Projected Cancer Incidence Rates in Bulgaria, 1968–2017

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Background. Incidence predictions are applicable when planning preventive or screening health care programmes, diagnostic, treatment and rehabilitation facilities. The aim of this study was to predict future (1993–2017) incidence rates of the most common sites of cancer in Bulgaria: breast, cervix and corpus uteri in females, and lung, prostate and stomach in males.

Method. Observed numbers of incident cases in the period 1968–1992 and observed (predicted) population size were employed. Age-cohort and age-cohort-period log-linear models were fitted to the observed data, assuming no change in the observed trends.

Results. The incidence rates for all the studied primary sites, except stomach cancer, were predicted to increase. The observed rates in the period 1988–1992 and the predicted rates in the period 2013–2017 per 100 000 were in females: breast—from 38.8 to 64.6, cervix—from 12.8 to 19.3, corpus uteri—from 12.4 to 26.5. In males similar rates were: lung—from 41.0 to 73.8, prostate—from 10.1 to 15.0 and stomach—from 17.5 to 10.2. Due to the increasing incidence rates and ageing of the population the predicted number of new cases in the studied sites of cancer in the period 2013–2017 is 62% higher than that observed in the period 1988–1992.

Keywords: cancer incidence, prediction, Bulgaria

In Bulgaria a nationwide Cancer Registry was established in 1952. The registration of each newly diagnosed incident case is compulsory. Notifications are sent to the regional oncological centres by every physician, pathological laboratory, or radiotherapy unit. Cases registered by death certificates only are also registered as new cases. Data is collected for cancers in situ for some primary sites, e.g. cervical cancer. At the end of each year the data from the regional registries are collected at the National Cancer Registry.

The total number of new cases registered in Bulgaria1 in 1992 was 22,956 (in men 11,875 and in women 11,081 cases). The age-adjusted, world standard (WS), incidence in males was 187.7 per 100,000 person years and in females 161.5 per 100,000 person years. Cancer incidence has been continuously increasing in both sexes since the establishment of the Cancer Registry. The most frequent primary sites of cancer in men in 1992 were lung, stomach, prostate, rectum and colon. In women the most common cancer sites were breast, corpus uteri, cervix uteri, stomach and ovary.

An incidence prediction can be useful when planning different health care programmes such as preventive and screening policies or diagnostic, treatment and rehabilitation facilities. From the research point of view predictions are useful for evaluation of changes in the environmental exposures and other risk factors. They can also be an appropriate base for assessment of the effect of primary prevention and screening programmes.

The aim of this study was to predict future incidence rates of the most common sites of cancer in Bulgaria in the period 1993–2017 if present trends in risk factors and diagnostic practices persist, i.e. the prediction is based on the assumption that cancer incidence will follow the same age, period and cohort patterns in the future period, 1993–2017, as in the observed period, 1968–1992.

MATERIAL AND METHODS
The numbers of incident cases of breast cancer, cancer of corpus uteri and cervical cancer in females and lung, prostate and stomach cancers in males were considered in this study. Observed numbers of new incident cases registered between 1968 and 1992 were obtained from the Bulgarian Cancer Registry. Data were provided by 5-year calendar period (1968–1972, 1973–1977, 1978–1982, 1983–1987, 1988–1992) and 5-year age group (0–4, 5–9, 10–14, ..., 80–84, 85+ years) by sex.
The population of Bulgaria was 8.5 million in 1992. Data on the observed and predicted population size were provided by the National Statistical Office of Bulgaria. Observed population numbers for the period 1968–1992 by sex, 5-year calendar period and 5-year age group, as above, were employed in the evaluation of the observed incidence trends. Predicted population numbers for the periods 1993–1997, 1998–2002, 2003–2007, 2008–2012, 2013–2017 and the same age group as above were applied for the prediction of the incidence in the future. Five-year birth cohorts were defined. For example, the birth cohort which was 0–4 years old in 1938–1942 was aged 25–29 in 1963–1967, and aged 30–34 in 1968–1972.

Longitudinal trends in the occurrence of a disease can be analysed as a function of three time dependent components: age, calendar period and birth cohort. They are linearly dependent and it is difficult to separate and interpret the effect of each of them on changes in incidence rates. In the analysis of incidence data, assuming independence of the events, multiplicative Poisson regression models were fitted to the observed incidence rates by primary site. Age-cohort and age-cohort-period log-linear models shown in Table 1 were chosen for the predictions on the basis of these modelling procedures. Particular age groups were included in the models according to the following considerations:

(i) The natural history of the disease: occurrence of cancer is occasional in the youngest age groups, for cervical cancer before age of 25, for prostate cancer before age of 45 and for the other primary sites before the age of 30. (ii) Goodness of fit of the model: each of the factors (age, period and cohort) of the final models improved statistically significantly \((P < 0.05)\) the fit of the particular model. However, in spite of the insignificant fit of the breast cancer model for the observed period we did not include higher order terms which could increase the uncertainty of the prediction.

The number of new cases was predicted by the following scheme: (i) observed incidence rates were employed to forecast future incidence rates; (ii) numbers of new cases were calculated as a product of the predicted incidence rates and predicted population size.

The statistical package GLIM was used for the predictions. The future incidence was calculated on the basis of estimated age and cohort trend components and new period and future cohort’s estimates. For the predicted period it was assumed that the cohort estimates will follow the log-linear trend of those in the observed period. Age-adjusted (WS) incidence rates were calculated for the future period on the basis of the age groups included in the prediction models, assuming zero incidence rate in the youngest age groups, which were excluded from the prediction models.

**RESULTS**

Since 1968 the age-adjusted incidence of breast cancer has increased continuously in Bulgarian females from 23.29 per 100 000 woman years in the period 1968–1972 to 38.78 per 100 000 in the period 1988–1992 (Figure 1). The highest age-specific incidence during the entire period was observed in women aged 60–74 years (Figures 2a and 2b). The incidence increased in each of the age groups over time and every succeeding birth cohort experienced higher risk of breast cancer than the previous one. The relative risk of breast cancer in the cohort aged 30–34 in 1988–1992 was more than twice that of the cohort aged 80–84 at that time. The increasing trend in the incidence of breast cancer was predicted to continue in the future period 1993–2017, and at the end of the period the age-adjusted incidence was expected to be 64.60 per 100 000 woman years.

The age-adjusted incidence of cervical cancer increased during the observed period, from 9.87 per 100 000 woman years in the period 1968–1972 to 12.79 in the period 1988–1992 (Figure 1). The incidence was relatively stable in all those aged over 49 during the period 1968–1992 (Figures 3a and 3b), while substantial increases in the incidence rates were observed in the younger age groups. The prediction for the future period, 1993–2017, was made assuming that the cohort estimates of the risk of cervical cancer in the future cohorts will remain on the same level as that estimated for the youngest cohort observed in the period 1988–1992. The age-specific incidence was predicted to increase in the women between 40 and 69 years old and to remain constant after that age. The age-adjusted incidence was predicted to follow the increasing trend up to the period

<table>
<thead>
<tr>
<th>Site of cancer</th>
<th>Age limits</th>
<th>Model</th>
<th>Goodness of fit</th>
<th>d.f.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>30+</td>
<td>Ac+Cc+Pc(^a)</td>
<td>55.1</td>
<td>30</td>
</tr>
<tr>
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<td>25+</td>
<td>Ac+Cc</td>
<td>46.7</td>
<td>36</td>
</tr>
<tr>
<td>Corpus uteri</td>
<td>30+</td>
<td>Ac+Cc+Pc</td>
<td>31.6</td>
<td>30</td>
</tr>
<tr>
<td>Lung</td>
<td>30+</td>
<td>Ac+Cc+Pc</td>
<td>41.3</td>
<td>30</td>
</tr>
<tr>
<td>Stomach</td>
<td>30+</td>
<td>Ac+Cc+Pc</td>
<td>34.6</td>
<td>30</td>
</tr>
<tr>
<td>Prostate</td>
<td>45+</td>
<td>Ac+Cc+Pc</td>
<td>22.1</td>
<td>21</td>
</tr>
</tbody>
</table>

\(^a\) Where Ac is age component, Cc is cohort component and Pc is period component.
2013–2017, when a rate of 19.30 per 100 000 woman years can be expected.

The age-adjusted incidence of cancer of corpus uteri was 6.28 per 100 000 woman years in the period 1968–1972, but it has rapidly increased and in the period 1988–1992 the rate was already twofold higher, at 12.36 per 100 000 (Figure 1). The increasing trend was similar in all age groups and the highest age-specific incidence was observed in women between 50 and 74 years old (Figures 4a and 4b). The cohort component estimates of risk show that the youngest observed birth cohorts have substantially higher risk compared to the older ones. A higher incidence rate is expected to be attributable to those cohorts as they grow older. By the end of the period 1993–2017 age-adjusted incidence of the disease was predicted to increase up to 26.50 per 100 000 woman years as a result of expected increase in the relative risk in all ages and by birth cohorts.

The highest cancer incidence in men was that of lung cancer, 38.03 per 100 000 man years in the period
1968–1972 and it increased to 40.95 per 100,000 in the period 1988–1992 (Figure 5). The incidence of lung cancer increased with age up to 70–74 years. The calendar time pattern of the incidence of lung cancer showed an increase in the age groups from 30 to 64, whereas after that age a stable decreasing trend was observed (Figures 6a and 6b). According to the age and cohort risk estimates based on the observed data, a substantial increase in the incidence of lung cancer in men was predicted for the future period. Following the same trends the incidence may reach 73.80 per 100,000 man years in the period 2013–2017. The relative risk of lung cancer in the younger observed cohorts was nine times higher compared to the oldest one. Therefore, the total incidence was predicted to increase rapidly when those high risk cohorts grow older.

The incidence of prostate cancer has increased during the observed period, from 7.91 per 100,000 man years in the period 1968–1972 to 10.11 per 100,000 in the period 1988–1992 (Figure 4). Incident cases of prostate cancer were occasional in men under 45. After that age the age-specific incidence increased, and the highest rate was observed in the age group 75–84 years (Figures 7a and 7b). The incidence rates in the age group 45–49 were relatively stable, whereas the incidence in men over 50 increased. The cohort estimates showed that the relative risk of prostate cancer increased by birth cohort. Age-adjusted incidence of prostate cancer was predicted to increase from 10.90 per 100,000 man years in the period 1993–1997 to 15.00 per 100,000 in the period 2013–2017. The same stable increasing trend was predicted for the future period by age groups and cohorts.

Stomach cancer was the only one of the studied primary sites to show a declining incidence trend. The age-adjusted incidence decreased in the observed period and in the period 1988–1992 it was about a half of that in the period 1968–1972; 17.52 and 32.29 per 100,000 man years respectively. The age-specific incidence rates (Figures 8a and 8b) decreased in all the age groups over the period and the relative risk by birth
cohorts has decreased. The age-adjusted incidence of stomach cancer is expected to follow the observed decreasing trend, and the predicted rate was 10.20 per 100,000 man years in the period 2013–2017. The highest incidence rate is expected to remain in the age group 70–79, but reductions in age-specific incidence rates in all the age groups were predicted.

The prediction in terms of number of new cases is presented in Table 2.

DISCUSSION

The assumption that the observed trends by age and birth cohorts will remain unchanged in future cannot be expected to be valid always. It is known that the extent to which a prediction can be realized in future may be influenced in three different ways: by the extrapolation of time trends, by the changes in the risk factors, and by incorporation of the effects of intervention. However, it is not always possible to estimate all the changes that can affect the predictions and the assumption that time trends will remain unchanged is often employed when predicting future occurrence of cancer. Stomach and lung cancers are good examples for the influence of changes in risk factors on risk of disease. The worldwide decrease in stomach cancer in the last decades is attributed to changes in diet such as increasing availability and consumption of fruits and vegetables, increasing intake of vitamins C, E and A, and replacement of traditional salty and smoked food by fresh and frozen food. A similar decreasing trend by birth cohorts to that estimated in Bulgarian males has been estimated in Sweden. An overall declining incidence of stomach cancer in the future has been predicted for the period 1988–2012 in the Nordic countries.

Lung cancer is a rather hypothetical example of the effect of changes in exposures on occurrence of the disease. It was estimated that about 87% of lung cancers are due to tobacco smoking, and a reduction in smoking will cause a proportional reduction in incidence of lung cancer. Tobacco smoking usually starts at young ages, therefore the cohort pattern of the risk is an important component when evaluating the overall incidence trend. The cohort risk estimates calculated in this study showed that the risk of lung cancer in men in the younger birth cohorts increases continuously. Although the predicted increase in lung cancer incidence may seem too rapid, there is no reason to believe that the total incidence has been overestimated. The growth can be explained as a reasonable consequence of epidemic extension of the smoking habit in the previous decades. A similar increasing trend related to high risk of lung cancer in the youngest birth cohorts was predicted recently in the Czech and Slovak Republics. The possible effect of changes in prevalence of smoking was studied by Hakulinen and Pukkala. The authors estimated the expected effect of six alternative changes in smoking at population level. They estimated that if 10% of smokers in different age groups and smoking categories stop smoking in each successive 5-year period, 25 years later the incidence of lung cancer will be about 30% lower. However, if no changes in the trends are assumed, Bulgaria can be attached to the group of European countries with presently low but rapidly increasing lung cancer incidence.

Another kind of intervention that can affect the pattern of occurrence of a disease is screening. Mass screening for cervical cancer is known to be the most

<table>
<thead>
<tr>
<th>Period</th>
<th>Breast</th>
<th>Cervix</th>
<th>Corpus</th>
<th>Lung (males)</th>
<th>Prostate</th>
<th>Stomach (males)</th>
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</thead>
<tbody>
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<td>1993–1997</td>
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<td>3962</td>
<td>4954</td>
<td>14294</td>
<td>4090</td>
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<tr>
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<td>16064</td>
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<td>2003–2007</td>
<td>18057</td>
<td>4769</td>
<td>7053</td>
<td>18214</td>
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<td>4221</td>
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<tr>
<td>2008–2012</td>
<td>20131</td>
<td>5149</td>
<td>8270</td>
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<td>3805</td>
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<tr>
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<td>5474</td>
<td>9561</td>
<td>22985</td>
<td>5959</td>
<td>3471</td>
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</tbody>
</table>
effective screening for cancer at present. Incidence of cervical cancer has been decreasing in most European countries in the last two decades. In some of them the declining trend is attributed to organized mass screening, but a slight decreasing trend has been observed also in countries where there is only spontaneous mass screening for cancer. An explanation for the increasing mortality from cervical cancer in Bulgaria was suggested by Beral, and this can also be adopted for the incidence trend. The incidence is increasing up to about the same level as that observed in other countries without organized screening programmes or before the establishment of mass screening. It can be assumed that the increase is rather due to improvements in diagnostic practices than to change in the risk of the disease.

Independently of the broad variations by country, incidence of breast cancer in females and prostate cancer in males are constantly increasing in most European countries. The incidence of both cancer sites in Bulgaria is similar to that in the other Eastern European countries; relatively low and rapidly increasing. Predictions for the future showed that a further increase in the incidence is expected by age and birth cohort. Due to the increasing proportion of elderly in the population the number and the proportion of new cases of breast and prostate cancers will increase even more rapidly; compared to age-adjusted incidence. Risk factors have been studied, but no effective primary prevention has been proposed so far. Screening for early detection of breast cancer was established in some countries or regions, but no empirical population-based data on the effect of screening programmes are available at present.

The incidence of cancer of corpus uteri in the past decades was relatively stable in most European populations, although some variations were observed. The risk of the disease is decreasing by birth cohort, even in those countries where the total incidence is still increasing. However, the observed incidence of cancer of corpus uteri in Bulgaria is very low, in terms of European populations, and the trend is increasing by birth cohort. There is no reason to believe that the trend difference is a result of essential differences in the risk factors for the disease. Therefore, as for cervical cancer, the increase may be attributed to improvement in diagnostic and registration practices.

This study intended to provide a description of the present and a prediction for future patterns of occurrence of the most frequent cancer sites in Bulgaria. These accounted for 40% of the incident cases in females and 38% of those in males in 1992. The incidence of all of the considered cancer sites, except stomach cancer, is expected to increase in the future and they will become a larger public health problem. Usually the information on occurrence of cancer is presented in terms of incidence rate which is a function of the number of new cases and population size, and provides one dimension of the problem. However, when the predictions are used for planning health care facilities, the number of cases is as important as the risk of disease. Due to the increasing incidence rates and ageing of the population the number of new cases in the period 2013–2017 is expected to be 62% higher than the number of cases observed in the period 1988–1992 (47% for breast, 78% for cervix, 129% for corpus uteri, 76% for lung in males and 62% for prostate, respectively). The number of stomach cancer patients (male) is predicted to decline by about 40% in the same period. A growth of more than 5000 new cases would imply a substantial increase in the need for resources devoted to cancer control, if the present standards are assumed. Particularly important is the establishment of organized screening programmes for cervical and breast cancer as soon as possible as well as the development of efficient programmes for primary prevention of lung cancer.


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