ICO/IARC Information Centre on HPV and Cancer

INDICATOR GUIDELINES

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ICO
Institut Català d'Oncologia

Contents

1 Introduction

The Catalan Institute of Oncology (ICO) and the International Agency for Research on Cancer (IARC) have joined forces to expand the HPV Information Centre. The HPV Information Centre is being developed by the Cancer Epidemiology Research Program (CERP) of the ICO. The Centre was originally launched by ICO with the collaboration of World Health Organization, WHO's Immunisation, Vaccines and Biologicals (IVB) department and support from the Bill and Melinda Gates Foundation to to accelerate the introduction of HPV vaccines in countries with the highest burden of cervical cancer and reduce the incidence of this disease and related lesions among women.

Aggregated information is derived from data and official reports produced by the WHO, IARC, United Nations, The World Bank, and published literature. Indicators include relevant statistics on HPV-related cancer sites, epidemiological determinants of cervical cancer such as demographics, socioeconomic factors and other risk factors, estimates on the burden of HPV infection, data on immunization and cervical cancer screening.

2 Region and Country Definitions

2.1 Member States, by sub-regions

Countries have been grouped into either developed and developing regions, five continents (Africa, Americas, Asia, Europe, and Oceania) and 21 sub-regions outlined by the United Nations for geographic disaggregation of the statistics (http://unstats.un.org/unsd/methods/m49/m49regin.htm). The categorization of countries or areas is for statistical convenience and does not imply any assumption regarding political or other affiliation of countries or territories by the United Nations or the ICO/IARC Information Centre on HPV and Cancer.

Table 1: Developed and developing regions classification

Term	Definition
Developed regions	Northern America, Europe, Japan, Australia and New Zealand
Developing regions	Africa, Americas (excluding Northern America), Caribbean, Central America, South America, Asia excluding Japan, and Oceania excluding Australia and New Zealand

Table 2: Member States, by Sub-Regions.

Continent	Region	Countries
Africa	Eastern Africa	Burundi, Comoros, Djibouti, Eritrea, Ethiopia, Kenya, Madagascar, Mozambique, Mauritius, Malawi, Rwanda, Somalia, South Sudan, Seychelles, United Republic of Tanzania, Uganda, Zambia, Zimbabwe
	Middle Africa	Angola, Central African Republic, Cameroon, Democratic Republic of the Congo, Congo, Gabon, Equatorial Guinea, Sao Tome and Principe, Chad
	Northern Africa	Algeria, Egypt, Western Sahara, Libya, Morocco, Sudan, Tunisia
	Southern Africa	Botswana, Lesotho, Namibia, Eswatini, South Africa
	Western Africa	Benin, Burkina Faso, Côte d'Ivoire, Cabo Verde, Ghana, Guinea, Gambia, Guinea-Bissau, Liberia, Mali, Mauritania, Niger, Nigeria, Senegal, Sierra Leone, Togo
America	Caribbean	Antigua and Barbuda, Bahamas, Barbados, Cuba, Dominica, Dominican Republic, Grenada, Haiti, Jamaica, Saint Kitts and Nevis, Saint Lucia, Trinidad and Tobago, Saint Vincent and the Grenadines & The Grenadines, Trinidad & Tobago
	Central America	Belize, Costa Rica, Guatemala, Honduras, Mexico, Nicaragua, Panama, El Salvador
	South America	Argentina, Bolivia, Brazil, Chile, Colombia, Ecuador, Guyana, Peru, Paraguay, Suriname, Uruguay, Venezuela (Bolivarian Republic of)
	Northern America	Canada, United States of America
Asia	Eastern Asia	China, Japan, Republic of Korea, Mongolia, Democratic People's Republic of Korea, Taiwan
	South-Eastern Asia	Brunei Darussalam, Indonesia, Cambodia, Lao People's Democratic Republic, Myanmar, Malaysia, Philippines, Singapore, Thailand, Timor-Leste, Viet Nam
	Southern Asia	Afghanistan, Bangladesh, Bhutan, India, Iran, Sri Lanka, Maldives, Nepal, Pakistan
	Central Asia	Kazakhstan, Kyrgyzstan, Tajikistan, Turkmenistan, Uzbekistan
	Western Asia	Armenia, Azerbaijan, Bahrain, Georgia, Iraq, Israel, Jordan, Kuwait, Lebanon, Oman, State of Palestine, Qatar, Saudi Arabia, Syrian Arab Republic, Turkey, United Arab Emirates, Yemen
Europe	Eastern Europe	Bulgaria, Belarus, Czechia, Hungary, Republic of Moldova, Poland, Romania, Russian Federation, Slovakia, Ukraine
	Northern Europe	Channel Islands, Denmark, Estonia, Finland, United Kingdom of Great Britain and Northern Ireland, Ireland, Iceland, Lithuania, Latvia, Norway, Sweden
	Southern Europe	Albania, Andorra, Bosnia and Herzegovina, Cyprus, Spain, Greece, Croatia, Italy, Republic of North Macedonia, Malta, Montenegro, Portugal, San Marino, Serbia, Slovenia
	Western Europe	Austria, Belgium, Switzerland, Germany, France, Liechtenstein, Luxembourg, Monaco, Netherlands
Oceania	Australia/New Zealand	Australia, New Zealand
	Melanesia	Fiji, Papua New Guinea, Solomon Islands, Vanuatu
	Micronesia	Micronesia, Kiribati, Marshall Islands, Nauru, Palau
	Poynesia	Cook Islands, Niue, Samoa, Tonga, Tuvalu

3 Glossary of cancer sites, histologies and cytology

3.1 Histology/cytology of the cervix

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.

3.2 Other anogenital cancers

Terminology

Cancer of the anus
Cancer that forms in tissues of the anus, which is the opening of the rectum (last part of the large intestine) to the outside of the body.

Cancer of the penis
Cancer that forms on the skin or in the tissues of the penis.

Cancer of the vagina
Cancer that forms in the tissues of the vagina (birth canal). The vagina leads from the cervix (the opening of the uterus) to the outside of the body.

Cancer of the vulva
Cancer of the vulva occurs in the external female genital organs which include the clitoris, vulvar lips, and the opening to the vagina.

3.3 Head and Neck cancers

Terminology

Oral cavity cancer
Cancer (mainly squamous cell carcinoma) that arises in mucosal surfaces of the oral cavity (the mouth). Those include the anterior two thirds of the tongue, the lips, the gum, the floor of the mouth, the hard palate and other and unspecified parts of the oral cavity such as the buccal mucosa and the retromolar area.

Oropharyngeal cancer
Cancer (mainly squamous cell carcinoma) that arises in mucosal surfaces of the oropharynx. Those include the tonsils, the base of tongue, the uvula, the soft palate, the Waldeyer's ring and other and unspecified parts of the oropharynx such as the vallecula and the lateral and posterior walls of the oropharynx.

Larynx cancer
Cancer (mainly squamous cell carcinoma) that arises in mucosal surfaces of the larynx. Those include the glottis, the supraglottis, the subglottis and other and unspecified parts of the larynx such as the laryngeal cartilague.

4 Cancer statistics

Table 3: Classification of cancer sites.

Cancer	International Classification of Disease (ICD, 10th revision) code	
	GLOBOCAN 2020	Cancer Incidence 5 Continents
Cervical	C53	C53
Anal	C21	C21
Vulvar	C51	C51
Vaginal	C52	C52
Penile	C60	C60
Oral Cavity	C00-C06	C00-C06
Oropharynx	C09-C10	C09-C10
Larynx	C32	C32

4.1 Incidence

Incidence is the number of new cases that occurs during a given period of time in a specified population. It can be expressed as an absolute number of cases per year or as a rate per 100,000 persons per year.

Incidence data are available from cancer registries. They cover entire national populations, or samples of such populations from selected regions.

Crude incidence rate
For a specific cancer site and population, a crude rate is calculated by dividing the number of new cancers observed during a given time period by the corresponding number of people at risk in the population. The result is usually given as a rate per 100000 person-years of observation.

This rate is called crude because it relates to each population as a whole and is influenced by the age structure of each population.

It cannot be used for comparison purposes.

Age-specific incidence rate
The age-specific rate in each age class can be calculated by dividing the number of cases in the age-class by the corresponding population.

Age-specific incidence rates should always be the starting point and foundation of any thorough analysis of the incidence data.

Age-standardised incidence rate
The age-standardised rate is a summary of the individual age-specific rates using an external population called a standard population. This is the incidence that would be observed if the population had the age structure of the standard population, and corresponds to the crude incidence rate in the standard population. The age-standardised incidence rate is expressed, as is the crude incidence rate, as the number of new cases per 100 000 person-years.

The standard worldwide used is the Segi standard population (Segi, 1960).

It should be stressed that the objective of age standardisation is essentially to establish rates for comparison purposes.

Cumulative Risk
The cumulative rate is an approximation of the probability to develop a cancer during a certain period-for example, a lifetime. For cancer, it is often expressed as the risk accumulated over the age period 0-74. This has the advantage of summarising the age-specific rates independently of the age structure of the population, and gives the probability of an individual developing a cancer. This calculation is theoretical and assumes that no death occurs in the period, and that the age-specific incidence rates will be stable for an individual.

Like the age-standardised rate, it permits comparisons between populations with different age structures.

The cumulative risk is expressed as a percentage.

Annual number of new cancer cases
The number of new cases that occurs during a given period of time in a specified population. Usually they are expressed as an absolute number of cases per year.

In the HPV Information Centre, cancer incidence data presented are only from the cancer registries compiled by the IARC.

Cancer data are always collected and compiled sometime after the events to which they relate, so that the most recent statistics available are always 'late'. GLOBOCAN 2020 presents estimates for the year 2020. However, although the populations of the different countries are those estimated for the middle of 2020, the disease rates are not those for the year 2020, but from the most recent data available, generally 2-5 years earlier.

In Cancer Incidence in Five Continents (CI5), Volume XI, numbers of cancer cases are reported for the period 2008-2012.

These estimates are based on the most recent incidence data available at IARC, but more recent figures may be available directly from local sources.

Ranking of cervical cancer among other cancers
The order of frequency of cervical cancer resulting of sorting crude incidence rates by cancer site. Reflects burden of disease. Ranking based on age-standardized rates may differ.

Data Sources
Cancer incidence from cancer registries
Bray F, Colombet M, Mery L, Piñeros M, Znaor A, Zanetti R and Ferlay J, editors (2017)

Cancer Incidence in Five Continents, Vol. XI (electronic version). Lyon: International Agency for Research on Cancer. Available from: https://ci5.iarc.fr

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

Disaggregation
Age and sex

Comments
None

4.2 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.

Mortality data by cause are available for many countries through the registration of vital events, although the degree of detail and quality of the data vary considerably.

Crude mortality rate
For a specific cancer site and population, a crude rate is calculated by dividing the number of cancer deaths observed during a given time period by the corresponding number of people at risk in the population. The result is usually given as a rate per 100000 person-years of observation.

This rate is called crude because it relates to each population as a whole and is influenced by the age structure of each population.

It cannot be used for comparison purposes.

Age-specific mortality rate
The age-specific rate in each age class can be calculated by dividing the number of deaths in the age-class by the corresponding population.

Age-specific mortality rates should always be the starting point and foundation of any thorough analysis of the mortality data.

Age-standardised mortality rate
The age-standardised rate is a summary of the individual age-specific rates using an external population called a standard population. This is the mortality that would be observed if the population had the age structure of the standard population, and corresponds to the crude mortality rate in the standard population. The age-standardised mortality rate is expressed, as is the crude mortality rate, as the number of deaths per 100 000 person-years.

The standard worldwide used is the Segi standard population (Segi, 1960).

It should be stressed that the objective of age standardisation is essentially to establish rates for comparison purposes

Cumulative Risk
The cumulative rate is an approximation of the probability of dying from a cancer during a certain period-for example, a lifetime. For cancer, it is often expressed as the risk accumulated over the age period 0-74. This has the advantage of summarising the age-specific rates independently of the age structure of the population, and gives the probability of an individual dying from a cancer. This calculation is theoretical and assumes assuming no other causes of death are in operation, and that the age-specific mortality rates will be stable for an individual.

Like the age-standardised rate, it permits comparisons between populations with different age structures.

The cumulative risk is expressed as a percentage.

Annual number of deaths
The number of deaths that occurs during a given period of time in a specified population. Usually they are expressed as an absolute number of deaths per year.

In the HPV Information Centre, cancer mortality data presented are compiled by the International Agency for Research on Cancer (IARC) from country-specific national mortality data. These estimates are based on the most recent mortality data available at IARC, but more recent figures may be available directly from local sources.

Ranking of cervical cancer among other cancers
The order of frequency of cervical cancer resulting of sorting crude mortality rates by cancer site. Reflects burden of disease. Ranking based on age-standardized rates may differ.

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 on 27 January 2021.

For specific estimation methodology refer to https://gco.iarc.fr/today/data-sources-methods

Disaggregation
Age and sex

Comments
None

5 Human papillomavirus (HPV) related statistics

Definitions

HPV Prevalence

HPV prevalence is the proportion of subjects infected by the human papillomavirus (HPV) according to an HPV DNA test at a specific time point.

Type-specific HPV prevalence

HPV-type prevalence is the proportion of subjects infected by a specific HPV genotype according to a type-specific HPV DNA test at a given time point.

Data source

HPV Infection statistics in the HPV Information Centre are generated from the findings of systematic review of the literature. Systematic reviews of the literature are performed at the Institut Català d´Oncologia or the International Agency for Research on Cancer. These reviews have been published in the peer-reviewed literature, and the resulting papers represent the basis of further updates. Once initially published, all these analyses are periodically updated and uploaded in the website. Table 4 presents the different sections of HPV infection statistics and their reference publications.

Table 4: Reference publications for HPV prevalence and type distribution statistics by site and lesion

Site/lesion for HPV prevalence statistics	References	Date of update of the most recent original publication	Date of update HPV Information centre in October, 2021
Women with normal cytology	Bruni L, Diaz M, Castellsagué X, Ferrer E, Bosch FX, de Sanjosé S. Cervical human papillomavirus prevalence in 5 continents: meta-analysis of 1 million women with normal cytological findings. J Infect Dis. 2010;202(12):1789-99. De Sanjosé S, Diaz M, Castellsagué X, Clifford G, Bruni L, Munoz N, Bosch FX. Worldwide prevalence and genotype distribution of cervical human papillomavirus DNA in women with normal cytology: a meta-analysis. Lancet Infect Dis. 2007;7(7):453-9.	Jun 2014	Jun 2015
Low-grade cervical lesions	Guan P, Howell-Jones R, Li N, Bruni L, de Sanjosé S, Franceschi S, Clifford GM. Human papillomavirus types in 115,789 HPV-positive women: a meta-analysis from cervical infection to cancer. Int J Cancer. 2012;131(10):2349-59.	Nov 2011	Jun 2015

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Table 4 – continued from previous page

Site/lesion for HPV prevalence statistics	References	Date of update of the most recent original publication	Date of update HPV Information centre in October, 2021
	Clifford GM, Rana RK, Franceschi S, Smith JS, Gough G, Pimenta JM. Human papillomavirus genotype distribution in low-grade cervical lesions: comparison by geographic region and with cervical cancer. Cancer Epidemiol Biomarkers Prev. 2005;14(5):1157-64.		
High-grade cervical lesions	Guan P, Howell-Jones R, Li N, Bruni L, de Sanjosé S, Franceschi S, Clifford GM. Human papillomavirus types in 115,789 HPV-positive women: a meta-analysis from cervical infection to cancer. Int J Cancer.2012;131(10):2349-59. Smith JS, Lindsay L, Hoots B, Keys J, Franceschi S, Winer R, Clifford GM. Human papillomavirus type distribution in invasive cervical cancer and high-grade cervical lesions: a meta-analysis update. Int J Cancer. 2007;121(3):621-32. Clifford GM, Smith JS, Aguado T, Franceschi S. Comparison of HPV type distribution in high-grade cervical lesions and cervical cancer: a meta-analysis. Br J Cancer. 2003 Jul 7;89(1):101-5.	Nov 2011	Jun 2015
Invasive cervical cancer	Guan P, Howell-Jones R, Li N, Bruni L, de Sanjosé S, Franceschi S, Clifford GM. Human papillomavirus types in 115,789 HPV-positive women: a meta-analysis from cervical infection to cancer. Int J Cancer. 2012;131(10):2349-59. Li N, Franceschi S, Howell-Jones R, Snijders PJ, Clifford GM. Human papillomavirus type distribution in 30,848 invasive cervical cancers worldwide: Variation by geographical region, histological type and year of publication. Int J Cancer. 2011;128(4):927-35.	Nov 2011	Jun 2015

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Table 4 – continued from previous page

Site/lesion for HPV prevalence statistics	References	Date of update of the most recent original publication	Date of update HPV Information centre in October, 2021
	Smith JS, Lindsay L, Hoots B, Keys J, Franceschi S, Winer R, Clifford GM. Human papillomavirus typedistribution in invasive cervical cancer and high-grade cervical lesions: a meta-analysis update. Int J Cancer. 2007;121(3):621-32. Clifford GM, Smith JS, Plummer M, Munoz N, Franceschi S. Human papillomavirus types in invasive cervical cancer worldwide: a meta-analysis. Br J Cancer. 2003;88(1):63-73. Clifford GM, Smith JS, Aguado T, Franceschi S. Comparison of HPV type distribution in high-grade cervical lesions and cervical cancer: a meta-analysis. Br J Cancer. 2003 Jul 7;89(1):101-5.		
Anal, vulvar, vaginal cancers and precancerous lesions	Bouvard V, Baan R, Straif K, Grosse Y, Secretan B, El Ghissassi F, Benbrahim-Tallaa L, Guha N, Freeman C, Galichet L, Cogliano V,on behalf of the WHO International Agency for Research on Cancer Monograph Working Group. 2012. A review of human carcinogens-Part B: biological agents. De Vuyst H, Clifford GM, Nascimento MC, Madeleine MM, Franceschi S. Prevalence and type distribution of human papillomavirus in carcinoma and intraepithelial neoplasia of the vulva, vagina and anus: a meta-analysis. Int J Cancer. 2009;124(7):1626-36	Jun 2015	Jun 2015
Penile cancer and precancerous lesions	Bouvard V, Baan R, Straif K, Grosse Y, Secretan B, El Ghissassi F, Benbrahim-Tallaa L, Guha N, Freeman C, Galichet L, Cogliano V,on behalf of the WHO International Agency for Research on Cancer Monograph Working Group. 2012. A review of human carcinogens-Part B: biological agents	Jun 2014	Jun 2015

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Table 4 – continued from previous page

Site/lesion for HPV prevalence statistics	References	Date of update of the most recent original publication	Date of update HPV Information centre in October, 2021
	Miralles-Guri C, Bruni L, Cubilla AL, Castellsagué X, Bosch FX, de Sanjosé S. Human papillomavirus prevalence and type distribution in penile carcinoma. J Clin Pathol. 2009 Oct;62(10):870-8.		
Anogenital sites in Men from the general population or from special subgroups	Smith JS, Gilbert PA, Melendy A, Rana RK, Pimenta JM. Age-specific prevalence of human papillomavirus infection in males: a global review. J Adolesc Health. 2011 Jun;48(6):540-52. Dunne EF, Nielson CM, Stone KM, Markowitz LE, Giuliano AR. Prevalence of HPV infection among men: A systematic review of the literature. J Infect Dis 2006;194:1044–57. Olesen TB, Munk C, Christensen J, Andersen KK, Kjaer SK. Human papillomavirus prevalence among men in sub-Saharan Africa: a systematic review and meta-analysis. Sex Transm Infect 2014. Hebnes JB, Olesen TB, Duun-Henriksen AK, Munk C, Norrild B, Kjaer SK. Prevalence of Genital Human Papillomavirus among Men in Europe: Systematic Review and Meta-Analysis. J Sex Med 2014;11:2630–44.	Oct 2015	Oct 2015
Head and neck cancers	Ndiaye C, Mena M, Alemany L, Arbyn M, Castellsagué X, Laporte L, et al. HPV DNA, E6/E7 mRNA, and p16INK4a detection in head and neck cancers: a systematic review and meta-analysis. Lancet Oncol 2014;15:1319–31. Kreimer AR, Clifford GM, Boyle P, Franceschi S. Human papillomavirus types in head and neck squamous cell carcinomas worldwide: a systematic review. Cancer Epidemiol Biomarkers Prev 2005;14:467–75.	Feb 2012	Feb 2012

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Table 4 – continued from previous page

Site/lesion for HPV prevalence statistics	References	Date of update of the most recent original publication	Date of update HPV Information centre in October, 2021
Head and neck in healthy population	Mena M, Taberna M, Monfil L, Arbyn M, de Sanjosé S, Bosch FX, Alemany L, Bruni L. Might Oral Human Papillomavirus (HPV) Infection in Healthy Individuals Explain Differences in HPV-Attributable Fractions in Oropharyngeal Cancer? A Systematic Review and Meta-analysis. J Infect Dis 2019;219(10):1574-1585.	May 2015	Oct 2021

Methods of estimation

HPV prevalence estimates are computed following the methodology of the papers above (table 4) and as follows.

Systematic review of the literature

The HPV Information Centre follows standardized procedures to review the literature (Figure 1). First search is performed through MESH terms and key words depending on the indicator in search engines such as Pubmed or Scopus. Other search engines include LILACS, IME, Google scholar. A first screening round is done using were very sensitive search terms but unspecific, such as "HPV". Additionally, to improve specificity, a second round of searches and screening is made specifying the generic search terms as before but together with the name of each country one by one.

Selection of papers is done according to pre-established inclusion/exclusion criteria (Table 5). A first triage is done by title and abstract, but a second triage is done at full text level. Full texts are also screened for further references that may meet inclusion criteria but are missed by search engines.

Quality control ensures that at least a fraction of the papers are reviewed by another reviewer as well. Discrepancies and doubts are resolved by consensus within the reviewers. Eventually, authors are requested to provide further detail of data if targeted data is incomplete. Data is entered in the system database by the reviewers themselves and afterwards is validated and statistically analysed.

Figure 1: Algorithm for the systematic review

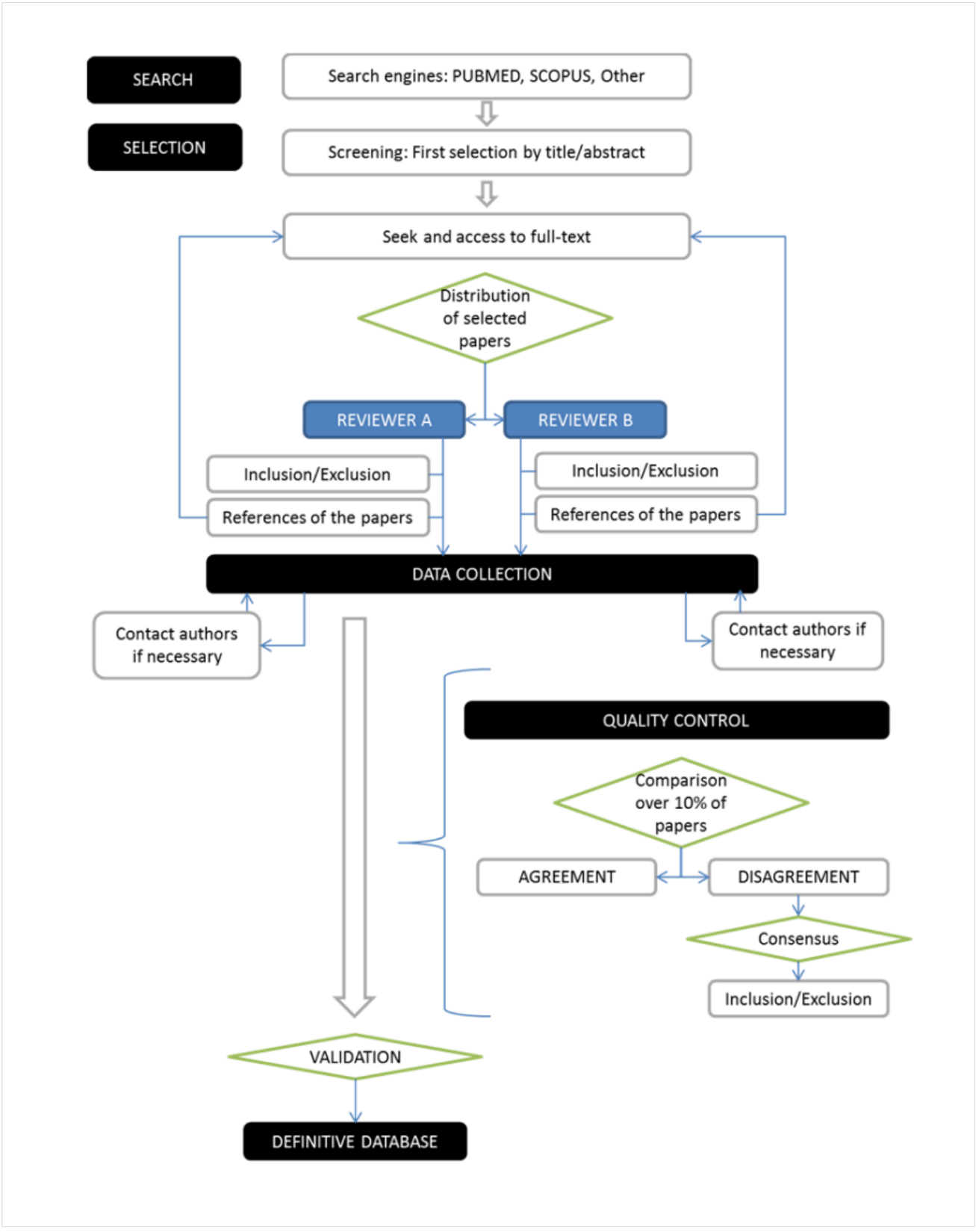

Table 5: Search terms and inclusion and exclusion criteria for HPV statistics

Site/lesion for HPV prevalence statistics	Generic search terms	Criteria
Women with normal cytology	1st round: "HPV" AND "cerv*" 2nd round: "HPV" AND specific country name	Detailed description of HPV detection methodology HPV DNA detection by means of PCR or HC2 Minimum number of cases: - Initially (until 2009): at least 100 cases - 2011-onwards: • 100 cases in the absence of other studies in the country • Same magnitude or more cases than studies already included in the country (USA/-Canada, pending Europe)
Low- and high-grade cervical lesions	1st round: "HPV" AND "cerv*" 2nd round: "HPV" AND specific country name	Detailed description of HPV detection methodology HPV DNA detection by means of PCR Genotype distribution performed. Since 2011 only studies genotyping at least 2 HPV types in the absence of other studies in the country, otherwise at least 5 genotypes tested Minimum number of cases: - Initially (until 2011): At least 20 - 2011-onwards: 20 cases in the absence of other studies in the country, otherwise at least 100 cases tested

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Table 5 – continued from previous page

Site/lesion for HPV prevalence statistics	Generic search terms	Criteria
Invasive cervical cancer	1st round: "HPV" AND "cerv*" 2nd round: "HPV" AND specific country name	Detailed description of HPV detection methodology HPV DNA detection by means of PCR Genotype distribution performed. Since 2011 only studies genotyping at least 2 HPV types in the absence of other studies in the country, otherwise at least 5 genotypes tested Minimum number of cases: - Initially (until 2011): At least 20 cases - 2011-onwards: 20 cases in the absence of other studies in the country, otherwise at least 50 cases tested
Anal, penile, vulvar, vaginal cancers and precancerous lesions	"HPV" AND ("anus" OR "anal") OR ("penile") OR "vagin*" OR "vulv*"	Detailed description of HPV detection methodology HPV DNA detection by means of PCR Genotype distribution performed Minimum number of cases: at least 10 cases
Anogenital sites in Men from the general population or from special subgroups	"HPV" AND "Male"	Detailed description of HPV detection methodology HPV DNA detection by means of PCR or HC2. (ISH if there is no country data)
Head and neck cancers	"papillomaviridae" and "head and neck neoplasms" in combination with keywords "polymerase chain reaction" or "PCR"	Detailed description of HPV detection methodology HPV DNA detection by means of PCR At least one of the following cancer sites or subsites: oral cavity, oropharynx, hypopharynx, and larynx Identification of the histological classification as squamous cell carcinoma Primary tumour Diagnosis of a tumour confined in only one site Minimum number of cases: at least 20 cases

Continued on next page

Table 5 – continued from previous page

Site/lesion for HPV prevalence statistics	Generic search terms	Criteria
Head and neck in healthy population	"oral" and ("papillomavirus" or "HPV").	Detailed description of HPV detection methodology. Minimum number of cases: at least 50 healthy individuals. The following exclusion criteria were used: studies involving subjects vaccinated against HPV, individuals with HPV-related pathology and other high-risk populations; studies involving pregnant women or infants and children (age <=13 years); studies that had HPV test results for <50 subjects and did not use DNA-based HPV testing methods; and studies that did not provide information on the sex distribution of participants.

Statistical analysis
For each study included in any of the categories above, at least the following data are collected: the number of cases tested, the number of cases positive for HPV, the number of cases positive for each specific HPV type tested, and the HPV detection technique. These numbers can be stratified by age group in the case of women with normal cytology, histology in the case of cancers, sex when applicable and some special populations such as MSM or HIV.

The number of cases tested and HPV positive extracted for each study are pooled to estimate the prevalence of HPV DNA and the HPV type distribution by country, geographical region and globally. Pools are made by the summation of the number of cases positives for HPV divided by the summation of cases tested from all the studies. HPV prevalences are presented as percentages and binomial 95% confidence intervals using the score method (Wilson) are calculated for each of them.

Disaggregation
Data are presented disaggregated by sex, age and histological groups (squamous cell carcinoma, adenocarcinoma, and unspecified histology) when available.

Comments
Because of limitations of the HPV DNA detection techniques and study designs used, data should be interpreted cautiously and used only as a guidance to assess the burden of HPV infection in the population.

6 Factors contributing to HPV-related cancers

6.1 Smoking (Current smoking of any tobacco prevalence, Daily smoking of any tobacco prevalence, Current cigarette smoking prevalence, Daily cigarette smoking prevalence)

Definitions
The percentage of men and women who smoke:

Smoking any tobacco product
Smoking any form of tobacco, including cigarettes, cigars, pipes, or any other smoked tobacco products and excluding smokeless products.

Smoking cigarettes
Smoking manufactured cigarettes.

Current smoking
Smoking at the time of the survey, including both daily and non-daily or occasional smoking.

Daily smoking
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/i/item/who-global-report-on-trends-in-prevalence-of-tobacco-use-2000-2025-third-edition

Methods of estimation
WHO global report on trends in prevalence of tobacco use 2000–2025, third edition. Geneva: World Health Organization; 2019. Available at https://www.who.int/publications/i/item/who-global-report-on-trends-in-prevalence-of-tobacco-use-2000-2025-third-edition

Disaggregation
Sex

Comments
None

6.2 Parity

Definitions
Parity is the number of times a woman has given birth. High parity has been associated with an increased risk of invasive cervical cancer.

Total fertility rate
Total fertility rate is the average number of live births per woman, assuming the age-specific fertility rate observed in a given year or period.

Age-specific fertility rate
Age-specific fertility rate is the annual number of births per 1000 women in a particular age group in a given year or period.

Data Sources
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].

Methods of estimation
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].

Disaggregation
Age

Comments
None

6.3 Oral Contraceptive Use

Refer to Contraceptive Use (7.3) in the Reproductive Health section of the indicator guidelines for definition, source and methods of estimation.

6.4 Human immunodeficiency virus (HIV) prevalence

Definitions

Adults and children HIV estimates
Estimated number of adults (15+ years) and children (0-14 years) living with HIV.

Adults (15+ years) HIV estimate
Estimated number of adults (15+ years) living with HIV.

Adults (15-49 years) HIV prevalence (%)
The percentage of adults aged 15-49 years living with HIV.

Women (15+ years) HIV estimate
Estimated number of women (15+ years) living with HIV.

Young women (15-24 years) HIV rate (%)
Estimated percentage of young women aged 15-24 living with HIV.

Young men (15-24 years) HIV rate (%)
Estimated percentage of young men aged 15-24 living with HIV.

AIDS deaths in adults and children
Estimated number of AIDS deaths in adults (15+ years) and children (0-14 years).

HIV prevalence among female sex workers in the capital city
Estimated percentage of female sex workers in the capital city living with HIV.

HIV prevalence among men who sex with men in capital city
Estimated percentage of men who have sex with men in the capital city living with HIV.

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

Methods of estimation
Figures are based on modelled HIV estimates. Please see the "Annex on methods" from "Seizing the moment—Tackling entrenched inequalities to end epidemics" for more information on HIV estimates methodology. Available at: https://www.unaids.org/en/resources/documents/2020/global-aids-report

Disaggregation
Sex

Comments
None

7 Sexual and reproductive health behaviour indicators

7.1 Time of sexual intercourse/High-risk sexual behaviour

Definitions

Time of sexual intercourse

Median age at first sexual intercourse among young men and women
The age by which half of young people aged 15-24 have had penetrative sex (median age).

Median age at first sexual intercourse among men (25-54 years) and women (25-49 years)
The age by which half of people aged 25-54 years have had penetrative sex (median age).

Sex before age of 15
% of young people aged 15-24 who had penetrative sexual intercourse before the age of 15.

Abstinence of never-married young men and women
Proportion of never married young women and men aged 15-24 who have never had sex.

High-risk sexual behaviour

Extramarital sex
Percentage of respondents who have had sex with a non-marital, non-cohabiting partner in the last 12 months of all respondents who have reported sexual activity in the last 12 months.

Commercial sex in the last year
Percentage of male respondents reporting sex with a sex worker in the last 12 months.

Multiple partners in the last year among sexually active respondents aged 15-49
Percentage of women and men age 15-49 who have had sexual intercourse with more than one partner in the last 12 months, among respondents aged 15-49, who were sexually active in the last 12 months.

Data Sources
Welling K, Collumbien M, Slaymaker E, Singh S, Hodges Z, Patel D, Bajos N. Sexual behaviouir in context: a global perspective. Lancet 2006; 368(9548):1706-28.

Estimates are derived from available survey data from nationally representative population-based surveys undertaken such as the MEASURE DHS (Demographic and Health Surveys, http://www.measuredhs.com) project, national survey data, and from Reproductive Health Surveys.

Methods of estimation
Methods are specific to each survey used. Refer to country-specific reference for full description of methodologies used.

Disaggregation
Age and sex

Comments
None

7.2 Marriage Patterns

Definitions

Average Age at first marriage
Average age at which men or women ever married between the ages of 15 and 50 years, an age after which first marriages are rare.

Percentage of ever married, (%)
Proportion of ever married persons aged 15-19, 20-24, and 40-48.

Difference in Average Age at First Marriage between Men and Women
% of young people aged 15-24 who had penetrative sexual intercourse before the age of 15.

Women aged 15-49, married or in union
Number of women of reproductive age (15-49 years) who are married or in a union. A union is involves a man and a woman regularly cohabiting in a marriage-like relationship.

Data Sources
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

Methods of estimation
Estimates are derived from censuses, surveys, and civil registries. The data is housed within databases maintained by the Population Division and the Statistics Division of the United Nations Department of Economic and Social Affairs.
Estimates and projections of the number of married or in-union women of reproductive-age (15-49 years) are provided for the period from 1970 to 2030 for 201 countries or areas, and for regions and development groups. Estimates and projections of the proportions of married or in-union women, by five-year age group and for women of reproductive-age (15-49 years), are provided for the period from 2000 to 2030 for 201 countries or areas.

Disaggregation
Age and sex

Comments
None

7.3 Contraceptive Use

Definitions

Any contraceptive use, (%)
Contraceptive prevalence is the proportion of women who are using (or whose partner is using) a contraceptive method among those of reproductive age (15-49 years) who are married or in union.

Prevalence of modern methods, (%)
Prevalence of modern methods is the proportion of women using modern method contraception among those of reproductive age (15-49 years) who are married or in union.
Modern methods include: sterilization (male/female); oral contraceptives/pill; injectable or implant; intrauterine device (IUD); condoms; vaginal barrier methods (diaphragms, cervical caps and spermicidal foams, jelly, cream and sponges); other methods (emergency contraception, female condom and modern methods not reported separately).

Sterilization, (%)
Proportion of women or male partners who were sterilized, among women of reproductive age (15-49 years) who are married or in union.

Oral Contraceptive Use / Pill, (%)
Proportion of women using oral contraceptives, also known as the pill, among those of reproductive age (15-49 years) who are married or in union.

Injectable (%)
Proportion of women using hormonal contraception in the form of injections among those of reproductive age (15-49 years) who are married or in union.

Implant (%)
Proportion of women using hormonal contraception in the form of implants among those of reproductive age (15-49 years) who are married or in union.

Intrauterine device (IUD), (%)
Proportion of women using intrauterine device as a form of birth control among those of reproductive age (15-49 years) who are married or in union.

Condom use, (%)
Proportion of male partners who are using condoms with their female partners of reproductive age (15-49 years) who are married or in union.

Vaginal barrier method, (%)
Proportion of women using barrier methods among those of reproductive age (15-49 years) who are married or in union.
Vaginal barrier methods include diaphragms, cervical caps and spermicidal foams, jelly, cream and sponges.

Other modern methods, (%)
Proportion of women using other methods among those of reproductive age (15-49 years) who are married or in union. Other modern methods include emergency contraception, female condom and modern methods not reported separately.

Contraception of other traditional methods, (%)
Proportion of women using traditional methods among those of reproductive age (15-49 years) who are

married or in union.
Traditional methods include rhythm (periodic abstinence or the calendar method), withdrawal and other methods (Including prolonged abstinence, breastfeeding, douching, various folk methods and traditional methods not reported separately).

Rhythm, (%)
Proportion of women using the traditional contraceptive method of rhythm, also known as periodic abstinence or the calendar method, among those of reproductive age (15-49 years) who are married or in union.

Withdrawal, (%)
Proportion of women using the traditional contraceptive method of withdrawal among those of reproductive age (15-49 years) who are married or in union.

Other traditional method, (%)
Proportion of women using other traditional contraceptive methods among those of reproductive age (15-49 years) who are married or in union. Other traditional methods include prolonged abstinence, breastfeeding, douching, various folk methods and traditional methods not reported separately.

Data Sources
United Nations, Department of Economic and Social Affairs, Population Division (2020). World Contraceptive Use 2020 (POP/DB/CP/Rev2020). Available at https://www.un.org/en/development/desa/population/publications/dataset/contraception/wcu2020.asp

Methods of estimation
The indicators presented have been estimated using data from nationally-representative household surveys for women of reproductive age (from 15 to 49 years). Data pertain to countries or areas of the world from 1950 or later. For country estimates, the most recent data came from the United Nations Population Division based on survey data. Weights used are the estimated numbers of women aged 15-49 who are married or in a consensual union.

The number of women of reproductive age who are married or in a consensual union was estimated based on data on the proportion of women married or in union in each country containined in World Marriage Data and on estimates of the number of women by age group obtained from World Population Prospects.

Disaggregation
Sex (prevalence of sterilization)

Comments
None

8 HPV Preventive strategies

8.1 Cervical cancer screening practices

Cervical cancer screening, recommended age for screening, screening interval, estimated screening coverage, screening tests

Definitions

Pap smear
Cervical cancer screening is a public health intervention used on a population at risk or target population. A Papanicolau (or Pap) smear is a cervical screening test used to detect premalignant and malignant (cancerous) processes in the ectocervix. A medical professional uses a swab or stick to wipe cells off from the cervix, the opening lining of the womb (uterus) and these cells are then evaluated to determine presence or absence of abnormalities. Screening is not undertaken to diagnose cervical cancer disease, but to identify individuals with a high probability of having or developing cervical cancer (by detecting precancerous changes in the cervix uteri, which untreated, may lead to cancer). Histological diagnosis is the "gold standard" for identifying precancerous and cancerous lesions.

Screening interval (years) or frequency of screens
The recommended interval between one screening test and the subsequent test when the result is negative for abnomalities. Recommendations may vary between organizations and guidelines, so a range of the screening interval is recorded in some instances.

Lifetime number of recommended smears
Proportion of women in the target age group who are screened at the recommended age intervals during a given time period. The number of screening tests performed is not considered coverage, since this number may include women outside the target group, and women may be screened more often than recommended.

Number of women
Number of women in the sample who have been asked about their Pap smear history.

Age range
Age interval of the sample of women who received a Pap smear ranging form the youngest to the oldest woman.

Estimated coverage of cervical screening within the last year(s)
Proportion of women in the total sample of the mentioned age range in the country or region that reported having a Pap smear during a given time period (e.g., last year, last 2, 3, 5 years or ever).

Populations studied

General female population
Sample of women representative of the general population of the specific country and the specific age range. The information is generally collected directly from households through national censuses, or more commonly through household surveys. The latter may be collected as part of a broader national

survey or may be focused only on health topics.

National screening programme
Women of a determined age range are invited (actively or not) to attend the screening programme throughout the whole nation or country. National guidelines specify who are at risk of cervical cancer and eligible to attend the programme. Eligible women may attend regularly within the specified interval. Different screening intervals may apply depending on age. This sample of women is based on information extracted from the registry data and it generally addresses women of reproductive age.

Regional screening programme
Women attending a screening programme in a specific region or city. The sample may not represent women from the whole country.

Women attending health services
Women visiting health care facilities: primary health care centres, antenatal clinics, sexually transmitted infections clinics, family planning clinics, gynaecology/obstetrics wards or hospitals for any reason who receive a Pap smear. This sample of women may be more health conscious or wealthy than the general population, thus classified separately to avoid selection bias as they may not be representative of the whole female population. More information on the sample may be included in the comments section.

Selected sample
Group of women with specific attributes that have been asked regarding their last Pap smear. See description of sample in the comments section.

Health care personnel
Sample of female health care attendants asked for their level of utilization of Pap smears to provide an insight into the general knowledge and awareness of the community. Health care providers may play a significant role in dissemination of medical information in the community, and increase the utilization of cytology services if aware of the benefits of screening.

National or regional coverage
National coverage presents data representative of the majority of women in the mentioned country. Regional data applies to the screening coverage representative of the majority of women in the mentioned region or city.

Data Sources
IARC Handbooks of Cancer Prevention Vol. 10: Cervix Cancer Screening. IARC Press. Lyon, 2005.

Ronco G, van Ballegooijen M, Becker N, Chil A, Fender M, Giubilato P, et al. Process performance of cervical screening programmes in Europe. Eur. J. Cancer. 2009 Oct;45(15):2659-2670.

Country-specific references identified in each country-specific report as general recommendation from relevant scientific organizations and/or publications.

Disaggregation
When available, data are disaggregated by rural or urban; by region when available; by type of population (general population, national screening programme, or other).

Comments
A summary of facts and figures are reported from the data sources of cervical cancer screening in the defined country, which is complementary to the other data presented, providing a screening profile within their health system setting and an overview of each country's cervical cancer situation. Data may be

contradictory for the same country in some instances but it reflects the available literature of the different sources.

For additional data that may aid in the understanding of the presented values, refer to the original references for the population studied.

8.2 HPV vaccination

Definitions

HPV vaccine introduction
HPV vaccine introduction into national immunization programmes

HPV vaccination program coverage
Describes the vaccination coverage according to the national schedule and the program's eligibility criteria for each calendar year. It represents the number of doses of HPV vaccines provided in the calendar year as a fraction of the program's target population up to 14 years of age. Note that most countries vaccinate a single cohort and current estimate excludes the population aged 15 and above even if they were vaccinated in the given calendar year.

Vaccine in schedule
Whether or not the HPV vaccine is introduced as part of the vaccination schedule in the country and the schedule of the doses vaccine.

Introduction in entire/part of the country
Year of introduction of the HPV vaccine in the entire or part of the country.

Vaccine schedule
Immunisation schedules for each country.

Recommendation for primary target population
Primary target ages for HPV vaccination.

Recommendation for catch-up population
Whether or not there is a program for catch-up vaccination for those not included in the primary target population.

Data Sources
Human papillomavirus (HPV) vaccination coverage. World Health Organization. 2021. Available from: https://immunizationdata.who.int/pages/coverage/hpv.html, accessed [20 sep 2021]

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.

Methods of estimation:
WHO and UNICEF collect information on new vaccines introduction. Refer to the reference Bruni L et al. Prev Med.2021;144(106399):106399.

Disaggregation
First dose and the full recommended schedule, and sex

Comments
None

9 Protective factors for cervical cancer

9.1 Male circumcision

Definitions

Circumcision
Surgical removal of the foreskin on the penis or prepuce.

Prevalence of circumcision
The prevalence of circumcision (or circumcision rate) refers to the proportion of males that are circumcised in a given population. It may also refer to the proportion of newborn males that are circumcised.

Data Sources

Refer to country report for specific references. The main data sources are:

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.

Williams BG, Lloyd-Smith JO, Gouws E, Hankins C, Getz WM, Hargrove J, de Zoysa I, Dye C, Auvert B. The potential impact of male circumcision on HIV in Sub-Saharan Africa. PLoS Med. 2006;3(7):e262.

Drain PK, Halperin DT, Hughes JP, Klausner JD, Bailey RC. Male circumcision, religion, and infectious diseases: an ecologic analysis of 118 developing countries. BMC Infect Dis. 2006 Nov 30;6:172.

World Health Organization, Department of Reproductive Health and Research and Joint United Nations Programme on HIV/AIDS (UNAIDS). Male circumcision: global trends and determinants of prevalence, safety and acceptability. 2007. Available from: http://www.who.int/reproductivehealth/publications/rtis/9789241596169/en.

Methods of estimation

Refer to country-specific reference(s) in the country-specific report for full methodologies.

Disaggregation

None

Comments

None

9.2 Condom use

Refer to Condom use (7.3) in the Reproductive Health section of the indicator guidelines for definition, source and methods of estimation.

10 Demographic and socioeconomic factors

10.1 Population

Definitions

Total Population
Population estimates include all residents regardless of legal status or citizenship.

Data Sources
United Nations, Department of Economic and Social Affairs, Population Division (2019). World Population Prospects 2019, Online Edition. Rev. 1. Available at: https://population.un.org/wpp/Download/Standard/Population/

Methods of estimation
World Bank staff estimates are derived from civil registration, population registers, other administrative records, population and censuses, social and demographic surveys.

Disaggregation
Age and sex

Comments
None

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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.
Although efforts have been made by the HPV Information Centre to prepare and include as accurately as possible the data presented, mistakes may occur. Readers are requested to communicate any errors to the HPV Information Centre, so that corrections can be made in future volumes.

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