

Original Article

Attributable Causes of Breast Cancer and Ovarian Cancer in China: Reproductive Factors, Oral Contraceptives and Hormone Replacement Therapy

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ABSTRACT

Objective: To provide an evidence-based, consistent assessment of the burden of breast cancer attributable to reproductive factors (RFs, including nulliparity, mean number of children, age at first birth and breastfeeding), use of oral contraceptives (OCs, restricted to the age group of 15–49 years), and hormone replacement therapy (HRT), as well as of the burden of ovarian cancer attributable to the mean number of children in China in 2005.

Methods: We derived the prevalence of these risk factors and the relative risk of breast and ovarian cancer from national surveys or large-scale studies conducted in China. In the case of RFs, we compared the exposure distributions in 2001 and counterfactual exposure.

Results: Exposure of RFs in 2001 was found to account for 6.74% of breast cancer, corresponding to 9,617 cases and 2,769 deaths, and for 2.78% of ovarian cancer (711 cases, 294 deaths). The decrease in mean number of children alone was responsible for 1.47% of breast cancer and 2.78% of ovarian cancer. The prevalence of OC use was 1.74% and the population attributable fraction (PAF) of breast cancer was 0.71%, corresponding to 310 cases and 90 deaths. The PAF of breast cancer due to HRT was 0.31%, resulting in 297 cases and 85 deaths.

Conclusion: RFs changes in China contributed to a sizable fraction of breast and ovarian cancer incidence and mortality, whereas HRT and OCs accounted for relatively low incidence of breast cancer in China.

Key words: Reproductive factors; Oral contraceptives; Hormone replacement therapy; Cancer; Population attributable fraction

INTRODUCTION

Breast cancer is the most frequent cancer of women with an estimated 1.4 million new cases in 2008 worldwide, according to GLOBOCAN 2008^[1].

There are generally increasing rates of breast cancer in the world, and incidence rates are high in most of the developed areas and low in most of Asia including China^[2]. However, cancer registries in China are recording annual increases in incidence of 3% to 4%, which is much higher than average increasing rates (about 0.5%) in other countries^[2]. Ovarian cancer ranks the seventh most common cancer in women worldwide. Incidence rates are highest in developed countries. There are relative low age-standardized incidence and mortality rates in China (3.8 and 1.5 per 100,000)^[1].

Reproductive factors (RFs), and exogenous

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hormones, majorly oral contraceptive (OC) and hormone replacement therapy (HRT), are known risk factors to breast cancer and ovarian cancer. The RFS for which the evidence of a causal link with breast cancer is established include parity, age at first birth, total number of children, and duration of breast-feeding^[3-6]. In addition, total number of children is also causally associated with ovarian cancer^[7, 8]. Current or recent OC use contributes to the increased risk of breast cancer, particularly in young women and a history of OC use has clearly been shown to reduce the risk of ovarian cancer. Prolonged HRT use is found to be one of the important risk factors of breast cancer^[9]. There is also evidence that HRT is associated with ovarian cancer occurrence^[7].

As major risk factors, the unfavorable trend of RF change and prevalent OC and HRT use can lead to increasing incidence rates of breast cancer and/or ovarian cancer. The weight of these three risk factors to the burden of cancer in a given population is critical for better understanding of the relative importance of risk factors and for prioritization of public health efforts. Since one-fifth of new cancer cases worldwide occurs in China every year^[8], attributable causes of cancers in China is in need of investigation to guide efforts in cancer control and prevention.

Attributable risks of these risk factors to breast cancer and ovarian cancer have been studied systematically in developed countries such as the United States and France^[10, 11]. In contrast, the distribution of these factors in China is different from European and North American countries: HRT use in China is restricted to menopausal women who have peri-menopause symptoms. OC use is only one of the contraception methods used among women. The family planning policy implemented three decades ago and the lifestyle changes from economic improvement during this period in China have led to changes in RFs. No systematic assessment of the use of HRT and OC and the impact of RF on breast and ovarian cancer is available for China. Based on the rising incidence of breast and ovarian cancer and the different exposure situation regarding risk factors in China, we aimed to evaluate the proportion of breast and ovarian cancer risk attributable to these three factors in China.

MATERIALS AND METHODS

Overview

This study was to estimate the contribution of reproductive and hormonal factors to the burden of cancer through the calculation of proportion of specific cancers occurring in China in 2005 attributable to these

risk factors (population attributable fraction, PAF). Our estimate of PAF was calculated based on the counterfactual scenario of total avoidance of exposure, except evaluation for RFs. We obtained estimates of relative risk (RR) and prevalence of each risk factor in Chinese women to derive estimate of PAF.

For three risk factors in this study, there is no lag time considered between at which time prevalence of specific factor was drawn and at which time cancer statistics was obtained. The latency period in PAF study does not apply to RFs, for which recent exposure is more important to determine cancer risk. Because current OC use is associated with breast cancer and such risk would disappear after cessation of OC use^[12]. No lag time was considered for OC use in PAF analysis. Similarly, past HRT, defined as use of HRT ceased at least one year previously, has been associated rarely with a significant small increase in breast cancer risk^[13].

To evaluate RR of breast cancer or ovarian cancer associated with RF, OC and HRT or their prevalence in China, we conducted a systematic publication search on PubMed, Medical Database of China Online Journals, Database for Chinese Technical Periodicals, China National Knowledge Infrastructure, On-line Visual Display Unit Interrogation of Databases, Excerpta Medical Database, the Cochrane Library, and cited references. Language was limited to English and Chinese. Search terms included risk factor, RF, OCs, HRT, menopause, perimenopausal women, China, Asia, breast cancer, ovarian cancer, social science, investigation, attitude, and health. Criteria for priority selection of data sources are: studies on national population or a representative sample preferred over studies of selected populations; meta-analyses over single studies; and Chinese data over data from other Asian countries or regions.

RFs

To collect population-based data on the prevalence of RFs, we browsed yearbooks^[14-20] of health, population, family planning, fertility and reproductive health in China from 1980 to 2008. Additionally, we searched publications or data analysis books^[21-30] from related national surveys or investigations of representative samples conducted during this period. Department of Health or National Population and Family Planning Commission performed these surveys or investigations in 1985, 1987, 1988, 1992, 1995, 1997, 2001, and 2004. Two dataset books^[31, 32] were also used to include data from national population and fertility surveys conducted in 1982 and 1990. We also examined a few studies^[33, 34] presenting prevalence of RFs, although