ORIGINAL ARTICLE

Is cervical cancer screening necessary or the "Paradox" example of Bulgaria

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Summary

Purpose: The present study aimed at analyzing the results of cervical screening carried out in Bulgaria, its effect on basic epidemiological indices, age-related incidence of cervical cancer and their dynamics. It also highlighted the way in which the suspension of organized screening has influenced the epidemiological data for cervical cancer.

Methods: Analyses were carried out, based on data from the National Cancer Register, the Central Institute of Statistics and the Oncological Dispensaries. Simple mathematical methods were used to analyze the attendance rate, the rate of inadequate smears and share of biopsies in women with abnormal cytology. Cohort analysis was utilized in determining age-specific incidence.

Results: Incidence and mortality were stable during the first 15 years of screening activities, followed by a constant increase which became most obvious after the final interruption of organized screening. The ratio between invasive cancer and carcinoma in situ ranged from 2:1 in 1982 to over 5:1 in 2002 and was due to the faster increasing rates of invasive cancer. Age groups' and birth-cohort analysis for 3 time points (1975, 1990, and 2005) with different screening characteristics showed highest incidence in middle-aged women and a higher risk of cervical cancer for every subsequent generation.

Conclusion: Bulgaria gives yet another, though "paradoxical", example in support of the importance of organized cervical screening. This conclusion has been reinforced by a distinct deterioration of epidemiological characteristics of cervical cancer in our country as a result of absence of an organized screening. This serious situation lends valid reasons to recommend that the relevant health authorities take a political decision to launch a programme in compliance with the European standards.

Key words: Bulgaria, carcinoma in situ, cervical cancer, cervical screening, incidence, mortality

Introduction

Since the beginning of the 1960s cervical cancer screening programmes, based on cytological examination, have been carried out in many countries, most intensively in north America, the Scandinavian countries and the United Kingdom (UK). The main achievements of screening programmes are improvement of stage distribution of cases with cervical cancer on first diagnosis (early stages), increase in the number of cases with carcinoma *in situ*, decrease of incidence of invasive cancer and reduction of mortality.

The importance of the Papanicolaou smears examination (PAP test) in reducing the risk of invasive cancer and mortality has been firmly established, and it is estimated that regular screening reduces the risk of invasive cancer by 80%. Organized cervical screening programmes have been shown to be more effective than opportunistic or non-organized screening, because opportunistic screening tends to omit women at greatest risk [1-3].

As a result of screening, the countries applying effective programmes feature significant reduction in mortality and incidence of invasive cancer. The most successful screening programmes have been implemented in the Scandinavian countries, the UK, the USA and Canada, while the programme in Finland is considered to be the best example. Finnish authorities have reported a screening range of 75-80%, resulting in a decrease in incidence by 60% and in mortality from 7 to 3‰ [4].

In Bulgaria, preventive examinations of the female genital tract were introduced in 1956, and cytological screening was launched in 1970. This comprised

all women over the age of 30 at one-year screening interval. PAP smears were taken by obstetrician-gynecologists and midwives and cytological diagnostics was carried out in 14 centralized laboratories. Most laboratories were staffed with a pathologist, biologists and technicians. Later on, due to lack of organized screening programme, there was an imbalance in human resources' policy, expressed by a shortage of cytopathologists and insufficient number of biologists in different regions, their number been rather inadequate considering the anticipated volume of screening activities. Classification of cytological results was carried out according to the Papanicolaou numerical system. No quality control system had been officially introduced [5].

Since 1970 registration has been going on for cervical cancer cases and since 1975 it included also carcinoma *in situ* cases. Unfortunately, the lack of a nationwide screening registry, a modern information system for registration and follow-up of women with abnormal cytology and dysplastic lesions were factors which determined the inefficiency of registration of screening activities as a whole [5,6].

At the end of the 1980s - the period when political, economic and social changes started taking place in the country - organized screening activities were suspended, which in turn led to alterations of the objective indicators for screening activities and epidemiological indices of cervical cancer.

The present study aimed at analyzing the organization and results of cervical screening carried out in Bulgaria, its effect on some basic epidemiological indices, age-related incidence of cervical cancer and their dynamics. This research also highlighted the way in which the suspension of organized screening has influenced the epidemiological data for cervical cancer.

Methods

Different sources of information were used. Data about new cases of cervical cancer, incidence and mortality for the period 1970-2005 and *in situ* cancer for 1975-2005 were obtained from the National Cancer Register annual reports **[**6]. Information regarding the number and dynamics of the population as well as the number of deaths due to cervical cancer (1970-2005) were drawn from the Central Statistics Institute annual reports [7]. Data about screening activities at Regional Oncological Dispensaries (1978-1996) were taken from their registers and annual reports [8].

The survey focused on indicators of actual incidence and mortality, incidence of carcinoma *in situ*, and age-standardized incidence and mortality (World stan-

dard). Simple mathematical methods were used to analyze the attendance rate, the rate of inadequate smears and share of biopsies in women with abnormal cytological results. Cohort analysis was utilized in determining age-specific incidence. These data were processed by means of SPSS / v. 11.01 for Windows.

Results

The population subjected to screening consisted of approximately 1.5 million women. Analysis of the screening range showed that for the period up until the end of the 1980s, screening was regularly carried out at a constantly high level of coverage (over 85%). Later, there was a significant drop in the intensity of organized cervical screening, with the 1996 data reporting only 205,081 screening tests performed (a 7-fold decrease of the number of women examined). Thus, due to political, social and economic reasons, screening activities actually ceased. They were performed on an opportunistic basis only, without any nation-wide registration of screening results.

Over the period under study, the average share of women with inadequate smears was 5.4%, ranging from 0.2 to 27.1% at different regional laboratories, in different years.

In a 1970-2005 survey, the number of new cervical cancer cases varied from 509 (at the beginning of the period) to 1,096 cases (at the end of the mentioned period). There was a distinct trend of steady increase in the number of new cases.

In the period 1970-2005 the crude incidence of cervical cancer ranged from 12.7 to 27.4‰₀₀. After certain stabilization until 1985/86, the incidence showed a marked upward tendency, most obvious over the last 15 years. Age-standardized incidence (World) (1970-2005) was in the range of 9.9 to 19.5‰₀₀ (Figure 1).

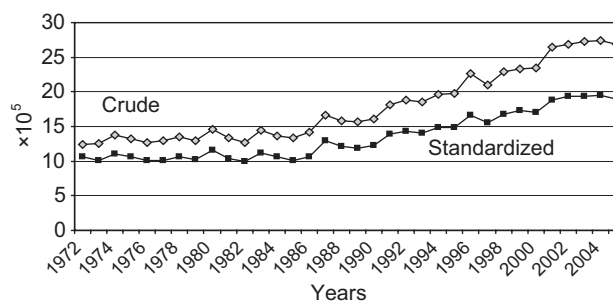Cervical cancer deaths for the period 1979-2005 ranged from 179 to 411 women.

Figure 1. Crude and standardized incidence of cervical cancer, Bulgaria, 1970-2005.
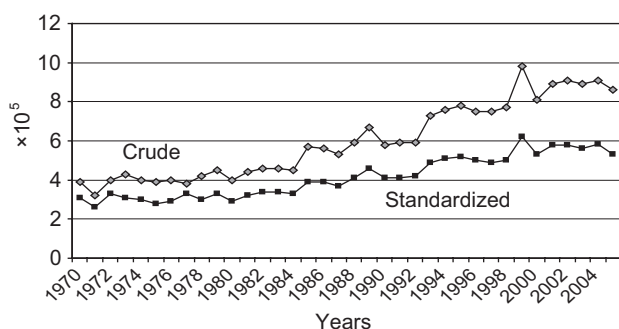
Figure 2. Crude and standardized mortality of cervical cancer, Bulgaria, 1970-2005.
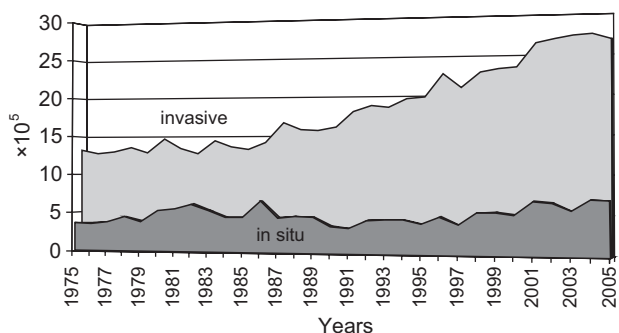

Figure 4. Cervical cancer incidence by age, Bulgaria, 1975, 1990, 2005.

Figure 3. Ratio between patients with cancer *in situ* and invasive cervical cancer, Bulgaria, 1975-2005.

Analysis of the incidence curves by 5-year age groups in 1975 and 1990 revealed that the results were relatively close, especially in women over 40 (Figure 4). Both curves were markedly different from the one for 2005, most pronounced in young and middle age groups (35-64 years).

As a result of the cohort's analysis performed in 3 separate years with different characteristics of cervical screening (namely, 1975, 1990 and 2005), we found that every subsequent generation had a higher risk of cervical cancer for a particular age group.

Discussion

Analysis of cervical screening activities in Bulgaria showed that, at first, the programme launched in 1970 met the international standards and its principles were not different from those of the programmes in western Europe and north America. It clearly outlined the subject population, the screening interval, the screening method applied, as well as the way women with abnormal cytology were specified. The call for screening, registration and data storage at the launch of the programme were in compliance with the international institutions recommendations of that time [9,10].

The expected outcomes of screening should have resulted in meeting its major goals: a decrease in incidence of invasive cancer and mortality. Unfortunately, after a certain stabilization of these indices after 1985-86, there was a kind of a "drop" in screening activities which is demonstrated by a strong falling trend in the attendance rate (from 1.5 million to about 200,000 women). This means that the former organization of screening had some disadvantages which is one of the reasons why it did not achieve a severe impact on the epidemiological data of the disease.

In contrast to Bulgaria, countries with successful screening programmes conducted extensive research

For the period 1970-2005 the crude mortality increased from 3.2 to 9.1‰₀₀ women. Similar was the case with age-standardized mortality (World) which ranged from 2.6 to 5.8‰₀₀ with a marked rising tendency (Figure 2).

The absolute number of cervical carcinoma *in situ* cases ranged from 140 to 275 women for the period 1975-2005. Among all the women who underwent cytologic screening only 1% turned out to have cervical carcinoma *in situ*. The actual carcinoma *in situ* incidence for the same period of time was a direct indicator for screening inefficiency and varied from 3.1 to 7.0‰₀₀ (Figure 3). The considerably lower value of this indicator determined the unfavorable ratio with invasive carcinoma cases and ranged from 2:1 in 1982 to over 5:1 in 2002 due to the faster rates of invasive cervical cancer incidence compared to the lower carcinoma *in situ* frequency.

The study of the basic epidemiological indices for the whole screening programme period showed the following trends: there was certain stabilization at the beginning of the period (1970-1985/86), followed by a steady increase in incidence and mortality rates, which became most obvious after the final suspension of organized screening activities.
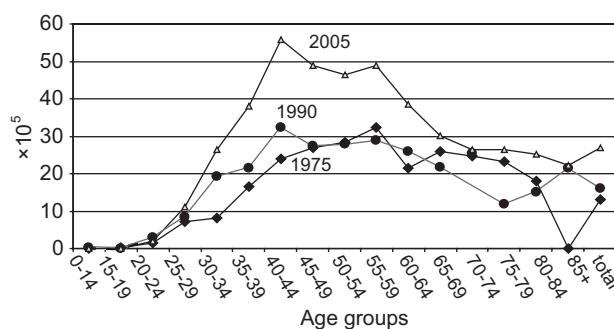
to find how effective screening is. Our country proved that absence of screening leads to aggravation of the epidemiological indices for cervical cancer.

In Bulgaria the unfavorable changes of these indices have been established against a background of total lack of re-organization and updating of the cervical screening programme since it was launched in 1970 up to the present day. This, together with the interruption of the organized character of the programme after 1989, has resulted in the negative epidemiological characteristics of the disease and, hence, to an unsatisfactory assessment of the programme efficiency [10].

Unlike Bulgaria, the Scandinavian countries provide convincing evidence for the importance of cervical screening. In these countries its implementation has resulted in the greatest reduction in cervical cancer incidence and mortality ever.

The evidence in the UK serves as yet another example that an adequately organized screening programme is actually indispensable. Cervical screening was introduced there in 1964 and the first results proved no significant efficiency. At the beginning of 1970s an increase in cervical cancer incidence was reported for women under the age of 45. Mortality decreased by 20% for the period 1967-87, but in younger women a marked increase was observed. According to Cuzick and Boyle, the major cause for these results was inadequate screening coverage of the population at risk [11]. An editorial in The Lancet titled *Death by Incompetence* admitted that another major cause was the inefficient utilisation of resources [12]. After programme re-organization, the foundation of a National Coordinating Network followed by the introduction of a centrally organized computerised system for screening invitations, as well as purpose-oriented payment to GPs, screening coverage increased to 80% and all screening parameters improved [13-15].

By contrast with our data (Figure 3) over the frequency of carcinoma *in situ* in the UK for the period 1971-91, there was 8-fold increase of the levels of *in situ* carcinoma, due to the improved screening activities and registration. The ratio of *in situ* to invasive cancer increased with increased numbers of carcinoma *in situ* in all birth cohorts since 1932-36 [16].

According to the analysis of Herbert in the UK after the introduction of a highly successful centrally organized cervical screening programme in 1988, the incidence of invasive cervical cancer has fallen by more than 40% [15].

Analysis of the age-related incidence in 1975, 1990 and 2005 (Figure 4) indicates that the highest incidence rate was observed in 2005 in middle-aged women who had not been covered by cervical screening because of its suspension in the 1990s.

On the basis of a birth cohort analysis of incidence in 3 time points, i.e. 1975 (with functioning cervical screening), 1990 (when the screening programme started deteriorating) and 2005 (characterized by a lack of organized screening activities) we noticed a higher risk of cervical cancer for every subsequent generation with a main increase among women born between 1941-45 and 1946-51, as reported in many other countries across Europe [16,17]. The stability of incidence and mortality between 1975 and 1990, the steady increase of these indices following that period of time, as well as the increase in the ratio between invasive carcinoma and carcinoma *in situ* on the one hand suggest that the screening had a limited effect during the first 15 years, and, on the other hand, underscored the strong impact of the suspension of organized screening after 1990.

Opposite to our results are those reported by Bray et al., who analyzed similar programmes in 13 European countries. The decreased incidence in most of them was a consequence of the implementation of effective cytological screening. Similar to Bulgaria are the results in 4 of the countries (Spain, Slovenia, Slovakia, and Estonia), in which no effective screening takes place. The main difference with other countries in terms of unfavorable epidemiological changes is exhibited in the level of the indices which is higher in our country. Conversely, the beneficial effects of organized screening programmes gain special prominence in the period-specific decreases in the Nordic countries and in the UK at much the same time as incidence and mortality increased in Bulgaria [17].

Conclusion

The unfavorable changes and trends have given us grounds to admit that Bulgaria gives yet another, though 'paradoxical', example in support of the importance of organized cervical screening in order to efficiently control the disease. This conclusion has been reinforced by a distinct deterioration of cervical cancer epidemiological characteristics in the country as a result of the loss of an organized screening programme.

The extremely serious situation in our country lends valid reasons to recommend that the relevant health authorities take a political decision to launch a programme in compliance with European standards and outline steps in carrying out cervical screening throughout the country.

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