

## SECTION 11

# Reproductive History and Health Screening for Women and Mortality in the Japan Collaborative Cohort Study for Evaluation of Cancer (JACC)

Fumio Sakauchi

## Abstract

Reproductive history and participation in health screening for women were surveyed among female subjects, and interesting results were obtained in the present analyses. Women who had never experienced pregnancy had significantly increased risks of death from all causes and cerebrovascular disorders compared with those who had experienced 1 or 2 pregnancies. In contrast, women who had experienced 3 or 4 pregnancies had significantly decreased risks of death from all causes, all cancers, rectal cancer, and breast cancer. Among women who had ever undergone mass screening examination for uterine cervical cancer, there were significantly lower risks of death from all causes, all cancers, stomach cancer, uterine cervical cancer, urinary tract cancer, and ischemic heart diseases compared with those who had not had such experience.

**Keywords:** Reproductive history - screening history - mortality - cancer - circulatory disease

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## Introduction

Reproductive history and participation in health screening for women were surveyed among female subjects in the JACC Study.

## Materials and Methods

The subjects were asked about number of pregnancies and deliveries, age at first delivery, age at menopause, use

of sex hormones, and participation in health screening. The hazard ratios (HRs) adjusted for age and area of study and 95% confidence intervals (95% CIs) of major causes of death were calculated.

## Results

*Number of pregnancies* (Table 1)

Women who had never experienced pregnancy had a significantly increased risks of death from all causes

**Table 1. Hazard Ratios (HRs)<sup>#</sup> and 95% Confidence Intervals (95% CI) for Mortality According to Reproductive History**

| Cause ICD                  | Observed person years | Number of pregnancies |                                |           |      |           |                                |          |                    |
|----------------------------|-----------------------|-----------------------|--------------------------------|-----------|------|-----------|--------------------------------|----------|--------------------|
|                            |                       | none                  |                                | 1-2 times |      | 3-4 times |                                | ≥5 times |                    |
|                            |                       | No                    | HR (95%CI)                     | No        | HR   | No        | HR (95%CI)                     | No       | HR (95%CI)         |
| All causes                 | 7,174                 | 346                   | 1.28 (1.13, 1.45)**            | 1,284     | 1.00 | 2,467     | 0.93 (0.87, 1.00)*             | 1,997    | 0.99 (0.92, 1.06)  |
| All cancer C00-90          | 2,325                 | 87                    | 0.99 (0.79, 1.25)              | 505       | 1.00 | 865       | 0.88 (0.79, 0.98)*             | 564      | 0.91 (0.80, 1.03)  |
| Esophagus C15              | 27                    | 3                     | 2.75 (0.63, 11.9)              | 5         | 1.00 | 9         | 0.86 (0.29, 2.58)              | 7        | 0.93 (0.28, 3.06)  |
| Stomach C16                | 386                   | 16                    | 1.12 (0.65, 1.94)              | 79        | 1.00 | 147       | 0.95 (0.72, 1.25)              | 93       | 0.86 (0.63, 1.19)  |
| Colon C18                  | 220                   | 7                     | 0.76 (0.34, 1.70)              | 44        | 1.00 | 86        | 0.93 (0.65, 1.34)              | 51       | 0.80 (0.53, 1.22)  |
| Rectum C19-20              | 89                    | 0                     | NA                             | 25        | 1.00 | 24        | 0.49 (0.28, 0.87)*             | 26       | 0.92 (0.51, 1.66)  |
| Liver C22                  | 227                   | 8                     | 1.16 (0.54, 2.49)              | 46        | 1.00 | 96        | 1.03 (0.72, 1.46)              | 54       | 0.91 (0.60, 1.37)  |
| Gall bladder C23           | 95                    | 4                     | 1.38 (0.45, 4.20)              | 17        | 1.00 | 38        | 1.22 (0.68, 2.19)              | 24       | 1.25 (0.64, 2.43)  |
| Pancreas C25               | 217                   | 5                     | 0.46 (0.18, 1.16) <sup>+</sup> | 49        | 1.00 | 77        | 0.79 (0.55, 1.14)              | 61       | 0.96 (0.64, 1.43)  |
| Lung C33-34                | 268                   | 16                    | 1.55 (0.88, 2.73)              | 63        | 1.00 | 91        | 0.74 (0.53, 1.03) <sup>+</sup> | 66       | 0.84 (0.59, 1.21)  |
| Breast C50                 | 103                   | 3                     | 0.77 (0.23, 2.53)              | 40        | 1.00 | 35        | 0.56 (0.36, 0.89)*             | 13       | 0.52 (0.27, 1.00)* |
| Uterine cervix C53         | 36                    | 0                     | NA                             | 6         | 1.00 | 20        | 2.02 (0.81, 5.06)              | 7        | 1.46 (0.47, 4.54)  |
| Kidney C64                 | 19                    | 1                     | 1.02 (0.11, 9.34)              | 5         | 1.00 | 5         | 0.50 (0.14, 1.73)              | 4        | 0.61 (0.15, 2.48)  |
| Urothelium C65-67          | 41                    | 3                     | 2.02 (0.49, 8.38)              | 6         | 1.00 | 13        | 1.05 (0.40, 2.78)              | 11       | 1.20 (0.42, 3.40)  |
| Non-Hodgkin's C82-85       | 65                    | 3                     | 1.61 (0.44, 5.83)              | 12        | 1.00 | 25        | 1.02 (0.51, 2.05)              | 14       | 0.99 (0.44, 2.20)  |
| Multiple myeloma C90       | 49                    | 2                     | 0.90 (0.20, 4.13)              | 12        | 1.00 | 17        | 0.70 (0.33, 1.48)              | 14       | 0.88 (0.39, 1.99)  |
| Myeloid leukemia C92       | 33                    | 0                     | NA                             | 5         | 1.00 | 14        | 1.49 (0.53, 4.16)              | 7        | 1.38 (0.42, 4.60)  |
| Ischemic heart dis I20-25  | 458                   | 28                    | 1.52 (0.98, 2.38) <sup>+</sup> | 75        | 1.00 | 148       | 0.93 (0.70, 1.24)              | 138      | 0.94 (0.70, 1.27)  |
| Cerebrovascular dis I60-69 | 1,151                 | 65                    | 1.51 (1.13, 2.02)**            | 172       | 1.00 | 404       | 1.08 (0.90, 1.29)              | 338      | 1.06 (0.87, 1.28)  |

<sup>#</sup>Adjusted for age and area of study. \*\*, p<0.01; \*, p<0.05; <sup>+</sup>, p<0.10 NA: not applicable

Department of Public Health, Sapporo Medical University School of Medicine, S1W17, Chuo-ku, Sapporo, 060-8556, Japan, Fax +81-11-641-8101, E-mail: sakauchi@sapmed.ac.jp

**Table 2. Hazard Ratios (HRs)<sup>#</sup> and 95% Confidence Intervals (CI) for Mortality According to Reproductive History Among Women - Deliveries**

| Cause ICD                      | Observed person years | Number of deliveries |                     |           |      |          |                    | Age at first delivery |                     |       |      |       |                    |
|--------------------------------|-----------------------|----------------------|---------------------|-----------|------|----------|--------------------|-----------------------|---------------------|-------|------|-------|--------------------|
|                                |                       | none                 |                     | 1-2 times |      | ≥3 times |                    | ≤22                   |                     | 23-25 |      | ≥26   |                    |
|                                |                       | No                   | HR(95%CI)           | No        | HR   | No       | HR(95%CI)          | No                    | HR(95%CI)           | No    | HR   | No    | HR(95%CI)          |
| All causes                     | 7,174                 | 356                  | 1.38 (1.23, 1.55)** | 1,698     | 1.00 | 3,890    | 1.00 (0.94, 1.07)  | 1,802                 | 1.14 (1.07, 1.23)** | 1,908 | 1.00 | 2,026 | 1.08 (1.01, 1.15)* |
| All cancer C00-90              | 2,325                 | 90                   | 1.10 (0.88, 1.38)   | 691       | 1.00 | 1,193    | 0.97 (0.87, 1.07)  | 575                   | 1.16 (1.02, 1.31)*  | 653   | 1.00 | 707   | 1.14 (1.02, 1.27)* |
| Esophagus C15                  | 27                    | 3                    | 3.06 (0.73, 12.8)   | 6         | 1.00 | 14       | 1.09 (0.40, 2.99)  | 8                     | 1.63 (0.51, 5.17)   | 6     | 1.00 | 7     | 1.37 (0.45, 4.14)  |
| Stomach C16                    | 386                   | 16                   | 1.17 (0.68, 2.01)   | 107       | 1.00 | 204      | 0.99 (0.77, 1.27)  | 97                    | 1.11 (0.82, 1.50)   | 106   | 1.00 | 117   | 1.17 (0.90, 1.53)  |
| Colon C18                      | 220                   | 8                    | 0.92 (0.44, 1.96)   | 61        | 1.00 | 115      | 0.93 (0.67, 1.30)  | 43                    | 0.74 (0.49, 1.13)   | 72    | 1.00 | 64    | 0.93 (0.66, 1.31)  |
| Rectum C19-20                  | 89                    | 0                    | N.A                 | 31        | 1.00 | 43       | 0.80 (0.49, 1.32)  | 28                    | 1.75 (0.96, 3.20)*  | 23    | 1.00 | 25    | 1.14 (0.64, 2.02)  |
| Liver C22                      | 227                   | 8                    | 1.17 (0.55, 2.47)   | 68        | 1.00 | 126      | 1.02 (0.74, 1.40)  | 63                    | 1.19 (0.80, 1.79)   | 61    | 1.00 | 71    | 1.21 (0.85, 1.71)  |
| Gall bladder C23               | 95                    | 4                    | 1.58 (0.53, 4.72)   | 22        | 1.00 | 55       | 1.51 (0.88, 2.58)  | 22                    | 1.16 (0.62, 2.17)   | 26    | 1.00 | 31    | 1.26 (0.74, 2.14)  |
| Pancreas C25                   | 217                   | 8                    | 0.87 (0.41, 1.84)   | 60        | 1.00 | 119      | 1.04 (0.75, 1.46)  | 55                    | 1.52 (1.00, 2.30)*  | 51    | 1.00 | 76    | 1.46 (1.02, 2.11)* |
| Lung C33-34                    | 268                   | 16                   | 1.86 (1.07, 3.23)*  | 78        | 1.00 | 136      | 0.99 (0.74, 1.34)  | 68                    | 1.37 (0.95, 1.96)*  | 68    | 1.00 | 81    | 1.30 (0.94, 1.81)  |
| Breast C50                     | 103                   | 4                    | 1.13 (0.40, 3.18)   | 54        | 1.00 | 32       | 0.57 (0.36, 0.91)* | 19                    | 0.74 (0.37, 1.48)   | 31    | 1.00 | 38    | 1.43 (0.88, 2.32)  |
| Uterine cervix C53             | 36                    | 0                    | N.A                 | 10        | 1.00 | 23       | 1.98 (0.90, 4.35)* | 8                     | 1.57 (0.57, 4.28)   | 9     | 1.00 | 14    | 1.73 (0.74, 4.04)  |
| Kidney C64                     | 19                    | 1                    | 1.23 (0.14, 11.0)   | 6         | 1.00 | 7        | 0.62 (0.19, 2.00)  | 2                     | 0.54 (0.10, 2.79)   | 6     | 1.00 | 6     | 1.00 (0.31, 3.22)  |
| Urothelial tract C65-67        | 41                    | 3                    | 1.45 (0.30, 7.12)   | 8         | 1.00 | 22       | 1.21 (0.51, 2.86)  | 9                     | 1.17 (0.45, 3.02)   | 12    | 1.00 | 11    | 0.80 (0.35, 1.85)  |
| Non-Hodgkin's C82-85           | 65                    | 3                    | 1.53 (0.44, 5.31)   | 19        | 1.00 | 30       | 0.97 (0.53, 1.76)  | 17                    | 1.08 (0.56, 2.09)   | 24    | 1.00 | 14    | 0.68 (0.35, 1.34)  |
| Multiple myeloma C90           | 49                    | 2                    | 0.79 (0.18, 3.53)   | 19        | 1.00 | 22       | 0.56 (0.29, 1.08)* | 13                    | 1.37 (0.59, 3.19)   | 13    | 1.00 | 18    | 1.43 (0.69, 2.96)  |
| Myeloid leukemia C92           | 33                    | 0                    | N.A                 | 9         | 1.00 | 17       | 1.19 (0.50, 2.82)  | 8                     | 1.06 (0.38, 2.94)   | 11    | 1.00 | 8     | 0.68 (0.27, 1.72)  |
| Ischemic heart disease I20-25  | 458                   | 27                   | 1.50 (0.97, 2.34)*  | 94        | 1.00 | 258      | 0.97 (0.75, 1.24)  | 121                   | 1.09 (0.82, 1.45)   | 116   | 1.00 | 131   | 1.17 (0.90, 1.51)  |
| Cerebrovascular disease I60-69 | 1,151                 | 66                   | 1.56 (1.18, 2.07)** | 229       | 1.00 | 661      | 1.08 (0.92, 1.26)  | 291                   | 1.19 (0.99, 1.42)*  | 294   | 1.00 | 326   | 1.07 (0.91, 1.26)  |

<sup>#</sup> Adjusted for age and area of study. \*\*, p<0.01; \*, p<0.05; +, p<0.10

**Table 3. Hazard Ratios (HRs)<sup>#</sup> and 95% Confidence Intervals (CI) for Mortality According to Menarche and Menopause among Women**

| Observed person-years          | Age at menarche |                   |       |      |       |                                | Age at menopause |                                |       |      |       |                                | Type of menopause |      |           |                                |
|--------------------------------|-----------------|-------------------|-------|------|-------|--------------------------------|------------------|--------------------------------|-------|------|-------|--------------------------------|-------------------|------|-----------|--------------------------------|
|                                | ≤13             |                   | 14-15 |      | ≥16   |                                | ≤47              |                                | 48-50 |      | ≥51   |                                | Natural           |      | Operative |                                |
|                                | No              | HR (95%CI)        | No    | HR   | No    | HR (95%CI)                     | No               | HR (95%CI)                     | No    | HR   | No    | HR (95%CI)                     | No                | HR   | No        | HR (95%CI)                     |
| All causes                     | 752             | 1.07 (0.98, 1.16) | 2,270 | 1.00 | 2,838 | 1.02 (0.96, 1.08)              | 1,506            | 1.10 (1.03, 1.18)**            | 1,996 | 1.00 | 1,499 | 0.94 (0.88, 1.01) <sup>+</sup> | 3,012             | 1.00 | 315       | 1.03 (0.92, 1.16)              |
| All cancer C00-C97             | 299             | 1.05 (0.91, 1.20) | 802   | 1.00 | 898   | 1.02 (0.92, 1.12)              | 464              | 1.11 (0.98, 1.26) <sup>+</sup> | 623   | 1.00 | 512   | 0.98 (0.87, 1.10)              | 1,015             | 1.00 | 120       | 1.05 (0.87, 1.27)              |
| Esophagus C15                  | 1               | 0.47 (0.06, 3.87) | 7     | 1.00 | 15    | 1.56 (0.63, 3.87)              | 7                | 2.08 (0.66, 6.56)              | 5     | 1.00 | 7     | 1.74 (0.55, 5.48)              | 11                | 1.00 | 2         | 0.68 (0.15, 3.19)              |
| Stomach C16                    | 52              | 1.07 (0.77, 1.49) | 139   | 1.00 | 140   | 0.87 (0.69, 1.11)              | 81               | 1.14 (0.85, 1.53)              | 104   | 1.00 | 88    | 1.03 (0.78, 1.37)              | 176               | 1.00 | 15        | 1.35 (0.80, 2.30)              |
| Colon C18                      | 27              | 1.02 (0.66, 1.59) | 83    | 1.00 | 75    | 0.80 (0.58, 1.10)              | 44               | 1.01 (0.69, 1.48)              | 67    | 1.00 | 40    | 0.72 (0.49, 1.07)              | 87                | 1.00 | 10        | 1.02 (0.53, 1.97)              |
| Rectum C19-20                  | 10              | 0.88 (0.43, 1.79) | 33    | 1.00 | 35    | 1.01 (0.62, 1.65)              | 6                | 0.34 (0.14, 0.81) <sup>+</sup> | 27    | 1.00 | 22    | 1.02 (0.58, 1.79)              | 28                | 1.00 | 8         | 0.42 (0.19, 0.93)*             |
| Liver C22                      | 29              | 1.01 (0.66, 1.55) | 83    | 1.00 | 83    | 0.93 (0.68, 1.26)              | 59               | 1.56 (1.09, 2.24) <sup>+</sup> | 58    | 1.00 | 45    | 0.91 (0.62, 1.34)              | 116               | 1.00 | 14        | 1.06 (0.60, 1.85)              |
| Gall bladder C23               | 12              | 1.11 (0.55, 2.24) | 29    | 1.00 | 38    | 1.18 (0.72, 1.94)              | 26               | 1.60 (0.91, 2.80)              | 24    | 1.00 | 20    | 1.00 (0.55, 1.82)              | 43                | 1.00 | 5         | 1.11 (0.43, 2.84)              |
| Pancreas C25                   | 28              | 1.23 (0.78, 1.94) | 67    | 1.00 | 100   | 1.29 (0.94, 1.77)              | 46               | 1.03 (0.71, 1.51)              | 67    | 1.00 | 44    | 0.78 (0.53, 1.14)              | 88                | 1.00 | 18        | 0.63 (0.38, 1.06) <sup>+</sup> |
| Lung C33-C34                   | 39              | 1.26 (0.85, 1.86) | 82    | 1.00 | 110   | 1.26 (0.94, 1.69)              | 51               | 1.05 (0.73, 1.52)              | 72    | 1.00 | 62    | 1.02 (0.72, 1.43)              | 126               | 1.00 | 14        | 1.13 (0.64, 1.97)              |
| Breast C50                     | 21              | 0.98 (0.57, 1.67) | 44    | 1.00 | 32    | 0.96 (0.60, 1.54)              | 12               | 0.79 (0.38, 1.64)              | 21    | 1.00 | 20    | 1.06 (0.58, 1.96)              | 35                | 1.00 | 10        | 0.60 (0.29, 1.25)              |
| Uterine cervix C53             | 5               | 0.86 (0.30, 2.46) | 13    | 1.00 | 12    | 1.10 (0.49, 2.49)              | 4                | 1.07 (0.30, 3.79)              | 6     | 1.00 | 10    | 1.86 (0.68, 5.14)              | 17                | 1.00 | 0         | NA                             |
| Kidney C64                     | 1               | 0.57 (0.07, 4.78) | 6     | 1.00 | 8     | 1.17 (0.40, 3.43)              | 3                | 0.96 (0.23, 4.02)              | 5     | 1.00 | 4     | 0.92 (0.25, 3.42)              | 6                 | 1.00 | 1         | 0.71 (0.08, 5.99)              |
| Urothelial tract C65-C67       | 1               | 0.30 (0.04, 2.34) | 12    | 1.00 | 18    | 1.19 (0.57, 2.48)              | 5                | 0.49 (0.18, 1.35)              | 15    | 1.00 | 3     | 0.25 (0.07, 0.87)*             | 13                | 1.00 | 1         | 1.57 (0.20, 12.2)              |
| Non-Hodgkin's C82-85           | 7               | 0.76 (0.32, 1.77) | 24    | 1.00 | 27    | 1.16 (0.66, 2.03)              | 18               | 1.91 (0.96, 3.79) <sup>+</sup> | 15    | 1.00 | 16    | 1.21 (0.60, 2.46)              | 32                | 1.00 | 3         | 1.44 (0.44, 4.74)              |
| Multiple myeloma C90           | 6               | 0.89 (0.36, 2.23) | 21    | 1.00 | 18    | 0.74 (0.39, 1.40)              | 12               | 1.43 (0.65, 3.13)              | 13    | 1.00 | 14    | 1.31 (0.61, 2.79)              | 21                | 1.00 | 1         | 2.89 (0.39, 21.8)              |
| Myeloid leukemia C92           | 4               | 1.23 (0.37, 4.04) | 9     | 1.00 | 15    | 1.64 (0.71, 3.83)              | 8                | 2.01 (0.70, 5.78)              | 6     | 1.00 | 10    | 1.90 (0.69, 5.23)              | 14                | 1.00 | 3         | 0.67 (0.19, 2.39)              |
| Ischemic heart disease I20-25  | 47              | 1.19 (0.85, 1.68) | 140   | 1.00 | 185   | 1.02 (0.82, 1.27)              | 96               | 1.19 (0.91, 1.57)              | 115   | 1.00 | 114   | 1.31 (1.01, 1.70)*             | 194               | 1.00 | 20        | 0.95 (0.60, 1.52)              |
| Cerebrovascular disease I60-69 | 90              | 0.98 (0.77, 1.24) | 335   | 1.00 | 489   | 1.13 (0.98, 1.30) <sup>+</sup> | 233              | 1.02 (0.86, 1.20)              | 336   | 1.00 | 242   | 0.94 (0.79, 1.11)              | 476               | 1.00 | 40        | 1.17 (0.85, 1.62)              |

<sup>#</sup> Adjusted for age and area of study. \*\*, p<0.01; \*, p<0.05; +, p<0.10 NA: not applicable

**Table 4. Hazard Ratios (HRs)<sup>#</sup> and 95% Confidence Intervals (95% CI) for Mortality and Sex Hormone Use**

| Observed person yrs<br>Site ICD10 | History of sex hormone use |      |        |                                | Frequency of use |      |          |                   |           |                   |
|-----------------------------------|----------------------------|------|--------|--------------------------------|------------------|------|----------|-------------------|-----------|-------------------|
|                                   | No                         |      | Yes    |                                | Never use        |      | <6months |                   | 6 months+ |                   |
|                                   | No                         | HR   | No     | HR (95% CI)                    | No               | HR   | No       | HR (95% CI)       | No        | HR (95% CI)       |
|                                   | 574,072                    |      | 29,425 |                                | 574,072          |      | 10,083   |                   | 10,670    |                   |
| All causes                        | 4,491                      | 1.00 | 177    | 1.03 (0.88, 1.19)              | 4,491            | 1.00 | 59       | 1.07 (0.83, 1.39) | 60        | 0.92 (0.71, 1.19) |
| All cancer C00-97                 | 1,521                      | 1.00 | 65     | 0.99 (0.77, 1.27)              | 1,521            | 1.00 | 21       | 0.97 (0.63, 1.49) | 27        | 1.12 (0.76, 1.63) |
| Esophagus C15                     | 17                         | 1.00 | 3      | 4.60 (1.33, 15.9)              | 17               | 1.00 | 2        | 8.46 (1.91, 37.6) | 0         | NA                |
| Stomach C16                       | 256                        | 1.00 | 7      | 0.68 (0.32, 1.45)              | 256              | 1.00 | 3        | 0.90 (0.29, 2.80) | 1         | 0.26 (0.04, 1.85) |
| Colon C18                         | 158                        | 1.00 | 4      | 0.59 (0.22, 1.60)              | 158              | 1.00 | 3        | 1.36 (0.43, 4.28) | 1         | 0.38 (0.05, 2.68) |
| Rectum C19-20                     | 57                         | 1.00 | 1      | 0.39 (0.06, 2.85)              | 57               | 1.00 | 0        | NA                | 1         | 1.05 (0.15, 7.62) |
| Liver C22                         | 138                        | 1.00 | 9      | 1.46 (0.74, 2.88)              | 138              | 1.00 | 2        | 1.00 (0.25, 4.07) | 4         | 1.88 (0.69, 5.10) |
| Gall bladder C23                  | 62                         | 1.00 | 2      | 0.75 (0.18, 3.09)              | 62               | 1.00 | 0        | NA                | 2         | 2.04 (0.49, 8.40) |
| Pancreas C25                      | 158                        | 1.00 | 4      | 0.59 (0.22, 1.59)              | 158              | 1.00 | 1        | 0.45 (0.06, 3.23) | 1         | 0.40 (0.06, 2.83) |
| Lung C33-34                       | 166                        | 1.00 | 13     | 1.71 (0.97, 3.01) <sup>+</sup> | 166              | 1.00 | 5        | 1.89 (0.77, 4.63) | 5         | 1.77 (0.72, 4.33) |
| Breast C50                        | 64                         | 1.00 | 5      | 1.51 (0.61, 3.78)              | 64               | 1.00 | 2        | 1.84 (0.45, 7.56) | 1         | 0.91 (0.13, 6.60) |
| Uterine cervix C53                | 26                         | 1.00 | 1      | 0.77 (0.10, 5.74)              | 26               | 1.00 | 0        | NA                | 1         | 2.16 (0.29, 16.1) |
| Kidney C64                        | 11                         | 1.00 | 0      | N.A                            | 11               | 1.00 | 0        | NA                | 0         | NA                |
| Urothelium C65-67                 | 23                         | 1.00 | 1      | 1.35 (0.18, 10.1)              | 23               | 1.00 | 0        | NA                | 1         | 3.83 (0.51, 29.0) |
| Non-Hodgkin lymphoma              |                            |      |        |                                |                  |      |          |                   |           |                   |
| C82-85                            | 48                         | 1.00 | 1      | 0.45 (0.06, 3.29)              | 48               | 1.00 | 1        | 1.28 (0.18, 9.35) | 0         | NA                |
| Multiple myeloma C90              | 28                         | 1.00 | 0      | N.A                            | 28               | 1.00 | 0        | NA                | 0         | NA                |
| Myeloid leukemia C92              | 20                         | 1.00 | 0      | N.A                            | 20               | 1.00 | 0        | NA                | 0         | NA                |
| IHD I20-I25                       | 287                        | 1.00 | 8      | 0.82 (0.41, 1.66)              | 287              | 1.00 | 3        | 0.98 (0.31, 3.07) | 2         | 0.55 (0.14, 2.21) |
| CVD I60-I69                       | 742                        | 1.00 | 18     | 0.69 (0.43, 1.10)              | 742              | 1.00 | 8        | 1.02 (0.51, 2.05) | 6         | 0.60 (0.27, 1.33) |

<sup>#</sup> Adjusted for age and area of study. Significance level: \*\* p<0.01, \* p<0.05, + p<0.1 NA: not applicable

(HR=1.28) and cerebrovascular disorders (HR=1.51) compared with those who had experienced 1 or 2 pregnancies. In contrast, women who had experienced 3 or 4 pregnancies had significantly decreased risks of death from all causes (HR=0.93), all cancers (HR=0.88), rectal cancer (HR=0.49), and breast cancer (HR=0.56). Additionally, women who had experienced more than 5 pregnancies also had a decreased risk of death from breast cancer (HR=0.52).

#### Number and age of deliveries (Table 2)

Results regarding number of delivered babies were similar to those regarding the number of pregnancies. Women who had never experienced delivery had significantly increased risks of death from all causes (HR=1.38), lung cancer (HR=1.86), and cerebrovascular disorders (HR=1.56) compared with those who had experienced 1 or 2 deliveries. In contrast, women who had experienced more than 3 deliveries had a significantly decreased risk of death from breast cancer (HR=0.57).

Age at first delivery of less than 23 years or more than 25 years was positively associated with risk of death from all causes (HR=1.14 for less than 23 years, and HR=1.08 for more than 25 years, respectively), all cancers (HR=1.16 for less than 23 years, and HR=1.14 for more than 25 years), and that of more than 25 years was also positively associated with risk of death from pancreatic cancer (HR=1.46) compared with those who experienced their first delivery between 23 and 25 years old.

#### Age at menarche and menopause (Table 3)

Age at natural menopause less than 48 years was positively associated with risks of death from all causes (HR=1.10), and liver cancer (HR=1.56) compared with those who experienced their natural menopause between

48 and 50 years old, but, it was inversely associated with risk of death from rectal cancer (HR=0.34). At the same time, age at natural menopause of more than 50 years was positively associated with risk of death from ischemic heart diseases (HR=1.31), but inversely linked with risk of death from urinary tract cancers (HR=0.25).

#### Sex hormone use (Table 4)

In the present study, no significant effects were found regarding risks of death from breast, ovarian, and uterine cervical cancer associated with the use of sex hormones.

#### Participation in health screening (Table 5)

There were significantly lower risks of death from all causes (HR=0.76), all cancers (HR=0.81), stomach cancer (HR=0.65), uterine cervical cancer (HR=0.40), urinary tract cancer (HR=0.29), and ischemic heart diseases (HR=0.67) among women who had ever undergone mass screening examination for uterine cervical cancer compared with those who had not had such experience. There were also significantly lower risks of death from all causes (HR=0.74), all cancers (HR=0.75, 95% CI 0.66-0.85), stomach cancer (HR=0.63, 95% CI 0.45-0.88), uterine cervical cancer (HR=0.19, 95% CI 0.04-0.81), ischemic heart diseases (HR=0.65, 95% CI 0.47-0.92), and cerebrovascular disorders (HR=0.81, 95% CI 0.66-0.99) among women who had ever undergone a mass screening examination for breast cancer. Similar results were found among those who habitually performed self examination for breast cancer.

## Discussion

Results regarding number of pregnancies were similar to those of delivered babies. For example, women who

**Table 5. Hazard Ratios (HRs)<sup>#</sup> and 95% Confidence Intervals (CI) of Selected Causes of Death for Health Screening among Women**

| Observed person years          | ICD     | Participation in cervical cancer screening |      |       |                                | Participation in breast cancer screening |      |     |                     | Self-examination of breast cancer |      |       |                                |                      |                                |
|--------------------------------|---------|--|------|-------|--------------------------------|--|------|-----|---------------------|-----------------------------------|------|-------|--------------------------------|----------------------|--------------------------------|
|                                |         | No   |      | Yes   |                                | No                                       |      | Yes |                     | No                                |      | Yes   |                                | Don't know how to do |                                |
|                                |         | N  | HR   | N     | HR(95%CI)                      | No                                       | HR   | No  | HR(95%CI)           | No                                | HR   | No    | HR(95%CI)                      | No                   | HR(95%CI)                      |
| All causes                     |         | 3,485                                      | 1.00 | 1,446 | 0.76 (0.72, 0.82)**            | 3,866                                    | 1.00 | 861 | 0.74 (0.69, 0.80)** | 3,010                             | 1.00 | 1,113 | 0.76 (0.71, 0.82)**            | 334                  | 1.01 (0.90, 1.13)              |
| All cancers                    | C00-C97 | 1,072                                      | 1.00 | 584   | 0.81 (0.73, 0.91)**            | 1,251                                    | 1.00 | 337 | 0.75 (0.66, 0.85)** | 925                               | 1.00 | 473   | 0.87 (0.77, 0.97)*             | 78                   | 0.82 (0.65, 1.03) <sup>+</sup> |
| Esophagus                      | C15     | 11   | 1.00 | 8     | 1.69 (0.62, 4.61)              | 10                                       | 1.00 | 5   | 1.44 (0.46, 4.57)   | 12                                | 1.00 | 2     | 0.34 (0.07, 1.60)              | 0                    | N.A.                           |
| Stomach                        | C16     | 188  | 1.00 | 81    | 0.65 (0.49, 0.85)**            | 214                                      | 1.00 | 46  | 0.63 (0.45, 0.88)** | 162                               | 1.00 | 67    | 0.76 (0.56, 1.02) <sup>+</sup> | 12                   | 0.63 (0.35, 1.14)              |
| Colon                          | C18     | 107  | 1.00 | 64    | 0.97 (0.69, 1.35)              | 132                                      | 1.00 | 36  | 0.81 (0.55, 1.19)   | 90                                | 1.00 | 52    | 1.11 (0.77, 1.58)              | 11                   | 1.17 (0.62, 2.21)              |
| Rectum                         | C19-C20 | 38   | 1.00 | 26    | 0.84 (0.49, 1.41)              | 47                                       | 1.00 | 15  | 0.72 (0.40, 1.33)   | 24                                | 1.00 | 25    | 1.67 (0.93, 2.98) <sup>+</sup> | 3                    | 1.36 (0.40, 4.64)              |
| Liver                          | C22     | 110  | 1.00 | 54    | 0.77 (0.54, 1.08)              | 128                                      | 1.00 | 33  | 0.76 (0.51, 1.14)   | 99                                | 1.00 | 47    | 0.77 (0.54, 1.11)              | 6                    | 0.68 (0.29, 1.57)              |
| Gall bladder                   | C23     | 44   | 1.00 | 18    | 0.69 (0.39, 1.24)              | 49                                       | 1.00 | 11  | 0.68 (0.34, 1.34)   | 36                                | 1.00 | 18    | 0.92 (0.51, 1.66)              | 5                    | 1.17 (0.45, 3.05)              |
| Pancreas                       | C25     | 98   | 1.00 | 60    | 1.00 (0.71, 1.42)              | 115                                      | 1.00 | 37  | 0.91 (0.62, 1.35)   | 90                                | 1.00 | 46    | 0.89 (0.61, 1.30)              | 4                    | 0.40 (0.14, 1.09) <sup>+</sup> |
| Lung                           | C33-34  | 122  | 1.00 | 62    | 0.75 (0.54, 1.03) <sup>+</sup> | 136                                      | 1.00 | 41  | 0.88 (0.61, 1.26)   | 103                               | 1.00 | 55    | 0.89 (0.63, 1.26)              | 11                   | 1.06 (0.56, 2.01)              |
| Breast                         | C50     | 43   | 1.00 | 34    | 0.92 (0.58, 1.47)              | 55                                       | 1.00 | 20  | 0.77 (0.45, 1.31)   | 37                                | 1.00 | 30    | 1.03 (0.63, 1.69)              | 2                    | 0.74 (0.18, 3.12)              |
| Uterine cervix                 | C53     | 21   | 1.00 | 7     | 0.40 (0.16, 0.97)*             | 23                                       | 1.00 | 2   | 0.19 (0.04, 0.81)*  | 19                                | 1.00 | 4     | 0.29 (0.10, 0.87)*             | 2                    | 1.24 (0.28, 5.45)              |
| Kidney                         | C64     | 6  | 1.00 | 6     | 1.60 (0.47, 5.49)              | 6  | 1.00 | 3   | 1.85 (0.41, 8.44)   | 6                                 | 1.00 | 1     | 0.31 (0.04, 2.71)              | 0                    | N.A.                           |
| Urothelium                     | C65-67  | 23   | 1.00 | 3     | 0.29 (0.08, 1.00)*             | 22                                       | 1.00 | 3   | 0.51 (0.15, 1.80)   | 18                                | 1.00 | 4     | 0.51 (0.17, 1.58)              | 1                    | 0.60 (0.08, 4.66)              |
| Non-Hodgkin and other lymphoma | C82-85  | 24   | 1.00 | 22    | 1.17 (0.63, 2.17)              | 32                                       | 1.00 | 9   | 0.73 (0.34, 1.56)   | 22                                | 1.00 | 15    | 1.12 (0.56, 2.23)              | 3                    | 1.20 (0.35, 4.11)              |
| Multiple myeloma, plasmacytoma | C90     | 22   | 1.00 | 11    | 0.75 (0.34, 1.62)              | 27                                       | 1.00 | 6   | 0.62 (0.25, 1.55)   | 20                                | 1.00 | 10    | 0.82 (0.37, 1.82)              | 1                    | 0.51 (0.07, 3.86)              |
| Myeloid leukemia               | C92     | 15   | 1.00 | 7     | 0.68 (0.26, 1.74)              | 14                                       | 1.00 | 7   | 1.35 (0.52, 3.52)   | 10                                | 1.00 | 7     | 2.21 (0.81, 6.00)              | 2                    | 3.53 (0.71, 17.7)              |
| Ischemic heart disease         | I20-25  | 256  | 1.00 | 73    | 0.67 (0.50, 0.88)**            | 271                                      | 1.00 | 43  | 0.65 (0.47, 0.92)*  | 213                               | 1.00 | 61    | 0.72 (0.53, 0.97)              | 31                   | 1.17 (0.79, 1.72)              |
| Cerebrovascular disease        | I60-69  | 549  | 1.00 | 223   | 0.88 (0.74, 1.04)              | 603                                      | 1.00 | 129 | 0.81 (0.66, 0.99)*  | 132                               | 1.00 | 507   | 0.61 (0.50, 0.75)              | 55                   | 0.91 (0.68, 1.21)              |

<sup>#</sup> Adjusted for age and area of study. \*\*, p<0.01; \*, p<0.05; +, p<0.10

had never experienced pregnancy or delivery had significantly increased risks of death from all causes, and cerebrovascular disorders compared with those who had experienced them. In contrast, women who had experienced more than 3 pregnancies or deliveries had a significantly decreased risk of death from breast cancer. Adjusted for potential confounding factors, there was still a significant decline in the risk of incidence of breast cancer with increasing parity among parous women in previous report from the JACC Study (Tamakoshi et al., 2005). It is reported that parity has a dual effect on breast cancer risk: it transiently increases the risk after childbirth but reduces the risk in later years (Zografos et al., 2004). Female subjects in the JACC Study were 40-79 years old, and the increasing number of pregnancy and delivery was inversely associated with the risk of the death of breast cancer.

Age at first delivery of less than 23 years or more than 25 years was positively associated with the risk of death from all causes compared with those who experienced their first delivery between 23 and 25 years old. There may be preferable age at first delivery for female health. Age at natural menopause less than 48 years was positively associated with the risk of death from all causes compared with those who experienced their natural menopause between 48 and 50 years old. Meanwhile, age at natural menopause of more than 50 years was positively associated with risk of death from ischemic heart diseases. But, in multivariable adjusted analysis Cui et al. reported that no significant association was observed between duration of menstruation and mortality from stroke, coronary heart disease (Cui et al, 2006).

Use of sex hormones is a very influential factor affecting the development of female cancers such as breast, ovarian, and endometrial cancer (Pike et al., 2004; Zografos et al., 2004). In the present study, being adjusted for only age, no significant effect was found between risks of death from breast, and ovarian cancer and the use of sex hormones. But in other result from the JACC Study, experience of using sex hormones may increase risk of endometrial cancer death (Khan et al, 2006), and this finding may support previous report that estrogen therapy increases risk of developing endometrial cancer (Pike et al., 2004). It is expected that mass screening of the endometrial cancer is generally conducted in the future.

There were significantly lower risks of death from several causes including uterine cervical cancer among women who had ever undergone mass screening examination for uterine cervical cancer compared with women who had not had such experience. There were also significantly lower risks of death from all causes and cancers among women who had ever undergone mass screening examination for breast cancer. Similar results were found among those who habitually administered self examination for breast cancer. One report in the JACC Study revealed that men and women with low interest and with no participation in health screening were at high risk for developing cardiovascular disease and all-causes of mortality (Ikeda et al., 2005; Aklimunnessa et al., 2006). It is well known that people who volunteer for cancer screening are generally more health conscious than

who do not, and they have better lifestyle. This is one of reasons why those subjects who participated in cancer screening for female had reduced mortality.

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