

# The Burden of Cervical Cancer in South-East Europe at the Beginning of the 21<sup>st</sup> Century

Marc Arbyn<sup>1,2</sup>, Maja Primic-Žakelj<sup>3</sup>, Amidu O. Raifu<sup>1</sup>, Magdalena Grce<sup>4</sup>, Evangelos Paraskevidis<sup>5</sup>, Emanuel Diakomanolis<sup>6</sup>, Vesna Kesić<sup>7</sup>, Florian A. Nicula<sup>8</sup>, Ofelia Suteu<sup>8</sup> and Lawrence von Karsa<sup>9</sup>

<sup>1</sup> Scientific Institute of Public Health, Unit of Cancer Epidemiology, Brussels, Belgium

<sup>3</sup> Cancer Registry of Slovenia, Institute of Oncology, Ljubljana, Slovenia

<sup>4</sup> Ruder Bošković Institute, Division of Molecular Medicine, Zagreb, Croatia

<sup>5</sup> Department of Obstetrics and Gynaecology, University Hospital of Ioannina, Ioannina, Greece

<sup>6</sup> Department of Obstetrics and Gynaecology, University of Athens, Alexandra Hospital, Athens, Greece; President of the European Federation for Colposcopy

<sup>7</sup> Department for Gynaecologic Diagnostics and Oncology, Institute of Obstetrics and Gynaecology, University Clinical Centre, Beograd, Serbia

<sup>8</sup> Institute of Oncology, Cluj, Romania

<sup>9</sup> European Cancer Network, European Network for Information on Cancer, IARC, Lyon, France

## ABSTRACT

*The situation of cervical cancer prevention in South-East Europe is hardly documented, in spite of the fact that it encloses the most affected countries of Europe. We estimated the number of cases of cervical cancer, the number of deaths from this malignancy and the corresponding rates for 11 countries located in South-East Europe, in the period 2002–2004. Each year, approximately 9,000 women develop cervical cancer and about 4,600 die from the disease in this subcontinent. The most affected country is Romania with almost 3,500 cases and more than 2,000 deaths per year. High world-age standardised mortality rates (>7.5 [expressed per 100,000 women-years]) are observed in 7 countries: FYROM (7.6), Moldova (7.8), Bulgaria (8.0), Bosnia & Herzegovina (8.0), Albania (9.8), Serbia & Montenegro (10.1) and Romania (13.0). A matter of concern is the increasing mortality rate, in younger women, in the countries with the highest burden of cervical cancer. Thus, appropriate cervical cancer prevention programmes should be set up without delay in this part of Europe.*

**Key words:** cervical cancer, prevention, mortality, incidence, Europe, South-East Europe

## Introduction

This paper has been written as a contribution to a special issue of *Collegium Anthropologicum* edited at the occasion of the International Workshop on Human Papillomaviruses and Consensus Recommendations for Cervical Cancer Prevention, Dubrovnik-Cavtat (Croatia), 18–20 April, 2007. This workshop offers an excellent opportunity to attract the attention of clinicians, epidemiologists and health authorities on a public health problem which is responsible for considerable human suffering and loss of lives but which is highly preventable if preventive activities are well organized. In the present study, we evaluate the burden of cervical cancer in 11 countries in the South-Eastern part of Europe based on the most recent available data and on estimates of the in-

cidence and the cause-specific mortality, computed by the International Agency for Research on Cancer, for the period 2002–2004.

## Material and Methods

We describe the estimated number of cases of cervical cancer, the number of deaths from cervical cancer and the corresponding crude and age-standardised rates with the world standard population as reference for 11 countries located in the South-Eastern part of Europe (Albania, Bosnia & Herzegovina, Bulgaria, Croatia, Cyprus, Greece, FYROM [Former Yugoslavian Republic of Mace-

donia], Moldova, Romania, Serbia & Montenegro and Slovenia) for the period 2002–2004. We identified countries as defined in 2004, therefore we did not separate Serbia and Montenegro. Registered data were available from the Cancer Registry of Slovenia for the year 2003<sup>1</sup>. Estimates for 2004 were available for two countries (Cyprus and Greece)<sup>2</sup>. For the other 8 countries, estimates were derived from GLOBOCAN 2002<sup>3</sup>.

Methods used for estimation have been described previously<sup>3,4</sup>. Shortly: the most recent mortality rates were derived from the published vital statistics, stored at the World Health Organisation (WHO) Mortality Database (<http://www.who.int/whosis/mort>) for all countries except Cyprus and Bosnia & Herzegovina. Mortality for Bosnia & Herzegovina was estimated by averaging rates from neighbouring countries. The mortality in Cyprus was estimated from national incidence and pooled European survival data. For Albania, reported mortality rates were multiplied with a correction factor to compensate for under-registration of deaths. Mortality from cancer of the cervix uteri were adjusted by reallocating deaths from uterus cancer not otherwise specified using age-specific rules. Incidence data were available from national cancer registries for Bulgaria, Croatia, Cyprus and Slovenia. The incidence for Serbia & Montenegro was computed by taking the average of the regional registries of Vojvodina and Central Serbia. For the other countries incidence was estimated from reported or estimated national mortality rates using incidence/mortality (I/M) ratios computed by Poisson regression using representative regions where both incidence and mortality data were available.

Number of cases and deaths were computed by multiplying the most recent age-specific rates with the corresponding population size for 2002 or 2004, derived from

the World Population Prospects published by the United Nations Population Division (<http://esa.un.org/unpp/>). For Slovenia, the mid-year population of 2003, published in Cancer Incidence in Slovenia 2003 was used<sup>1</sup>.

## Results

The number of cases and deaths and the corresponding rates by country are shown in Table 1. The standardised rates, ranked by increasing mortality are displayed in a bar graph (Figure 1). The geographical distribution of the standardised mortality is mapped in Figure 2. In total, each year, approximately 9,000 women in South-Eastern Europe developed cervical cancer and about 4,600 died from the disease. A low to moderately high age-standardised mortality was observed in the North-West and the South-East margin of the region: Slovenia ( $4.1/10^5$ ), Croatia ( $5.0/10^5$ ), Greece ( $2.1/10^5$ ) and Cyprus ( $5.6/10^5$ ). However, in the core of the region, high to very high mortality rates were noted varying between  $7.8/10^5$  (Moldova) and  $13.0/10^5$  (Romania). The standardised incidence rate varied from  $7.2/10^5$  in Greece to more than  $20.0/10^5$  in Albania, Romania and Serbia & Montenegro. In general the crude incidence and mortality correlated well ( $r=0.88$ ). The parameter 1-M/I, a surrogate index for survival, varied between 39% in Albania and 66% in Serbia & Montenegro. However, the correlation coefficient and the survival surrogate index are rather artificial indicators since incidence often was derived from mortality.

## Discussion

South-East Europe is a region of major contrasts. It contains the 2 countries with the highest burden for the

**TABLE 1**  
INCIDENCE OF AND MORTALITY FROM CERVICAL CANCER IN 11 SOUTH-EAST EUROPEAN COUNTRIES: NUMBER OF CASES AND DEATHS (IN MULTIPLES OF HUNDRED), CRUDE AND WORLD-AGE STANDARDISED RATE (W-ASR) (PER 100,000 WOMEN-YEARS [WY])

Country	Incidence			Mortality			Year	Source
	Cases (x 100)	Crude Rate (/10 <sup>5</sup> WY)	W-ASR (/10 <sup>5</sup> WY)	Deaths (x 100)	Crude Rate (/10 <sup>5</sup> WY)	W-ASR (/10 <sup>5</sup> WY)		
Albania	3.9	25.1	25.2	1.5	9.4	9.8	2002	2
Bosnia & Herzegovina	5.5	26.6	21.3	2.3	11.1	8.0	2002	2
Bulgaria	9.8	24.4	18.7	5.1	12.6	8.0	2002	2
Croatia	4.3	18.0	13.3	2.1	8.7	5.0	2002	2
faautoCyprus	0.5	13.2	12.5	0.3	6.1	5.6	2004	1
Greece	4.8	8.9	7.2	2.1	3.9	2.1	2004	1
FYROM	1.7	16.4	13.9	1.0	9.7	7.6	2002	2
Moldova	4.8	21.4	18.0	2.2	9.9	7.8	2002	2
Romania	34.5	30.3	23.9	20.9	18.4	13.0	2002	2
Serbia & Montenegro	18.2	34.4	27.3	8.2	15.5	10.1	2002	2
Slovenia	2.1	20.4	18.5	0.8	7.9	4.1	2003	3

The estimates are derived from a recent study of the burden of cervical cancer in member states of the European Economic Area for 2004<sup>2</sup>, the Cancer Registry of Slovenia for 2003<sup>1</sup> and from GLOBOCAN 2002<sup>3</sup> for the other countries, figures are adjusted for mortality from not otherwise specified uterine cancer

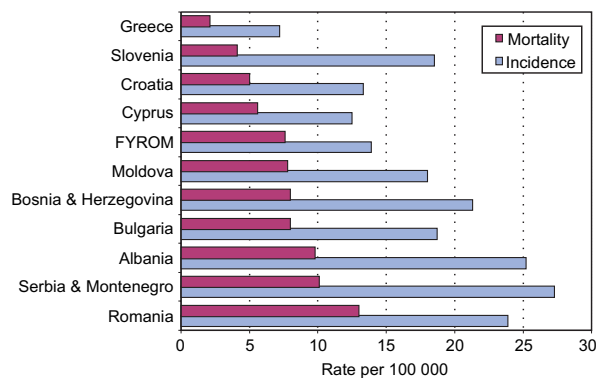


Fig. 1. Burden of cervical cancer: world age-standardised incidence and mortality in 11 countries of South-East Europe, estimates for 2002/2004 (Source: Globocan 2002<sup>3</sup>, Cancer Registry of Slovenia 2003<sup>1</sup>, Arbyn 2007<sup>2</sup>).

whole of Europe: Romania and Serbia & Montenegro. It contains, together with the Baltic countries, in Northern Europe, the 7 most affected states of the European continent with standardised rates of mortality from cervical cancer reaching 8/100,000 or higher (Romania, Serbia & Montenegro, Lithuania, Albania, Bosnia & Herzegovina, Bulgaria, Latvia)<sup>2,5</sup>. Otherwise, South-East Europe contains countries where the burden is low, for instance in Greece, where the standardised incidence is 3 to 4 times and the mortality 5 to 6 times lower than in Serbia & Montenegro or Romania.

The current cervical cancer incidence and mortality reflects exposure of successive generations to the main risk factor (infection of the cervix with oncogenic human

papillomavirus [HPV] types) and the impact of cytological screening for HPV induced cervical lesions and treatment of those lesions. A generally observed phenomenon in industrialised countries is that women born after 1940 are at higher risk compared to older cohorts due to changed sexual behaviour (and hence increased HPV transmission) since the 1960s<sup>6-8</sup>. Increased frequency of smoking and use of oral anti-conception might have enhanced this cohort effect<sup>6</sup>. In the Nordic and some West-European countries, incidence of and mortality from cervical cancer dropped substantially subsequent to cytological screening<sup>7,9-11</sup>. Little information is available on the screening situation in South-East Europe but it is expected that, in general, the coverage and quality are moderate to poor. Only in Slovenia, a formally organised cervical cancer screening programme is in place since 2003<sup>12</sup>. The current particularly high burden of cervical cancer in Romania and other South-East European countries can be explained most plausibly as an effect of elevated HPV transmission, over the past decades, not counteracted by screening. On the other hand the low incidence in Greece might be due to the rather low background risk, also observed in other Mediterranean countries such as Spain and Italy<sup>13</sup>. It is expected that ongoing studies assessing the prevalence and the geographical distribution of HPV types throughout Europe, conducted in the framework of the introduction of HPV vaccination, will clarify this hypothesis.

The data estimated in this study should be considered with caution, since their reliability is determined by the quality and completeness of cancer and death registration and further by the appropriateness of external data used to model unavailable data. In particular, the propor-

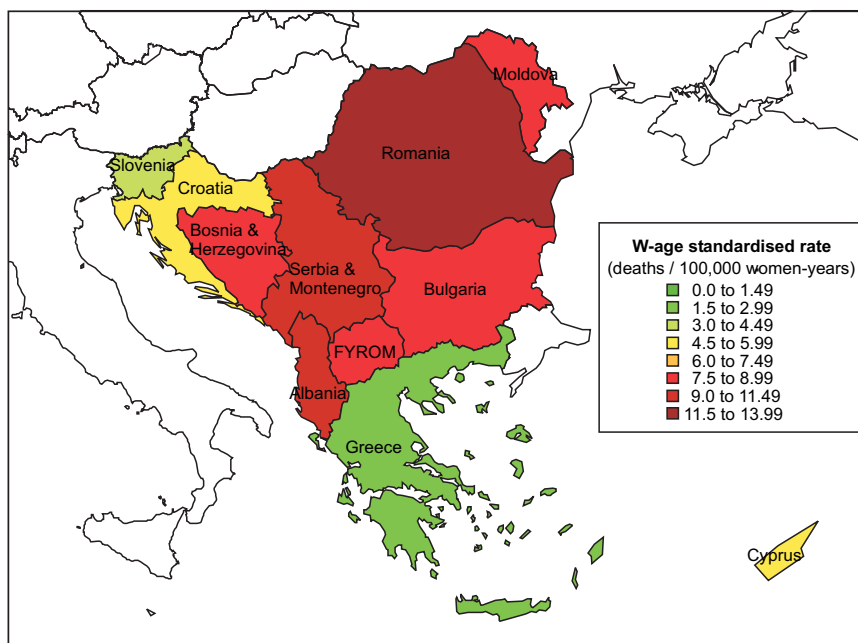


Fig. 2. Geographical distribution of the world age-standardised mortality (W-ASMR) from cervical cancer in 11 countries of South-East Europe, estimates for 2002/2004 (Source: Globocan 2002<sup>3</sup>, Cancer Registry of Slovenia 2003<sup>1</sup>, Arbyn 2007<sup>2</sup>).

tion of deaths from uterine cancer without specification of the exact topographic origin compromises the accuracy of the cause of death certification. We are currently conducting detailed trend studies, within the framework of the EU Network for Information on Cancer, where we look for the best possible solutions for the death cause certification problem and try to disentangle the dynamics of cervical cancer in all European countries. Preliminary results indicate that the mortality from uterus cancer, in age groups younger than 45 years – where nearly all deaths are caused by cervix uteri cancer, is falling in Greece, Croatia and Slovenia but continues to rise or remains stable at a high level in Bulgaria, Moldova, Romania and Serbia & Montenegro.

## Conclusion

We have highlighted the elevated burden of cervical cancer in some South-East European countries – in particular in Romania. The present study should motivate public health authorities to set-up well-organised cervical cancer prevention programmes without delay as rec-

ommended by the European Council<sup>14</sup>. It is hoped that the pending publication of the new European Guidelines for Quality Assurance in Cervical Cancer Screening will contribute in establishing this goal<sup>15</sup>. It is particularly challenging for public health experts to define, in the future, how prophylactic HPV vaccination besides screening will contribute in tackling this highly preventable disease.

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M. Arbyn

Scientific Institute of Public Health, Unit of Cancer Epidemiology, Brussels, Belgium  
e-mail: m.arbyn@iph.fgov.be

## BREME RAKA VRATA MATERNICE U JUGOISTOČNOJ EUROPI NA POČETKU 21. STOLJEĆA

### SAŽETAK

Stanje prevencije raka vrata maternice u jugoistočnoj Europi je slabo zabilježeno, unatoč činjenici da ovaj rak pogađa najviše te države u Europi. Procijenili smo broj slučajeva raka vrata maternice, smrtnost od ove bolesti te odgovarajuće odnose između njih za 11 zemalja jugoistočne Europe, u razdoblju od 2002. do 2004. g. Svake godine na ovom potkontinentu oboli od raka vrata maternice približno 9.000 žena, a oko 4.600 ih umre od ove bolesti. Najviše slučajeva bilježi Rumunjska, gotovo 3.500 te više od 2.000 smrtnih slučajeva godišnje. Visoka godišnja stopa smrtnosti u svijetu (>7,5 [brojevi se odnose na 100,000 žena godišnje]) je zabilježena u 7 zemalja: Bivša Jugoslavenska Republika Makedonija (7,6), Moldavija (7,8), Bugarska (8,0), Bosna i Hercegovina (8,0), Albanija (9,8), Srbija i Crna gora (10,1) te Rumunjska (13,0). Pitanje od važnosti je porast stope smrtnosti kod mladih žena u zemljama s visokom stopom obola od raka vrata maternice. Stoga bi, u ovom dijelu Europe, bez odgode trebali biti uspostavljeni odgovarajući programi prevencije raka vrata maternice.