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Breast and cervical cancer incidence and mortality trends in Russia 1980–2013

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ABSTRACT

Background: Breast and cervical cancer are among the leading causes of preventable cancer deaths in women in Russia. The aim of this study is to analyze changes in breast and cervical cancer incidence and mortality trends using data from the Russian State Cancer Registry.
Methods: The age-standardized rates of cervical cancer incidence (1993–2013) and mortality (1980–2013) were analyzed using piecewise linear regression. Age-period-cohort models were used to estimate the temporal effects and provide future predictions.
Results: Breast and cervical cancer incidence rates uniformly increased over two decades from 33.0 to 47.0 per 100,000 and from 10.6 to 14.2 per 100,000, respectively. Breast cancer mortality rates however declined from 17.6 to 15.7 in 2013, while cervical cancer mortality increased steadily from 5.6 to 6.7. Breakpoints in the risk occurred in cohorts born 1937–1953, indicating a recent generational decrease in breast cancer mortality, but a concomitant increase in cervical cancer. Cervical cancer has already surpassed breast cancer in terms of years of life lost (YLL) (23.4 per death vs 18.5 in 2009–2013), while future projections suggest that the annual YLL could reach 1.2 million for cervical cancer and (decline to) 1.8 million for breast cancer by the year 2030.
Conclusion: The temporal patterns of breast cancer incidence and mortality in Russia are in line with other countries in Europe, although cervical cancer rates and the risk of occurrence in recent generations is rapidly increasing; these trends underscore the need to place immediate priority in national cervical vaccination and screening programs.

1. Introduction

Breast cancer is the most common cancer type of women globally while cervical cancer is among most common cancer types in less developed regions [1]. Both breast and cervical cancer are among the leading causes of preventable cancer deaths in women in Russia [2]. Despite their high frequency, systematic large-scale efforts aimed at primary and secondary prevention to control breast and cervical tumours, while available [3–5], are not systematically implemented in the country [6].

A thorough quantification of the healthcare problem and its eligibility is the first of the WHO criteria for screening described by Wilson and Jungner [7]. Cost-effectiveness of interventions also depends on the cancer scale and profile, an assessment of trends, and projections evaluating possible impacts in the presence and absence of cancer control programmes [8,9]. Assessing cancer patterns and trends is essential for setting the health care priorities, identifying targets for intervention as well as guiding further research. Appropriate quantification requires valid, consistent and comparable data over time to reflect real trends and interpretation of the underlying changes [10].

Epidemiological data from Russia has not been extensively reported for several reasons: the language barrier, still limited formal education in epidemiology, scarce resources for cancer epidemiologic research and a lack of formal quality evaluation of registry data [11,12]. This is

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unfortunate given the vast proportion of the European population that Russia constitutes and the long history of the population-based cancer registration system in the country, established in the USSR in 1953 [12]. All medical facilities are obliged to notify the regional population-based cancer registries of all newly-diagnosed cancer cases and any new hospitalization of patients with cancer. The State Cancer Registry (SCR) based at the Herzen Research Institute of Oncology in Moscow aggregates the data from the regional registries and produces an annual report with crude data that is freely available [13]. Several changes in lifestyle, behavioral and reproductive factors in the last few decades in Russia, together with socioeconomic changes, likely influence the changing cancer profiles now observed [14].

The analysis of cancer trends and their changes in Russia are thus essential to understand the impact of cancer on the health care system in Russia. The aim of this study is to describe breast and cervical cancer incidence and mortality trends in Russia, quantifying changes using several indicators of the cancer burden including years of life lost (YLL), and a prediction of the future burden circa 2030, via an extrapolation of recent trends and demographic changes, as a baseline for cancer control action.

2. Materials and methods

2.1. Incidence, mortality, and population data

This study followed the data analysis protocol developed for the Russian cancer registries (details are described in *Supplementary Material 1*). Female breast and cervical cancer incidence (1993–2013) and mortality (1993–2013) data were acquired from the SCR based at the *P. Herzen Moscow Oncological Research Center* in Moscow. Obligatory cancer registration covers the entire population of the Russian Federation (143.5 million people in 2013) since 1953, but the SCR was officially established only in 1996 [15]. Registry operations are described in detail in the official order of the Ministry of Healthcare of Russian Federation (MOH) and involve the sending out of standardized paper-based notifications to the regional population-based cancer registries in Russia (at the moment more than 80 regional registries are operating in Russia), from which paper-based and electronic reports are then forwarded to the SCR [16]. The incidence data are collected under the supervision of the MOH, while the mortality data (based on death certificates) is collected independently as a part of the demographic data capture by the regional civil registries. At present, no comprehensive report is available about quality of the data in Russia. For cancers identified from death certificates only an overall number for all age groups and sexes for each regional cancer registry is provided [15].

All registered incident cancer cases and deaths were tabulated by age, sex and calendar period. Age-specific data was available for age-groups 20–24 and above for breast cancer incidence, breast and cervical cancer mortality, and for age-groups 15–19 and above for cervical cancer incidence. Overall number of cases and deaths registered for the study period was reported according to SCR. The number of cases and deaths registered before age of 20 was at most 0.08% (29 cases of breast cancer were registered in 1993 before age of 20). Population data were retrieved from the Federal State Statistics Service (FSSS) [17].

For comparative and validation purposes, additional sources of mortality data (1980–2011) were obtained from the World Health Organization (the WHO) Mortality Database and the Human Mortality Database [18,19]. Both databases use data reported by the MOH based on civil registration system. The mortality data before 1991 refer to the Russian Soviet Federative Socialist Republic (the RSFSR). The comparison of overlapping data from WHO and SCR (1993–2011) revealed only minor disparities. Most of them were for the years 2004 and 2005, for which the differences in the number of deaths were at most 0.4% and distributed equally by age group (e.g. for year 2004 overall 22,757 vs. 22,797 for breast cancer and 6003 vs. 6022 for cervical cancer as reported in the SRC and WHO data systems, respectively). For all years in this period, the disparities were less than 0.05% and the absolute difference was less than 10 cases. SCR data were thus used in the analysis.

In order to correct for possible inaccuracies in the reported deaths from uterine cancers (endometrial, cervical, and other and unspecified cancers), we applied the reallocation rules developed and applied in an earlier analysis of cervical cancer mortality trends [20]. Cervical cancer mortality in Russia was corrected using WHO mortality data for similar periods using the "gold standard" of Hungary (Fig. 1 and Table 1 in *Supplementary Material 2*). The incidence data reported by SCR did not include *uterus not otherwise specified* (NOS) cases (ICD-10 C55), hence the previously-used correction was not feasible, and in any case, the equivalent NOS proportions were minor, relative to mortality. The mortality trends from Uterus and Uterus NOS (C54, 55) and Uterus (C54) incidence are presented as Figs. 4 and 5 in *Supplementary Material 2*.

2.2. Statistical analysis

Age-standardized rates (ASR) of cancer incidence and mortality per 100,000 person-years were calculated using the Segi-Doll world standard population [21]. In order to find breakpoints (joinpoints) in trends, we fitted simple linear regression models with the ASR as response, calendar period the explanatory variable, using an iterative procedure proposed for estimation of regression models with piecewise linear relationships[22]. Estimates from the final model were plotted against the original trend with breakpoints and the annual percentage changes (EAPC) between linear segments were reported. Incidence and mortality ASRs per 100,000 person-years in 2008 and 2013 were obtained for 82 regional cancer registries in order to compare with national trends.

Age (A), calendar period (P), and birth cohort (C = P-A) effects on incidence and mortality were estimated using age-period-cohort models, that have been described elsewhere[23]. Briefly, the rates are described as a function of age, period, and cohort using a log-linear model, with Poisson errors and a logarithmic link function: $\log[l(A, P)] = a(A) + p(P) + c(C)$, where a, p, and c are the functions each parameterized with a limited number of parameters. We restricted our analyses to age intervals of 20–84 years and both maximum likelihood and sequential procedures for modelling were applied. A unique solution was provided by imposing constraints on the cohort and period effects ($C_o = 1945$ or $P_o = 2000$) with the first-order (linear) trend set to birth cohort, and the longitudinal age curve based on the reference cohort reported. The drift parameter was estimated as $\text{EAPC} = (\exp(\text{drift}) - 1) \times 100$). Natural splines were used to model the functions with seven knots applied to each effect category. In Table 2–5 of *Supplementary Material 2*, we present comparison based on the differences of residual deviances and degrees of freedom using χ^2 tests; the goodness-of-fit measures of the models are not reported as some have suggested they do not convey meaningful information about the actual model fit [23].

After comparing the likelihood ratio statistics, the final reported results were derived from the age-cohort model, with the age effects as rates for the reference cohort and cohort effects as rates relative to the reference cohort. Period effects were obtained from the model with the period term alone, using log (fitted values) from the age-cohort model as offset [24]. In order to simultaneously assess and present changes in incidence and mortality, we also show hodographs for cohort effect functions.

To predict future rates, we applied a validated approach that also utilizes age-period-cohort models (Nordpred) based on three plausible scenarios (Scenario 1: without reduction of drift; Scenario2: with 100% reduction for all periods; Scenario 3: 0–25%-50%-75% reduction in each following projection period) alongside official predicted population retrieved from FSSS [25](for details see *Supplementary Material 1*). The projection was done for four 5-year periods till (2014–2033) based