The economic burden of cancers attributable to metabolic syndrome in Korea

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Objectives: Metabolic syndrome is an important etiologic factor for the development of certain types of cancers. The economic costs for treatment of cancers were steadily increasing. So we estimated the economic burden of cancers attributable to metabolic syndrome in Korea.

Methods: We reviewed metabolic syndrome related cancers and relative risk then calculated population attributable fractions. We analyzed insurance claims data for metabolic syndrome related cancers in 2012 to estimate the direct cost including hospitalization, outpatient visits, transportation costs and caregivers’ costs and indirect cost including loss of productivity due to cancer treatment and premature death.

Results: The patients of cancers attributable to metabolic syndrome were 18,070 in 2012. The economic burden was USD 199.8 million and direct and indirect cost was USD 124.5 million and USD 75.3 million respectively.

Conclusions: We found the economic burden of cancers attributable to metabolic syndrome in Korea and the effort is necessary to reduce this burden.

Key words: Metabolic syndrome, Cancer, Economic burden
Introduction

Metabolic syndrome (MS) is an overall concept that includes diabetes, hypertension, obesity and dyslipidemia. In early days, the insulin resistance was a key factor in MS, diagnostic criteria was proposed in 2001 by the National Cholesterol Education Program Adult Treatment Panel (NCEP ATP) III and the Harmonizing definition was presented in 2009. The prevalence of MS is increasing steadily worldwide and Korea is not an exception, so the prevalence of MS in Korea was increasing from 24.9% in 1998 to 32.4% in 2009[1,2].

MS is a well-known risk factor of cardiovascular diseases but also some biological studies suggests that it may be an important etiologic factor for the development of certain types of cancer[3]. The positive association between colon cancer and obesity, one of the components making up the MS has been known and the effects of each component on cancer occurrence were reported. However there were few studies about effects of MS as risk factor of cancer because diagnostic criteria of MS were modified several times and may be applied differently depending on the country or regions. Nevertheless, a few large-scaled cohort studies were reported supporting the positive association between the MS and some cancers[4] and several meta-analysis about MS and risk of cancer were reported[5].

The occurrence of cancers are increasing steadily in Korea, 1.3 million people were registered as patients with cancer in 2012[6], the number of deaths from cancer in 2012 is 73,759 and death rate from cancer(per 100,000 population) in 2012 was 146.5[7]. The economic costs for treatment of cancers were steadily increasing and the health insurance benefit amount of National Health Insurance Service of Korea was USD 3.6 billion in 2012[6].

The effects of obesity and fasting glucose on cancer occurrence have been reported and a population attributable fraction (PAF) of obesity was reported[8]. But the measure of the impact of MS to cancers was not reported so we reviewed articles about the effect of MS on cancer occurrence and estimated PAF of MS.

Several studies about economic burden of cancers in Korea were reported[9, 10] but these estimated economic cost of a single cancer or total cancers and economic burden of cancers attributable to MS has not been studied. So we estimated the economic burden of MS related
cancers in Korea and the economic burden of cancers attributable to MS by using PAF.

Materials & Methods

1. Selection of metabolic syndrome related cancers and Relative risk

There were a few studies about the association between not a single component like obesity, hypertension and fasting glucose but MS and cancers. We investigated systematic reviews with meta-analysis about metabolic syndrome(MS) related cancers. MS was associated with an increased risk of colorectal cancer incidence in men (Relative Risk, RR: 1.33, 95 % CI 1.18-1.50) and women (RR: 1.41, 95 % CI 1.18-1.70)[11]. In men, MS was associated with an increased risk of liver cancer (RR: 1.43, 95% CI 1.23-1.65) and bladder cancer(RR : 1.10, 95 % CI 1.02-1.18)[5]. In women, MS was associated with an increased risk of pancreatic cancer (RR: 1.58, 95 % CI 1.35-1.84), postmenopausal(PM) breast cancer(RR: 1.56, 95% CI 1.08-2.24), uterine corpus(RR : 1.61, 95 % CI 1.20-2.15) and ovarian cancer(RR : 1.26, 95 % CI 1.00-1.59)[5]. The association with ovarian cancer in women was of borderline significance.

As the risk of premenopausal breast cancer[5], kidney cancer[12], cervical cancer[13], skin cancer[14], prostate cancer, thyroid cancer and bladder cancer in women[5] in MS were not significant, these cancers were excluded.

2. Calculation of population attributable fraction (PAF) and Prevalence of metabolic syndrome

We used the population attributable fraction(PAF) of MS in order to calculate the economic burden of cancers attributable to MS. The PAF of MS is calculated using the formula[15]:

\[
PAF = \frac{P \times (RR - 1)}{P \times (RR - 1) + 1}
\]
where P is the prevalence of exposure to the risk factor (metabolic syndrome) in the total population and RR is the relative risk of a risk factor for a specific cancer.

For the prevalence of MS, 22.4% for men and 27.9% for women in the 1998 Korean National Health and Nutrition Examination Survey (KNHANES) were applied [1] considering the time lag for cancer occurrence [8]. In KNHANES, diagnostic criteria of MS was NCEP and ATP III with Asia-Pacific criteria for abdominal obesity (>90 cm for men; >80 cm for women). In addition, we applied the prevalence of MS in 2001 KNHANES (26.9% in men, 31.8% in women) and 2005 KNHANES (31.7% in men, 29.5% in women) for sensitivity analysis [1].

The PAF of MS for colorectal cancer in men and women was 6.88% and 10.26%. The PAF of MS for pancreatic cancer in men, postmenopausal breast cancer, uterine corpus cancer and ovarian cancer in women was 13.93%, 13.51%, 14.54% and 6.76%. The PAF of MS for bladder cancer in men was 2.19%. Meanwhile, the proportion of liver cancer attributable to infectious agent such as hepatitis B virus or hepatitis C virus very high (84%) in Korea [16], so PAF for liver cancer was modified by multiplying proportion of liver cancer not attributable to infectious agents. The PAF of MS for liver cancer in men was 1.47%.

3. Estimation of economic burden

The economic burden of disease can include direct costs, indirect costs and intangible costs [17]. Intangible costs such as pain and suffering or bereavement are omitted in most studies on costs of disease because it is difficult to quantify these costs in monetary terms. So these costs were not included in this study. Direct costs consist of medical costs including hospitalization, outpatient visits and medication for the purpose of treatment of cancers and non-medical costs including transportation cost and caregivers’ cost. Indirect costs include loss of productivity associated with admissions or outpatient visits in addition to costs related to premature death. The economic burden of cancers attributable to MS was estimated using the total costs of each cancer and PAF in the following equation:
\[ \sum S_i \times PAF_j \]

i= metabolic syndrome related cancer

j = sex

Si; Sum of direct and indirect cost in metabolic syndrome related ‘i’cancer

3.1. Direct costs

To estimate the economic costs of MS related cancers, a prevalence-based approach was employed that targeted existing and newly diagnosed patients[21].

MS related cancers were defined according to the International Classification of Disease 10th revision (ICD-10) codes and included colorectal cancer (C18-C20), liver cancer (C22), pancreatic cancer (C25), postmenopausal breast cancer (C50), endometrial cancer (uterine corpus) (C54), ovarian cancer (C56) and bladder cancer (C67). Postmenopausal breast cancers were considered as 50 years of age or older. The target participants of this study were patients who had claimed health insurance benefits with the special cancer claim codes (V193) in 2012. In addition, we analyzed the patients who had been hospitalized more than once or visited outpatient clinics more than three times[10] with the mentioned cancer code of ICD-10 for sensitivity analysis. Patients under 20 year were excluded considering time lag for cancer occurrence and lower incidence rates of MS related cancers. All calculated costs were converted to U.S. dollars (1 USD=1,127 Korean won)[18].

To measure the direct medical costs, we requested the 2012 data from the Health Insurance Review and Assessment Service (HIRA). Non-covered medical costs were estimated by the proportion of total direct medical cost and that of outpatient and inpatient service was 16.4% and 22.8% respectively[19]. Outpatient pharmaceutical cost was excluded because of difficulty in calculation of the cost or small portion in total direct cost[9].

For transportation cost, we analyzed the raw data of Korea Health Panel- Year Data (Version 1.0) of the Korea Institute for Health and Social Affairs (KIHASA) and the average one-way cost among outpatients and inpatients with their guardians was USD 1.60 and USD 11.15 respectively in 2011. The 2011 price was converted to the 2012 price index
by multiplying by the inflation rate.

Caregivers’ cost was estimated as USD 57.68 for 24 hours by averaging USD 53.24 for moderate disease and USD 62.11 for serious disease[20]. Inpatients were assumed to be accompanied by caregivers for all day and the costs were multiplied by numbers of admission. For outpatients, the Caregivers’ cost was calculated by multiplying one-day caregivers’ fee and total outpatient visits and estimated as one third of that.

The protocol was approved by Institutional Review Board of Korea University(1040548-KU-IRB-13-118-A-1)

3.2. Indirect cost

Loss of productivity due to premature deaths is accepted in Human Capital Approach and estimated by calculation of present value of lost future income. Loss of productivity due to premature deaths in each cancer was in the following formula[21]:

$$\sum \sum \sum_{m=1}^{n} (N_{jk} \times \frac{Y_{jk(t+m)} \times P_{jk(t+m)}}{(1+r)^{m}})$$

j=Sex, k= Age

m=1,2,…,n(n is difference between age of death and life expectancy of age-cohort)

t=Age at death, r=Discount rate

N_{jk}=Number of death in each cancer

Y_{jk(t+m)}=Annual wage income at time(t+m) by sex and age

P_{jk(t+m)} =Employment rate at time(t+m)

The number of death in each MS related cancer and annual income by age and sex were obtained in Korean Statistical Information Service[7]. The discount rate of 3%[23] was applied and for sensitivity analysis the discount rate of 5%[9, 10] was applied also.
Loss of productivity due to hospitalization was calculated with days of admission due to each MS related cancer in the following formula:

\[ \sum D_{jk} \times Y_{jk} \times P_{jk} \]

\( j = \text{Sex}, \ k = \text{Age} \)
\( D_{jk} = \text{Days for inpatient care due to each cancer} \)
\( Y_{jk} = \text{Average daily wage income by sex and age} \)
\( P_{jk} = \text{Employment rate by sex and age} \)

For loss of productivity, the patients aged between 20 and 69yr participating in productive activities were included. To estimate loss of productivity due to outpatient visits, a third of the average daily income was multiplied by the number of outpatient visits.

For statistical analyses, SAS version 9.2 (SAS Inc., Cary, NC, USA) was used.

Results

Patients of metabolic syndrome (MS) related cancers in 2012 were 347,657 and the patients attributable to MS were 18,070, 5.2% of total cancer patients (Table 1). The patients with postmenopausal breast cancer were 6,584 occupying the largest proportion, followed by colorectal cancer in men. Among age-groups, the patients aged 50~59 were occupied the largest proportion 6,953 patients, followed by patients aged 60~69, 4,950 patients.

The economic burden of MS related cancers in 2012 were USD 3.32 billion and the burden attributable to MS were USD 199.8 million, 6.02% of the total costs. In the costs of MS related cancers, liver cancer of men was highest but the economic cost attributable to MS was highest in colorectal cancer of men.
Direct costs of cancers attributable to MS in Korean adults aged 20 years and older were estimated at about USD 124.5 million (Table 2). In outpatient care, the cost was USD 37.2 million and the cost for postmenopausal breast cancer occupied the largest proportion, USD 19.5 million, followed by colorectal cancer in men, USD 6.8 million. The estimated costs for inpatient care of patients attributable to MS were approximately USD 67.8 million, nearly 1.8 times outpatient care. In inpatient care, the cost for colorectal in men and women were USD 17.3 million to USD 17.2 million, ranked first and second.

Indirect costs of cancers attributable to MS in Korean adults aged 20 years and older were estimated at about USD 75.3 million (Table 3). Numbers of death due to premature deaths were 1,414 and the numbers of death due to colorectal cancer in women occupied the largest proportion, 360 patients. The estimated loss of productivity due to outpatient care, admission and premature death was about USD 2.7 million, USD 9.1 million and USD 63.4 million respectively.

Total economic burden of cancers attributable to MS was approximately USD 199.8 million (Figure 1). By cost item, the costs for inpatient care occupied the largest proportion, USD 67.8 million, followed by loss of productivity due to premature death, USD 63.4 million. By cancer site in sex, economic burden for colorectal cancer in men occupied the largest proportion, about USD 55.8 million, followed by postmenopausal breast cancer, USD 52.8 million. The economic burden per patient was highest in liver cancer of men as USD 36.2 thousand.

Sensitivity analysis was performed according to the prevalence of MS. The economic burden was USD 242.5 million using the prevalence of MS in 2001 and USD 249.2 million in 2005 (Table 4). In another sensitivity analysis performed according to the patient selection criteria and discount rate, the economic burden was from at least USD 193.3 million in special codes for cancer patients with 5% up to USD 205.2 million in frequency of visits with 3% (Table 5).

Discussion
This study estimated the economic burden of cancers attributable to metabolic syndrome (MS) in Korean adults aged 20 years and older in 2012 and it was approximately USD 199.8 million. Several studies about economic burden of cancers in Korea and other countries were reported but there are few studies about economic burden attributable to MS in cancers. So given that prevalence of MS and incidence of MS related cancers are increasing, it is meaningful to analysis the attributable fraction of MS and estimate economic burden due to MS. Furthermore, population attributable fractions (PAF) attributable to MS are higher than obesity[8] and the economic burden of cancers attributable to metabolic syndrome is much more than cancers due to obesity[25] so the management of metabolic syndrome has a higher health policy priority.

Meanwhile because there is no cancer site-specific PAF attributable to MS in Korea yet except obesity[8] we applied relative risk (RR) in meta-analysis of other countries. This is a limitation of this study although Korea is becoming westernized rapidly and PAF of liver cancer is modified. The PAFs attributable to MS were calculated to each cancer and varied from 2.2% of bladder cancer in men to 14.5% of uterine corpus. And in the case that there is difference in RR such as colorectal cancer[5,11], 15% of the difference occurred in the economic burden from USD 78.9 thousand to USD 92.7 thousand in sensitivity analysis.

In this study we assumed that MS affects the development of cancers but does not affect results of the treatment such as the survival or death because the relative risk is naturally effects on the occurrence. So the further study about the effects of MS on the treatment is necessary for more accurate measurement of economic burden attributable to MS.

As we mentioned earlier, we assumed the time lag for cancer occurrence as 15 or 20 year[8] and conducted sensitivity analysis for the induction period. As a result, the economic burden of cancers attributable to MS in 2012 were increased to USD 242.5 million and USD 249.2 million respectively as the prevalence of MS is increasing by the year 2001 and 2005(Table 4). In addition, though the time lag may differ depending on the type of cancer, applying that equally to all cancers is regarded as one of the limitations of this study.

In patient selection for analysis, we selected the patient with the special cancer claim code. In Korea, the fee reduction system for medical cost paid by patients with serious disease such as cancer, stroke and myocardial infarction has been operated from 2005. We supposed the numbers of the cancer patients with the special code were more accurate than with frequency
of visits because medical institutions providing medical services to cancer patients have to claim health insurance benefits with these codes. In sensitivity analysis, the numbers of patients were selected slightly less than selected based on frequency of visits with more than once admission or more than three times outpatient visits (Table 5). Colorectal and breast cancer have high prevalence in Korea (colorectal cancer: 211 per 100,000 people, breast cancer: 175 per 100,000 people) [24] and cancer patients attributable to MS were also 5,684 of postmenopausal breast cancer, 4,184 of colorectal cancer in men and 4,058 of colorectal cancer in women in order of frequency.

To estimate the economic burden of MS-related cancers, we utilized the 2012 data from HIRA. The direct costs were about USD 124.5 million and the costs for outpatient care and for inpatient care was 29% and 54% respectively. The cost paid by patient was 4 or 5% and it was reduced compared with 11.8% of previous study [9] because deductibles for the treatment of cancers decreased from 10% to 5% since 2010. The proportion of transportation cost was also less than that of previous study [9, 10] due to higher proportion of ambulatory outpatients with breast cancer. The indirect costs were about USD 75.3 million and this was 37.7% of the economic burden of cancers attributable to MS. This was smaller portion compared with 76% of previous study [9] or 41.2% in economic burden of cancer across the European Union [23]. In indirect comparison with foreign countries by multiplying the total economic burden of cancers and PAFs, the per capita economic burden of colorectal cancer in Korea was USD 1.86 and it was 50% of the United States and 75% of the UK [23, 26].

In Human Capital Approach accepted in our study, overestimation of productivity loss is often pointed out as a limitation of study [21] but this effect was attenuated a little in our study because of lower portion of fatal cancers such as lung cancer, stomach cancer or liver cancer. Sometimes the friction period approach was adopted for costing method [23] but it has the potential to be underestimation of productivity loss and the friction period of Korea has not been studied yet so we did not consider it [21].

There are a few additional limitations in our study and one of them is that outpatient pharmaceutical cost was excluded. But the total cost of outpatient anti-cancer drug multiplied by PAFs was estimated as about USD 4.4 million, 2.19% of total economic burden of cancers attributable to MS so it is necessary to calculate more accurate outpatient pharmaceutical cost completely matched with each cancer. In transportation cost, the applied average one-way
cost was public transportation fee mainly so it may be underestimated. The cost of alternative and complementary medicine was not excluded due to limitation of data.

In spite of some limitations, this is the first study on the economic burden attributable to MS in cancers. And it is rather significant considering that MS has been evaluated mainly with diabetes or cardiovascular events in terms of costs and complications. In addition, individual risk factor of cancers like obesity is important but the evaluation of MS as comprehensive concept is necessary in preventing cancer occurrence.

Conclusion

The cancer patients attributable to MS were 18,757 and the economic burden was USD 213.6 million. To reduce this economic, it is necessary to manage MS comprehensively and to evaluate the occurrence of MS related cancers and future studies will conduct these areas.

Conflicts of Interest

The authors have no conflicts of interest with the material presented in this paper.

Acknowledgments

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References


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Table 1. The patients attributable to metabolic syndrome in metabolic syndrome related cancers

<table>
<thead>
<tr>
<th>Cancer Site</th>
<th>sex</th>
<th>20-29</th>
<th>30-39</th>
<th>40-49</th>
<th>50-59</th>
<th>60-69</th>
<th>70-79</th>
<th>80-89</th>
<th>90+</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colon and rectum</td>
<td>men</td>
<td>12</td>
<td>87</td>
<td>358</td>
<td>1,042</td>
<td>1,353</td>
<td>1,091</td>
<td>229</td>
<td>12</td>
<td>4,184</td>
</tr>
<tr>
<td></td>
<td>women</td>
<td>14</td>
<td>104</td>
<td>381</td>
<td>937</td>
<td>1,072</td>
<td>1,135</td>
<td>389</td>
<td>27</td>
<td>4,058</td>
</tr>
<tr>
<td>Liver</td>
<td>men</td>
<td>1</td>
<td>9</td>
<td>65</td>
<td>186</td>
<td>164</td>
<td>105</td>
<td>20</td>
<td>1</td>
<td>550</td>
</tr>
<tr>
<td>Pancreas</td>
<td>women</td>
<td>2</td>
<td>10</td>
<td>32</td>
<td>99</td>
<td>150</td>
<td>193</td>
<td>87</td>
<td>8</td>
<td>583</td>
</tr>
<tr>
<td>Breast, postmenopausal</td>
<td>women</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>3,937</td>
<td>1,772</td>
<td>746</td>
<td>121</td>
<td>8</td>
<td>6,584</td>
</tr>
<tr>
<td>Uterine corpus</td>
<td>women</td>
<td>16</td>
<td>94</td>
<td>240</td>
<td>496</td>
<td>232</td>
<td>74</td>
<td>12</td>
<td>0</td>
<td>1,165</td>
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<tr>
<td>Ovary</td>
<td>women</td>
<td>34</td>
<td>61</td>
<td>135</td>
<td>195</td>
<td>107</td>
<td>57</td>
<td>11</td>
<td>1</td>
<td>601</td>
</tr>
<tr>
<td>Bladder</td>
<td>men</td>
<td>1</td>
<td>5</td>
<td>19</td>
<td>61</td>
<td>100</td>
<td>119</td>
<td>38</td>
<td>3</td>
<td>346</td>
</tr>
<tr>
<td>Subtotal</td>
<td></td>
<td>80</td>
<td>370</td>
<td>1,230</td>
<td>6,953</td>
<td>4,950</td>
<td>3,519</td>
<td>907</td>
<td>61</td>
<td>18,070</td>
</tr>
</tbody>
</table>
Table 2. Direct costs* of the patients attributable to metabolic syndrome in metabolic syndrome related cancers

<table>
<thead>
<tr>
<th>Cancer Site</th>
<th>sex</th>
<th>Outpatient care</th>
<th>Inpatient care</th>
<th>Transportation costs</th>
<th>Caregivers’ costs</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colon and rectum men</td>
<td>6,751,215</td>
<td>17,315,755</td>
<td>302,513</td>
<td>3,909,621</td>
<td>28,279,104</td>
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<tr>
<td>Colon and rectum women</td>
<td>5,819,308</td>
<td>17,230,783</td>
<td>290,144</td>
<td>4,400,262</td>
<td>27,740,497</td>
<td></td>
</tr>
<tr>
<td>Liver men</td>
<td>1,112,147</td>
<td>4,133,576</td>
<td>42,830</td>
<td>693,289</td>
<td>5,981,842</td>
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<tr>
<td>Liver women</td>
<td>1,128,316</td>
<td>5,304,996</td>
<td>62,729</td>
<td>1,270,303</td>
<td>7,766,343</td>
<td></td>
</tr>
<tr>
<td>Pancreas men</td>
<td>19,517,915</td>
<td>15,866,794</td>
<td>519,235</td>
<td>5,888,985</td>
<td>41,792,928</td>
<td></td>
</tr>
<tr>
<td>Pancreas women</td>
<td>1,503,487</td>
<td>2,676,507</td>
<td>61,102</td>
<td>818,156</td>
<td>5,059,252</td>
<td></td>
</tr>
<tr>
<td>Breast, postmenopausal women</td>
<td>987,023</td>
<td>4,545,684</td>
<td>66,637</td>
<td>1,013,607</td>
<td>6,612,951</td>
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<tr>
<td>Uterine corpus women</td>
<td>361,417</td>
<td>686,450</td>
<td>17,525</td>
<td>215,376</td>
<td>1,280,767</td>
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<tr>
<td>Ovary women</td>
<td>1,270,303</td>
<td>1,013,607</td>
<td>818,156</td>
<td>5,059,252</td>
<td>41,792,928</td>
<td></td>
</tr>
<tr>
<td>Bladder men</td>
<td>1,362,715</td>
<td>18,209,599</td>
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<td></td>
<td>124,513,684</td>
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</tr>
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</table>

* Unit: USD
Table 3. Indirect costs* of the patients attributable to metabolic syndrome in metabolic syndrome related cancers

<table>
<thead>
<tr>
<th>Cancer Site</th>
<th>sex</th>
<th>Frequency of outpatient visits</th>
<th>Loss of productivity due to outpatient care</th>
<th>Days of admission</th>
<th>Loss of productivity due to admission</th>
<th>No. of Death</th>
<th>Loss of productivity due to premature death</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colon and rectum</td>
<td>men</td>
<td>41,311</td>
<td>933,658</td>
<td>54,901</td>
<td>3,455,587</td>
<td>323</td>
<td>23,165,743</td>
<td>27,554,988</td>
</tr>
<tr>
<td></td>
<td>women</td>
<td>37,049</td>
<td>294,548</td>
<td>64,941</td>
<td>1,222,846</td>
<td>360</td>
<td>7,845,459</td>
<td>9,362,853</td>
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<tr>
<td>Liver</td>
<td>men</td>
<td>5,771</td>
<td>157,533</td>
<td>10,702</td>
<td>814,156</td>
<td>110</td>
<td>12,930,714</td>
<td>13,902,403</td>
</tr>
<tr>
<td></td>
<td>women</td>
<td>6,783</td>
<td>47,827</td>
<td>20,052</td>
<td>318,073</td>
<td>301</td>
<td>5,576,478</td>
<td>5,942,378</td>
</tr>
<tr>
<td>Pancreas</td>
<td>women</td>
<td>6,783</td>
<td>47,827</td>
<td>20,052</td>
<td>318,073</td>
<td>301</td>
<td>5,576,478</td>
<td>5,942,378</td>
</tr>
<tr>
<td>Breast, postmenopausal</td>
<td>women</td>
<td>96,336</td>
<td>1,028,588</td>
<td>71,328</td>
<td>2,276,355</td>
<td>191</td>
<td>7,671,262</td>
<td>10,976,204</td>
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<tr>
<td>Uterine corpus</td>
<td>women</td>
<td>10,602</td>
<td>136,738</td>
<td>10,837</td>
<td>389,062</td>
<td>48</td>
<td>2,208,244</td>
<td>2,734,043</td>
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<tr>
<td>Ovary</td>
<td>women</td>
<td>6,805</td>
<td>87,119</td>
<td>15,536</td>
<td>559,350</td>
<td>61</td>
<td>3,455,026</td>
<td>4,101,495</td>
</tr>
<tr>
<td>Bladder</td>
<td>men</td>
<td>2,958</td>
<td>44,695</td>
<td>2,797</td>
<td>104,083</td>
<td>20</td>
<td>565,029</td>
<td>713,807</td>
</tr>
<tr>
<td>Subtotal (%)</td>
<td></td>
<td>207,615</td>
<td>2,730,705</td>
<td>251,094</td>
<td>9,139,511</td>
<td>1,414</td>
<td>63,417,955</td>
<td>75,288,171</td>
</tr>
</tbody>
</table>

*Unit: USD
Table 4. Sensitivity Analysis for the prevalence of MS

<table>
<thead>
<tr>
<th>Year</th>
<th>Prevalence of MS(%)</th>
<th>Direct costs*</th>
<th>Indirect costs*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>men</td>
<td>22.4</td>
<td>124,513,684</td>
</tr>
<tr>
<td></td>
<td>women</td>
<td>27.9</td>
<td></td>
</tr>
<tr>
<td>1998</td>
<td></td>
<td>26.9</td>
<td>141,802,168</td>
</tr>
<tr>
<td></td>
<td>men</td>
<td>31.8</td>
<td></td>
</tr>
<tr>
<td></td>
<td>women</td>
<td>31.8</td>
<td></td>
</tr>
<tr>
<td>2001</td>
<td></td>
<td>31.7</td>
<td>142,287,672</td>
</tr>
<tr>
<td></td>
<td>men</td>
<td>29.5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>women</td>
<td>29.5</td>
<td></td>
</tr>
</tbody>
</table>

* Unit: USD
Table 5. Sensitivity Analysis for patient selection criteria and discount rate

<table>
<thead>
<tr>
<th>Selection Criteria</th>
<th>Numbers of Patients</th>
<th>Economic burden* to discounts rate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>3%</td>
</tr>
<tr>
<td>Special Code</td>
<td>18,070</td>
<td>199,801,855</td>
</tr>
<tr>
<td>Frequency of Visits</td>
<td>19,340</td>
<td>205,194,706</td>
</tr>
</tbody>
</table>

*Unit: USD
Figure 1. The economic burden of cancers attributable to metabolic syndrome (unit: USD)