Cancer Epidemiology 39 (2015) 1148–1151

Contents lists available at ScienceDirect

Cancer Epidemiology

The International Journal of Cancer Epidemiology, Detection, and Prevention

journal homepage: www.cancerepidemiology.net

Reprint of "Cancer of the cervix: A sexually transmitted infection?"☆

Valerie Beral

Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, United Kingdom

ARTICLE INFO

Article history:
Available online 4 November 2015

ABSTRACT

When mortality patterns for cancer of the uterine cervix were compared with trends in incidence of sexually transmitted diseases in both England and Wales and in Scotland, there were striking associations between the temporal, social class, occupational, and geographic distributions of these diseases. The data suggest that exposure to sexually transmitted infection is an important determinant of cervical cancer. Although they are still young, women born after 1940 are already experiencing increased cervical-cancer mortality. If cervical-cancer prevention and therapy remain unchanged, this generation's high risk of death from cervical cancer will probably continue to operate throughout their lives.

1. Introduction

Since the observation that cancer of the uterine cervix is almost unknown in nuns [1], it has been established that sexual activity is a major factor in the genesis of cervical cancer [2–7]. Detailed epidemiological studies have shown that factors associated with an increased risk of this malignancy include: marriage [2–10], broken marriage [2–5,8], multiple marriages [2,4,5,9], extramarital sexual activity [3,5,6], premarital sexual activity [3], early age of first marriage [2–5,8–10], early age of first inter-course [2,3,5,6], illegitimacy [3], multiple sexual partners of the woman [2,5,6] and of her husband [5,6], history of prostitution [11], history of syphilis [8,11], low socioeconomic status [3,8,10], and urban residence [3,10].

There are two current aetiological hypotheses based on these observations. The first stresses the association of cervical cancer with factors related to an early age of first intercourse. It proposes that during adolescence the cervical epithelial cells are especially vulnerable to carcinogens [7,12]. The suggested carcinogens include chronic cervicitis, hormonal imbalance, coal-tar douches, repeated cervical infection, smegma, trauma, or sperm DNA [12]. The second hypothesis stresses the association of cervical cancer with factors related to the multiplicity of sexual partners, not only of the woman herself, but also of her husband. It proposes that malignant change is induced by a sexually transmitted infection [5]. The herpesvirus type II, which causes genital herpes, has been implicated as the specific agent [13].

I have examined the two hypotheses in the light of trends in cervical-cancer mortality and their relation to the incidence of sexually transmitted infections in England and Wales and in Scotland.

2. Incidence of sexually transmitted infections in women

Venereal-disease clinics were established throughout Britain by the Venereal Disease Act of 1916. Since then the number of new cases of gonorrhoea, syphilis, and chancroid treated each year in the clinics has been recorded. The figures are collected separately in England and Wales and in Scotland, and published in the annual reports of the respective departments of health [14–18].

These routinely collected data may be inadequate for several reasons. Firstly, the proportion of persons with venereal disease who actually attend a clinic may have changed with time. Secondly, even if clinic attendance were complete, new cases treated do not provide a measure of actual incidence of the disease. This is especially true of syphilis, in which a "new case" may be an infection acquired years before. In 1972, 56% of women treated for syphilis in England and Wales had the infection for one year or longer [15]. Thirdly, with the widespread use of antibiotics, undiagnosed infections may be inadvertently treated when antibiotics are given for some unrelated illness. This is more likely to occur with syphilis than with gonorrhoea, since syphilis has a relatively longer incubation period and duration than gonorrhoea. Fourthly, chancroid-rates are erratic, because of the small number of cases each year. Therefore, of the diseases for which data exist, gonorrhoea-rates offer the most sensitive measure of actual incidence of infection. I have used gonorrhoea-rates to indicate time trends and distribution of sexually transmitted infections in general.

There were pronounced fluctuations in the reported rates of gonorrhoea among females in England and Wales and in Scotland

☆ Reprinted with permission of *The Lancet*. Beral, V. Cancer of the cervix: A sexually transmitted infection? *Lancet* 1974;303(7865):1037–1040.

http://dx.doi.org/10.1016/j.canep.2015.08.005
1877-7821/

between 1925 and 1972 (Figs. 1 and 2). Periods of increasing gonorrhoea incidence are synchronous in both parts of Britain and coincide with recognised times of social stress and change—i.e., with the economic depression in the early 1930s, with the 1939–1945 war, and with changes in sexual mores of recent years. Incidence-rates during the latest epidemic are continuing to rise.

In England and Wales information on age has been recorded since 1963. Each year peak rates in females have been in the 18–19 age-group. The proportion of infections in women aged between 16 and 24 is very large and has increased each year from 63% in 1963 to 76% in 1972 [14,15]. In Scotland age recording dates from before 1925 but the age-groups are not comparable with those of England and Wales. Since that time, peak rates in women have remained in the 20–24 year age-group. In the past 10 years, however, rates in the 15–19 age-group have been approaching those of the 20–24-year-olds. Since 1925 the proportion of infections seen in women aged between 15 and 24 has varied from 41% to 68% [16–18]. Scottish data also reveal that incidence-rates in women over 30 years of age are negligible. Despite the fluctuations in gonorrhoea incidence, it could be concluded that the age-distribution of those affected has remained relatively constant. In general, there is a concentration of cases in the narrow age-range between 16 and 24 and maximum incidence occurs at around age 20.

I shall therefore assume that during a woman's life her risk of exposure to gonorrhoea is limited to a relatively short period in early adulthood. Furthermore I shall also assume that a woman's chance of becoming infected depends on the level of gonorrhoea in the community when her risk of infection is greatest—i.e., the incidence of gonorrhoea when she is aged 20.

3. Mortality from cervical cancer

Against a background of declining mortality from cancer of the cervix among successive generations of women in England and Wales, the generations born between 1911 and 1924 and around 1941 were noted to be experiencing higher mortality-rates from this disease than women born before them [19,20]. In Scotland, women born around 1919 were also found to have higher mortality-rates from carcinoma of the uterus, that is of the cervix and body of the uterus combined, than women born before or after them [21].

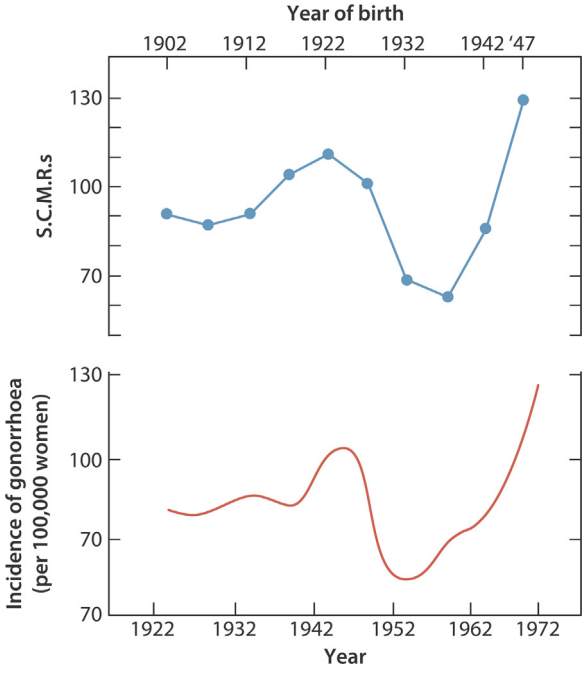

Fig. 1. SCMRs from cervical cancer among women born between 1902 and 1947 in England and Wales and incidence of gonorrhoea among women in England and Wales, 1925–1972.

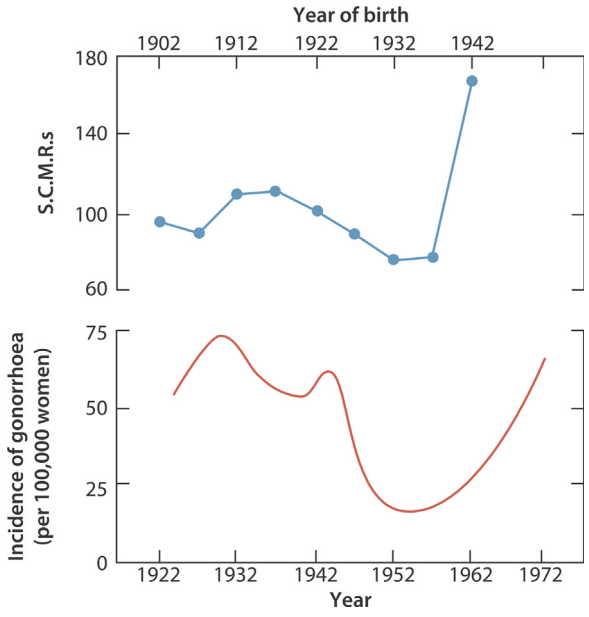

Fig. 2. SCMRs from cervical cancer among women born between 1902 and 1942 in Scotland and incidence of gonorrhoea among women in Scotland, 1925–1972.

I have examined mortality-rates from cervical cancer in successive generations of women in England and Wales born between 1902 and 1947 and between 1902 and 1942 for Scotland. The data were taken from the annual reports of the Registrar Generals of England and Wales [22] and of Scotland [23]. Each generation or cohort was identified by the average year of birth of the women in that group. Their mortality-rates in each 5-year age-grouping were calculated using the quinary-quinquennial method of Case [24].

In general, for any cohort the mortality at any given age was lower than the rate for its preceding cohort at the same age. The exceptions in England and Wales were seen in the 1917, 1942, and 1947 cohorts at all ages and in the 1922 and 1912 cohorts at certain ages. In Scotland, reversals of the general downward mortality trends were not as clearly defined as in England and Wales, but were seen mainly in the 1912, 1917, and 1942 cohorts.

As noted previously [21], the remarkable feature of these mortality patterns is the stability of cohort trends—i.e., a group with a high mortality at one age, compared with another group, retains a similar high mortality at other ages. This finding could be explained by an event occurring in early life and determining subsequent mortality. Alternative explanations are more complex and involve assumptions of changing outcome of treatment in each age-group at different times. The first is a simpler explanation, and furthermore stable cohort trends are described for other diseases in which mortality is thought to reflect events in early life [25].

To simplify the data a summary age-standardised statistic was calculated for each birth cohort. It is equal to the total observed deaths within the cohort, divided by the total deaths expected if average age-specific rates were to apply in each 5-year period, multiplied by 100. This method is therefore a form of indirect standardisation, where cohort rates are used instead of the usual period rates to calculate a standardised mortality ratio (SMR).This statistic is called a standardised cohort mortality ratio or SCMR.