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# **Human Papillomavirus and Related Diseases Report**

## **REPUBLIC OF NORTH MACEDONIA**

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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 Republic of North Macedonia 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

<b>Population</b>		
Women at risk for cervical cancer (Female population aged >=15 yrs)		890,171
<b>Burden of cervical cancer and other HPV-related cancers</b>		
Annual number of cervical cancer cases		113
Annual number of cervical cancer deaths		62
Crude incidence rates per 100,000 population:		
	Male	Female
Cervical cancer	-	10.9
Anal cancer	0.48	0.19
Vulva cancer	-	1.25
Vaginal cancer	-	0.58
Penile cancer	3.17	-
Oropharyngeal cancer	1.25	0.19
Oral cavity cancer	3.65	1.34
Laryngeal cancer	15.9	1.44
<b>Burden of cervical HPV infection</b>		
Prevalence (%) of HPV 16 and/or HPV 18 among women with:		
	Normal cytology	3.8
	Low-grade cervical lesions (LSIL/CIN-1)	27.1
	High-grade cervical lesions (HSIL/CIN-2/CIN-3/CIS)	54.5
	Cervical cancer	74.0
<b>Other factors contributing to cervical cancer</b>		
Smoking prevalence (%) [95% UI], women		- [—]
Total fertility rate (live births per women)		1.5
Oral contraceptive use (%)		1.60
HIV prevalence (%) [95% UI], women (15-49 years)		<0.1 [<0.1 -<0.1]
<b>Sexual behaviour</b>		
Percentage of 15-year-old who have had sexual intercourse (men/women)		36.0/3.0
Range of median age at first sexual intercourse (men/women)		15.5/16.3
<b>Cervical screening practices and recommendations</b>		
Existence of official national recommendations		Yes
Starting year of current recommendations		2006
Active invitation to screening		Yes
Screening ages (years), primary screening test used, and screening interval or frequency of screenings		24-60 (cytology, 3 years)
<b>HPV vaccine in females</b>		
HPV vaccination programme		Introduced
Year of introduction		2009
Year of estimation of HPV vaccination coverage		2021
HPV coverage – first dose (%)		32
HPV coverage – last dose (%)		21

\* Please see the specific sections for more information.

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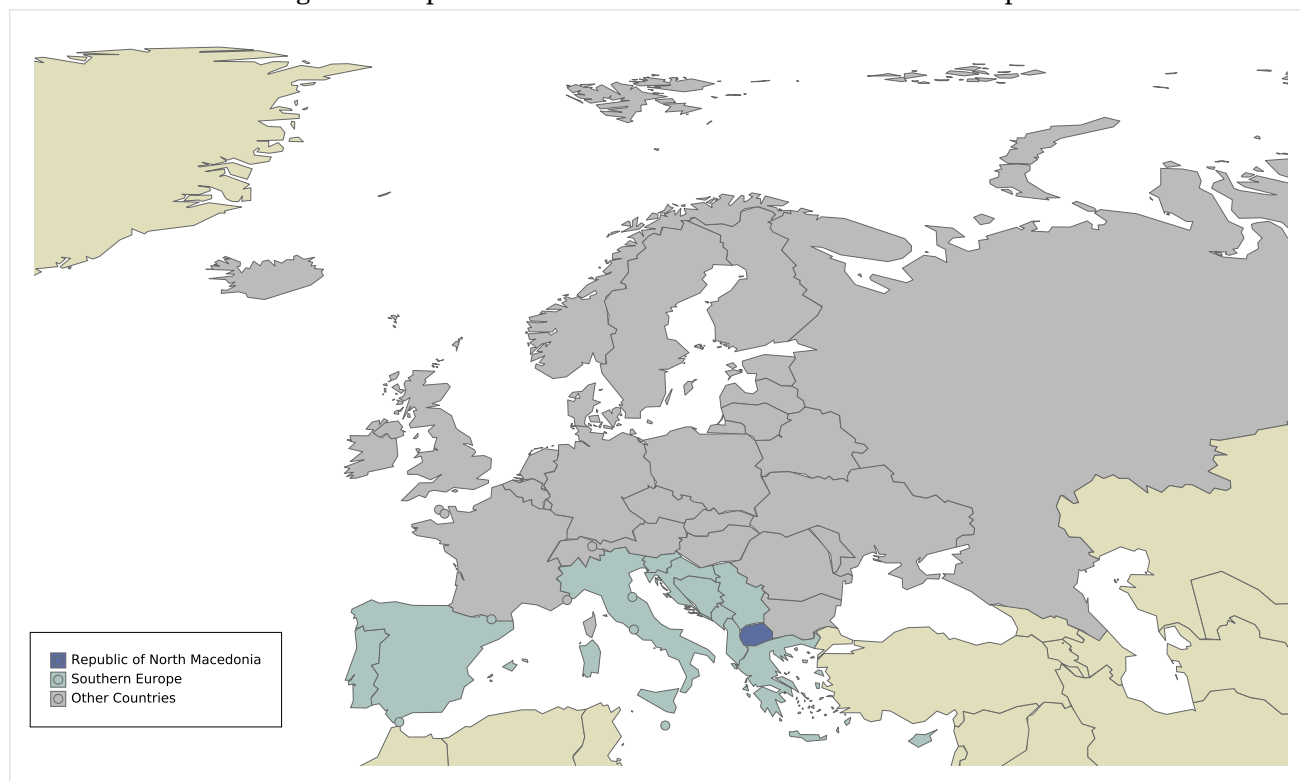
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# 1 Introduction

Figure 1: Republic of North Macedonia and Southern 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 Republic of North Macedonia 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 Republic of North Macedonia. For analytical purposes, Republic of North Macedonia is classified in the geographical region of Southern Europe (Figure 1, lighter blue), which is composed of the following countries: Andorra, Bosnia and Herzegovina, Cyprus, Spain, Gibraltar, Greece, Croatia, Italy, Malta, Montenegro, Portugal, San Marino, Serbia, Slovenia, and Holy See. Throughout the report, Republic of North Macedonia 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 Republic of North Macedonia with 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 Republic of North Macedonia, 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.

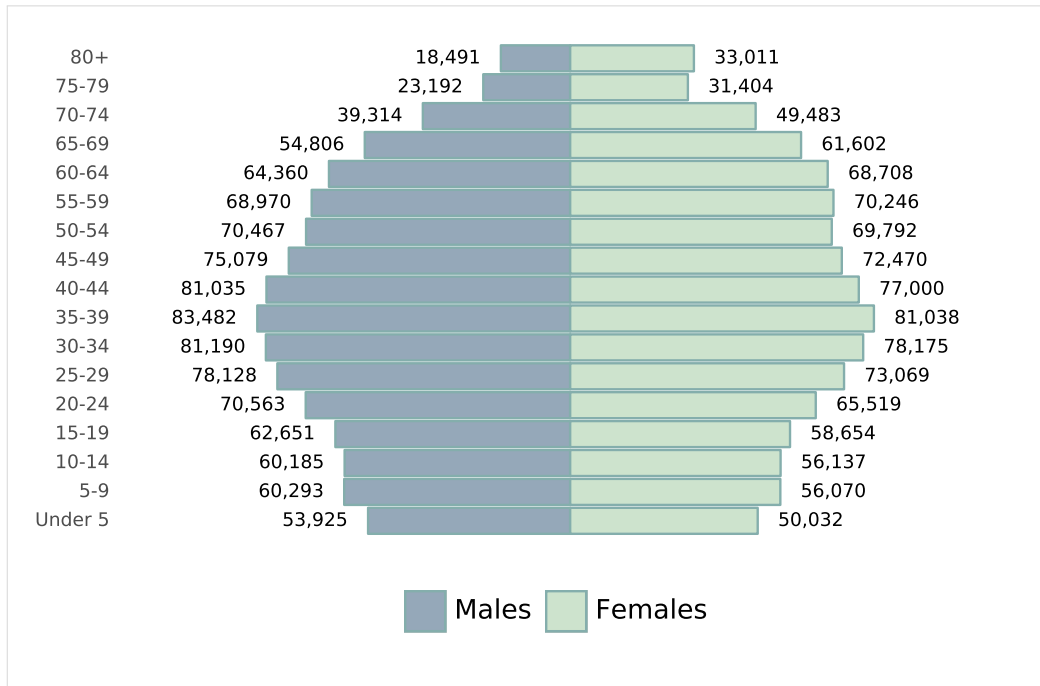
**Section 6, Sexual and reproductive health behaviour indicators.** This section presents sexual and reproductive behaviour indicators that may be used as proxy measures of risk for HPV infection and anogenital cancers, such as age at first sexual intercourse, average number of sexual partners, and anal 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 Republic of North Macedonia for 2022



Data accessed on 30 Jul 2022

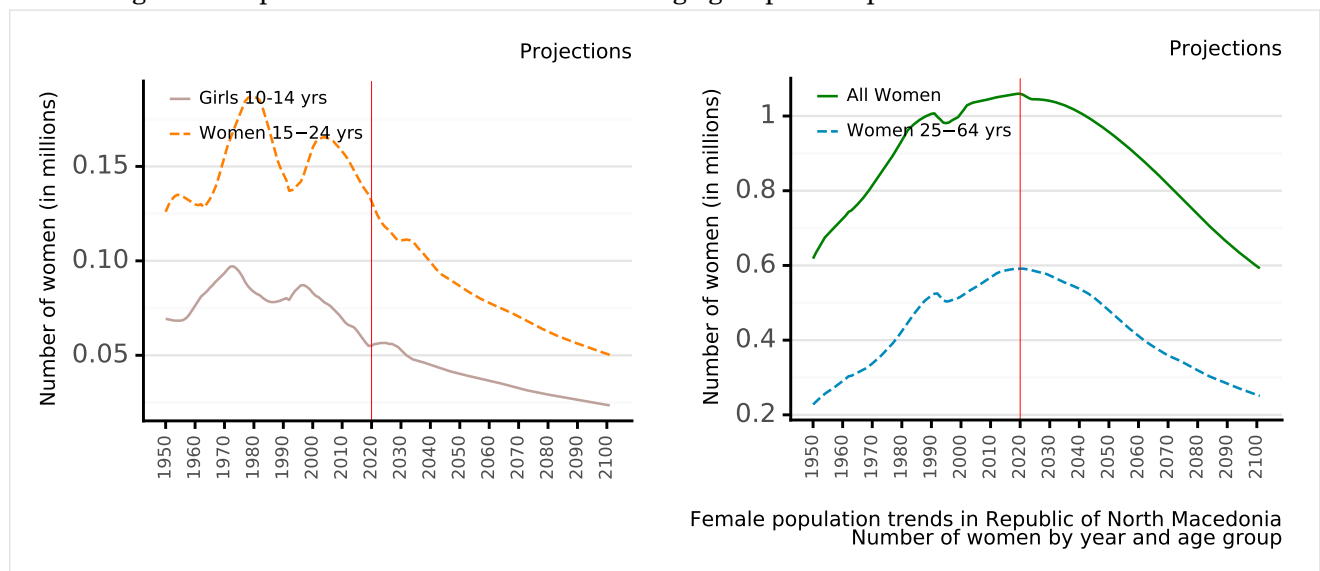
Please refer to original source for methods of estimation.

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 Republic of North Macedonia



Data accessed on 30 Jul 2022

Please refer to original source for methods of estimation.

Year of estimate: 2022

Data Sources:

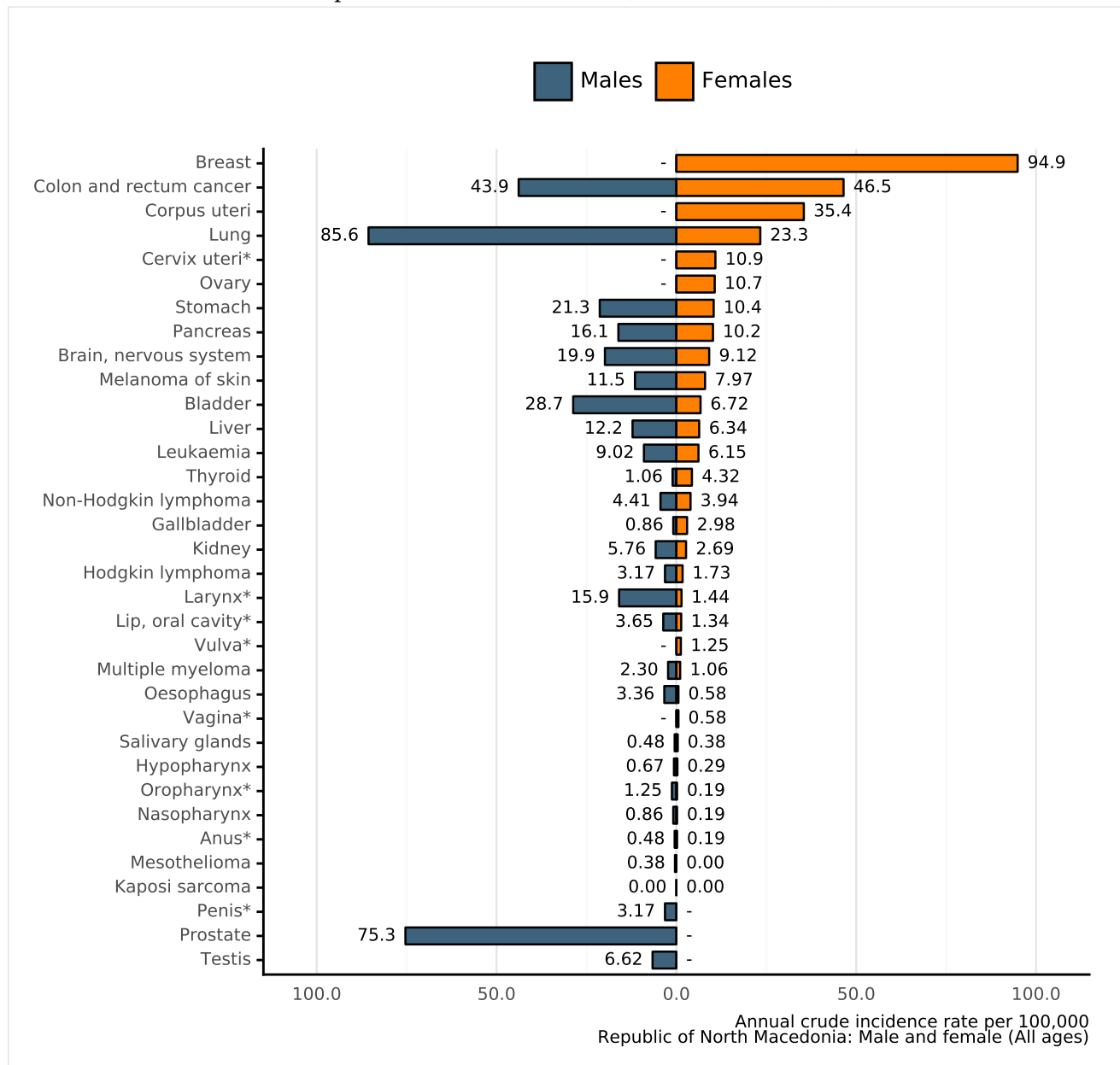
United Nations, Department of Economic and Social Affairs, Population Division (2022). World Population Prospects 2022, Online Edition. [Accessed on July 30, 2022].

### 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 Republic of North Macedonia (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

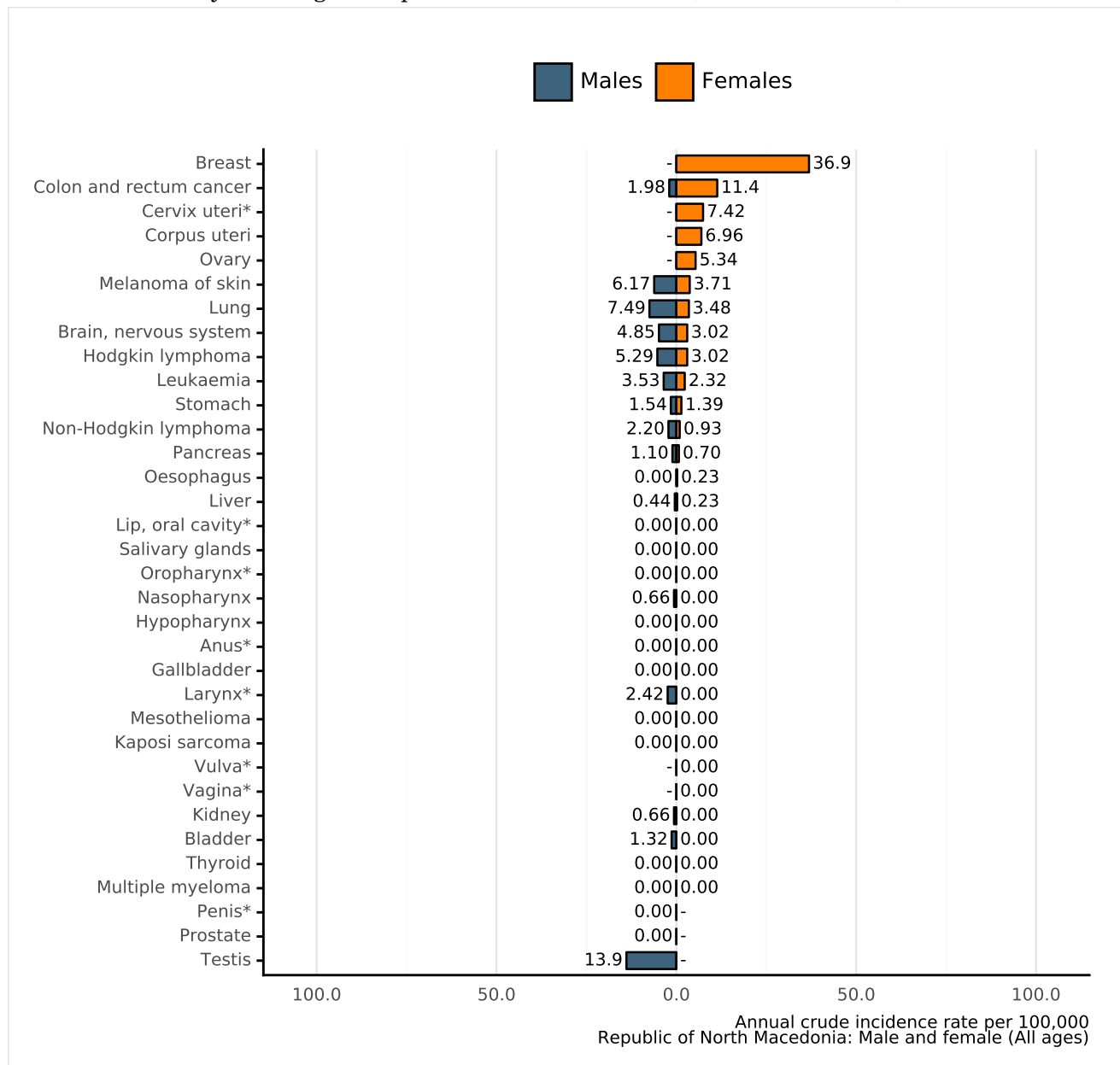
Rates per 100,000 men per year.

Rates per 100,000 women per year.

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 5: Comparison of HPV related cancers incidence to other cancers among men and women 15-44 years of age in Republic of North Macedonia (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.

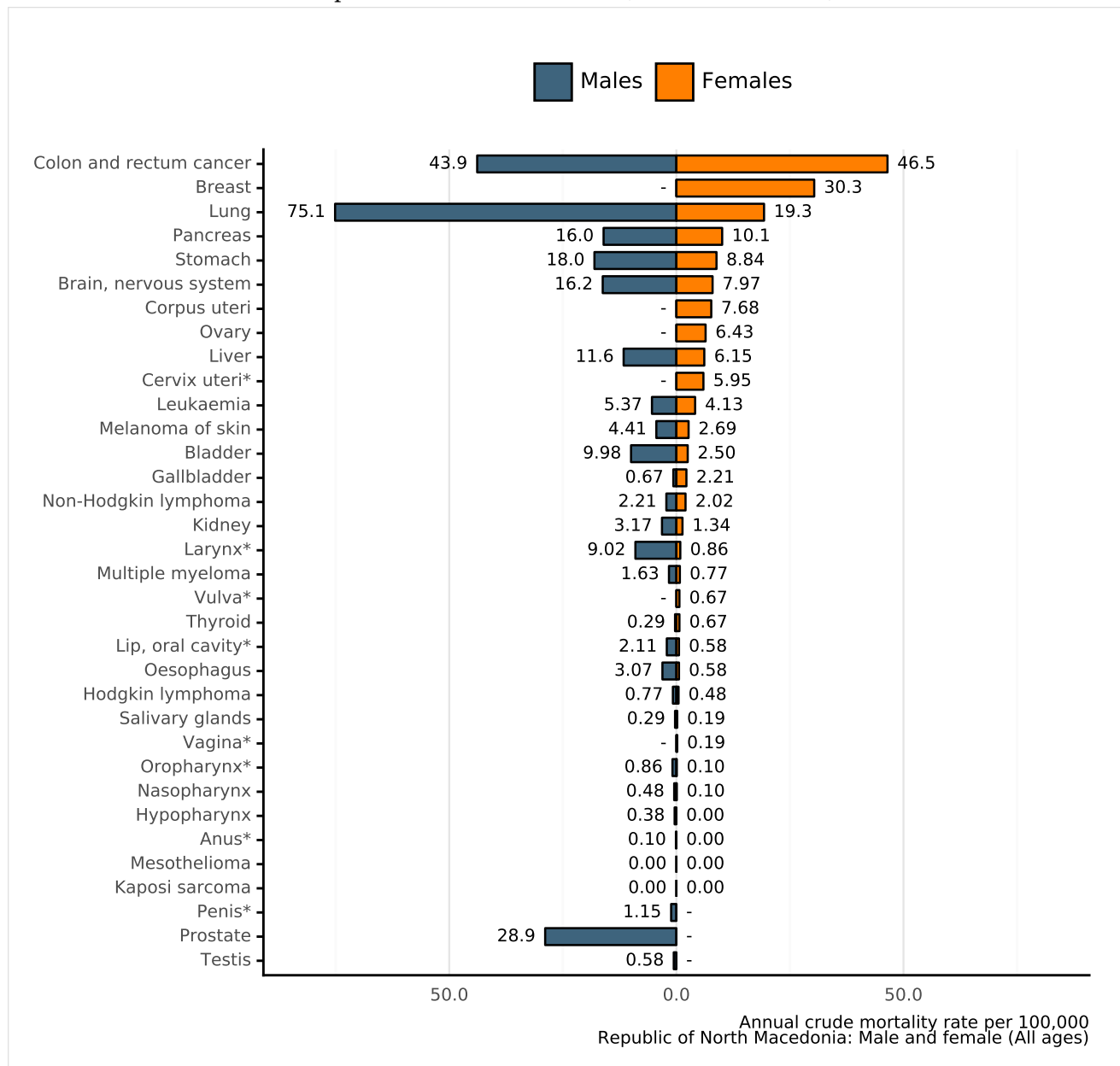
Data Sources:

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].



### 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 Republic of North Macedonia (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

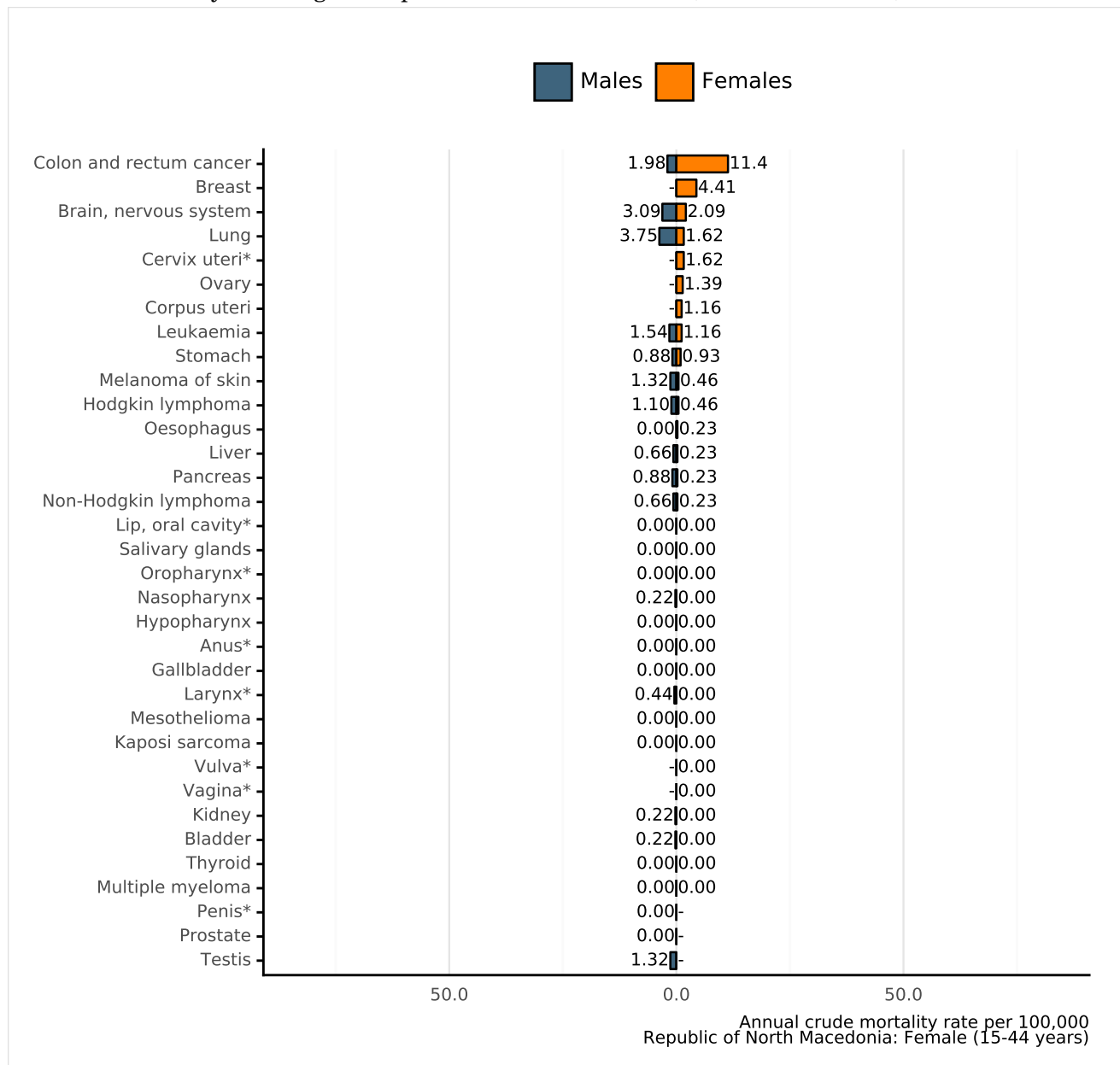
Rates per 100,000 men per year.

Rates per 100,000 women per year.

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 7: Comparison of HPV related cancers mortality to other cancers among men and women 15-44 years of age in Republic of North Macedonia (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.

**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].

### 3.3 Cervical cancer

Cancer of the cervix uteri is the 4<sup>th</sup> 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 Republic of North Macedonia 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 Republic of North Macedonia

##### Key Stats.

About **113 new cervical cancer cases** are diagnosed **annually** in **Republic of North Macedonia** (estimations for 2020).

Cervical cancer **ranks\* as the 5<sup>th</sup> leading cause** of female cancer in **Republic of North Macedonia**.

Cervical cancer is the **3<sup>rd</sup> most common** female cancer in **women aged 15 to 44 years in Republic of North Macedonia**.

\* 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.

Table 2: Cervical cancer incidence in Republic of North Macedonia (estimates for 2020)

Indicator	Republic of North Macedonia	Southern Europe	World
Annual number of new cancer cases	113	9,053	604,127
Uncertainty intervals of new cancer cases [95% UI]	[79-162]	[8,181-10,018]	[582,031-627,062]
Crude incidence rate <sup>b</sup>	10.9	11.5	15.6
Age-standardized incidence rate <sup>b</sup>	7.51	7.72	13.3
Cumulative risk (%) at 75 years old <sup>a</sup>	0.77	0.76	1.39

##### 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> 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.

##### 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].

Table 3: Cervical cancer incidence in Republic of North Macedonia by cancer registry

Cancer registry	Period	N cases <sup>a</sup>	Crude rate <sup>b</sup>	ASR <sup>b</sup>
-	-	-	-	-

**Data accessed on 5 Oct 2018**

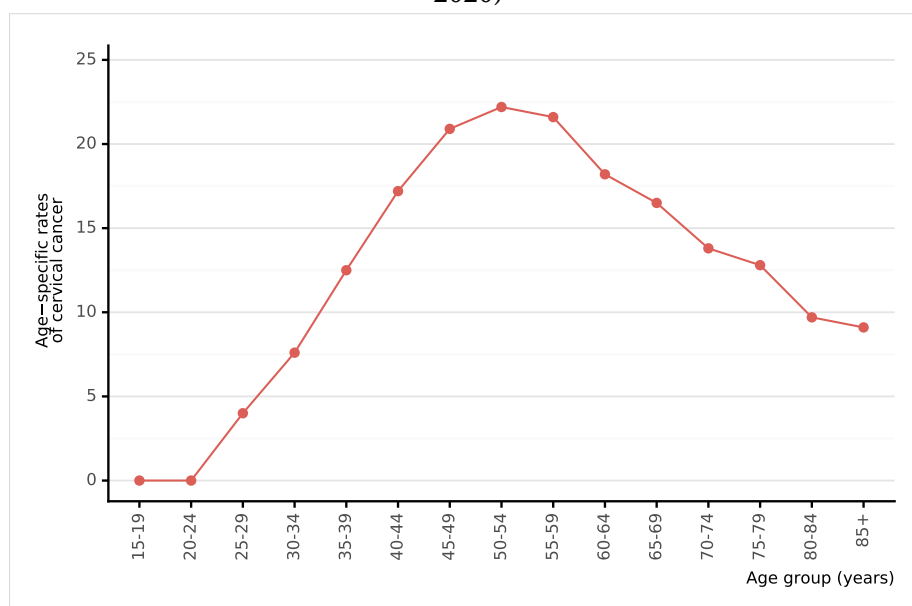
Please refer to original source (available at <http://ci5.iarc.fr/CI5-XI/Default.aspx>)

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

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



Data accessed on 27 Jan 2021

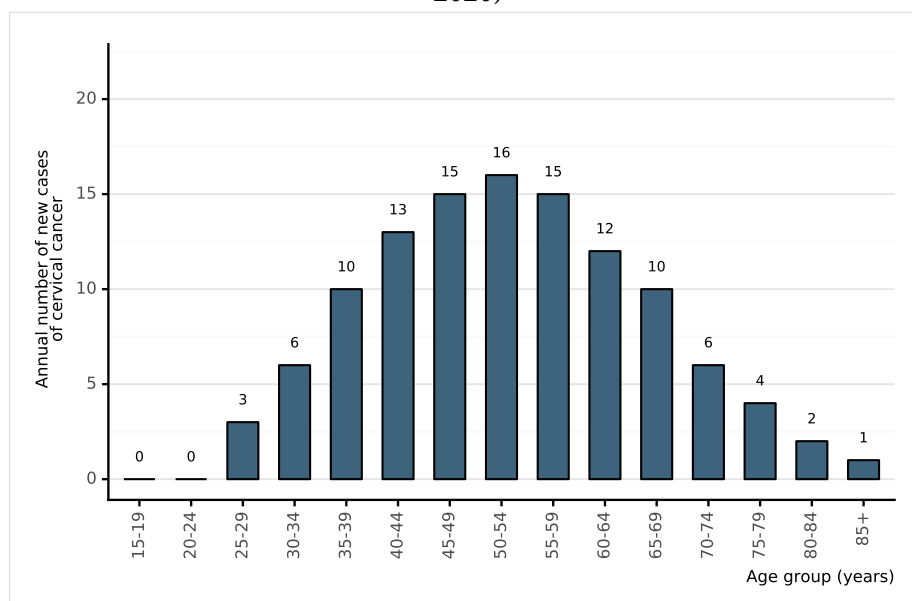
For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>

<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].

Figure 9: Annual number of new cases of cervical cancer in Republic of North Macedonia (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:

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].

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

### 3.3.2 Cervical cancer incidence by histology in Republic of North Macedonia

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

Cancer registry	Period	Squamo	Adeno	Other	Unspec.
-	-	-	-	-	-

**Data accessed on 5 Oct 2018**

Rates per 100,000 women per year.

Standardized rates have been estimated using the direct method and the World population as the references.

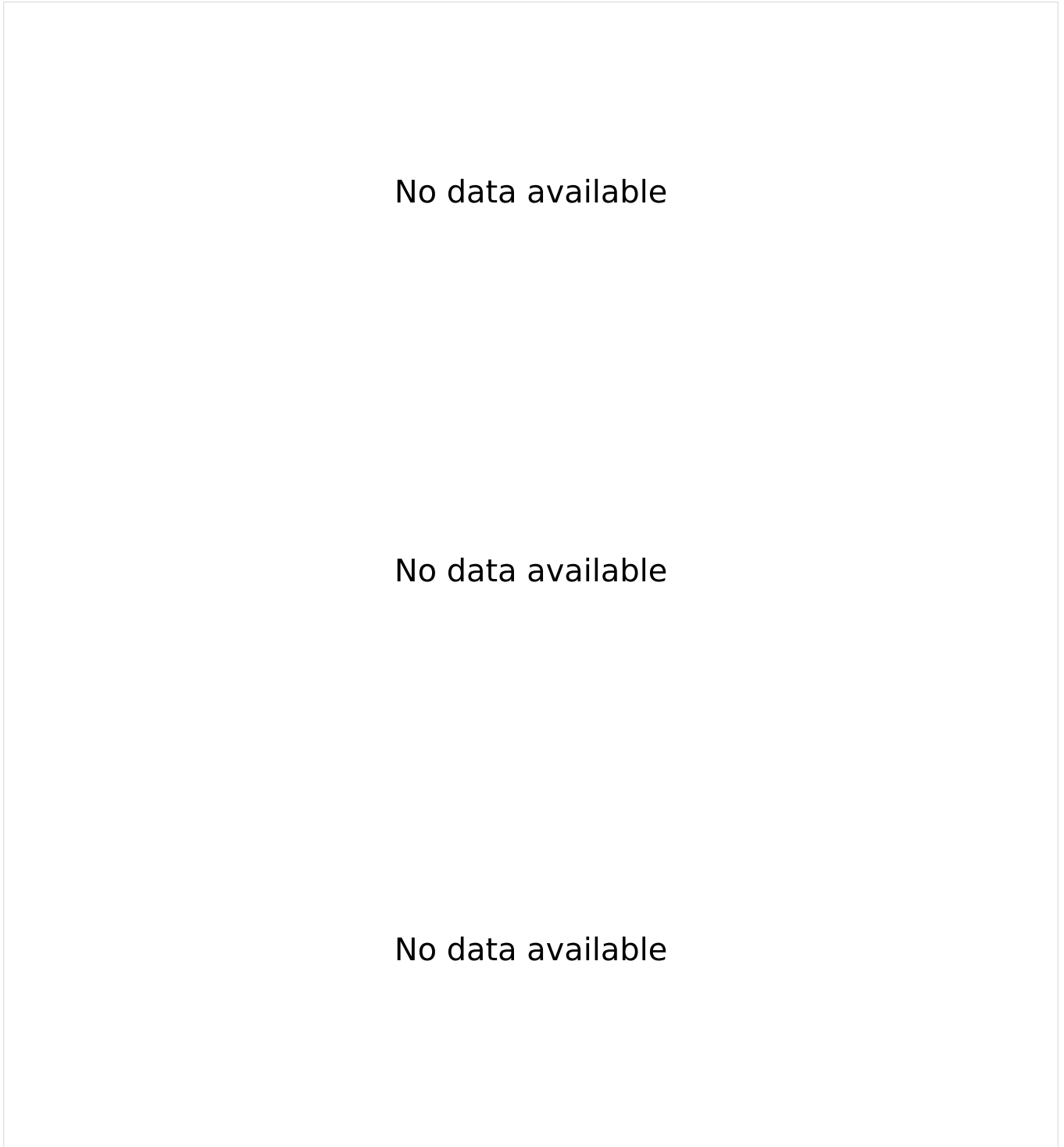
Adeno: adenocarcinoma; Other: Other carcinoma; Squamous: Squamous cell carcinoma; Unspec: Unspecified carcinoma;

**Data accessed on 28 Aug 2018**

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>

Figure 10: Time trends in cervical cancer incidence in Republic of North Macedonia (cancer registry data)





### 3.3.3 Cervical cancer mortality in Republic of North Macedonia

#### Key Stats.

About **62 cervical cancer deaths occur annually in Republic of North Macedonia** are diagnosed **annually** (estimations for 2020).

Cervical cancer **ranks\* as the 10<sup>th</sup> leading cause of cancer deaths** of female cancer deaths in **Republic of North Macedonia**.

Cervical cancer is the **4<sup>th</sup> leading cause of cancer deaths in women aged 15 to 44 years in Republic of North Macedonia**.

\* 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.

Table 5: Cervical cancer mortality in Republic of North Macedonia (estimates for 2020)

Indicator	Republic of North Macedonia	Southern Europe	World
Annual number of deaths	62	3,705	341,831
Uncertainty intervals of mortality cancer cases [95% UI]	[46-84]	[3,431-4,001]	[324,231-360,386]
Crude mortality rate <sup>b</sup>	5.95	4.72	8.84
Age-standardized mortality rate <sup>b</sup>	3.64	2.31	7.25
Cumulative risk (%) at 75 years old <sup>a</sup>	0.41	0.25	0.82

#### Data accessed on 27 Jan 2021

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

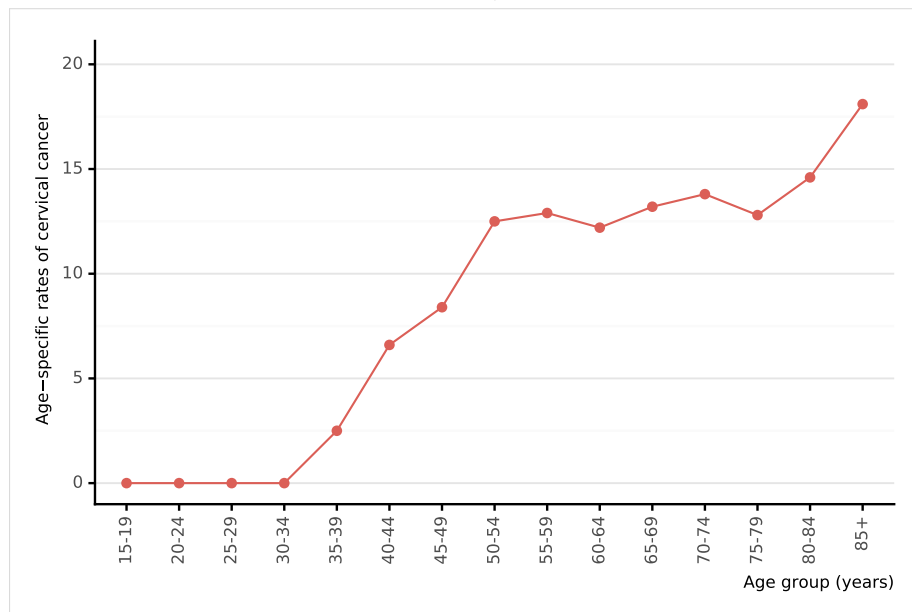
<sup>a</sup> Cumulative risk (mortality) is the probability or risk of individuals dying from the disease during ages 0-74 years. For cancer, it is expressed as the % of new born children who would be expected to die from a particular cancer before the age of 75 if they had the rates of cancer observed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

<sup>b</sup> Rates per 100,000 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 11: Age-specific mortality rates of cervical cancer in Republic of North Macedonia (estimates for 2020)



Data accessed on 27 Jan 2021

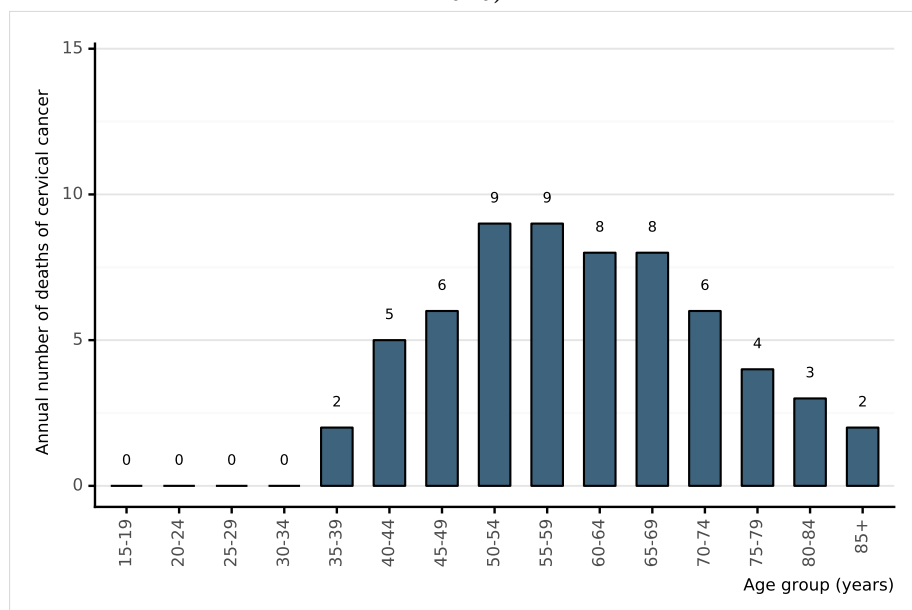
For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>

<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].

Figure 12: Annual number of deaths of cervical cancer in Republic of North Macedonia (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>

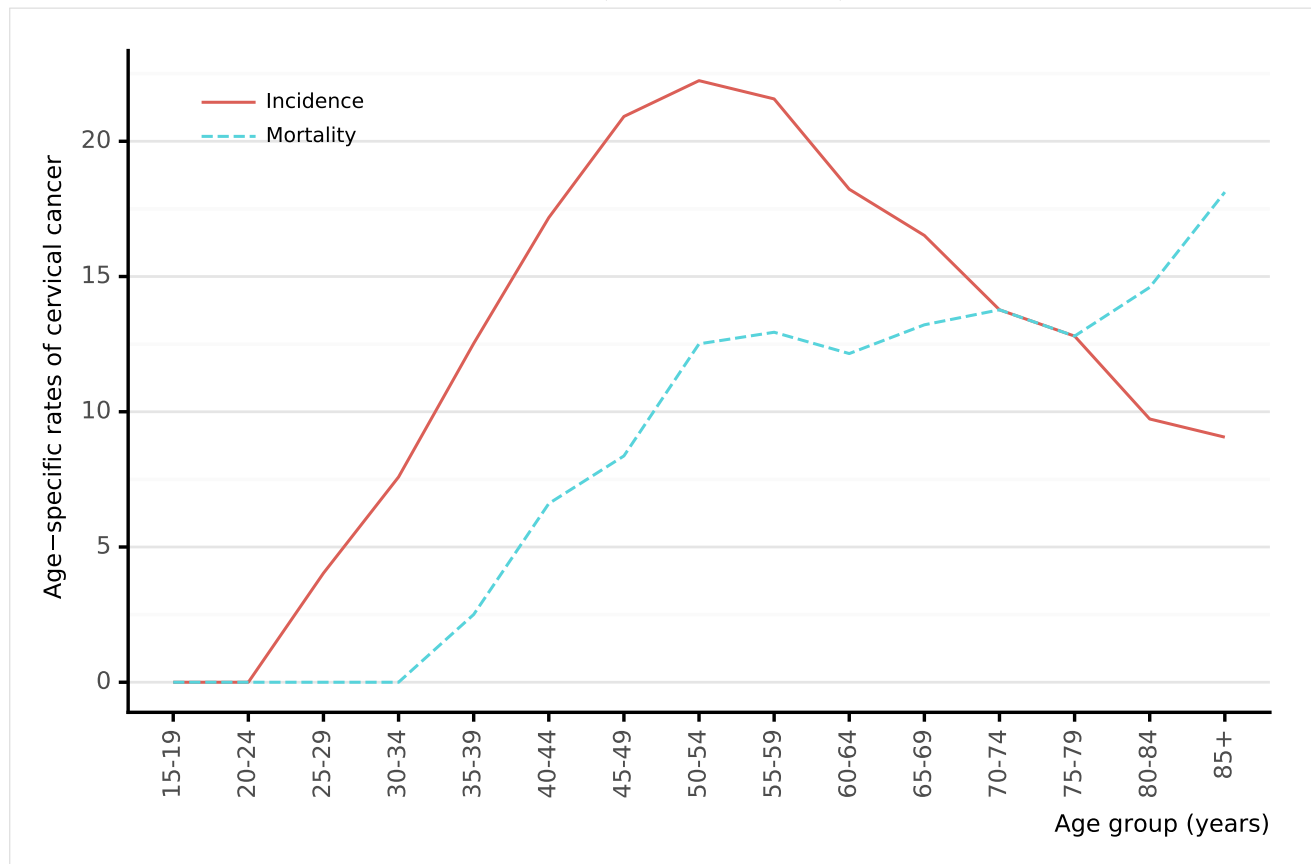
Data Sources:

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].

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

### 3.3.4 Cervical cancer incidence and mortality comparison in Republic of North Macedonia

Figure 13: Comparison of age-specific cervical cancer incidence and mortality rates in Republic of North Macedonia (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].

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

Indicator	Republic of North Macedonia		Europe		World	
	Number	Rate	Number	Rate	Number	Rate
DALYs (95% UI) <sup>a</sup>	2,886 (2,076-3,854)	272 (196-364)	824,336 (726,198-913,992)	189 (166-209)	8,955,013 (7,547,733-9,978,462)	232 (196-259)
YLLs (95% UI) <sup>b</sup>	2,792 (2,005-3,726)	264 (189-352)	793,756 (703,004-877,841)	182 (161-201)	8,712,962 (7,365,279-9,728,886)	226 (191-252)
YLDs (95% UI) <sup>c</sup>	94 (58-141)	9 (5-13)	30,580 (21,266-42,064)	7 (5-10)	242,051 (171,644-326,024)	6 (4-8)

Data accessed on 29 Apr 2021

Rate per 100,000 women

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

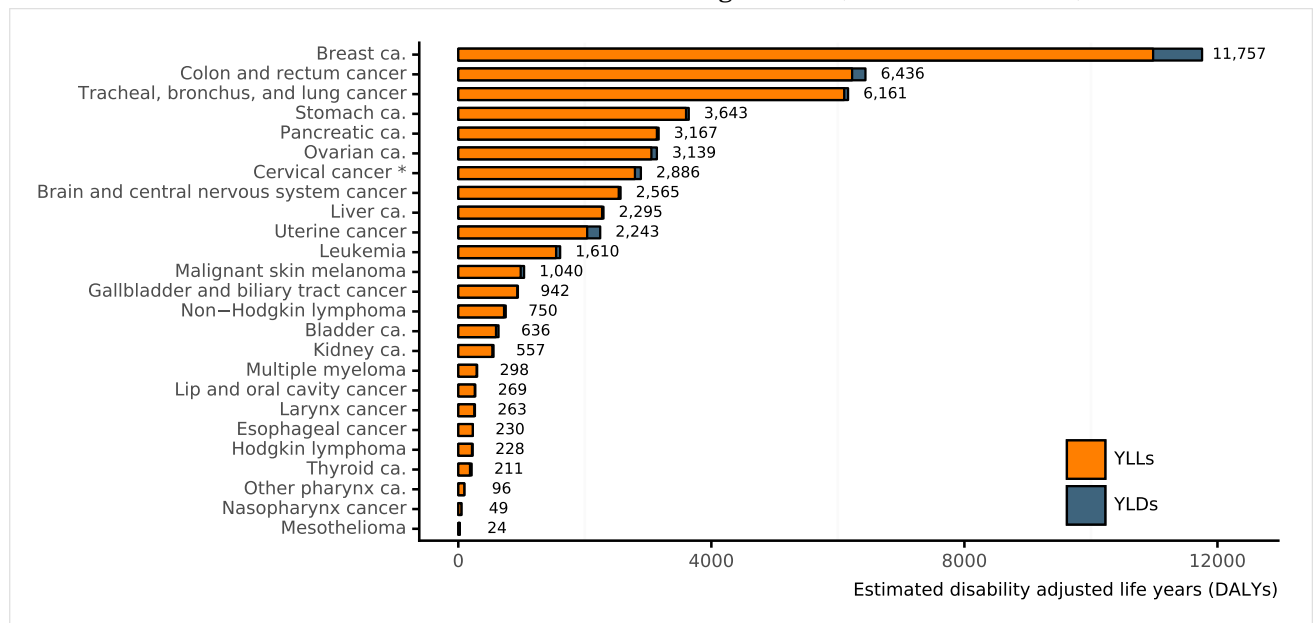
<sup>b</sup> YLLs (95% UI): years of life lost (95% uncertainty interval)

<sup>c</sup> 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

Figure 14: Comparison of annual premature deaths and disability from cervical cancer in Republic of North Macedonia to other cancers among women (estimates for 2019)



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 Republic of North Macedonia

Table 7: Anal cancer incidence in Republic of North Macedonia (estimates for 2020)

Indicator	Republic of North Macedonia	Southern Europe	World
<b>MEN</b>			
Annual number of new cancer cases	5	966	21,706
Uncertainty intervals of new cancer cases [95% UI]	[3-8]	[704-1,325]	[18,432-25,561]
Crude incidence rate <sup>b</sup>	0.48	1.29	0.55
Age-standardized incidence rate <sup>b</sup>	0.28	0.62	0.49
Cumulative risk (%) at 75 years old <sup>a</sup>	0.04	0.07	0.06
<b>WOMEN</b>			
Annual number of new cancer cases	2	1,385	29,159
Uncertainty intervals of new cancer cases [95% UI]	[1-3]	[1,082-1,773]	[25,656-33,140]
Crude incidence rate <sup>c</sup>	0.19	1.77	0.75
Age-standardized incidence rate <sup>c</sup>	0.09	0.70	0.58
Cumulative risk (%) at 75 years old <sup>a</sup>	0.01	0.08	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.

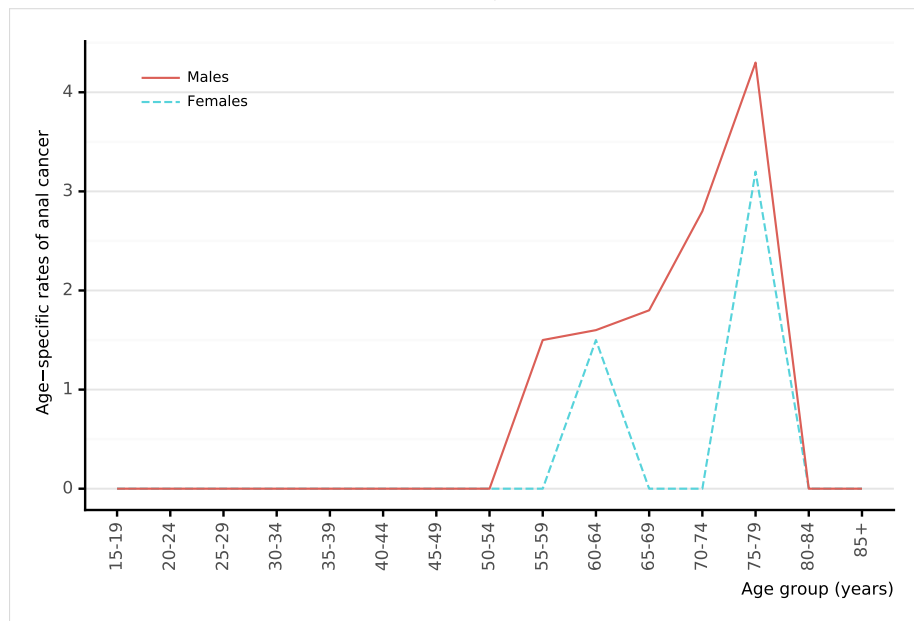
<sup>b</sup> Rates per 100,000 men per year.

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

#### Data Sources:

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 15: Age-specific incidence rates of anal cancer in Republic of North Macedonia (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>

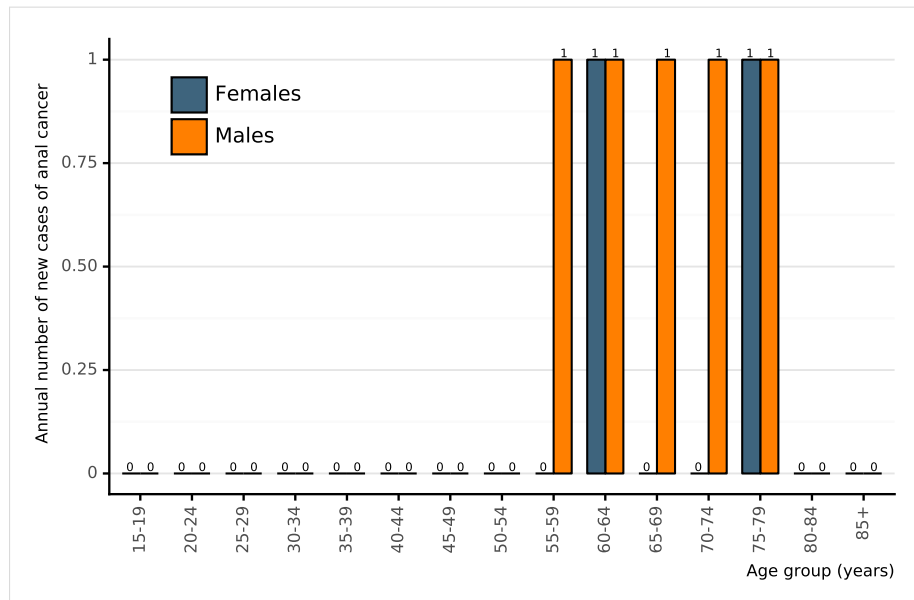
<sup>a</sup> Rates per 100,000 men per year.

<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: <https://gco.iarc.fr/today>, accessed [27 January 2021].

Figure 16: Annual number of new cases of anal cancer in Republic of North Macedonia (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:

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].

## 3.4.1.2 Anal cancer mortality in Republic of North Macedonia

Table 8: Anal cancer mortality in Republic of North Macedonia (estimates for 2020)

Indicator	Republic of North Macedonia	Southern Europe	World
<b>MEN</b>			
Annual number of new cancer cases	1	266	9,416
Uncertainty intervals of new cancer cases [95% UI]	[0-10]	[207-342]	[7,282-12,175]
Crude incidence rate <sup>b</sup>	0.10	0.35	0.24
Age-standardized incidence rate <sup>b</sup>	0.06	0.15	0.21
Cumulative risk (%) at 75 years old <sup>a</sup>	0.01	0.02	0.02
<b>WOMEN</b>			
Annual number of new cancer cases	0	376	9,877
Uncertainty intervals of new cancer cases [95% UI]	[0-10]	[307-460]	[7,795-12,516]
Crude incidence rate <sup>c</sup>	0	0.48	0.26
Age-standardized incidence rate <sup>c</sup>	0	0.16	0.19
Cumulative risk (%) at 75 years old <sup>a</sup>	0.0	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.

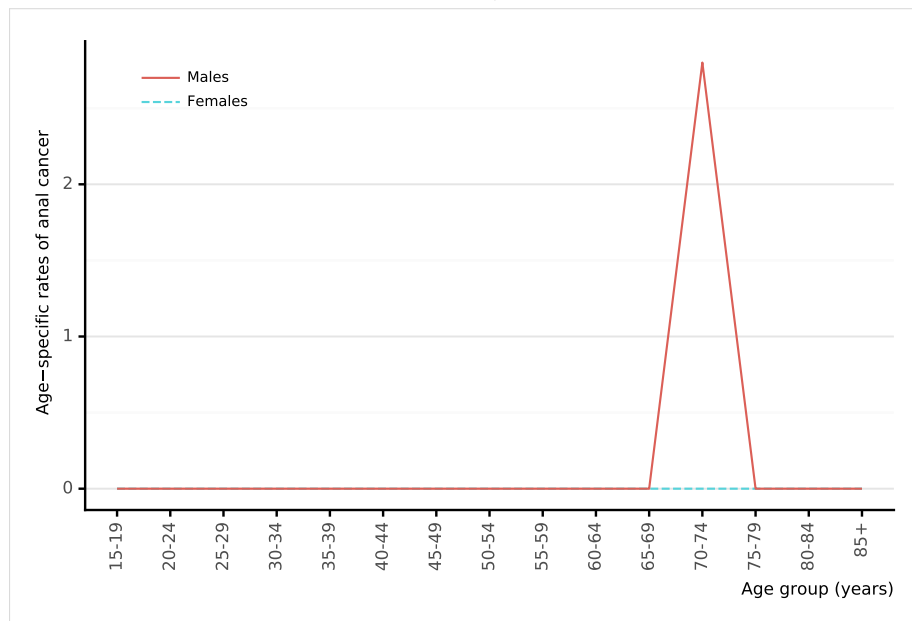
<sup>b</sup> Rates per 100,000 men per year.

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

**Data 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 17: Age-specific mortality rates of anal cancer in Republic of North Macedonia (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>

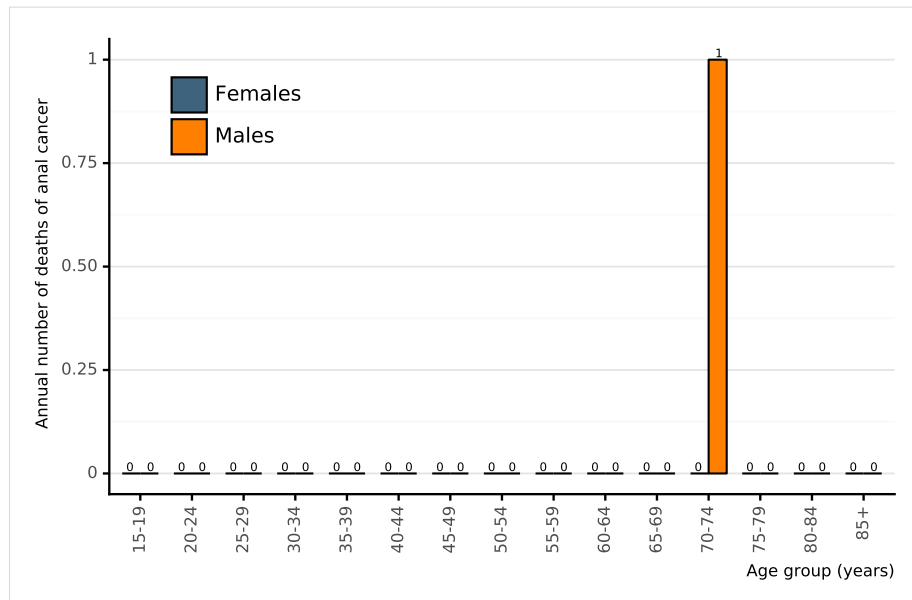
<sup>a</sup> Rates per 100,000 men per year.

<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: <https://gco.iarc.fr/today>, accessed [27 January 2021].

Figure 18: Annual number of deaths of of anal cancer in Republic of North Macedonia (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>

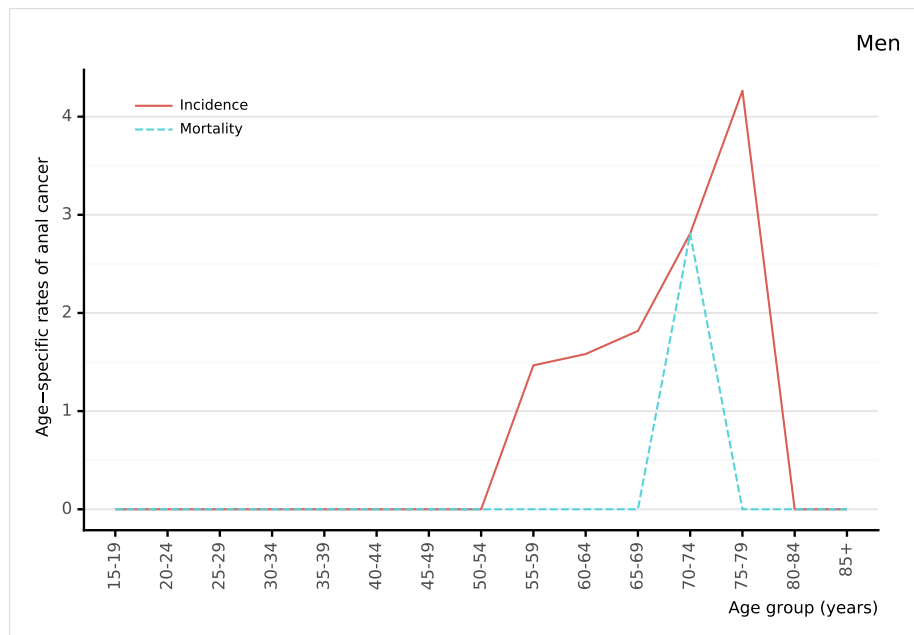
Data Sources:

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].



### 3.4.1.3 Anal cancer incidence and mortality comparison in Republic of North Macedonia

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



Data accessed on 27 Jan 2021

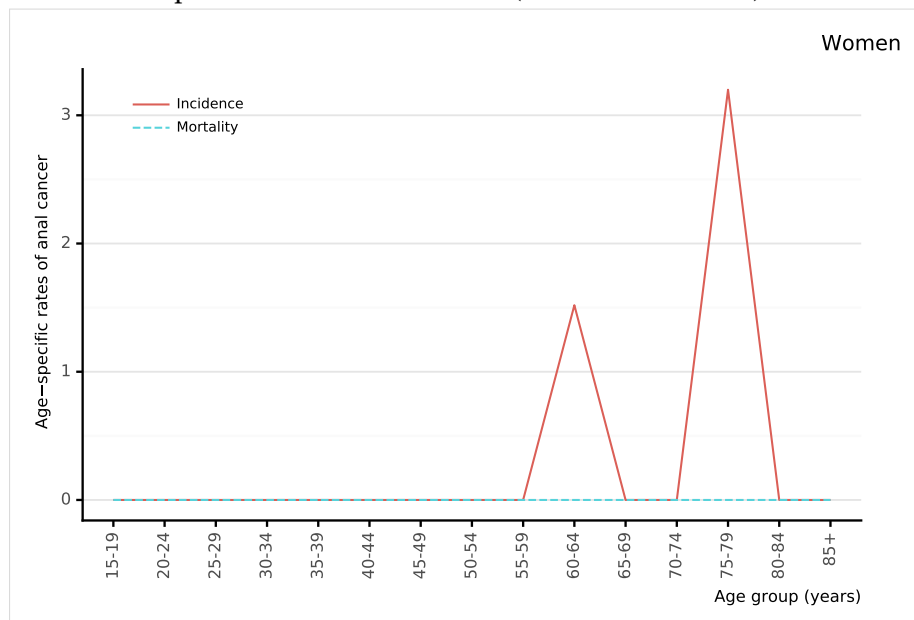
For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>

<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 20: Comparison of age-specific anal cancer incidence and mortality rates among women in Republic of North Macedonia (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].

### 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):e180-e190). 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 Republic of North Macedonia

Table 9: Vulva cancer incidence in Republic of North Macedonia (estimates for 2020)

Indicator	Republic of North Macedonia	Southern Europe	World
Annual number of new cancer cases	13	3,048	45,240
Uncertainty intervals [95% UI]	[4-40]	[2,592-3,584]	[40,656-50,342]
Crude incidence rate <sup>b</sup>	1.25	3.89	1.17
Age-standardized incidence rate <sup>b</sup>	0.60	1.35	0.85
Cumulative risk (%) at 75 years old <sup>a</sup>	0.09	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>

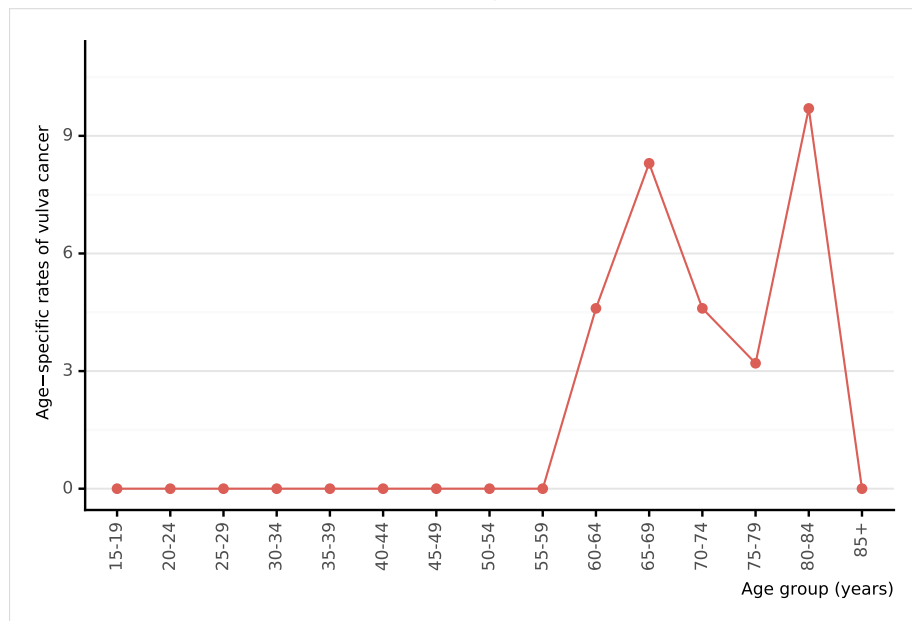
<sup>a</sup> Cumulative risk (incidence) is the probability or risk of individuals getting from the disease during ages 0-74 years. For cancer, it is expressed as the % of new born children who would be expected to develop from a particular cancer before the age of 75 if they had the rates of cancer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

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

**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 21: Age-specific incidence rates of vulva cancer in Republic of North Macedonia (estimates for 2020)



Data accessed on 27 Jan 2021

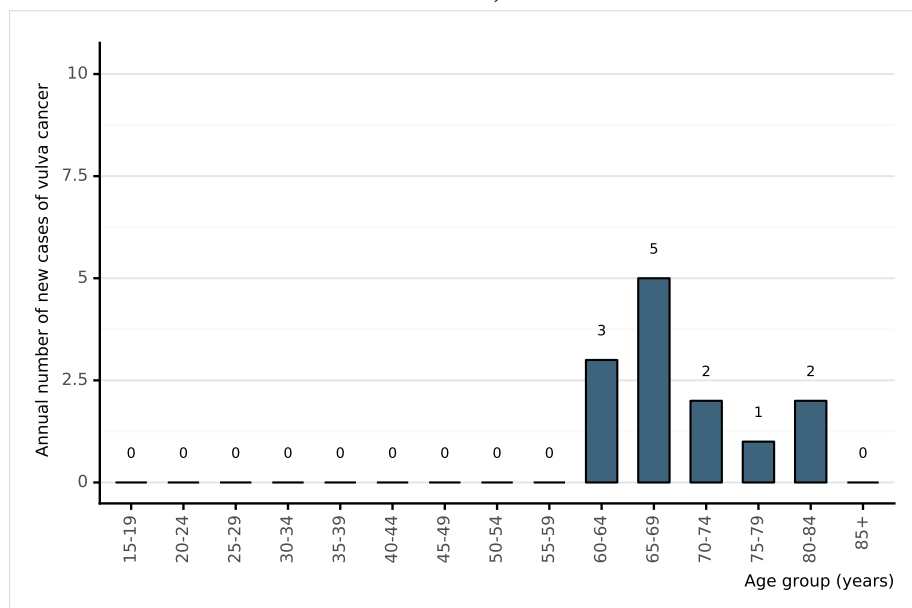
For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>

<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].

Figure 22: Annual number of new cases of vulva cancer in Republic of North Macedonia (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:

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].

### 3.4.2.2 Vulva cancer mortality in Republic of North Macedonia

Table 10: Vulva cancer mortality in Republic of North Macedonia (estimates for 2020)

Indicator	Republic of North Macedonia	Southern Europe	World
Annual number of deaths	7	1,293	17,427
Uncertainty intervals [95% UI]	[3-18]	[1,156-1,446]	[14,497-20,950]
Crude mortality rate <sup>b</sup>	0.67	1.65	0.45
Age-standardized mortality rate <sup>b</sup>	0.29	0.40	0.30
Cumulative risk (%) at 75 years old <sup>a</sup>	0.04	0.04	0.03

**Data accessed on 27 Jan 2021**

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

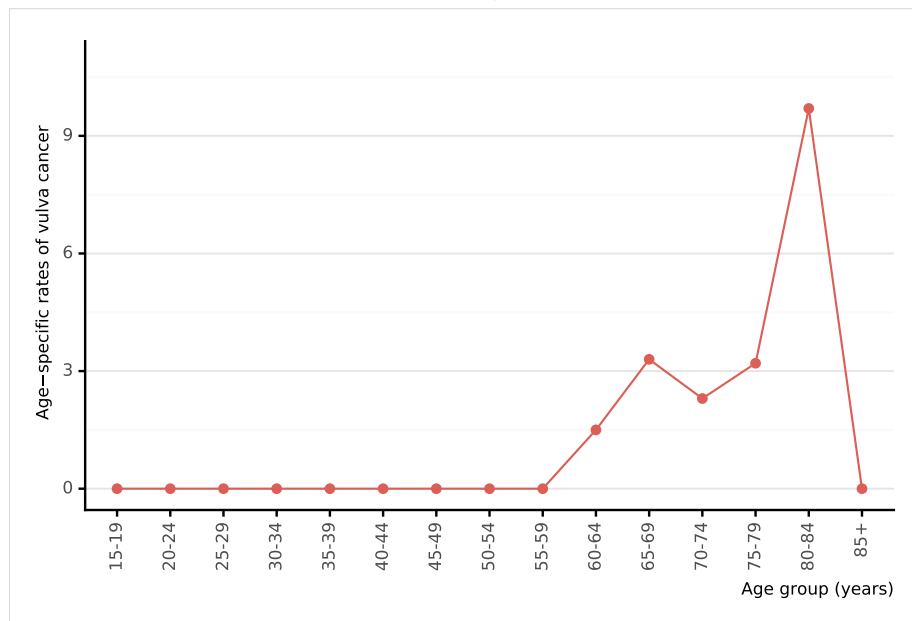
<sup>a</sup> Cumulative risk (mortality) is the probability or risk of individuals dying from the disease during ages 0-74 years. For cancer, it is expressed as the % of new born children who would be expected to die from a particular cancer before the age of 75 if they had the rates of cancer observed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

<sup>b</sup> Rates per 100,000 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 23: Age-specific mortality rates of vulva cancer in Republic of North Macedonia (estimates for 2020)



Data accessed on 27 Jan 2021

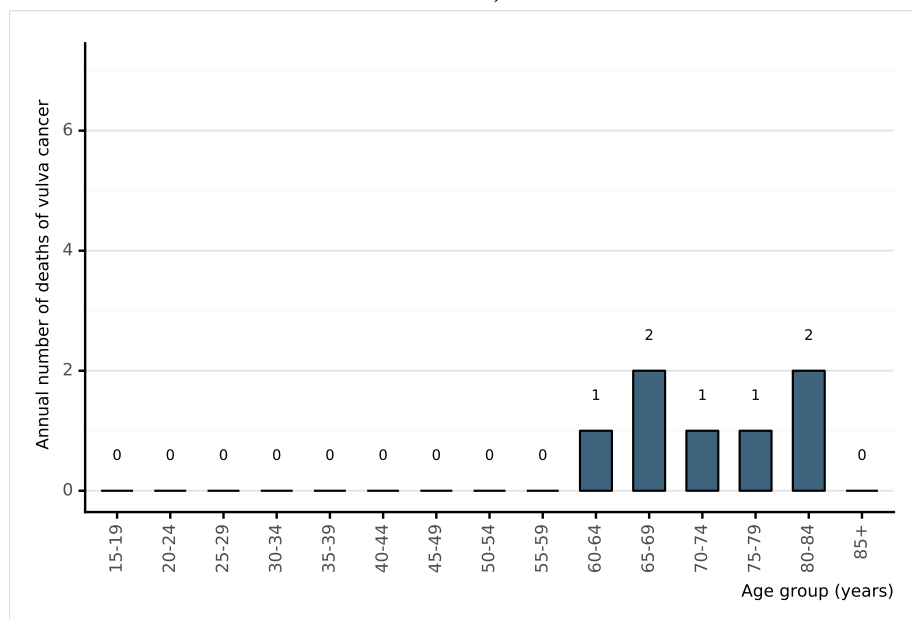
For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>

<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].

Figure 24: Annual number of deaths of vulva cancer in Republic of North Macedonia (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>

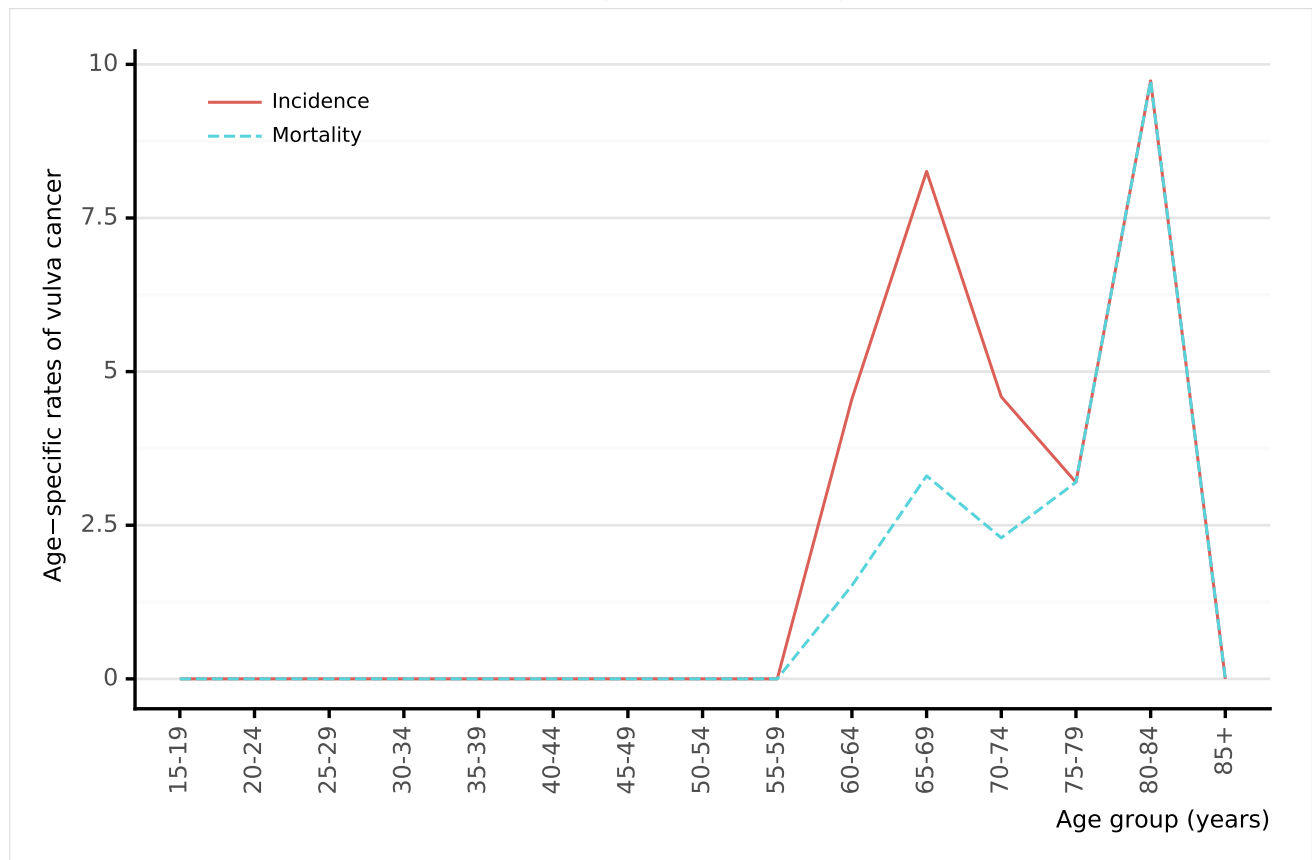
<sup>a</sup> Rates per 100,000 women per year.

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].

### 3.4.2.3 Vulva cancer incidence and mortality comparison in Republic of North Macedonia

Figure 25: Comparison of age-specific vulva cancer incidence and mortality rates in Republic of North Macedonia (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].

### 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 ( $\geq 65$  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 Republic of North Macedonia

Table 11: Vaginal cancer incidence in Republic of North Macedonia (estimates for 2020)

Indicator	Republic of North Macedonia	Southern Europe	World
Annual number of new cancer cases	6	553	17,908
Uncertainty intervals [95% UI]	[1-51]	[385-794]	[14,678-21,848]
Crude incidence rate <sup>b</sup>	0.58	0.70	0.46
Age-standardized incidence rate <sup>b</sup>	0.27	0.29	0.36
Cumulative risk (%) at 75 years old <sup>a</sup>	0.03	0.03	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>

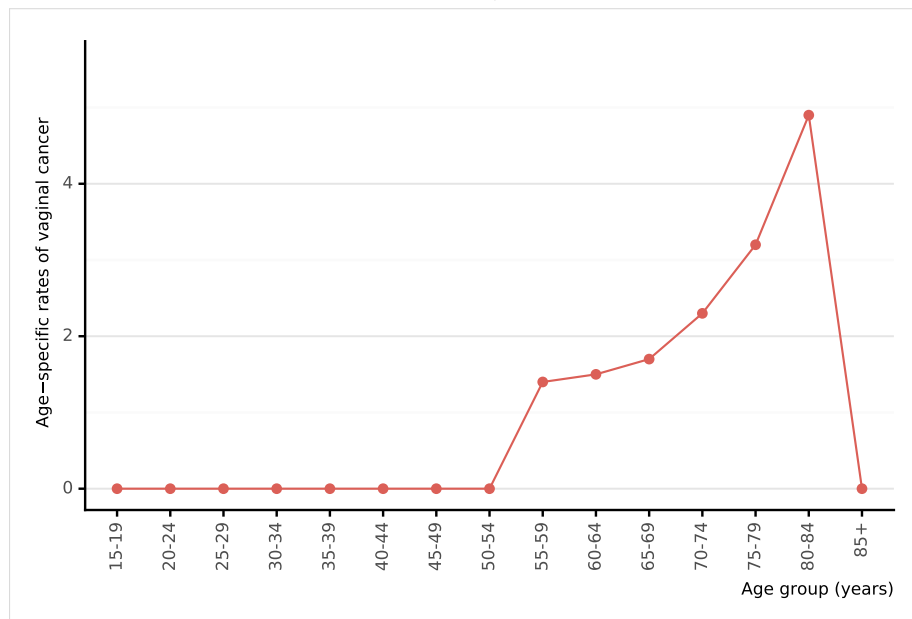
<sup>a</sup> Cumulative risk (incidence) is the probability or risk of individuals getting from the disease during ages 0-74 years. For cancer, it is expressed as the % of new born children who would be expected to develop from a particular cancer before the age of 75 if they had the rates of cancer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

<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 26: Age-specific incidence rates of vaginal cancer in Republic of North Macedonia (estimates for 2020)



Data accessed on 27 Jan 2021

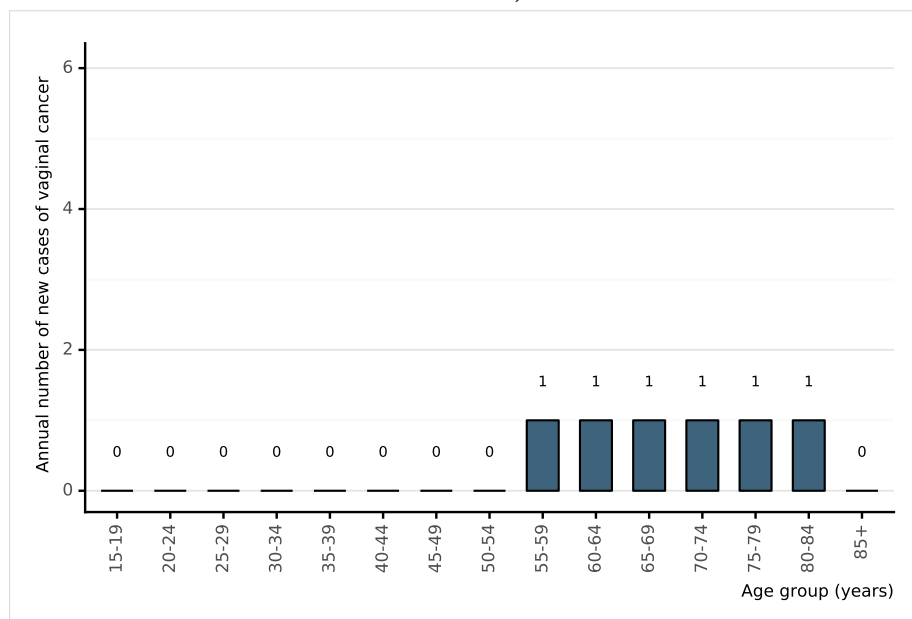
For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>

<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].

Figure 27: Annual number of new cases of vaginal cancer in Republic of North Macedonia (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:

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].



### 3.4.3.2 Vaginal cancer mortality in Republic of North Macedonia

Table 12: Vaginal cancer mortality in Republic of North Macedonia (estimates for 2020)

Indicator	Republic of North Macedonia	Southern Europe	World
Annual number of deaths	2	247	7,995
Uncertainty intervals [95% UI]	[0-12]	[190-322]	[5,983-10,684]
Crude mortality rate <sup>b</sup>	0.19	0.31	0.21
Age-standardized mortality rate <sup>b</sup>	0.11	0.09	0.16
Cumulative risk (%) at 75 years old <sup>a</sup>	0.02	0.01	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>

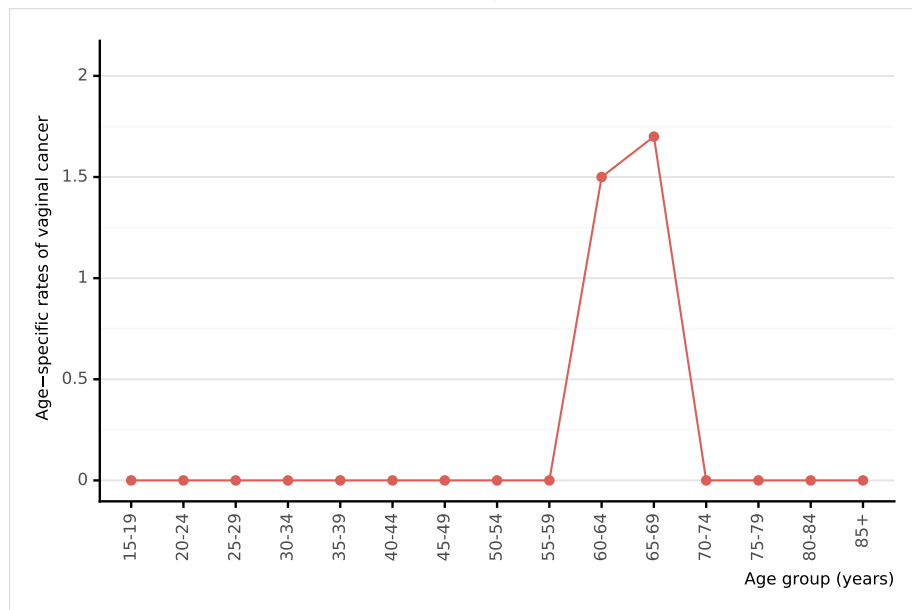
<sup>a</sup> Cumulative risk (mortality) is the probability or risk of individuals dying from the disease during ages 0-74 years. For cancer, it is expressed as the % of new born children who would be expected to die from a particular cancer before the age of 75 if they had the rates of cancer observed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

<sup>b</sup> Rates per 100,000 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 28: Age-specific mortality rates of vaginal cancer in Republic of North Macedonia (estimates for 2020)



Data accessed on 27 Jan 2021

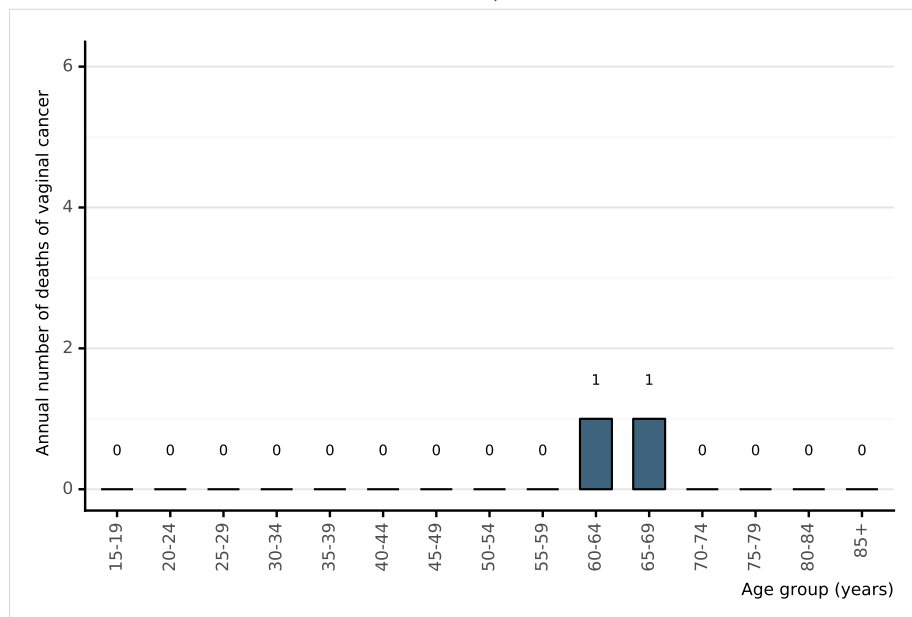
For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>

<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].

Figure 29: Annual number of deaths of vaginal cancer in Republic of North Macedonia (estimates for 2020)



Data accessed on 27 Jan 2021

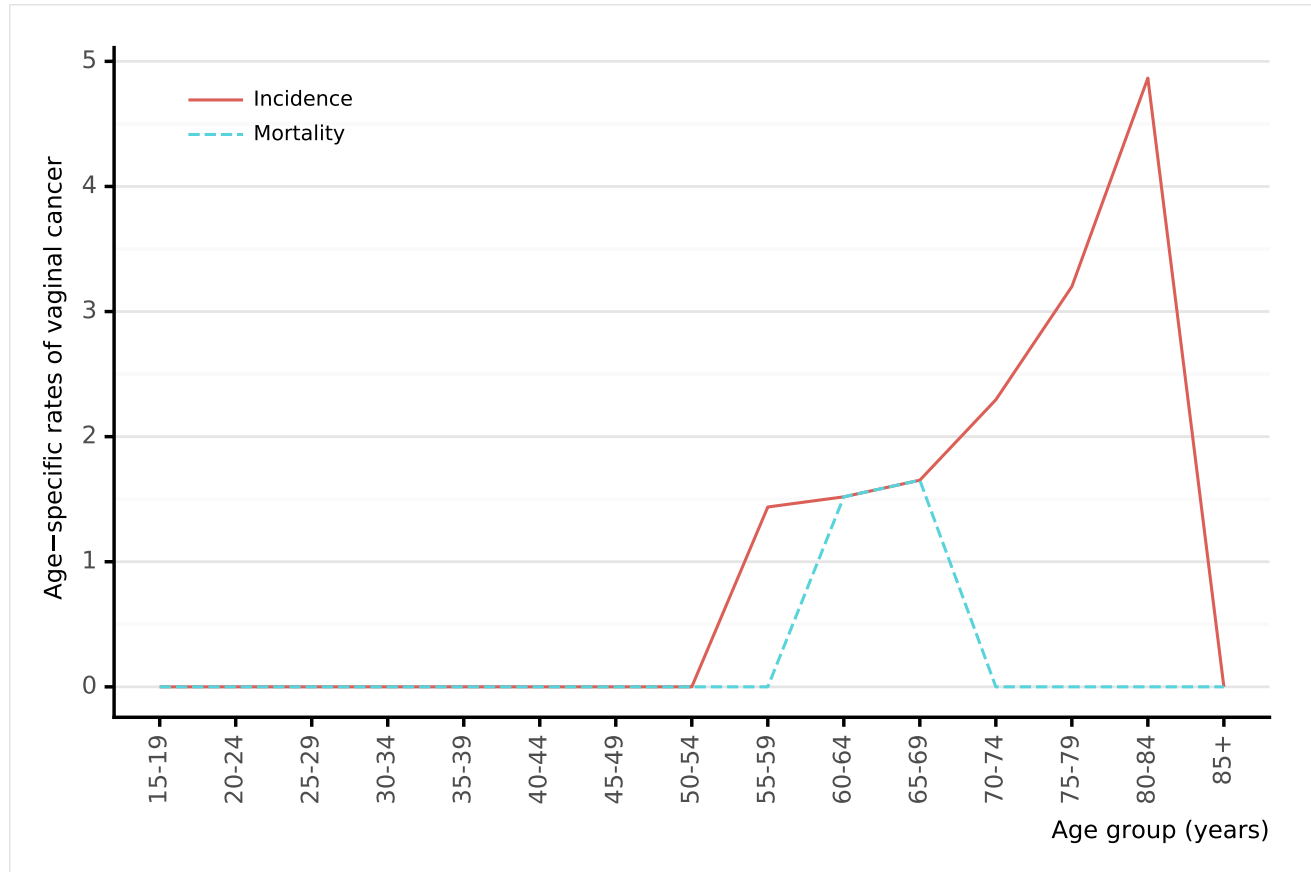
For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>

Data Sources:

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].

### 3.4.3.3 Vaginal cancer incidence and mortality comparison in Republic of North Macedonia

Figure 30: Comparison of age-specific vaginal cancer incidence and mortality rates in Republic of North Macedonia (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].

### 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 Republic of North Macedonia

Table 13: Penile cancer incidence in Republic of North Macedonia (estimates for 2020)

Indicator	Republic of North Macedonia	Southern Europe	World
Annual number of new cancer cases	33	1,471	36,068
Uncertainty intervals [95% UI]	[14-76]	[1,127-1,920]	[30,963-42,015]
Crude incidence rate <sup>b</sup>	3.17	1.96	0.92
Age-standardized incidence rate <sup>b</sup>	1.73	0.86	0.80
Cumulative risk (%) at 75 years old <sup>a</sup>	0.18	0.10	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>

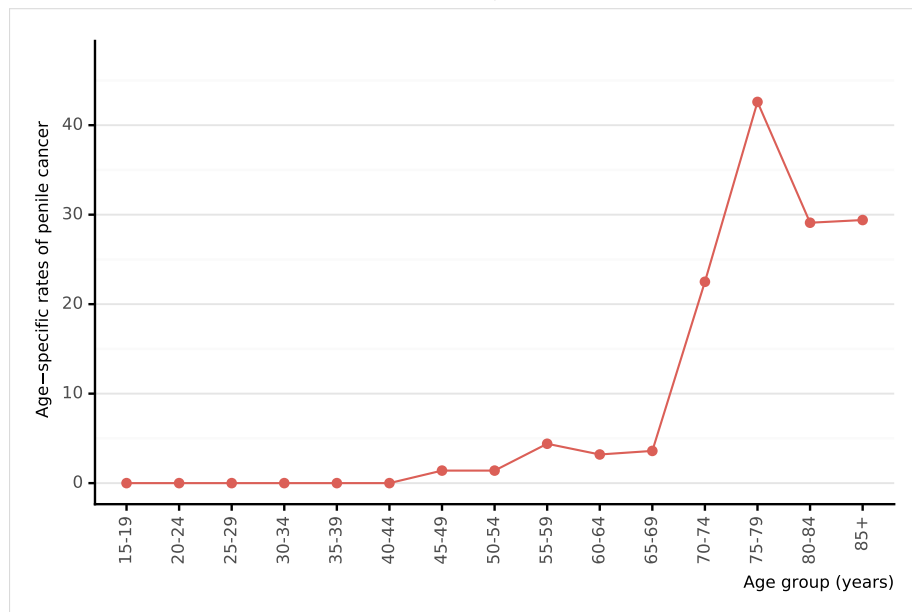
<sup>a</sup> Cumulative risk (incidence) is the probability or risk of individuals getting from the disease during ages 0-74 years. For cancer, it is expressed as the % of new born children who would be expected to develop from a particular cancer before the age of 75 if they had the rates of cancer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

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

#### Data Sources:

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 31: Age-specific incidence rates of penile cancer in Republic of North Macedonia (estimates for 2020)



Data accessed on 27 Jan 2021

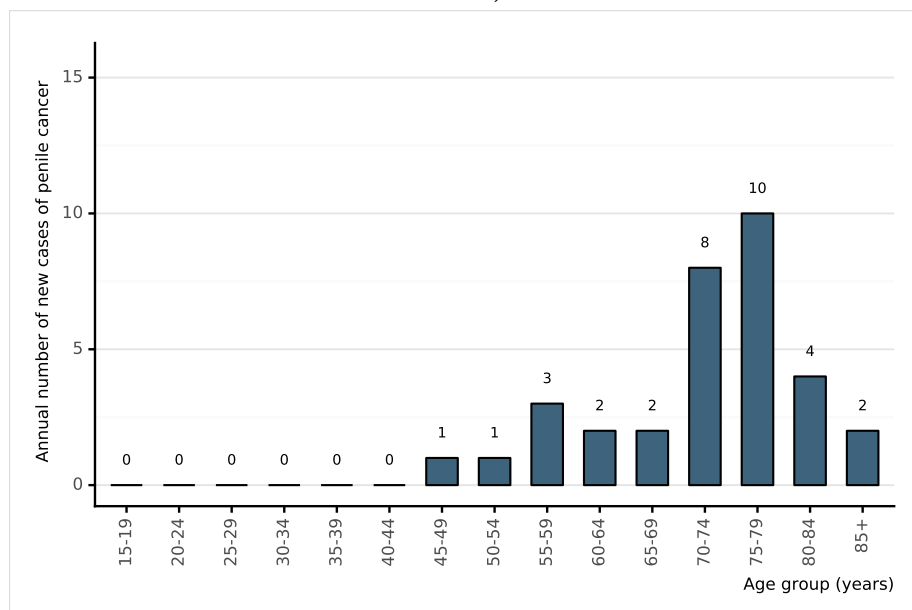
For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>

<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 32: Annual number of new cases of penile cancer in Republic of North Macedonia (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:

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].

### 3.4.4.2 Penile cancer mortality in Republic of North Macedonia

Table 14: Penile cancer mortality in Republic of North Macedonia (estimates for 2020)

Indicator	Republic of North Macedonia	Southern Europe	World
Annual number of deaths	12	414	13,211
Uncertainty intervals [95% UI]	[6-24]	[336-510]	[10,687-16,332]
Crude mortality rate <sup>b</sup>	1.15	0.55	0.34
Age-standardized mortality rate <sup>b</sup>	0.62	0.21	0.29
Cumulative risk (%) at 75 years old <sup>a</sup>	0.05	0.02	0.03

**Data accessed on 27 Jan 2021**

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

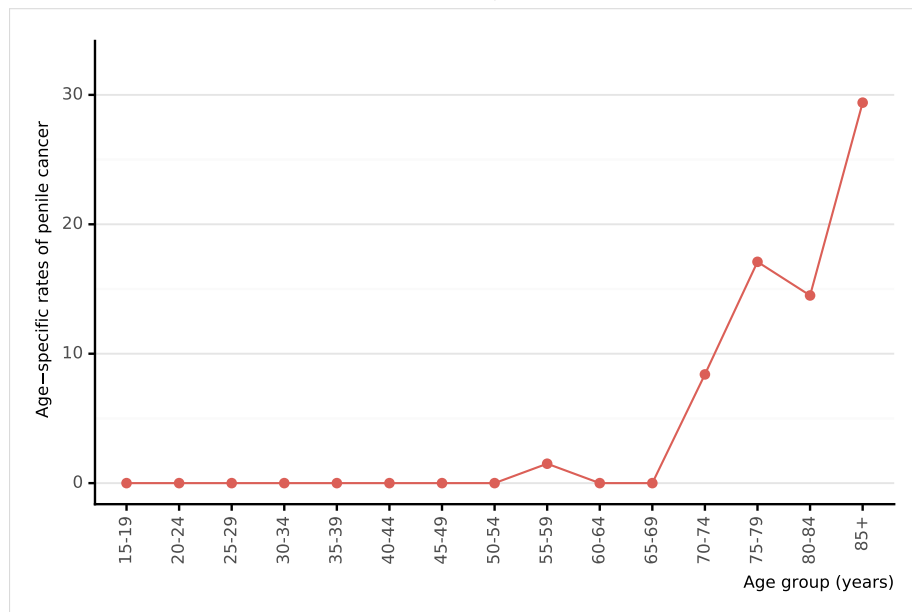
<sup>a</sup> Cumulative risk (mortality) is the probability or risk of individuals dying from the disease during ages 0-74 years. For cancer, it is expressed as the % of new born children who would be expected to die from a particular cancer before the age of 75 if they had the rates of cancer observed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

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

**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 33: Age-specific mortality rates of penile cancer in Republic of North Macedonia (estimates for 2020)



Data accessed on 27 Jan 2021

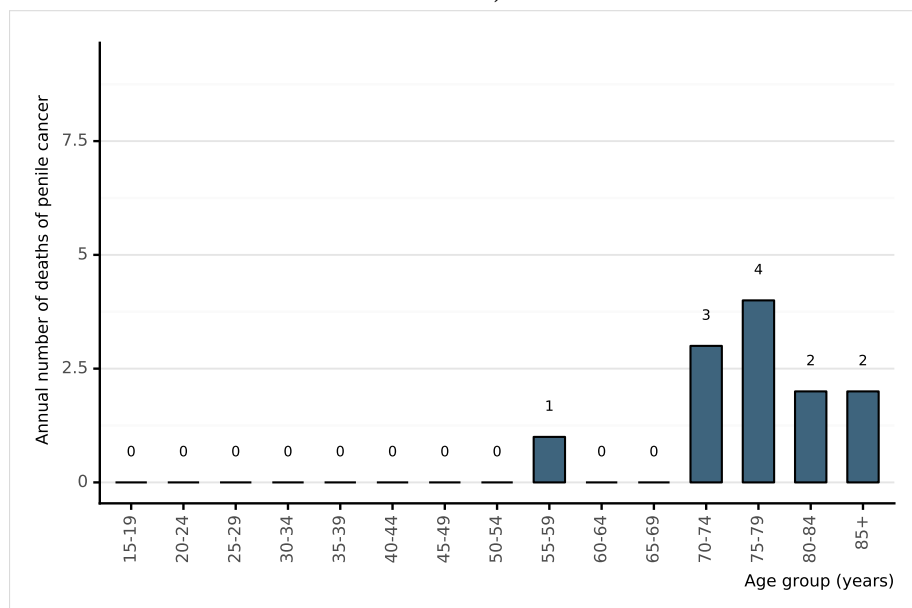
For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>

<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 34: Annual number of deaths of penile cancer in Republic of North Macedonia (estimates for 2020)



Data accessed on 27 Jan 2021

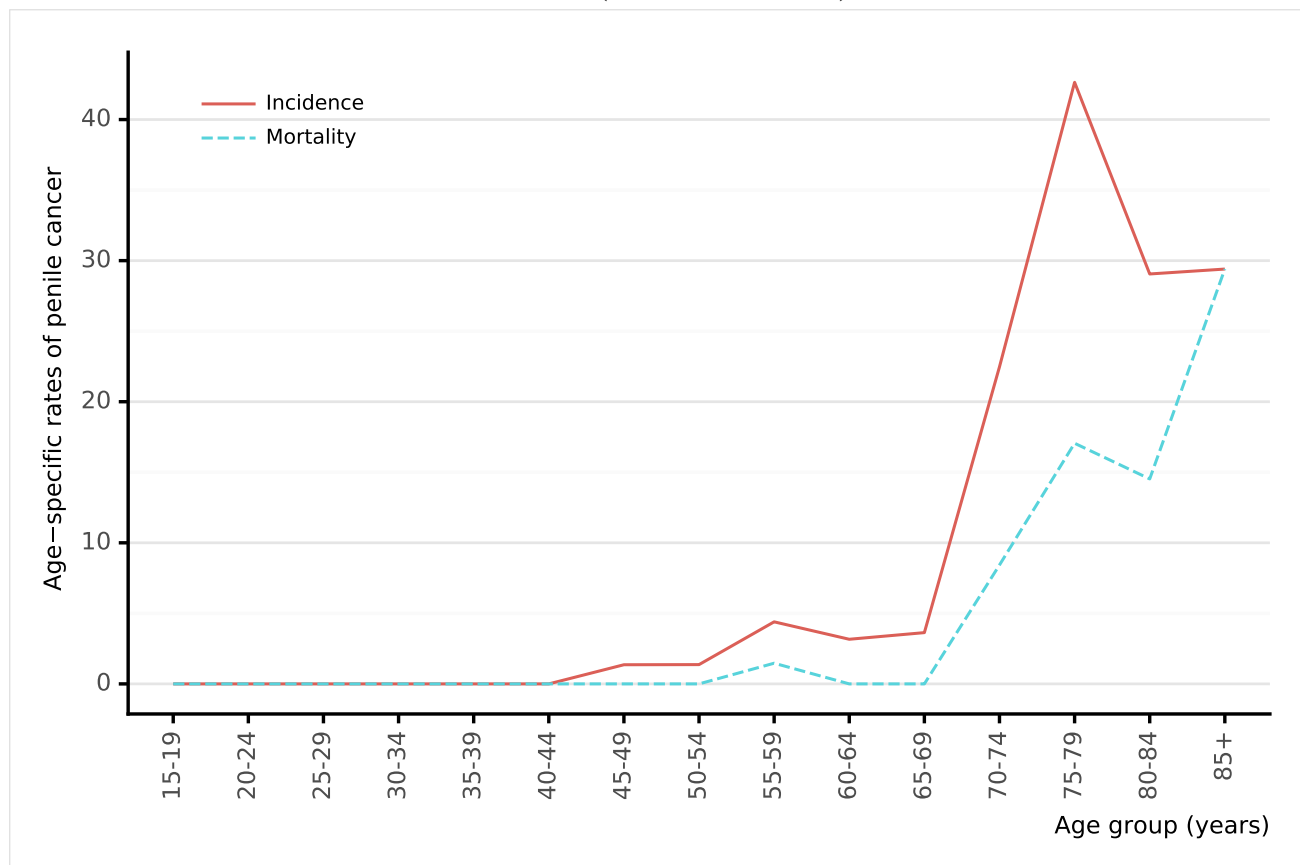
For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>

Data Sources:

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].

### 3.4.4.3 Penile cancer incidence and mortality comparison in Republic of North Macedonia

Figure 35: Comparison of age-specific penile cancer incidence and mortality rates in Republic of North Macedonia (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].



### 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 Republic of North Macedonia

Table 15: Oropharyngeal cancer incidence in Republic of North Macedonia (estimates for 2020)

Indicator	Republic of North Macedonia	Southern Europe	World
<b>MEN</b>			
Annual number of new cancer cases	13	2,941	79,045
Uncertainty intervals of new cancer cases [95% UI]	[5-32]	[2,484-3,483]	[72,769-85,862]
Crude incidence rate sa <sup>b</sup>	1.25	3.92	2.01
Age-standardized incidence rate sa <sup>b</sup>	0.77	2.11	1.79
Cumulative risk (%) at 75 years old <sup>a</sup>	0.09	0.27	0.22
<b>WOMEN</b>			
Annual number of new cancer cases	2	770	19,367
Uncertainty intervals of new cancer cases [95% UI]	[0-17]	[547-1,084]	[16,279-23,041]
Crude incidence rate sa <sup>c</sup>	0.19	0.98	0.50
Age-standardized incidence rate sa <sup>c</sup>	0.08	0.45	0.40
Cumulative risk (%) at 75 years old <sup>a</sup>	0.0	0.06	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.

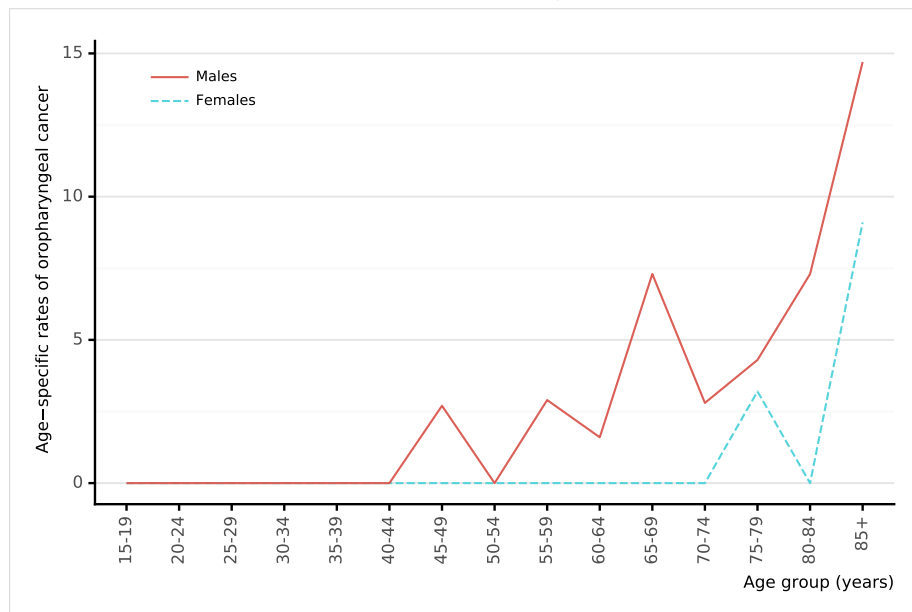
<sup>b</sup> Rates per 100,000 men per year.

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

**Data Sources:**

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 36: Age-specific incidence rates of oropharyngeal cancer in Republic of North Macedonia (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>

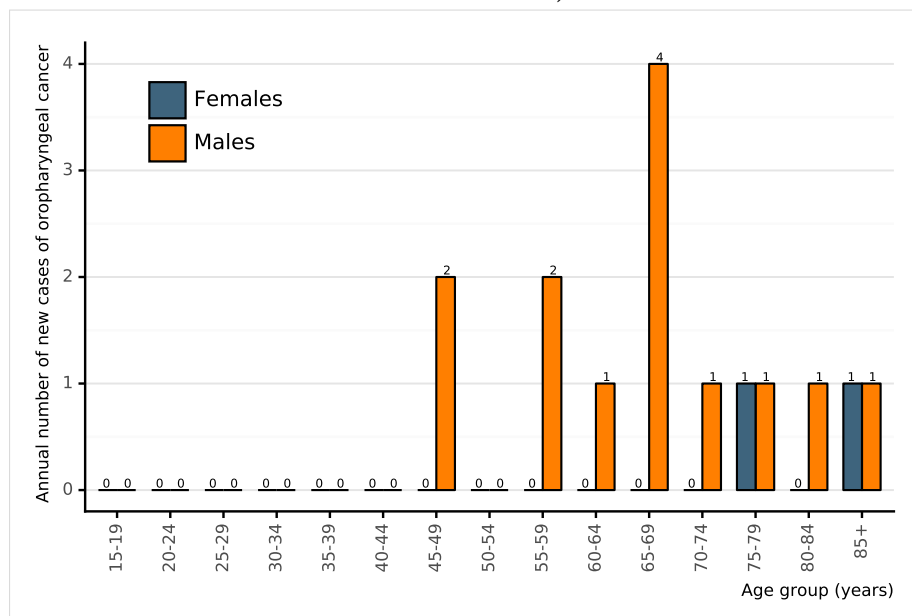
<sup>a</sup> Rates per 100,000 men per year.

<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: <https://gco.iarc.fr/today>, accessed [27 January 2021].

Figure 37: Annual number of new cases of oropharyngeal cancer in Republic of North Macedonia (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:

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].

### 3.5.1.2 Oropharyngeal cancer mortality in Republic of North Macedonia

Table 16: Oropharyngeal cancer mortality in Republic of North Macedonia (estimates for 2020)

Indicator	Republic of North Macedonia	Southern Europe	World
<b>MEN</b>			
Annual number of deaths	9	1,605	39,590
Uncertainty intervals of mortality cancer cases [95% UI]	[4-19]	[1,446-1,782]	[35,255-44,458]
Crude mortality rate sa <sup>b</sup>	0.86	2.14	1.01
Age-standardized mortality rate sa <sup>b</sup>	0.52	1.07	0.89
Cumulative risk (%) at 75 years old <sup>a</sup>	0.07	0.13	0.11
<b>WOMEN</b>			
Annual number of deaths	1	393	8,553
Uncertainty intervals of mortality cancer cases [95% UI]	[0-6]	[324-478]	[6,684-10,945]
Crude mortality rate sa <sup>c</sup>	0.10	0.50	0.22
Age-standardized mortality rate sa <sup>c</sup>	0.03	0.19	0.17
Cumulative risk (%) at 75 years old <sup>a</sup>	0.0	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.

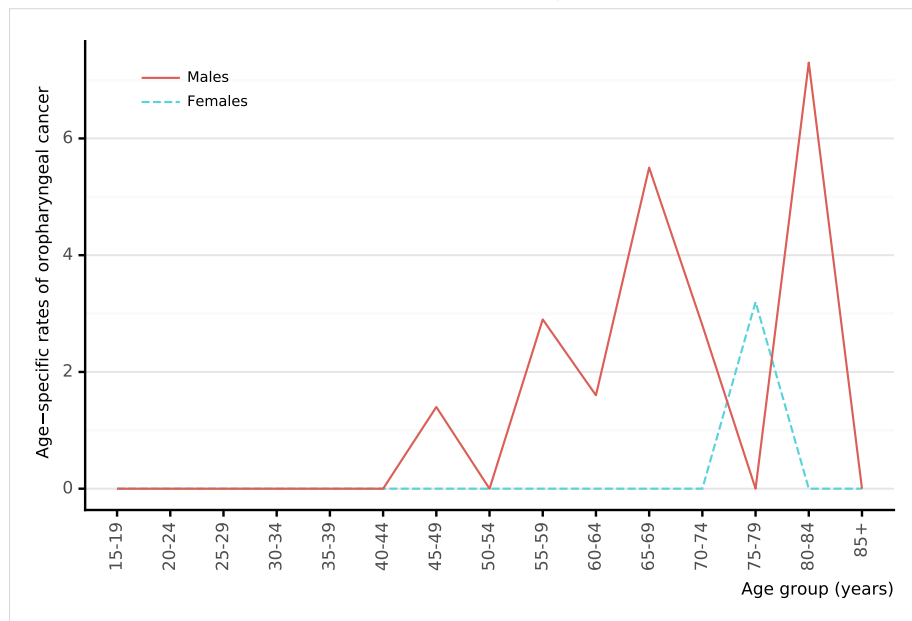
<sup>b</sup> Rates per 100,000 men per year.

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

**Data 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 38: Age-specific mortality rates of oropharyngeal cancer in Republic of North Macedonia (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>

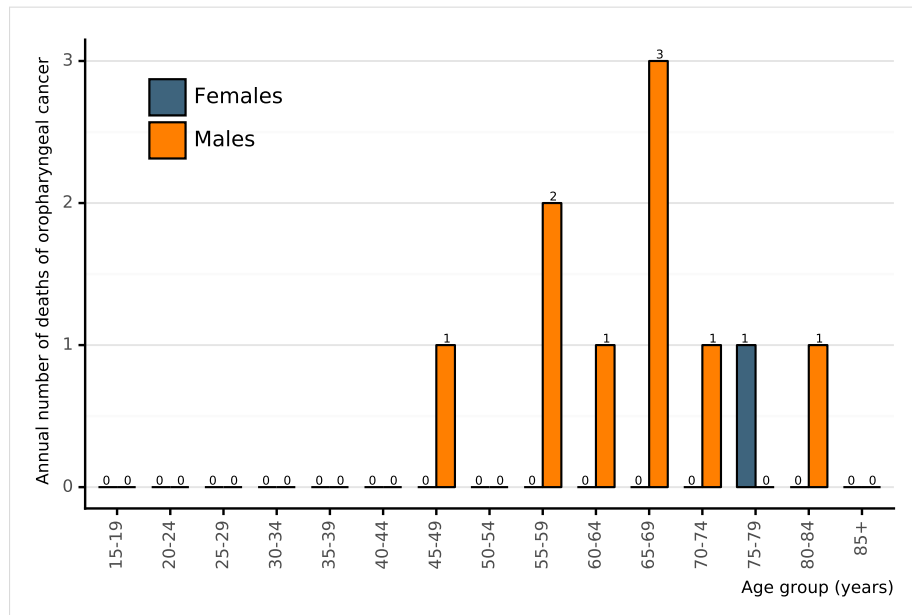
<sup>a</sup> Rates per 100,000 men per year.

<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: <https://gco.iarc.fr/today>, accessed [27 January 2021].

Figure 39: Annual number of deaths of oropharyngeal cancer in Republic of North Macedonia (estimates for 2020)



Data accessed on 27 Jan 2021

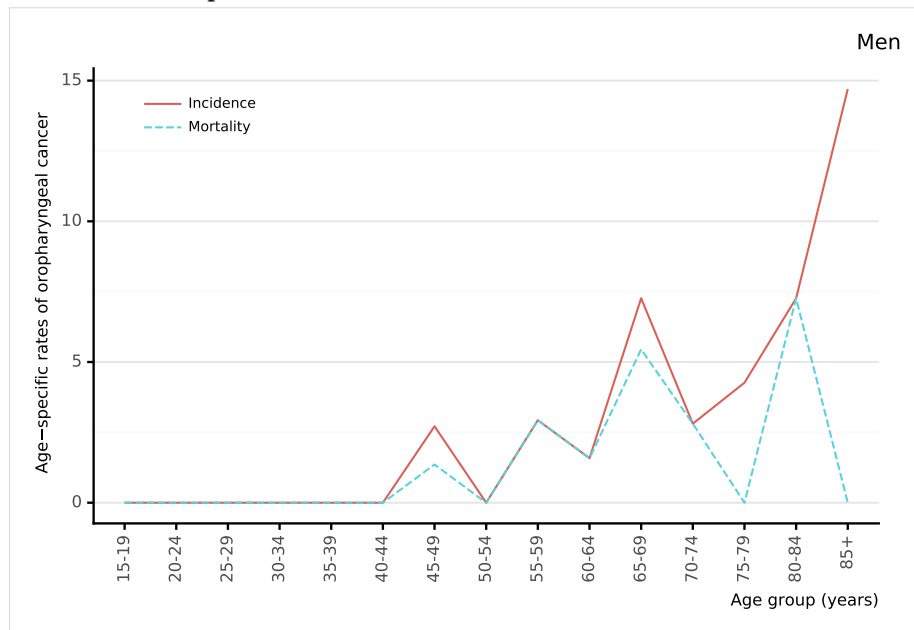
For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>

Data Sources:

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].

### 3.5.1.3 Oropharyngeal cancer incidence and mortality comparison in Republic of North Macedonia

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



Data accessed on 27 Jan 2021

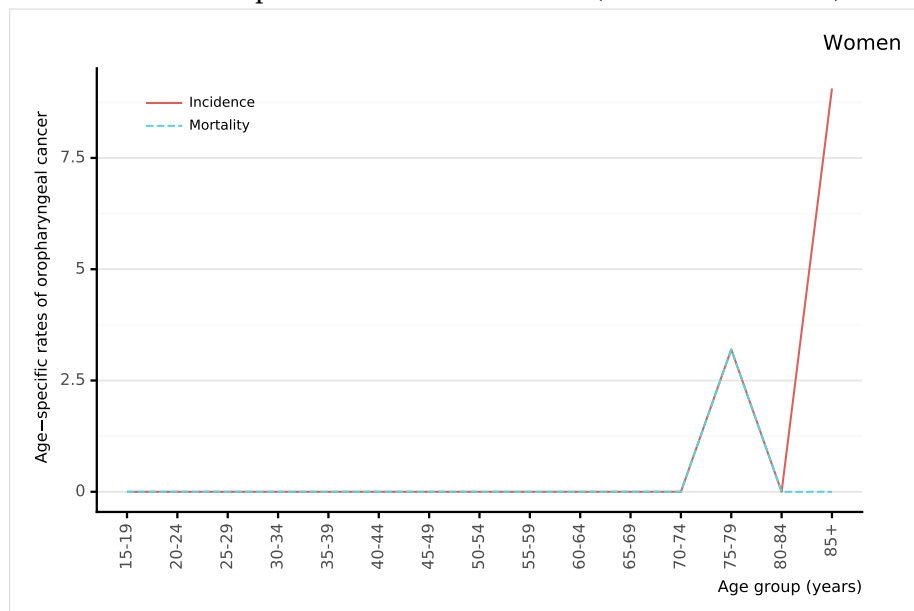
For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>

<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 Republic of North Macedonia (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].

### 3.5.2 Oral cavity cancer

#### 3.5.2.1 Oral cavity cancer incidence in Republic of North Macedonia

Table 17: Oral cavity cancer incidence in Republic of North Macedonia (estimates for 2020)

Indicator	Republic of North Macedonia	Southern Europe	World
<b>MEN</b>			
Annual number of new cancer cases	38	7,926	264,211
Uncertainty intervals of new cancer cases [95% UI]	[20-70]	[7,159-8,776]	[251,153-277,948]
Crude incidence rate sa <sup>b</sup>	3.65	10.6	6.72
Age-standardized incidence rate sa <sup>b</sup>	2.15	5.18	5.96
Cumulative risk (%) at 75 years old <sup>a</sup>	0.26	0.61	0.68
<b>WOMEN</b>			
Annual number of new cancer cases	14	4,461	113,502
Uncertainty intervals of new cancer cases [95% UI]	[4-44]	[3,852-5,166]	[105,599-121,997]
Crude incidence rate sa <sup>c</sup>	1.34	5.69	2.94
Age-standardized incidence rate sa <sup>c</sup>	0.59	2.08	2.28
Cumulative risk (%) at 75 years old <sup>a</sup>	0.07	0.23	0.26

**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.

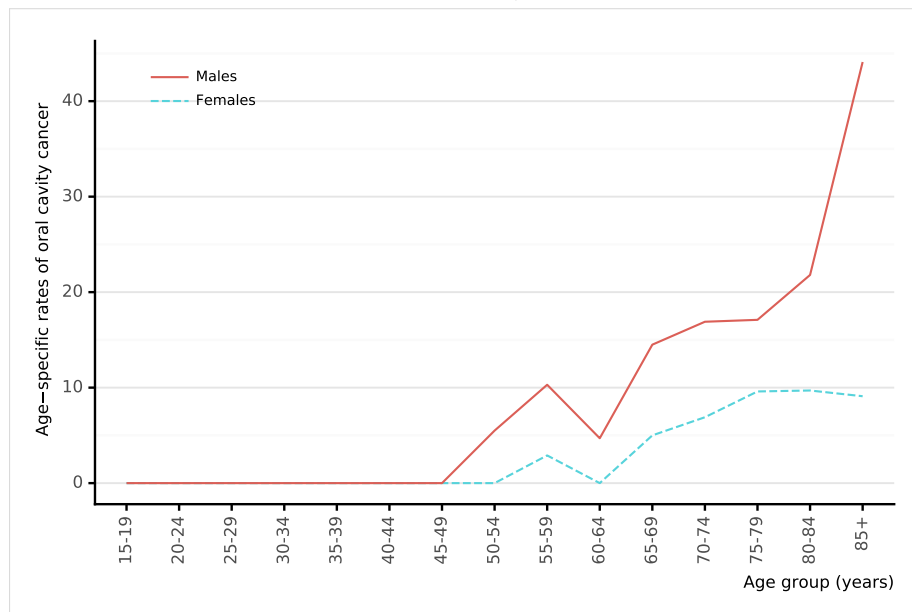
<sup>b</sup> Rates per 100,000 men per year.

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

**Data Sources:**

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 42: Age-specific incidence rates of oral cavity cancer in Republic of North Macedonia (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>

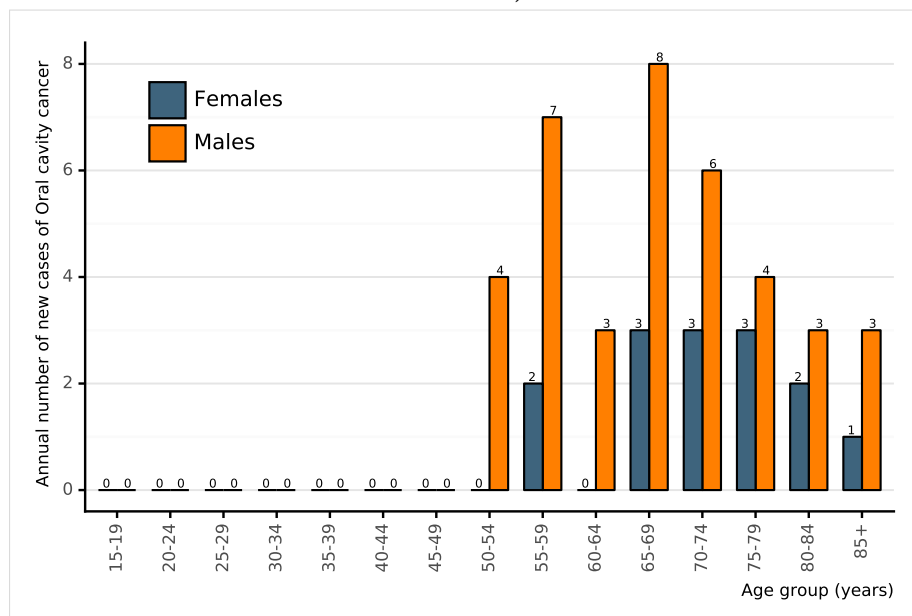
<sup>a</sup> Rates per 100,000 men per year.

<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: <https://gco.iarc.fr/today>, accessed [27 January 2021].

Figure 43: Annual number of new cases of oral cavity cancer in Republic of North Macedonia (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:

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].

### 3.5.2.2 Oral cavity cancer incidence and mortality comparison in Republic of North Macedonia

Table 18: Oral cavity cancer mortality in Republic of North Macedonia (estimates for 2020)

Indicator	Republic of North Macedonia	Southern Europe	World
<b>MEN</b>			
Annual number of deaths	22	2,751	125,022
Uncertainty intervals of mortality cancer cases [95% UI]	[13-37]	[2,537-2,983]	[116,573-134,084]
Crude mortality rate sa <sup>b</sup>	2.11	3.67	3.18
Age-standardized mortality rate sa <sup>b</sup>	1.26	1.67	2.82
Cumulative risk (%) at 75 years old <sup>a</sup>	0.14	0.20	0.32
<b>WOMEN</b>			
Annual number of deaths	6	1,483	52,735
Uncertainty intervals of mortality cancer cases [95% UI]	[2-16]	[1,340-1,641]	[47,690-58,313]
Crude mortality rate sa <sup>c</sup>	0.58	1.89	1.36
Age-standardized mortality rate sa <sup>c</sup>	0.25	0.56	1.04
Cumulative risk (%) at 75 years old <sup>a</sup>	0.03	0.06	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.

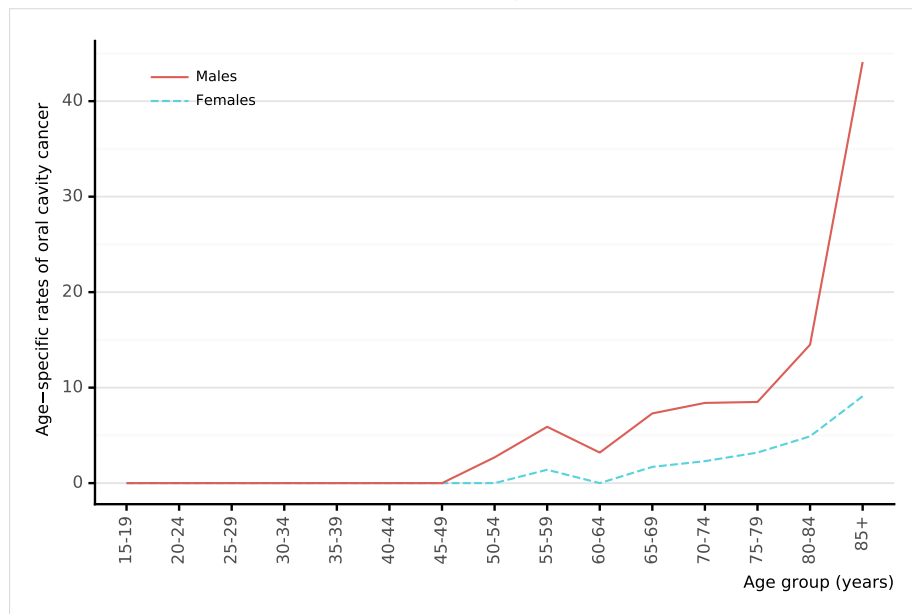
<sup>c</sup> Rates per 100,000 women per year.

**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 44: Age-specific mortality rates of oral cavity cancer in Republic of North Macedonia (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>

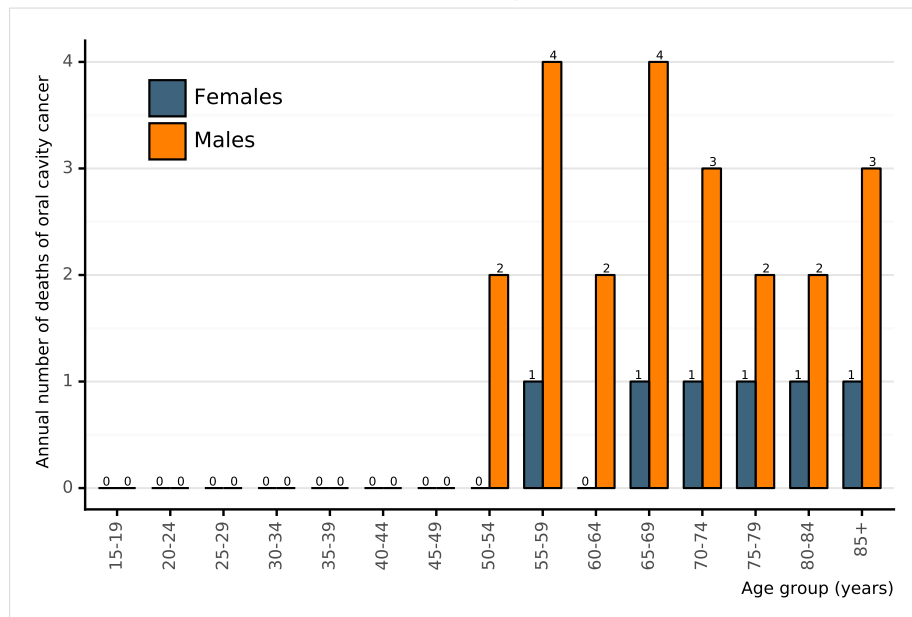
<sup>a</sup> Rates per 100,000 men per year.

<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: <https://gco.iarc.fr/today>, accessed [27 January 2021].

Figure 45: Annual number of deaths of oral cavity cancer in Republic of North Macedonia (estimates for 2020)



Data accessed on 27 Jan 2021

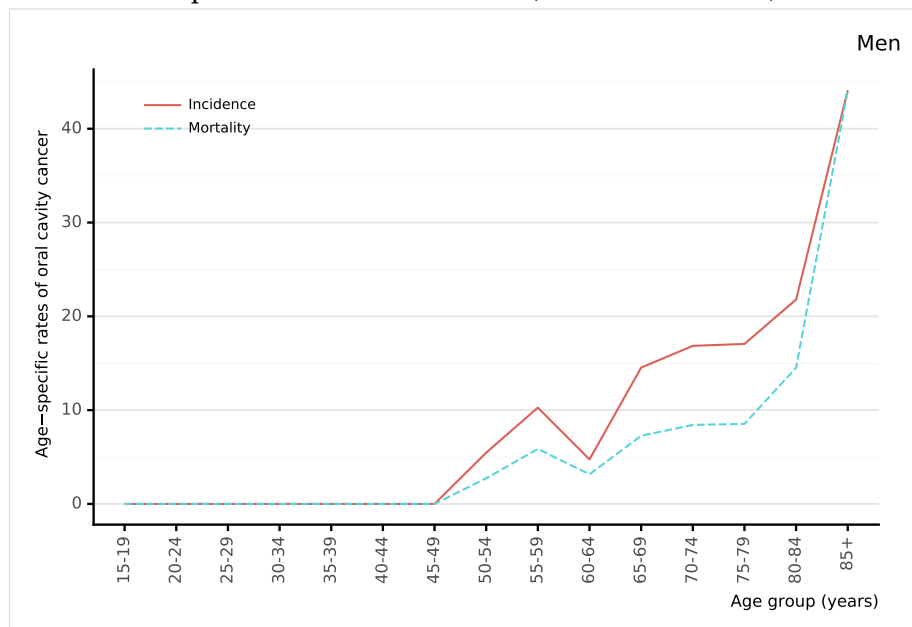
For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>

Data Sources:

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].

### 3.5.2.3 Oral cavity cancer incidence and mortality comparison in Republic of North Macedonia

Figure 46: Comparison of age-specific oral cavity cancer incidence and mortality rates among men in Republic of North Macedonia (estimates for 2020)



**Data accessed on 27 Jan 2021**

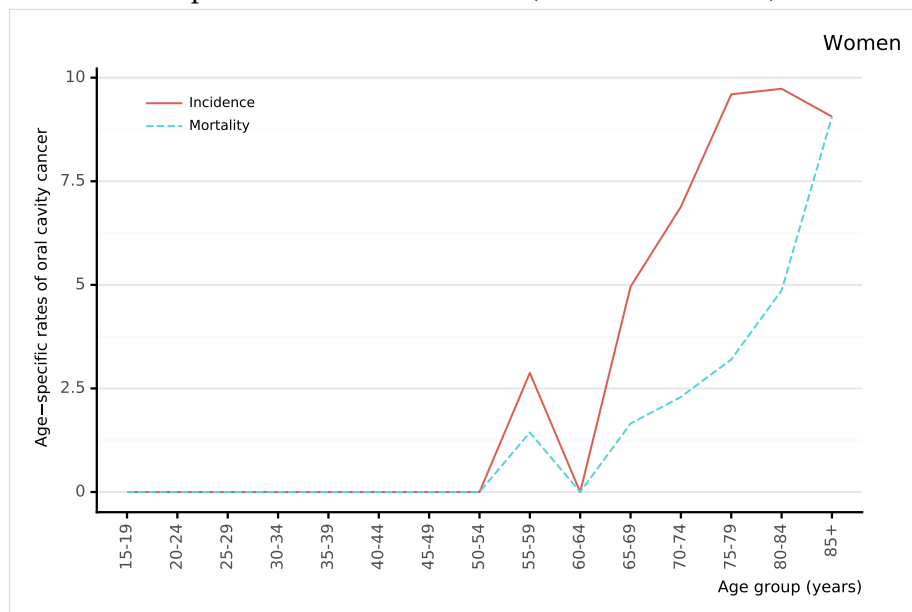
For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>

<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 47: Comparison of age-specific oral cavity cancer incidence and mortality rates among women in Republic of North Macedonia (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].

### 3.5.3 Laryngeal cancer

#### 3.5.3.1 Laryngeal cancer incidence in Republic of North Macedonia

Table 19: Laryngeal cancer incidence in Republic of North Macedonia (estimates for 2020)

Indicator	Republic of North Macedonia	Southern Europe	World
<b>MEN</b>			
Annual number of new cancer cases	166	8,174	160,265
Uncertainty intervals of new cancer cases [95% UI]	[97-285]	[7,471-8,944]	[150,633-170,513]
Crude incidence rate sa <sup>b</sup>	15.9	10.9	4.08
Age-standardized incidence rate sa <sup>b</sup>	10.2	5.38	3.59
Cumulative risk (%) at 75 years old <sup>a</sup>	1.21	0.67	0.45
<b>WOMEN</b>			
Annual number of new cancer cases	15	1,101	24,350
Uncertainty intervals of new cancer cases [95% UI]	[6-40]	[848-1,429]	[20,845-28,444]
Crude incidence rate sa <sup>c</sup>	1.44	1.40	0.63
Age-standardized incidence rate sa <sup>c</sup>	0.82	0.64	0.49
Cumulative risk (%) at 75 years old <sup>a</sup>	0.10	0.08	0.06

**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.

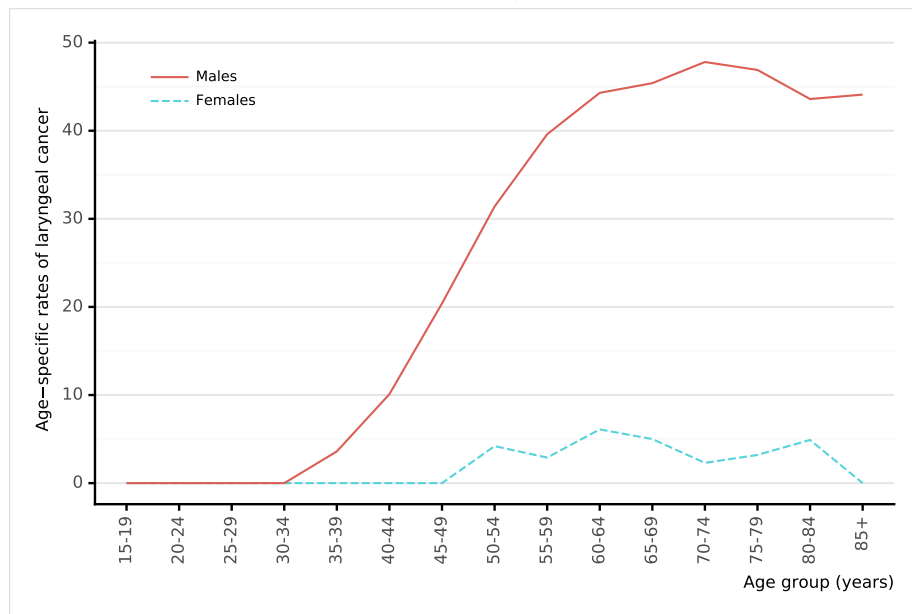
<sup>b</sup> Rates per 100,000 men per year.

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

**Data Sources:**

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 48: Age-specific incidence rates of laryngeal cancer in Republic of North Macedonia (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>

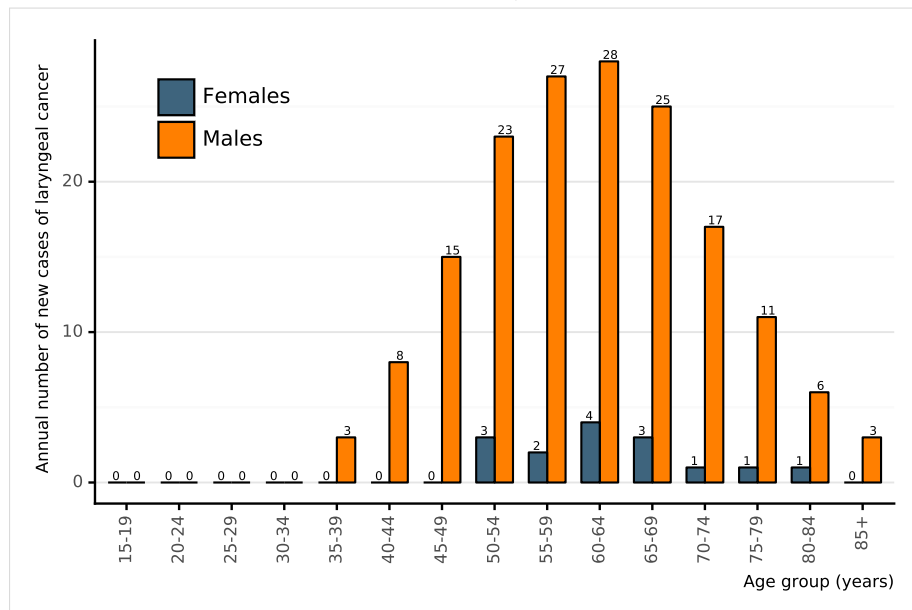
<sup>a</sup> Rates per 100,000 men per year.

<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: <https://gco.iarc.fr/today>, accessed [27 January 2021].

Figure 49: Annual number of new cases of laryngeal cancer in Republic of North Macedonia (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:

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].

### 3.5.3.2 Laryngeal cancer incidence and mortality comparison in Republic of North Macedonia

Table 20: Laryngeal cancer mortality in Republic of North Macedonia (estimates for 2020)

Indicator	Republic of North Macedonia	Southern Europe	World
<b>MEN</b>			
Annual number of deaths	94	4,054	85,351
Uncertainty intervals of mortality cancer cases [95% UI]	[62-142]	[3,790-4,337]	[78,895-92,335]
Crude mortality rate sa <sup>b</sup>	9.02	5.41	2.17
Age-standardized mortality rate sa <sup>b</sup>	5.49	2.31	1.89
Cumulative risk (%) at 75 years old <sup>a</sup>	0.69	0.28	0.23
<b>WOMEN</b>			
Annual number of deaths	9	475	14,489
Uncertainty intervals of mortality cancer cases [95% UI]	[4-20]	[391-577]	[11,902-17,639]
Crude mortality rate sa <sup>c</sup>	0.86	0.61	0.37
Age-standardized mortality rate sa <sup>c</sup>	0.45	0.22	0.28
Cumulative risk (%) at 75 years old <sup>a</sup>	0.06	0.03	0.03

**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.

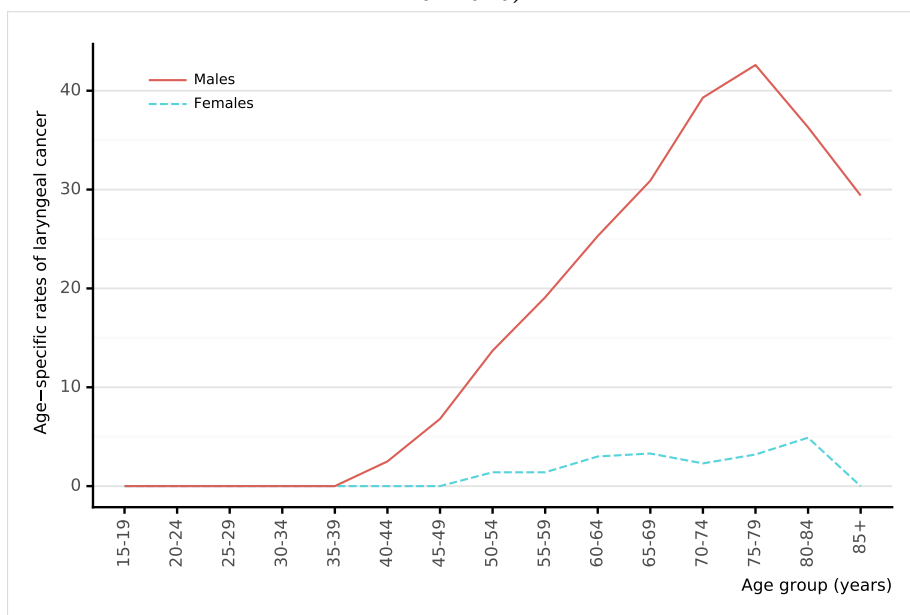
<sup>b</sup> Rates per 100,000 men per year.

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

**Data 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 50: Age-specific mortality rates of laryngeal cancer in Republic of North Macedonia (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>

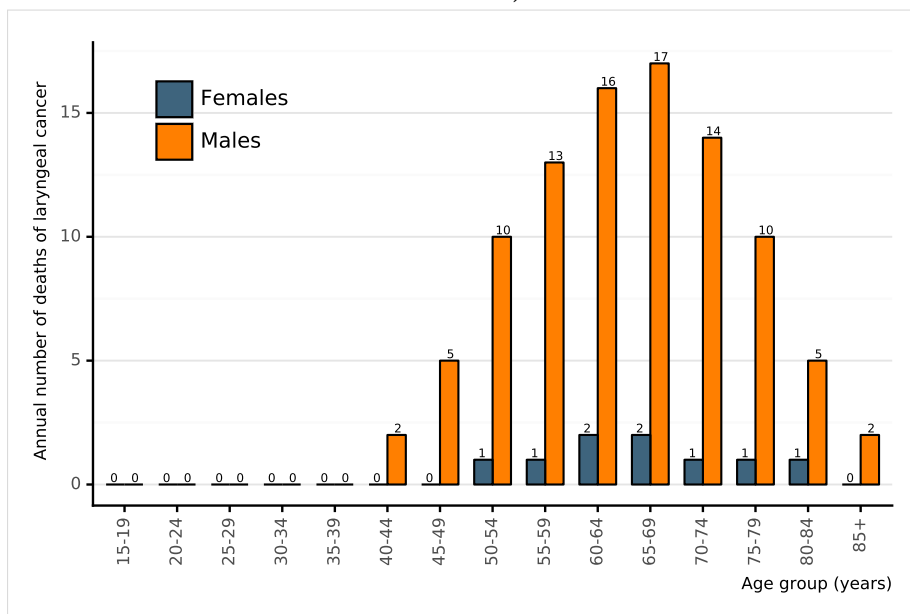
<sup>a</sup> Rates per 100,000 men per year.

<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: <https://gco.iarc.fr/today>, accessed [27 January 2021].

Figure 51: Annual number of deaths of of laryngeal cancer in Republic of North Macedonia (estimates for 2020)



Data accessed on 27 Jan 2021

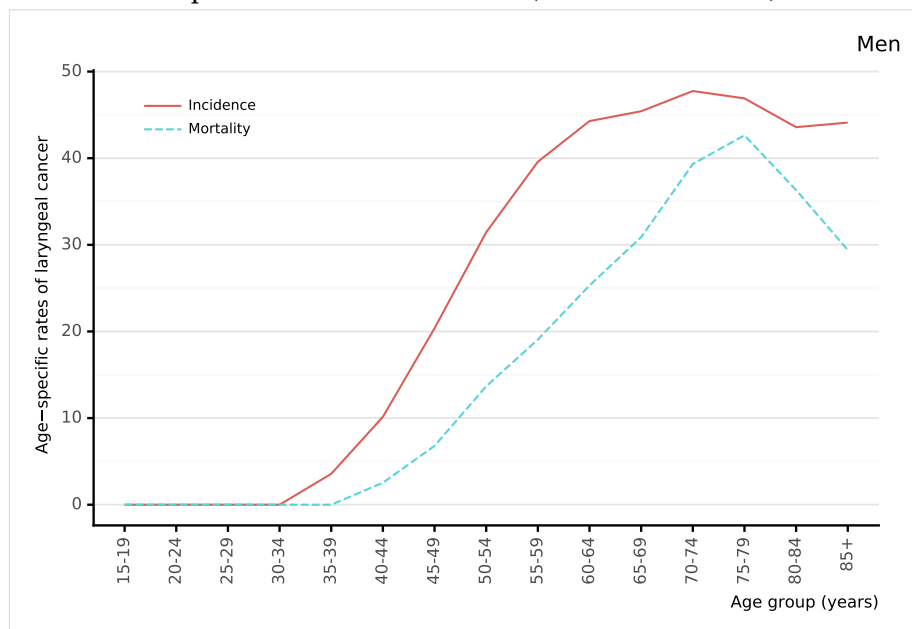
For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>

Data Sources:

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].

### 3.5.3.3 Laryngeal cancer incidence and mortality comparison in Republic of North Macedonia

Figure 52: Comparison of age-specific laryngeal cancer incidence and mortality rates among men in Republic of North Macedonia (estimates for 2020)



Data accessed on 27 Jan 2021

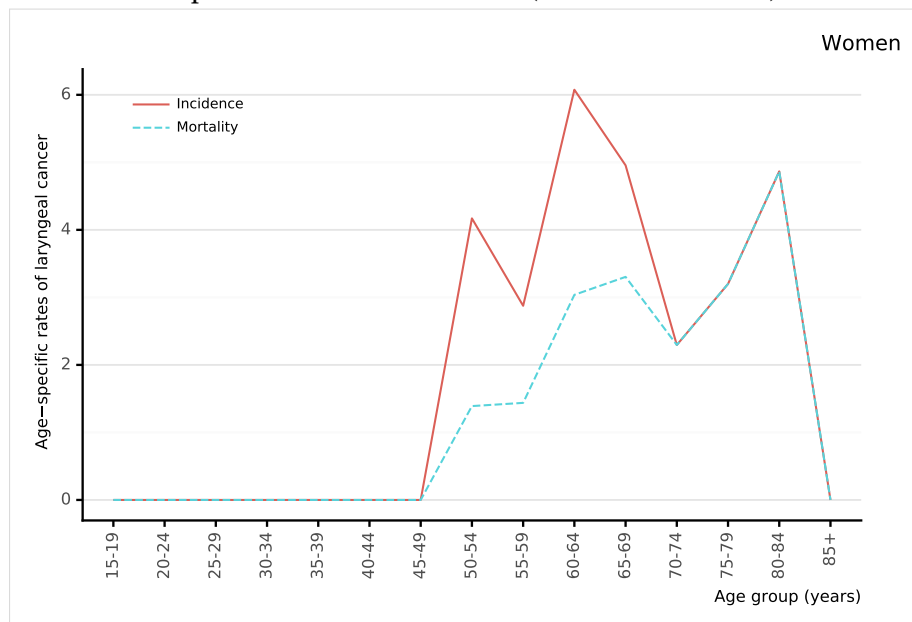
For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>

<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 53: Comparison of age-specific laryngeal cancer incidence and mortality rates among women in Republic of North Macedonia (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].

## 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).

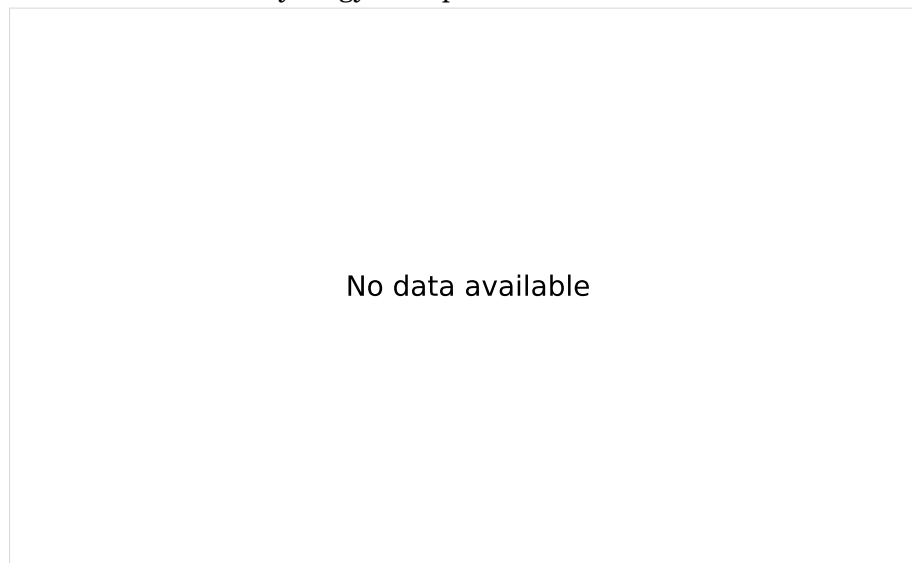
#### **Methods: Prevalence and type distribution of human papillomavirus in cervical carcinoma, low-grade cervical lesions, high-grade cervical lesions and normal cytology: systematic review and meta-analysis**

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 Republic of North Macedonia

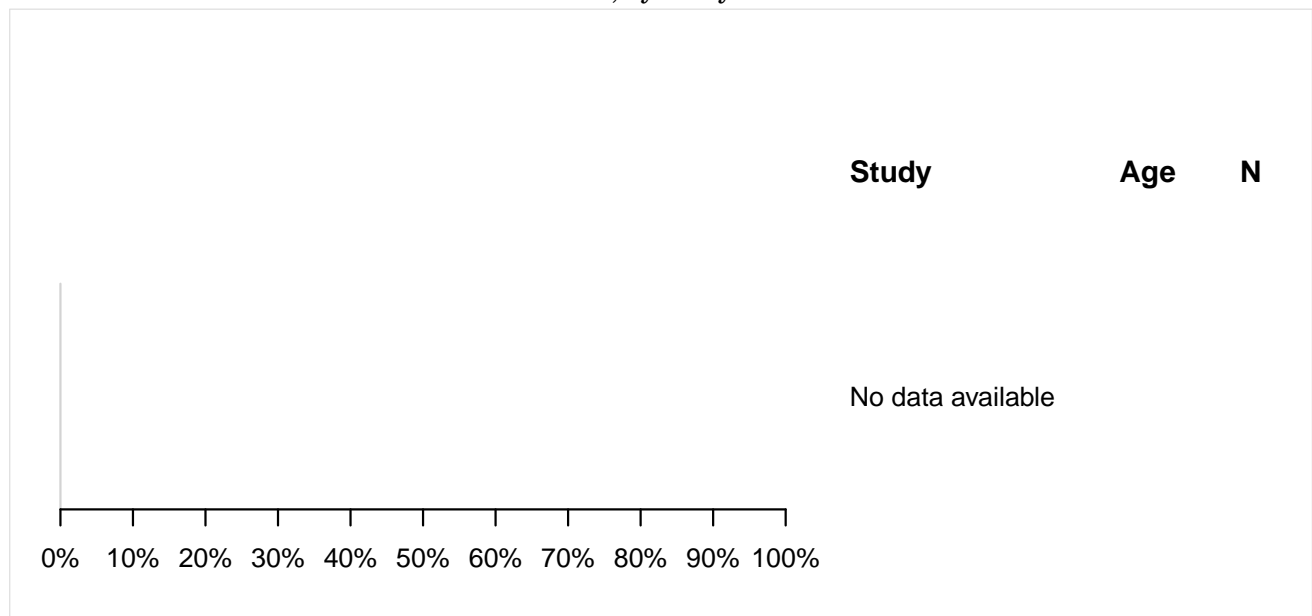


Data updated on 30 Jun 2015 (data as of 30 Jun 2014)

**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 Republic of North Macedonia, 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)

<sup>a</sup> 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

Table 21: Prevalence of HPV16 and HPV18 by cytology in Republic of North Macedonia

	No. tested	HPV 16/18 Prevalence % (95% CI)
Normal cytology <sup>1</sup>	-	--
Low-grade lesions <sup>2</sup>	-	--
High-grade lesions <sup>3</sup>	-	--
Cervical cancer <sup>4</sup>	-	--

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)

<sup>a</sup> Number of women tested

<sup>b</sup> 95% Confidence Interval

Data Sources:

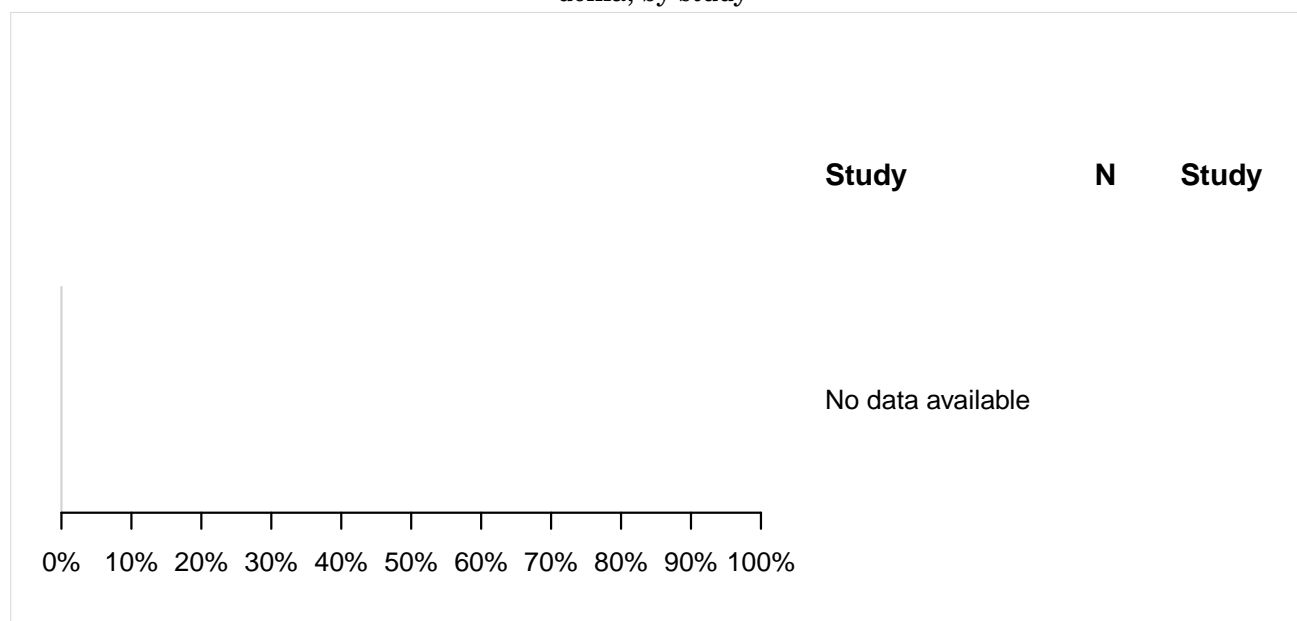
<sup>1</sup> Based on systematic reviews and meta-analysis performed by ICO. The ICO HPV Information Centre has updated data until November 2014. Reference publications: 1) Bruni L, J Infect Dis 2010; 202: 1789. 2) De Sanjosé S, Lancet Infect Dis 2007; 7: 453

<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.

<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) 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 Republic of North Macedonia, by study



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

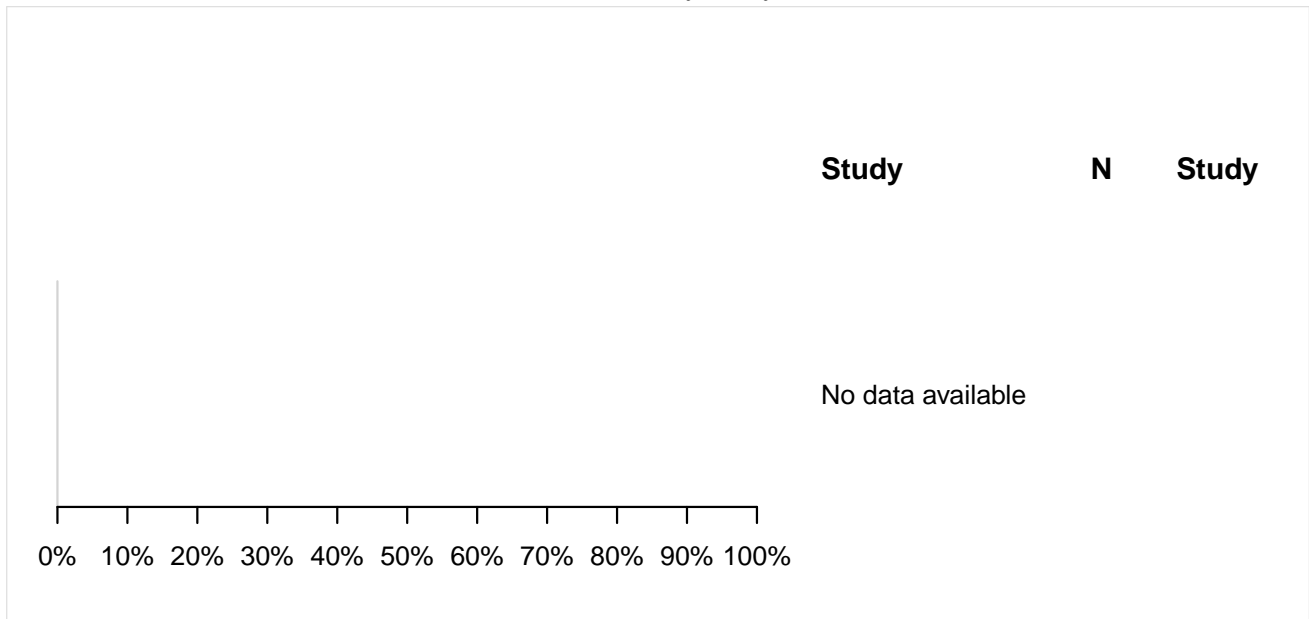
The samples for HPV testing come from cervical specimens (fresh/fixed biopsies or exfoliated cells)

<sup>a</sup> 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 Republic of North Macedonia, by study



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

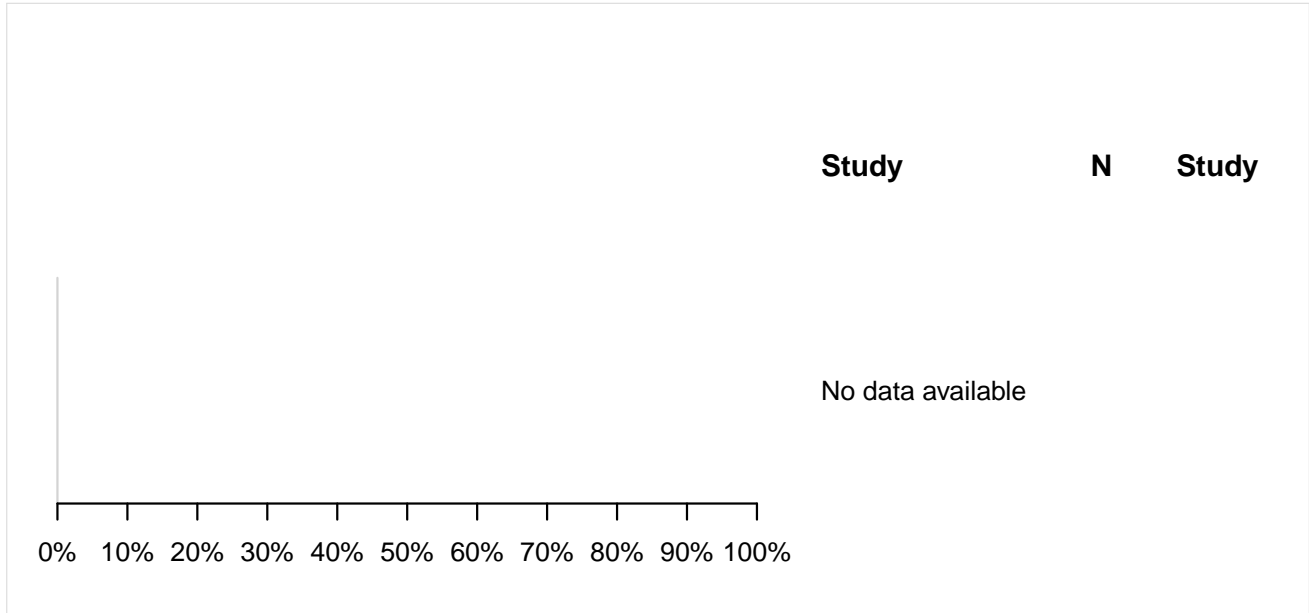
The samples for HPV testing come from cervical specimens (fresh/fixed biopsies or exfoliated cells)

<sup>a</sup> 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 Republic of North Macedonia, by study



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

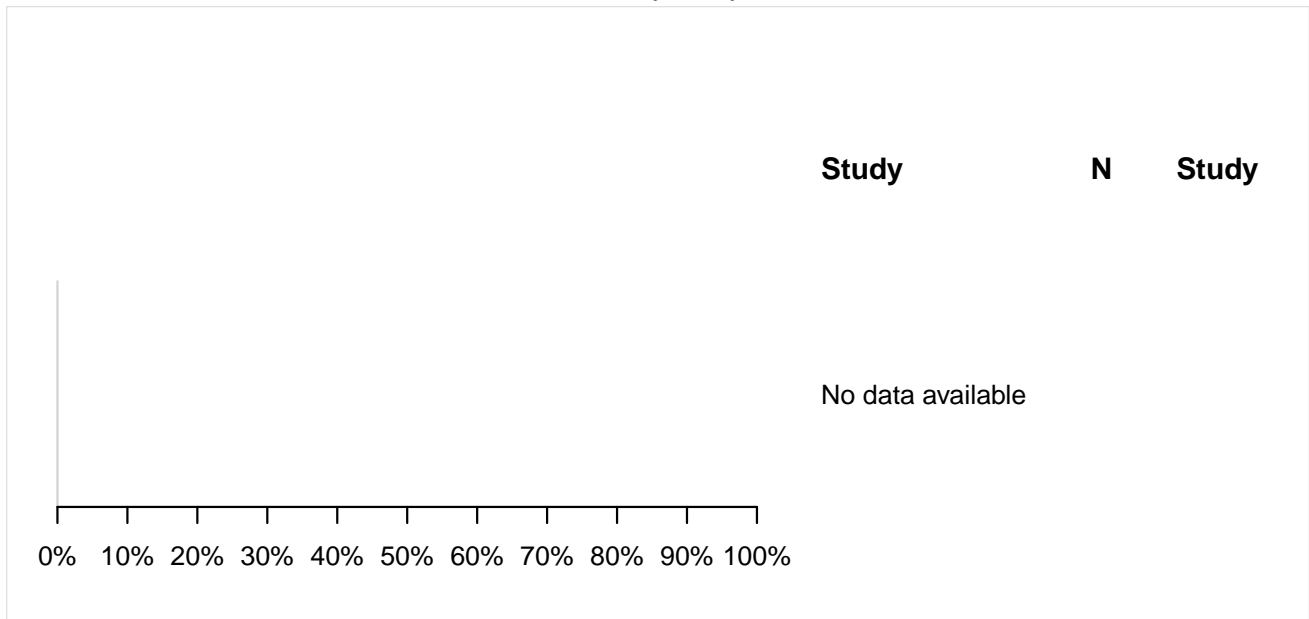
The samples for HPV testing come from cervical specimens (fresh/fixed biopsies or exfoliated cells)

<sup>a</sup> 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 Republic of North Macedonia, by study



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

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) 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 Republic of North Macedonia 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>1</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.

<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) Smith JS, *Int J Cancer* 2007;121:621 3) 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) Clifford GM, *Cancer Epidemiol Biomarkers Prev* 2005;14:1157

<sup>4</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

Figure 61: Comparison of the ten most frequent HPV oncogenic types in Republic of North Macedonia among women with invasive cervical cancer by histology

No data available

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

\* No data available. No more types than shown were tested or were positive

Data Sources:

<sup>1</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>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.

Table 22: Type-specific HPV prevalence in women with normal cervical cytology, precancerous cervical lesions and invasive cervical cancer in Republic of North Macedonia

HPV Type	Normal cytology <sup>1</sup>		Low-grade lesions <sup>2</sup>		High-grade lesions <sup>3</sup>		Cervical cancer <sup>4</sup>	
	No. tested	HPV Prev % (95% CI)	No. tested	HPV Prev % (95% CI)	No. tested	HPV Prev % (95% CI)	No. tested	HPV Prev % (95% CI)
<b>ONCOGENIC HPV TYPES</b>								
<b>High-risk HPV types</b>								
16	-	-	-	-	-	-	-	-
18	-	-	-	-	-	-	-	-
31	-	-	-	-	-	-	-	-
33	-	-	-	-	-	-	-	-
35	-	-	-	-	-	-	-	-
39	-	-	-	-	-	-	-	-
45	-	-	-	-	-	-	-	-
51	-	-	-	-	-	-	-	-
52	-	-	-	-	-	-	-	-
56	-	-	-	-	-	-	-	-
58	-	-	-	-	-	-	-	-
59	-	-	-	-	-	-	-	-
<b>Probable/possible carcinogen</b>								
26	-	-	-	-	-	-	-	-
30	-	-	-	-	-	-	-	-
34	-	-	-	-	-	-	-	-
53	-	-	-	-	-	-	-	-
66	-	-	-	-	-	-	-	-
67	-	-	-	-	-	-	-	-
68	-	-	-	-	-	-	-	-
69	-	-	-	-	-	-	-	-
70	-	-	-	-	-	-	-	-
73	-	-	-	-	-	-	-	-
82	-	-	-	-	-	-	-	-
85	-	-	-	-	-	-	-	-
97	-	-	-	-	-	-	-	-
<b>LOW RISK HPV TYPES</b>								
6	-	-	-	-	-	-	-	-
11	-	-	-	-	-	-	-	-
32	-	-	-	-	-	-	-	-
40	-	-	-	-	-	-	-	-
42	-	-	-	-	-	-	-	-
43	-	-	-	-	-	-	-	-
44	-	-	-	-	-	-	-	-
54	-	-	-	-	-	-	-	-
55	-	-	-	-	-	-	-	-
57	-	-	-	-	-	-	-	-
61	-	-	-	-	-	-	-	-
62	-	-	-	-	-	-	-	-
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)

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.<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) 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 23: Type-specific HPV prevalence among invasive cervical cancer cases in Republic of North Macedonia by histology

HPV Type	Any Histology		Squamous cell carcinoma		Adenocarcinoma		Unspecified	
	No. tested	HPV Prev % (95% CI)	No. tested	HPV Prev % (95% CI)	No. tested	HPV Prev % (95% CI)	No. tested	HPV Prev % (95% CI)
<b>ONCOGENIC HPV TYPES</b>								
<b>High-risk HPV types</b>								
16	-	-	-	-	-	-	-	-
18	-	-	-	-	-	-	-	-
31	-	-	-	-	-	-	-	-
33	-	-	-	-	-	-	-	-
35	-	-	-	-	-	-	-	-
39	-	-	-	-	-	-	-	-
45	-	-	-	-	-	-	-	-
51	-	-	-	-	-	-	-	-
52	-	-	-	-	-	-	-	-
56	-	-	-	-	-	-	-	-
58	-	-	-	-	-	-	-	-
59	-	-	-	-	-	-	-	-
<b>Probable/possible carcinogen</b>								
26	-	-	-	-	-	-	-	-
30	-	-	-	-	-	-	-	-
34	-	-	-	-	-	-	-	-
53	-	-	-	-	-	-	-	-
66	-	-	-	-	-	-	-	-
67	-	-	-	-	-	-	-	-
68	-	-	-	-	-	-	-	-
69	-	-	-	-	-	-	-	-
70	-	-	-	-	-	-	-	-
73	-	-	-	-	-	-	-	-
82	-	-	-	-	-	-	-	-
85	-	-	-	-	-	-	-	-
97	-	-	-	-	-	-	-	-
<b>LOW RISK HPV TYPES</b>								
6	-	-	-	-	-	-	-	-
11	-	-	-	-	-	-	-	-
32	-	-	-	-	-	-	-	-
40	-	-	-	-	-	-	-	-
42	-	-	-	-	-	-	-	-
43	-	-	-	-	-	-	-	-
44	-	-	-	-	-	-	-	-
54	-	-	-	-	-	-	-	-
55	-	-	-	-	-	-	-	-
57	-	-	-	-	-	-	-	-
61	-	-	-	-	-	-	-	-
62	-	-	-	-	-	-	-	-
64	-	-	-	-	-	-	-	-
71	-	-	-	-	-	-	-	-
72	-	-	-	-	-	-	-	-
74	-	-	-	-	-	-	-	-
81	-	-	-	-	-	-	-	-
83	-	-	-	-	-	-	-	-
84	-	-	-	-	-	-	-	-
86	-	-	-	-	-	-	-	-
87	-	-	-	-	-	-	-	-
89	-	-	-	-	-	-	-	-
90	-	-	-	-	-	-	-	-
91	-	-	-	-	-	-	-	-

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

<sup>b</sup> 95% Confidence Interval

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) 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 Republic of North Macedonia

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

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

<sup>a</sup> Number of women tested

<sup>b</sup> 95% Confidence Interval

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.

## **4.2 HPV burden in anogenital cancers other than cervix**

### **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 Republic of North Macedonia are presented.

Table 25: Studies on HPV prevalence among anal cancer cases in Republic of North Macedonia (male and female)

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

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 Republic of North Macedonia

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

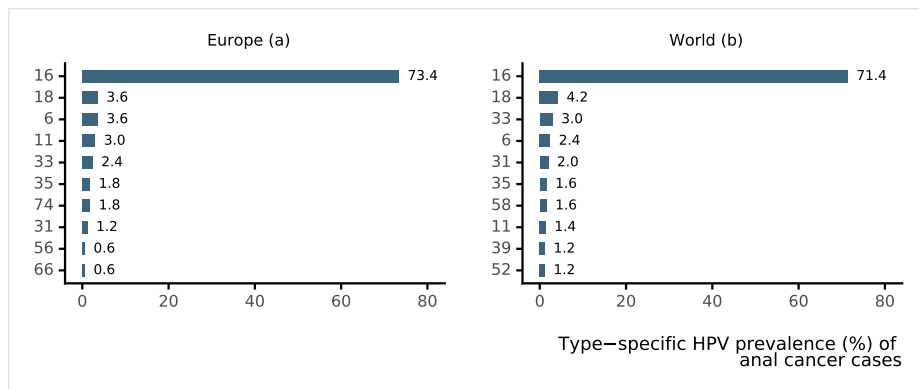
AIN 2/3: Anal intraepithelial neoplasia of grade 2/3

<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 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)

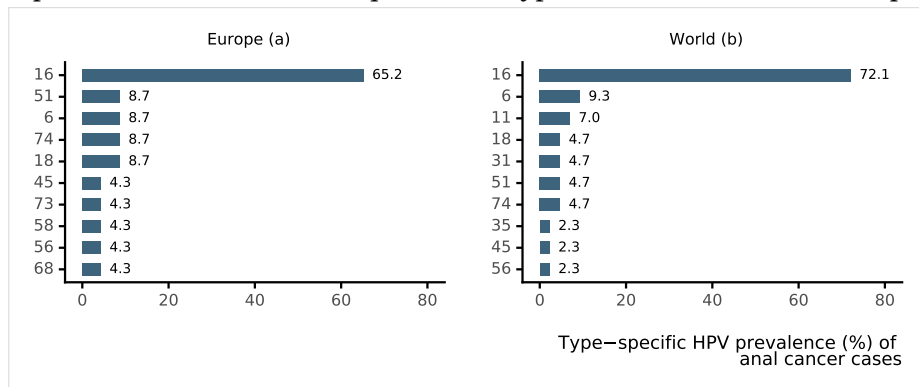
<sup>a</sup> Includes cases from Bosnia-Herzegovina, Czech Republic, France, Germany, Poland, Portugal, Slovenia, Spain and United Kingdom

<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

<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)

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 Republic of North Macedonia are presented.

Table 27: Studies on HPV prevalence among vulvar cancer cases in Republic of North Macedonia

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

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 28: Studies on HPV prevalence among VIN 2/3 cases in Republic of North Macedonia

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

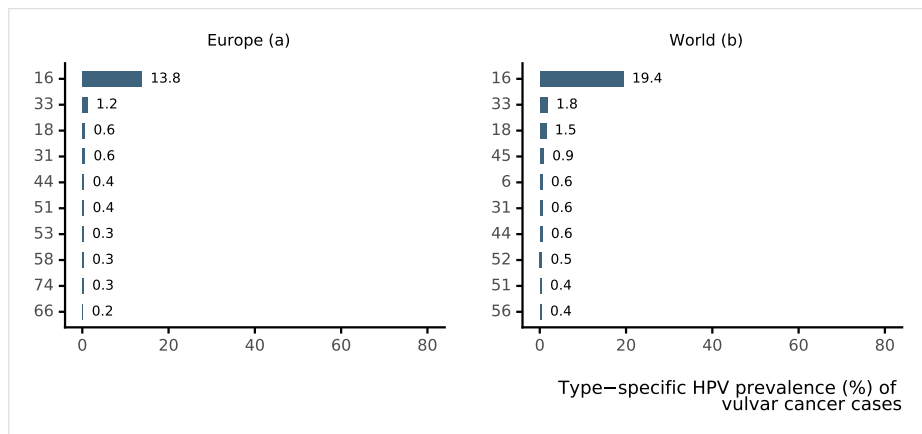
VIN 2/3: Vulvar intraepithelial neoplasia of grade 2/3

<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)

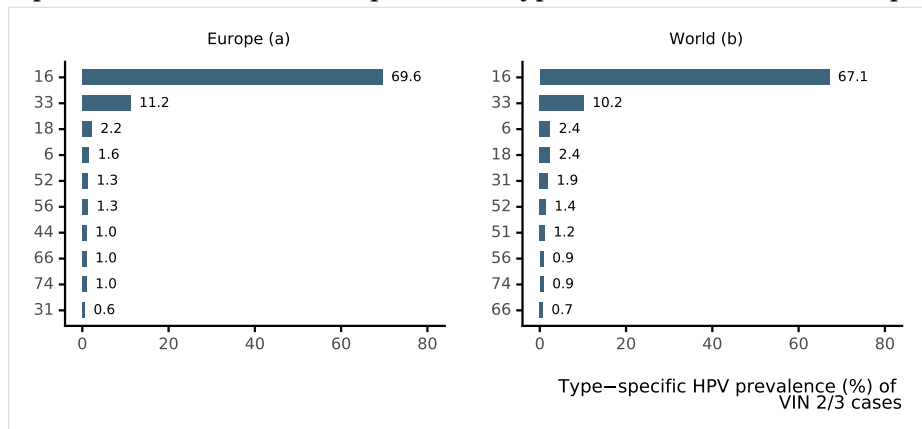
<sup>a</sup> Includes cases from Austria, Belarus, Bosnia-Herzegovina, Czech Republic, France, Germany, Greece, Italy, Poland, Portugal, Spain and United Kingdom.

<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, 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.

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 Republic of North Macedonia are presented.

Table 29: Studies on HPV prevalence among vaginal cancer cases in Republic of North Macedonia

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

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 Republic of North Macedonia

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

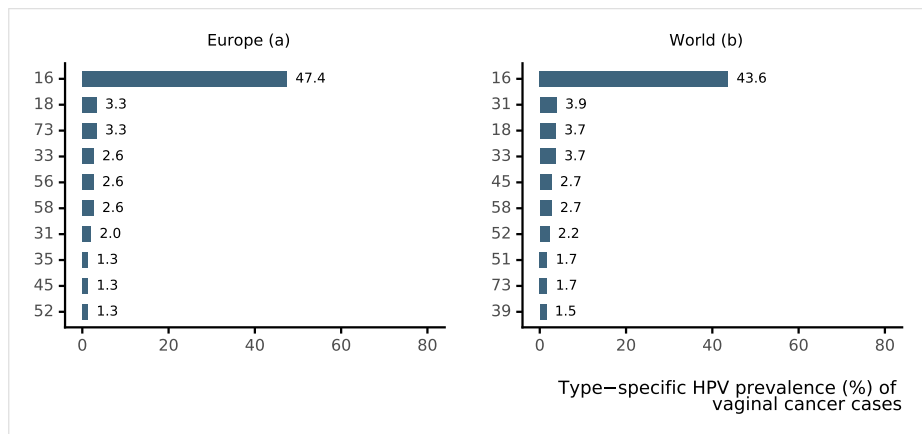
VAIN 2/3: Vaginal intraepithelial neoplasia of grade 2/3

<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 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)

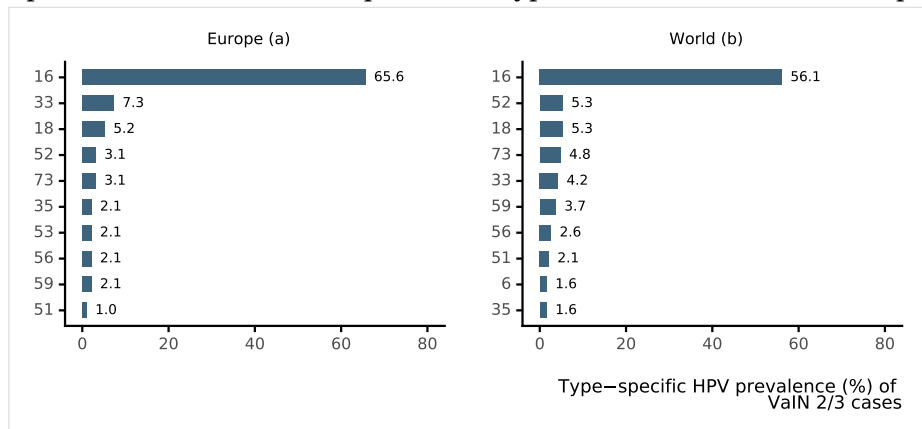
<sup>a</sup> Includes cases from Austria, Belarus, Czech Republic, France, Germany, Greece, Poland, Spain and United Kingdom.

<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.

<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); 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.

#### 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 Republic of North Macedonia are presented.

Table 31: Studies on HPV prevalence among penile cancer cases in Republic of North Macedonia

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

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

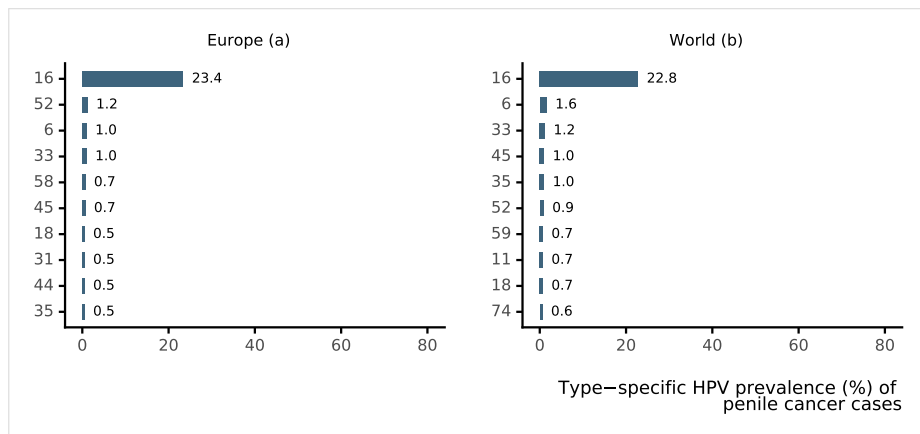
DBH: Dot Blot Hybridization; EIA: Enzyme ImmunoAssay; HC2: Hybrid Capture 2; ISH: In Situ Hybridization; LBA: Line-Blot Assay; LiPA: Line Probe Assay; PCR: Polymerase Chain Reaction; RFLP: Restriction Fragment Length Polymorphism; RLBH: Reverse Line Blot Hybridization; RT-PCR: Real Time Polymerase Chain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

<sup>a</sup> 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)

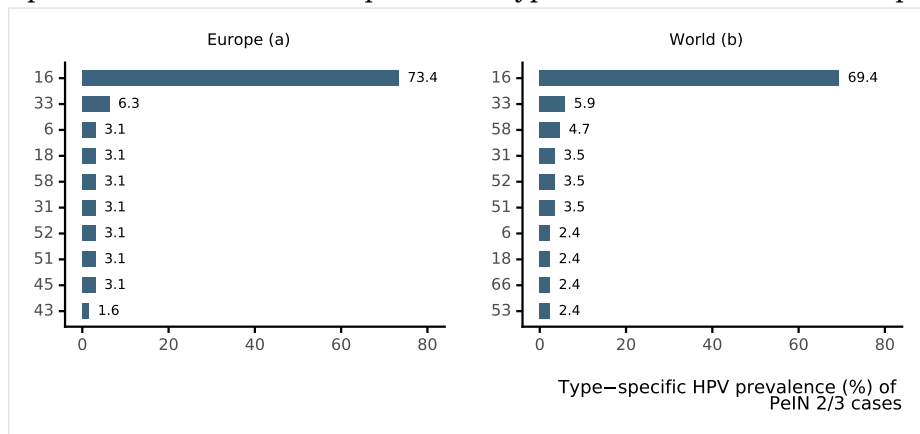
<sup>a</sup> Includes cases from Czech Republic, France, Greece, Poland, Portugal, Spain and United Kingdom

<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:

Alemanly 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 Republic of North Macedonia 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.

Table 33: Studies on HPV prevalence among men in Republic of North Macedonia

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

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 Republic of North Macedonia

Study	Anatomic sites samples	HPV detection method	Population	Age (years)	No. Tested	HPV Prevalence	
						%	(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 Republic of North Macedonia is presented.

### 4.4.1 Burden of oral HPV infection in healthy population

Table 35: Studies on oral HPV prevalence among healthy in Republic of North Macedonia

Study	Specimen collection method / anatomic site	HPV detection 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>
-	-	-	-	-	-	-	-	-	-

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

<sup>b</sup> NS: not specified

<sup>c</sup> number of cases tested for HPV DNA

<sup>d</sup> 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

Table 36: Studies on HPV prevalence among cases of oral cavity cancer in Republic of North Macedonia

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

Table 37: Studies on HPV prevalence among cases of oropharyngeal cancer in Republic of North Macedonia

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

Table 38: Studies on HPV prevalence among cases of hypopharyngeal or laryngeal cancer in Republic of North Macedonia

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

Table 39: Factors contributing to cervical carcinogenesis (cofactors) in Republic of North Macedonia

INDICATOR		MALE	FEMALE	TOTAL
<b>Smoking</b>				
Smoking of any tobacco adjusted prevalence (%) [95% UI]	Current <sup>a</sup>	- [—]	- [—]	- [—]
	Daily <sup>b</sup>	- [—]	- [—]	- [—]
Cigarette smoking adjusted prevalence (%) [95% UI]	Current <sup>c</sup>	- [—]	- [—]	- [—]
	Daily <sup>d</sup>	- [—]	- [—]	- [—]
<b>Parity</b>				
Total fertility rate per woman		-	1.5	-
	15-19 yrs	-	15.8	-
	20-24 yrs	-	60.4	-
	25-29 yrs	-	97.3	-
Age-specific fertility rate (per 1000 women)	30-34 yrs	-	75.4	-
	35-39 yrs	-	32.6	-
	40-44 yrs	-	5.8	-
	45-49 yrs	-	0.3	-
<b>Hormonal contraception</b>				
Oral contraceptive use (%) among women who are married or in union		-	1.60	-
Injectable contraception use (%) among women who are married or in union		-	0.20	-
Implant contraceptive use (%) among women who are married or in union		-	0	-
<b>HIV</b>				
Estimated percent of adults aged 15-49 who are living with HIV [95% UI]		<0.1 [<0.1-<0.1]	<0.1 [<0.1-<0.1]	<0.1 [<0.1-<0.1]
Estimated percent of young adults aged 15-24 who are living with HIV [95% UI]		<0.1 [<0.1-<0.1]	<0.1 [<0.1-<0.1]	- [—]
HIV prevalence (%) among sex workers		0	0	0
HIV prevalence (%) among men who have sex with men		5.4000001	-	5.4000001
Estimated number of people living with HIV [95% UI]		-	-	<500 [<500-<1000]
Estimated number of adults (15+ yrs) living with HIV [95% UI]		<500 [<500-<500]	<100 [<100-<100]	<500 [<500-<1000]
Estimated number of AIDS-related deaths [95% UI]		-	-	<100 [<100-<100]

### Data accessed on 12 Nov 2019

Crude adjusted prevalence (%) estimates of tobacco use among people aged  $\geq 15$  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.

<sup>d</sup> "Daily" means smoking every day at the time of the survey.

### 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/item/who-global-report-on-trends-in-prevalence-of-tobacco-use-2000-2025-third-edition>

Eurostat - Statistical office of the European Commission [web site]. Luxembourg: European Commission; 2017. Available at: <https://ec.europa.eu/eurostat/web/products-datasets/-/denofrate>. [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]

<sup>1</sup> <http://iph.mk/wp-content/uploads/2019/03/SW-2018.pdf>

<sup>2</sup> Respondent-Driven Sampling among MSM in the capital city, latest study in 2017.





## 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 Republic of North Macedonia are presented.

Table 40: Percentage of 15-year-olds who have had sexual intercourse in Republic of North Macedonia

Indicator	Male	Female
Percentage of 15-year-old subjects who report sexual intercourse	36.0	3.0

### 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](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 Republic of North Macedonia

Study <sup>b,1,a</sup>	Year/period	Birth cohort N	N	MALE		FEMALE		TOTAL
				Median age at first sex	N	Median age at first sex	N	Median age at first sex
Delva 2007	2004	1989-1993	418	15.5	232	16.3	-	-

### Data accessed on 16 Mar 2017

Please refer to original source for methods of estimation

<sup>a</sup> Data pertain to high school students in Bosnia (Sarajevo), the FYR of Macedonia (Skopje), and Serbia and Montenegro (Belgrade and Podgorica).

<sup>b</sup> Mean age at first sex.

### Data Sources:

<sup>1</sup> Delva W, Wuillaume F, Vansteelandt S, Claeys P, Verstraelen H, Temmerman M. Sexual behaviour and contraceptive use among youth in the Balkans. Eur J Contracept Reprod Health Care. 2007 Dec;12(4):309-316.

Table 42: Marriage patterns in Republic of North Macedonia

Indicator		Male	Female
Average age at first marriage <sup>1</sup>		26.7	25.5
Age-specific % of ever married <sup>2</sup>	15-19 years	1.48	4.3
	20-24 years	21.7	32.52
	25-29 years	62.02	68.33
	30-34 years	83.62	88.92
	35-39 years	92.24	94.01
	40-44 years	95.87	96.76
	45-49 years	97.36	98.6
	50-54 years	97.93	-
	55-59 years	98.15	-
	60-64 years	98.4	-
	65-69 years	98.52	-
	70-74 years	98.52	-
	+75	98.58	-

**Data accessed on 20 Feb 2020**

Please refer to original source for methods of estimation.

<sup>a</sup> 1994 Census<sup>b</sup> UNSD<sup>c</sup> 2011 MICS<sup>d</sup> MICS

Data Sources:

<sup>1</sup> 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 Republic of North Macedonia

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 Republic of North Macedonia

Study	Year/Period	Birth cohort	N surveyed	FEMALE	
				N sexual active	% among sexually active
-	-	-	-	-	-

**Data accessed on 8 Aug 2013**

Please refer to original source for methods of estimation

## 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 Republic of North Macedonia.

### 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.

Table 45: Main characteristics of cervical cancer screening in Republic of North Macedonia

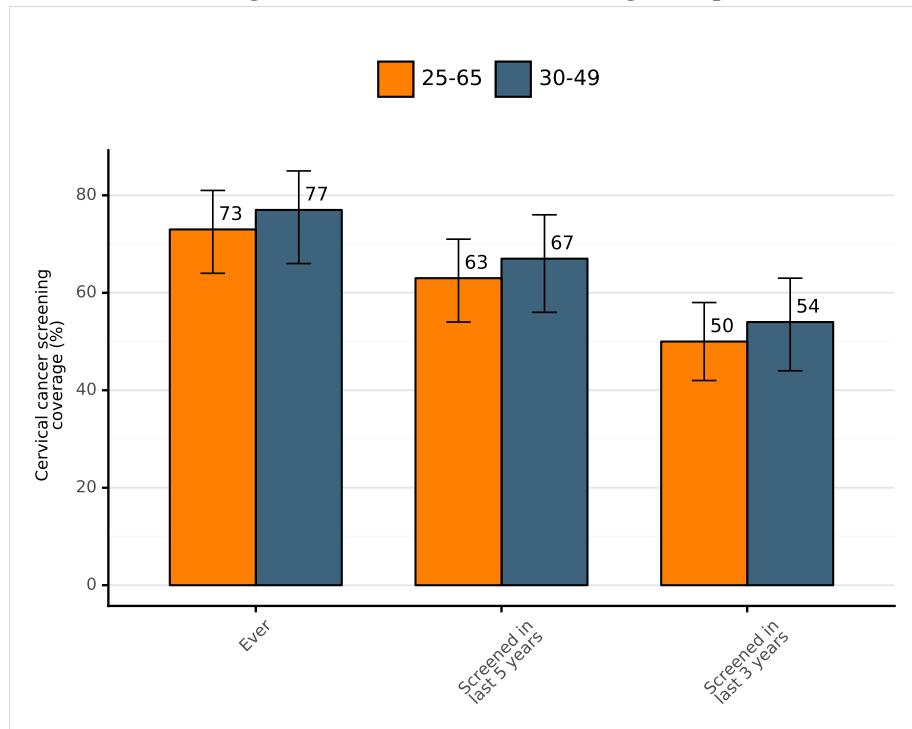
Region	Existence of official national recommendations	Starting year of current recommendations	Active invitation to screening	Screening ages (years), primary screening test used, and screening interval or frequency of screenings
Macedonia, TFYR	Yes	2006	Yes	24-60 (cytology, 3 years)

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):e11115.

Figure 70: Estimated coverage\* of cervical cancer screening in Republic of North Macedonia



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

Table 46: National HPV Immunization programme in Republic of North Macedonia

	Female	Male
HPV vaccination programme	Introduced	Not Available/Not Introduced
Year of introduction	2009	-
Year of estimation of HPV vaccination coverage	2021	-
HPV coverage – first dose (%)	32	-
HPV coverage – last dose (%)	21	-

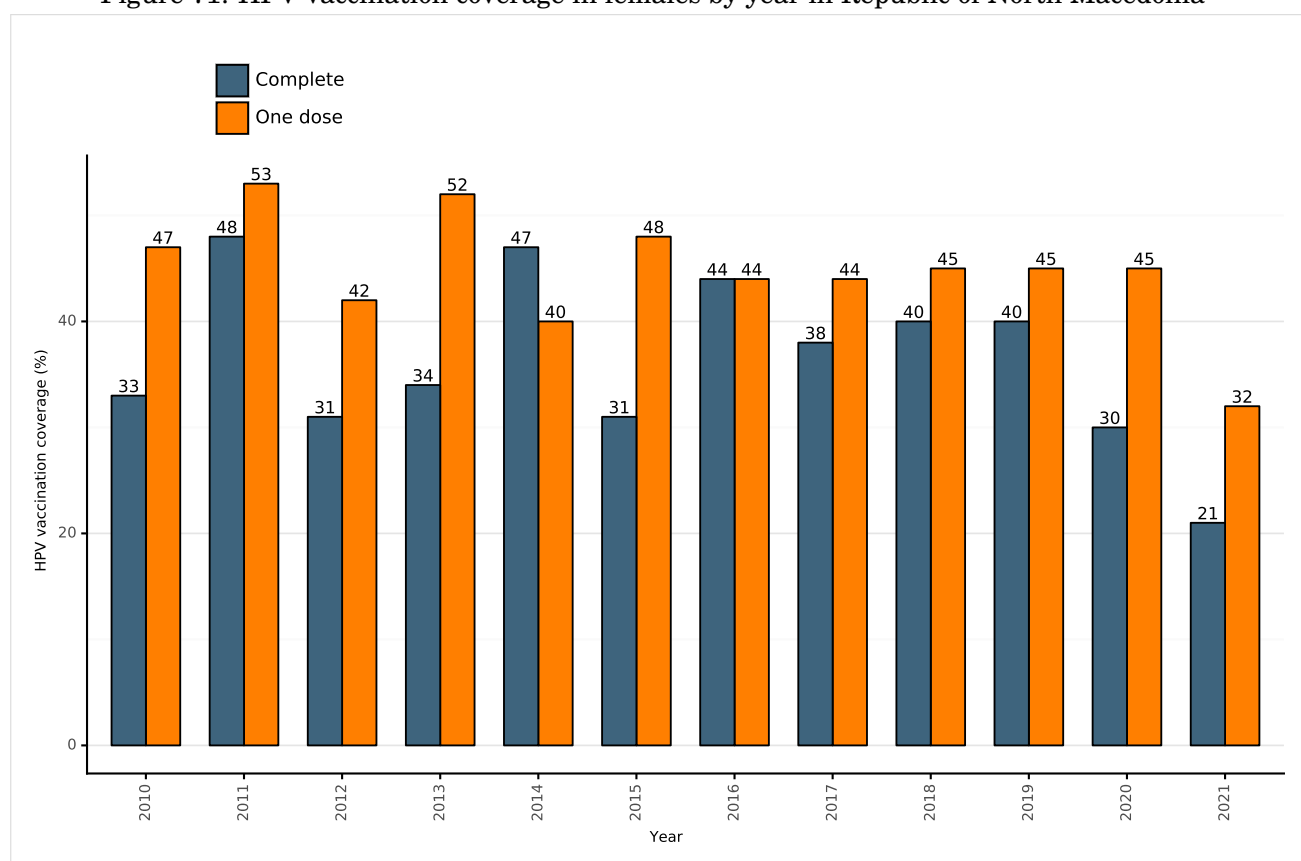
Data accessed on 24 Oct 2022

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 Republic of North Macedonia



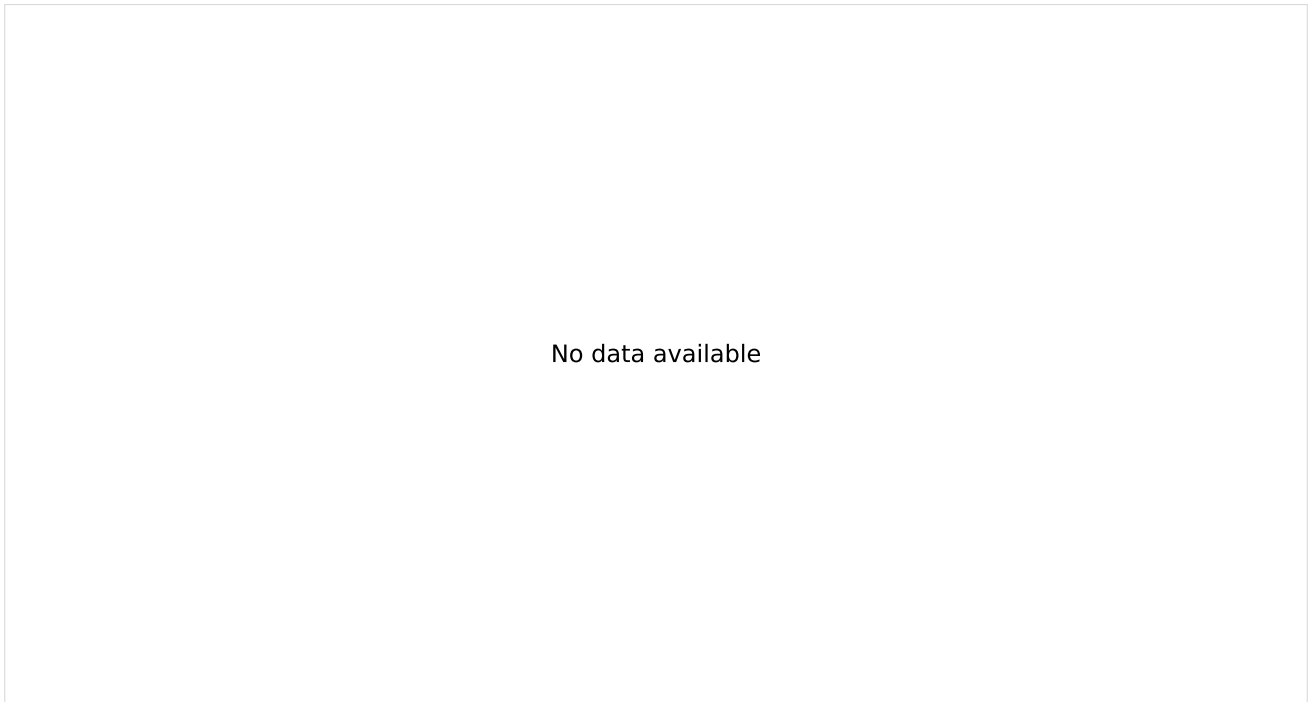
Data accessed on 24 Oct 2022

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 Republic of North Macedonia



**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.



## 8 Protective factors for cervical cancer

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

Table 47: Prevalence of male circumcision in Republic of North Macedonia

Reference	Prevalence % (95% CI)	Methods
Drain 2006	20-80	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	20-80	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 Republic of North Macedonia

Indicator	Age range	Year of estimate	Prevalence % <sup>a</sup>
Condom use	15-49	2011	8.3

**Data accessed on 18 Nov 2019**

Please refer to original source for methods of estimation.

<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:**

2011 MICS

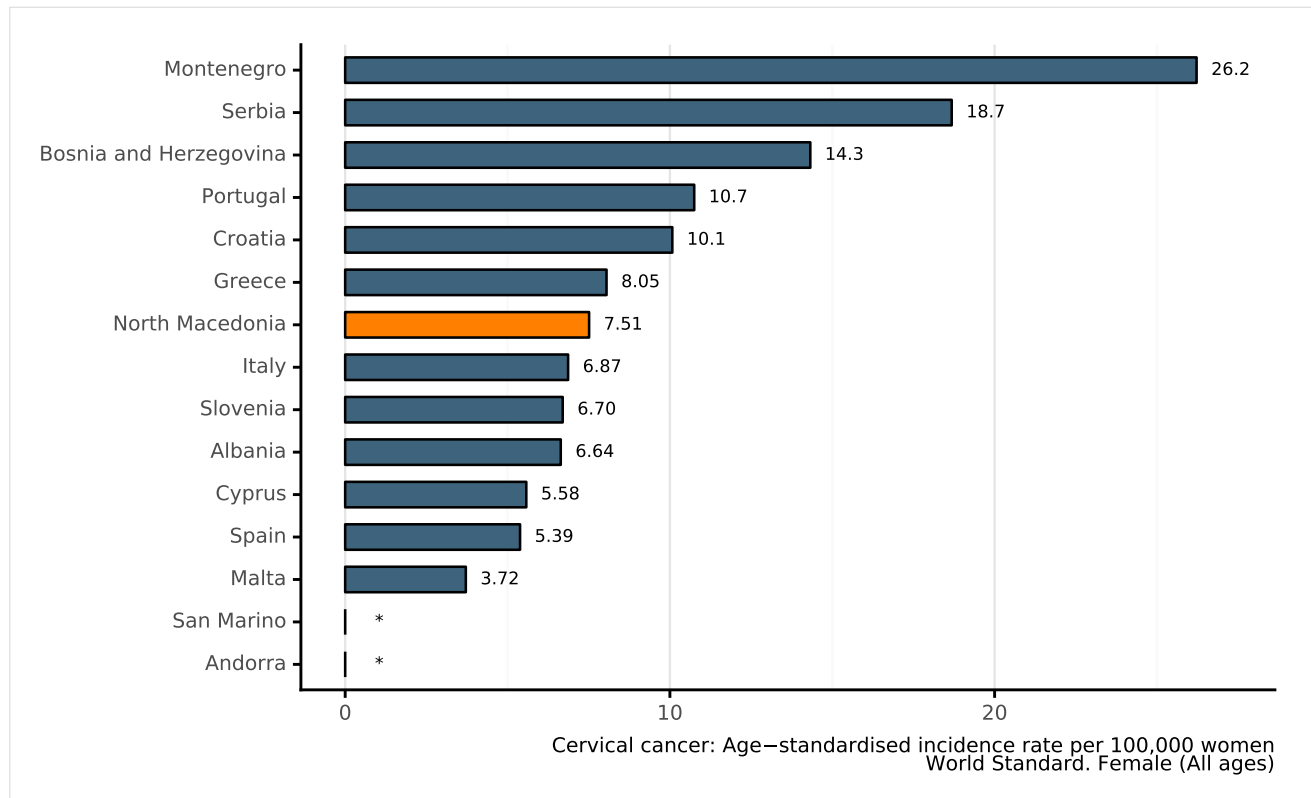
United Nations, Department of Economic and Social Affairs, Population Division (2019). World Contraceptive Use 2019 (POP/DB/CP/Rev2019). <https://www.un.org/en/development/desa/population/publications/dataset/contraception/wcu2019.asp>. Available at: [Accessed on November 18, 2019].

## 9 Annex

### 9.1 Incidence

#### 9.1.1 Cervical cancer incidence in Republic of North Macedonia across Southern Europe

Figure 73: Age-standardised incidence rates of cervical cancer of Republic of North Macedonia (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>

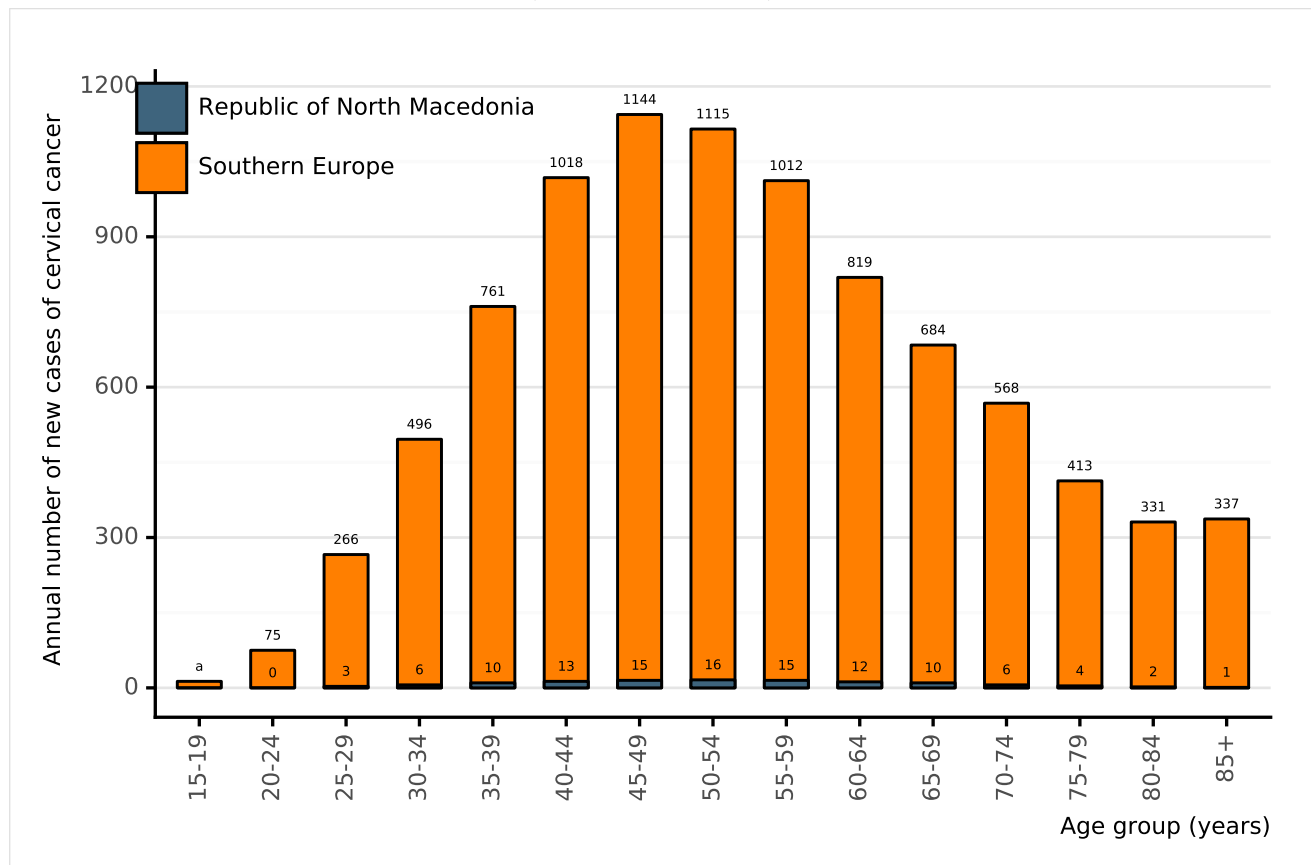
<sup>a</sup> Rates per 100,000 women per year.

\* Rates are not available

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 74: Annual number of new cases of cervical cancer by age group in Republic of North Macedonia (estimates for 2020)



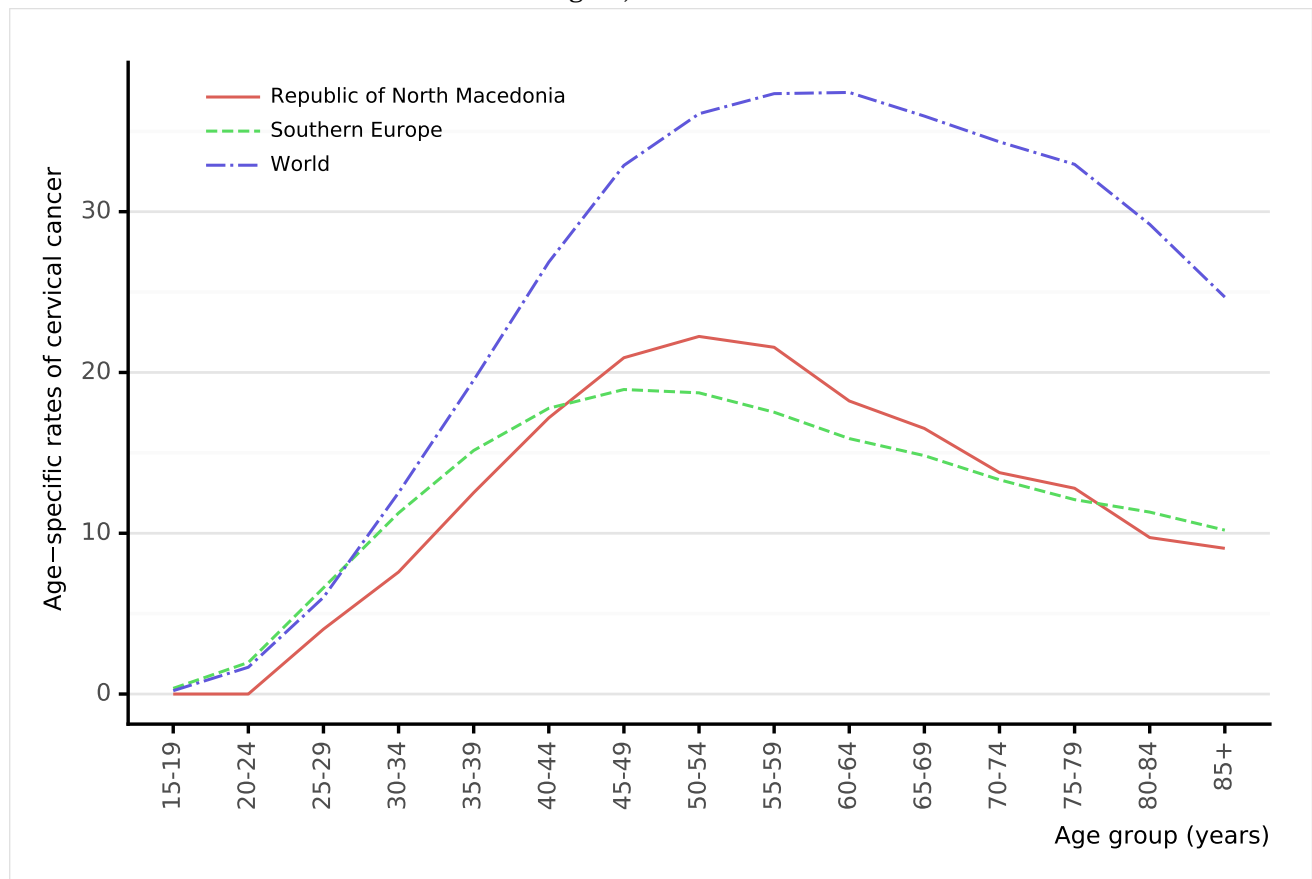
**Data accessed on 27 Jan 2021**

For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>  
<sup>a</sup> 0 cases for Republic of North Macedonia and 13 cases for Southern Europe in the 15-19 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 75: Comparison of age-specific cervical cancer incidence rates in Republic of North Macedonia, 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>

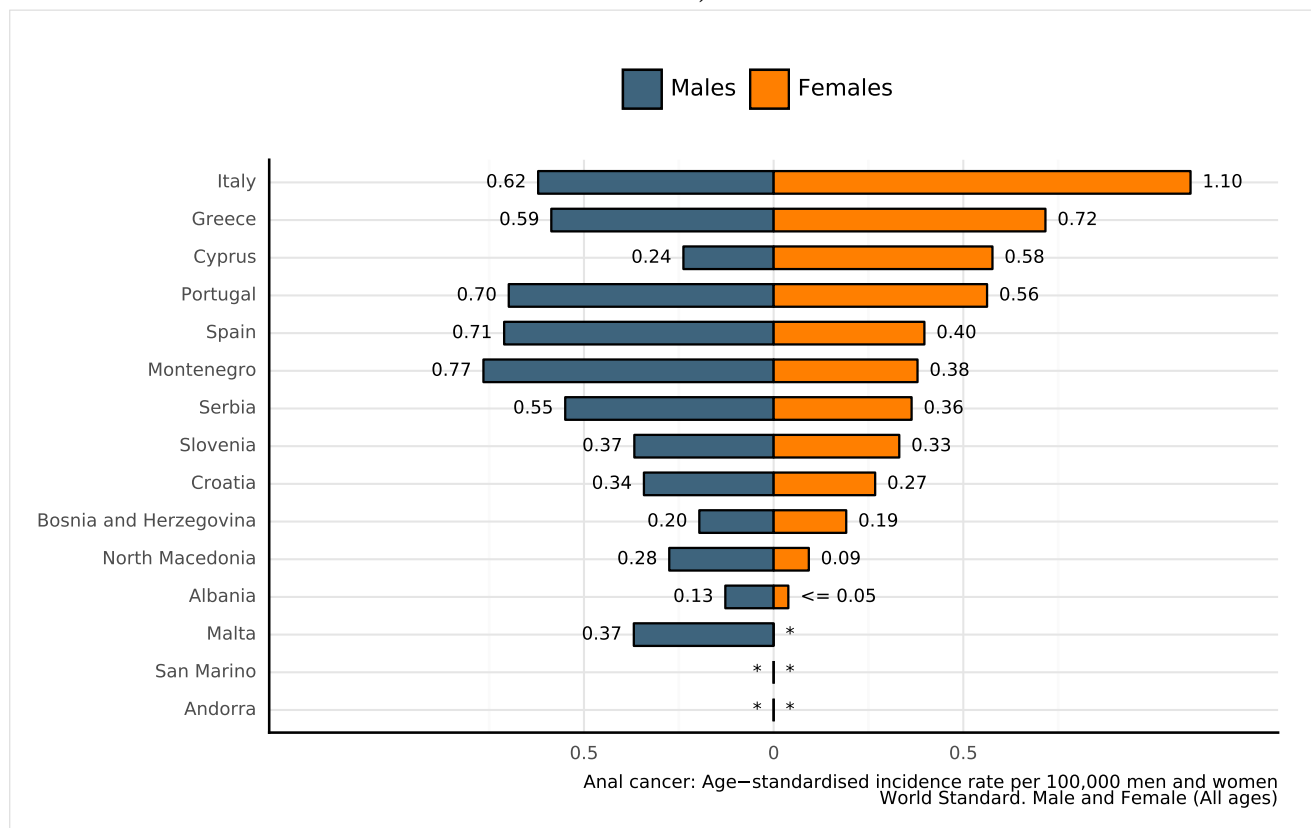
<sup>a</sup> Rates per 100,000 women per year.

**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].

### 9.1.2 Anal cancer incidence in Republic of North Macedonia across Southern Europe

Figure 76: Age-standardised incidence rates of anal cancer of Republic of North Macedonia (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.

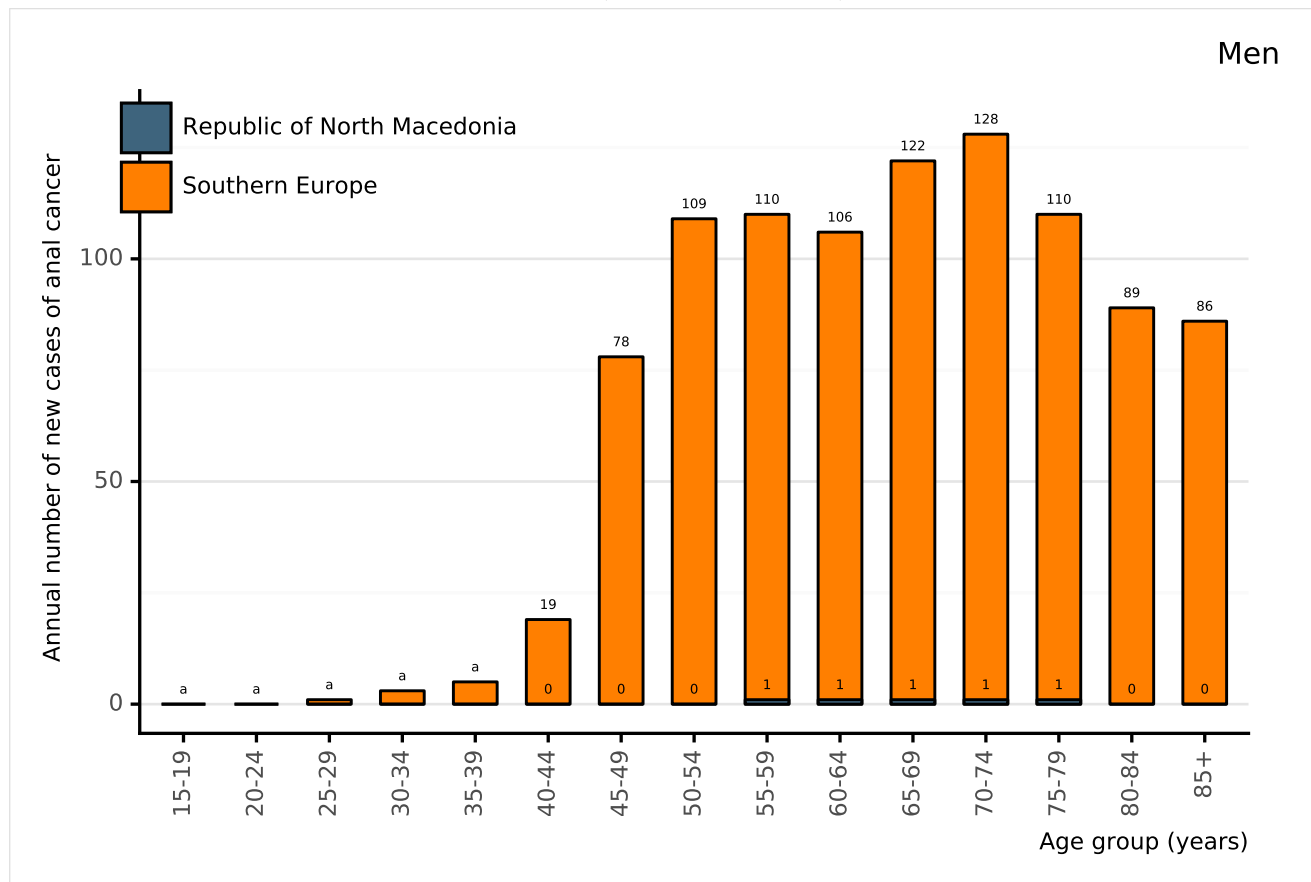
<sup>b</sup> Rates per 100,000 women per year.

\* Rates are not available

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 77: Annual number of new cases of anal cancer among men by age group in Republic of North Macedonia (estimates for 2020)



**Data accessed on 27 Jan 2021**

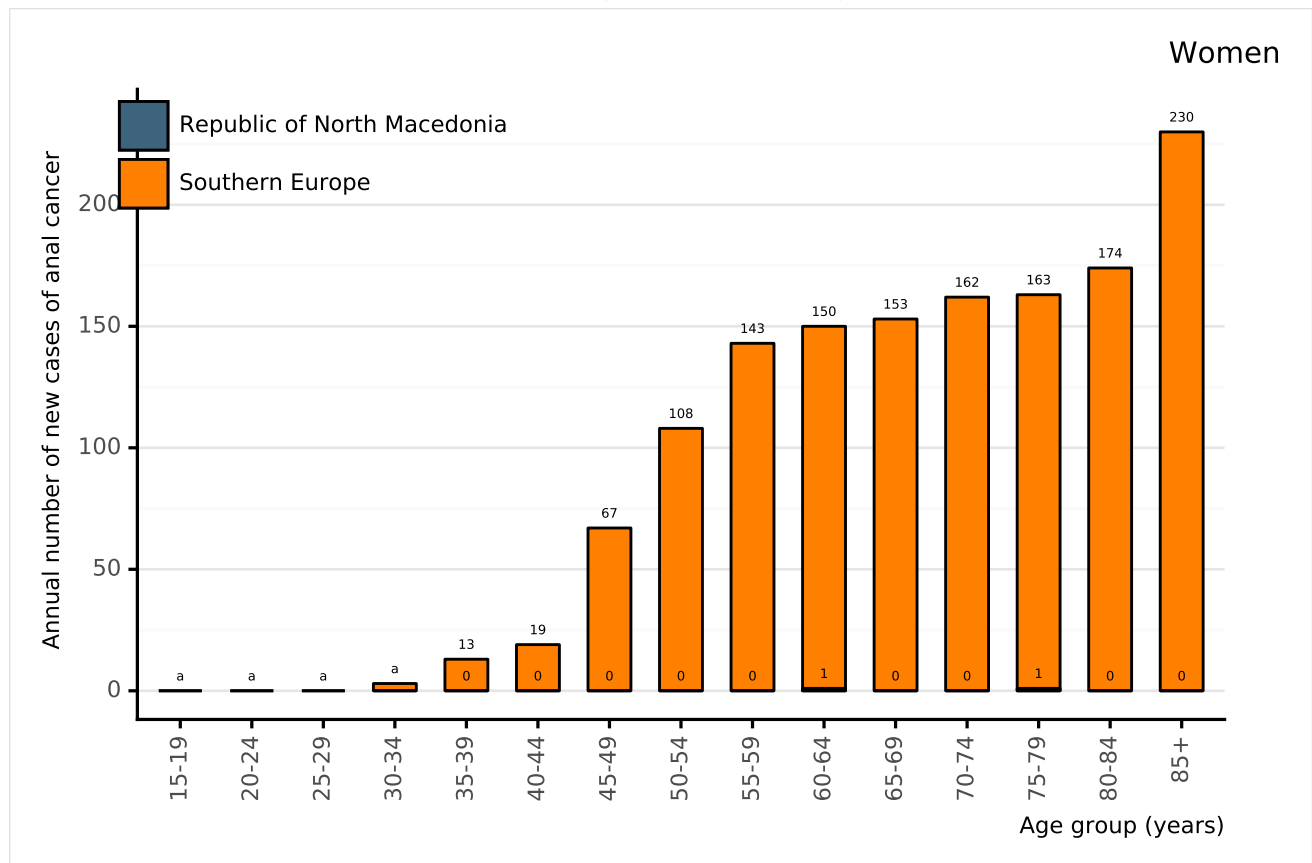
For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>

<sup>a</sup> 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 15-19 age group. 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 20-24 age group. 0 cases for Republic of North Macedonia and 1 cases for Southern Europe in the 25-29 age group. 0 cases for Republic of North Macedonia and 3 cases for Southern Europe in the 30-34 age group. 0 cases for Republic of North Macedonia and 5 cases for Southern Europe in the 35-39 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 78: Annual number of new cases of anal cancer among women by age group in Republic of North Macedonia (estimates for 2020)



Data accessed on 27 Jan 2021

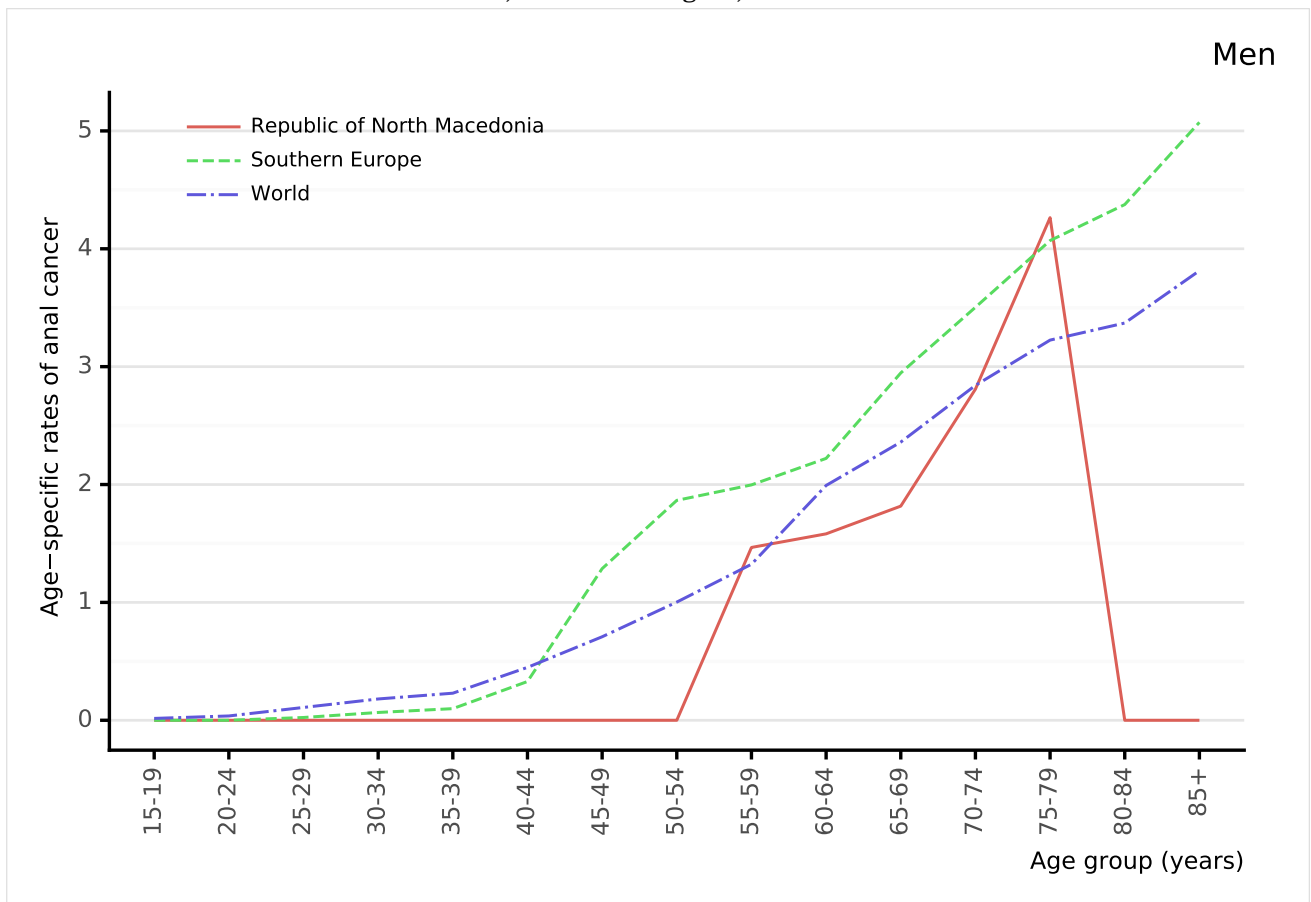
For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>

<sup>a</sup> 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 15-19 age group. 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 20-24 age group. 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 25-29 age group. 0 cases for Republic of North Macedonia and 3 cases for Southern Europe in the 30-34 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 79: Comparison of age-specific anal cancer incidence rates among men by age in Republic of North Macedonia, 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>

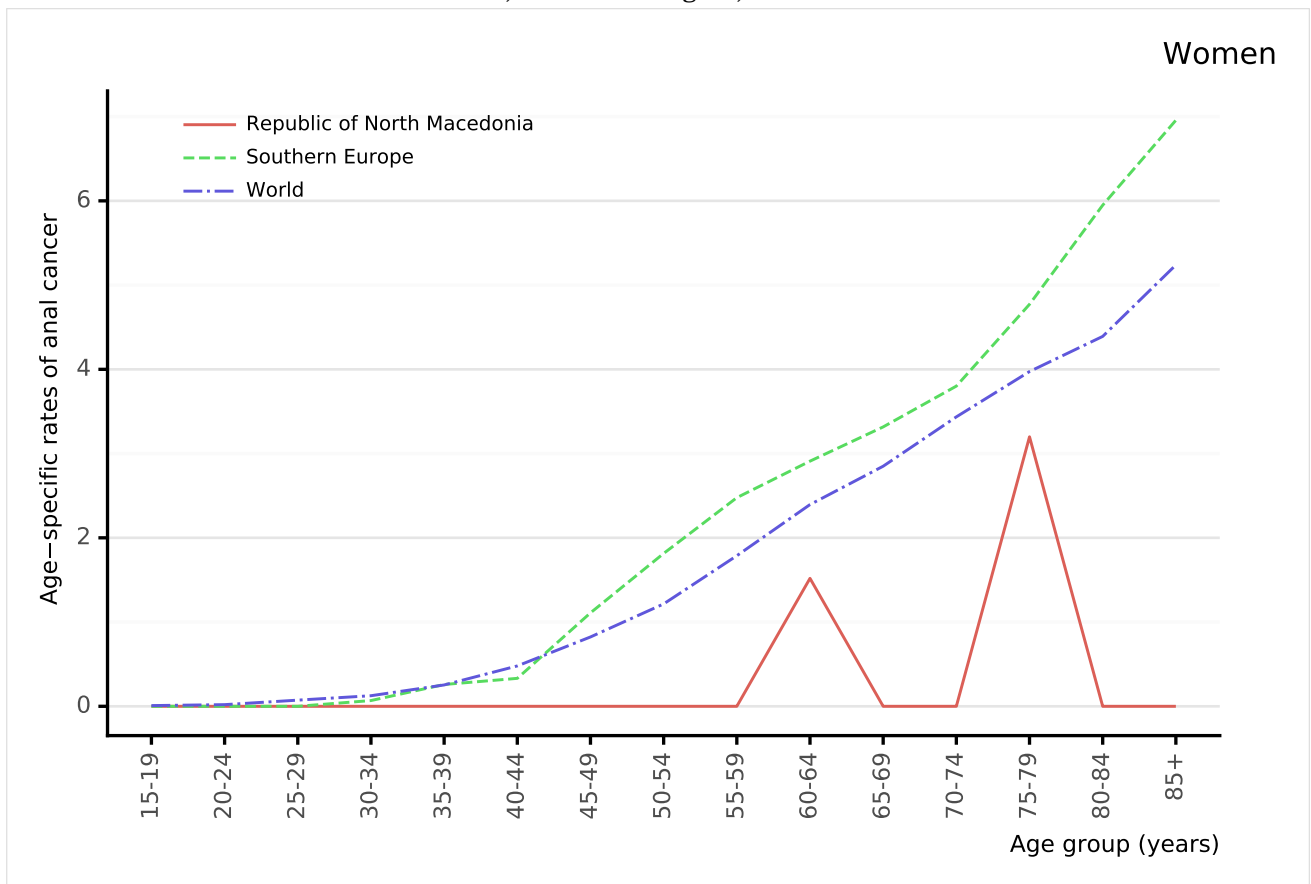
<sup>a</sup> Rates per 100,000 men per year.

Data Sources:

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 Republic of North Macedonia, 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>

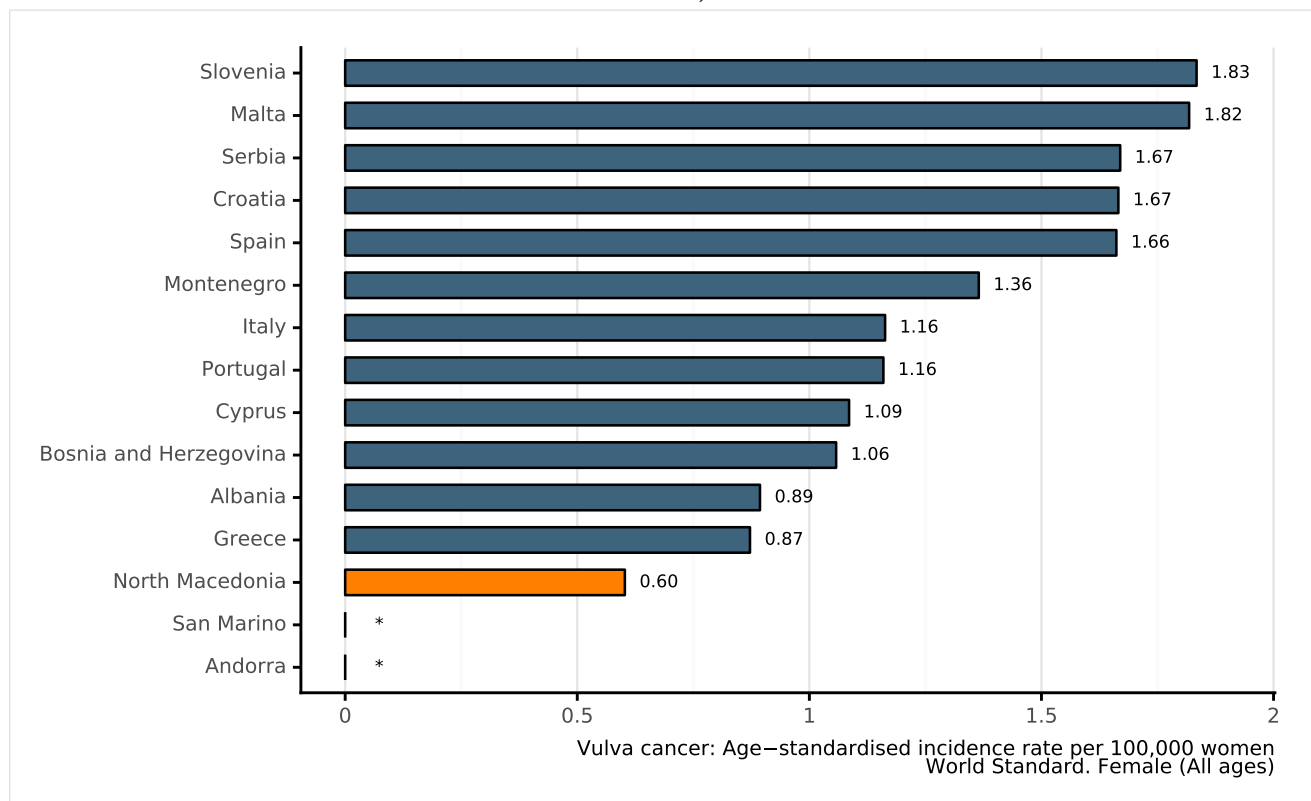
<sup>a</sup> Rates per 100,000 women per year.

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].

### 9.1.3 Vulva cancer incidence in Republic of North Macedonia across Southern Europe

Figure 81: Age-standardised incidence rates of vulva cancer of Republic of North Macedonia (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>

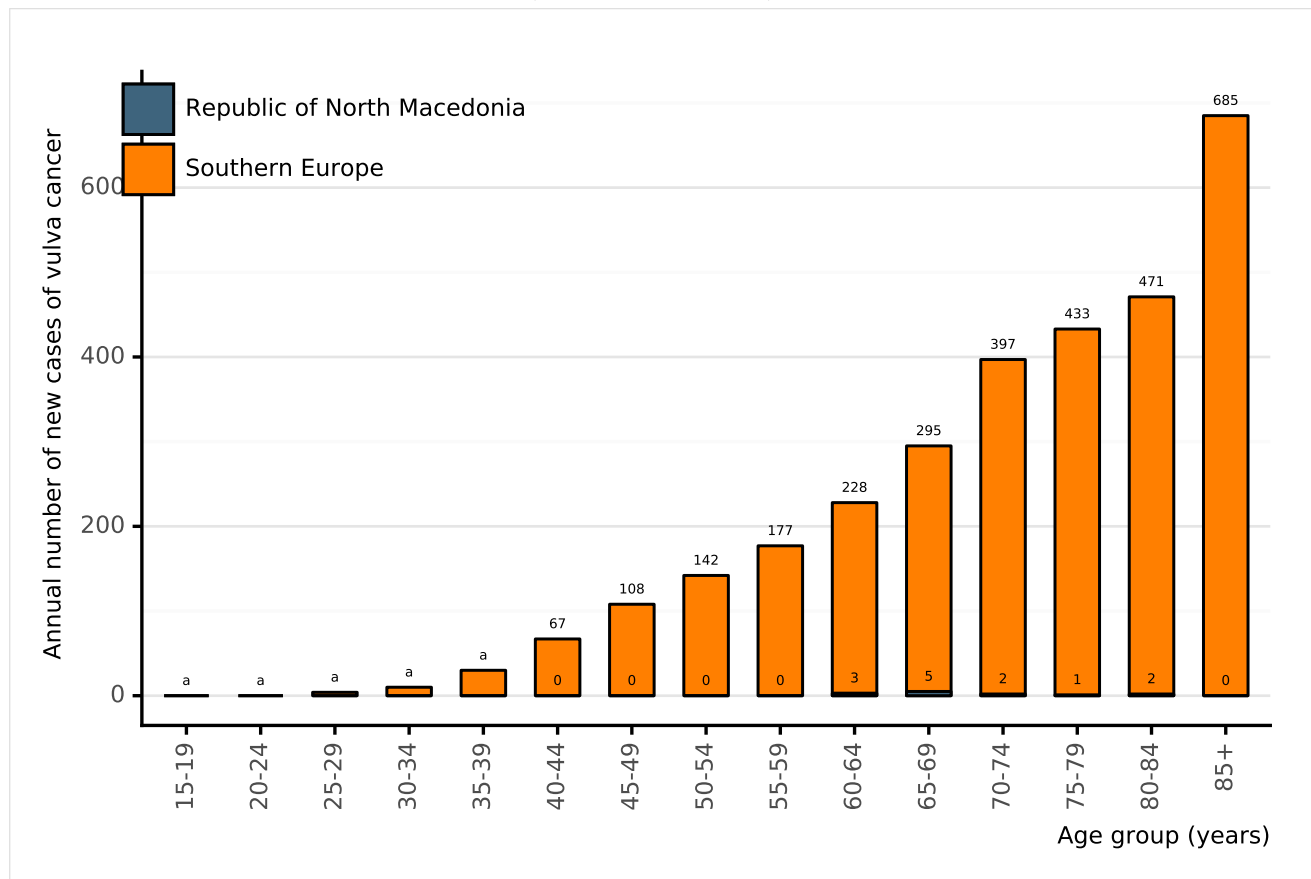
<sup>a</sup> Rates per 100,000 women per year.

\* Rates are not available

**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 82: Annual number of new cases of vulva cancer by age group in Republic of North Macedonia (estimates for 2020)



**Data accessed on 27 Jan 2021**

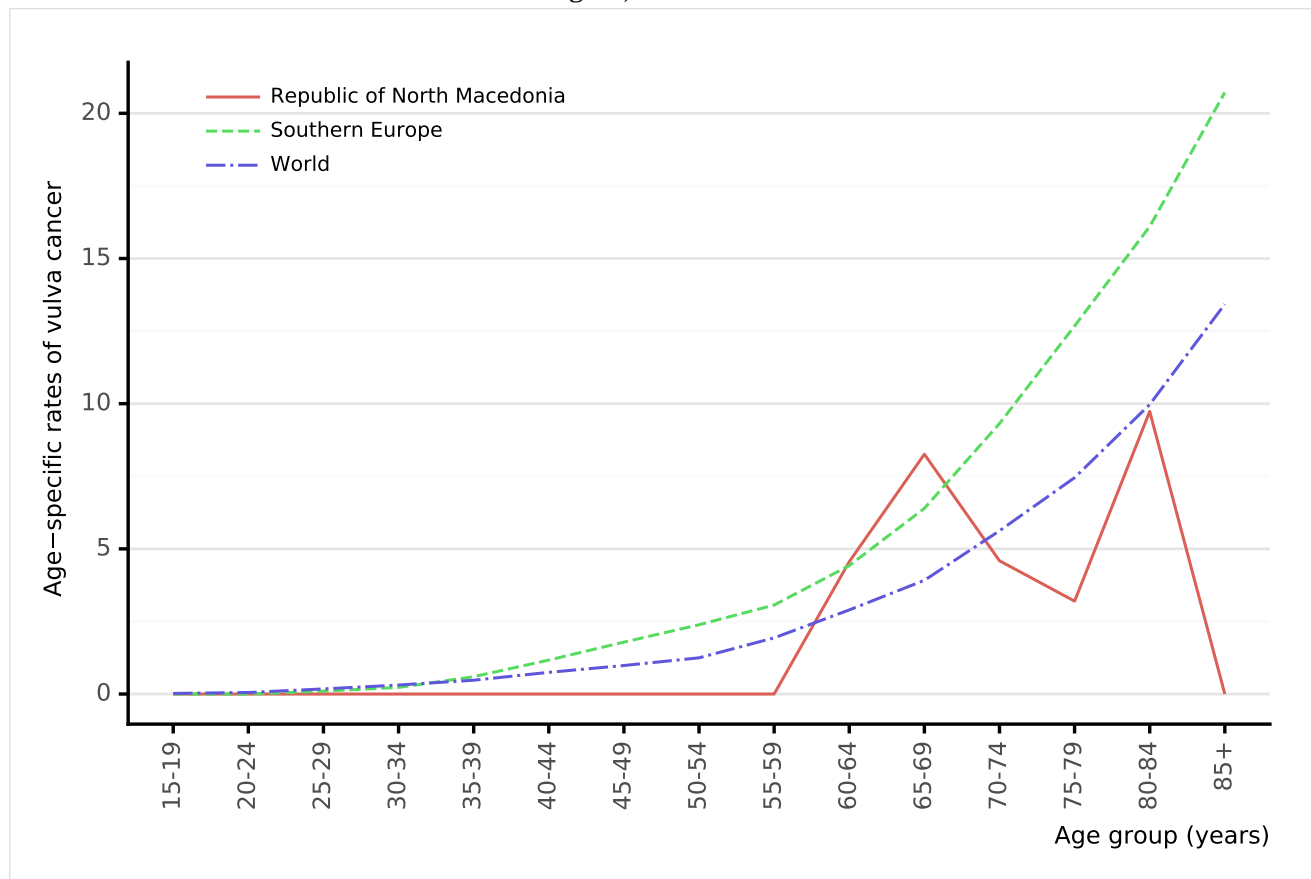
For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>

<sup>a</sup> 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 15-19 age group. 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 20-24 age group. 0 cases for Republic of North Macedonia and 4 cases for Southern Europe in the 25-29 age group. 0 cases for Republic of North Macedonia and 10 cases for Southern Europe in the 30-34 age group. 0 cases for Republic of North Macedonia and 30 cases for Southern Europe in the 35-39 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 83: Comparison of age-specific vulva cancer incidence rates in Republic of North Macedonia, 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>

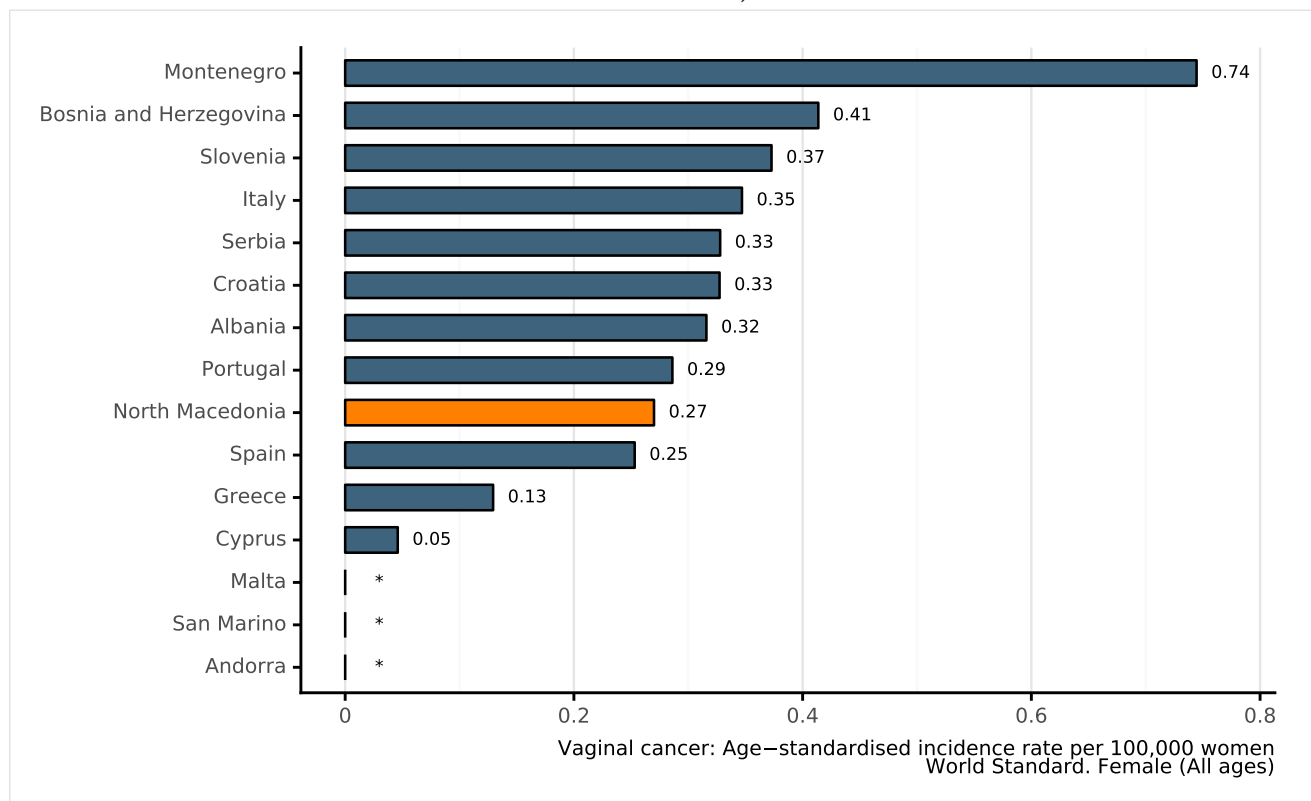
<sup>a</sup> Rates per 100,000 women per year.

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 Republic of North Macedonia across Southern Europe

Figure 84: Age-standardised incidence rates of vaginal cancer of Republic of North Macedonia (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>

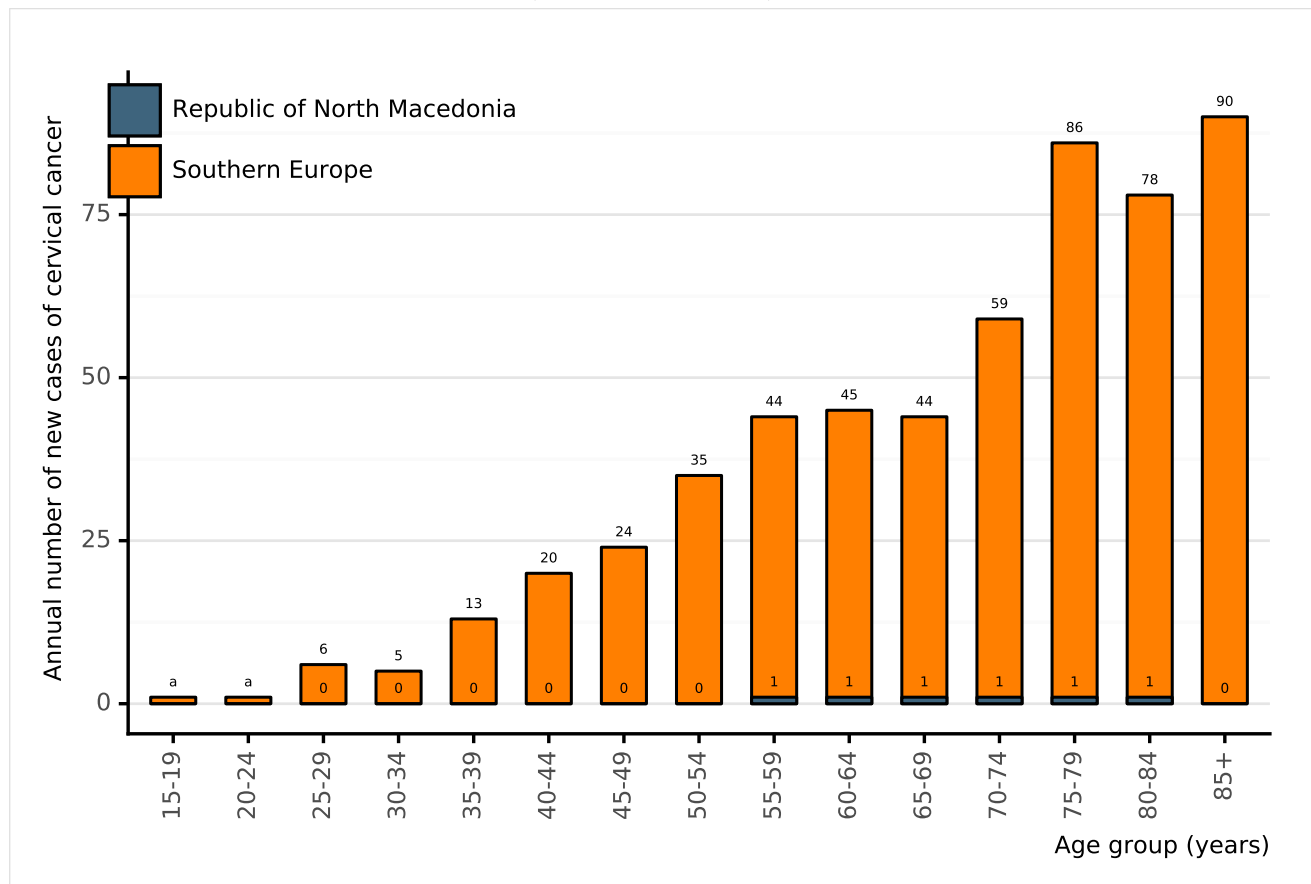
<sup>a</sup> Rates per 100,000 women per year.

\* Rates are not available

**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 85: Annual number of new cases of cervical cancer by age group in Republic of North Macedonia (estimates for 2020)



**Data accessed on 27 Jan 2021**

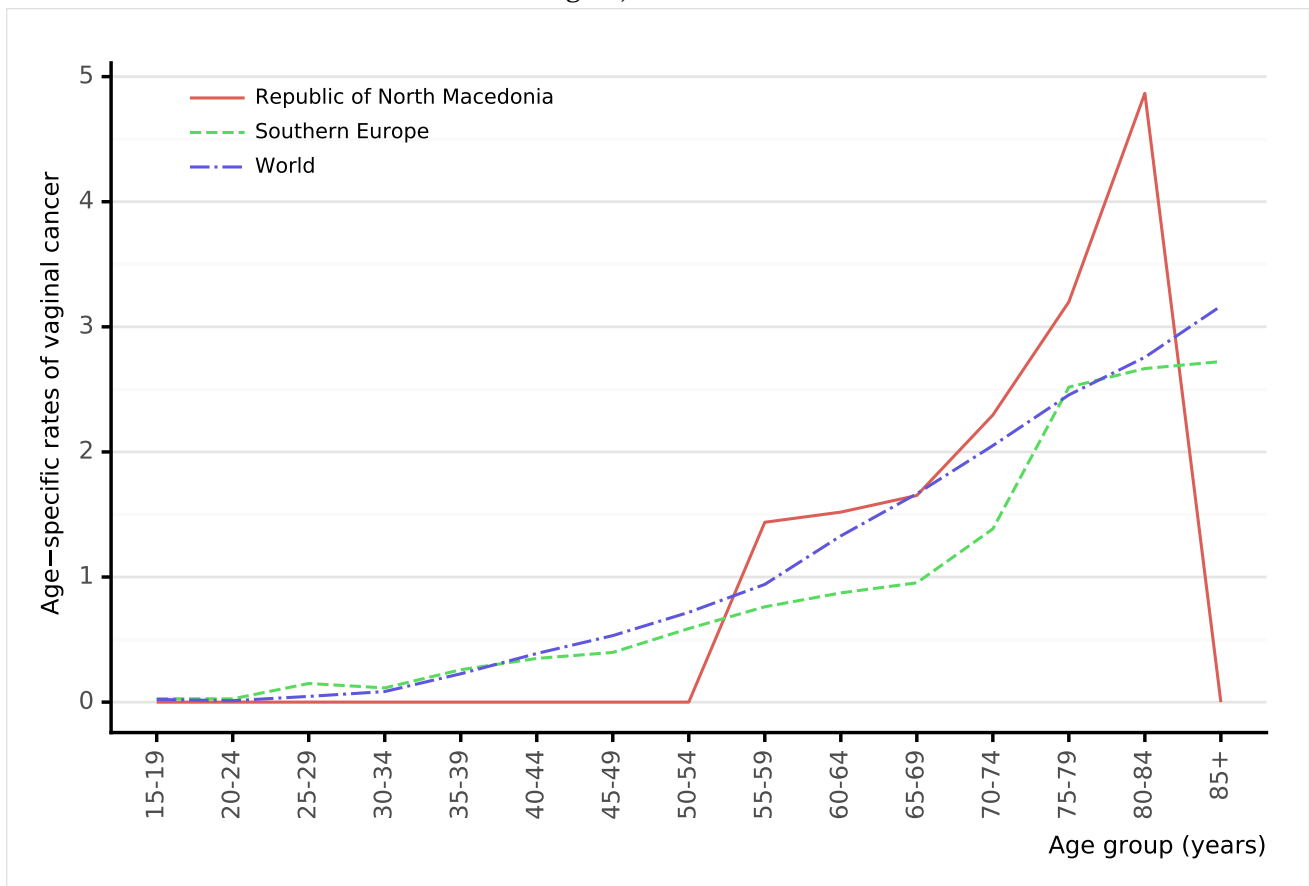
For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>

<sup>a</sup> 0 cases for Republic of North Macedonia and 1 cases for Southern Europe in the 15-19 age group. 0 cases for Republic of North Macedonia and 1 cases for Southern Europe in the 20-24 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 86: Comparison of age-specific vaginal cancer incidence rates in Republic of North Macedonia, 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>

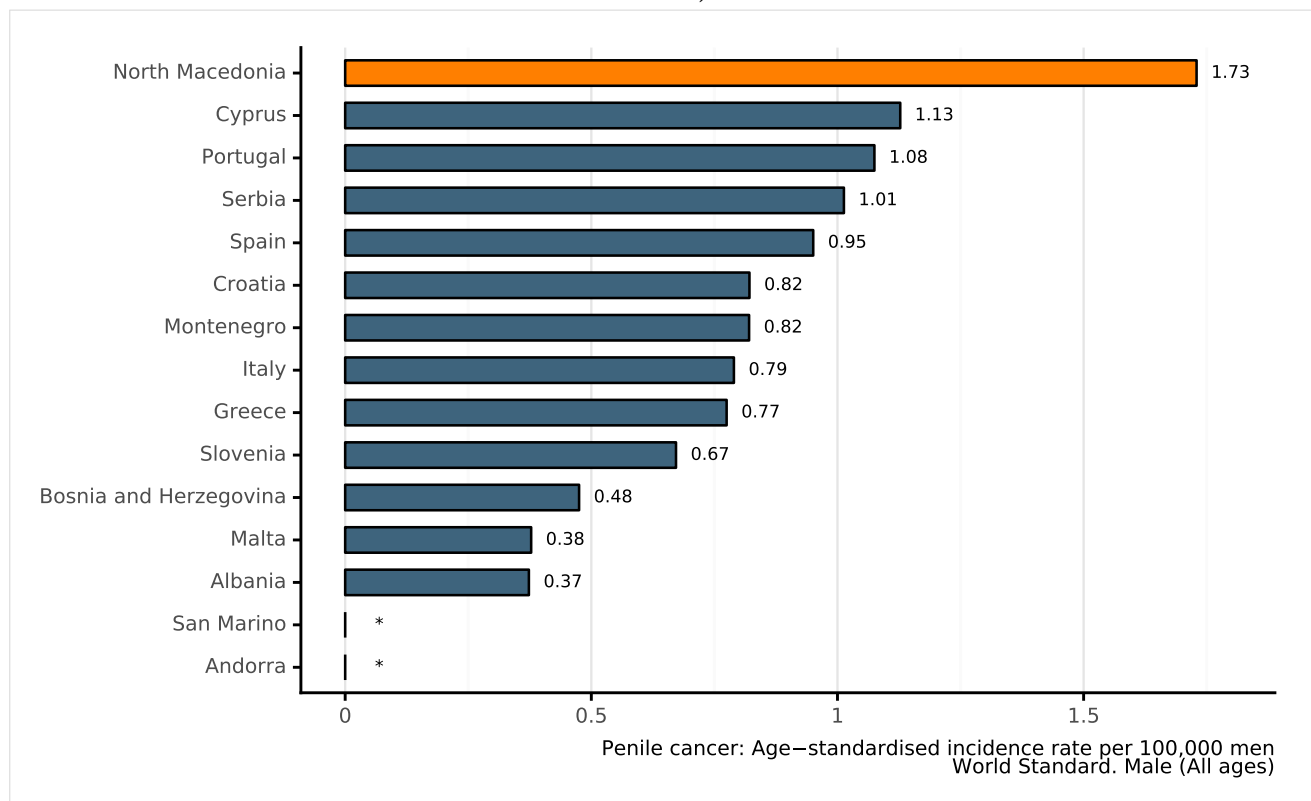
<sup>a</sup> Rates per 100,000 women per year.

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].

### 9.1.5 Penile cancer incidence in Republic of North Macedonia across Southern Europe

Figure 87: Age-standardised incidence rates of penile cancer of Republic of North Macedonia (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.

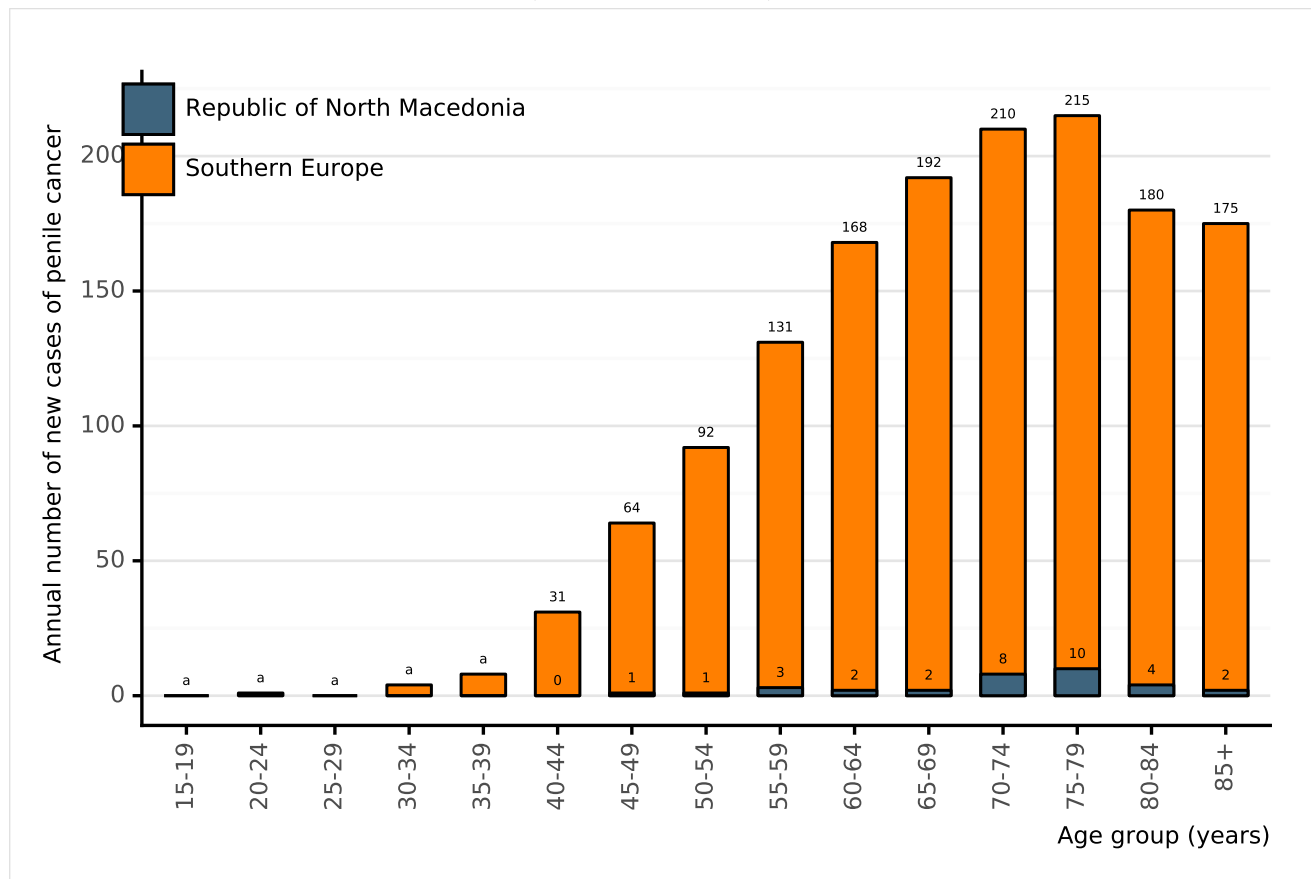
\* Rates are not available

**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 88: Annual number of new cases of penile cancer by age group in Republic of North Macedonia (estimates for 2020)



**Data accessed on 27 Jan 2021**

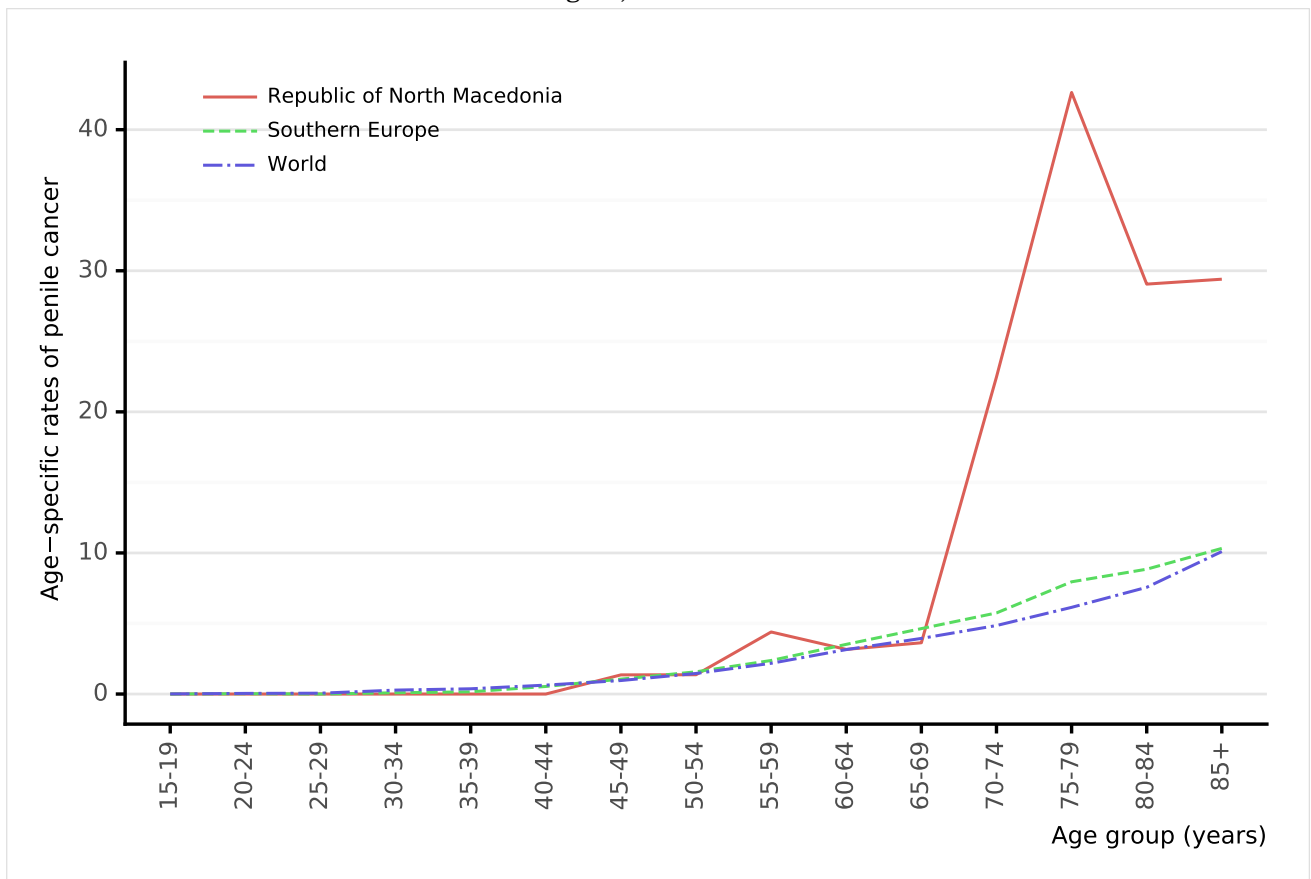
For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>

<sup>a</sup> 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 15-19 age group. 0 cases for Republic of North Macedonia and 1 cases for Southern Europe in the 20-24 age group. 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 25-29 age group. 0 cases for Republic of North Macedonia and 4 cases for Southern Europe in the 30-34 age group. 0 cases for Republic of North Macedonia and 8 cases for Southern Europe in the 35-39 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 89: Comparison of age-specific penile cancer incidence rates in Republic of North Macedonia, 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>

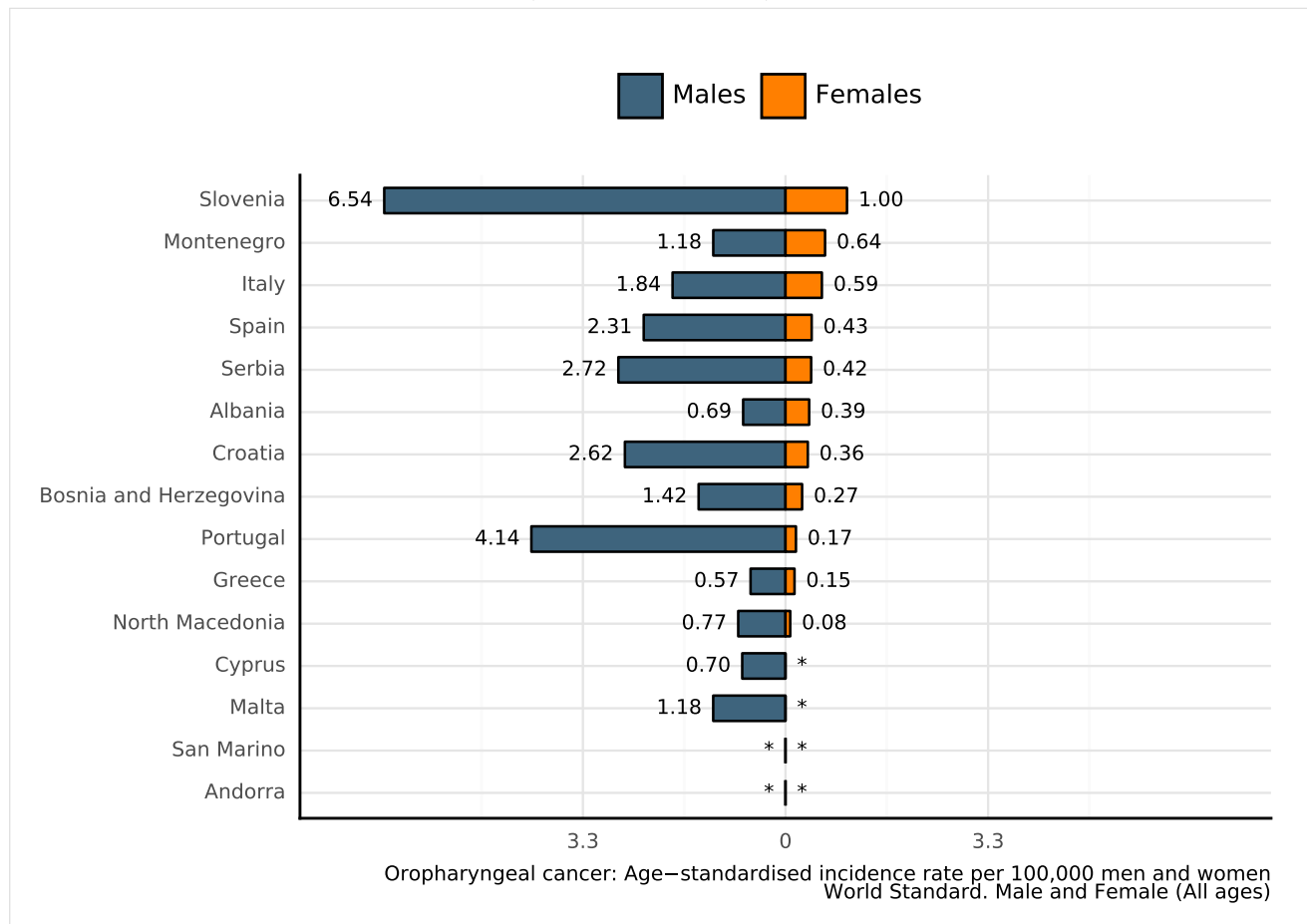
<sup>a</sup> Rates per 100,000 men per year.

Data Sources:

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].

### 9.1.6 Oropharyngeal cancer incidence in Republic of North Macedonia across Southern Europe

Figure 90: Age-standardised incidence rates of oropharyngeal cancer of Republic of North Macedonia (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.

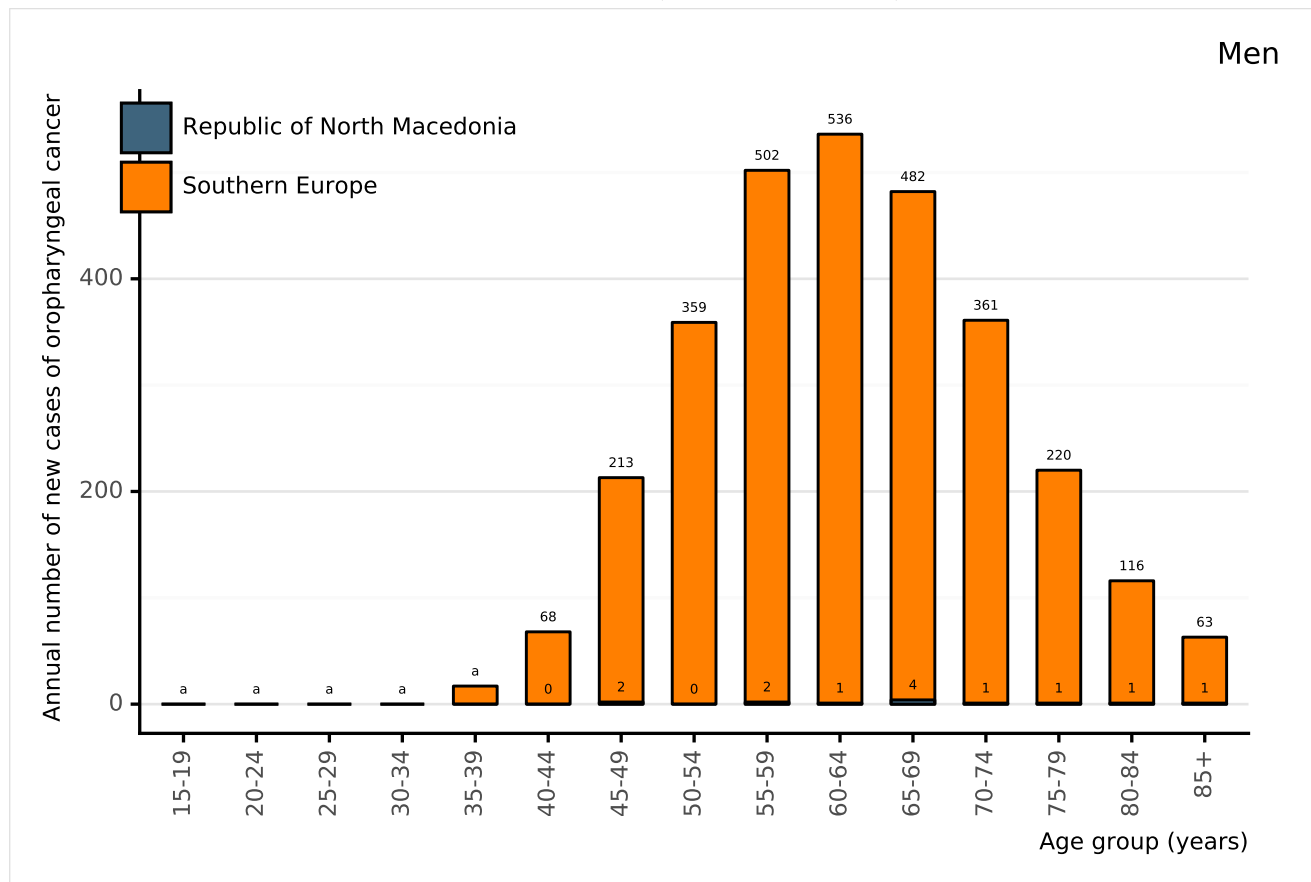
<sup>b</sup> Rates per 100,000 women per year.

\* Rates are not available

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 91: Annual number of new cases of oropharyngeal cancer among men by age group in Republic of North Macedonia (estimates for 2020)



**Data accessed on 27 Jan 2021**

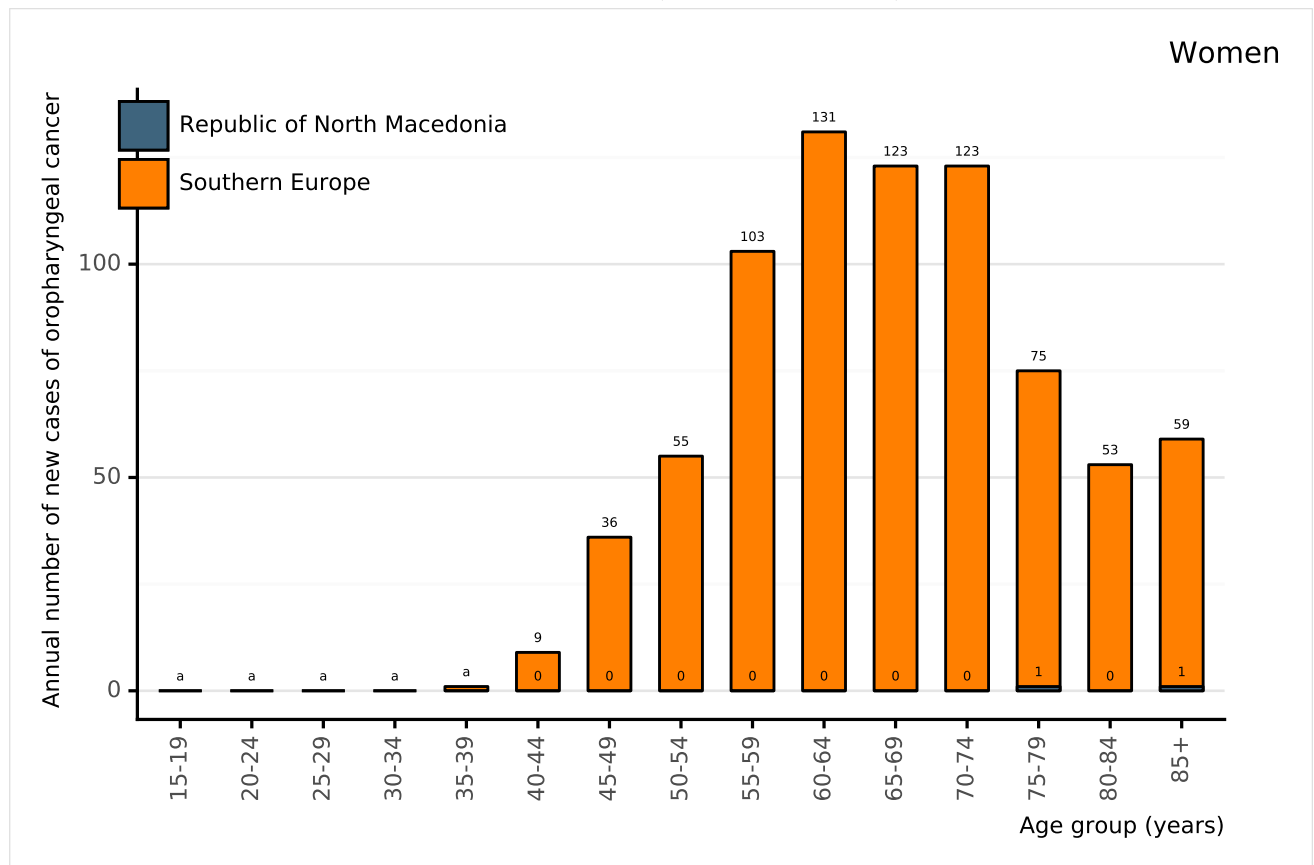
For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>

<sup>a</sup> 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 15-19 age group. 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 20-24 age group. 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 25-29 age group. 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 30-34 age group. 0 cases for Republic of North Macedonia and 17 cases for Southern Europe in the 35-39 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 92: Annual number of new cases of oropharyngeal cancer among women by age group in Republic of North Macedonia (estimates for 2020)



Data accessed on 27 Jan 2021

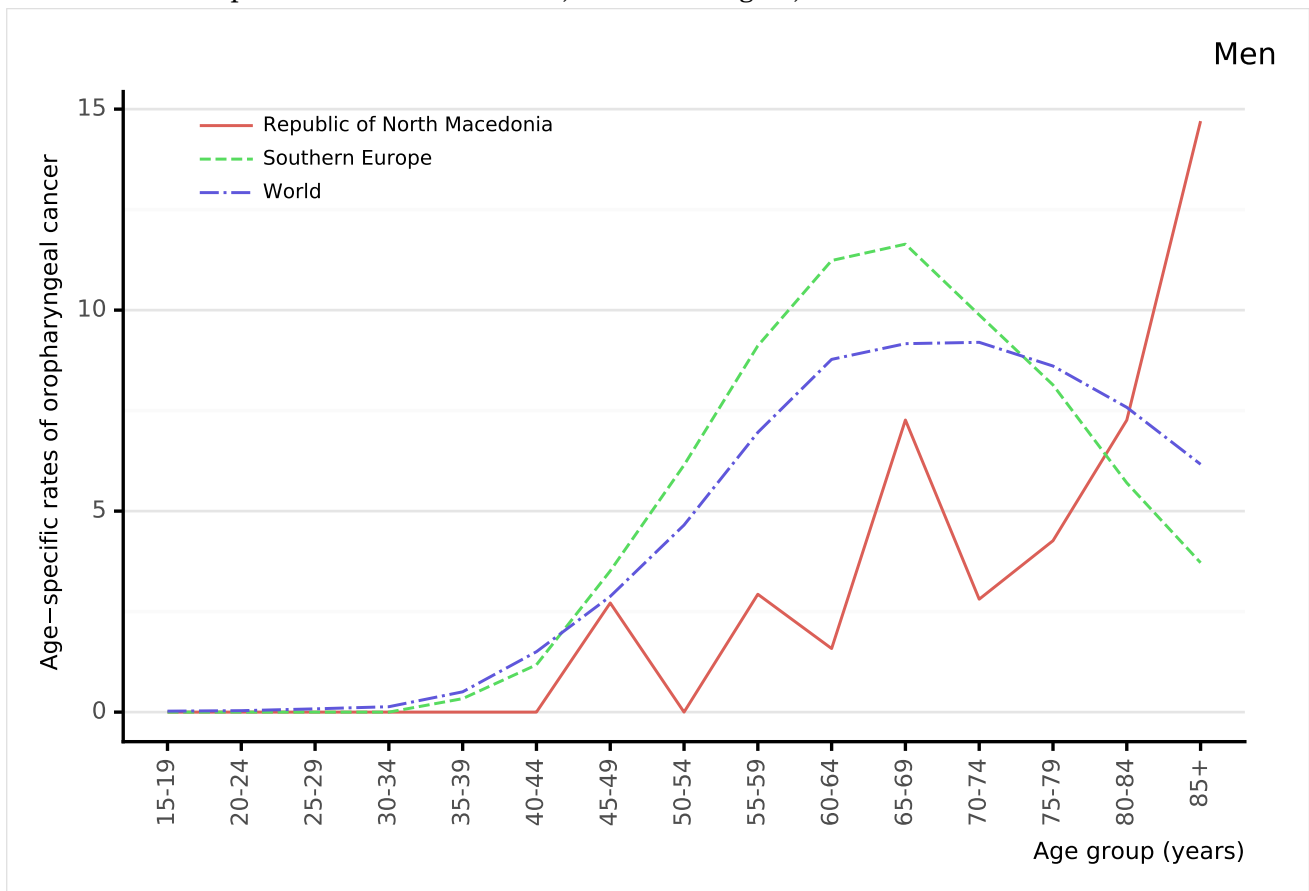
For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>

<sup>a</sup> 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 15-19 age group. 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 20-24 age group. 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 25-29 age group. 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 30-34 age group. 0 cases for Republic of North Macedonia and 1 cases for Southern Europe in the 35-39 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 93: Comparison of age-specific oropharyngeal cancer incidence rates among men by age in Republic of North Macedonia, within the region, and the rest of world



Data accessed on 27 Jan 2021

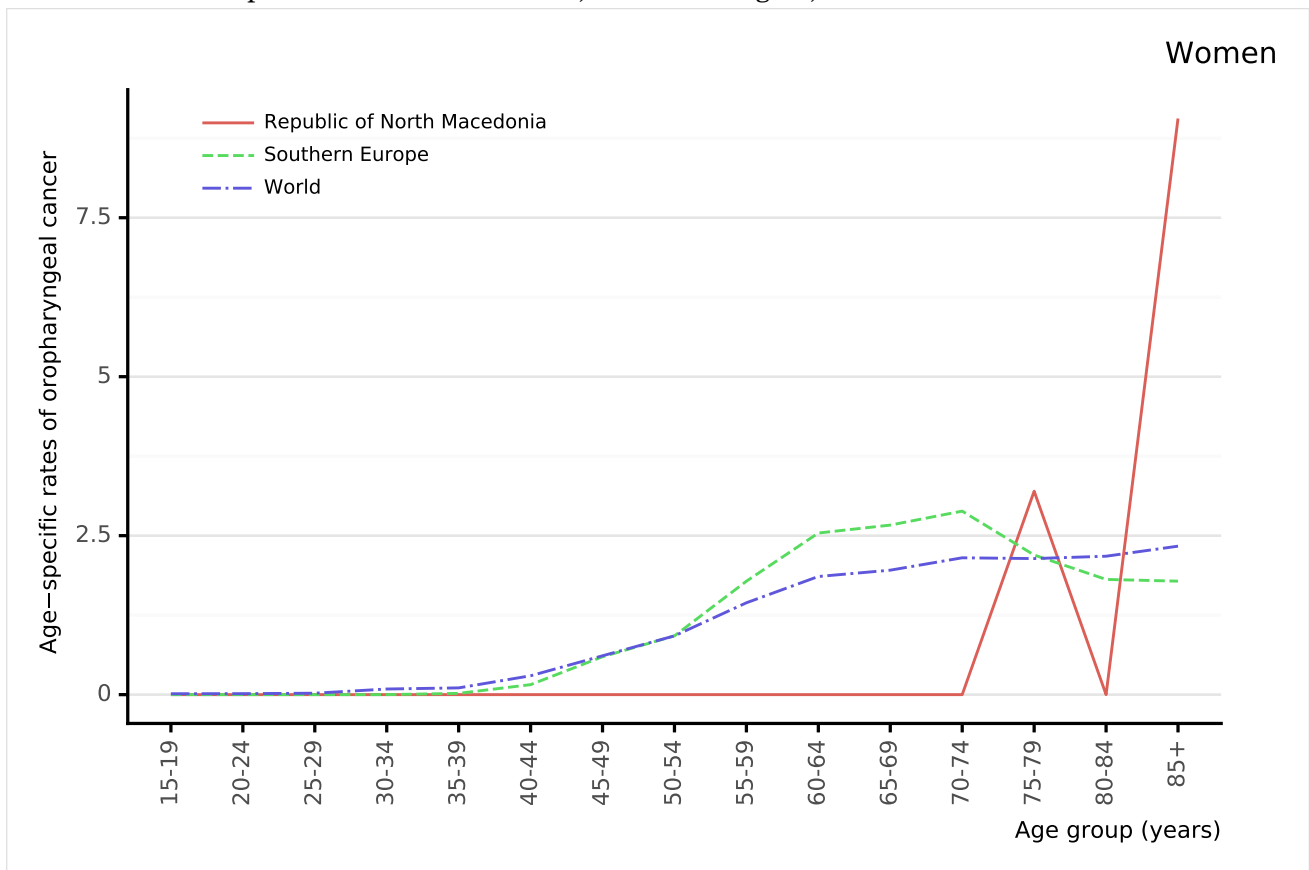
For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>

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

Data Sources:

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 94: Comparison of age-specific oropharyngeal cancer incidence rates among women by age in Republic of North Macedonia, 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>

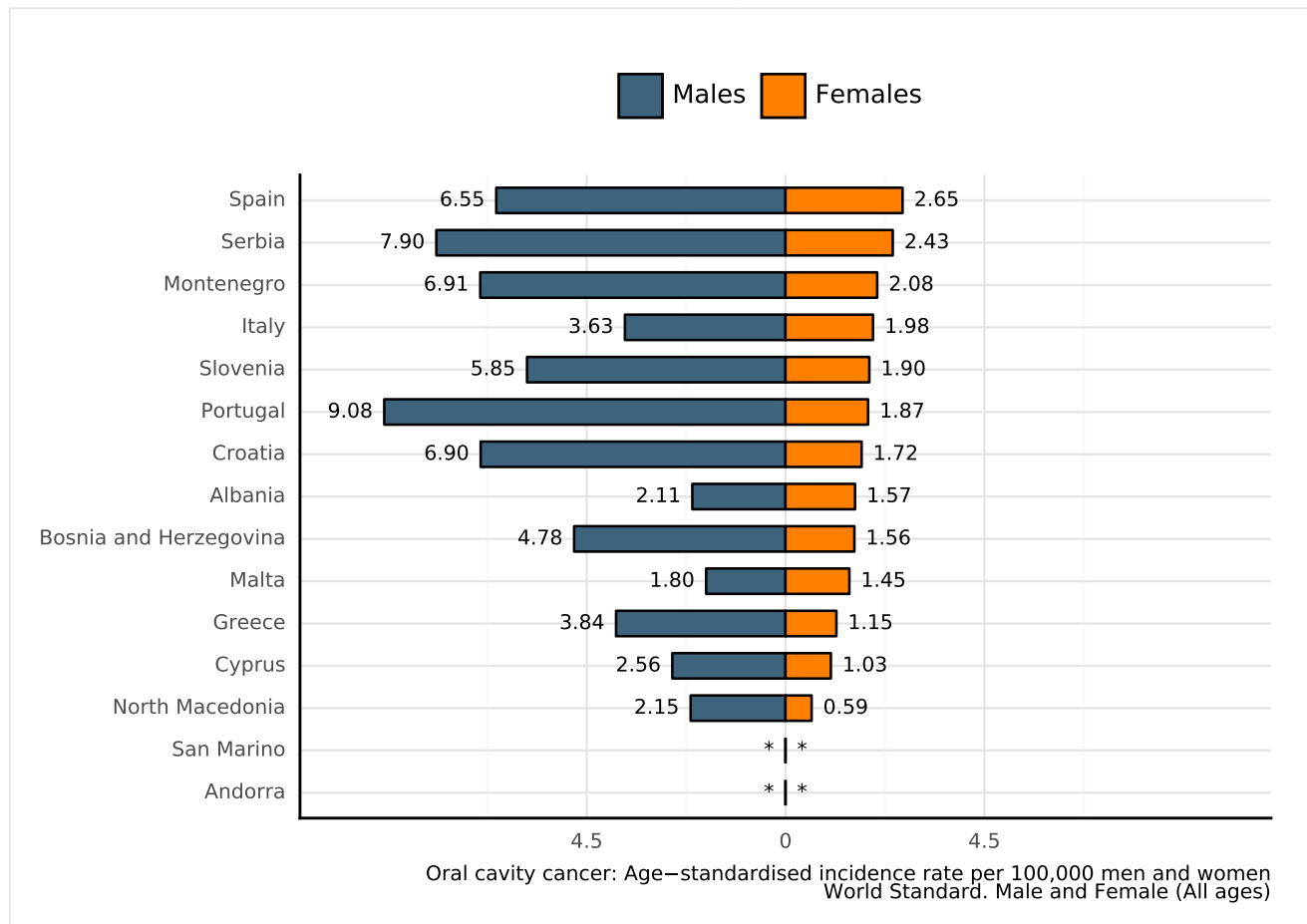
<sup>a</sup> Rates per 100,000 women per year.

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].

### 9.1.7 Oral cavity cancer incidence in Republic of North Macedonia across Southern Europe

Figure 95: Age-standardised incidence rates of oral cavity cancer of Republic of North Macedonia (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.

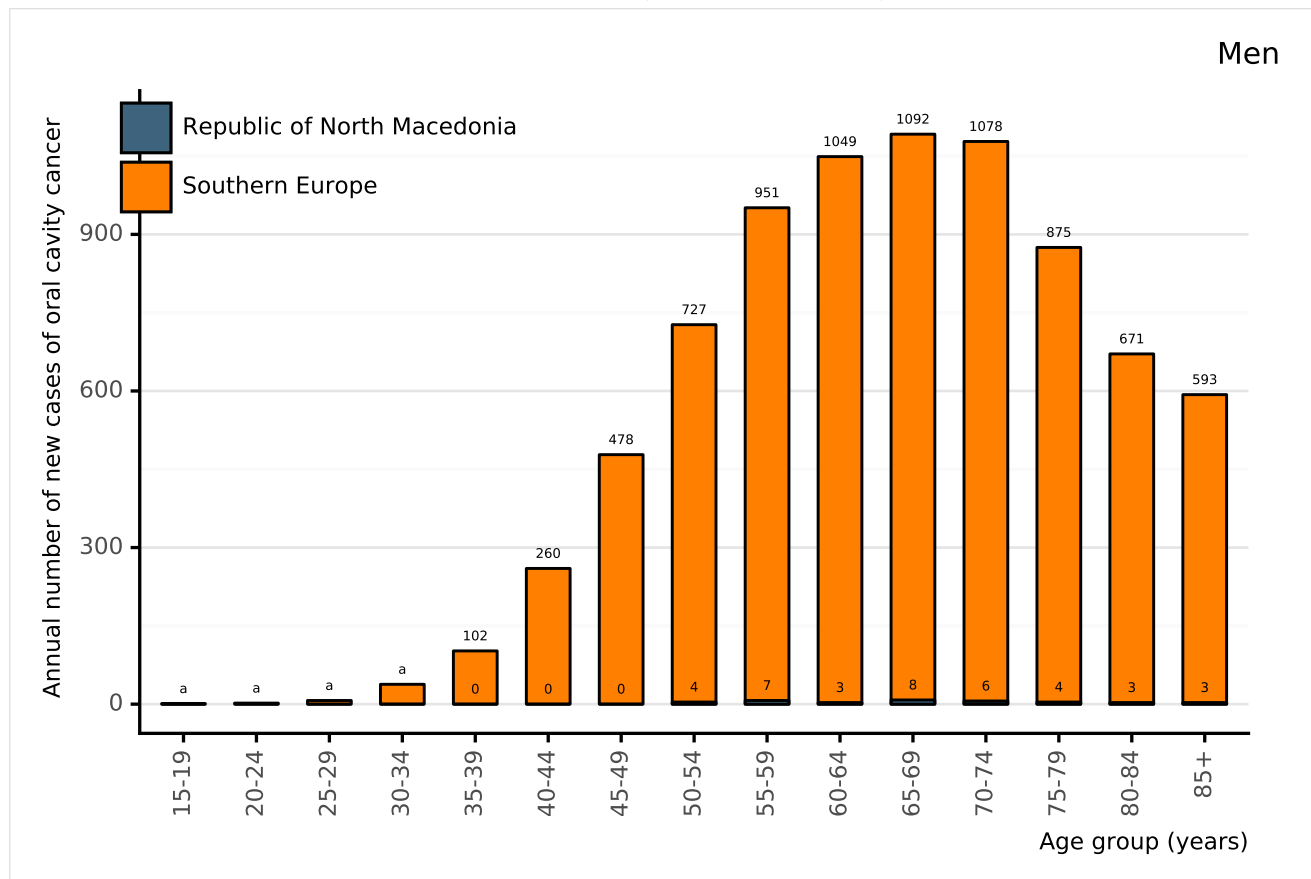
<sup>b</sup> Rates per 100,000 women per year.

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: <https://gco.iarc.fr/today>, accessed [27 January 2021].



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



**Data accessed on 27 Jan 2021**

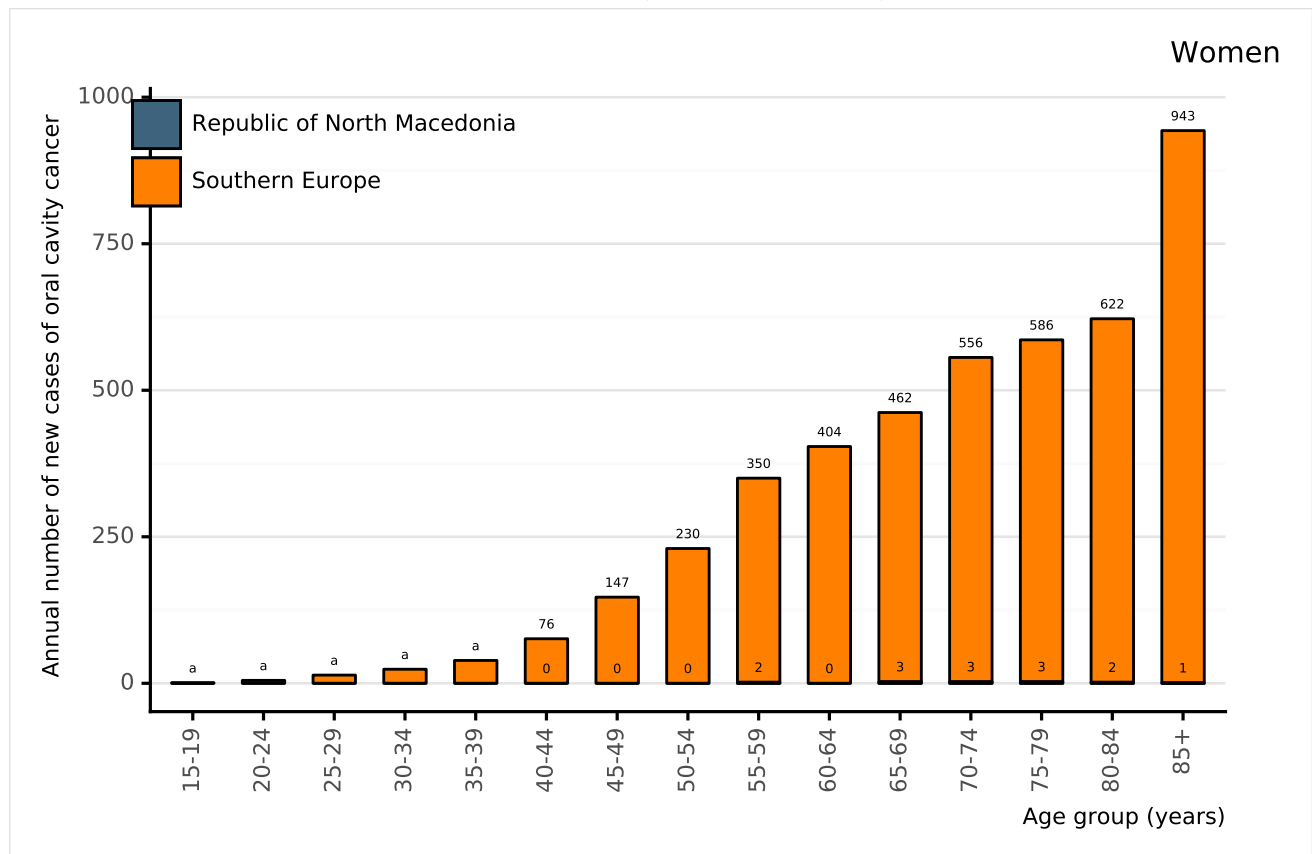
For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>

<sup>a</sup> 0 cases for Republic of North Macedonia and 1 cases for Southern Europe in the 15-19 age group. 0 cases for Republic of North Macedonia and 2 cases for Southern Europe in the 20-24 age group. 0 cases for Republic of North Macedonia and 7 cases for Southern Europe in the 25-29 age group. 0 cases for Republic of North Macedonia and 38 cases for Southern Europe in the 30-34 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 97: Annual number of new cases of oral cavity cancer among women by age group in Republic of North Macedonia (estimates for 2020)



**Data accessed on 27 Jan 2021**

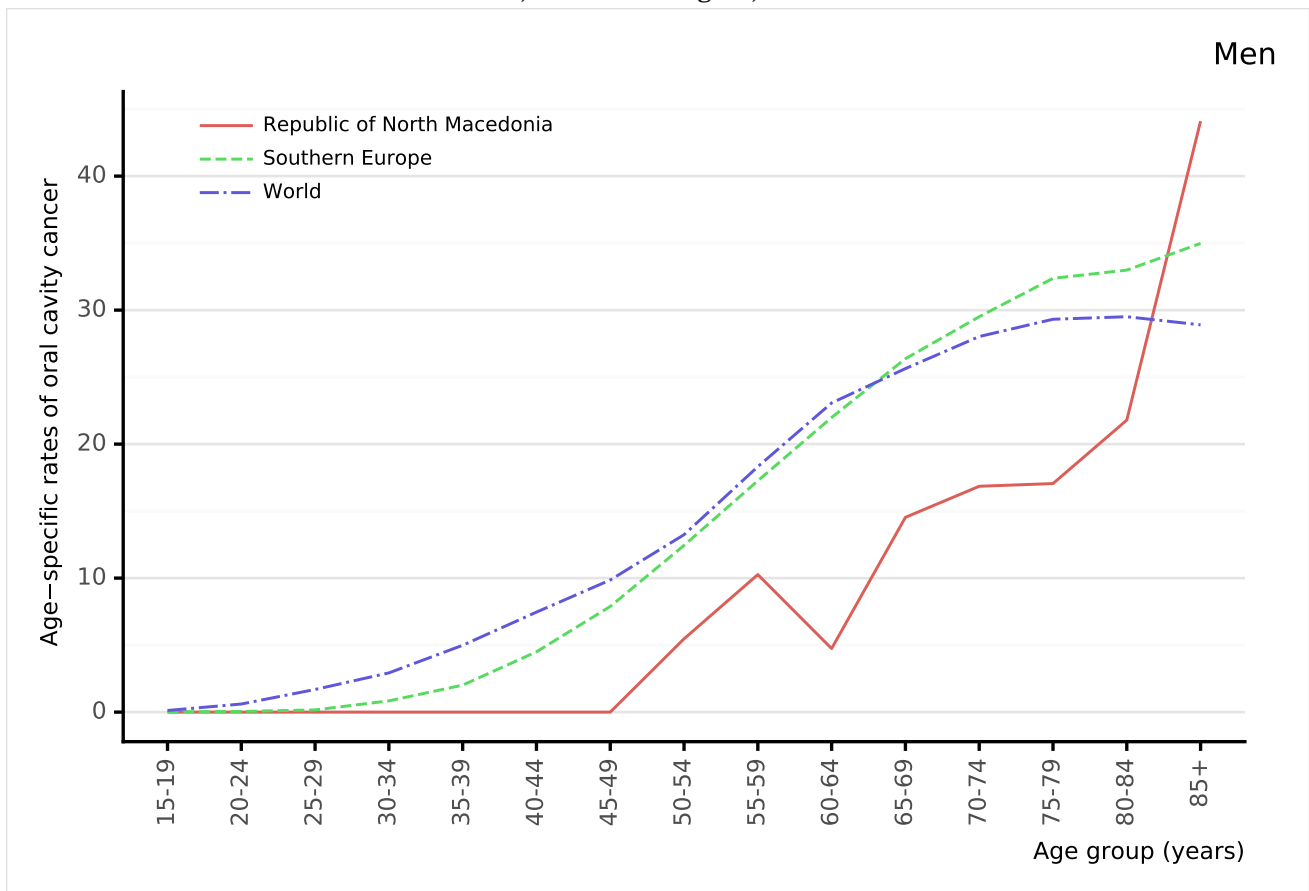
For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>

<sup>a</sup> 0 cases for Republic of North Macedonia and 1 cases for Southern Europe in the 15-19 age group. 0 cases for Republic of North Macedonia and 5 cases for Southern Europe in the 20-24 age group. 0 cases for Republic of North Macedonia and 14 cases for Southern Europe in the 25-29 age group. 0 cases for Republic of North Macedonia and 24 cases for Southern Europe in the 30-34 age group. 0 cases for Republic of North Macedonia and 39 cases for Southern Europe in the 35-39 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 98: Comparison of age-specific oral cavity cancer incidence rates among men by age in Republic of North Macedonia, within the region, and the rest of world



Data accessed on 27 Jan 2021

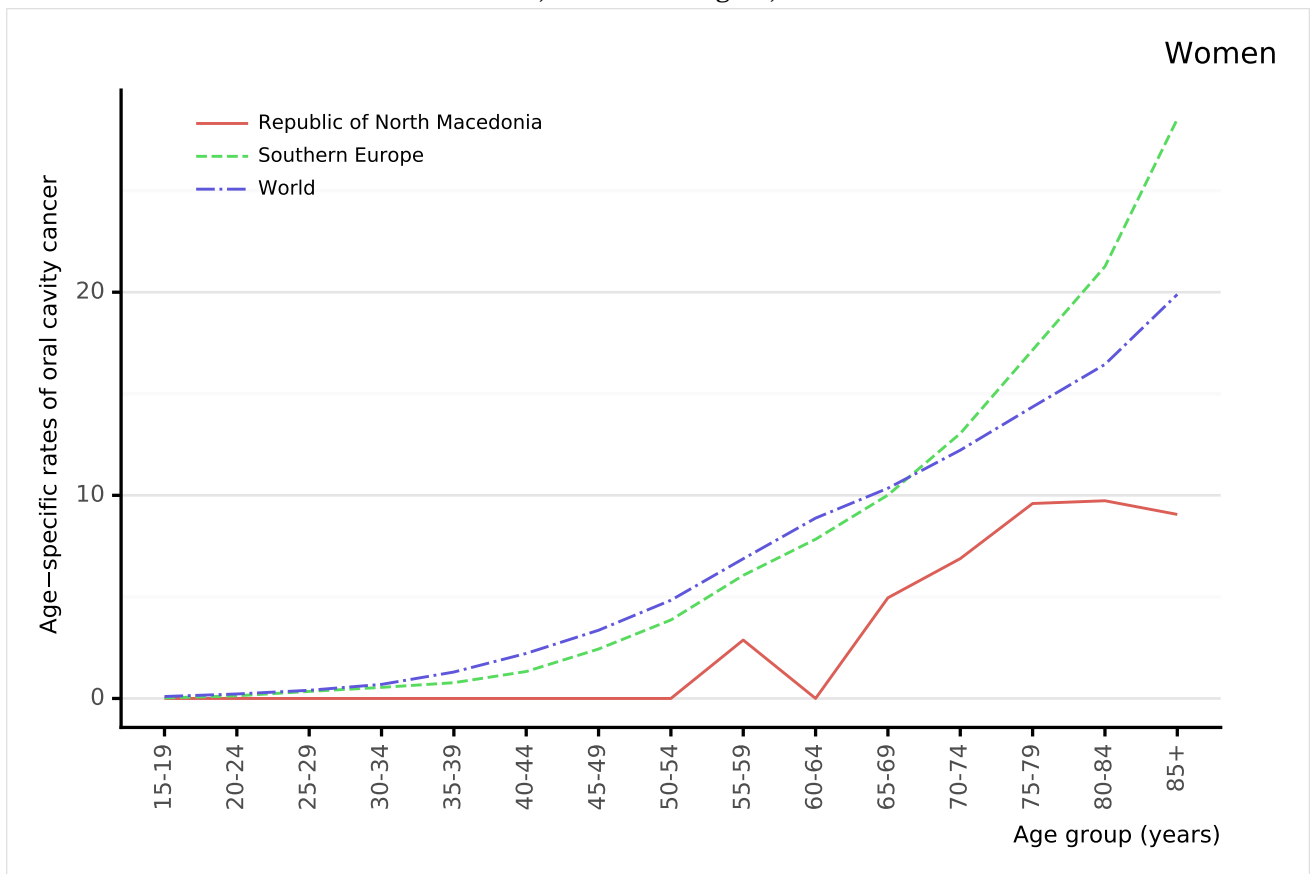
For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>

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

Data Sources:

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 Republic of North Macedonia, 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>

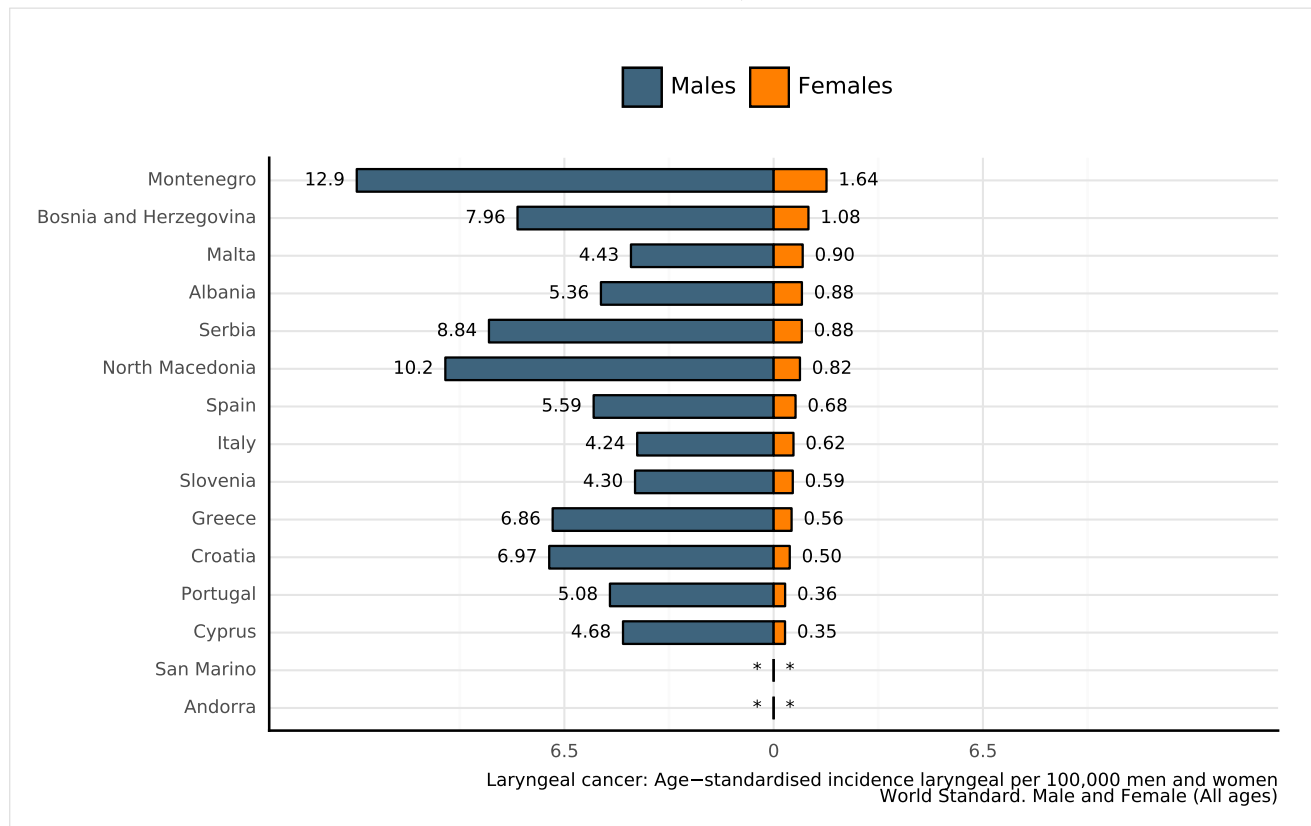
<sup>a</sup> Rates per 100,000 women per year.

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].

### 9.1.8 Laryngeal cancer incidence in Republic of North Macedonia across Southern Europe

Figure 100: Age-standardised incidence rates of laryngeal cancer of Republic of North Macedonia (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>

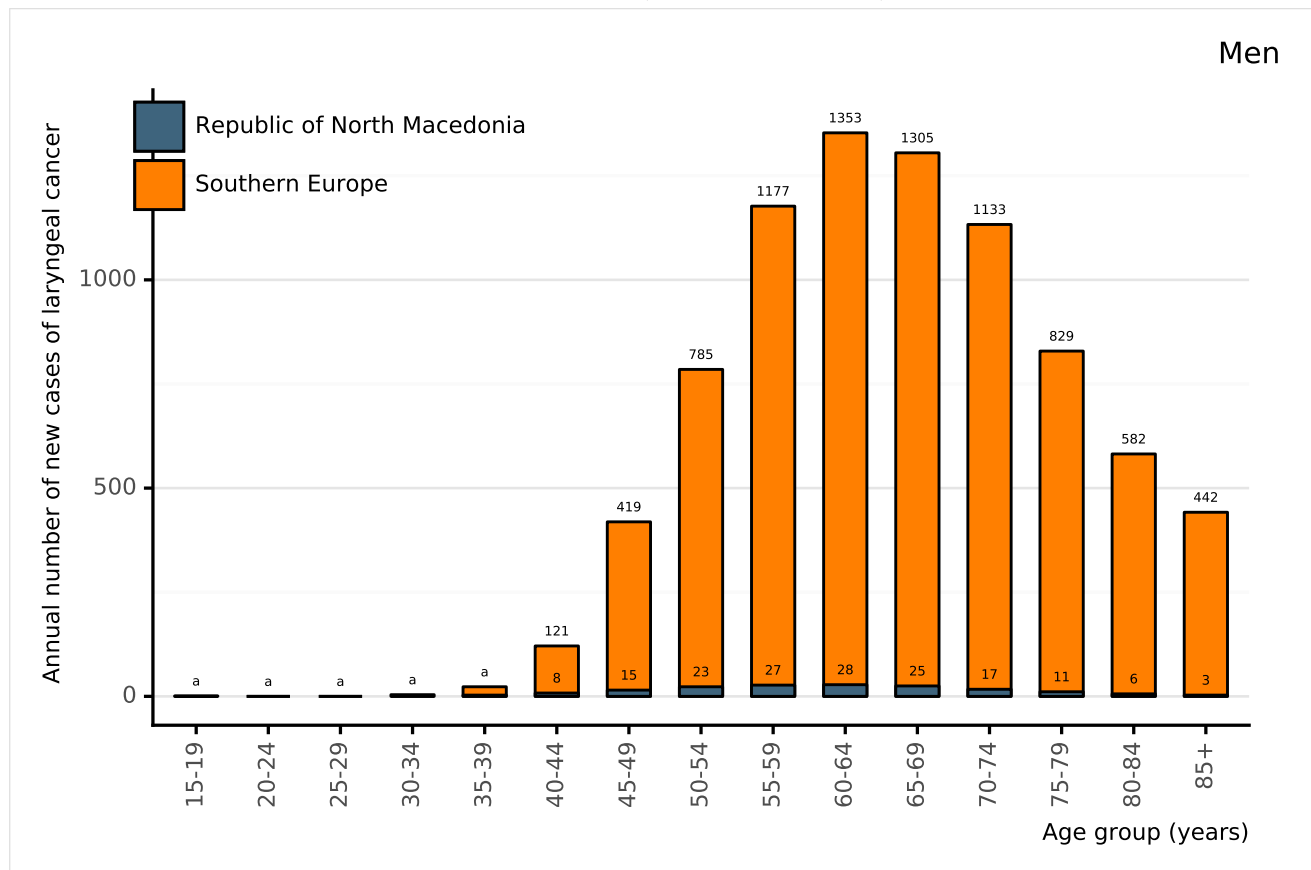
<sup>a</sup> Rates per 100,000 men per year.

<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: <https://gco.iarc.fr/today>, accessed [27 January 2021].

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



**Data accessed on 27 Jan 2021**

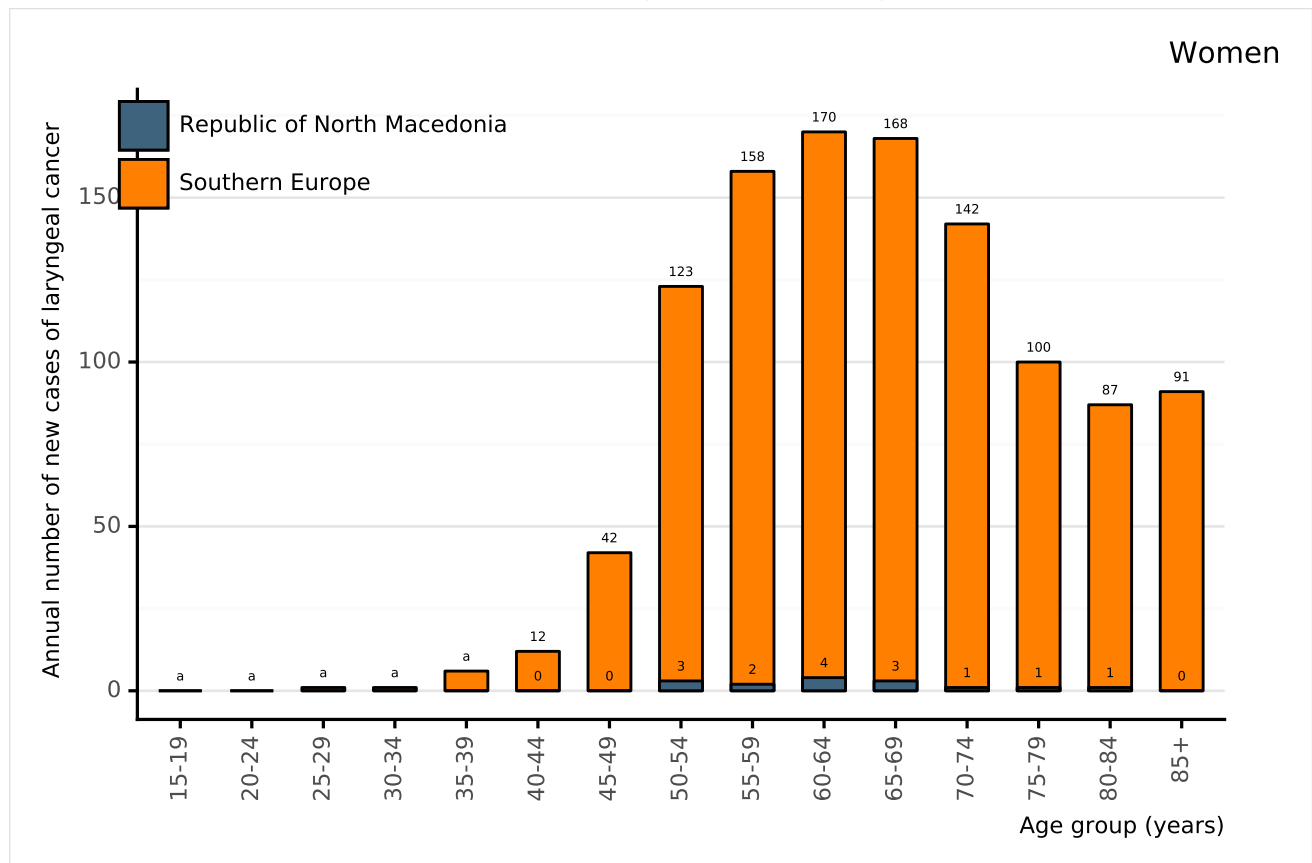
For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>

<sup>a</sup> 0 cases for Republic of North Macedonia and 1 cases for Southern Europe in the 15-19 age group. 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 20-24 age group. 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 25-29 age group. 0 cases for Republic of North Macedonia and 4 cases for Southern Europe in the 30-34 age group. 3 cases for Republic of North Macedonia and 23 cases for Southern Europe in the 35-39 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 102: Annual number of new cases of laryngeal cancer among women by age group in Republic of North Macedonia (estimates for 2020)



Data accessed on 27 Jan 2021

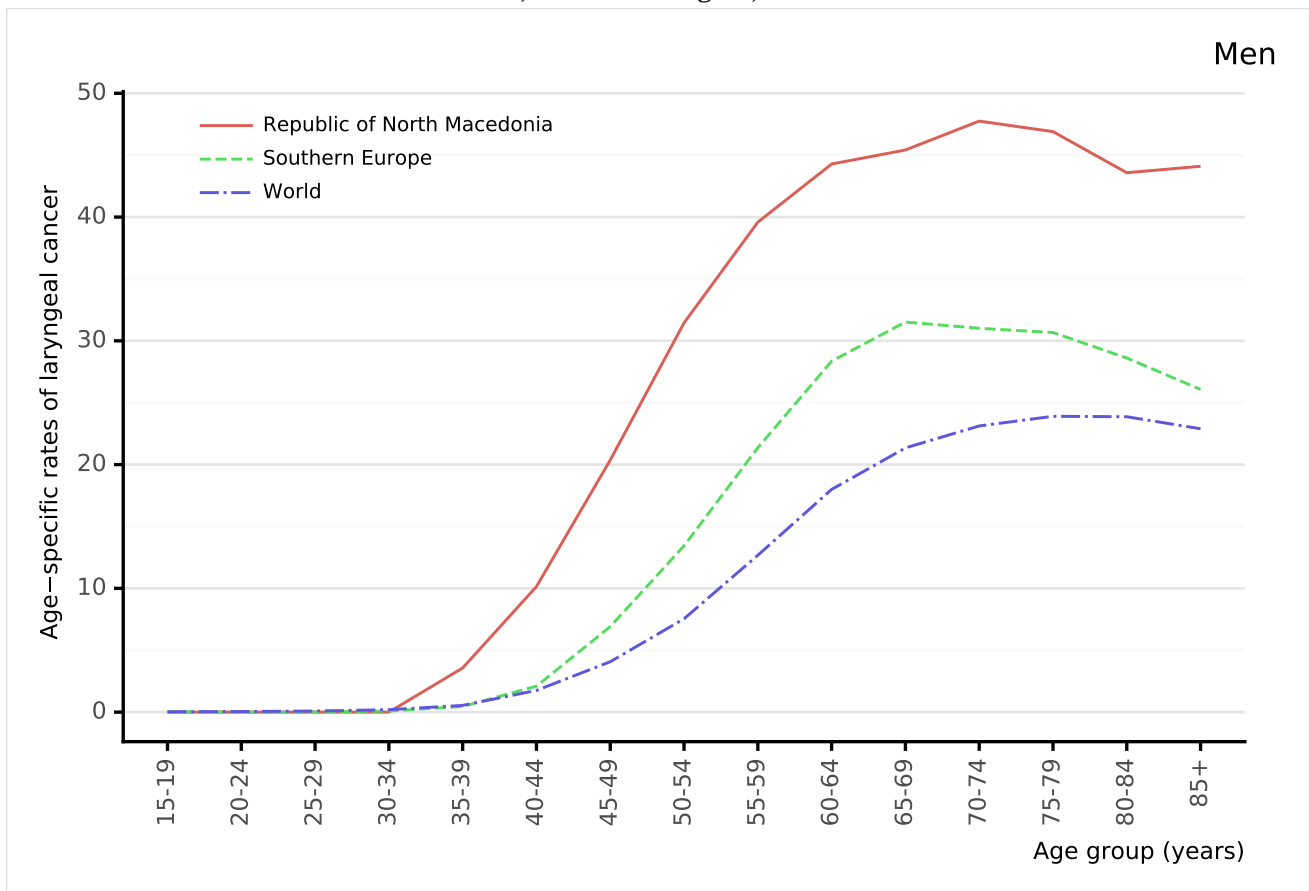
For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>

<sup>a</sup> 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 15-19 age group. 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 20-24 age group. 0 cases for Republic of North Macedonia and 1 cases for Southern Europe in the 25-29 age group. 0 cases for Republic of North Macedonia and 1 cases for Southern Europe in the 30-34 age group. 0 cases for Republic of North Macedonia and 6 cases for Southern Europe in the 35-39 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 103: Comparison of age-specific laryngeal cancer incidence rates among men by age in Republic of North Macedonia, 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>

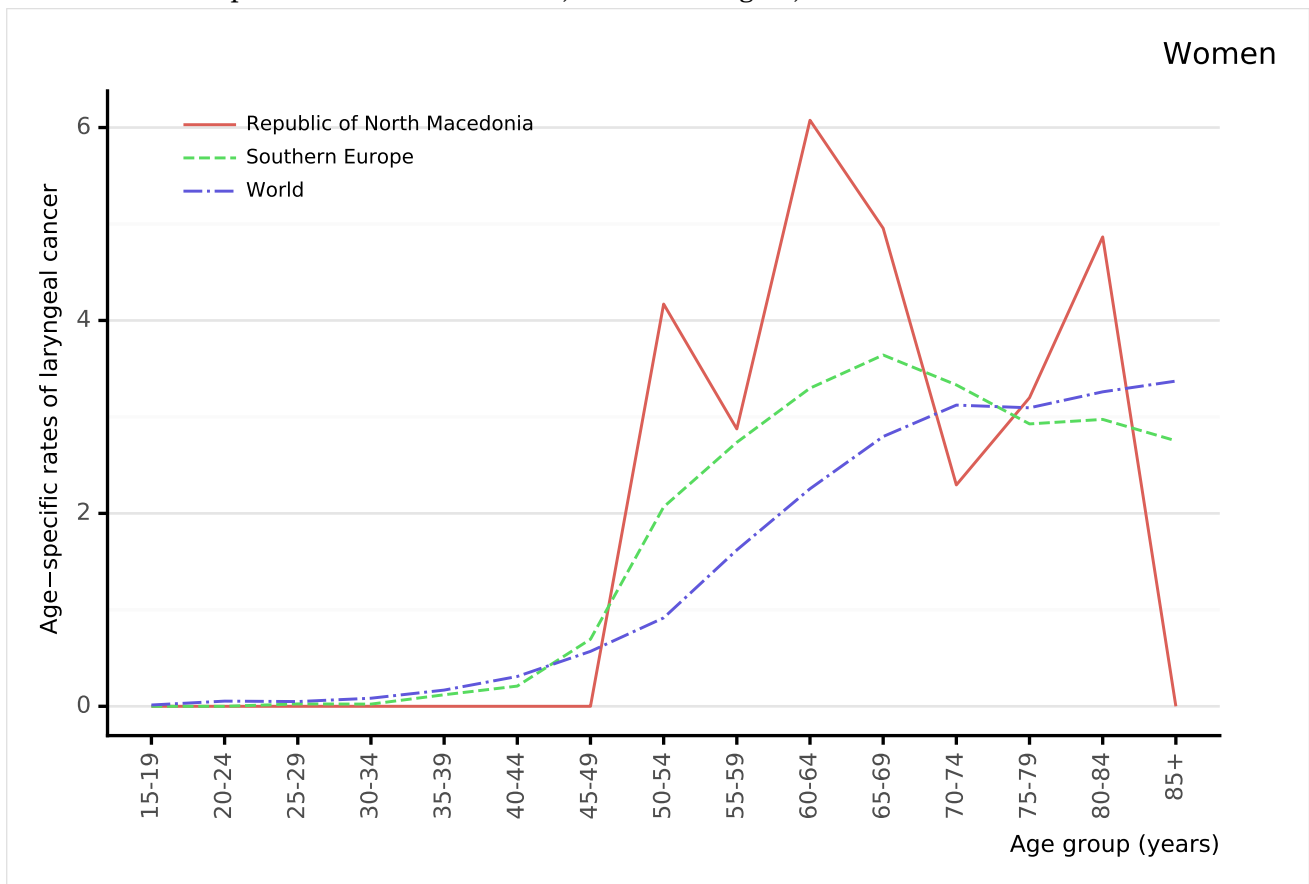
<sup>a</sup> Rates per 100,000 men per year.

Data Sources:

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 Republic of North Macedonia, 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.

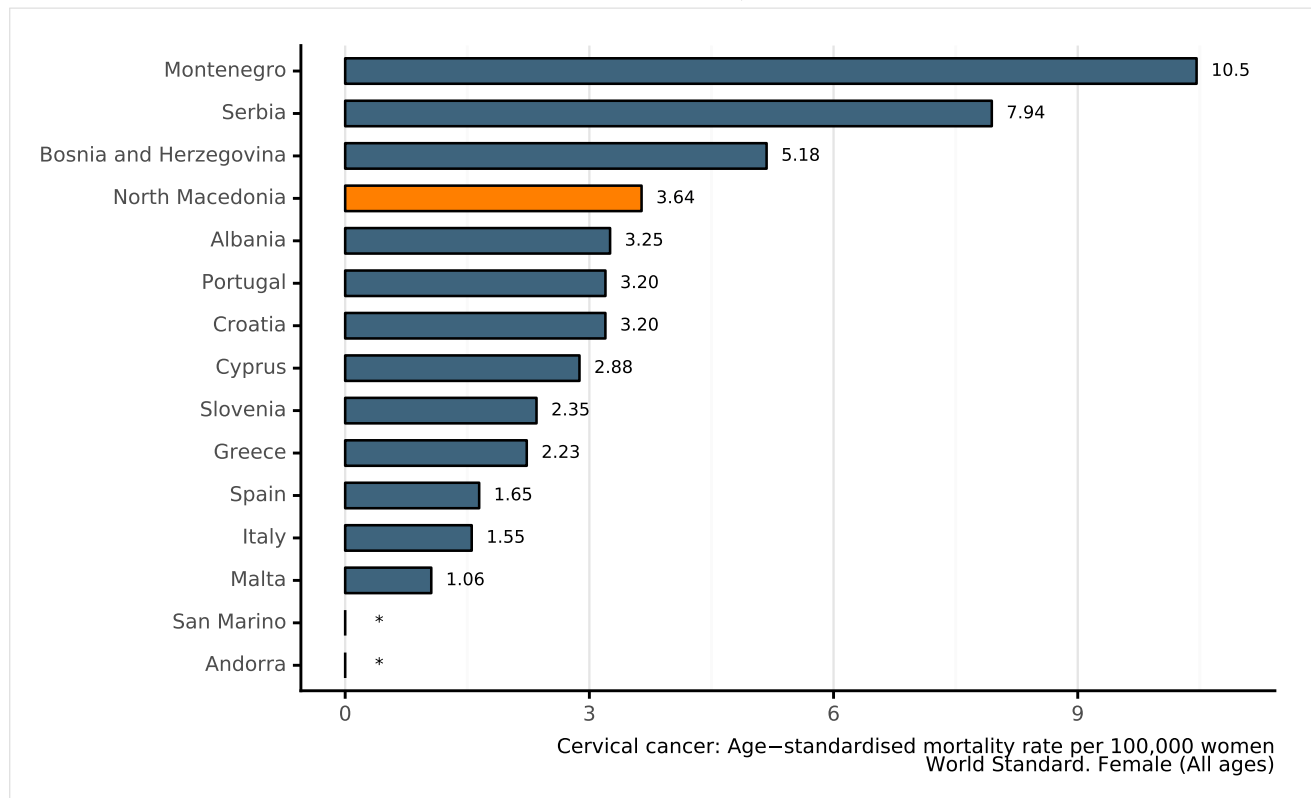
Data Sources:

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].

## 9.2 Mortality

### 9.2.1 Cervical cancer mortality in Republic of North Macedonia across Southern Europe

Figure 105: Age-standardised mortality rates of cervical cancer of Republic of North Macedonia (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>

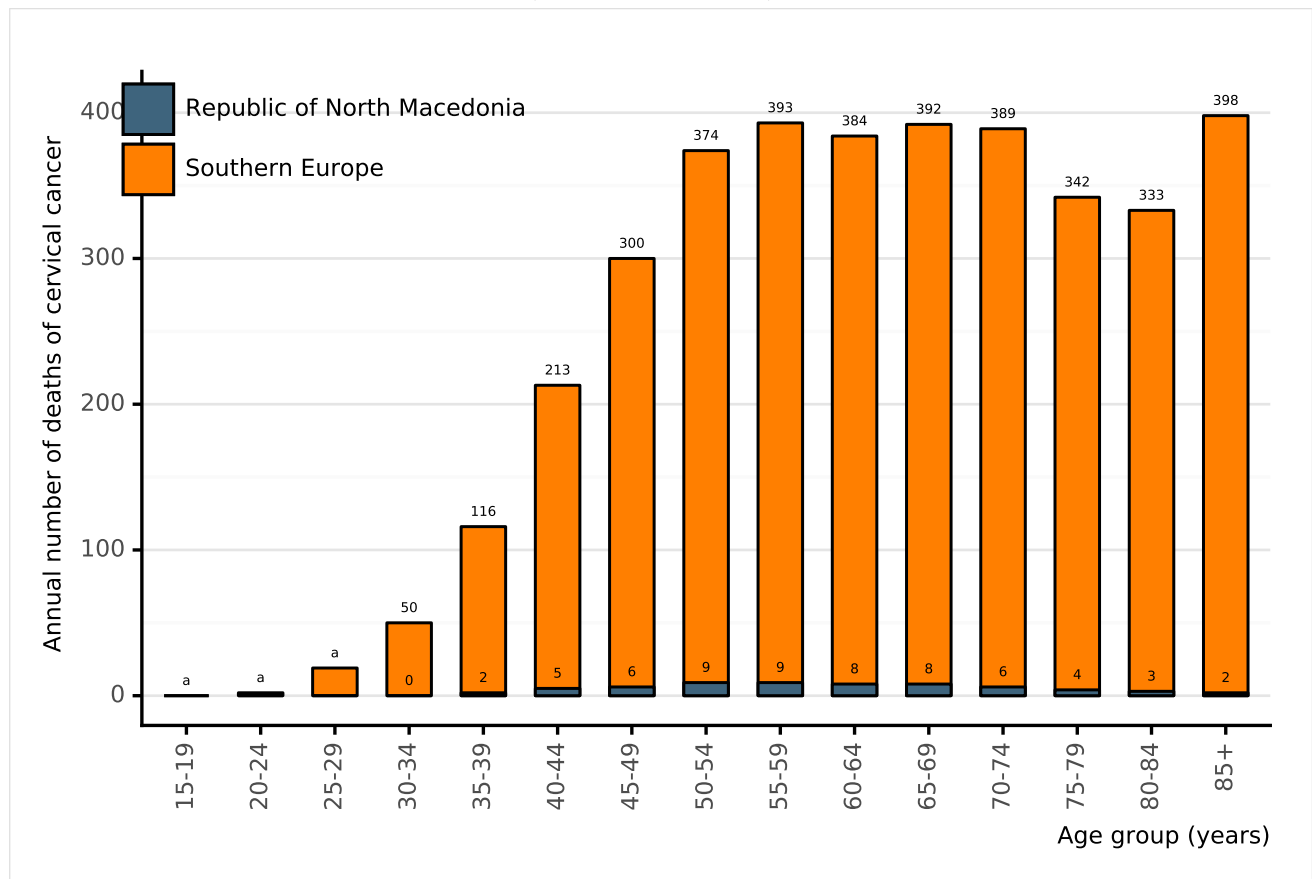
<sup>a</sup> Rates per 100,000 women per year.

\* Rates are not available

#### 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 106: Annual number of deaths of cervical cancer by age group in Republic of North Macedonia (estimates for 2020)



**Data accessed on 27 Jan 2021**

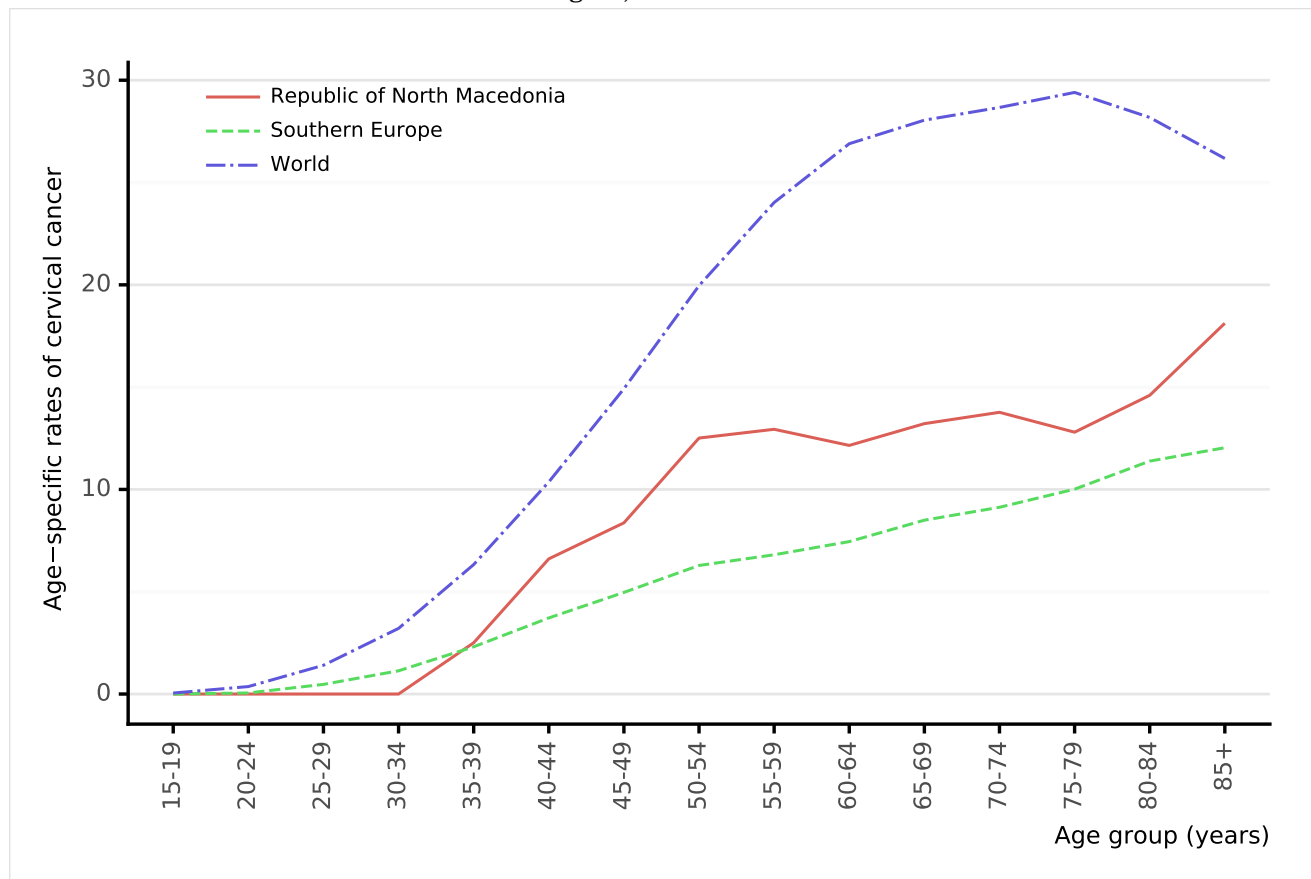
For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>

<sup>a</sup> 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 15-19 age group. 0 cases for Republic of North Macedonia and 2 cases for Southern Europe in the 20-24 age group. 0 cases for Republic of North Macedonia and 19 cases for Southern Europe in the 25-29 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 107: Comparison of age-specific cervical cancer mortality rates in Republic of North Macedonia, 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>

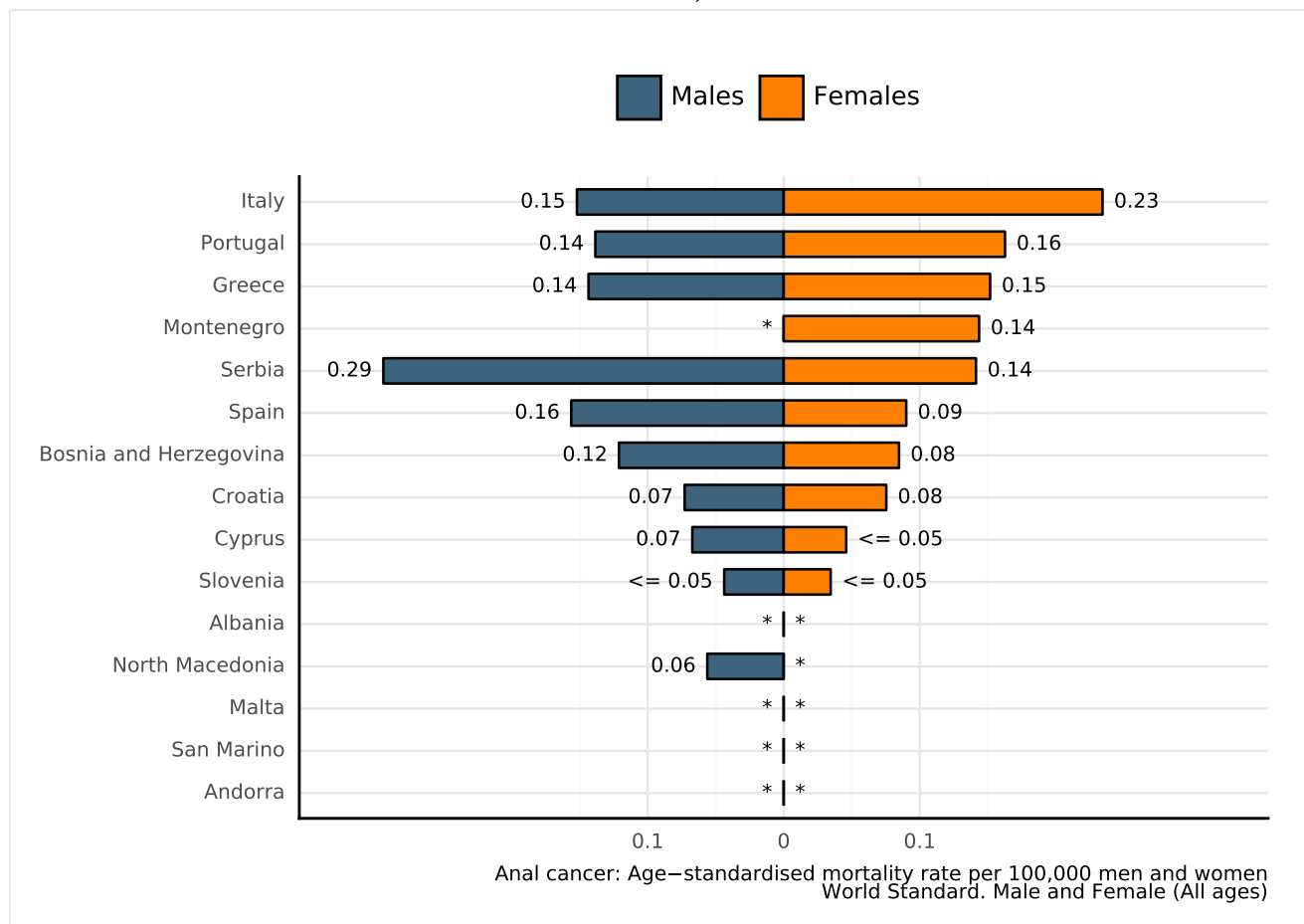
<sup>a</sup> Rates per 100,000 women per year.

**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].

## 9.2.2 Anal cancer mortality in Republic of North Macedonia across Southern Europe

Figure 108: Age-standardised mortality rates of anal cancer of Republic of North Macedonia (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.

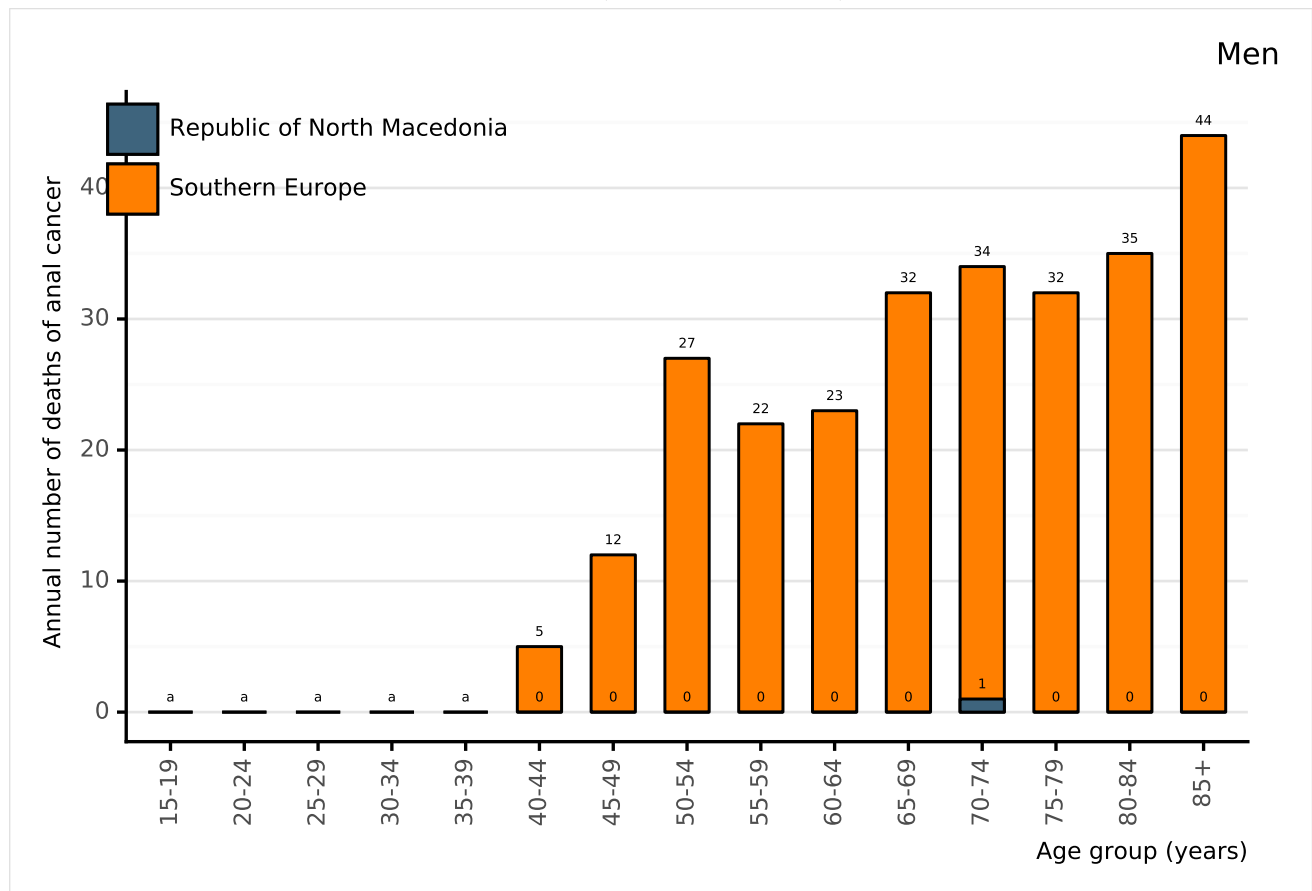
<sup>b</sup> Rates per 100,000 women per year.

\* Rates are not available

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



**Data accessed on 27 Jan 2021**

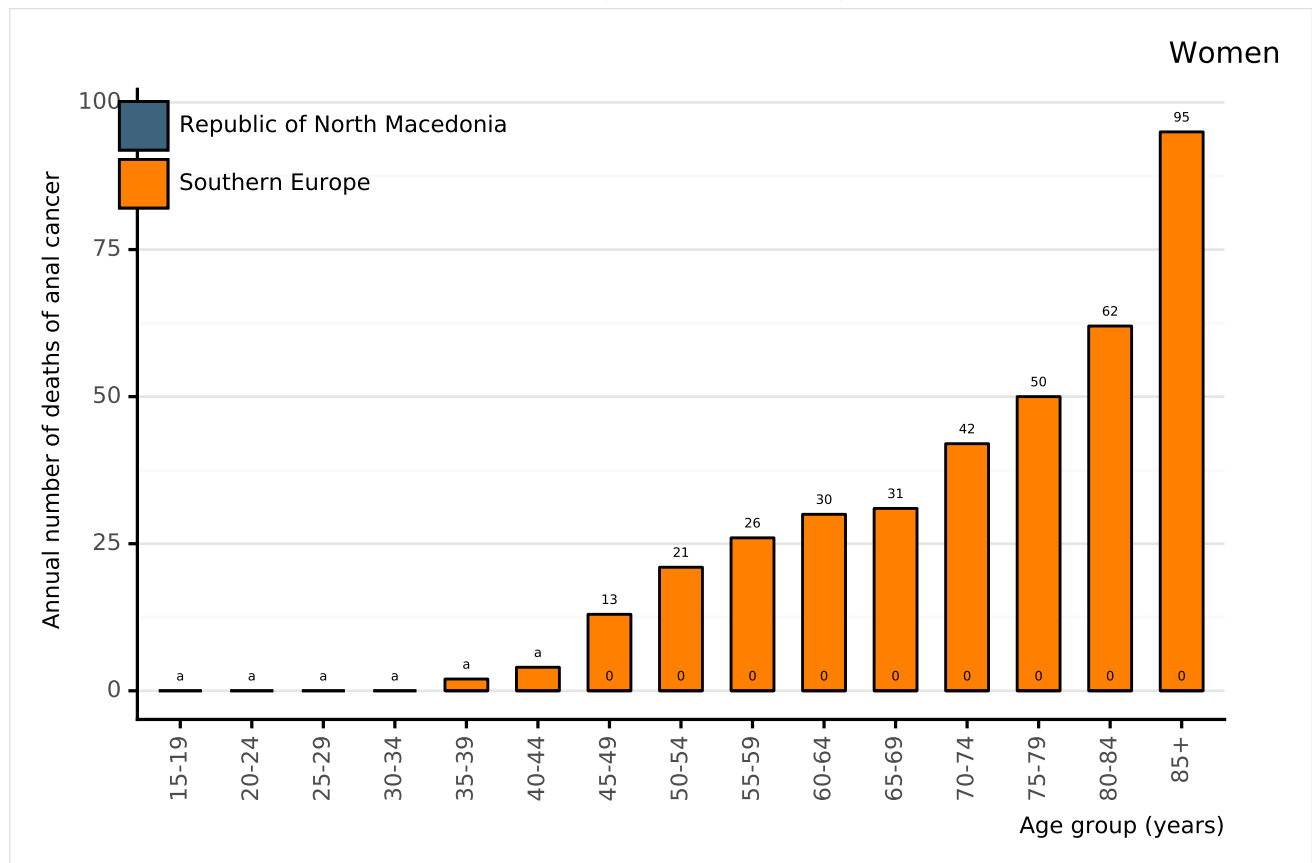
For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>

<sup>a</sup> 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 15-19 age group. 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 20-24 age group. 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 25-29 age group. 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 30-34 age group. 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 35-39 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 110: Annual number of deaths of anal cancer among women by age group in Republic of North Macedonia (estimates for 2020)



Data accessed on 27 Jan 2021

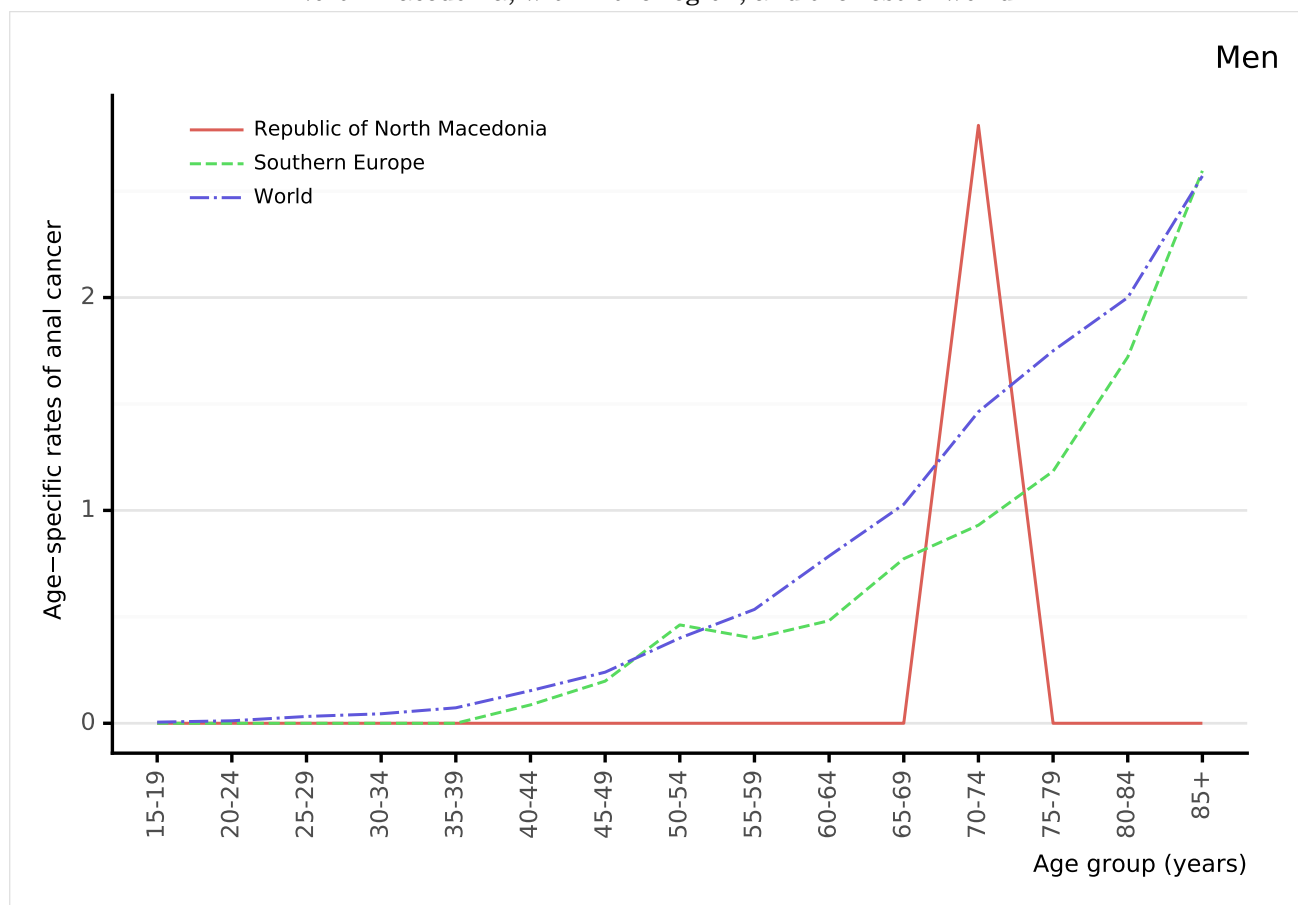
For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>

<sup>a</sup> 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 15-19 age group. 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 20-24 age group. 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 25-29 age group. 0 cases for Republic of North Macedonia and 2 cases for Southern Europe in the 35-39 age group. 0 cases for Republic of North Macedonia and 4 cases for Southern Europe in the 40-44 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 111: Comparison of age-specific anal cancer mortality rates among men by age in Republic of North Macedonia, 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>

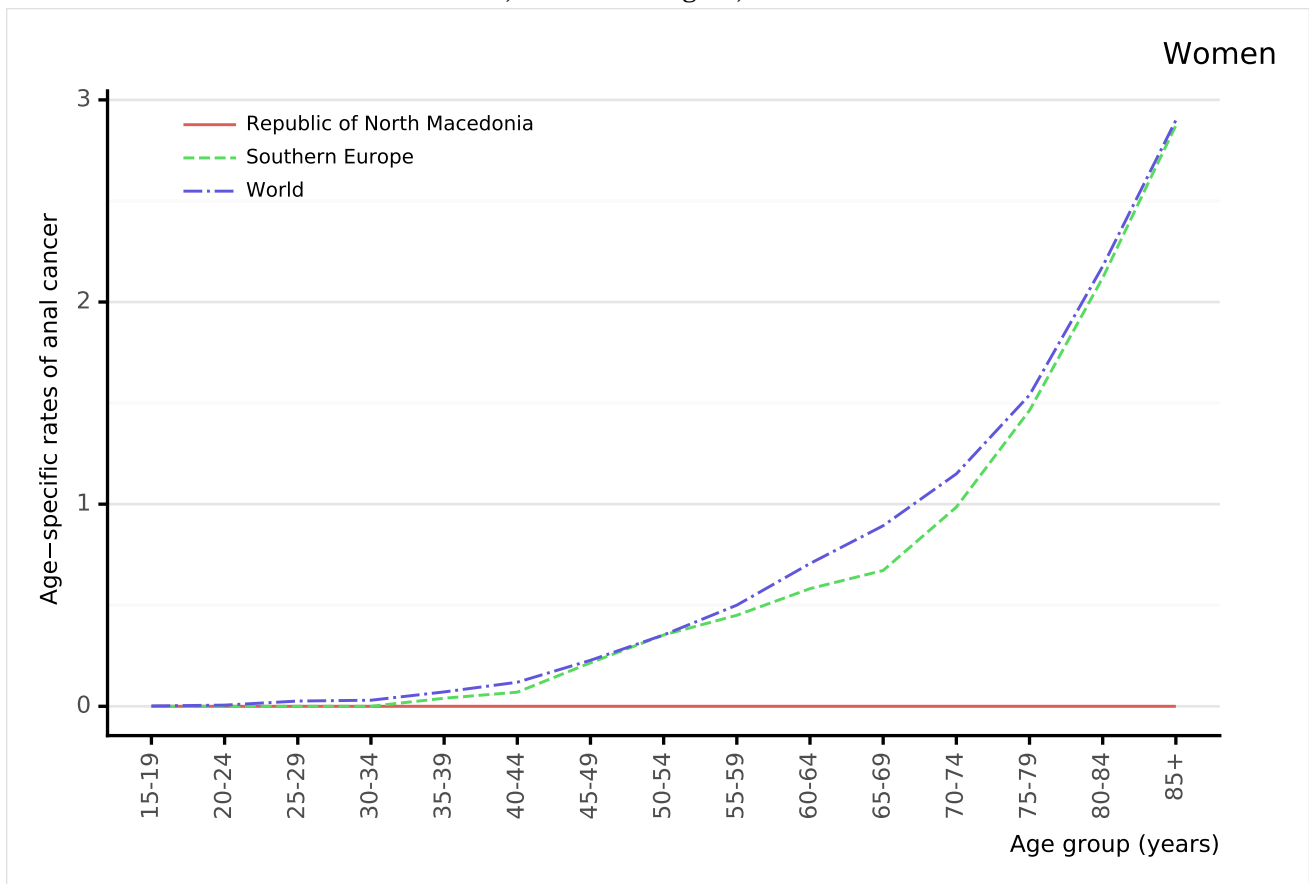
<sup>a</sup> Rates per 100,000 men per year.

Data Sources:

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 Republic of North Macedonia, 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>

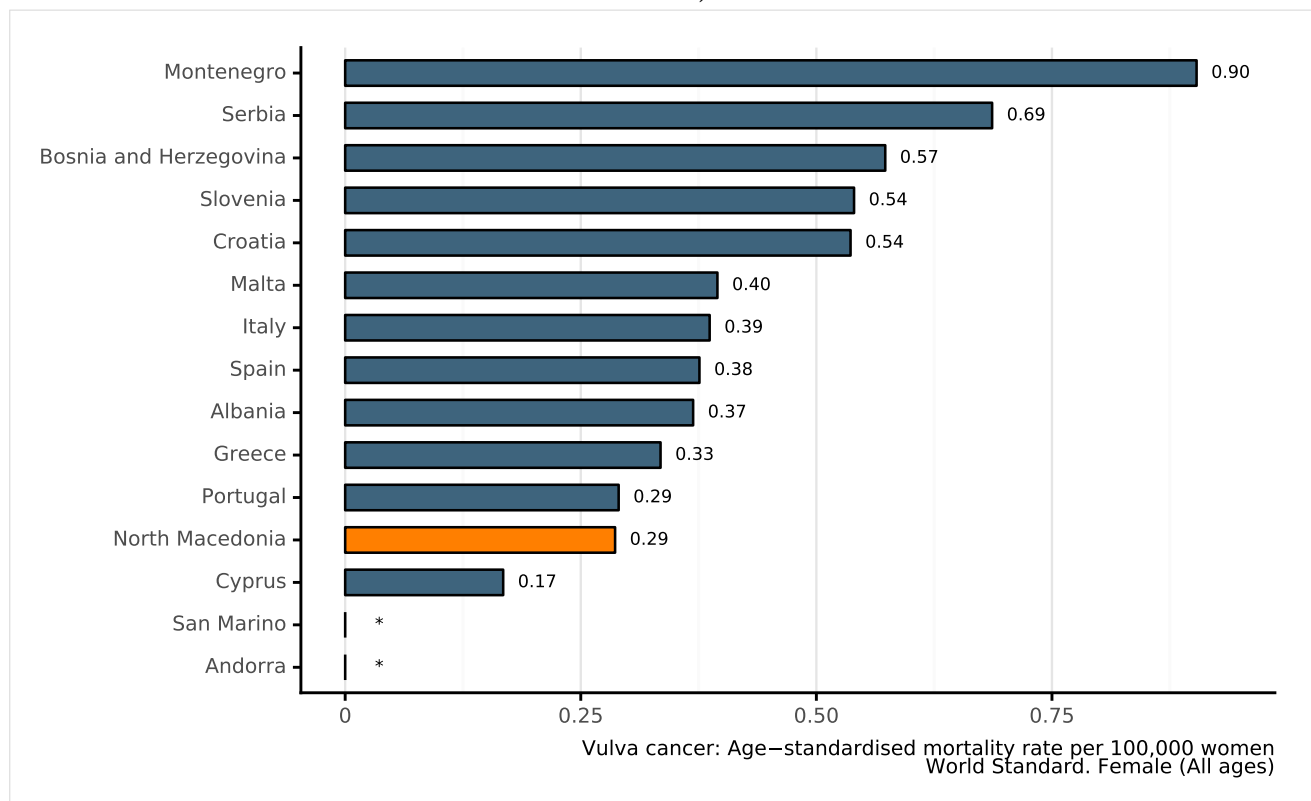
<sup>a</sup> Rates per 100,000 women per year.

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].

### 9.2.3 Vulva cancer mortality in Republic of North Macedonia across Southern Europe

Figure 113: Age-standardised mortality rates of vulva cancer of Republic of North Macedonia (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>

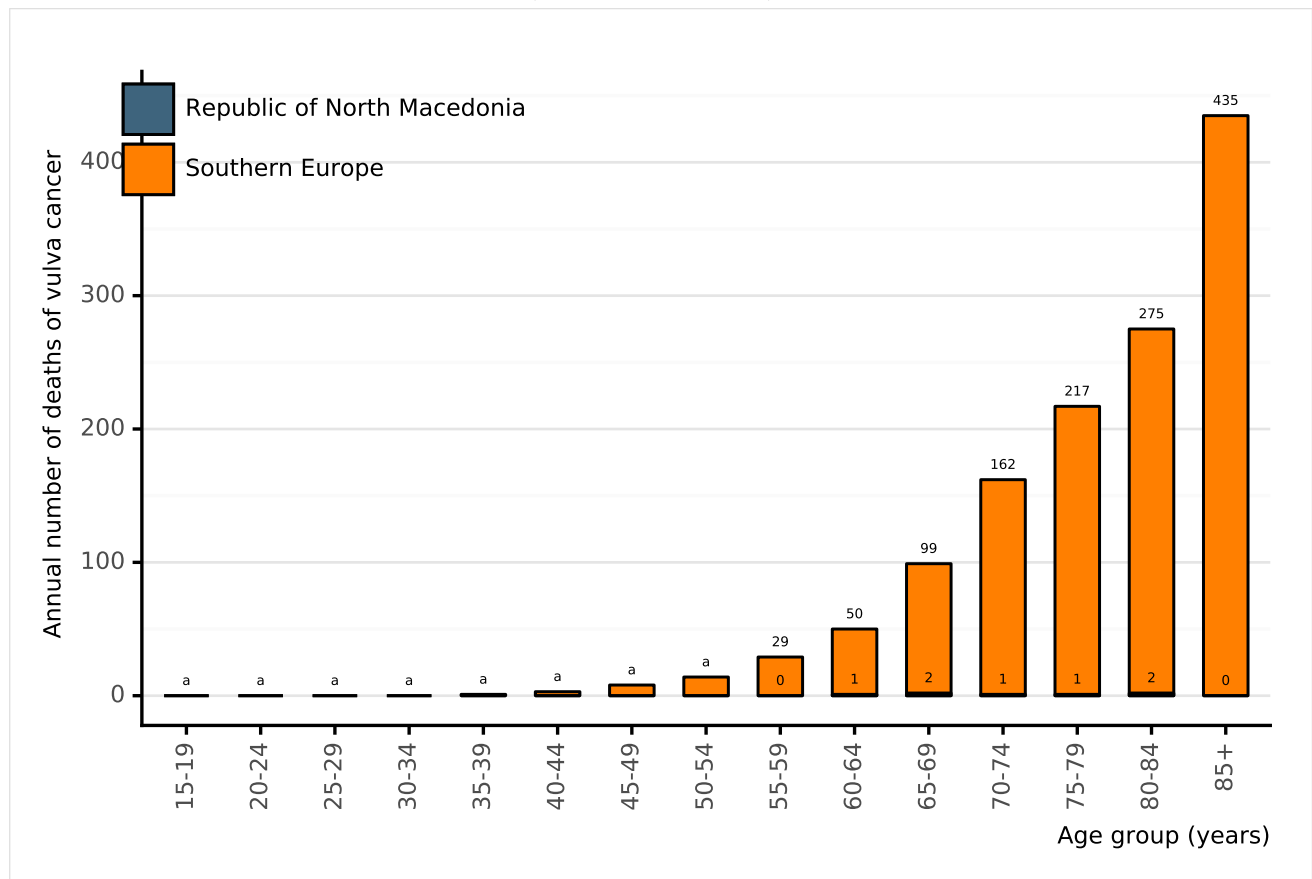
<sup>a</sup> Rates per 100,000 women per year.

\* Rates are not available

**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 114: Annual number of deaths of vulva cancer by age group in Republic of North Macedonia (estimates for 2020)



**Data accessed on 27 Jan 2021**

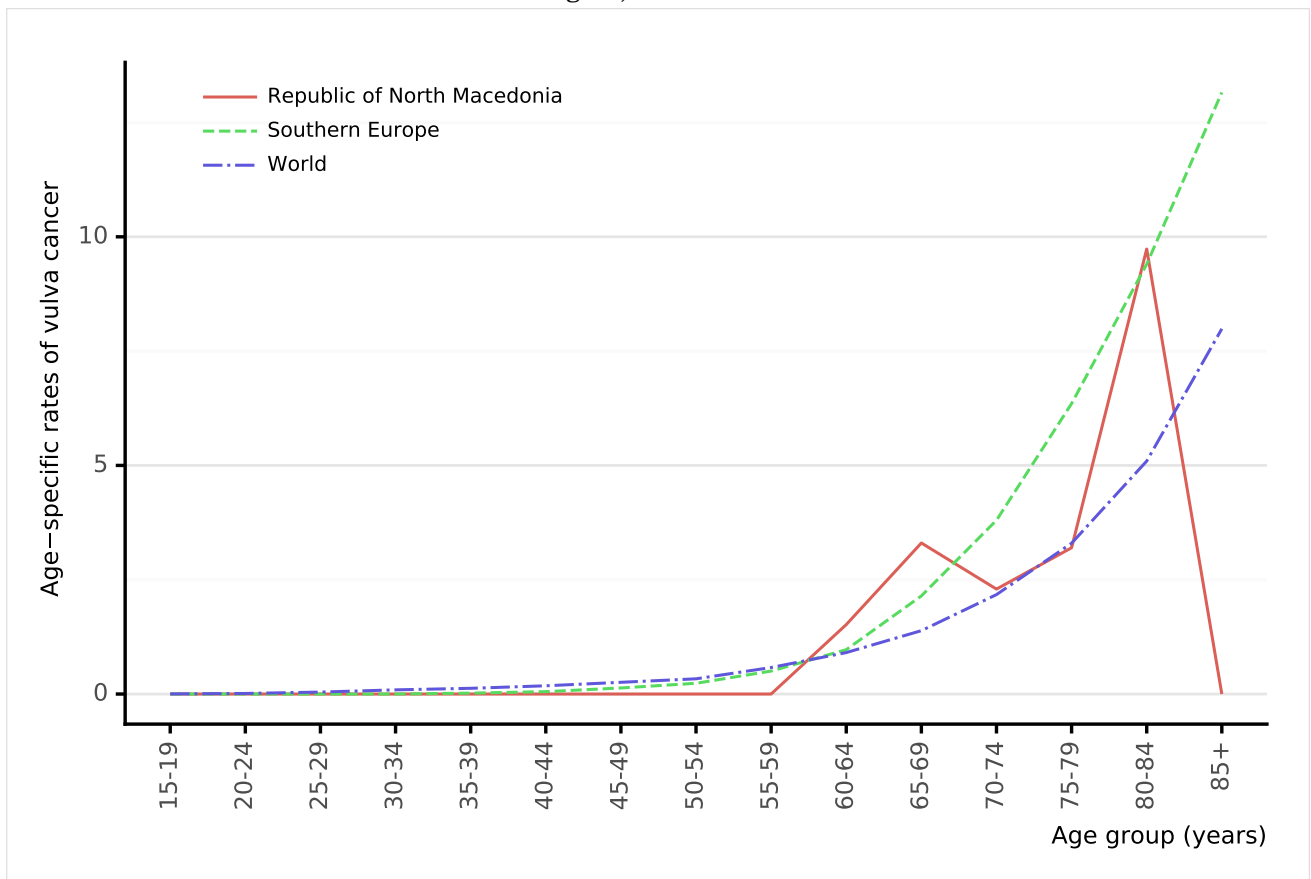
For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>

<sup>a</sup> 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 15-19 age group. 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 20-24 age group. 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 25-29 age group. 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 30-34 age group. 0 cases for Republic of North Macedonia and 1 cases for Southern Europe in the 35-39 age group. 0 cases for Republic of North Macedonia and 3 cases for Southern Europe in the 40-44 age group. 0 cases for Republic of North Macedonia and 8 cases for Southern Europe in the 45-49 age group. 0 cases for Republic of North Macedonia and 14 cases for Southern Europe in the 50-54 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 Republic of North Macedonia, 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>

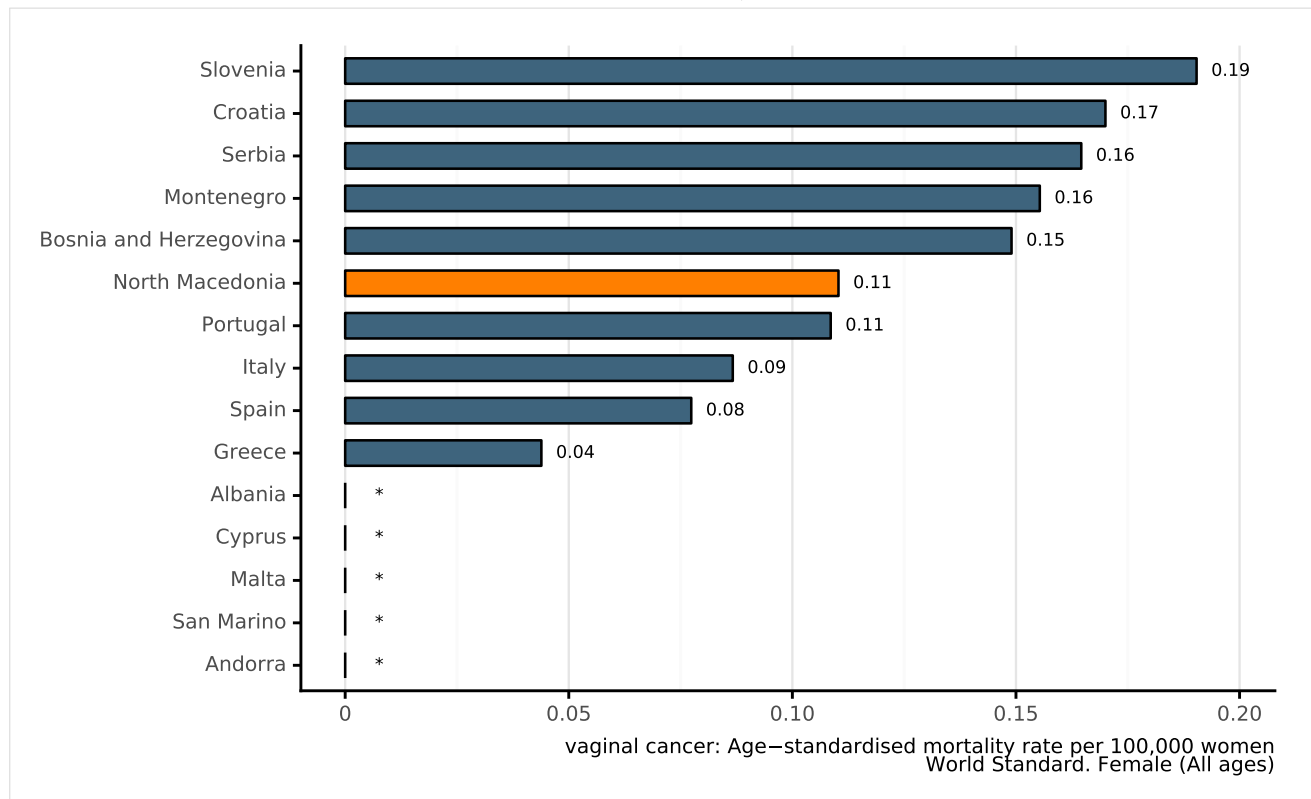
<sup>a</sup> Rates per 100,000 women per year.

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].

### 9.2.4 Vaginal cancer mortality in Republic of North Macedonia across Southern Europe

Figure 116: Age-standardised mortality rates of vaginal cancer of Republic of North Macedonia (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>

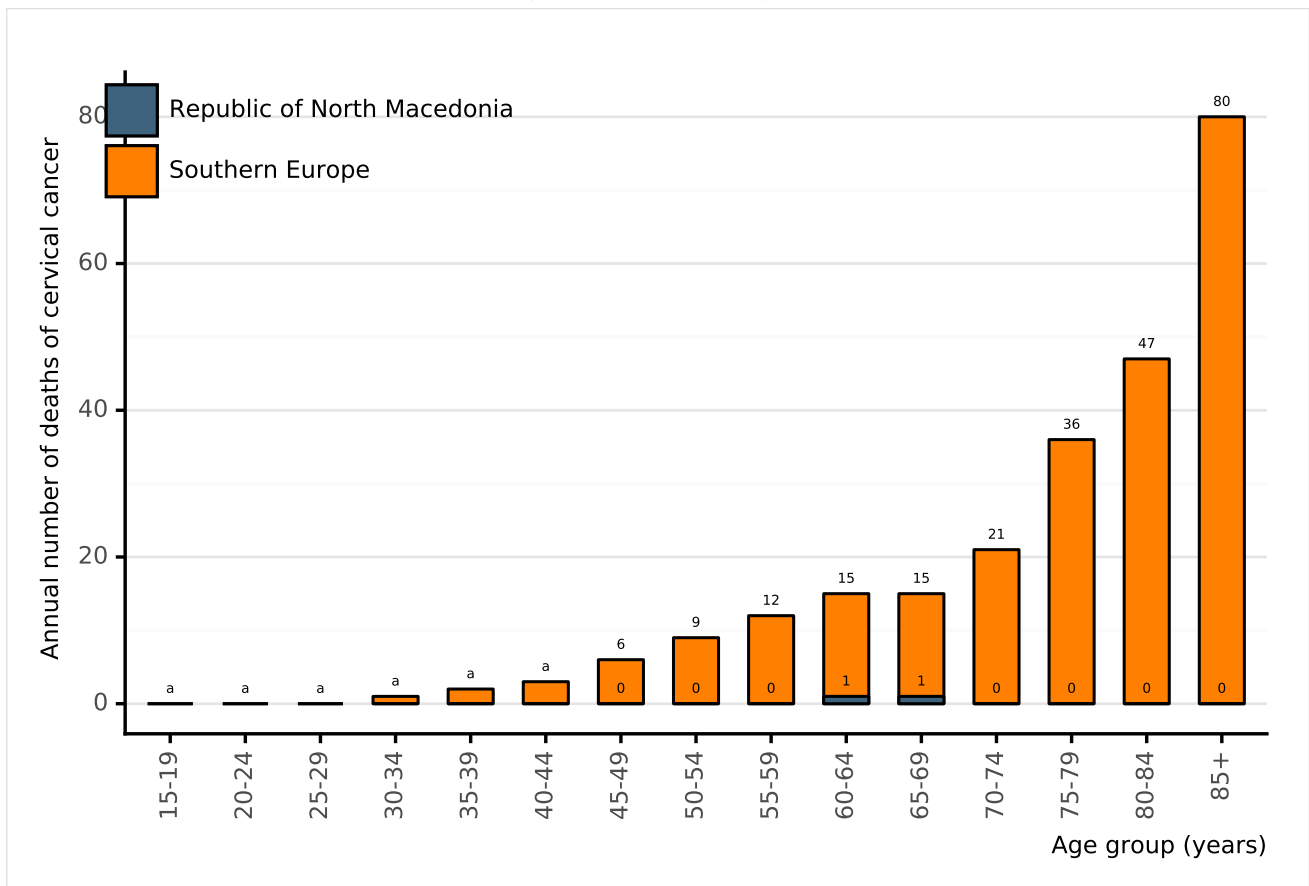
<sup>a</sup> Rates per 100,000 women per year.

\* Rates are not available

**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 117: Annual number of deaths of cervical cancer by age group in Republic of North Macedonia (estimates for 2020)



**Data accessed on 27 Jan 2021**

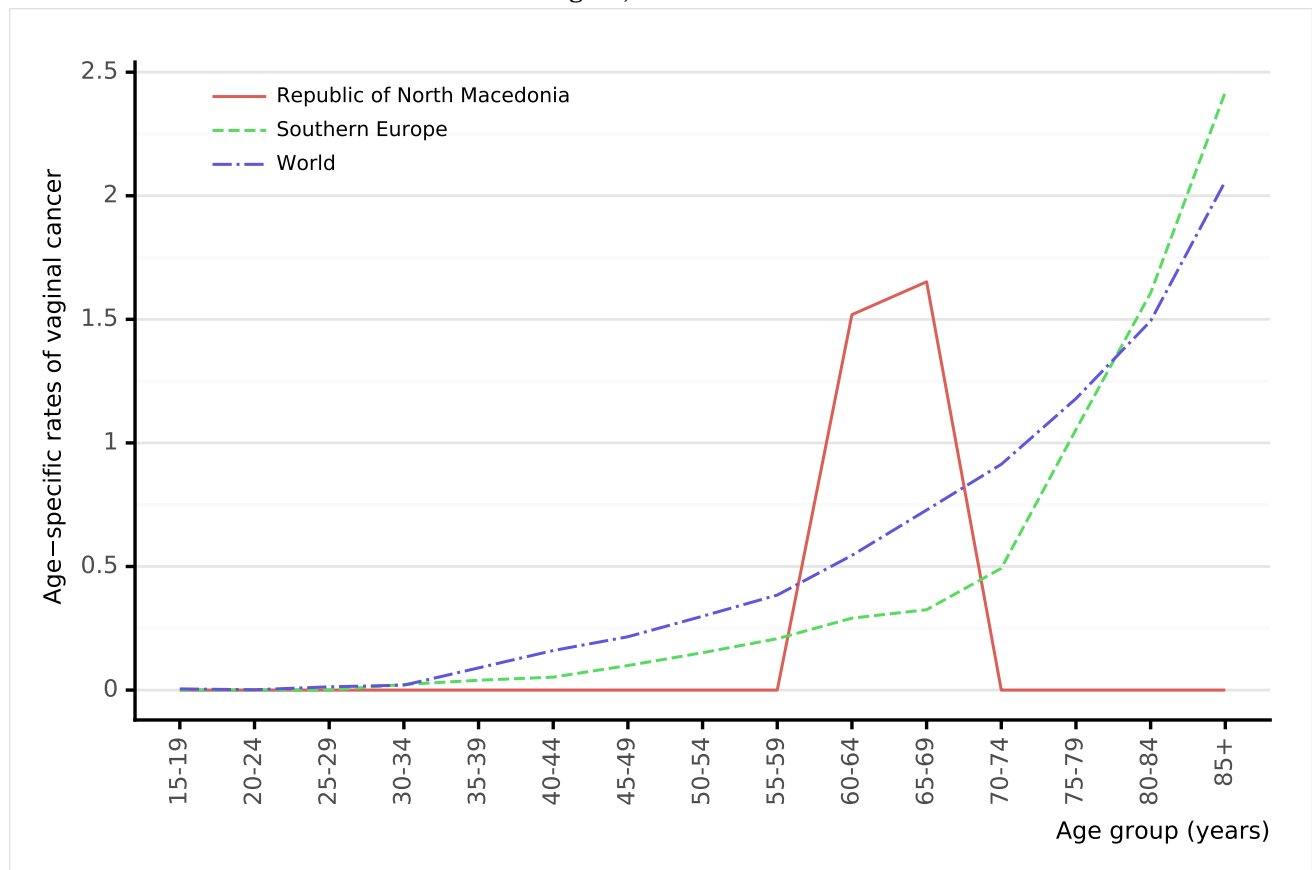
For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>

<sup>a</sup> 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 15-19 age group. 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 20-24 age group. 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 25-29 age group. 0 cases for Republic of North Macedonia and 1 case for Southern Europe in the 30-34 age group. 0 cases for Republic of North Macedonia and 2 cases for Southern Europe in the 35-39 age group. 0 cases for Republic of North Macedonia and 3 cases for Southern Europe in the 40-44 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 118: Comparison of age-specific vaginal cancer mortality rates in Republic of North Macedonia, 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>

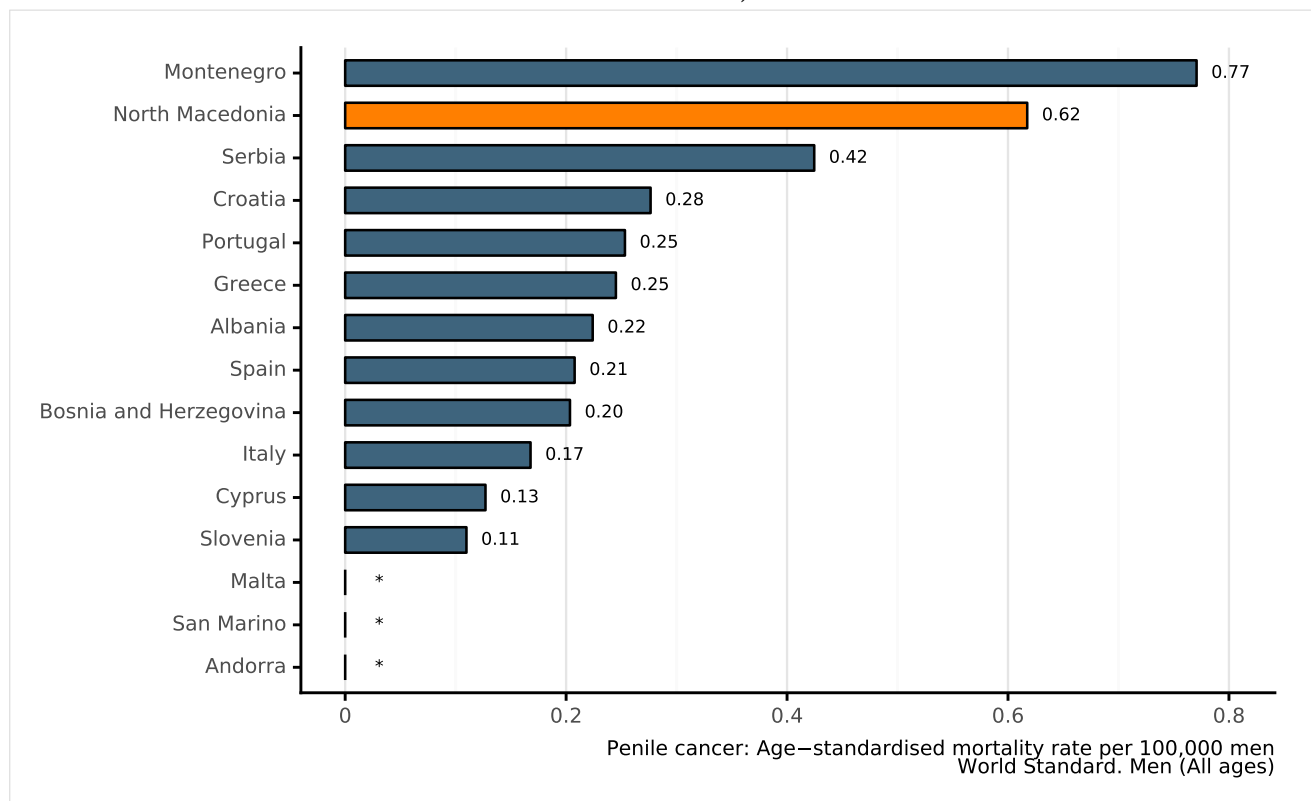
<sup>a</sup> Rates per 100,000 women per year.

**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].

### 9.2.5 Penile cancer mortality in Republic of North Macedonia across Southern Europe

Figure 119: Age-standardised mortality rates of penile cancer of Republic of North Macedonia (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.

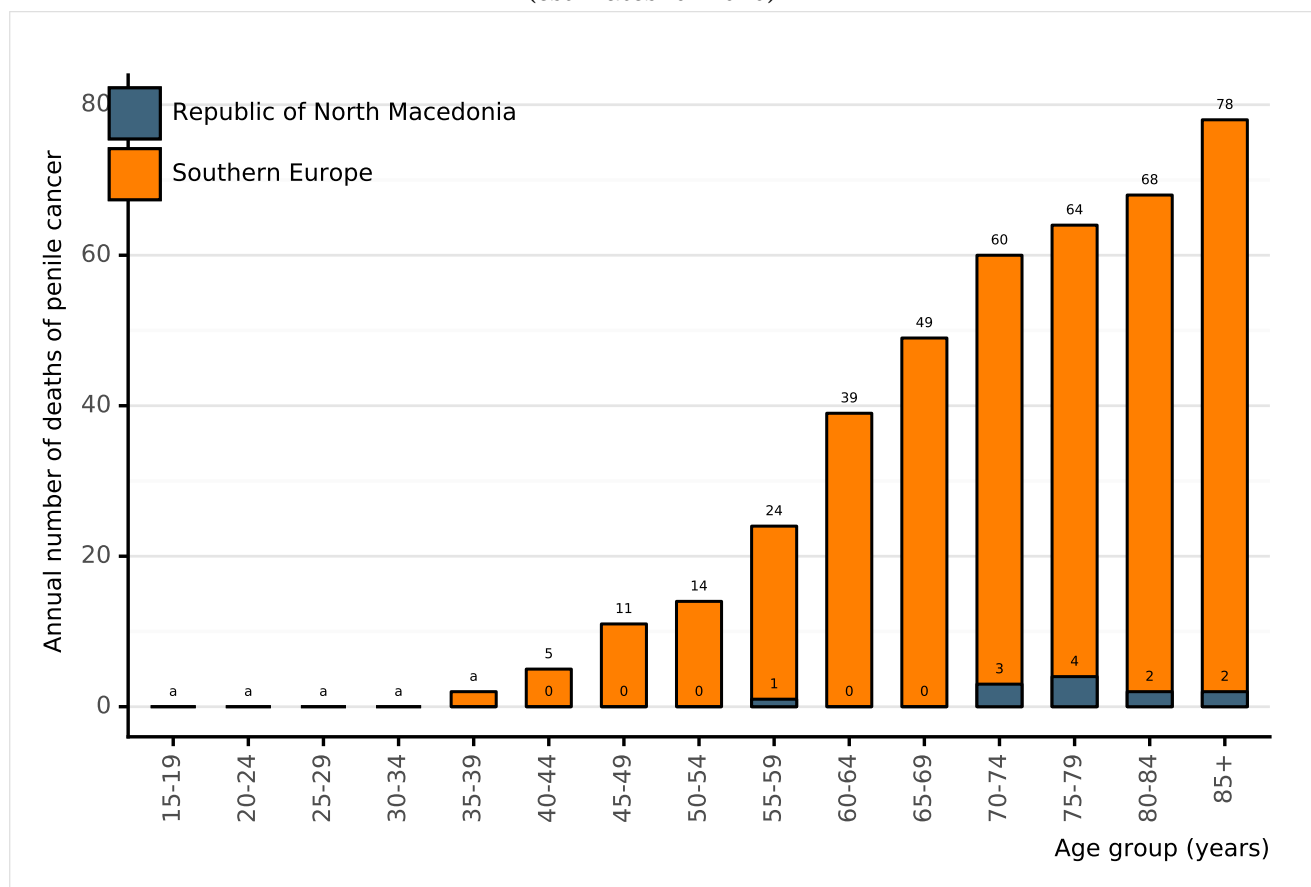
\* Rates are not available

**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 120: Annual number of new deaths of penile cancer by age group in Republic of North Macedonia (estimates for 2020)



**Data accessed on 27 Jan 2021**

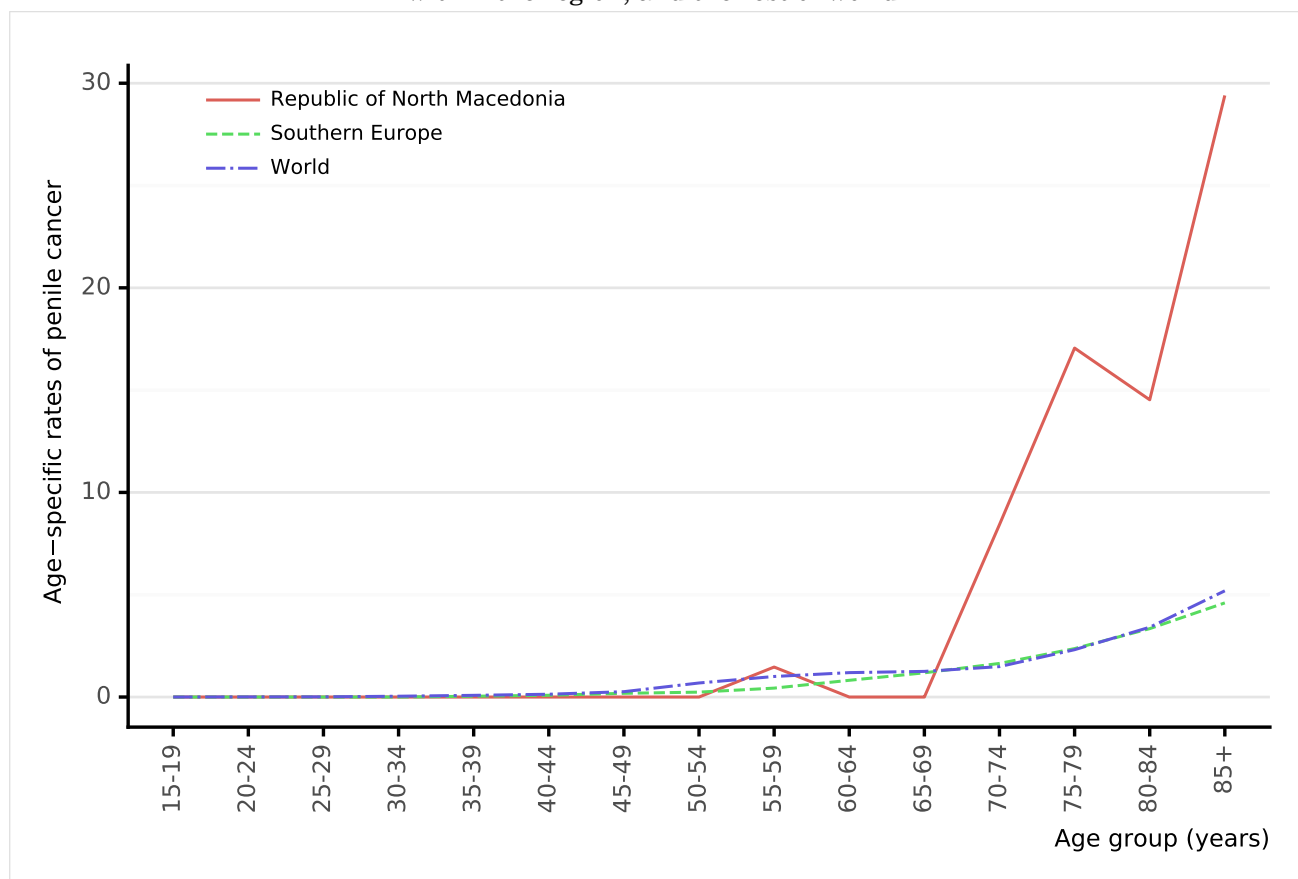
For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>

<sup>a</sup> 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 15-19 age group. 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 20-24 age group. 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 25-29 age group. 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 30-34 age group. 0 cases for Republic of North Macedonia and 2 cases for Southern Europe in the 35-39 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 121: Comparison of age-specific penile cancer mortality rates in Republic of North Macedonia, 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>

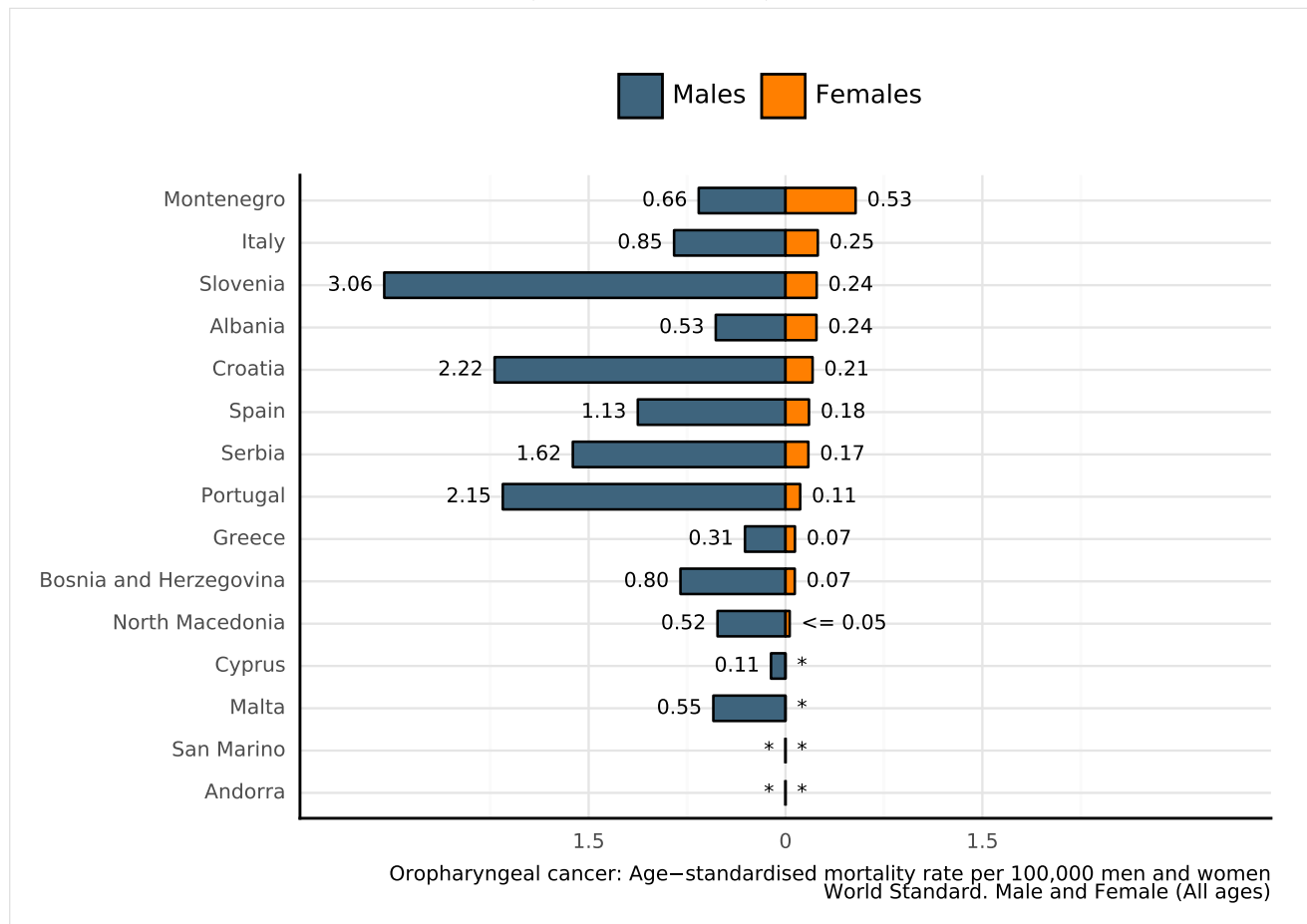
<sup>a</sup> Rates per 100,000 men per year.

Data Sources:

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].

## 9.2.6 Oropharyngeal cancer mortality in Republic of North Macedonia across Southern Europe

Figure 122: Age-standardised mortality rates of oropharyngeal cancer of Republic of North Macedonia (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.

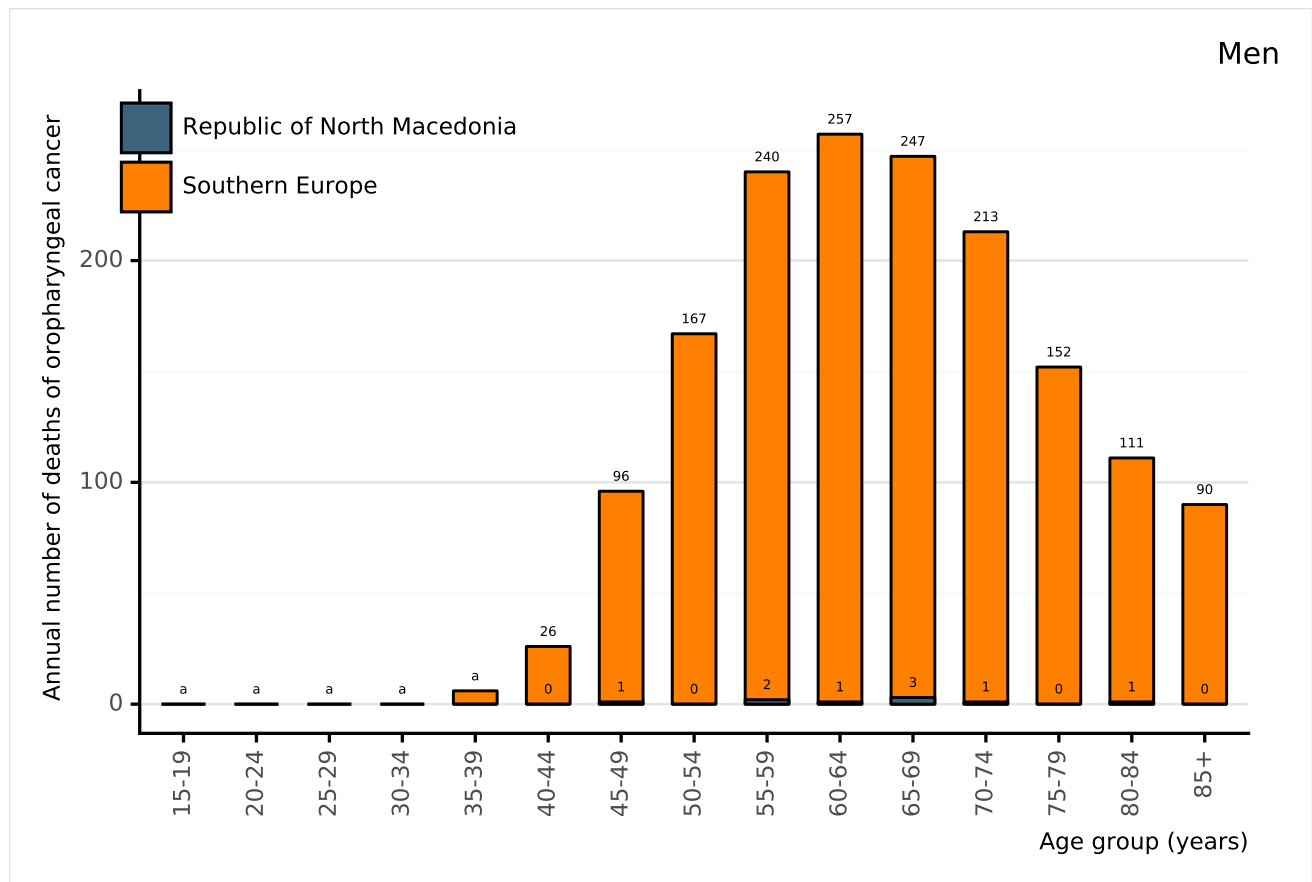
<sup>b</sup> Rates per 100,000 women per year.

\* Rates are not available

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 123: Annual number of deaths of oropharyngeal cancer among men by age group in Republic of North Macedonia (estimates for 2020)



**Data accessed on 27 Jan 2021**

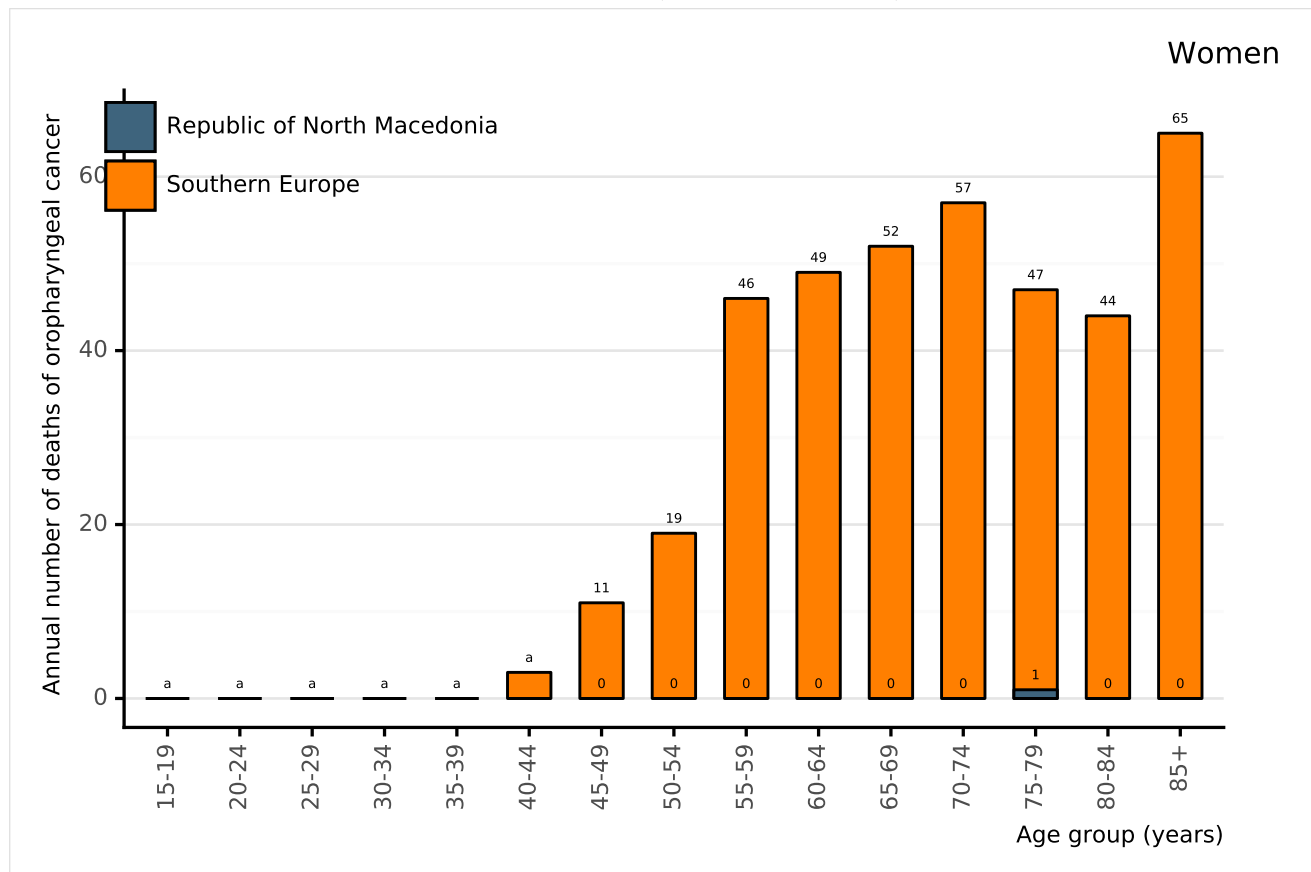
For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>

<sup>a</sup> 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 15-19 age group. 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 20-24 age group. 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 25-29 age group. 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 30-34 age group. 0 cases for Republic of North Macedonia and 6 cases for Southern Europe in the 35-39 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 124: Annual number of deaths of oropharyngeal cancer among women by age group in Republic of North Macedonia (estimates for 2020)



**Data accessed on 27 Jan 2021**

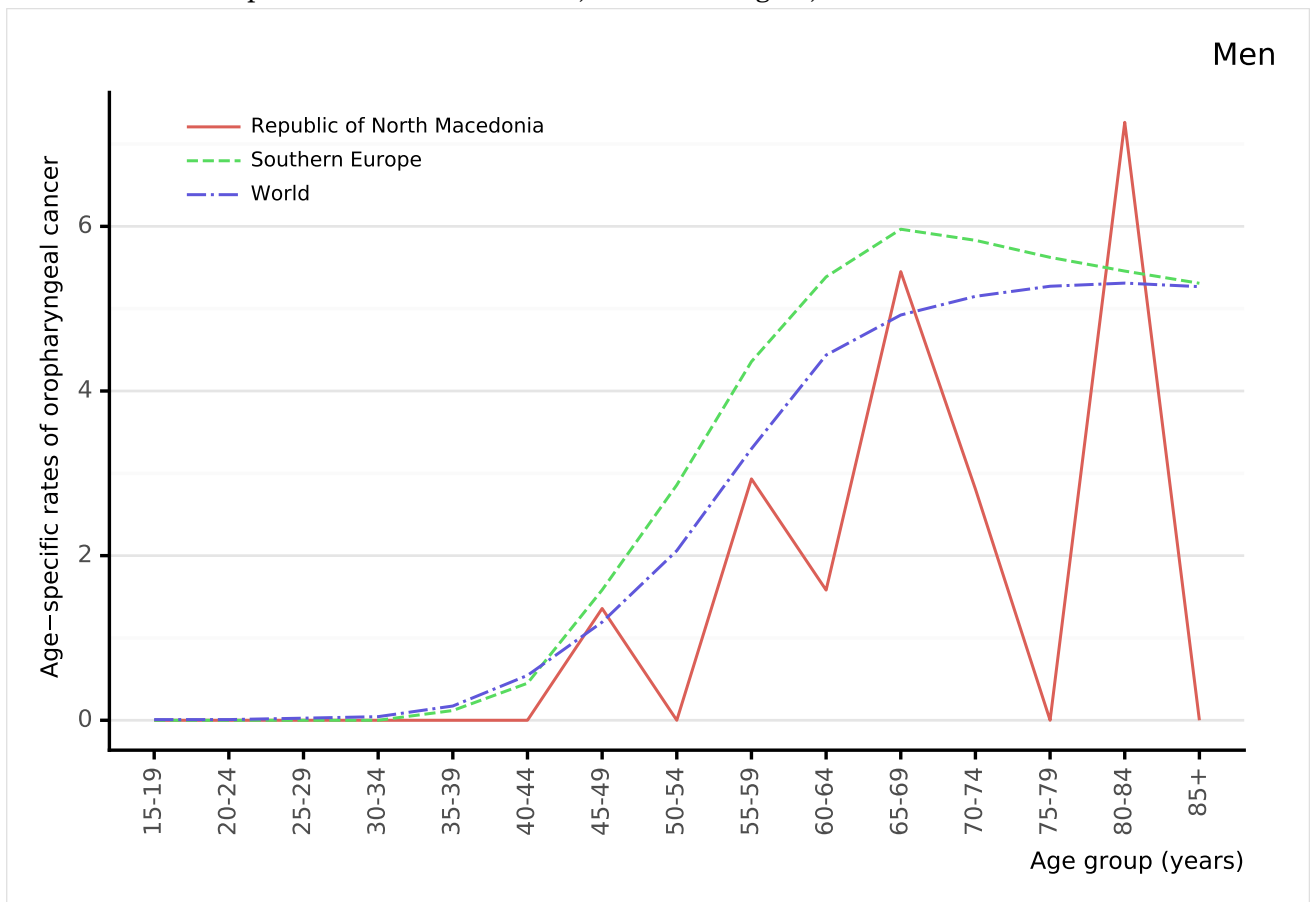
For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>

<sup>a</sup> 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 15-19 age group. 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 20-24 age group. 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 25-29 age group. 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 30-34 age group. 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 35-39 age group. 0 cases for Republic of North Macedonia and 3 cases for Southern Europe in the 40-44 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 125: Comparison of age-specific oropharyngeal cancer mortality rates among men by age in Republic of North Macedonia, within the region, and the rest of world



Data accessed on 27 Jan 2021

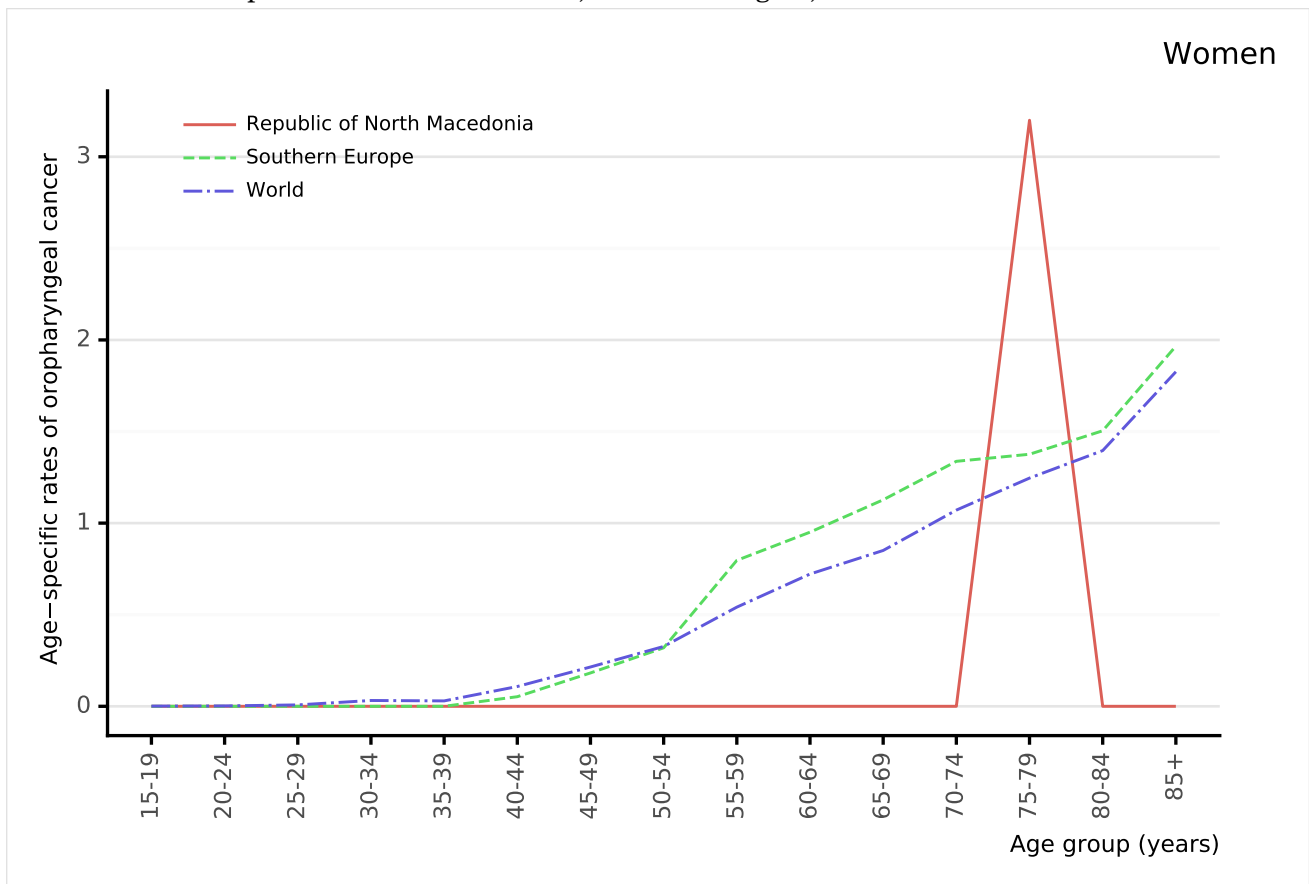
For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>

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

Data Sources:

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 126: Comparison of age-specific oropharyngeal cancer mortality rates among women by age in Republic of North Macedonia, 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>

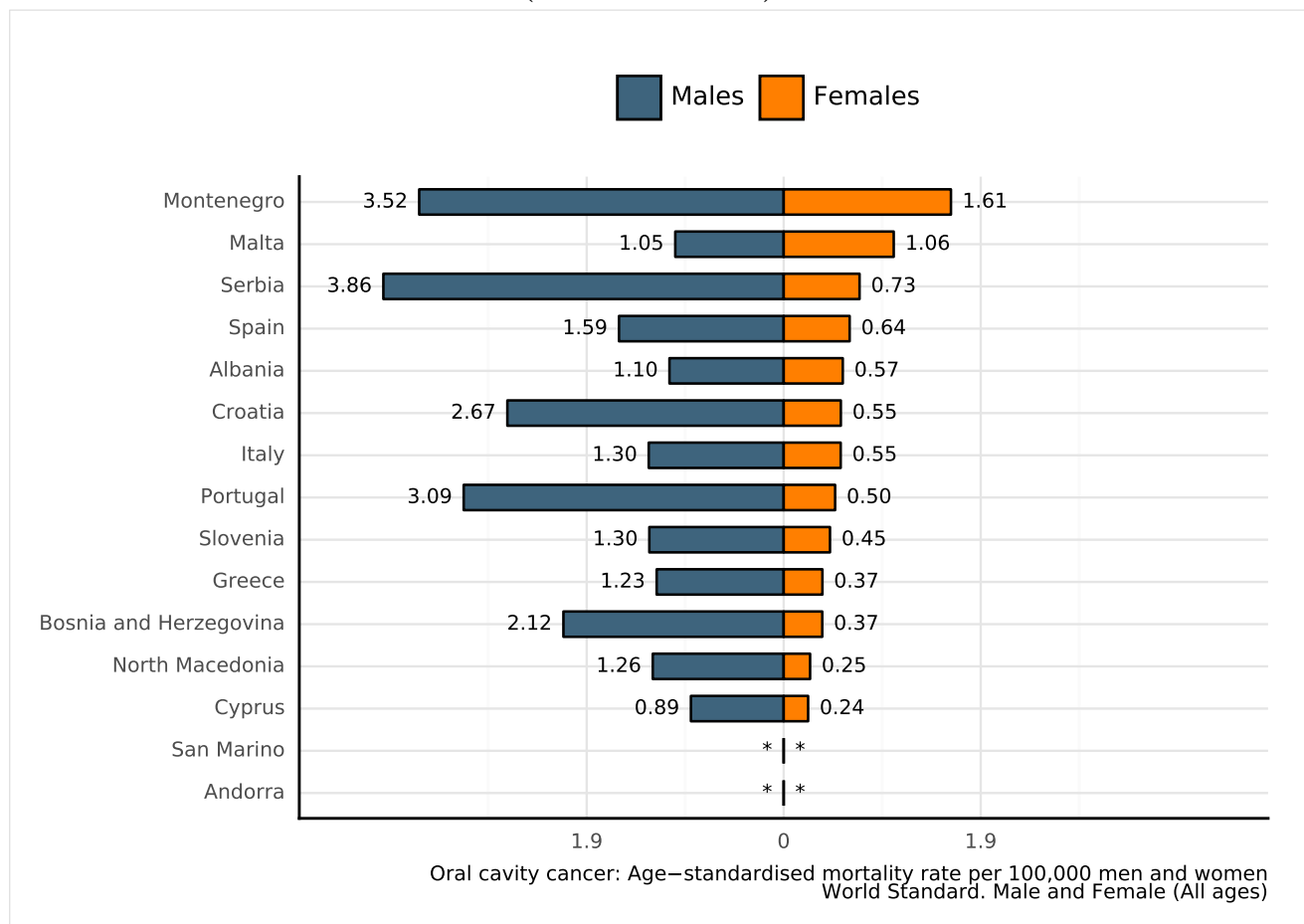
<sup>a</sup> Rates per 100,000 women per year.

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].

### 9.2.7 Oral cavity cancer mortality in Republic of North Macedonia across Southern Europe

Figure 127: Age-standardised mortality rates of oral cavity cancer of Republic of North Macedonia (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.

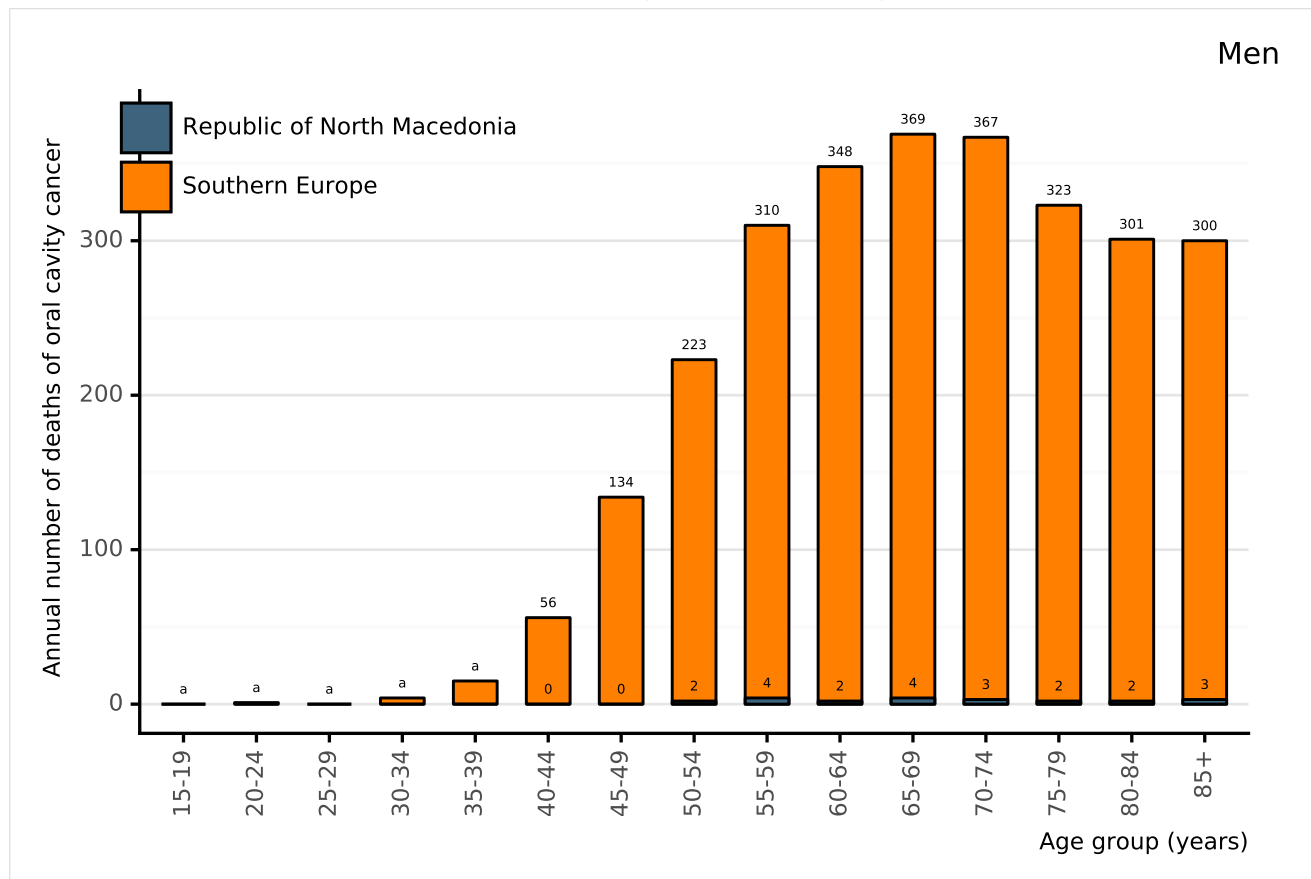
<sup>b</sup> Rates per 100,000 women per year.

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: <https://gco.iarc.fr/today>, accessed [27 January 2021].



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



**Data accessed on 27 Jan 2021**

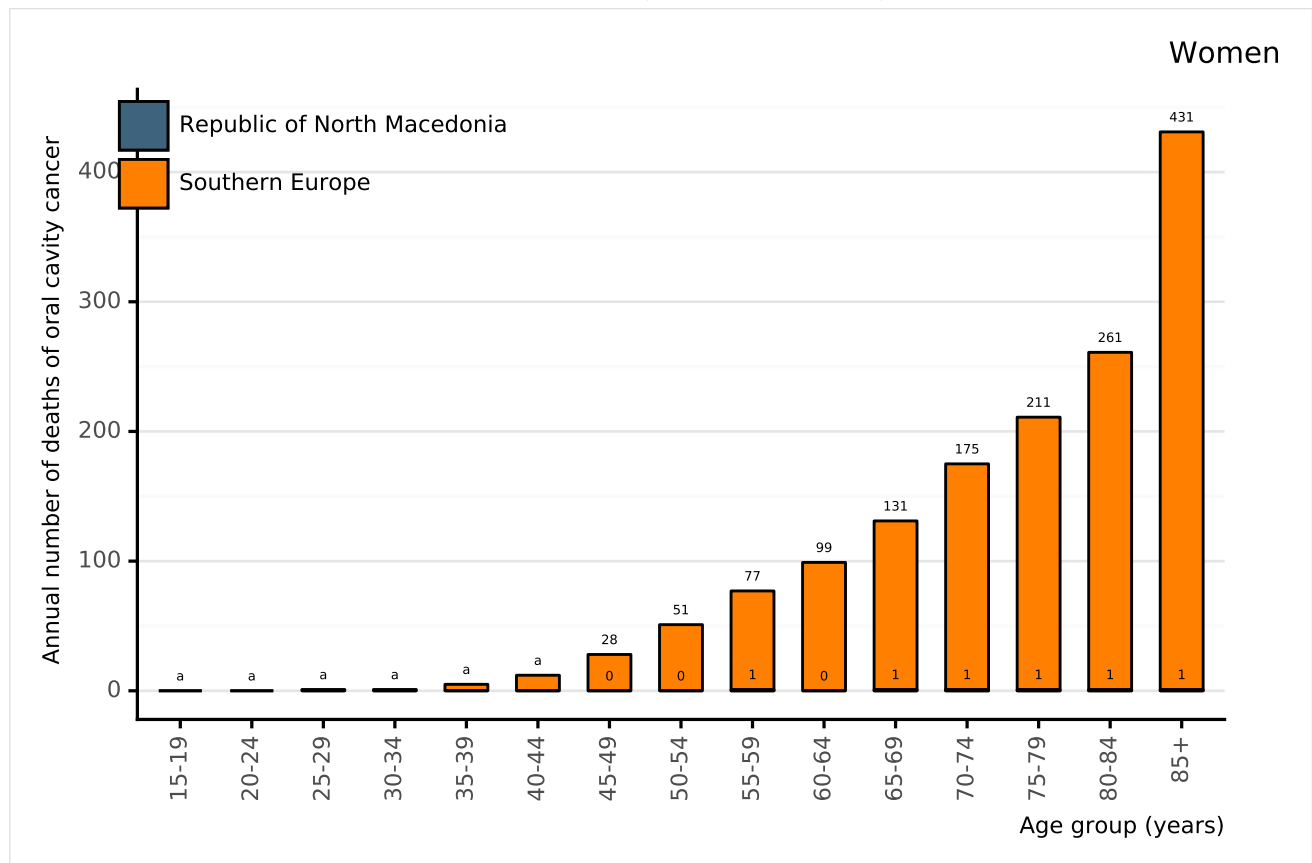
For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>

<sup>a</sup> 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 15-19 age group. 0 cases for Republic of North Macedonia and 1 cases for Southern Europe in the 20-24 age group. 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 25-29 age group. 0 cases for Republic of North Macedonia and 4 cases for Southern Europe in the 30-34 age group. 0 cases for Republic of North Macedonia and 15 cases for Southern Europe in the 35-39 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 129: Annual number of deaths of oral cavity cancer among women by age group in Republic of North Macedonia (estimates for 2020)



**Data accessed on 27 Jan 2021**

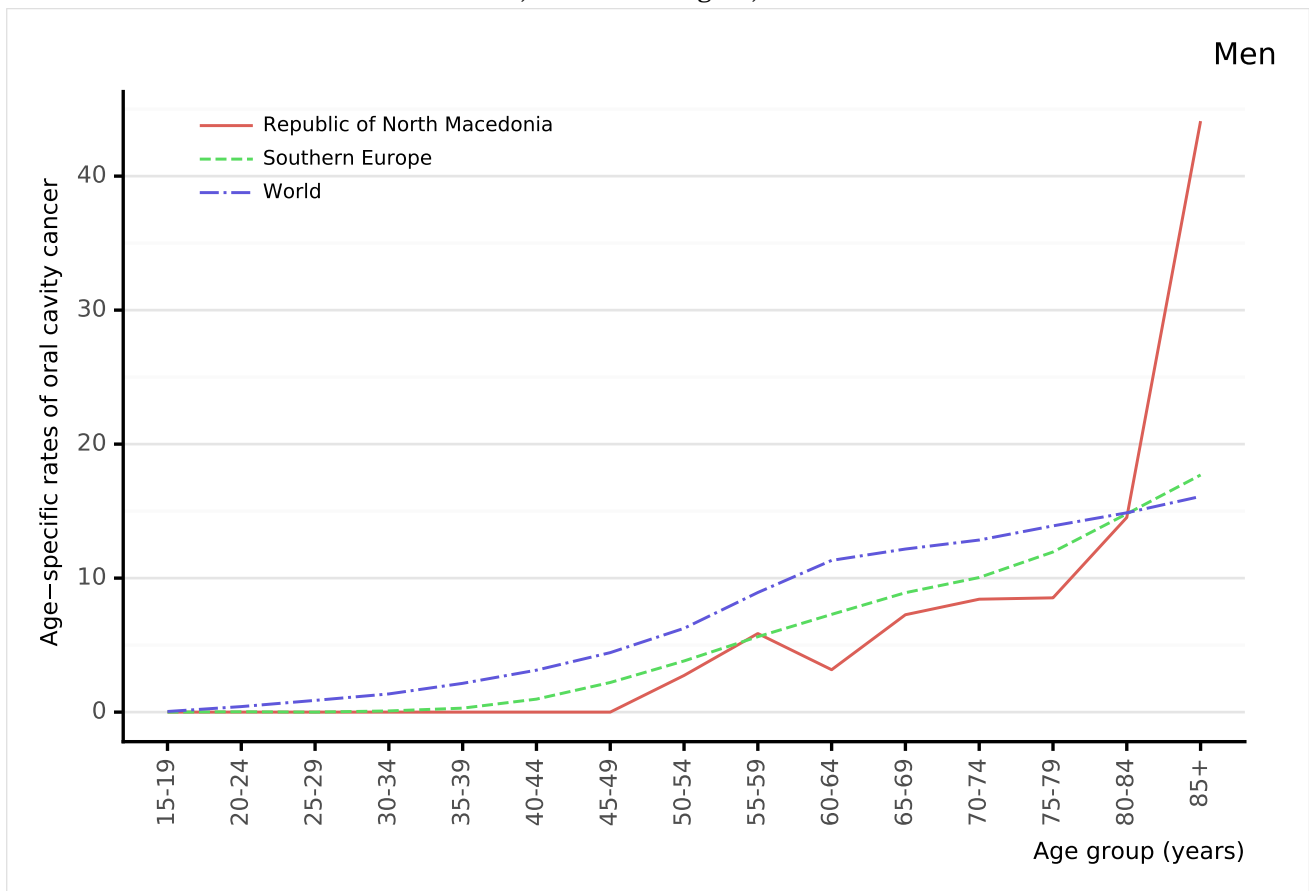
For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>

<sup>a</sup> 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 15-19 age group. 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 20-24 age group. 0 cases for Republic of North Macedonia and 1 cases for Southern Europe in the 25-29 age group. 0 cases for Republic of North Macedonia and 1 cases for Southern Europe in the 30-34 age group. 0 cases for Republic of North Macedonia and 5 cases for Southern Europe in the 35-39 age group. 0 cases for Republic of North Macedonia and 12 cases for Southern Europe in the 40-44 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 130: Comparison of age-specific oral cavity cancer mortality rates among men by age in Republic of North Macedonia, within the region, and the rest of world



Data accessed on 27 Jan 2021

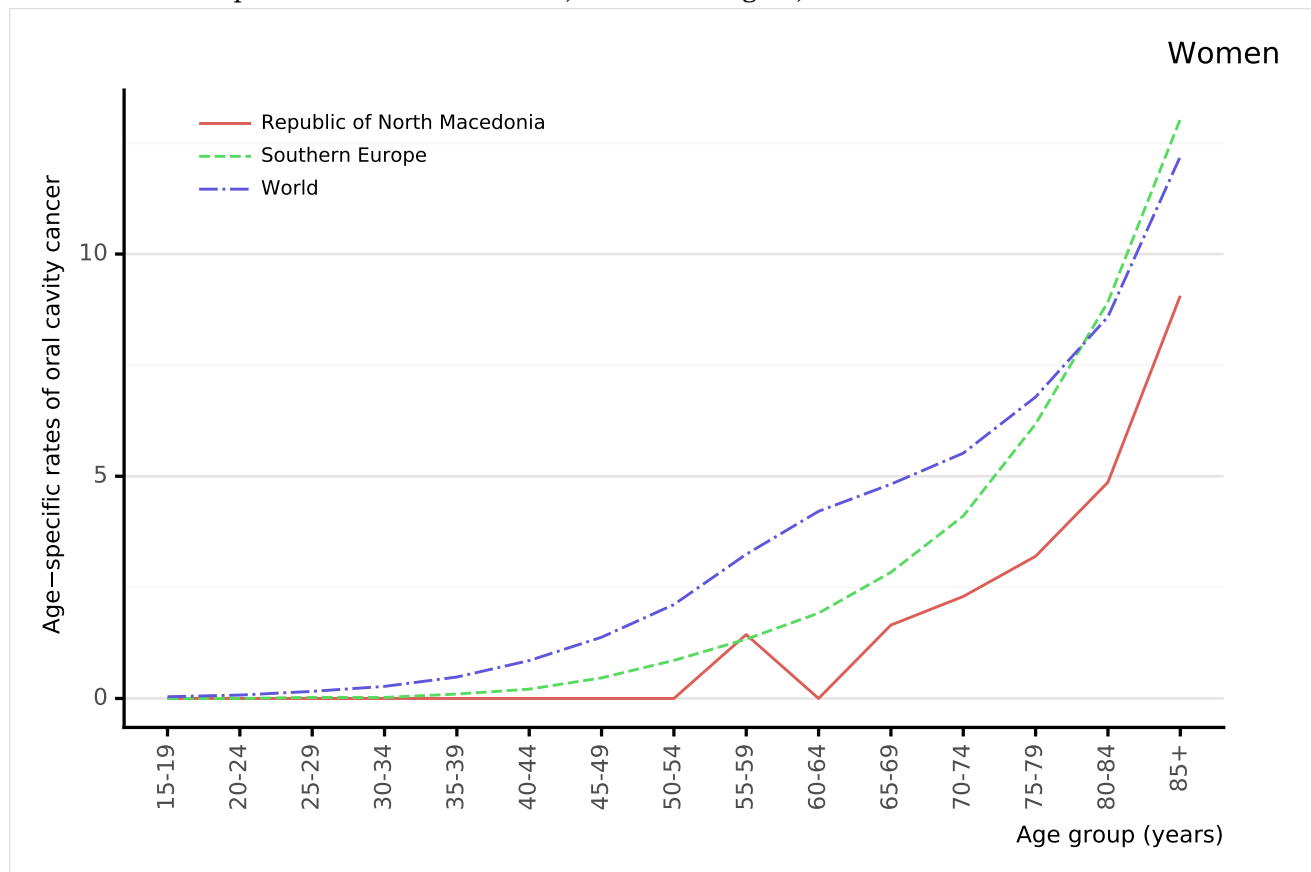
For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>

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

Data Sources:

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 Republic of North Macedonia, 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>

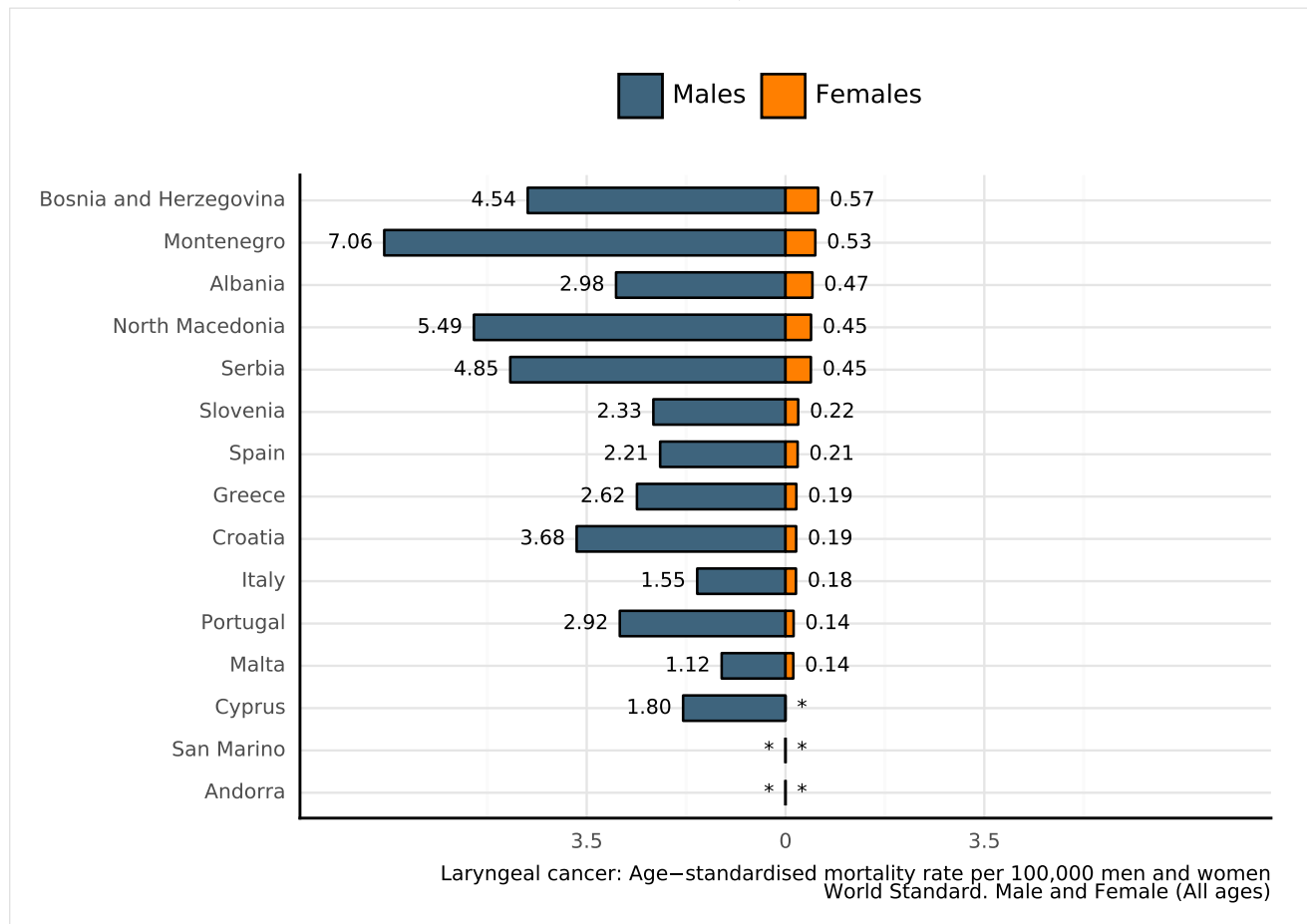
<sup>a</sup> Rates per 100,000 women per year.

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].

### 9.2.8 Laryngeal cancer mortality in Republic of North Macedonia across Southern Europe

Figure 132: Age-standardised mortality rates of laryngeal cancer of Republic of North Macedonia (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.

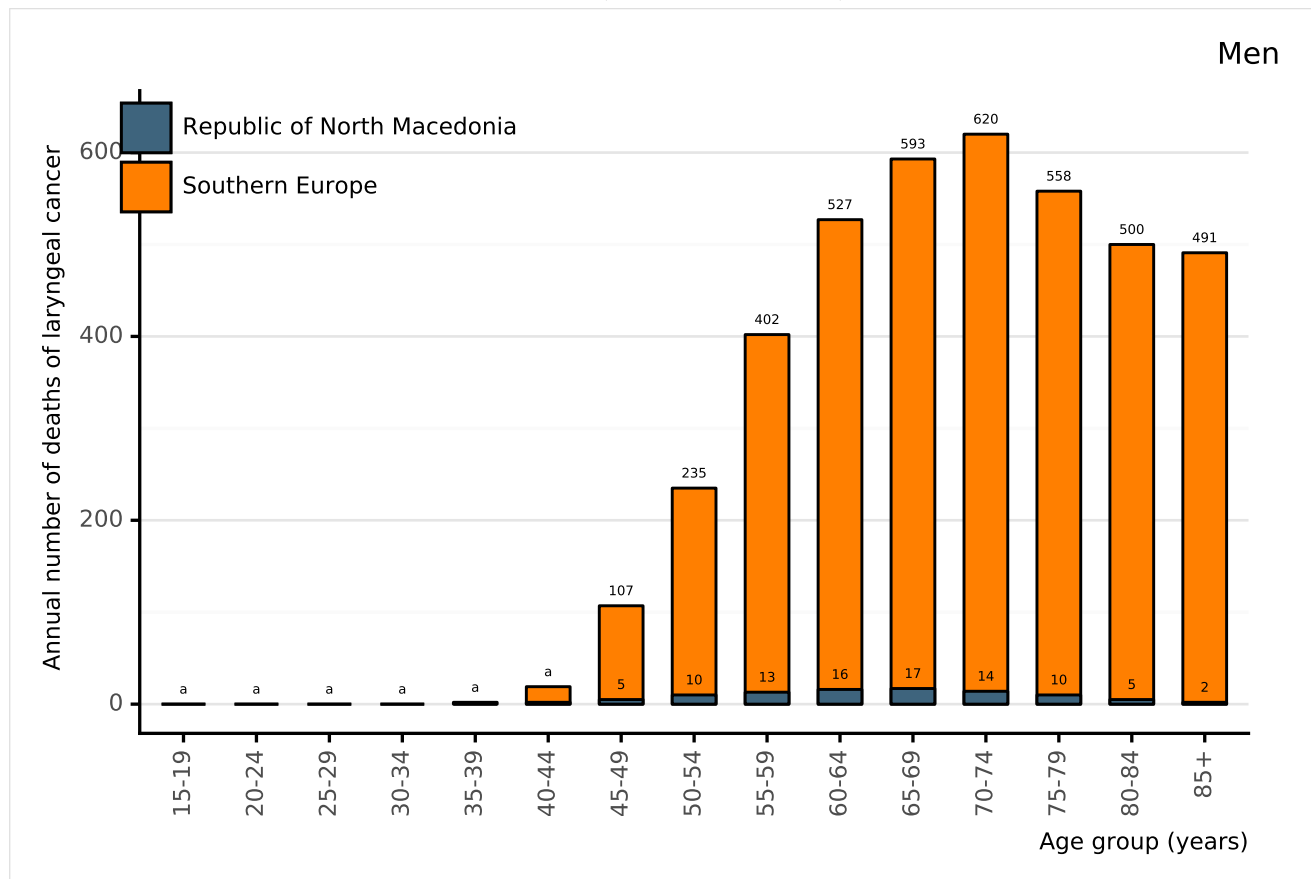
<sup>b</sup> Rates per 100,000 women per year.

\* Rates are not available

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 133: Annual number of deaths of laryngeal cancer among men by age group in Republic of North Macedonia (estimates for 2020)



**Data accessed on 27 Jan 2021**

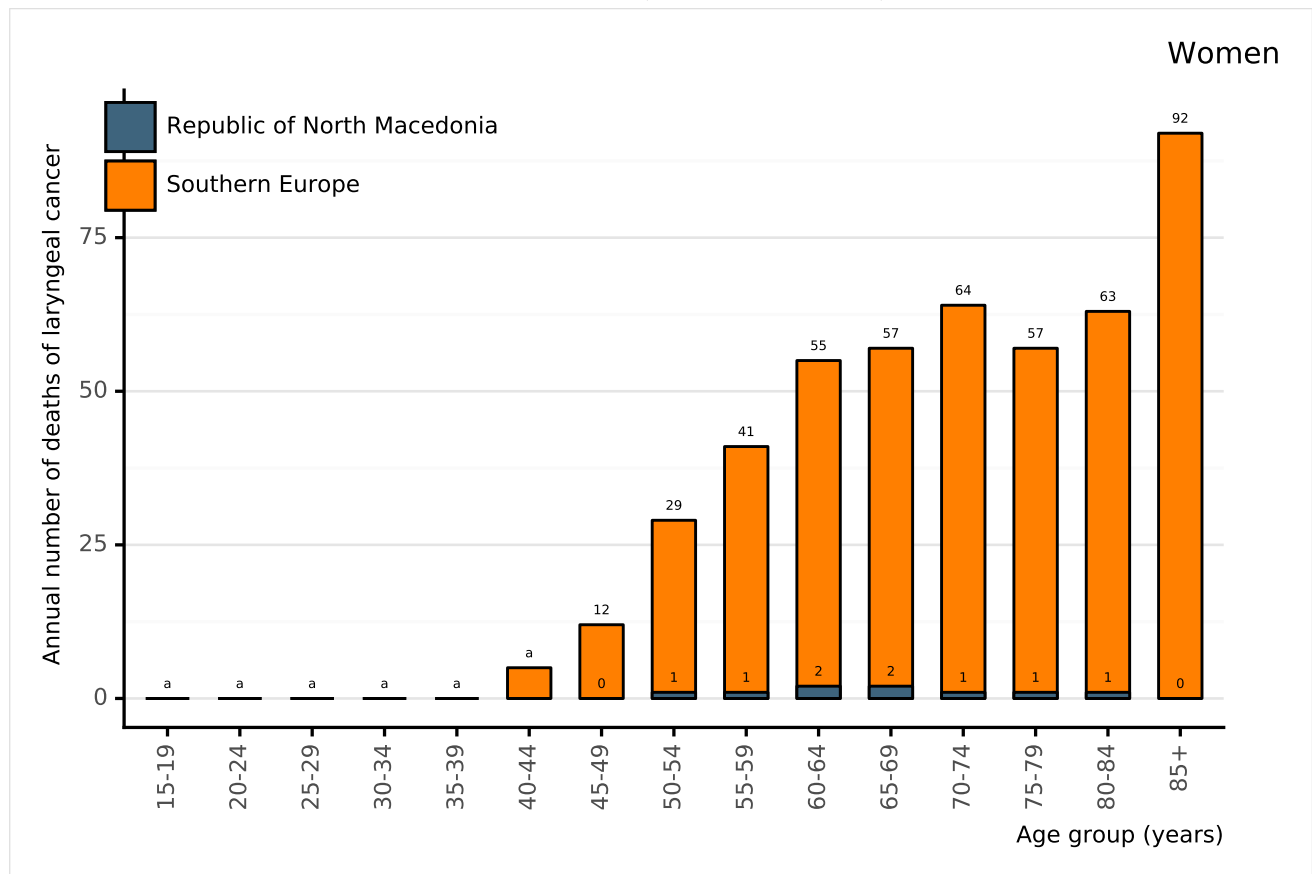
For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>

<sup>a</sup> 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 15-19 age group. 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 20-24 age group. 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 25-29 age group. 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 30-34 age group. 0 cases for Republic of North Macedonia and 2 cases for Southern Europe in the 35-39 age group. 2 cases for Republic of North Macedonia and 19 cases for Southern Europe in the 40-44 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 134: Annual number of deaths of laryngeal cancer among women by age group in Republic of North Macedonia (estimates for 2020)



**Data accessed on 27 Jan 2021**

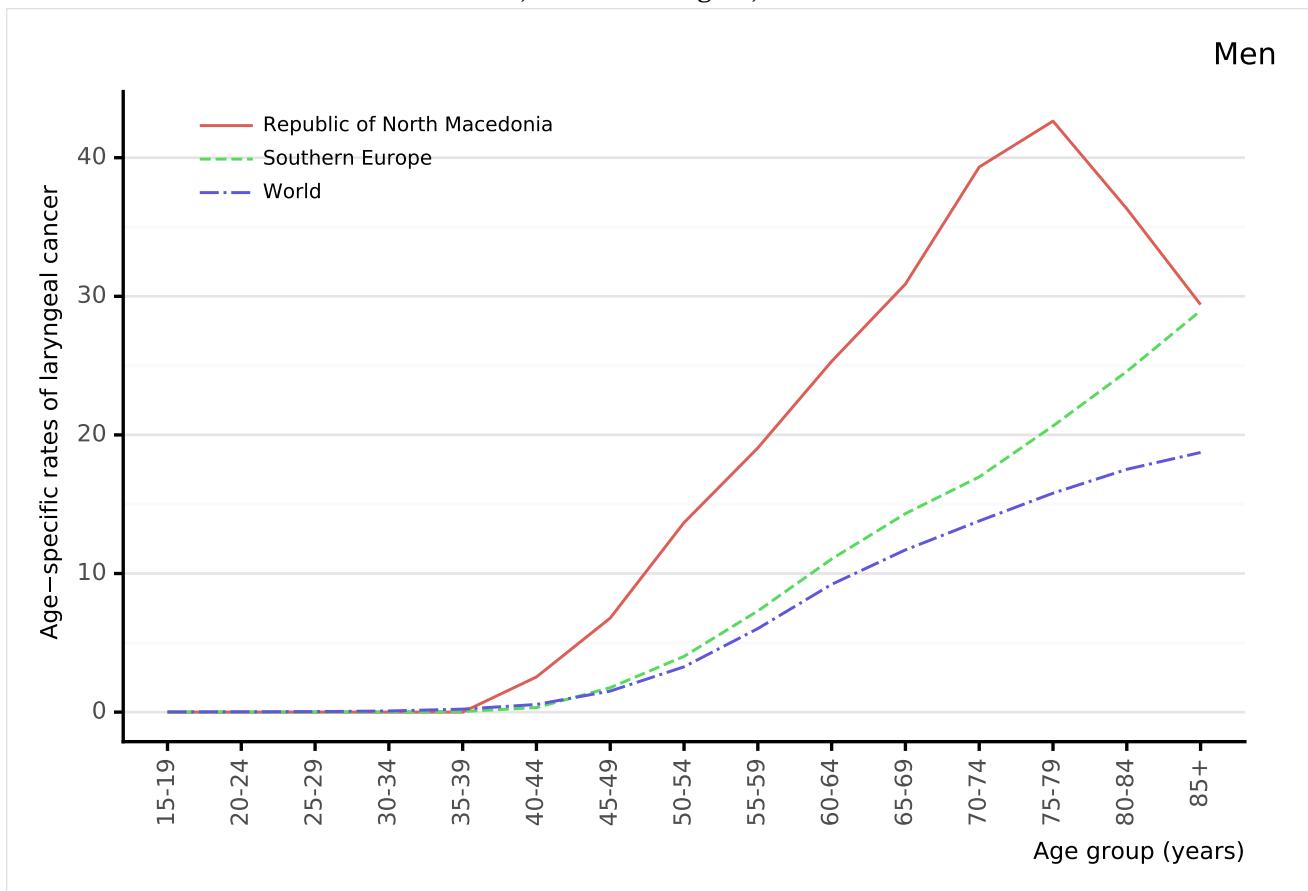
For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>

<sup>a</sup> 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 15-19 age group. 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 20-24 age group. 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 25-29 age group. 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 30-34 age group. 0 cases for Republic of North Macedonia and 0 cases for Southern Europe in the 35-39 age group. 0 cases for Republic of North Macedonia and 5 cases for Southern Europe in the 40-44 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 135: Comparison of age-specific laryngeal cancer mortality rates among men by age in Republic of North Macedonia, within the region, and the rest of world



Data accessed on 27 Jan 2021

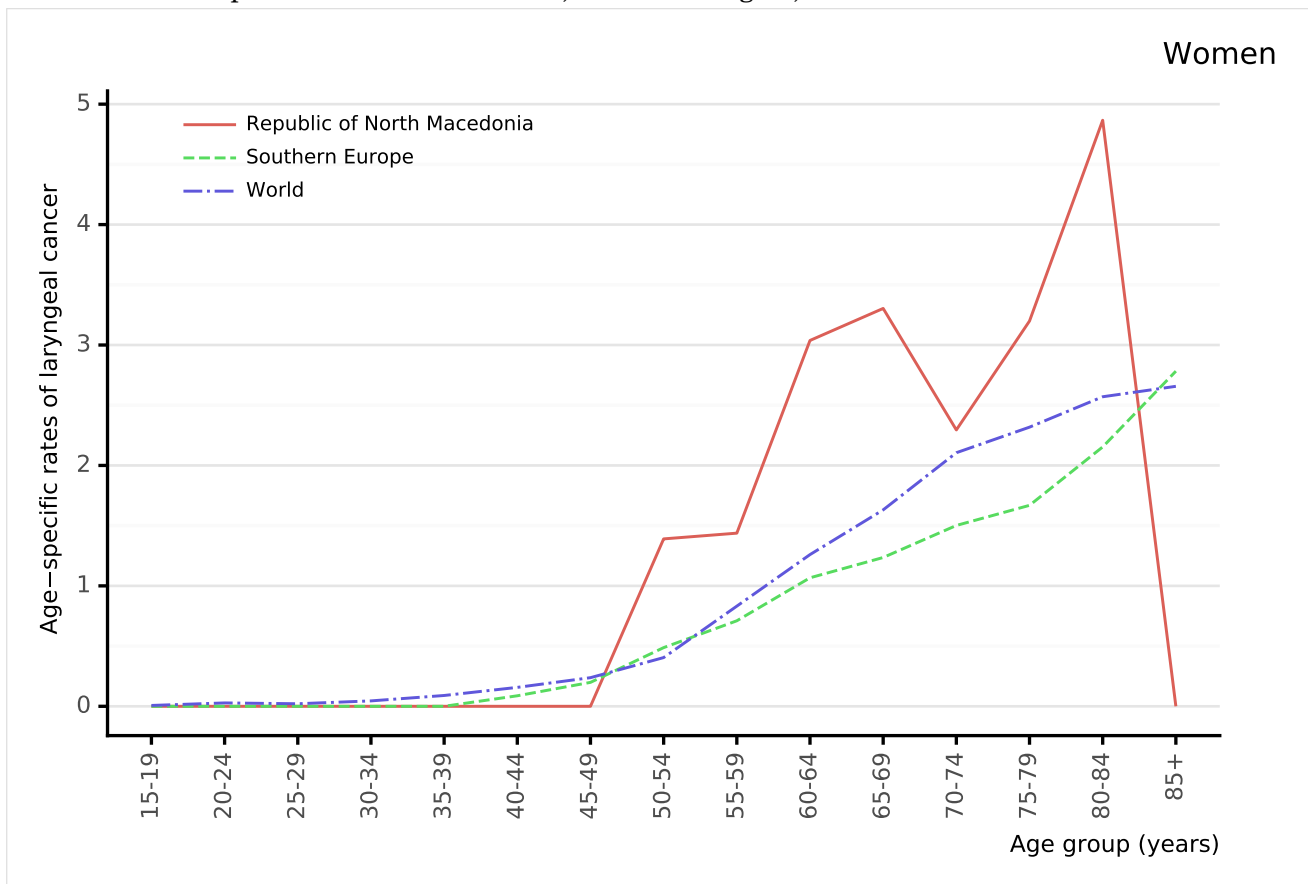
For more detailed methods of estimation please refer to <http://gco.iarc.fr/today/data-sources-methods>  
<sup>a</sup> Rates per 100,000 men per year.

Data Sources:

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 136: Comparison of age-specific laryngeal cancer mortality rates among women by age in Republic of North Macedonia, 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.

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].

## 10 Glossary

Table 49: Glossary

Term	Definition
Incidence	Incidence is the number of new cases arising in a given period in a specified 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 persons 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. Complete 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 considered 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 years are presented as they are likely to be of relevance 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 getting/dying from the disease during a specified period. For cancer, it is expressed 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 competing causes.
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).
Adenocarcinoma	Invasive tumour with glandular and squamous elements intermingled

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## Note to the reader

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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