

# Informing health policy in Japan: A mixed-model estimation to compare the cost of illness of cervical cancer and endometrial cancer

Running Head : cost of illness of uterine cancers

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## **Abstract**

### **Aim**

The objective of this study was to inform Japanese health policy by comparing these two diseases from the standpoint of economic burden and examining factors affecting future changes in economic burden.

### **Methods**

Using government-based nationwide statistical data, we used the cost of illness (COI) method to estimate the COIs from 1996 to 2011 and predicted future estimates for 2014, 2017, and 2020.

### **Results**

In 2011, the COI of cervical cancer was estimated at 159.9 billion yen and that of endometrial cancer was estimated at 99.5 billion yen. Assuming the current trends in health-related indicators, the COI of cervical cancer is predicted to temporarily decrease in 2014 and then remain constant. Meanwhile, the COI of endometrial cancer is predicted to temporarily decrease in 2014 before returning to an upward trend.

### **Conclusions**

The COI of both cervical cancer and endometrial cancer is estimated to remain constant or increase in the future. The average age of death from cervical cancer is predicted to remain relatively young and the high human capital value of patients who die in their sixties is the most likely explanation for the lack of decrease in future COI. As women's participation in society continues to increase, the future COI may also increase. Regarding endometrial cancer, the increase in direct costs, particularly hospitalization costs, are a likely factor resulting in the increase in the COI. This is

because women are surviving longer, and thus receiving care for longer durations,  
because of advancements in medical care.

## **Keywords**

Cost of illness (COI), Social burden of disease, Health economics, Cervical cancer of the uterus, Endometrial cancer of the uterus, Health policy

## Introduction

Cervical cancer (ICD-10 code: C53) and endometrial cancer (ICD-10 code: C54) are both malignant tumors occurring in the uterus. These cancers are considered separate disease entities and their clinical features differ greatly, including histological type, peak age of onset, risk factors, and treatments. Therefore, different profiles regarding the economic burdens resulting from cervical and endometrial cancers can also be expected. Since medical and economic resources are limited, prioritizing for distribution of resources is necessary by all means. Calculation and Comparison of the social burden of diseases is also necessary in prioritizing for distribution. In Japan, development and its applicability of cost of illness study have been introduced<sup>1</sup>, and made comparison of the social burden of 9 major cancers<sup>2</sup>. However, whereas a wide range of knowledge has been obtained regarding the clinical features of both cervical and endometrial cancers, no studies have compared them from the standpoint of economic burden. Data regarding economic burden is important for informing health policy decision-making on this topic, including policies regarding routine prophylactic vaccination against cervical cancer and expansion of outpatient services for the treatment of endometrial cancer. The purposes of the present study, expanded from a previous study are to estimate past cost of illness (COI) amounts, predict the future COI of cervical and endometrial cancers, and provide evidence to support policy-making in Japan<sup>3</sup>.

## Materials and Methods

### 1. Analytical method

In this study, we used government-based statistical data and the COI method proposed by Rice *et al.* to investigate the social burden of cervical and endometrial cancers in Japan<sup>4-11</sup>. The COI method incorporates both direct cost (DC) and indirect

cost (IC) (the IC is the sum of the morbidity cost (MbC) and mortality cost (MtC)).

The COI is calculated using the following equation:

$$\text{COI} = \text{DC} + \text{MbC} + \text{MtC}$$

DCs are medical costs that arise directly as a result of disease, such as costs of treatment, hospitalization, testing, and medication. We calculated the annual medical costs in the present study using the total medical expenses data reported in the Survey of National Medical Care Insurance Services<sup>12</sup>. This survey only contains data for calculating DCs starting with mid-level injuries and disease classifications such as uterine cancer (C53-55). It does not contain lower-level injury and disease classifications such as cervical cancer (C53) or endometrial cancer (C54). Therefore, using data from the Patient Survey of the Ministry of Health, Labour and Welfare, we calculated DCs by proportionally distributing total medical expenses based on the estimated number of patients (ENP) diagnosed with cervical cancer (C53), endometrial cancer (C54), and other uterine cancers (C55)<sup>13</sup>. Thus, for example, DC of cervical cancer (C53) was calculated using the following equation:

$$\text{DC (C53)} = \text{DC (C53-55)} \times \text{ENP (C53)} / \text{ENP(C53-55)}$$

ICs are opportunity costs lost as a result of disease or death. MbC and MtC were calculated using the following equations:

$$\text{MbC} = \text{TOVy} \times \text{LVd} / 2 + \text{THD} \times \text{LVd} \text{ and}$$

$$\text{MtC} = \text{NDy} \times \text{LVI},$$

TOVy is the total person-days of outpatient visits, LVd is the 1-day labor value per person, THD is the total person-days of hospitalization, NDy is the number of deaths, and LVI is the lifetime labor value per person.

The TOVy and THD according to 5-year age groups were calculated based on the above-mentioned Patient Survey <sup>13</sup>. The labor values were calculated according to 5-year age groups using the Basic Survey on Wage Structure <sup>14</sup>, Labor Force Survey <sup>15</sup>, Estimates of Monetary Valuation of Unpaid Work <sup>16</sup>, and Evaluations of Domestic Labor <sup>17</sup>. Each of these data sources is associated with a specific government office. The LVI was calculated by summing the income that could have been earned in the future if death had not occurred. We calculated the MbC by assuming a full day of labor-value loss for one hospitalized day and a half day of labor-value loss for one outpatient visit. We obtained the number of deaths because of cervical cancer according to 5-year age groups from the vital statistics reported by the Ministry of Health, Labour and Welfare <sup>18</sup>.

LVD and THD were calculated as follows:

$$LVD = (I_y + ULV_y) / 365 \text{ and}$$

$$THD = HP_y \times ALOS$$

$I_y$  is the annual income per person <sup>14</sup>,  $ULV_y$  is the annual monetary valuation of unpaid work per person <sup>16,17</sup>,  $HP_y$  is the annual number of hospitalized patients <sup>13</sup>, and  $ALOS$  is the average length of stay <sup>13</sup>. The future labor value was adjusted to a present value using a 3% discount rate because 3% is widely used as the discount rate in developed countries such as Japan and the United States, where application of the COI method is popular.

## 2. COI estimations

To examine changes overtime, we first estimated the COIs every 3 years from 1996 to 2011 using available data. The effect of introducing specific therapeutic techniques

was not examined in this study. Next, to make future predictions, we estimated the COIs for 2014, 2017, and 2020 using the two methods described below.

The first method involved fixing health-related indicators (mortality rate, average number of outpatient visits, average number of hospitalizations, average length of stay, and medical fees per examination) at the 2011 values and making estimates assuming changes in Japan's population and age composition (hereafter referred to as fixed-model estimation). The data regarding medical fees per examination were obtained from the Patient Survey<sup>14</sup>. Using 2011 as the standard year, we first calculated the mortality rate, average number of outpatient visits, average number of hospitalizations, and average length of stay according to 5-year age groups. These data were multiplied by the estimated populations for 2014, 2017, and 2020 according to 5-year age groups to obtain the predicted mortality rate, average number of outpatient visits, average number of hospitalizations, and average length of stay for each year. Using data from 2011, the estimated average length of stay, mean life expectancy, and labor value were used to estimate MbC and MtC. DCs were calculated by multiplying the outpatient and inpatient costs from 2011 by the rate of increase in outpatient visits and inpatient hospitalizations from 2011 to 2014, 2017, and 2020.

The second method involved making estimates assuming continued trends in health-related indicators as well as changes in population and age compositions. After calculating approximation curves (logarithmic and linear approximations) for each item using data after 1996, we obtained figures for 2014, 2017, and 2020. We then calculated the annual rate of increase in medical fees per examination (outpatient and inpatient)<sup>11</sup> from 1996 to 2011 and corrected this increase by multiplying it by the estimated outpatient and inpatient costs for 2014, 2017, and 2020. When making future predictions using this method, estimates varied depending on which

approximation for which they were calculated. Three patterns of estimates were made: Estimates made from logarithmic approximations of all items (logarithmic-model estimation), estimates made from linear approximations of all items (linear-model estimation), and estimates made from approximations of items with higher determination coefficients (mixed-model estimation). Logarithmic and linear estimates produce different annual trends depending on the item; thus, single estimates are likely to produce overestimated or underestimated values. We therefore compared determination coefficients within the same age group in both the logarithmic and linear approximation curves and performed a mixed estimate using the curve with the higher coefficient in each age group. Mixed-model estimation was considered the most reliable estimate in this study. The elements used for calculating the predicted future COI are shown in Table 1.

Data from 2011 were used to determine the average life expectancy and the labor value. Additionally, the Population Estimates<sup>19</sup> by the Ministry of Internal Affairs and Communications were used for 1996, 2002, 2005, 2008, and 2011 population statistics, whereas the Population Projections for Japan<sup>20</sup> from the National Institute of Population and Social Security Research were used to make estimates for 2014, 2017, and 2020.

For estimates using approximation curves, some future predicted values may be  $<0$ ; however, these are unlikely to reflect actual clinical conditions. Therefore, we defined minimum values in the present study as described below. For mortality and the number of outpatients visits and inpatient hospitalizations per person, the minimum value was set as the value from the year prior to that in which the estimate was  $<0$ . When examined according to age groups, we assumed that the value from the year prior to that when the estimate was  $<0$  would be maintained thereafter and thus we



applied this value when estimates for 2014, 2017, and 2020 fell to  $<0$ . The minimum value for the average length of stay was set at 7.8 days, which is the average in 28 countries (2010) that report data on neoplasms. This was based on the average length of stay by diagnostic categories in the OECD Health Data 2013 (statistics and indicators). According to the 2011 Patient Survey<sup>13</sup>, the average length of stay for uterine cancer (15 days) did not differ greatly from the overall mean hospitalization period for all malignant neoplasms (20.6 days). Thus, we set the mean value for neoplasms in this study as the minimum length of stay for uterine cancer and applied this to age groups with hospitalization periods of  $<7.8$  days in the estimates for 2014, 2017, and 2020.

The main model used in our analysis was the mixed model. The fixed model was used as a reference. The linear and logarithmic models provided low-end and high-end estimates, respectively, and can be regarded as sensitivity analyses that show the robustness of the mixed-model estimation.

### **3. Ethical considerations**

This study used only aggregated and published nationwide data that are freely available online. No humans or animals were used. In Japan, no institutional review board approval is required for this type of study<sup>21</sup>.

## **Results**

### **1. COI estimates from 1996 to 2011**

#### *Cervical cancer*

The COI of cervical cancer followed an upward trend from 96.1 billion yen in 1996 to 159.9 billion yen in 2011 and was estimated to have increased by 66% during this period. The number of deaths increased, but deaths of individuals aged  $\geq 65$  years as a percentage of all deaths remained mostly unchanged, and no increase in the average

age of death was observed. The fatality rate, calculated by dividing the crude mortality rate by the crude morbidity rate, did not change. The MtC per person, calculated by dividing the MtC by the number of deaths, followed an increasing trend.

### ***Endometrial cancer***

The COI of endometrial cancer followed an upward trend from 41.8 billion yen in 1996 to 99.5 billion yen in 2011 and was estimated to have increased by 138% during this period. While the number of deaths increased in a manner similar to that of cervical cancer, there was a greater increase in deaths of individuals aged  $\geq 65$  years as a percentage of all deaths and the average age of death. However, the fatality rate decreased and MtC per person followed a downward trend (Table 2).

## **2. COI estimates for 2014, 2017, and 2020 (fixed-model estimation)**

### ***Cervical cancer***

The COI of cervical cancer was estimated to remain unchanged at 159.5 billion yen in 2014, 158.9 billion yen in 2017, and 156.8 billion yen in 2020. DC, MbC, and MtC were also estimated to remain unchanged (Table 3). The predicted number of deaths followed an upward trend and is expected to increase by 7.9% from 2011 to 2020. The mortality rate of those aged  $\geq 65$  years and the average age of death are also expected to follow upward trends. MtC of patients aged  $\geq 65$  years as a percentage of the total is predicted to be 20.8% by 2020, whereas the MtC per person is expected to follow a downward trend.

### ***Endometrial cancer***

The COI of endometrial cancer was estimated to remain unchanged at 98.5 billion yen in 2014, 98.6 billion in 2017, and 99.1 billion yen in 2020. DC, MbC, and MtC were also estimated to remain unchanged (Table 4). The predicted number of deaths followed an upward trend, and is expected to increase by 6.1% from 2011 to 2020.

The mortality rate of those aged  $\geq 65$  years and the average age of death are also expected to follow upward trends. The MtC for patients aged  $\geq 65$  years as a percentage of the total MtC is predicted to increase to 40.8% by 2020, whereas the MtC per person is expected to follow a downward trend.

### **3. COI estimates for 2014, 2017, and 2020 (linear-, logarithmic-, and mixed-model estimations)**

#### ***Cervical cancer***

Linear-model estimation showed that the COI of cervical cancer would temporarily decrease to 145.9 billion yen in 2014 and then remain unchanged at 144.0 billion yen in 2017 and 145.3 billion yen in 2020. According to the logarithmic-model estimation, it appears that the COI will remain relatively unchanged at 159.8 billion yen in 2014, 163.4 billion yen in 2017, and 164.6 billion yen in 2020. The predicted number of deaths follows a downward trend with the linear-model estimation and an upward trend with the logarithmic-model estimation. The mixed-model estimation showed that the COI would temporarily decrease to 148.8 billion yen in 2014 before remaining unchanged at 146.9 billion yen in 2017 and 147.8 billion yen in 2020. The predicted number of deaths and MbC will decrease over time from 2011, and DC, MtC, and COI appear to temporarily decrease in 2014 and then remain mostly unchanged until 2020. The mortality rate of those aged  $\geq 65$  years is predicted to decrease to 48.0% in 2020 and the average age of death should decrease to 63.2 years. The MtC per person appears to increase to 44.3 million yen, and the proportion of those  $\geq 65$  years in the overall mortality cost will decrease to 16.0%. (Table 3)

#### ***Endometrial cancer***

Linear-model estimation showed that the COI of endometrial cancer would temporarily decrease to 92.1 billion yen in 2014 before following an upward trend

reaching 103 billion yen in 2017 and 116.3 billion yen in 2020. The COI will increase by 16.9% between 2011 and 2020. Using the logarithmic-model estimation, it appears that the COI will follow an upward trend of 98.5 billion yen in 2014, 102.1 billion yen in 2017, and 104.2 billion yen in 2020. The predicted number of deaths follows an upward trend using the linear-model estimation and remains mostly unchanged using the logarithmic-model estimation. The mixed-model estimation showed that the COI will temporarily decrease to 94.4 billion yen in 2014 before following an upward trend of 102.2 billion yen in 2017 and 108.7 billion yen in 2020. The COI is estimated to increase by 9.2% from 2011 to 2020. The predicted number of deaths, MbC, and MtC may temporarily decrease in 2014 before returning to an upward trend until 2020. Conversely, DC is estimated to increase consistently from 2011 to 2020. The mortality rate of those aged  $\geq 65$  years is expected to increase to 70.5% in 2020, and the average age of death is predicted to increase to 70.7 years. Furthermore, the MtC per person is predicted to decrease to 28.9 million yen and the proportion of those aged  $\geq 65$  years accounting for the overall mortality cost should increase to 40.1% (Table 4). The successive COI projections for cervical cancer and endometrial cancer starting from 1996 are shown in Figure 1. The COI of both diseases is not expected to decrease in the future. Configuration ratio of each cost for the cost of illness is shown in Figure 2. It remains mostly unchanged in cervical cancer, and the MtC and MbC of endometrial cancer as a proportion of the COI will decrease, whereas the proportion of DC will increase (Figure 2a and 2b). Time trends of the direct cost of endometrial cancer is shown in Figure 3. The DC for both have shown an upward trend. Medical fees of endometrial cancer and total patients with endometrial cancer are shown in Figure 4. The daily medical costs of inpatients have also been higher than those of outpatients, with the increase being particularly marked from 2005 onwards (Figure

4a). Conversely, the total number of hospitalization days per year has markedly declined beginning in 2005, despite an increase until that point (Figure 4b).

## Discussion

The COI of both cervical cancer and endometrial cancer showed an upward trend from 1996 to 2011. Factors that influenced the increase in the COI from 1996 to 2011 were greater DC and MtC. In our previous study on this topic <sup>3</sup>, we demonstrated that the increase in the medical fees per examination for cervical cancer and the estimated number of patients were factors causing the increase in DC. The increase in the number of deaths of young women with high human capital value and the increase in the annual labor value per person because of women's participation in society were factors resulting in the MtC increase.

Increases in DC and MtC also affected the increase in the COI of endometrial cancer. Similar to cervical cancer, increases in DC were affected by increases in the medical fees per examination and the ENP. However, the rate of increase of DC was greater than that of cervical cancer (cervical cancer: from 15.8 billion yen in 1996 to 31.0 billion yen in 2011, 96% increase; endometrial cancer: from 8.5 billion yen in 1996 to 27 billion yen in 2011, 218% increase). In contrast with cervical cancer, the average age of death from endometrial cancer increased, whereas the fatality rate decreased. The increase in medical costs resulting from the long-term survival of patients living with cancer was presumed to be a factor resulting in the increase in direct costs. With regard to the MtC for endometrial cancer, in contrast to cervical cancer, the rate of increase (from 27.6 billion yen in 1996 to 64.5 billion yen in 2011, 134% increase) was similar to the rate of deaths (from 971 individuals in 1996 to 2,092 individuals in

2011, 115% increase). Because of the increase in the average age of death, the wage increases for women during this time were negated. Moreover, because the MtC per person remained mostly unchanged, the MtC may have increased in proportion to the increase in the number of deaths.

According to our projections (mixed-model estimation), the COI of cervical cancer is expected to temporarily decrease in 2014 and then is predicted to follow a consistent upward trend. Similar trends were also observed for the number of deaths, DC, MbC, and MtC. The mortality rate of those aged  $\geq 65$  years is predicted to decrease (from 49.6% in 2011 to 48.0% in 2020) along with the average age of death (from 64.0 years in 2011 to 63.2 years in 2020). However, the mortality cost per person is predicted to follow an upward trend (from 43.5 million yen in 2011 to 44.3 million yen in 2020).

In our previous study<sup>1</sup>, no increase in the average age of death from cervical cancer and no decrease in the number of deaths of young women with high human capital value were observed. These were considered as factors preventing a future decrease in the COI. Instead, the COI may increase in the future if women's participation in the society further expands and their human capital values increase, suggesting that intervention in young women's health should be an important policy focus. Routine prophylactic vaccination against cervical cancer is currently being introduced in Japan. Prophylactic vaccination against cervical cancer is expected to further reduce the number of patients with cervical cancer and the related deaths, which should contribute to reducing the COI.

Our estimates showed that the COI of endometrial cancer would temporarily decrease in 2014 before returning to a consistent upward trend. The increase in DC is a factor behind the increase in COI that was predicted to begin in 2014. MtC and

MbC, however, will remain unchanged from 2014 onwards. In contrast with cervical cancer, the MtC and MbC of endometrial cancer as a proportion of the COI will decrease, whereas the proportion of DC will increase (Figure 2a and 2b). The MtC per person will decrease as the average age of death increases as a result of longer survival periods because of advancements in medical care. DC is estimated to increase concurrently with the controls placed on the MtC increases. Since 1996, the DC of endometrial cancer for patients who receive inpatient care has been consistently higher than the DC for patients who receive outpatient care; and the DC for both have shown an upward trend (Figure 3). The daily medical costs of inpatients have also been higher than those of outpatients, with the increase being particularly marked from 2005 onwards (Figure 4a). Conversely, the total number of hospitalization days per year has markedly declined beginning in 2005, despite an increase until that point (Figure 4b). This may have been because of the introduction of the Diagnosis Procedure Combination/Per-Diem Payment System (DPC/PDPS) in 2003. This is a case payment system for acute care hospitals in which the hospitals receive more money for discharging patients within a shorter period of time. It has been suggested that the overall duration of inpatient medical care is becoming shorter and that the volume of medical care administered within that time is increasing. Moreover, because the total number of outpatient visits per year is following a consistent upward trend, treatment is predicted to shift to outpatient settings, as exemplified by the introduction of outpatient chemotherapy. Further expansion of outpatient and homecare for endometrial cancer may contribute to a decrease in the COI.

Although these cancers both occur in the same organ, trends in the COI differ depending on the patient background and clinical features. By comparing the factors

that affect the COI of each of these cancers, we can assess the characteristics of the economic burden of each disease and contribute to future decisions regarding medical policies.

A limitation of the present study is the fact that the COI method only analyzes macro estimates of cost without taking into account the quality of medical care or quality of life, and it does not involve verification of the cost effectiveness of micro-level therapeutic techniques, vaccination, women's medical check-up. In addition, because we used fixed annual labor values from 2011 to make future predictions, MbC and MtC may have been underestimated because women's participation in society is expanding and their incomes are increasing. However, the COI method is important because it enables rational decision-making regarding the efficient use of limited medical resources by measuring the monetary value of disease burden<sup>3,4</sup>. Moreover, this method makes it possible to justify intervention plans and can provide basic information for policymaking associated with prevention and management activities for injuries and diseases<sup>7</sup>. We therefore believe that the knowledge obtained from this study can be applied to future policy-making efforts.

In conclusion, we predicted and compared the COI of cervical cancer and endometrial cancer using statistics from the Japanese government. Mixed-model estimation, which was considered the most valid estimation method, suggested that the COI of both cervical and endometrial cancer would probably not decrease during the period of time that was studied. The predictions also revealed that no increase in the average age of death and no decrease in the number of deaths of young women with high human capital value were considered as factors preventing a future decrease in the COI of cervical cancer. The future COI may increase with further expansion of women's participation in society. Interventions for young women are therefore



considered a top policy priority. The increase in DC, particularly inpatient medical costs, is likely a key contributor to the increase in the COI of endometrial cancer. This increase is because patients are surviving longer, and thus receiving care for longer durations, because of advancement in medical care. Further expansion of outpatient services and homecare for treatment of endometrial cancer may contribute to a decrease in the COI.

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## Disclosure

The authors declare that they have no competing interests.

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## Figure legends

**Figure 1: Time trends of the cost of illness (COI)**

**Figure 2: Configuration ratio of each cost for the cost of illness (COI; a: cervical cancer, b: endometrial cancer)**

**Figure 3: Time trends of the direct cost of endometrial cancer (2014–2020; mixed model)**

**Figure 4a: Medical fees of endometrial cancer (yen/person/days)**

Medical fees per outpatient examination: Calculated according to the number of outpatients in the “Patient Survey”<sup>11</sup>, and outpatient medical expenses per year in the “Survey of National Medical Care Insurance Services”<sup>10</sup>.

Medical fees per inpatient hospitalization: Calculated according to the number of inpatients in the “Patient Survey”<sup>11</sup>, and inpatient medical expenses per year in the “Survey of National Medical Care Insurance Services”<sup>10</sup>.

**Figure 4b: Total patients with endometrial cancer (person/days)**

Source of the number of endometrial cancer patients: “Patient Survey”<sup>11</sup>.

Table 1. Elements used for calculation of the predicted future cost of illness

| Model                    | Item              | Elements used for calculation                        | Fixed or Varied  |  |        |
|--------------------------|-------------------|--|--|--|--------|
| Fixed model              | Number of deaths  | Mortality rate                                       | Fixed  |  |        |
|                          |                   | The population estimates                             | Varied   |  |        |
|                          | Direct cost       | The expenses of outpatient visit and hospitalization |  | Fixed (Calculated using the unit cost in 2011)                               |        |
|                          |                   | Medical fees per examination                         | Fixed  |  |        |
|                          |                   | Total person-days of outpatient visit                | Varied   |  |        |
|                          |                   | Total person-days of hospitalizations                | Varied   |  |        |
|                          |                   | Average number of outpatients                        | Fixed  |  |        |
|                          | Morbidity cost    | Average number of hospitalizations                   | Fixed  |  |        |
|                          |                   | Average length of stay                               | Fixed  |  |        |
|                          | Mortality cost    | The population estimates                             |  | Varied   |        |
|                          |                   | Labor-value  | Fixed  |  |        |
|                          |                   | Number of deaths                                     | Varied   |  |        |
|                          |                   | Life expectancy                                      | Fixed  |  |        |
|                          |                   | Labor-value  | Fixed  |  |        |
|                          |                   |  | Discount rate: 3%  | Fixed  |        |
|                          | Logarithmic model | Number of deaths                                     | Mortality rate   | Varied (Calculated using the trend line formula)                             |        |
| The population estimates |                   |  | Varied   |  |        |
| Direct cost              |                   | The expenses of outpatient visit and hospitalization |  | Fixed (Calculated using the unit cost in 2011)                               |        |
|                          |                   | Medical fees per examination                         | Varied   |  |        |
|                          |                   | Total person-days of outpatient visit                | Varied   |  |        |
|                          |                   | Total person-days of hospitalization                 | Varied   |  |        |
|                          |                   | Average number of outpatient visits                  | Varied (Calculated using the trend line formula)<br>(Minimum value: the previous value before 0) |  |        |
| Linear model             |                   | Average number of hospitalizations                   | Varied (Calculated using the trend line formula)<br>(Minimum value: the previous value before 0) |  |        |
| Mixed model              |                   | Morbidity cost                                       | Average length of stay   | Varied (Calculated using the trend line formula)<br>(Minimum value: 7.8days) |        |
|                          |                   |  | The population estimates   |  | Varied |
|                          |                   |  | Labor-value  | Fixed  |        |
|                          |                   | Mortality cost                                       | Number of deaths   | Varied   |        |
|                          |                   |  | Life expectancy  | Fixed  |        |
|                          |                   |  | Labor-value  | Fixed  |        |
|                          |                   |  | Discount rate: 3%  |  | Fixed  |

Fixed: The value for 2011 was used. Varied: The values for 2014, 2017, and 2020 were calculated based on the trend line.

Source of medical fees per examination: Patient Survey. <sup>11</sup>.

Source of average length of stay: Patient Survey. <sup>11</sup>.

Table 2. Time trend of the cost of illness of cervical cancer and endometrial cancer

|   |                       | 1996    | 1999    | 2002    | 2005    | 2008    | 2011    |
|---|-----------------------|---------|---------|---------|---------|---------|---------|
| Population (thousand person)                              |                       | 125,864 | 126,686 | 127,435 | 127,768 | 127,692 | 127,799 |
|   | [% 65 years or older] | 15.1%   | 16.7%   | 18.5%   | 20.2%   | 22.1%   | 23.1%   |
| Number of cancer deaths (person)<br>[% 65 years or older] |                       | 2,219   | 2,260   | 2,443   | 2,465   | 2,486   | 2,737   |
|   | cervical cancer       | 51.7%   | 51.1%   | 47.7%   | 48.2%   | 47.7%   | 49.6%   |
|   | endometrial cancer    | 971     | 1,133   | 1,299   | 1,459   | 1,720   | 2,092   |
|   |                       | 51.3%   | 55.4%   | 59.0%   | 57.0%   | 62.6%   | 64.7%   |
| Average age of death (year)                               | cervical cancer       | 64.1    | 63.6    | 62.9    | 63.6    | 63.4    | 64.0    |
|   | endometrial cancer    | 64.9    | 66.2    | 67.2    | 66.7    | 68.8    | 69.5    |
| Crude incidence rate (per 100 thousand, female)           | cervical cancer       | 12.1    | 10.7    | 13.5    | 13.0    | 15.0    | NA      |
|   | endometrial cancer    | 7.2     | 8.8     | 10.2    | 12.5    | 16.5    | NA      |
| Crude mortality rate (per 100 thousand, female)           | cervical cancer       | 3.49    | 3.53    | 3.79    | 3.82    | 3.85    | 4.23    |
|   | endometrial cancer    | 1.53    | 1.77    | 2.02    | 2.26    | 2.67    | 3.14    |
| Fatality rate (female)                                    | cervical cancer       | 0.29    | 0.33    | 0.28    | 0.29    | 0.26    | NA      |
|   | endometrial cancer    | 0.21    | 0.20    | 0.20    | 0.18    | 0.16    | NA      |
| Direct cost (billion yen)                                 | cervical cancer       | 15.8    | 26.0    | 20.1    | 25.3    | 33.6    | 31.0    |
|   | endometrial cancer    | 8.5     | 15.6    | 14.4    | 26.6    | 25.6    | 27.0    |
| Morbidity cost (billion yen)                              | cervical cancer       | 10.4    | 10.1    | 12.8    | 10.3    | 10.6    | 9.9     |
|   | endometrial cancer    | 5.7     | 5.9     | 7.8     | 9.1     | 8.1     | 8.0     |
| Mortality cost (billion yen)<br>[% 65 years or older]     |                       | 69.9    | 74.5    | 98.8    | 97.8    | 101.3   | 119.0   |
|   | cervical cancer       | 16.6%   | 15.4%   | 15.8%   | 16.9%   | 15.2%   | 17.5%   |
|   | endometrial cancer    | 27.6    | 30.3    | 39.4    | 46.9    | 48.7    | 64.5    |
|   |                       | 22.7%   | 24.3%   | 30.3%   | 30.5%   | 32.2%   | 35.4%   |
| Mortality cost per person (million yen)                   | cervical cancer       | 31.5    | 33.0    | 40.4    | 39.7    | 40.7    | 43.5    |
|   | endometrial cancer    | 28.4    | 26.8    | 30.3    | 32.1    | 28.3    | 30.8    |
| COI (billion yen)   | cervical cancer       | 96.1    | 110.6   | 131.7   | 133.4   | 145.5   | 159.9   |
|   | endometrial cancer    | 41.8    | 51.8    | 61.5    | 82.5    | 82.4    | 99.5    |

Source of the population data: Ministry of Internal Affairs and Communications, "Population Estimates."

Source of the number of cervical and endometrial cancer deaths: Vital Statistics.

Average age of death: Calculated according to the number of deaths, age (5-year age grades), and cause of death in Vital Statistics.

Source of crude morbidity rate and crude mortality rate: Center for Cancer Control and Information Services, National Cancer Center, Japan.

Fatality rate: Calculated by dividing the crude mortality rate by the crude morbidity rate.

NA: Not available

Table 3. Future prediction of the cost of illness of cervical cancer

| Model             | Item                                      | 2011    | 2014    | 2017    | 2020    |
|-------------------|---|---------|---------|---------|---------|
|                   | Estimated population (thousand person)    | 127,799 | 126,949 | 125,739 | 124,223 |
|                   | [%65 years or older]                      | 23.1%   | 26.1%   | 28.0%   | 29.1%   |
| Fixed model       | Number of cervical cancer deaths (person) | 2,737   | 2,816   | 2,900   | 2,953   |
|                   | [% 65 years or older]                     | 49.6%   | 53.0%   | 55.5%   | 56.8%   |
|                   | Average age of death (year)               | 64.0    | 64.8    | 65.6    | 66.3    |
|                   | Direct cost (billion yen)                 | 31.0    | 31.1    | 31.0    | 30.8    |
|                   | Morbidity cost (billion yen)              | 9.9     | 9.9     | 9.8     | 9.7     |
|                   | Mortality cost (billion yen)              | 119.0   | 118.5   | 118.1   | 116.3   |
|                   | [% 65 years or older]                     | 17.5%   | 19.3%   | 20.5%   | 20.8%   |
|                   | Mortality cost per person (million yen)   | 43.5    | 42.1    | 40.7    | 39.4    |
|                   | COI (billion yen)                         | 159.9   | 159.5   | 158.9   | 156.8   |
| Linear model      | Number of cervical cancer deaths (person) | 2,737   | 2,611   | 2,598   | 2,553   |
|                   | [% 65 years or older]                     | 49.6%   | 48.3%   | 47.4%   | 45.0%   |
|                   | Average age of death (year)               | 64.0    | 63.1    | 62.8    | 62.3    |
|                   | Direct cost (billion yen)                 | 31.0    | 23.1    | 20.8    | 22.2    |
|                   | Morbidity cost (billion yen)              | 9.9     | 6.7     | 5.5     | 5.0     |
|                   | Mortality cost (billion yen)              | 119.0   | 116.1   | 117.7   | 118.1   |
|                   | [% 65 years or older]                     | 17.5%   | 16.4%   | 15.5%   | 13.9%   |
|                   | Mortality cost per person (million yen)   | 43.5    | 44.5    | 45.3    | 46.3    |
|                   | COI (billion yen)                         | 159.9   | 145.9   | 144.0   | 145.3   |
| Logarithmic model | Number of cervical cancer deaths (person) | 2,737   | 2,714   | 2,772   | 2,812   |
|                   | [% 65 years or older]                     | 49.6%   | 52.6%   | 54.0%   | 54.6%   |
|                   | Average age of death (year)               | 64.0    | 64.4    | 64.8    | 65.3    |
|                   | Direct cost (billion yen)                 | 31.0    | 36.9    | 40.5    | 43.1    |
|                   | Morbidity cost (billion yen)              | 9.9     | 9.6     | 8.9     | 8.1     |
|                   | Mortality cost (billion yen)              | 119.0   | 113.3   | 114.0   | 113.4   |
|                   | [% 65 years or older]                     | 17.5%   | 19.0%   | 19.4%   | 19.2%   |
|                   | Mortality cost per person (million yen)   | 43.5    | 41.7    | 41.1    | 40.3    |
|                   | COI (billion yen)                         | 159.9   | 159.8   | 163.4   | 164.6   |
| Mixed model       | Number of cervical cancer deaths (person) | 2,737   | 2,604   | 2,584   | 2,549   |
|                   | [% 65 years or older]                     | 49.6%   | 49.7%   | 49.3%   | 48.0%   |
|                   | Average age of death (year)               | 64.0    | 63.5    | 63.3    | 63.2    |
|                   | Direct cost (billion yen)                 | 31.0    | 27.7    | 26.6    | 28.4    |
|                   | Morbidity cost (billion yen)              | 9.9     | 7.8     | 6.8     | 6.4     |
|                   | Mortality cost (billion yen)              | 119.0   | 113.3   | 113.5   | 113.0   |
|                   | [% years or older]                        | 17.5%   | 17.5%   | 17.0%   | 16.0%   |
|                   | Mortality cost per person (million yen)   | 43.5    | 43.5    | 43.9    | 44.3    |
|                   | COI (billion yen)                         | 159.9   | 148.8   | 146.9   | 147.8   |

Source of estimated population, 2011: Ministry of Internal Affairs and Communications, "Population Estimates."

2014, 2017, and 2020: National Institute of Population and Social Security Research, Population Statistics of Japan.

Table 4. Future prediction of the cost of illness of endometrial cancer

| Model           | Item   | 2011    | 2014    | 2017    | 2020    |
|-----------------|--|---------|---------|---------|---------|
|                 | Estimated population (thousand person)       | 127,799 | 126,949 | 125,739 | 124,223 |
|                 | [% 65 years or older]                        | 23.1%   | 26.1%   | 28.0%   | 29.1%   |
| Fixed model     | Number of endometrial cancer deaths (person) | 2,092   | 2,103   | 2,169   | 2,220   |
|                 | [%65 years or older]                         | 64.7%   | 68.0%   | 70.4%   | 71.1%   |
|                 | Average age of death (year)                  | 69.5    | 69.8    | 70.4    | 70.9    |
|                 | Direct cost (billion yen)                    | 27.0    | 27.0    | 27.0    | 27.5    |
|                 | Morbidity cost (billion yen)                 | 8.0     | 7.9     | 7.9     | 8.0     |
|                 | Mortality cost (billion yen)                 | 64.5    | 63.6    | 63.7    | 63.6    |
|                 | [%65 years or older]                         | 35.4%   | 39.0%   | 40.9%   | 40.8%   |
|                 | Mortality cost per person (million yen)      | 30.8    | 30.2    | 29.4    | 28.6    |
|                 | COI (billion yen)                            | 99.5    | 98.5    | 98.6    | 99.1    |
| Linear model    | Number of endometrial cancer deaths (person) | 2,092   | 2,098   | 2,306   | 2,511   |
|                 | [%65 years or older]                         | 64.7%   | 67.8%   | 70.3%   | 71.2%   |
|                 | Average age of death (year)                  | 69.5    | 69.9    | 70.5    | 71.0    |
|                 | Direct cost (billion yen)                    | 27.0    | 22.3    | 28.7    | 37.8    |
|                 | Morbidity cost (billion yen)                 | 8.0     | 6.4     | 6.9     | 7.1     |
|                 | Mortality cost (billion yen)                 | 64.5    | 63.4    | 67.4    | 71.4    |
|                 | [%65 years or older]                         | 35.4%   | 38.3%   | 40.3%   | 40.3%   |
|                 | Mortality cost per person (million yen)      | 30.8    | 30.2    | 29.2    | 28.4    |
|                 | COI (billion yen)                            | 99.5    | 92.1    | 103.0   | 116.3   |
| Logarithm model | Number of endometrial cancer deaths (person) | 2,092   | 1,878   | 1,974   | 2,054   |
|                 | [%65 years or older]                         | 64.7%   | 67.3%   | 69.8%   | 70.6%   |
|                 | Average age of death (year)                  | 69.5    | 69.7    | 70.3    | 70.7    |
|                 | Direct cost (billion yen)                    | 27.0    | 33.2    | 36.3    | 38.1    |
|                 | Morbidity cost (billion yen)                 | 8.0     | 8.1     | 7.5     | 6.9     |
|                 | Mortality cost (billion yen)                 | 64.5    | 57.2    | 58.3    | 59.2    |
|                 | [%65 years or older]                         | 35.4%   | 38.3%   | 40.3%   | 40.1%   |
|                 | Mortality cost per person (million yen)      | 30.8    | 30.5    | 29.5    | 28.8    |
|                 | COI (billion yen)                            | 99.5    | 98.5    | 102.1   | 104.2   |
| Mixed model     | Number of endometrial cancer deaths (person) | 2,092   | 1,879   | 1,974   | 2,055   |
|                 | [%65 years or older]                         | 64.7%   | 67.3%   | 69.8%   | 70.5%   |
|                 | Average age of death (year)                  | 69.5    | 69.7    | 70.2    | 70.7    |
|                 | Direct cost (billion yen)                    | 27.0    | 29.9    | 36.3    | 41.9    |
|                 | Morbidity cost (billion yen)                 | 8.0     | 7.3     | 7.5     | 7.5     |
|                 | Mortality cost (billion yen)                 | 64.5    | 57.2    | 58.4    | 59.3    |
|                 | [%65 years or older]                         | 35.4%   | 38.3%   | 40.2%   | 40.1%   |
|                 | Mortality cost per person (million yen)      | 30.8    | 30.4    | 29.6    | 28.9    |
|                 | COI (billion yen)                            | 99.5    | 94.4    | 102.2   | 108.7   |

Source of estimated population, 2011: Ministry of Internal Affairs and Communications, "Population Estimates."  
2014, 2017, and 2020: National Institute of Population and Social Security Research, Population Statistics of Japan.



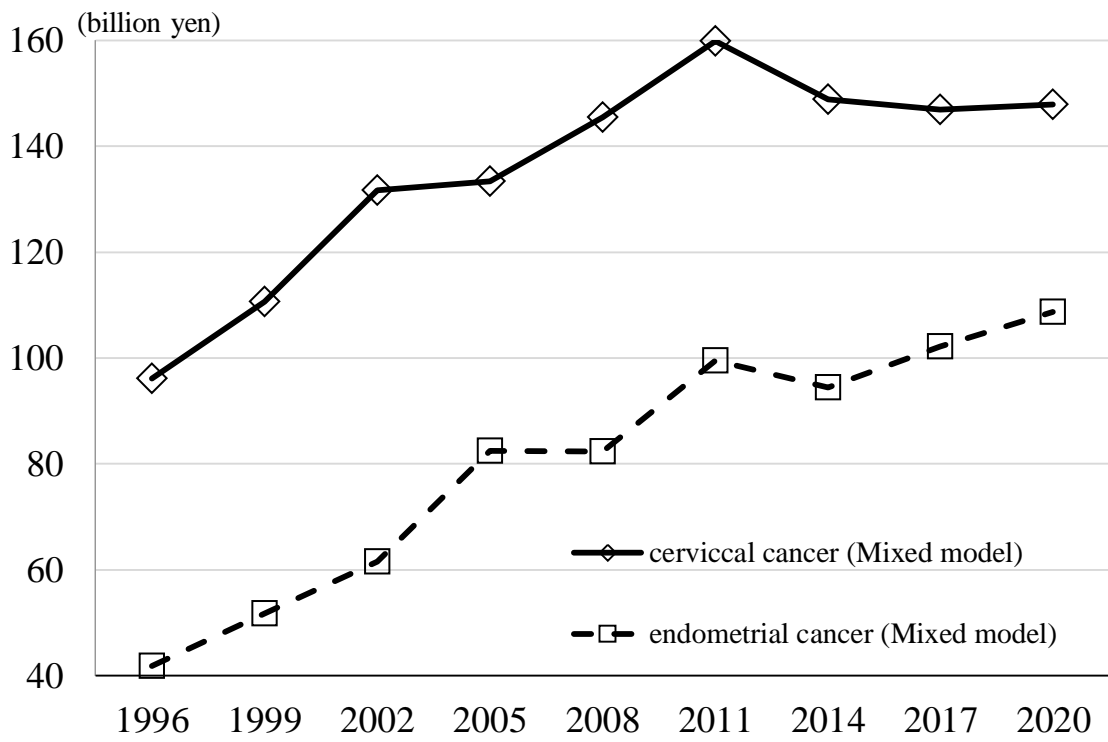
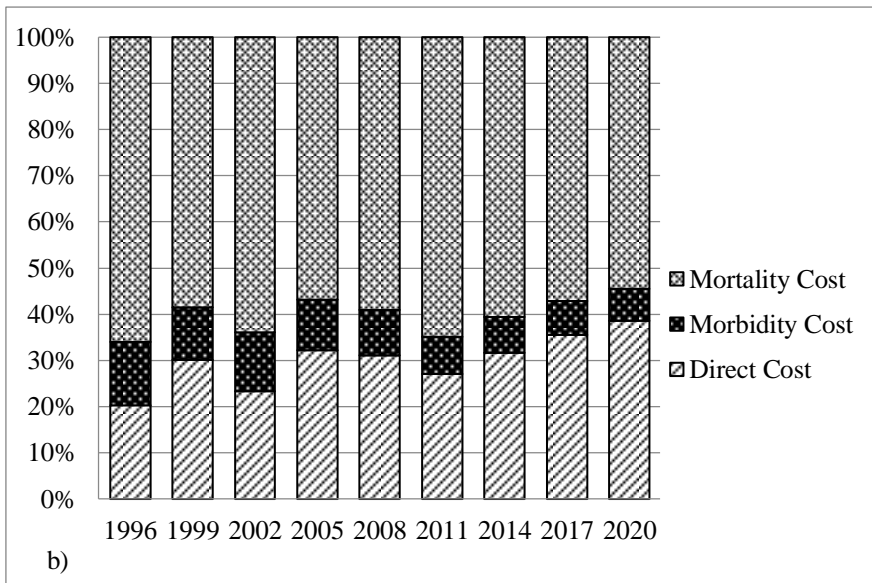
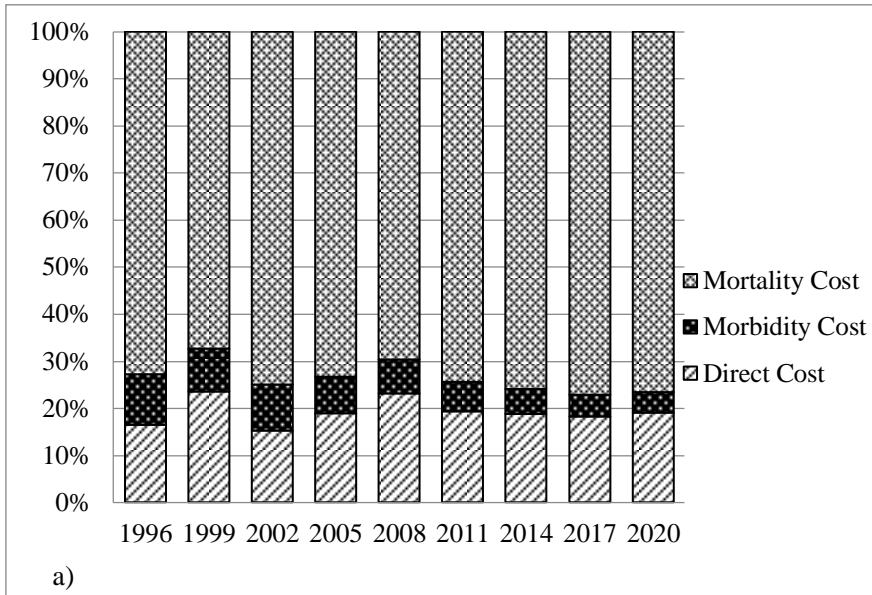


Figure1

Figure2



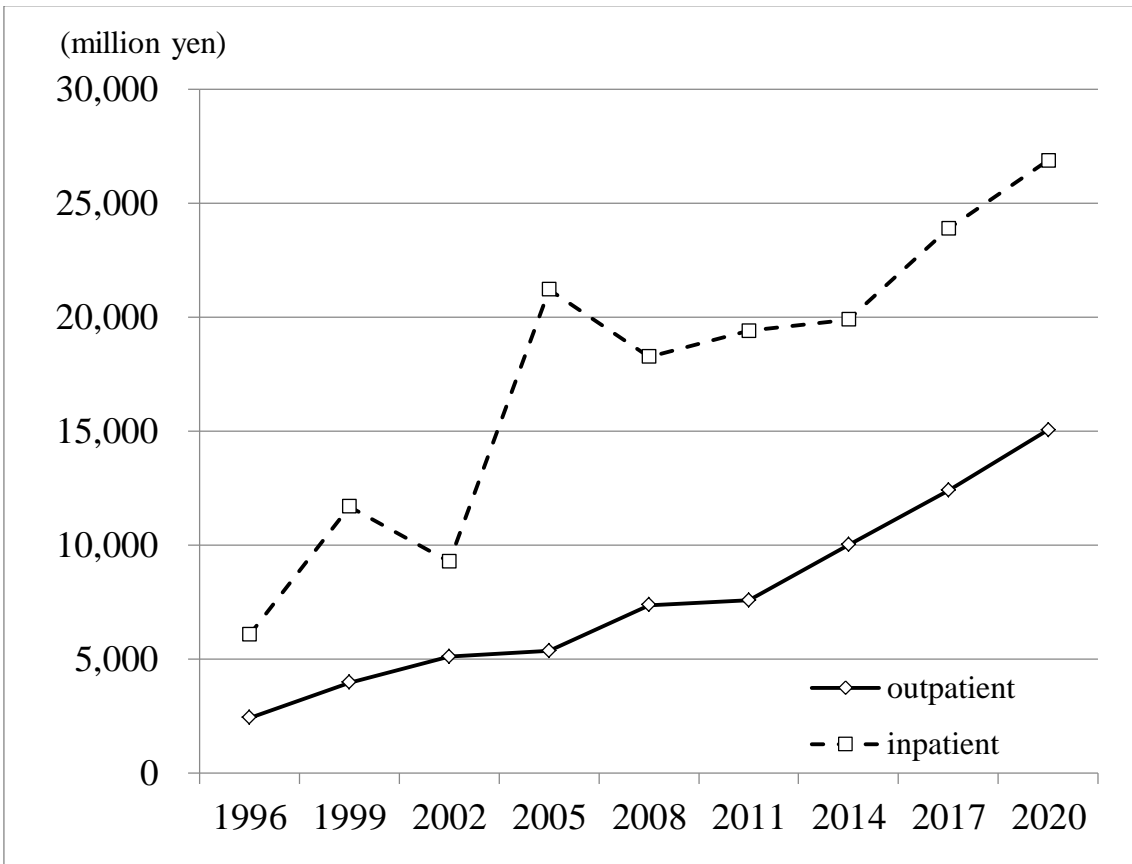


Figure3

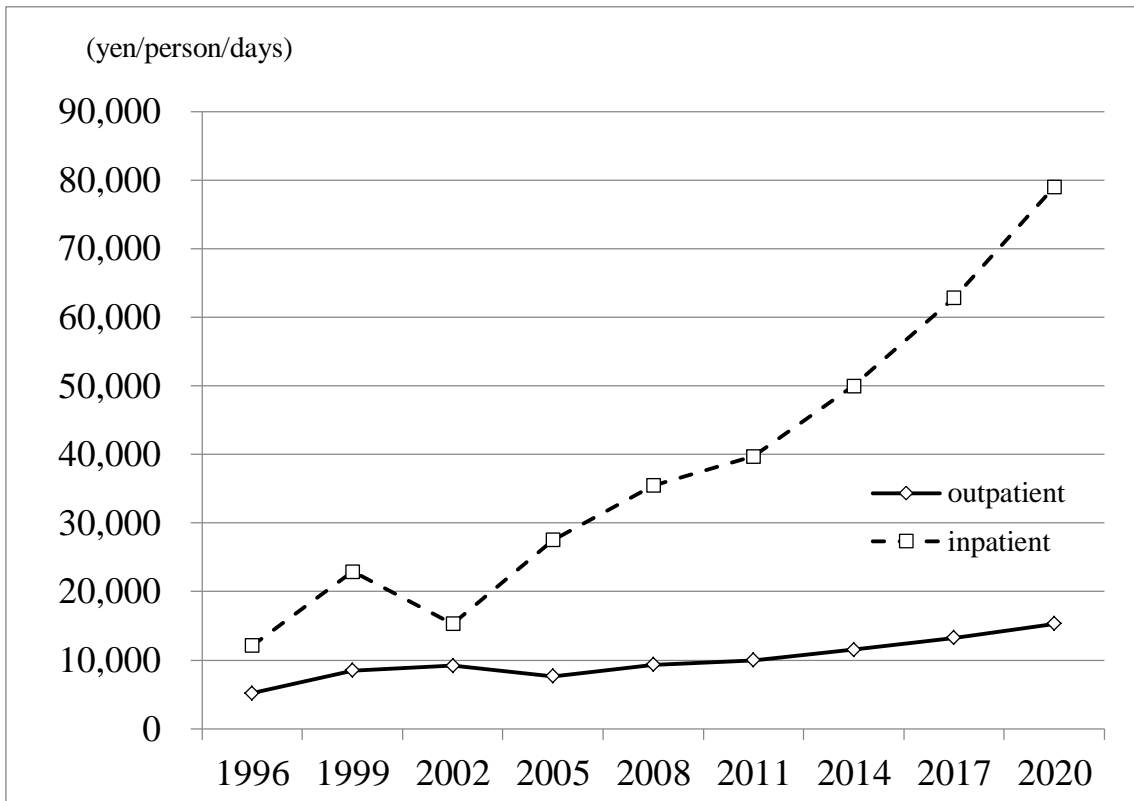


Figure4a

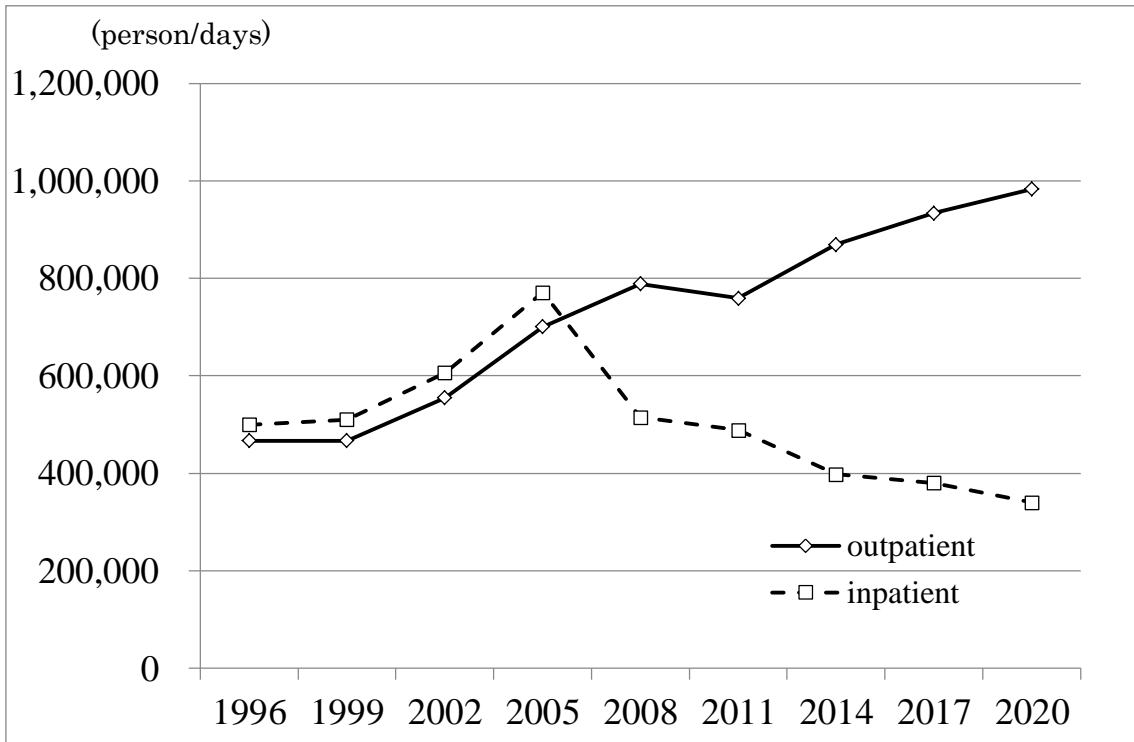


Figure4b