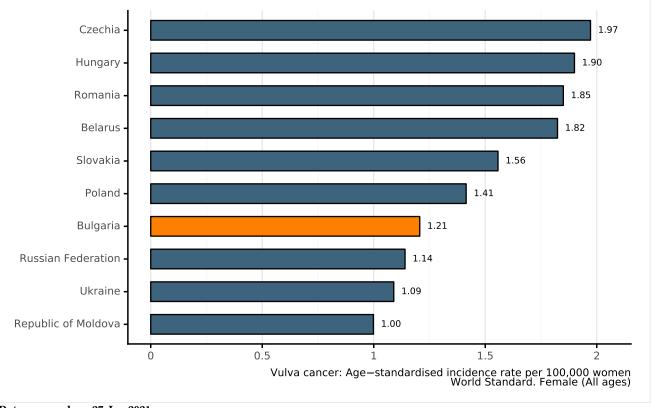
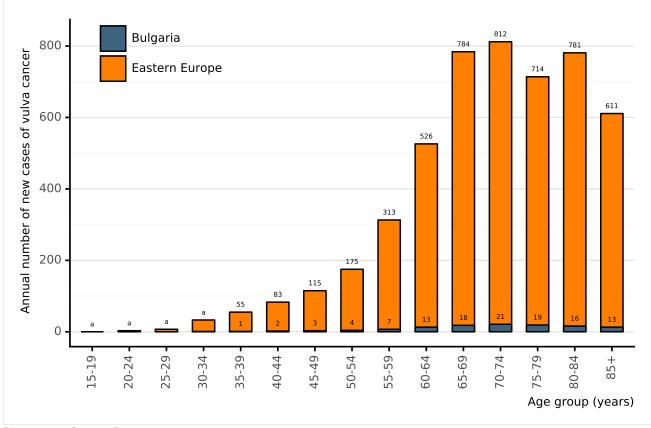


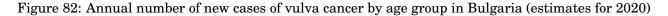
Figure 81: Age-standardised incidence rates of vulva cancer of Bulgaria (estimates for 2020)

#### Data accessed on 27 Jan 2021

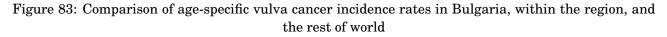
For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 women per year.

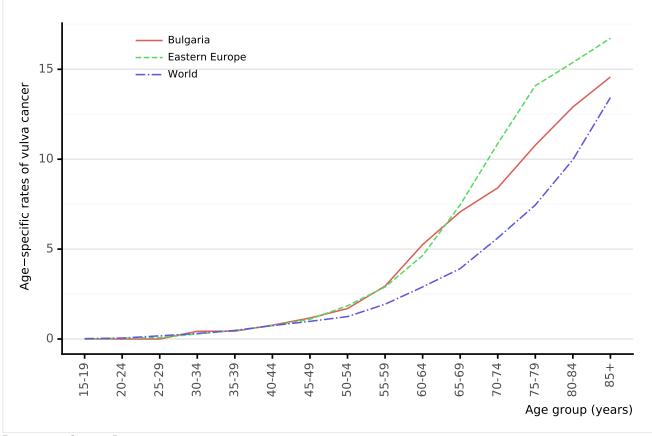
Data Sources:





Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> 0 cases for Bulgaria and 0 cases for Eastern Europe in the 15-19 age group. 0 cases for Bulgaria and 3 cases for Eastern Europe in the 20-24 age group. 0 cases for Bulgaria and 7 cases for Eastern Europe in the 25-29 age group. 1 cases for Bulgaria and 33 cases for Eastern Europe in the 30-34 age group.





#### Data accessed on 27 Jan 2021

Data accessed on 2/Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods a Rates per 100,000 women per year. Data Sources: Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2020). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer. Available from: https://gco.iarc.fr/today, accessed [27 January 2021].

## 9.1.4 Vaginal cancer incidence in Bulgaria across Eastern Europe

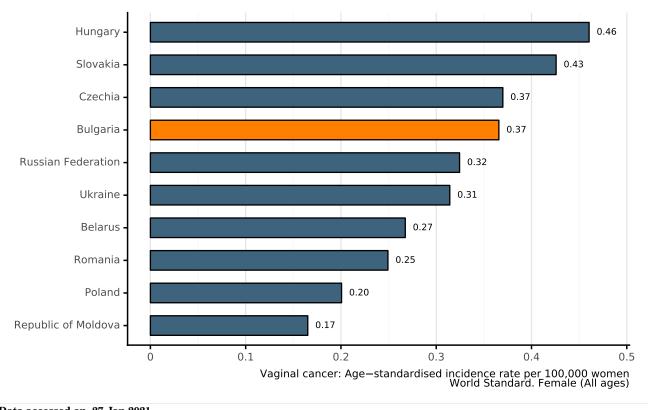
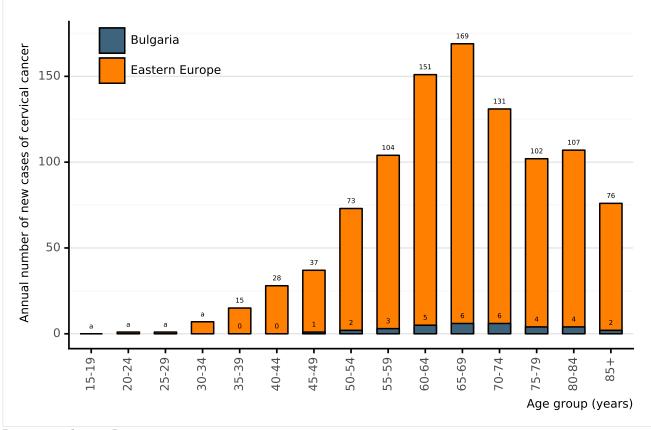


Figure 84: Age-standardised incidence rates of vaginal cancer of Bulgaria (estimates for 2020)

#### Data accessed on 27 Jan 2021

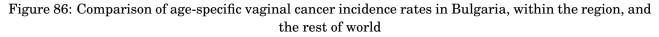
For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 women per year.

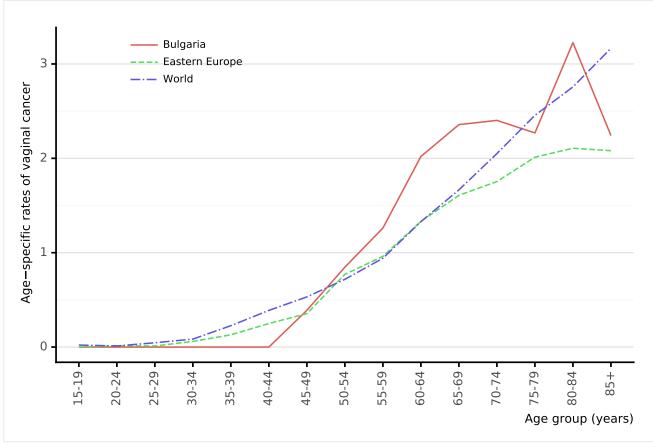
Data Sources:



### Figure 85: Annual number of new cases of cervical cancer by age group in Bulgaria (estimates for 2020)

Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> 0 cases for Bulgaria and 0 cases for Eastern Europe in the 15-19 age group. 0 cases for Bulgaria and 1 cases for Eastern Europe in the 20-24 age group. 0 cases for Bulgaria and 1 cases for Eastern Europe in the 25-29 age group. 0 cases for Bulgaria and 7 cases for Eastern Europe in the 30-34 age group.





Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 women per year. <u>Data Sources</u>: Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2020). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer. Available from: https://gco.iarc.fr/today, accessed [27 January 2021].

## 9.1.5 Penile cancer incidence in Bulgaria across Eastern Europe

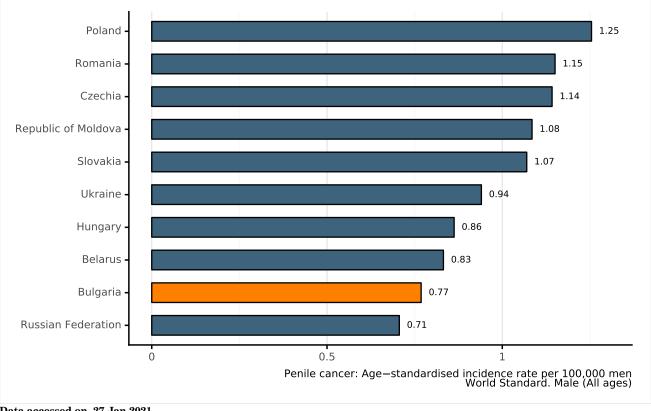
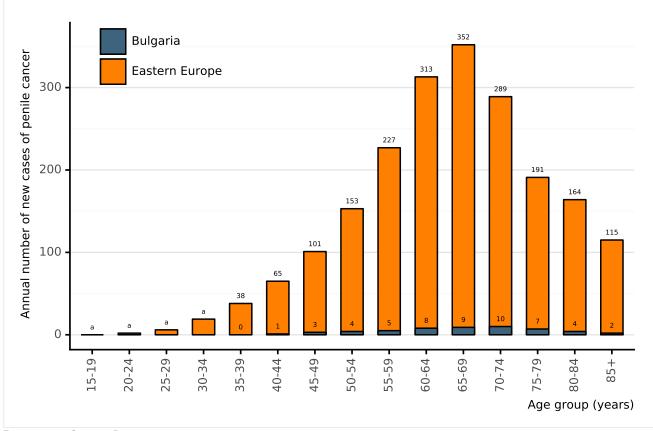


Figure 87: Age-standardised incidence rates of penile cancer of Bulgaria (estimates for 2020)

### Data accessed on 27 Jan 2021

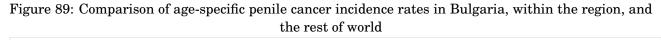
For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 men per year.

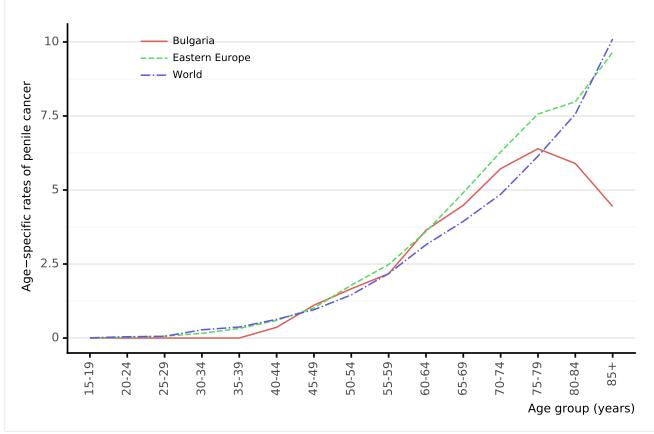
Data Sources:



### Figure 88: Annual number of new cases of penile cancer by age group in Bulgaria (estimates for 2020)

Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> 0 cases for Bulgaria and 0 cases for Eastern Europe in the 15-19 age group. 0 cases for Bulgaria and 2 cases for Eastern Europe in the 20-24 age group. 0 cases for Bulgaria and 6 cases for Eastern Europe in the 25-29 age group. 0 cases for Bulgaria and 19 cases for Eastern Europe in the 30-34 age group.





Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 men per year. Deta Sources

### 9.1.6 Oropharyngeal cancer incidence in Bulgaria across Eastern Europe

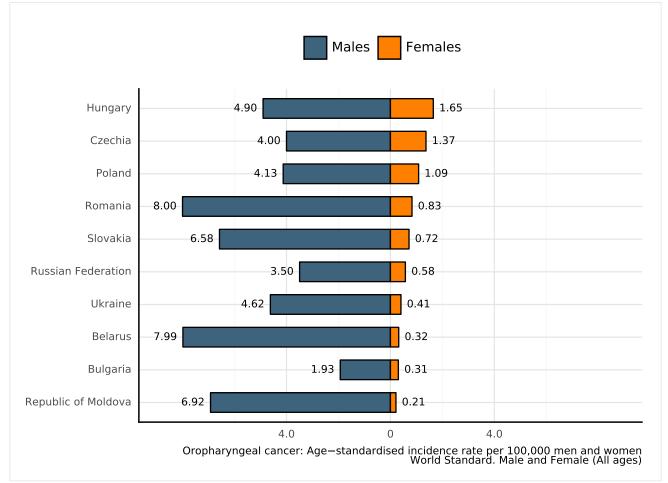
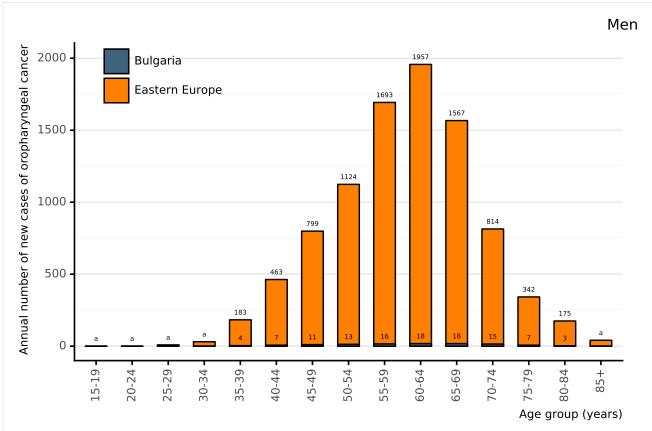


Figure 90: Age-standardised incidence rates of oropharyngeal cancer of Bulgaria (estimates for 2020)

Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods a Rates per 100,000 men per year.

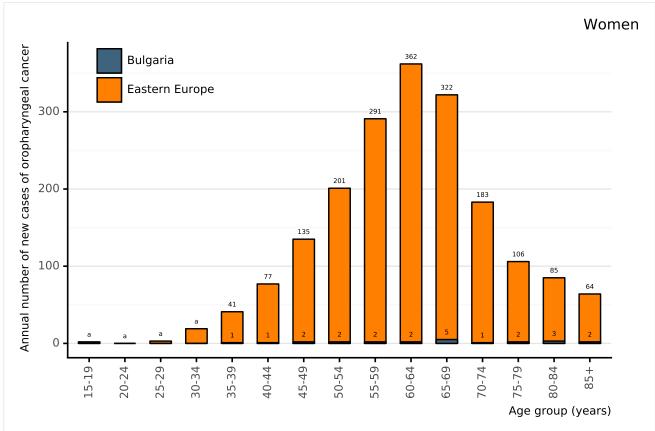
b Rates per 100,000 women per year.



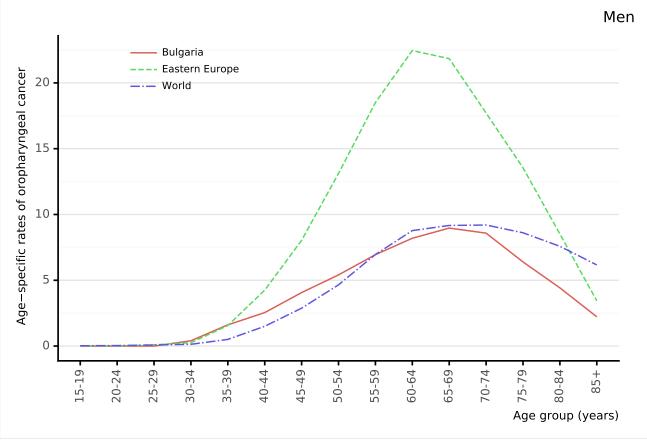
## Figure 91: Annual number of new cases of oropharyngeal cancer among men by age group in Bulgaria (estimates for 2020)

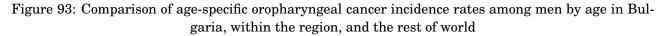
Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> 0 cases for Bulgaria and 1 cases for Eastern Europe in the 15-19 age group. 0 cases for Bulgaria and 1 cases for Eastern Europe in the 20-24 age group. 0 cases for Bulgaria and 9 cases for Eastern Europe in the 25-29 age group. 1 cases for Bulgaria and 31 cases for Eastern Europe in the 30-34 age group. 1 cases for Bulgaria and 41 cases for Eastern Europe in the 85+ age

for Eastern Europe in the 20-20 age group. I cases for Dargana and of c



Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> 0 cases for Bulgaria and 2 cases for Eastern Europe in the 15-19 age group. 0 cases for Bulgaria and 0 cases for Eastern Europe in the 20-24 age group. 0 cases for Bulgaria and 3 cases for Eastern Europe in the 25-29 age group. 0 cases for Bulgaria and 19 cases for Eastern Europe in the 30-34 age group.





### Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 men per year.

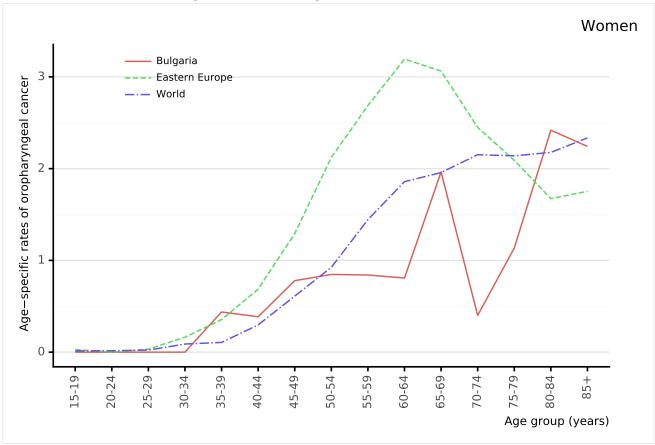


Figure 94: Comparison of age-specific oropharyngeal cancer incidence rates among women by age in Bulgaria, within the region, and the rest of world

#### Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 women per year.

## 9.1.7 Oral cavity cancer incidence in Bulgaria across Eastern Europe

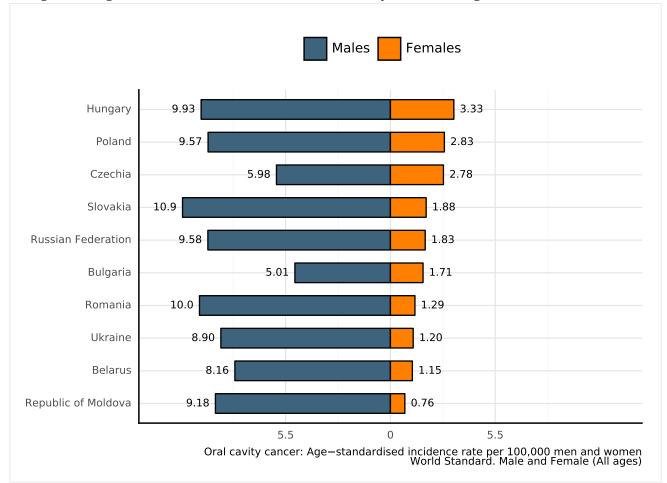
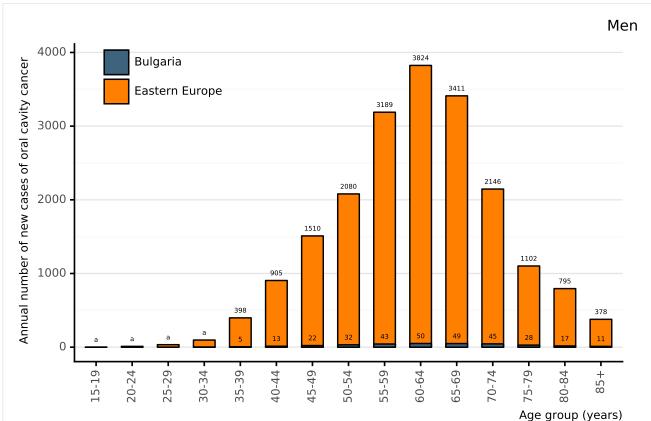


Figure 95: Age-standardised incidence rates of oral cavity cancer of Bulgaria (estimates for 2020)

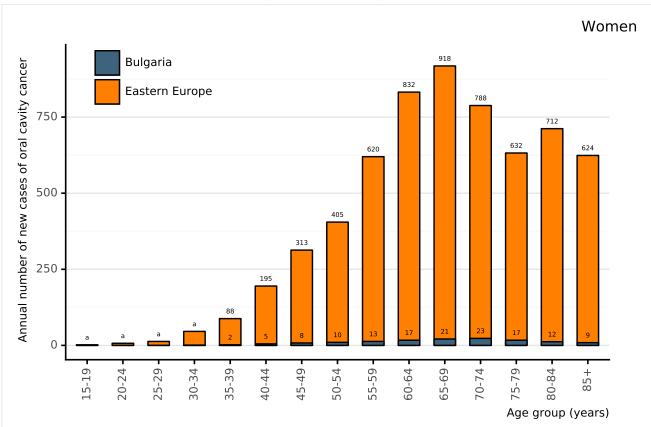
Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 men per year.

b Rates per 100,000 women per year.



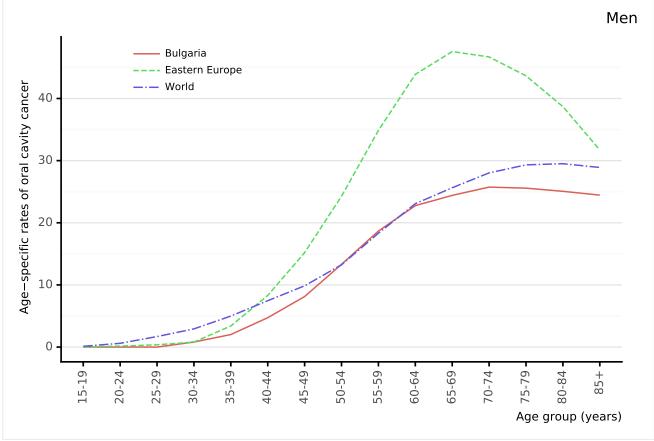
## Figure 96: Annual number of new cases of oral cavity cancer among men by age group in Bulgaria (estimates for 2020)

Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> 0 cases for Bulgaria and 1 cases for Eastern Europe in the 15-19 age group. 0 cases for Bulgaria and 11 cases for Eastern Europe in the 20-24 age group. 0 cases for Bulgaria and 34 cases for Eastern Europe in the 25-29 age group. 2 cases for Bulgaria and 97 cases for Eastern Europe in the 30-34 age group.



## Figure 97: Annual number of new cases of oral cavity cancer among women by age group in Bulgaria (estimates for 2020)

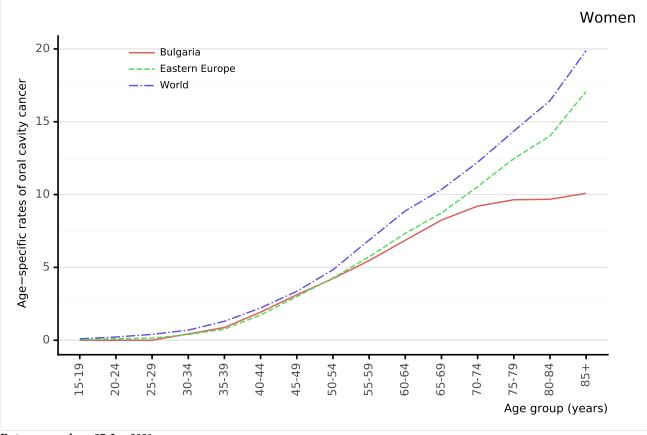
Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> 0 cases for Bulgaria and 2 cases for Eastern Europe in the 15-19 age group. 0 cases for Bulgaria and 7 cases for Eastern Europe in the 20-24 age group. 0 cases for Bulgaria and 13 cases for Eastern Europe in the 25-29 age group. 1 cases for Bulgaria and 46 cases for Eastern Europe in the 30-34 age group.



## Figure 98: Comparison of age-specific oral cavity cancer incidence rates among men by age in Bulgaria, within the region, and the rest of world

### Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods a Rates per 100,000 men per year. <u>Data Sources</u>: Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2020). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer. Available from: https://gco.iarc.fr/today, accessed [27 January 2021].

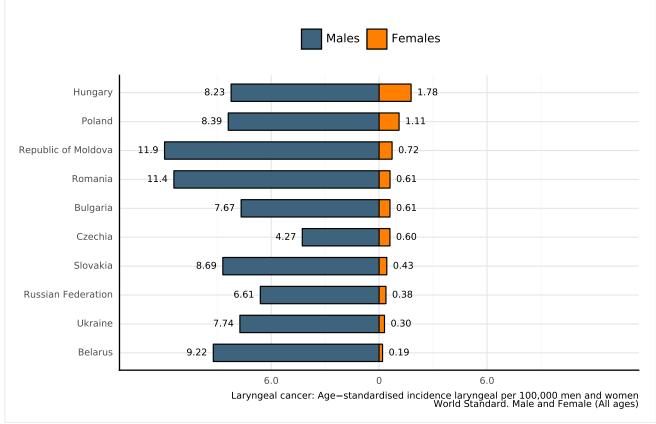


## Figure 99: Comparison of age-specific oral cavity cancer incidence rates among women by age in Bulgaria, within the region, and the rest of world

#### Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods a Rates per 100,000 women per year.

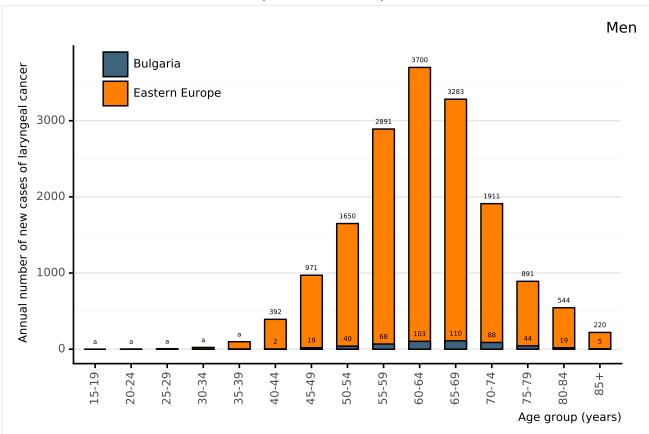
# 9.1.8 Laryngeal cancer incidence in Bulgaria across Eastern Europe Figure 100: Age-standardised incidence rates of laryngeal cancer of Bulgaria (estimates for 2020)



#### Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 men per year.

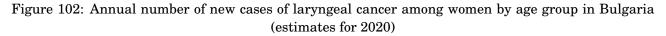
<sup>b</sup> Rates per 100,000 women per year.

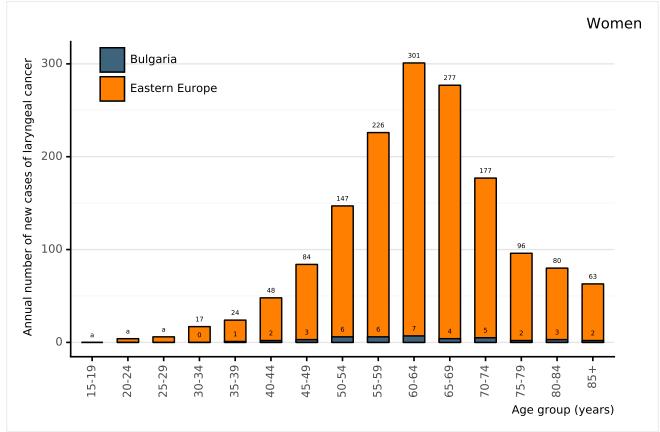


## Figure 101: Annual number of new cases of laryngeal cancer among men by age group in Bulgaria (estimates for 2020)

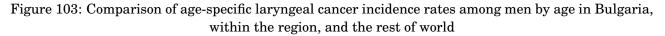
Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> 0 cases for Bulgaria and 0 cases for Eastern Europe in the 15-19 age group. 0 cases for Bulgaria and 1 cases for Eastern Europe in the 20-24 age group. 0 cases for Bulgaria and 5 cases for Eastern Europe in the 25-29 age group. 1 cases for Bulgaria and 23 cases for Eastern Europe in the 30-34 age group. 2 cases for Bulgaria and 98 cases for Eastern Europe in the 35-39

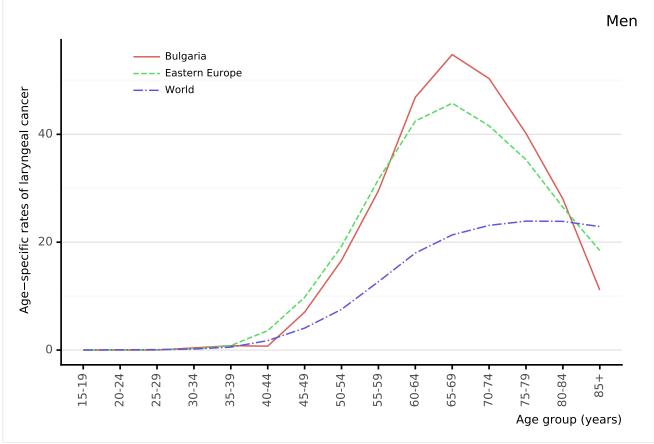
for Eastern Europe in the 20-20 age group. I tases for Dargana and 20 tases for Eastern Europe in the 21-20 ge group. Data Sources: Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2020). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer. Available from: https://gco.iarc.fr/today, accessed [27 January 2021].





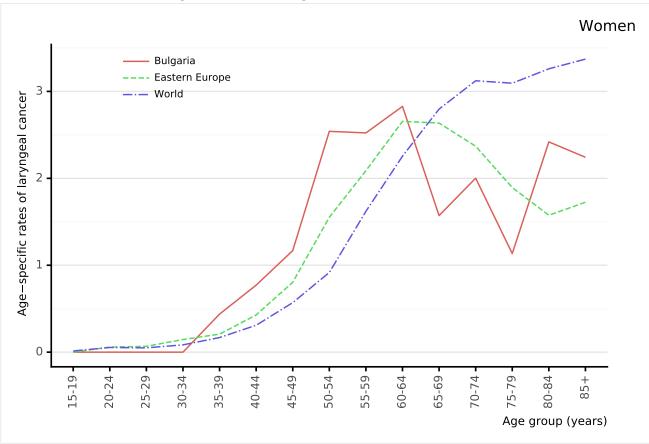
Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> 0 cases for Bulgaria and 0 cases for Eastern Europe in the 15-19 age group. 0 cases for Bulgaria and 4 cases for Eastern Europe in the 20-24 age group. 0 cases for Bulgaria and 6 cases for Eastern Europe in the 25-29 age group.





### Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods a Rates per 100,000 men per year. <u>Data Sources</u>: Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2020). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer. Available from: https://gco.iarc.fr/today, accessed [27 January 2021].



## Figure 104: Comparison of age-specific laryngeal cancer incidence rates among women by age in Bulgaria, within the region, and the rest of world

#### Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 women per year.

## 9.2 Mortality

## 9.2.1 Cervical cancer mortality in Bulgaria across Eastern Europe

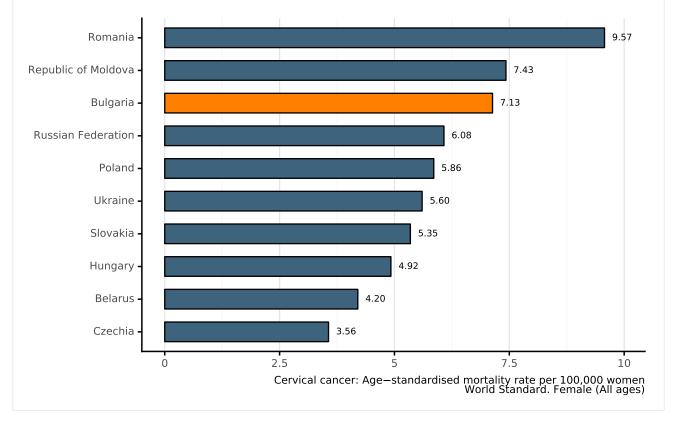
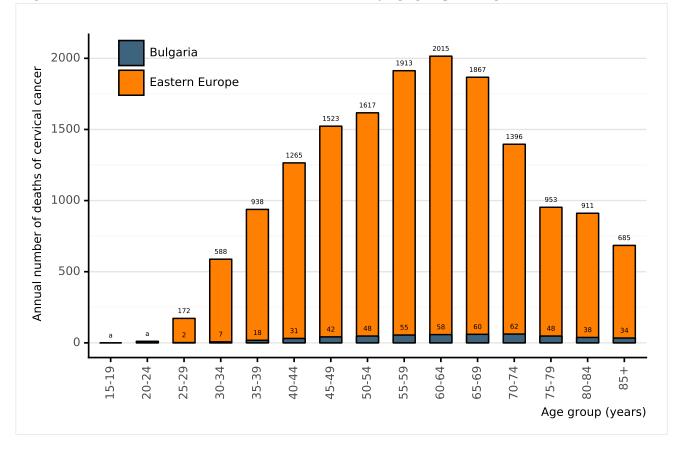


Figure 105: Age-standardised mortality rates of cervical cancer of Bulgaria (estimates for 2020)

#### Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 women per year.

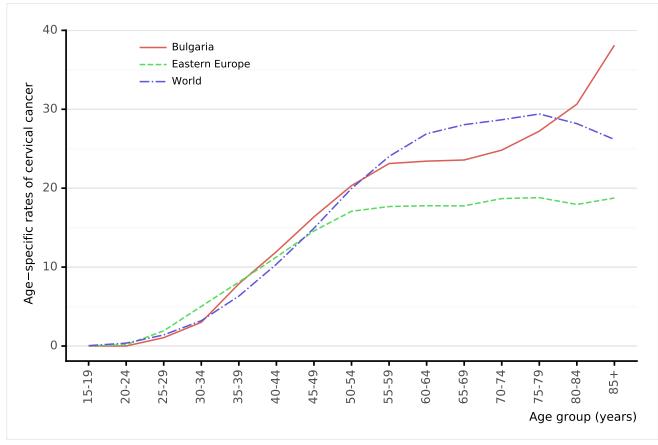
Data Sources:



### Figure 106: Annual number of deaths of cervical cancer by age group in Bulgaria (estimates for 2020)

### Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods
<sup>a</sup> 0 cases for Bulgaria and 0 cases for Eastern Europe in the 15-19 age group. 0 cases for Bulgaria and 11 cases for Eastern Europe in the 20-24 age group.

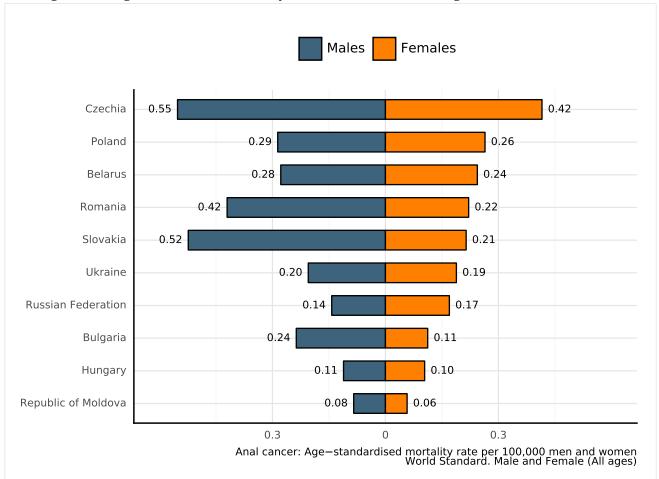


## Figure 107: Comparison of age-specific cervical cancer mortality rates in Bulgaria, within the region, and the rest of world

#### Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 women per year.

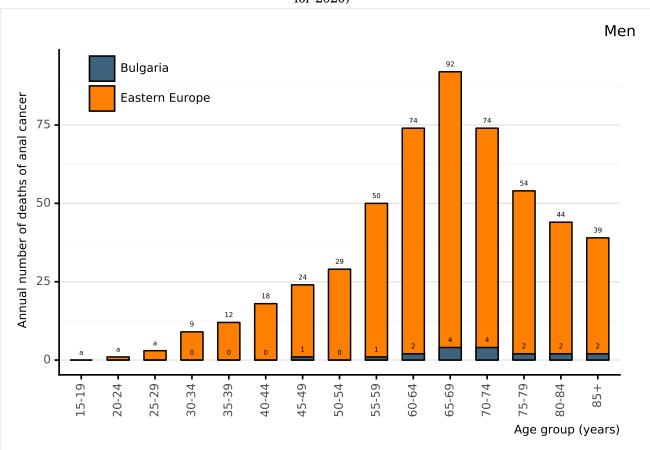
## 9.2.2 Anal cancer mortality in Bulgaria across Eastern Europe



### Figure 108: Age-standardised mortality rates of anal cancer of Bulgaria (estimates for 2020)

Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 men per year.

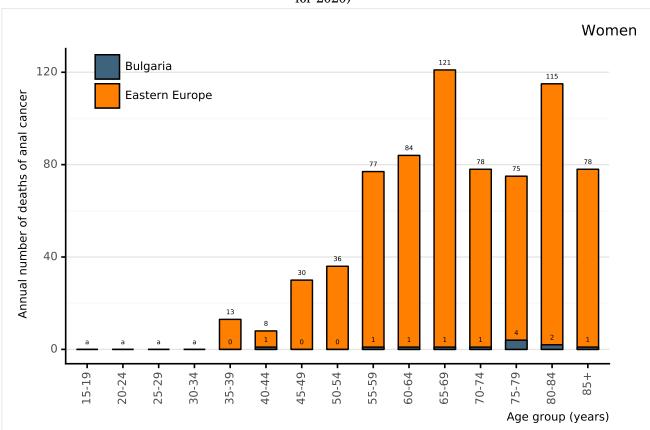
b Rates per 100,000 women per year.



## Figure 109: Annual number of deaths of anal cancer among men by age group in Bulgaria (estimates for 2020)

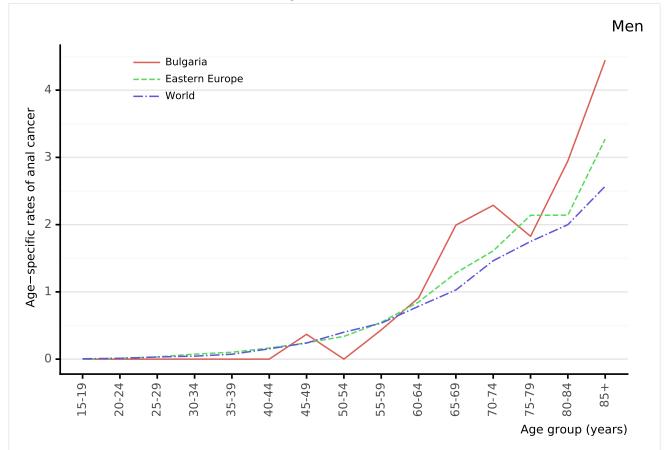
#### Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods
<sup>a</sup> 0 cases for Bulgaria and 0 cases for Eastern Europe in the 15-19 age group. 0 cases for Bulgaria and 1 cases for Eastern Europe in the 20-24 age group. 0 cases for Bulgaria and 3 cases for Eastern Europe in the 25-29 age group.



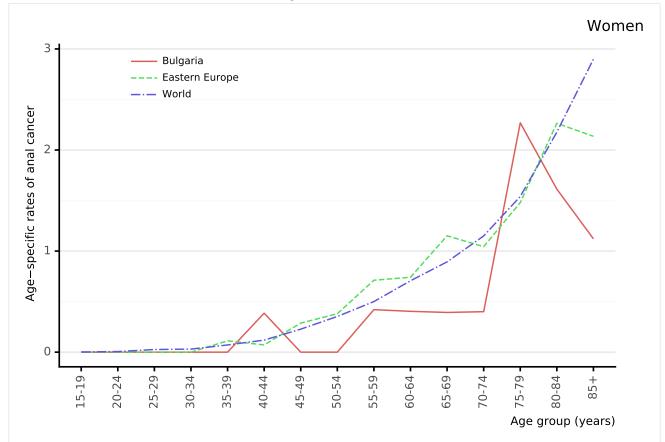
## Figure 110: Annual number of deaths of anal cancer among women by age group in Bulgaria (estimates for 2020)

Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> 0 cases for Bulgaria and 0 cases for Eastern Europe in the 15-19 age group. 0 cases for Bulgaria and 0 cases for Eastern Europe in the 20-24 age group. 0 cases for Bulgaria and 0 cases for Eastern Europe in the 25-29 age group. 0 cases for Bulgaria and 0 cases for Eastern Europe in the 25-29 age group. 0 cases for Bulgaria and 0 cases for Eastern Europe in the 30-34 age group.



## Figure 111: Comparison of age-specific anal cancer mortality rates among men by age in Bulgaria, within the region, and the rest of world

Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 men per year. <u>Data Sources:</u> Ferlay J. Ervik M, Lam F, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2020). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer. Available from: https://gco.iarc.fr/today, accessed [27 January 2021].



## Figure 112: Comparison of age-specific anal cancer mortality rates among women by age in Bulgaria, within the region, and the rest of world

#### Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 women per year.

### 9.2.3 Vulva cancer mortality in Bulgaria across Eastern Europe

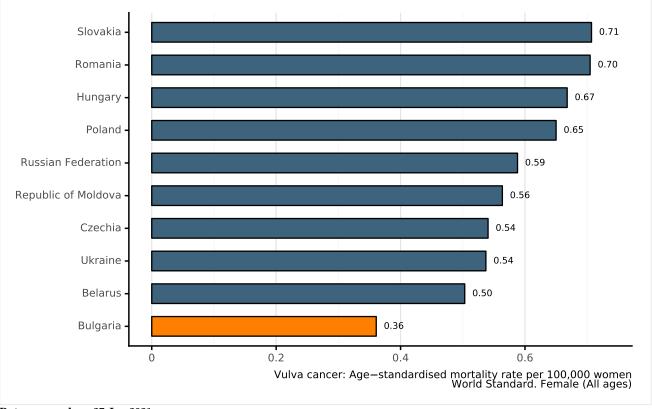
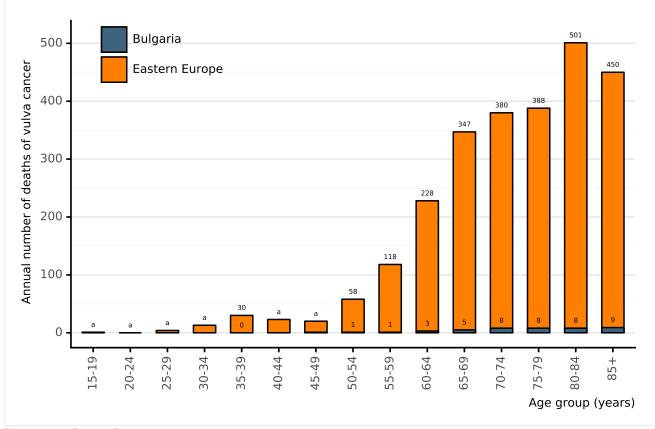


Figure 113: Age-standardised mortality rates of vulva cancer of Bulgaria (estimates for 2020)

Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 women per year.

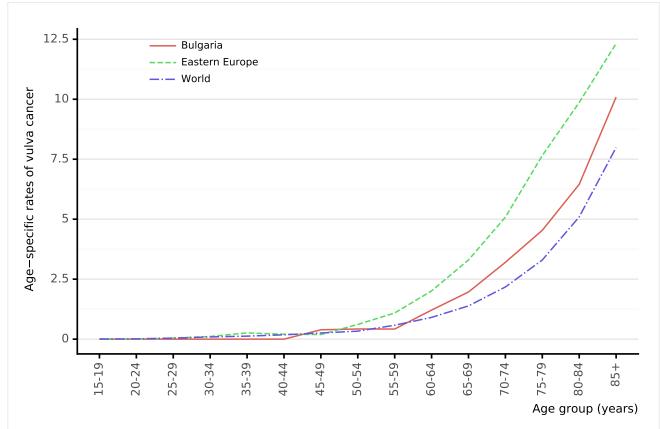
Data Sources:



### Figure 114: Annual number of deaths of vulva cancer by age group in Bulgaria (estimates for 2020)

### Data accessed on 27 Jan 2021

Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods @ 0 cases for Bulgaria and 1 cases for Eastern Europe in the 15-19 age group. 0 cases for Bulgaria and 0 cases for Eastern Europe in the 20-24 age group. 0 cases for Bulgaria and 4 cases for Eastern Europe in the 25-29 age group. 0 cases for Bulgaria and 13 cases for Eastern Europe in the 30-34 age group. 0 cases for Bulgaria and 23 cases for Eastern Europe in the 40-44 age group. 1 cases for Bulgaria and 20 cases for Eastern Europe in the 45-49 age group. Data Sources: Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2020). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer. Available from: https://gco.iarc.fr/today, accessed [27 January 2021].



## Figure 115: Comparison of age-specific vulva cancer mortality rates in Bulgaria, within the region, and the rest of world

Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 women per year. <u>Data Sources:</u> Ferlay J. Ervik M, Lam F, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2020). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer. Available from: https://gco.iarc.fr/today, accessed [27 January 2021].

### 9.2.4 Vaginal cancer mortality in Bulgaria across Eastern Europe

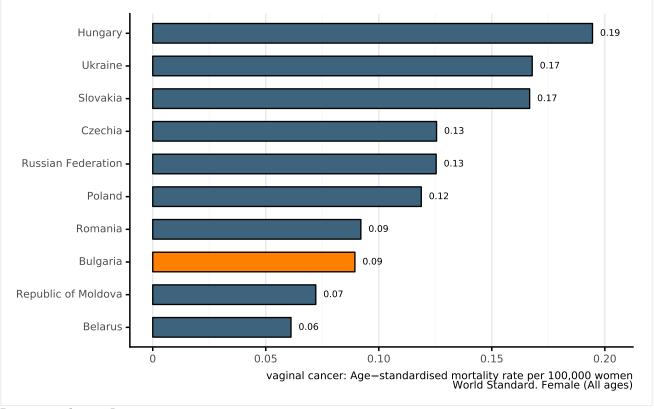
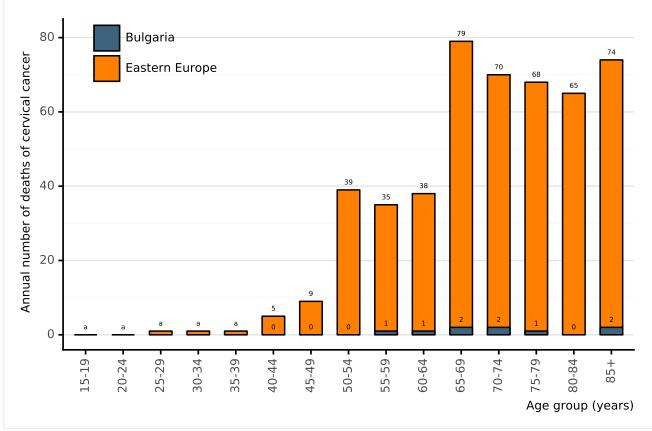


Figure 116: Age-standardised mortality rates of vaginal cancer of Bulgaria (estimates for 2020)

### Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 women per year.

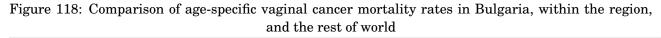
Data Sources:

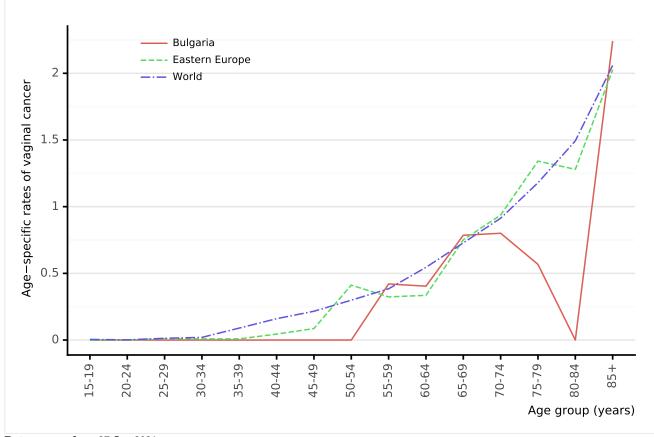


### Figure 117: Annual number of deaths of cervical cancer by age group in Bulgaria (estimates for 2020)

Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> 0 cases for Bulgaria and 0 cases for Eastern Europe in the 15-19 age group. 0 cases for Bulgaria and 0 cases for Eastern Europe in the 20-24 age group. 0 cases for Bulgaria and 1 cases for Eastern Europe in the 25-29 age group. 0 cases for Bulgaria and 1 cases for Eastern Europe in the 30-34 age group. 0 cases for Bulgaria and 1 cases for Eastern Europe in the 35-39 age

for Eastern Europe in the 20-20 age group. O cases for Dargania and Cases in Dargania an





Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 women per year. Deto Source:

### 9.2.5 Penile cancer mortality in Bulgaria across Eastern Europe

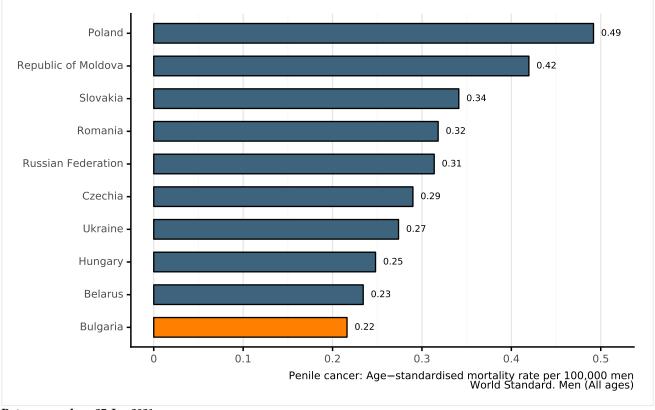
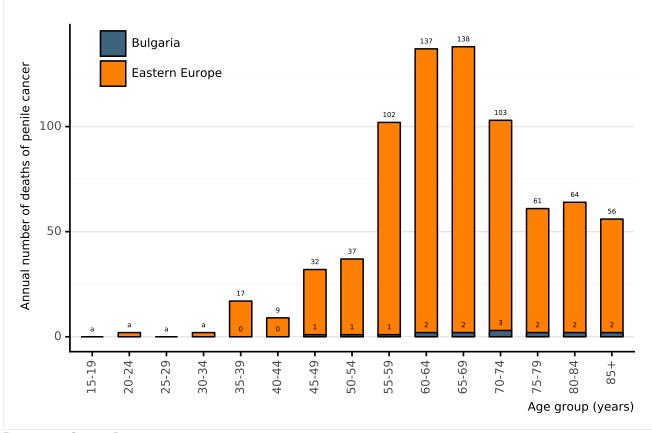


Figure 119: Age-standardised mortality rates of penile cancer of Bulgaria (estimates for 2020)

Data accessed on 27 Jan 2021

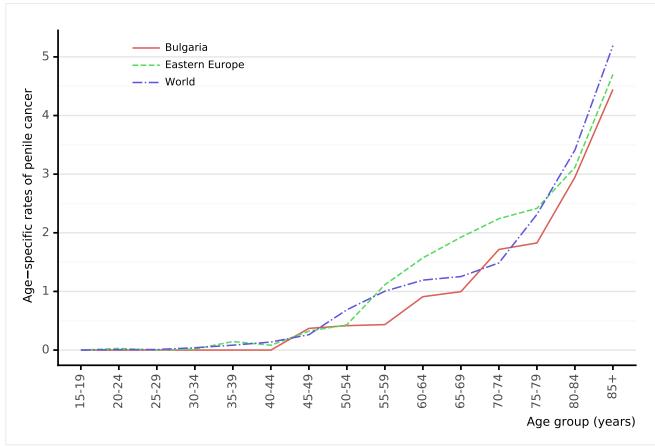
For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 men per year.

Data Sources:



#### Figure 120: Annual number of new deaths of penile cancer by age group in Bulgaria (estimates for 2020)

Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> 0 cases for Bulgaria and 0 cases for Eastern Europe in the 15-19 age group. 0 cases for Bulgaria and 2 cases for Eastern Europe in the 20-24 age group. 0 cases for Bulgaria and 0 cases for Eastern Europe in the 25-29 age group. 0 cases for Bulgaria and 2 cases for Eastern Europe in the 20-24 age group. 0 cases for Bulgaria and 0 cases for Eastern Europe in the 25-29 age group. 0 cases for Bulgaria and 2 cases for Eastern Europe in the 30-34 age group.



### Figure 121: Comparison of age-specific penile cancer mortality rates in Bulgaria, within the region, and the rest of world

Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 men per year. <u>Data Sources:</u> Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2020). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer. Available from: https://gco.iarc.fr/today, accessed [27 January 2021].

#### Oropharyngeal cancer mortality in Bulgaria across Eastern Europe 9.2.6

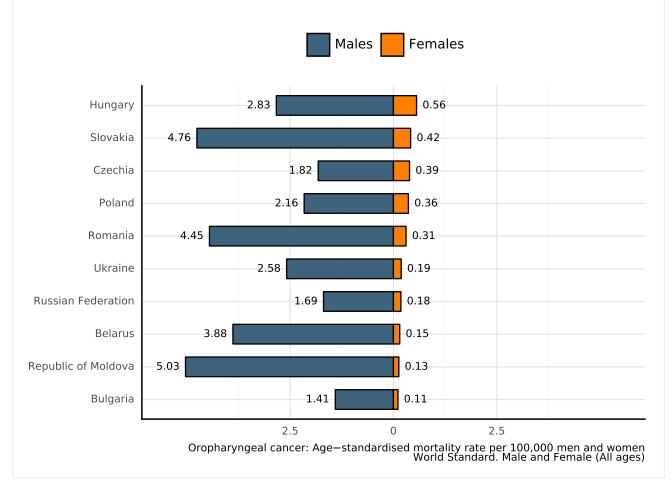
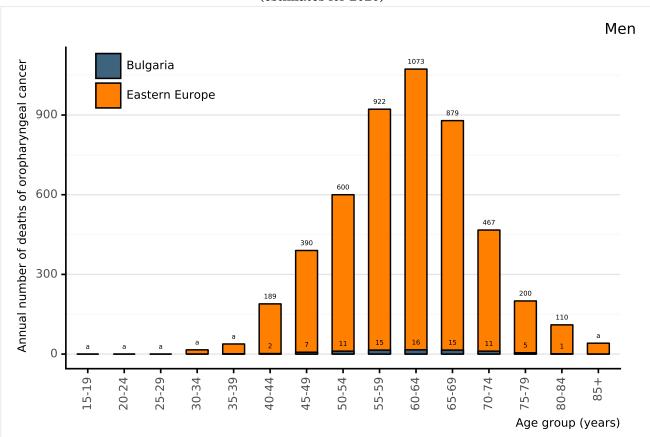


Figure 122: Age-standardised mortality rates of oropharyngeal cancer of Bulgaria (estimates for 2020)

Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 men per year.

b Rates per 100,000 women per year.



#### Figure 123: Annual number of deaths of oropharyngeal cancer among men by age group in Bulgaria (estimates for 2020)

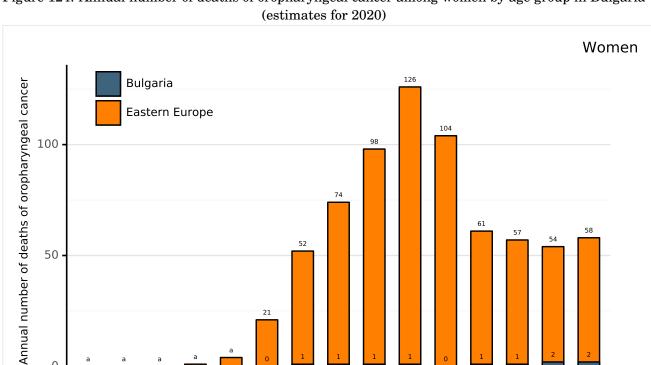
#### Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods a 0 cases for Bulgaria and 0 cases for Eastern Europe in the 15-19 age group. 0 cases for Bulgaria and 0 cases for Eastern Europe in the 20-24 age group. 0 cases for Bulgaria and 0 cases for Eastern Europe in the 25-29 age group. 0 cases for Bulgaria and 16 cases for Eastern Europe in the 25-29 age group. 0 cases for Bulgaria and 16 cases for Eastern Europe in the 30-34 age group. 1 cases for Bulgaria and 38 cases for Eastern Europe in the 35-39 age group. 0 cases for Eastern Europe in the 85+ age group.

100

50

0



74

52

45-49.

21

40-44

98

55-59.

60-64

65-69

70-74

61

57

75-79.

54

80-84

Age group (years)

# Figure 124: Annual number of deaths of oropharyngeal cancer among women by age group in Bulgaria

15-19.

20-24

25-29.

а

30-34

35-39

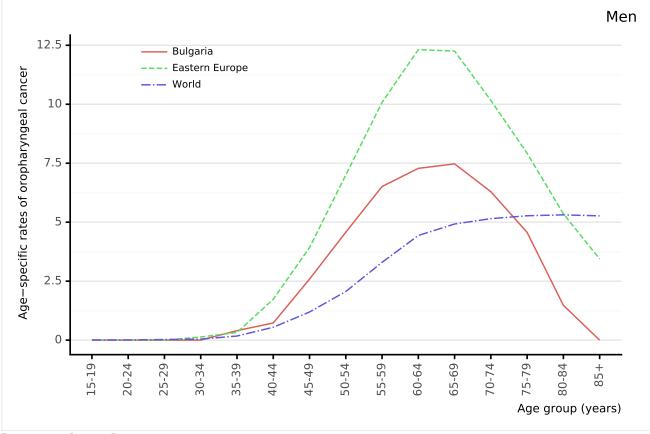
Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> 0 cases for Bulgaria and 0 cases for Eastern Europe in the 15-19 age group. 0 cases for Bulgaria and 0 cases for Eastern Europe in the 20-24 age group. 0 cases for Bulgaria and 0 cases for Eastern Europe in the 25-29 age group. 0 cases for Bulgaria and 1 cases for Eastern Europe in the 30-34 age group. 0 cases for Bulgaria and 4 cases for Eastern Europe in the 35-39 age

50-54

for Eastern Europe in Size 20 20 and 20 20 an

58

85+

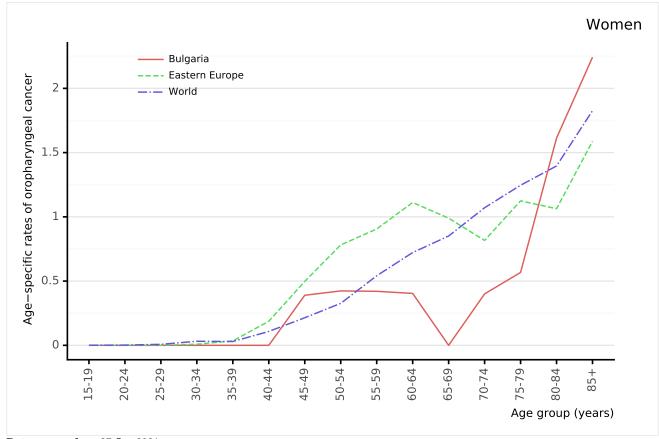


### Figure 125: Comparison of age-specific oropharyngeal cancer mortality rates among men by age in Bulgaria, within the region, and the rest of world

Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 men per year.

Data Sources:



### Figure 126: Comparison of age-specific oropharyngeal cancer mortality rates among women by age in Bulgaria, within the region, and the rest of world

Data accessed on 27 Jan 2021

Data accessed on 2/ Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 women per year. <u>Data Sources:</u> Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2020). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer. Available from: https://gco.iarc.fr/today, accessed [27 January 2021].

#### 9.2.7 Oral cavity cancer mortality in Bulgaria across Eastern Europe

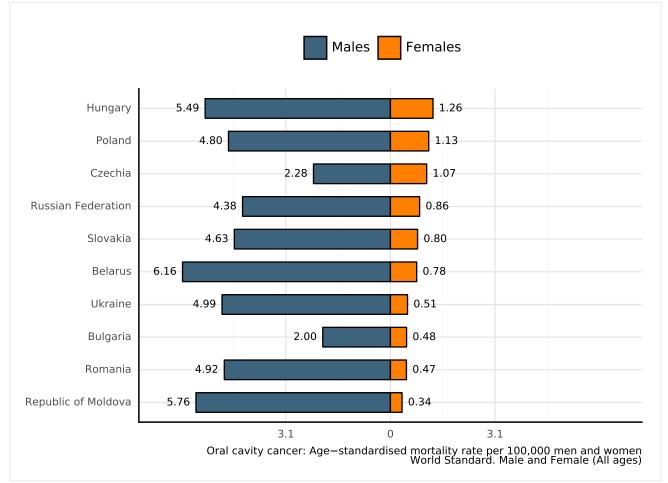
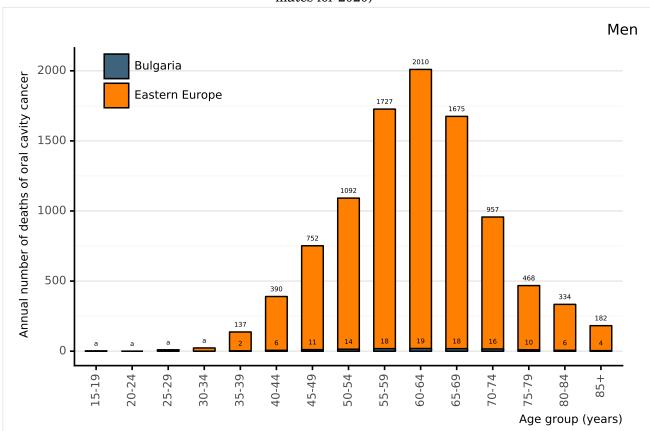


Figure 127: Age-standardised mortality rates of oral cavity cancer of Bulgaria (estimates for 2020)

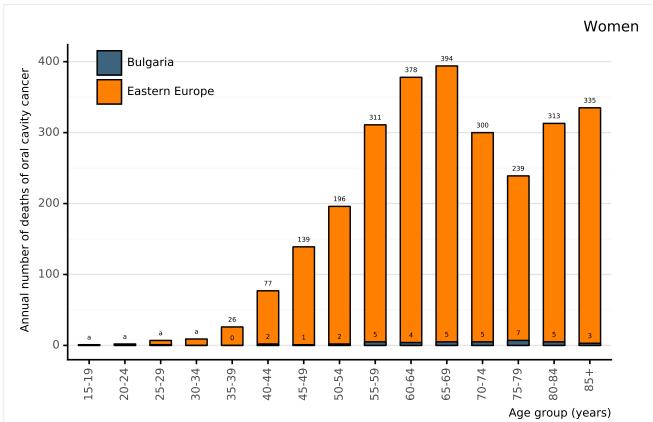
Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 men per year.

b Rates per 100,000 women per year.



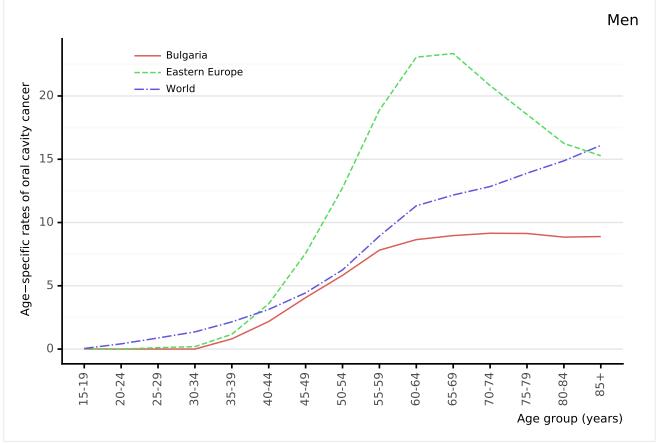
### Figure 128: Annual number of deaths of oral cavity cancer among men by age group in Bulgaria (estimates for 2020)

Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> 0 cases for Bulgaria and 2 cases for Eastern Europe in the 15-19 age group. 0 cases for Bulgaria and 0 cases for Eastern Europe in the 20-24 age group. 0 cases for Bulgaria and 10 cases for Eastern Europe in the 25-29 age group. 0 cases for Bulgaria and 23 cases for Eastern Europe in the 30-34 age group.



### Figure 129: Annual number of deaths of oral cavity cancer among women by age group in Bulgaria (estimates for 2020)

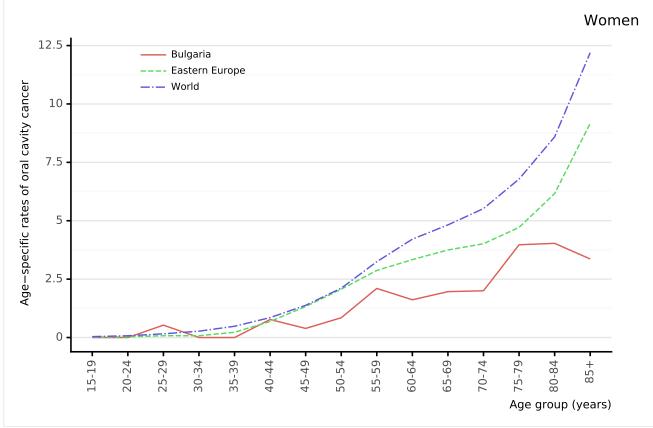
Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> 0 cases for Bulgaria and 1 cases for Eastern Europe in the 15-19 age group. 0 cases for Bulgaria and 2 cases for Eastern Europe in the 20-24 age group. 1 cases for Bulgaria and 7 cases for Eastern Europe in the 25-29 age group. 0 cases for Bulgaria and 9 cases for Eastern Europe in the 30-34 age group.



### Figure 130: Comparison of age-specific oral cavity cancer mortality rates among men by age in Bulgaria, within the region, and the rest of world

#### Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods a Rates per 100,000 men per year. <u>Data Sources</u>: Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2020). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer. Available from: https://gco.iarc.fr/today, accessed [27 January 2021].



### Figure 131: Comparison of age-specific oral cavity cancer mortality rates among women by age in Bulgaria, within the region, and the rest of world

Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods a Rates per 100,000 women per year.

#### 9.2.8 Laryngeal cancer mortality in Bulgaria across Eastern Europe

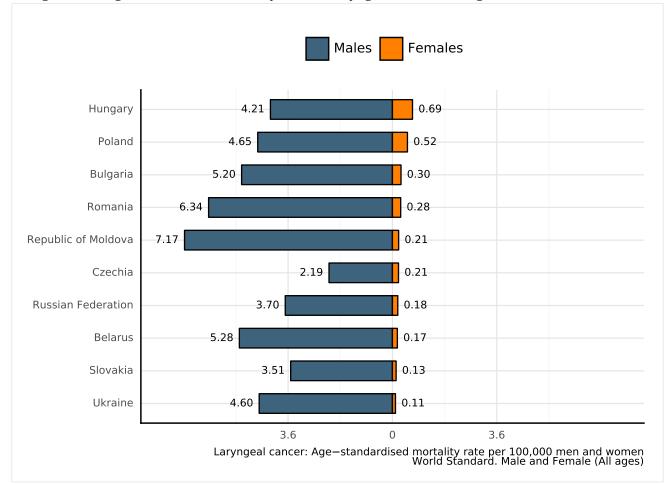
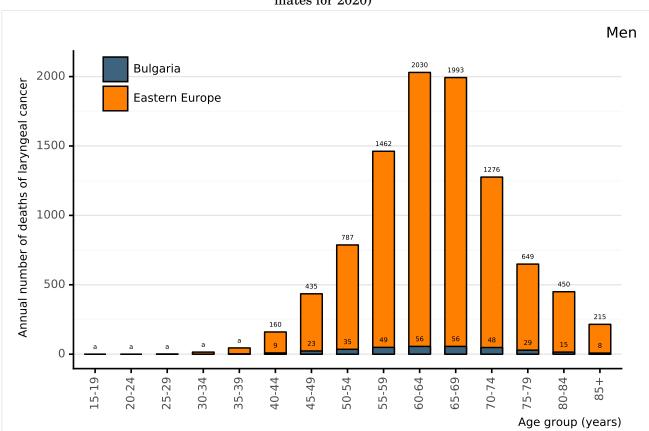


Figure 132: Age-standardised mortality rates of laryngeal cancer of Bulgaria (estimates for 2020)

Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 men per year.

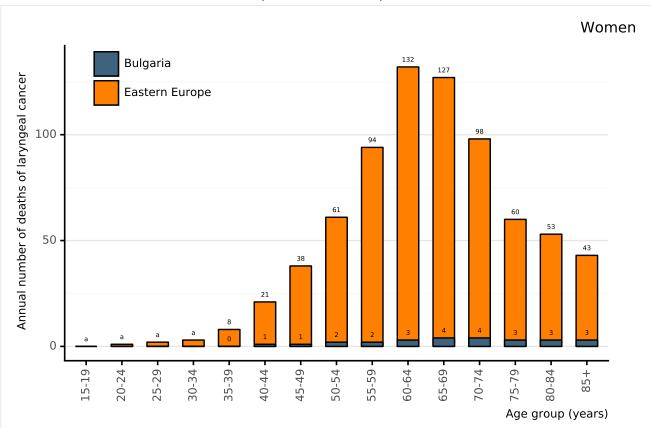
b Rates per 100,000 women per year.



### Figure 133: Annual number of deaths of laryngeal cancer among men by age group in Bulgaria (estimates for 2020)

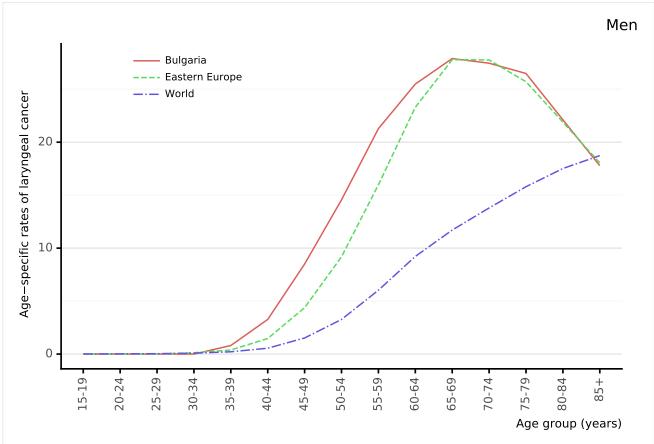
Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> 0 cases for Bulgaria and 0 cases for Eastern Europe in the 15-19 age group. 0 cases for Bulgaria and 0 cases for Eastern Europe in the 20-24 age group. 0 cases for Bulgaria and 1 cases for Eastern Europe in the 25-29 age group. 0 cases for Bulgaria and 15 cases for Eastern Europe in the 30-34 age group. 2 cases for Bulgaria and 45 cases for Eastern Europe in the 35-39

for Eastern Europe in the 20-20 age group. 0 tases for Europe in the 20-20 age group. <u>Data Sources:</u> Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2020). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer. Available from: https://gco.iarc.fr/today, accessed [27 January 2021].



### Figure 134: Annual number of deaths of laryngeal cancer among women by age group in Bulgaria (estimates for 2020)

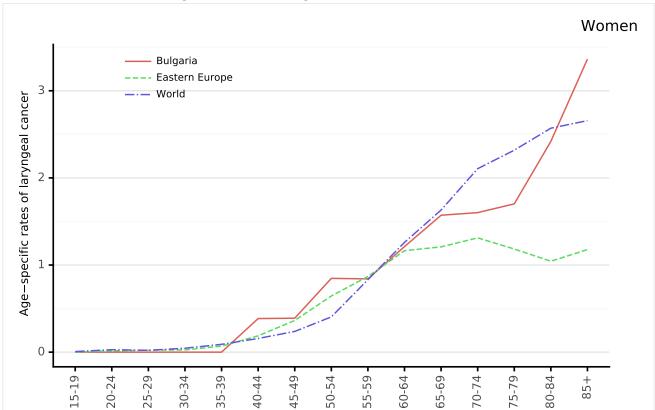
Data accessed on 27 Jan 2021 For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> 0 cases for Bulgaria and 0 cases for Eastern Europe in the 15-19 age group. 0 cases for Bulgaria and 1 cases for Eastern Europe in the 20-24 age group. 0 cases for Bulgaria and 2 cases for Eastern Europe in the 25-29 age group. 0 cases for Bulgaria and 3 cases for Eastern Europe in the 30-34 age group.



### Figure 135: Comparison of age-specific laryngeal cancer mortality rates among men by age in Bulgaria, within the region, and the rest of world

#### Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 men per year.



### Figure 136: Comparison of age-specific laryngeal cancer mortality rates among women by age in Bulgaria, within the region, and the rest of world

#### Data accessed on 27 Jan 2021

For more detailed methods of estimation please refer to http://gco.iarc.fr/today/data-sources-methods <sup>a</sup> Rates per 100,000 women per year.

30-34

35-39

Data Sources: Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2020). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer. Available from: https://gco.iarc.fr/today, accessed [27 January 2021].

50-54

55-59

60-64

62-69

70-74

75-79

80-84

Age group (years)

85+

45-49

# 10 Glossary

Table 49: Glossary		
Term	Definition	
Incidence	Incidence is the number of new cases arising in a given period in a speci- fied population. This information is collected routinely by cancer registries. It can be expressed as an absolute number of cases per year or as a rate per 100,000 persons per year (see Crude rate and ASR below). The rate provides an approximation of the average risk of developing a cancer.	
Mortality	Mortality is the number of deaths occurring in a given period in a specified population. It can be expressed as an absolute number of deaths per year or as a rate per 100,000 persons per year.	
Prevalence	The prevalence of a particular cancer can be defined as the number of per- sons in a defined population who have been diagnosed with that type of cancer, and who are still alive at the end of a given year, the survivors. Com- plete prevalence represents the number of persons alive at certain point in time who previously had a diagnosis of the disease, regardless of how long ago the diagnosis was, or if the patient is still under treatment or is con- sidered cured. Partial prevalence , which limits the number of patients to those diagnosed during a fixed time in the past, is a particularly useful measure of cancer burden. Prevalence of cancers based on cases diagnosed within one, three and five are presented as they are likely to be of rele- vance to the different stages of cancer therapy, namely, initial treatment (one year), clinical follow-up (three years) and cure (five years). Patients who are still alive five years after diagnosis are usually considered cured since the death rates of such patients are similar to those in the general population. There are exceptions, particularly breast cancer. Prevalence is presented for the adult population only (ages 15 and over), and is available both as numbers and as proportions per 100,000 persons.	
Crude rate	Data on incidence or mortality are often presented as rates. For a specific tumour and population, a crude rate is calculated simply by dividing the number of new cancers or cancer deaths observed during a given time period by the corresponding number of person years in the population at risk. For cancer, the result is usually expressed as an annual rate per 100,000 persons at risk.	
ASR (age-standardised rate)	An age-standardised rate (ASR) is a summary measure of the rate that a population would have if it had a standard age structure. Standardization is necessary when comparing several populations that differ with respect to age because age has a powerful influence on the risk of cancer. The ASR is a weighted mean of the age-specific rates; the weights are taken from population distribution of the standard population. The most frequently used standard population is the World Standard Population. The calculated incidence or mortality rate is then called age-standardised incidence or mortality rate (world). It is also expressed per 100,000. The world standard population used in GLOBOCAN is as proposed by Segi [1] and modified by Doll and al. [2]. The age-standardised rate is calculated using 10 age-groups. The result may be slightly different from that computed using the same data categorised using the traditional 5 year age bands.	

Continued on next page

Table 49 – continued from previous page		
Term	Definition	
Cumulative risk	Cumulative incidence/mortality is the probability or risk of individuals get- ting/dying from the disease during a specified period. For cancer, it is ex- pressed as the number of new born children (out of 100, or 1000) who would be expected to develop/die from a particular cancer before the age of 75 if they had the rates of cancer observed in the period in the absence of com- peting causes.	
Cytologically normal women	No abnormal cells are observed on the surface of their cervix upon cytology.	
Cervical Intraepithe- lial Neoplasia (CIN) / Squamous Intraepithe- lial Lesions (SIL)	SIL and CIN are two commonly used terms to describe precancerous lesions or the abnormal growth of squamous cells observed in the cervix. SIL is an abnormal result derived from cervical cytological screening or Pap smear testing. CIN is a histological diagnosis made upon analysis of cervical tis- sue obtained by biopsy or surgical excision. The condition is graded as CIN 1, 2 or 3, according to the thickness of the abnormal epithelium (1/3, 2/3 or the entire thickness).	
Low-grade cervical le- sions (LSIL/CIN-1)	Low-grade cervical lesions are defined by early changes in size, shape, and number of ab-normal cells formed on the surface of the cervix and may be referred to as mild dysplasia, LSIL, or CIN-1.	
High-grade cervical le- sions (HSIL / CIN-2 / CIN-3 / CIS)	High-grade cervical lesions are defined by a large number of precancerous cells on the sur-face of the cervix that are distinctly different from normal cells. They have the potential to become cancerous cells and invade deeper tissues of the cervix. These lesions may be referred to as moderate or severe dysplasia, HSIL, CIN-2, CIN-3 or cervical carcinoma in situ (CIS).	
Carcinoma in situ (CIS)	Preinvasive malignancy limited to the epithelium without invasion of the basement membrane. CIN 3 encompasses the squamous carcinoma in situ.	
Invasive cervical can- cer (ICC) / Cervical	If the high-grade precancerous cells invade the basement membrane is called ICC. ICC stages range from stage I (cancer is in the cervix or uterus	
cancer Adenocarcinoma	only) to stage IV (the cancer has spread to distant organs, such as the liver). Invasive tumour with glandular and squamous elements intermingled	

# Acknowledgments

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### Cancer Epidemiology Research Program, Catalan Institute of Oncology (ICO), Institut d'Investigació Biomèdica de Bellvitge (IDIBELL), in alphabetic order

Albero G, Amarilla S, Bosch FX, Bruni L, Collado JJ, de Sanjosé S, Gómez D, Mena M, Muñoz J, Ruiz FJ, Serrano B.

International Agency for Research on Cancer (IARC)

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Anyone who is aware of relevant published data that may not have been included in the present report is encouraged to contact the HPV Information Centre for potential contributions.

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