

Cervical Cancer Trends Related to Mortality in Japan

Kazuo AOKI¹, Junichi MİSUMİ¹, Jianru WANG², Hengli JİANG², Juan SUN³

¹Department of Environmental Health and Preventive Medicine, Faculty of Medicine, Oita University, Oita, Japan

²Hebei Medical University, Shijiazhuang, Hebei, China

³Department of Public Health and Hygiene, Tianjin Medical University, China

Received 29 May 2006; received in revised form 07 August 2006; accepted 09 August 2006

Abstract

Objective: Our study aims to identify the major trends in mortality from cancer of the *cervix uteri* in Japan during a 50-year period (1950-2000); and to consider the negative contribution of cancer of the *cervix uteri* to life expectancy.

Materials and Methods: The age specific rates for mortality of cervical cancer, were based on the data collected by Vital Statistics of Japan. The contribution of cervical cancer to the overall change in life expectancy was calculated by the cause-elimination life table.

Results: The mortality rates show a large variance during this 50-year period. The highest mortality rate was 3.74/100 000 in 2000, and the lowest mortality rate was 1.19/100 000 in 1950. The rate for 2000 was about 3 times higher than that for 1950. The high mortality rates occurred mainly in the elderly population during the period from 1950-2000. In addition, the difference observed in cervical cancer death was thus found to affect life expectancy. The highest negative contribution was 0.08 year in 1960 and the lowest was 0.02 year in 1950.

Discussion: The mortality rates of cervical cancer in Japan showed a large difference during the period from 1950 to 2000. This cancer had no negative effect on the prolongation in life expectancy in Japan.

Keywords: mortality, cancer, cervix uteri, life expectancy

Özet

Japonya'da Mortalite ile Serviks Kanseri Arasındaki İlişki

Amaç: Japonya'da 50 yıllık (1950-2000) dönemde servikal kansere bağlı mortalite sıklığını ve yaşam süresine olan negatif etkisini saptamak.

Materyal ve Metot: Servikal kansere bağlı yaşa özel mortalite oranları Japonya Yaşam İstatistikleri veri tabanı temel alınarak değerlendirildi. Yaşam beklentisindeki tüm değişkenler üzerine serviks kanserinin etkisi neden-çözüm yaşam tablosu kullanılarak hesaplandı.

Sonuçlar: Mortalite oranlarının 50 yıllık dönem süresince büyük farklılıklar gösterdiği saptandı. En yüksek mortalite oranı 2000 yılında 3.74/100 000, en düşük mortalite oranı da 1950 yılında 1.19/100 000 olarak saptanmıştır. İki bin yılı için oran 1950 yılına göre yaklaşık 3 kat daha fazla idi. 1950-2000 arasındaki dönemde yüksek mortalite oranları esas olarak yaşlı popülasyonda saptandı. Ek olarak, serviks kanseri ölümlerinde gözlenen farkın yaşam beklentisini etkilediği saptandı. En yüksek negatif etki 1960 yılında 0.08 yıl ve en düşük negatif etki 0.02 olup 1950 yılında hesaplandı.

Tartışma: Japonya'da serviks kanserinde ölüm oranları 1950-2000 yılları arasında önemli farklılık göstermektedir. Bu kanser, Japonya'da yaşam beklentisinde meydana gelen kayda değer uzama üzerinde etkili olmamıştır.

Anahtar sözcükler: mortalite, kanser, serviks uteri, yaşam beklentisi

Corresponding Authors: (1) Juan Sun, MD

Department of Public Health and Hygiene

Tianjin Medical University, China

E-mail: sunjuana@oita-med.ac.jp

(2) Kazuo Aoki, MD

Department of Environmental Health and Social Medicine

Faculty of Medicine, Oita University, Oita 879-5593 Japan

E-mail: aoki@med.oita-u.ac.jp

Introduction

The primary cause of death in women in the world is cancer (1). Cervical cancer is the second most common cancer after breast cancer among women worldwide (2) and it is also the major female site (3). In most developing countries, cancer of the cervix is the most prevalent cancer (1); however, in developed countries it is only the sixth most common malignancy among women (2). Invasive cervical cancer has been reported to be the second most common cancer in women worldwide, but 80% of the cases occur in developing countries (4). In Europe, Levi F. et al systematically evaluated the death certification data from the World Health Organization (WHO) mortality database for cancer of the cervix, corpus, and uterus unspecified, and analyzed trends in the age-standard rates between 1960 and 1998 in individuals under 45 years of age, when most deaths from uterine cancer are due to cervical neoplasms (5).

In Japan, the life expectancy for males was 78.53 years while that for females was 85.49 years (6). On the other hand, since the end of the Second World War (1945), infectious diseases have rapidly decreased and have been replaced by so-called life style related diseases such as malignant neoplasms (cancer), heart disease, and cerebrovascular diseases. The top three causes of death are malignant neoplasms (cancer), coronary heart diseases (CHD) and cerebrovascular diseases (CVD). The female mortality rate from malignant neoplasms has been steadily increasing from 12.4% in 1965 to 30.1 in 2005 (7). The mortality rate for total deaths from CHD, on the other hand, has fluctuated during the last few decades.

The male and female CVD mortality rates of all Japanese death have decreased remarkably.

Mortality from the above-mentioned top three causes of death is responsible for more than 50% of all Japanese deaths (7, 8). Among all deaths from malignant neoplasms (cancer), lung cancer is the most common, accounting for a 73.3 rate per 100 000 population of all cancer deaths for males, followed by stomach cancer with a 53.0 rate per 100 000 and hepatic cancer with a 37.6 rate per 100 000 while colorectal cancer in the most common females with a 28.9 rate per 100 000, followed by stomach cancer with 27.4 rate per 100 000 and lung cancer with 26.1 rate per 100 000 (7). Stomach cancer and cervix/corpus uteri cancer, which used to be major causes of death among the Japanese, are now showing a gradually decreasing trend, thus indicating that advances in medical techniques such as early detection and early treatment are also relevant factors (8).

One of the major cancers in Japanese women, as estimated from the vital statistics data and the cancer registry data, is known to be cervix (9). What is the time trend of cervical cancer mortality in Japan for the last half century when cervical cancer mortality has been decreasing in developed countries over the past several decades (10)? Based on the study of the time trend for the breast cancer mortality rate that has rapidly increased in Japan (11), we used the country-

death data in this study to analyze the cervical cancer mortality trends. We compared the time trends for the impact of cervical cancer death on life expectancy and provide an information dataset for the analysis of cervical cancer in Japan.

Materials and Methods

To study the mortality of stomach cancer for the entire population of Japan, principal sources of information were used: the total Japanese woman population, the total number of deaths as well as the number of deaths due to cervical cancer by 5-year age groups and calendar year. We obtained these data from the Vital Statistics of Japan, generated by the Ministry of Health, Labor and Welfare. The population data are drawn from a Population Census generated by the Statistics Bureau & Statistics Center, Ministry of Management. We analyzed the data from 1950 to 2000 in 10-year intervals. During the calendar period considered, five different revisions of the International Classification of Diseases (ICD) were used. The original data on the numbers of deaths were coded according to the Sixth, Seventh, Eighth, Ninth, and Tenth revisions of the International Classification of Diseases (ICD-6, ICD-7, ICD-8, ICD-9, ICD-10).

The trends in the mortality rates from cervical cancer over time were plotted to separate the effects of time. We next compared the change in the rates from 1950 to 2000 for all ages. Age-specific mortality rates from cancer were also computed and plotted on a graph.

Regarding demography, the effects of eliminating diseases are studied by cause-elimination life tables. In such life tables a cause for cervical cancer of death is eradicated and the life expectancy recalculated. The life expectancy is the sum of all the years of a life table in which a person is expected to live between the years 1950 and 2000. The contribution of cervical cancer to the overall change in life expectancy was calculated by cause-elimination life table in the abridged form with ages grouped into five-year intervals except the first 5 years as previously described (12) and it was expressed as the negative contribution to life expectancy of cervix cancer-related deaths. The change rate in the negative contribution to life expectancy in comparison to that in 2000 was computed to assess the age specific identical degree of the time trends.

Results

Figure 1 showed the curves of cervical cancer mortality rates during the past fifty years period. The time trends indicate that the mortality rates increased dramatically in Japan from 1950 to 1960 and the rate reached 3.7/100 000. Conversely, a decrease in the mortality rates with about 1/100 000 was seen from 1960 to 1970, and then it stabilized with a slightly upward trend until 1990. In 2000, the rates reached a level of 3.7/100 000 again.

The time trends of life expectancy at birth due to the elimination of cervical cancer deaths demonstrate a consistent pattern with the mortality rate (Figure 2). The highest

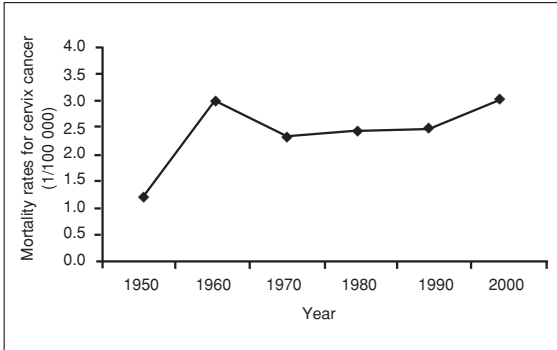


Figure 1. Mortality rates for cervical cancer from 1950 to 2000 in Japan

negative contribution occurred in 1960 and 2000, namely over 0.070 year. A negative contribution was 0.057-0.060 year in 1970, 1980, and 1990. On the other hand, the negative contribution as it was first observed (1950) was only 0.022 year.

The age-related mortality rates for 1950 through 2000 are shown in Figure 3. In individuals from 20 to 59 years (young and old age groups) the mortality rates were similar, while in groups over 75 years of age, the mortality rates increased by around 2-5 times. In comparison to the mortality rates of cervical cancer in 2000, the change in the rates in other observation years demonstrated a large variation in the young and old age groups, while that in the adult age groups showed only a small variation (data was not shown).

The age-specific curves of the negative contribution to cervical cancer in 1950 and 2000 are presented in Figure 4. The increase in the negative contribution between 1950 and 2000 was much greater in the young age groups. However, the differences decreased gradually with age after 30 years of age due to the fact that the life expectancy becomes shorter and shorter with age.

Table 1 displayed a negative contribution in the change rate of cervical cancer based on that in 2000 for some age

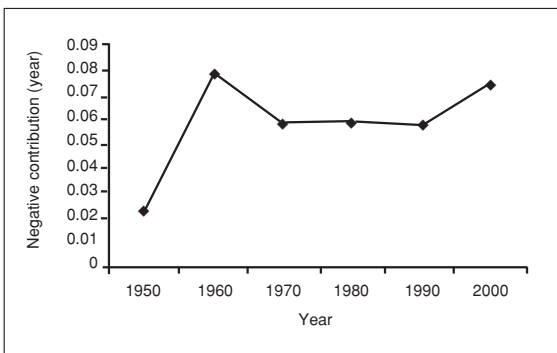


Figure 2. Negative contribution to life expectancy of cervical cancer-related deaths

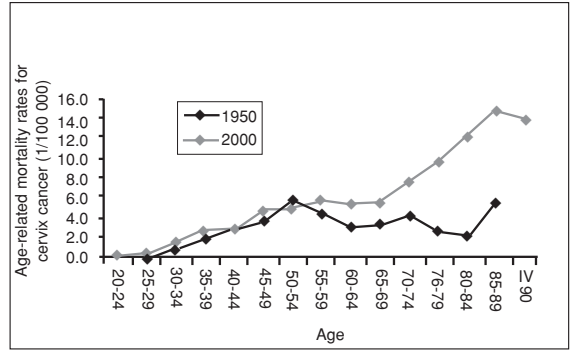


Figure 3. Age-specific mortality rates for cervical cancer in Japan

groups. The change in this negative contribution increased more than one fold for every age group in 1950 which have the lowest mortality in all observation years. The negative contribution for cervical cancer in 2000 increased by 2.24 times in comparison to that in 1950 at birth. In 1960 cervical cancer have the highest mortality, correspondingly, the change rate in the negative contribution showed a negative value in the age groups younger than 60 years of age. For example a negative contribution for cervical cancer in 2000 decreased 0.05 times more than that in 1960 at birth. However, in individuals over 60 years old, a negative contribution in 2000 showed an increase in comparison to that in 1960. For the oldest observed age group (85-89), a negative contribution for cervical cancer in 2000 increased 6.35 times more than that in 1950. Similar changes have been shown in other observation years. The most evident age changes occurred in the last three age groups (over 75 years of age). In every observation year, a negative contribution in these age groups showed an evident increase in comparison to other age groups in the same year and the change in the negative contribution was more than one fold except for 1990. The negative contribution for cervical cancer in 2000 increased 18.5 times more than that seen in 1950 for the 80-84 age group; and in 2000 it increased 1.14 times more than that in 1990 for the 85-89 age group, although there was only a ten year interval with 2000.

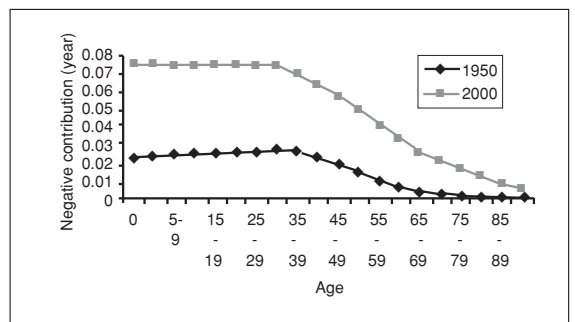


Figure 4. Negative contribution to life expectancy of cervical cancer-related deaths

Table 1. Changes in the negative contribution to life expectancy of cervix cancer-related deaths in Japan, based on those observed in 2000

Age (years)	Year				
	1950	1960	1970	1980	1990
0	2.24*	-0.05	0.29	0.26	0.31
1 - 4	2.06	-0.07	0.27	0.25	0.30
5 - 9	1.95	-0.08	0.27	0.25	0.30
10 - 14	1.93	-0.08	0.27	0.25	0.30
15 - 19	1.91	-0.08	0.27	0.25	0.30
20 - 24	1.88	-0.08	0.27	0.25	0.30
25 - 29	1.84	-0.09	0.26	0.25	0.31
30 - 34	1.74	-0.10	0.25	0.24	0.31
35 - 39	1.70	-0.14	0.20	0.19	0.27
40 - 44	1.73	-0.17	0.17	0.11	0.23
45 - 49	1.96	-0.16	0.18	0.07	0.20
50 - 54	2.17	-0.12	0.18	0.03	0.13
55 - 59	3.33	-0.03	0.24	0.04	0.10
60 - 64	4.76	0.11	0.34	0.04	0.08
65 - 69	5.77	0.40	0.76	0.18	0.08
70 - 74	7.72	0.86	1.40	0.49	0.22
75 - 79	14.14	2.17	2.31	1.01	0.33
80 - 84	18.50	3.82	5.03	1.68	0.63
85 - 89	14.64	6.35	9.41	3.55	1.14

* The numerical value indicates the change in the negative contribution to the life expectancy of cervical cancer (NCLECC) in 2000 which was calculated by $(\text{NCLECC in the 2000} - \text{NCLECC in the 1950}) / (\text{NCLECC in the 1950})$

Discussion

A general analysis of cervical cancer mortality rates in Japan was done based on a 50-year period (1950-2000) after we studied the uterine cancer (13). The real death rates for the population of all ages increased over three times between 1950 and 2000. It is notable that this cancer displayed a heterogeneous annual mortality change rate. The rate was similar in 1960 and 2000. In 1980s it was reported that “according to the Vital Statistics of Japan, the age-adjusted mortality rates for cancers of the cervix uteri have been decreasing” (14). In our study the real death rates demonstrated a consistent result. However, dramatic increases occurred between 1990 and 2000.

The Japanese people have the longest life expectancy in the world, which reached 85 years for women in 2000. This prolongation of life expectancy is partly ascribed to the rapid decrease in various cancer mortality rates (15,16) but not for cervix cancer. Corresponding to the mortality rate, a negative contribution to life expectancy from cervical cancer was similar in 2000 and 1960. The contribution for cervical cancer death in life expectancy at birth between 1950 and 2000 were found to be 0.023 years and 0.074 years, respectively, also giving the difference with three times folds.

Similar differences were seen for most of the young age groups until about 35 years of age, when such differences thus tend

to decrease as the life expectancy becomes shorter and shorter with age... The negative contribution to life expectancy is stable in children and young individuals due to the fact that cervical cancer is very rare in children and young individuals. Although time trend of a negative contribution in the 50-year period did not show any particular pattern of the age trend in each observation year showed the same pattern. The change in the rates of the negative contribution to life expectancy by elimination of cervical cancers displayed an increase with age in comparison to that in 2000 although the magnitude of the change varied. The largest change in the rates of negative contributions came from the last three age groups for each observation year. As previously reported, the main reason for the increase of cancer deaths seems to be largely due to the increase in the elderly population in Japan (9). In contrast to this age trend, in Canada large declines in the mortality from cervical cancer in younger women were observed between 1953 and 1972, whereas larger reductions in the mortality occurred in older age groups from 1973 to 1997 (17).

In Japan, since 1983 cancer screening has been supported by the Japanese government. Initially it covered gastric and cervical cancer with lung, breast and endometrial cancers supported since 1987 and colorectal cancer in 1992. Since 1998 support for cancer screening has been transferred to the local government. Estimates for Japan suggest that at least 30% of the eligible population participate in these services. In other parts of the world screening is more widely accepted, for example, 67% for breast and 79% for cervical cancer screening in the United States of America. Barriers within Japan for increasing screening are complex and include, ethical, financial, technical infrastructure, data related matters and the level of understanding and education of the general population (18). Sobue et al. have reported that 75% of cervical cancer mortality and 59% of invasive cervical cancer incidence among mass-screened women could be prevented by cervical cancer screening (19). Strong evidence for reduction in mortality was classified to have established for cervical cancer (cytology), breast cancer (mammography with classical touch for women aged more than and equal to 50 years of age), colorectal cancer (fecal occult blood test), gastric cancer, lung cancer and liver cancer, have been demonstrated based on an evaluation of cancer screening in terms of the usefulness and effectiveness by Ministry of Health, Labor and Welfare of Japan in 2000 (20).

The age-specific incidence rate per 100 000 populations in Japan of uterus cancer, including CIS, has increased from 1.0 in 1975 to 2.1 in 1999 and from 2.9 in 1975 to 11.4 in 1999 for females aged 20 to 24 years of age and females aged 25 to 29 years, respectively (21). Many types (HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, and 82) of human papillomavirus (HPV) have established as the central cause of cervical cancer worldwide (22,23). Bosch and de Sanjose comparatively investigated the prevalence of HPV-DNA in women from the general population in different regions of the world (24). These differences in the prevalence of HPV-DNA among different regions

and communities may be related to ethnicity and geographical factors. As a persistent infection with a high-risk human papillomavirus (HPV) is generally accepted to be a basic requirement of cervical cancer (25), these differences may thus be the association between HPV infection and mortality of cervical cancer although all subjects with HPV infection will not develop to cervical cancer and all cervical cancer patients will not be always die by suitable medical treatment. In Japan, the positivity of the HPV-DNA testing by routinely screening women was 7.0% among those aged from 30 to 78 years of age (26).

Steckley et al. comparatively studied cervical cancer, smoking rates and gross domestic production per capita by country, indicating extremely high mortality 61.08 and 52.16 (per 100 000) in Zambia and Swaziland in comparison to those in the Russian Federation (13.58), Japan (11.11), Canada (8.25) and USA (7.84) (27).

The newest mortality 8.3 per 100 000 in round numbers for cervical cancer in Japan was announced in the 2005 edition of Vital Statistics of Japan on June 1st, 2006 by the Japanese Ministry of Health, Labor and Welfare (7). These differences in the mortality of cervical cancer and prevalence of HPV by country may suggest that those differences may be explained by the type of HPV, the ethnicity of the subjects, geographical factors and socioeconomic status.

Karube et al. reported that an HPV type 16 infection is a significant risk factor for the progression of cervical cancer in a young population of women (28). In Japanese young women, the HPV-positive rate in patients aged 20 to 29 years old (29.0% in the normal cytology/histology group and 85.5% in the abnormal group) was higher than that in the patients aged 30 to 59 years old, and the rates declined until 60 years of age as an individual's age increased (29). According to our result, the negative contributions of cervical cancer were over 0.7 in young women under 40 years, thus suggesting that the effective preventive measures, such as cervical cancer screening should therefore be established for young women, especially in women from 20 to 29 years of age. Changes in the negative contribution to life expectancy of cervical cancer-related deaths were very high for elderly women at an advanced age. This result suggested that if medical treatment improves and the screening for cervical cancer increases, the life expectancy in the near future will be prolonged even more than now because the cervical cancer mortality would thus decrease in elderly woman at an advanced age.

In summary, the mortality rates of cervical cancer in Japan showed a large variation during the period from 1950-2000. The most pronounced mortality rates occurred in the elderly population. The mortality rates of cervical cancer in Japan showed a large difference during the period from 1950-2000. This cancer was not attributable to an increased coverage of a pronounced prolongation in life expectancy in Japan.

References

1. Stanley K, Stjernsward J, Korolitchouk V. Women and cancer. *World Health Stat Q* 1987;40:267-78.
2. Aleknaviciene B, Smailyte G, Elaawar B, Kurtinaitis J. Cervical cancer: recent trends of incidence and mortality in Lithuania. *Medicina (Kaunas)* 2002;38:223-30.
3. Sierra R, Parkin DM, Leiva GM. Cancer in Costa Rica. *Cancer Res* 1989; 49:717-24.
4. Quinn M, Babb P, Jones J, Allen E. Effect of screening on incidence of and mortality from cancer of cervix in England: evaluation based on routinely collected statistics. *BMJ* 1999;318:904-8.
5. Levi F, Lucchini F, Negri E, Franceschi S, la Vecchia C. Cervical cancer mortality in young women in Europe: patterns and trends. *Eur J Cancer* 2000;36:2266-71.
6. Ministry of Health, Labor, and Welfare of Japan. The 2005 edition of abridged life table in Japan, announced in 25 July, 2006.
7. Ministry of Health, Labor, and Welfare of Japan. Round numbers in the 2005 edition of Vital Statistics in Japan, announced in 24 July, 2006.
8. Nomura K (Editor in chief). *Cancer Statistics in Japan 2005* Tokyo: Foundation for promotion of cancer Research (FPCR), 2005.
9. Tominaga S. Cancer of the Japanese, from the view point of epidemiology. *Gan To Kagaku Ryoho* 1984;11:688-95. (in Japanese with English Abstract)
10. Llorca J, Prieto MD, Delgado-Rodriguez M. Increase in cervical cancer mortality in Spain 1951-1991. *J Epidemiol Community Health* 1999;53:408-11.
11. Kono A, Sun J, Misumi J. The time trend of breast cancer mortality in Japan. *Arch Gynecol Obstet* 2005;272:187-90.
12. Sun J, Kono A, Sun P, Misumi J. Population characteristics of traffic accident-related deaths in Japan and Ireland, 1950-2000. *J Emerg Med* 2004; 27:333-8.
13. Sun J, Sun P. The impact of uterine cancer on life expectancy in Japan. *Int J Gynecol Obstet* 2004;86:54-5.
14. Kato I, Tominaga S, Kuroishi T. The epidemiology of cancers of the female genital organs. *Gan No Rinsho* 1989;35:1-8.
15. Sun J, Misumi J, Shimaoka A et al. Stomach cancer-related mortality rate is higher in young Japanese women than in men. *Public Health* 2002;116:39-44.
16. Sun J, Misumi J, Shimaoka A et al. Stomach cancer mortality. *Eur J Cancer Prev* 2001;10:61-7.
17. Liu S, Semenciw R, Probert A, Mao Y. Cervical cancer in Canada: changing patterns in incidence and mortality. *Int J Gynecol Cancer* 2001;11:24-31.
18. Akaza H, Tsuruo T, Saijo N et al. Cancer screening. *Gan To Kagaku Ryoho* 2005;32:125-34. (in Japanese with English Abstract).
19. Sobue T et al. A case-control study of the effectiveness of cervical cancer screening in Osaka; Japan. *Jpn J Cancer Res* 1988;79:1269-75.
20. Hisamichi S. Evaluation of effectiveness for new method on cancer screening. Tokyo: Japan Public Health Association; 2001 (in Japanese).
21. The Research Group for Population-based Cancer Registry in Japan. Cancer incidence and incidence rates in Japan in 1999; Estimates based on data from 11 population-based cancer registries. *Jpn J Clin Oncol* 2004;34:352-6.
22. Bosch FX, Lorincz A, Munoz N et al. The causal relation between human papillomavirus and cervical cancer. *J Clin Pathol* 2002;55:244-65.
23. Munoz N, Bosch FX, de Sanjose S et al. International Agency for Research on Cancer Multicenter Cervical Cancer Study Group. Epidemiologic classification of human papillomavirus types associated with cervical cancer. *N Engl J Med* 2003;348:518-27.
24. Bosch FX, de Sanjose S. Chapter 1: Human papillomavirus and cervical cancer-burden and assessment of causality. *J Natl Cancer Inst Monogr* 2003;31:3-13.
25. Snijders PJ, Steenbergen RD, Heideman DA, Meijer CJ. HPV-mediated cervical carcinogenesis: concepts and clinical implications. *J Pathol* 2006; 208:152-64.
26. Zheng PS, Iwasaka T, Zhang ZM et al. Telomerase activity in Papanicolaou smear-negative exfoliated cervical cells and its association with lesions and oncogenic human papillomaviruses. *Gynecol Oncol* 2000;77:394-8.
27. Steckley SL, Pickworth WB, Haverkos HW. Cigarette smoking and cervical cancer: Part II: a geographic variability study. *Biomed Pharmacother*. 2003;57:78-83. Erratum in: *Biomed Pharmacother* 2003;57:377.
28. Karube A, Sasaki M, Tanaka H et al. Human papilloma virus type 16 infection and the early onset of cervical cancer. *Biochem Biophys Res Commun* 2004;323:621-4.
29. Masumoto N, Fujii T, Ishikawa M et al. Dominant human papillomavirus 16 infection in cervical neoplasia in young Japanese women; study of 881 outpatients. *Gynecol Oncol* 2004;94:509-14.