Future patient distribution and incidence in hemato-oncology: a study using data from the cancer registry in Kanagawa, Japan

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Original Article

Title: Future patient distribution and incidence in hemato-oncology: a study using data from the cancer registry in Kanagawa, Japan

Running title: Prediction of the incidence of hematological malignancy

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Abstract

BACKGROUND AND PURPOSE

The distribution of patients with hematological malignancies will probably markedly change because society is aging. We assessed the expected incidence rates of leukemia, malignant lymphoma, and multiple myeloma using estimates of the nation's population and Kanagawa Cancer Registry data.

METHODS

To estimate the future incidence, we multiplied the 2010 rate by the predicted population according to age groups.

RESULTS

The total number of patients newly diagnosed as having hematological malignancy in Kanagawa in 2010 was 1,970. This was predicted to increase to 2,581 in 2025 and to decrease to 2,712 in 2040. Trends were almost the same for all three hematological malignancies. The incidence rates of the three hematological malignancies were predicted to continuously increase in patients aged ≥65 years: a 169% (450/266) increase in leukemia, 167% (1205/722) increase in malignant lymphoma, and 169% (309/183) increase in multiple myeloma from 2010 to 2040. In the group of patients

aged <65 years, the incidence rates of these hematological malignancies were predicted to decrease.

CONCLUSIONS

The distribution of patients will change in the future: the number of elderly patients will increase, and the number of patients living in urban areas will increase. This prediction may have a great impact on the future health care plan.

(206 words)

Key words: Nordpred, leukemia, myeloma, lymphoma, hematopoietic stem cell transplantation.

Introduction

Japan is becoming a rapidly developed aging society like some of the developing countries[1]. Age is the most important risk factor of cancer[2]; thus, the number of patients with cancer will rapidly increase in the future. We recently predicted the future incidence of breast cancer[3] using data from the Kanagawa Cancer Registry[4], 2010 census population data from the National Census, and estimated data for future populations up to 2040 from the National Institute of Population and Social Security Research[2]. We demonstrated that the future distribution of patients with breast cancer would drastically change: the number of elderly patients in urban areas would increase. Kanagawa is the one of the biggest prefectures in Japan, which had a population of 9,048,331 people in 2010, including urban, suburbs, and rural areas[5]. Thus, this prediction could be applied to many areas in Japan. This change in distribution would induce a major change in the demands and supply of cancer medicine; thus, this information would have a great impact in medical providers.

Predicting the future incidence of hematological malignancies is also important. Treatments differ according to the type of diseases. The intensity of treatment is usually decided according to the patient's age. Highly intensive treatments require many medical resources, medical providers, and pieces of medical equipment. Thus, knowing

which age groups and diseases would increase in the future would be valuable for determining the required medical resources.

In this study, we described the future incidence of hematological diseases in areas with different characteristics. We also evaluated the demand and supply balance, which could give physicians an important outlook on the treatment for hematological malignancies.

Methods

Data collection

The methods of data collection have been described elsewhere[3]. Briefly, we used the population-based cancer registry data for the Kanagawa Prefecture (Kanagawa Cancer Registry). In 2010, the population in the Kanagawa Prefecture was 9,048,331 people, and only Tokyo had a larger population in Japan. All data from the Kanagawa Cancer Registry were retrieved from the database after obtaining permission from the Kanagawa Prefecture in April 2016. Results are presented for the following cancer sites, as defined by the International Classification of Diseases, tenth edition: Hodgkin lymphoma (C81), follicular lymphoma (C82), non-follicular lymphoma (C83), mature T/natural killer-cell lymphomas (C84), other specified and unspecified types of non-Hodgkin lymphoma (C85), malignant immunoproliferative diseases and certain other B-cell lymphomas (C88), multiple myeloma and malignant plasma cell neoplasms (C90), lymphoid leukemia (C91), myeloid leukemia (C92), monocytic leukemia (C93), other leukemias of specified cell type (C94), leukemia of unspecified cell type (C95), and other and unspecified malignant neoplasms of lymphoid and hematopoietic and related tissue (C96). Leukemia, malignantly lymphoma, and multiple myeloma included codes C91-C95, C81-C85 and C96, and C88 and C90, respectively.

To estimate the expected incidence of cancer for 2015, 2020, 2025, 2030, and 2035, we used three databases. Data of newly diagnosed patients with hematological malignancy by sex and 16 age groups (5-year intervals up to 79 years and >85 years old); the 1995 2000, 2005, and 2010 census population data; and estimated data for 2015, 2020, 2025, 2030, and 2035 populations were based on the Kanagawa Cancer Registry, National Census, and National Institute of Population and Social Security Research[6], respectively. Patients with hematological malignancy identified using a death certificate only (DCO) were excluded because detailed information, including the diagnosis date of cancer and incidence data, were not obtained for these patients (Figure 1). Patients with hematological malignancy identified using a DCO comprised 15.1% (351/2321) of all patients in 2010.

Data Analysis

Data analysis was conducted as previously described[3]. Briefly, future estimates of the incidence rates of hematological malignancies were calculated by multiplying the 2010 incidence rates according to sex and the 16 age groups by the future populations according to sex and the age groups. For example, the predicted incidence of hematological malignancies was calculated as follows:

$$Predicted\ incidence\ of\ hm\ in\ 2020$$

$$= \sum_{\substack{sex= \\ woman, \\ man}} \left\{ (the\ predicted\ number\ of\ individuals\ by\ sex\ aged > 85\ years\ in\ 2020) \right.$$

$$\times \frac{the\ incidence\ of\ hm\ by\ sex\ in\ those\ aged > 85\ years\ in\ 2010}{the\ number\ of\ residents\ by\ sex\ \ in\ those\ aged\ > 85\ years\ in\ 2010}$$

$$+ \sum_{i=0}^{16} (the\ predicted\ number\ of\ residents\ by\ sex\ \ in\ those\ aged\ \ 5i\ to\ 5i+4\ in\ 2020)$$

$$\left. \times \frac{the\ incidence\ of\ hm\ by\ sex\ in\ those\ aged\ 5i\ to\ 5i+4\ in\ 2010}{the\ number\ of\ residents\ by\ sex\ in\ those\ aged\ 5i\ to\ 5i+4\ in\ 2010} \right\},$$

where hm means hematological malignancies and $those\ aged\ 5i\ to\ 5i+4$ means a 5-year interval. We called this the simple 2010 model. We also used programmed software, Nordpred, to perform sensitivity analysis. Nordpred is an R-based software developed by the Cancer Registry of Norway, and it is basically an age-period-cohort model with a Poisson regression:

$$R_a^p = \mathrm{g}\left(A_a + D \cdot p + P_p + C_c\right),$$

where g is a link function and R_a^p, D, A_a, P_p, and C_c are defined as the incidence rates in the age group a and in the period p, common linear drift parameter, age component of the age group a, non-linear period component of the period p, and non-linear cohort component of the cohort c, respectively. We used two link functions: the exponential

function, and for better predictions to level off the exponential growth, the power 5 function (i.e., $g(x) = x^5$ by Moller et al[7].

The future estimated values are presented as an index value, and they are expressed as the relative value compared with the 2010 incidence as a proportion of 100.

Results

Estimation of the future incidence

The total numbers of patients newly diagnosed as having hematological malignancy in Kanagawa in 2010 were 1,970, including 547 with leukemia, 1,168 with malignant lymphoma, and 255 with multiple myeloma. The total number of patients newly diagnosed as having hematological malignancy was predicted to increase to 2,581 in 2025 and to decrease to 2,712 in 2040 (Figure 1). Trends were almost the same for all three hematological malignancies (Figure 2).

In the 2010 model, the incidence by age groups according to diseases, including malignant lymphoma, multiple myeloma, and leukemia, are shown in Table 1. The incidence rates of the three hematological malignancies was predicted to continuously increase in patients aged ≥65 years: a 169% (450/266) increase for leukemia, 167% (1205/722) increase for malignant lymphoma, and 169% (309/183) increase for multiple myeloma from 2010 to 2040 (Table 1). In the group of patients aged <65 year, the incidence rates of these hematological malignancies was predicted to decrease (Table 1).

Discussion

This study showed that the distribution of patients with leukemia, malignant lymphoma, and multiple myeloma would drastically change in the future. This prediction may have a great impact on the future health care plan for hematological malignancies.

We found that the future incidence rates of hematological malignancies would change. In the present study, the number of patients with cancer onset aged ≥65 years was predicted to continuously increase until 2040 (Figure 3), whereas that in patients aged <65 years would decrease (2010 model) or increase very little (Nordpred) (Figure 4). This change was almost consistent with our future prediction of patients with breast cancer[3]. In breast cancer[3], the aging baby boom generation, which includes individuals born during the first baby boom (1947–1949) after World War II, probably had a marked effect on this change in the distribution of patients. This group has been a dominant component of the Japanese population, and the total number of baby boomers is 8,060,000[8]. This prediction indicated that the demand for high-intensity treatments, such as allogeneic hematopoietic stem cell transplantation[9], will decrease; the number of patients with leukemia aged <40 years, who are candidates for myeloablative transplantation, will largely decrease to 67% (76/113, 2010 model) from 2010 to 2040 (Table 1). The number of patients with leukemia aged <60 years, who are candidates for

non-myeloablative transplantation, will also decrease to 78% (177/227, 2010 model) (Table 1). Similarly, the number of candidates for autologous hematopoietic transplantation with malignant lymphoma and multiple myeloma will decrease. In contrast, the number of patients aged ≥65 years would increase for all three diseases. Regarding the therapeutic strategy for these patients, maintaining quality of life is often emphasized[10]. Thus, in the near future, the role of intensive treatment for a cure would be lower and that of patients' management to maintain quality of life would be higher. With the increasing number of elderly patients with cancer, clinicians are increasingly recognizing the necessity to perform a clinical trial for this patient population. Clinical trials in geriatric hemato-oncology with endpoints for quality of life are needed[11].

Future regional disparity in distributions of patients with hematological malignancies is almost similar to that with breast cancer[3]; the number of elderly patients will grow in urban areas. This indicates that the supply of medical resources, such as hematological specialists, will be needed in these areas. In rural areas, patients' accessibility to medical professions would become difficult because the patient density would become lower. Currently, more treatments can be conducted in outpatient care centers for malignant lymphoma and multiple myeloma. Thus, as it would be difficult for patients living in rural areas to regularly visit hospitals to receive cancer treatments,

improving accessibility to medical institutions that provide cancer care is needed. For example, travel clinics in rural areas where the cancer patients could receive chemotherapy may be worth investigating.

Although this study provided important information about the future perspectives on hematological malignancies, one issue remains to be discussed. To estimate the future incidence according to each medical region, we multiplied the incidence rate of 2010 by the population in secondary medical regions. This estimation method, using the incidence data of a single year, can be applied to other municipalities, as our calculation did not consider the historical data of the cancer incidence; however, unlike other methods, the impact of the cohort effect cannot be considered. As per the epidemiologic definition, a cohort effect occurs when different distributions of disease arise from a changing or new environmental cause that affects age groups in a different manner. Thus, a cohort effect is conceptualized as a period effect that is differentially experienced through age-specific exposure or susceptibility to that event or cause (i.e., interaction or effect modification)[12,13]. Only the effect of aging was considered in this study; yet, this effect does not need to be considered in the prediction for hematological malignancies. Risk factors are unknown for most hematological diseases. Effective prevention of these diseases is also unknown. Thus, factors, except for age, are

neglected. To reduce the prospect of erroneous predictions because of inherently large random variation due to small numbers, models in Nordpred need at least 100 patients with cancer (all ages) per every 5-year period[14]. The numbers for leukemia, malignant lymphoma, and multiple myeloma in the Kanagawa Cancer Registry were not numerically strong.

In summary, the distribution of patients with hematological malignancies will change in the future: the number of elderly patients will increase, and the number of patients living in urban areas will increase. This prediction may have a great impact on the future health care plan.

(1816 words)

Figure legends

Figure 1: Predicted incidence of hematological malignancies in the Kanagawa Prefecture.

Figure 2: Predicted incidence rates of the three hematological malignancies in the 2010 model. Those for leukemia (a), malignant lymphoma (b), and multiple myeloma (c) are shown.

Figure 3: Predicted incidence rates of hematological malignancies in those aged 65 years and older in the 2010 model and according to NORDPRED. Those of the exponential and Power 5 as link functions are shown.

Figure 4: Predicted incidence rates of hematological malignancies in those aged 64 years and younger in the 2010 model and according to NORDPRED. Those of the exponential and Power 5 as link functions are shown.

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Author contributions

Conception and design: All authors

Collection and assembly of data: M Sakaguchi and K Katayama

Data analysis and interpretation: All authors

Manuscript writing: All authors

Final approval of manuscript: All authors

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Table 1: Future estimated values using 2010 model

	Age groups†	Year						
		Future estimated values*						
		2010	**2015**	**2020**	**2025**	**2030**	**2035**	**2040**
Leukemia	≥65	100	122	137	147	153	159	169
	<65	100	95	95	96	95	89	80
	<60	100	98	100	98	93	84	78
	<40	100	92	84	78	74	71	67
Malignant lymphoma	≥65	100	122	137	144	150	157	167
	<65	100	94	96	102	103	97	86
	<60	100	101	107	109	104	91	84
	<40	100	89	81	77	74	70	66
Multiple myeloma	≥65	100	123	140	151	154	159	169
	<65	100	90	90	101	107	103	89
	<60	100	99	107	114	111	96	87
	<40	100	83	72	66	63	62	58

*Future estimated values are presented as an index value, and they are expressed as the relative value compared with the 2010 incidence as a proportion of 100 by age.

†Age groups ≥65, <65, <60, and <40 years represent those aged 65 years and older, 64 years and younger, 59 years and younger, and 39 years and younger, respectively.

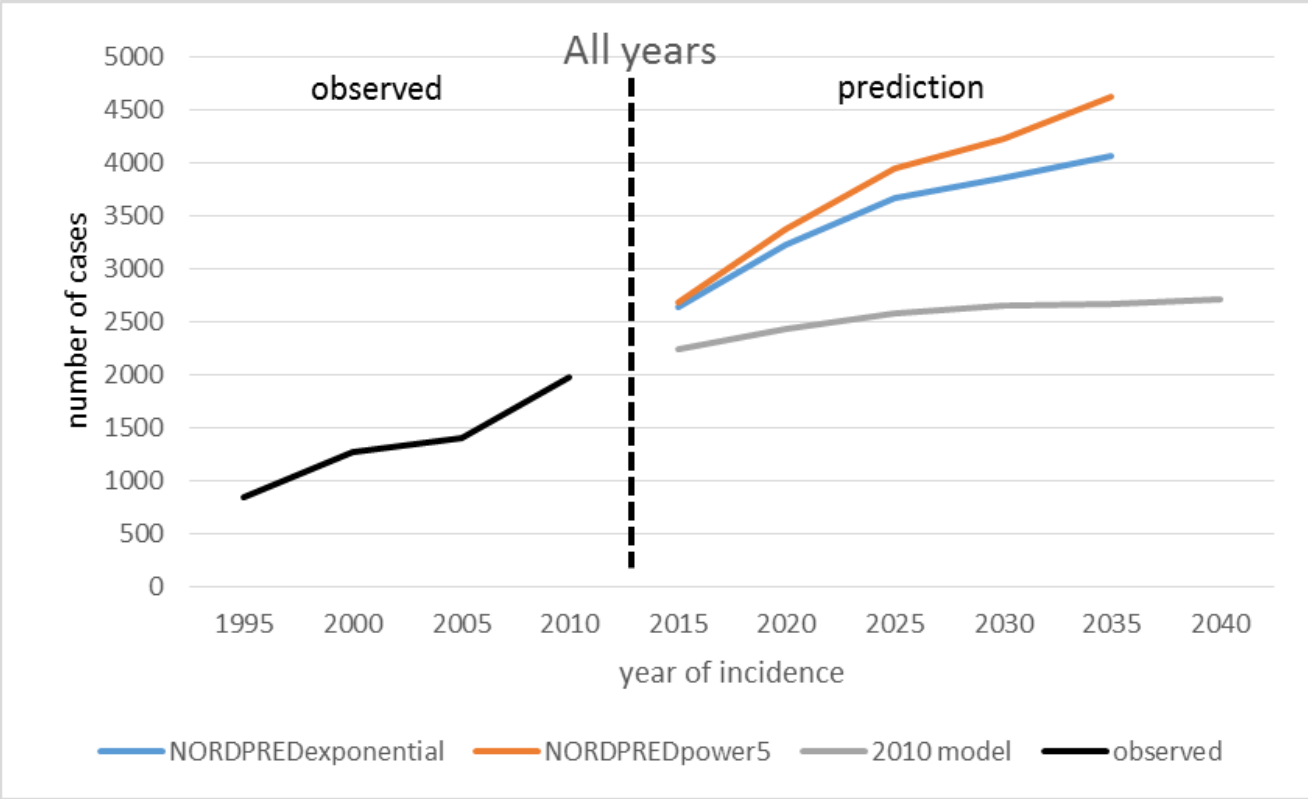

All years
observed
prediction
number of cases
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
1995
2000
2005
2010
2015
2020
2025
2030
2035
2040
year of incidence
NORDPREDexponential
NORDPREDpower5
2010 model
observed

Figure1

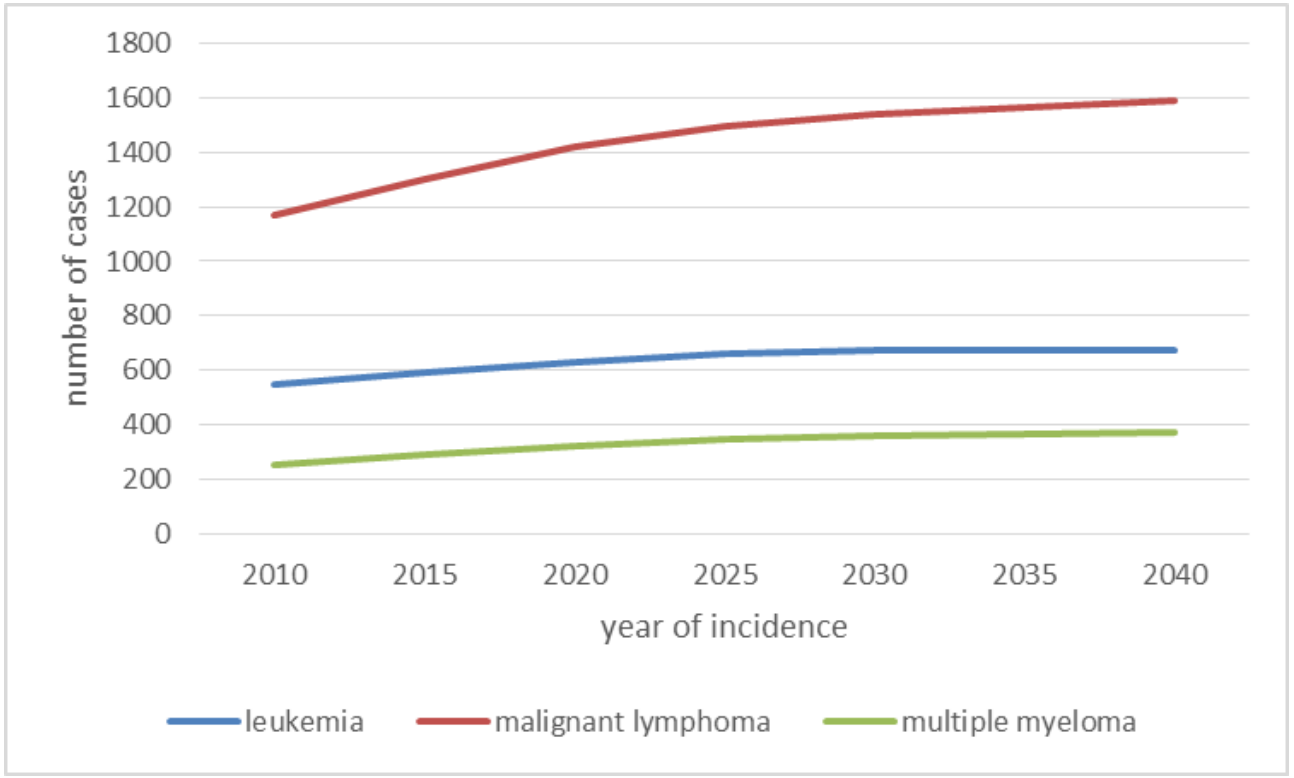
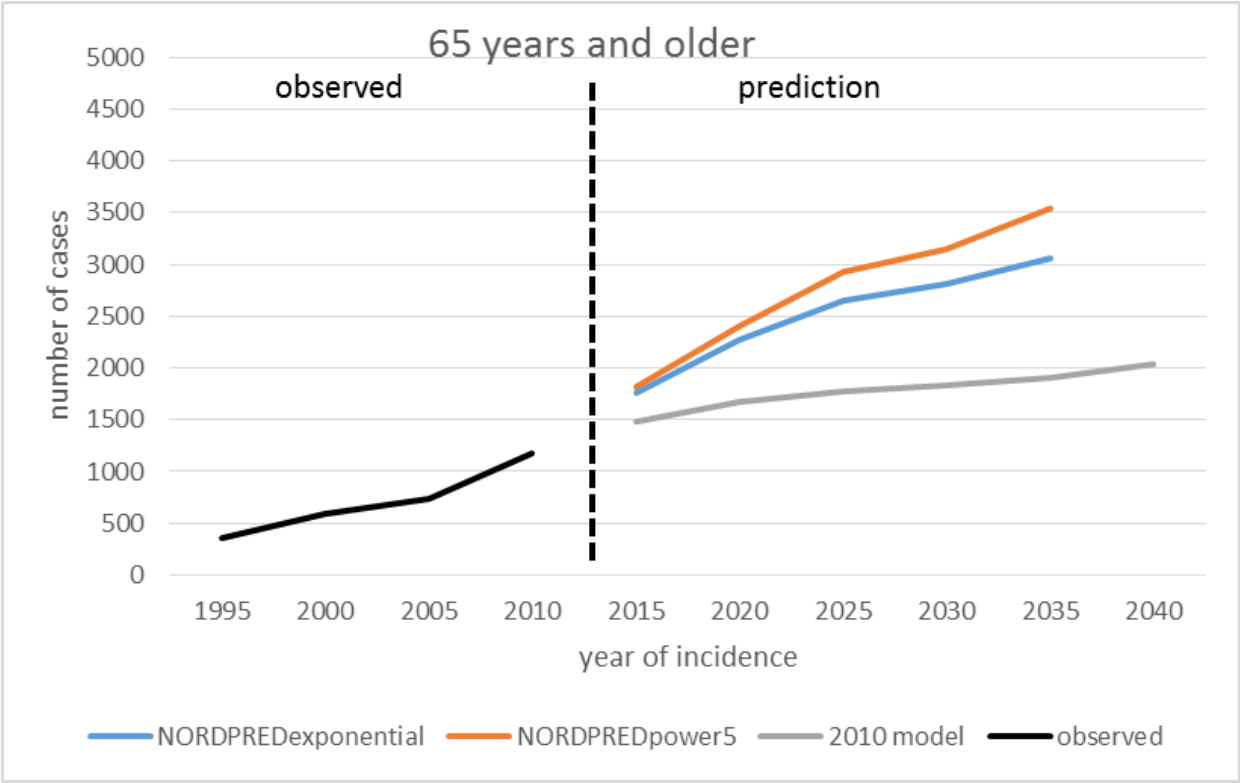

1800
1600
1400
1200
1000
800
600
400
200
0
number of cases
2010
2015
2020
2025
2030
2035
2040
year of incidence
leukemia
malignant lymphoma
multiple myeloma

Figure2


65 years and older
observed
prediction
number of cases
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
1995
2000
2005
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2015
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2025
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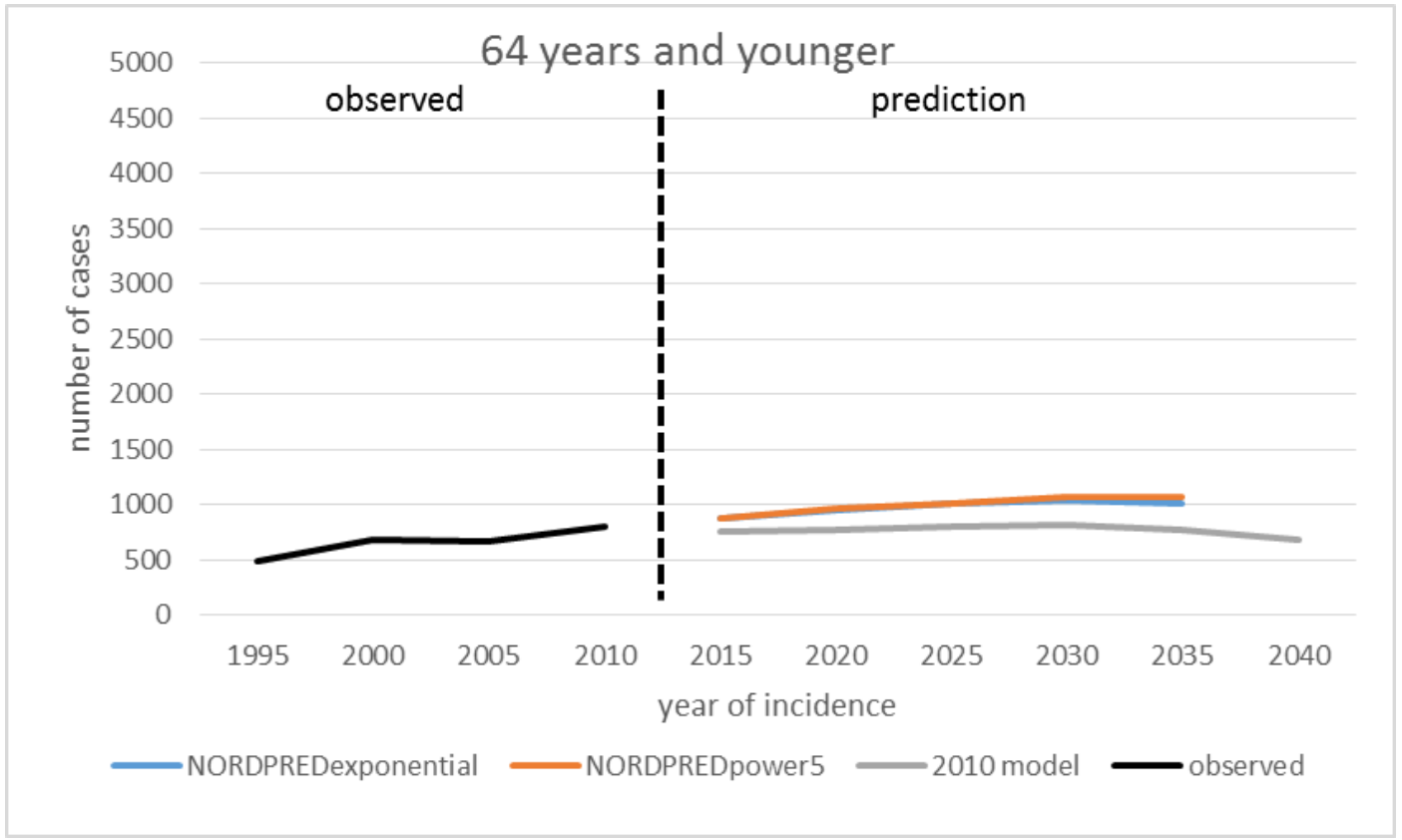
2040
year of incidence
NORDPREDexponential
NORDPREDpower5
2010 model
observed

Figure 3


64 years and younger
observed
prediction
number of cases
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
1995
2000
2005
2010
2015
2020
2025
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2035
2040
year of incidence
NORDPREDexponential
NORDPREDpower5
2010 model
observed

Figure 4

Figures

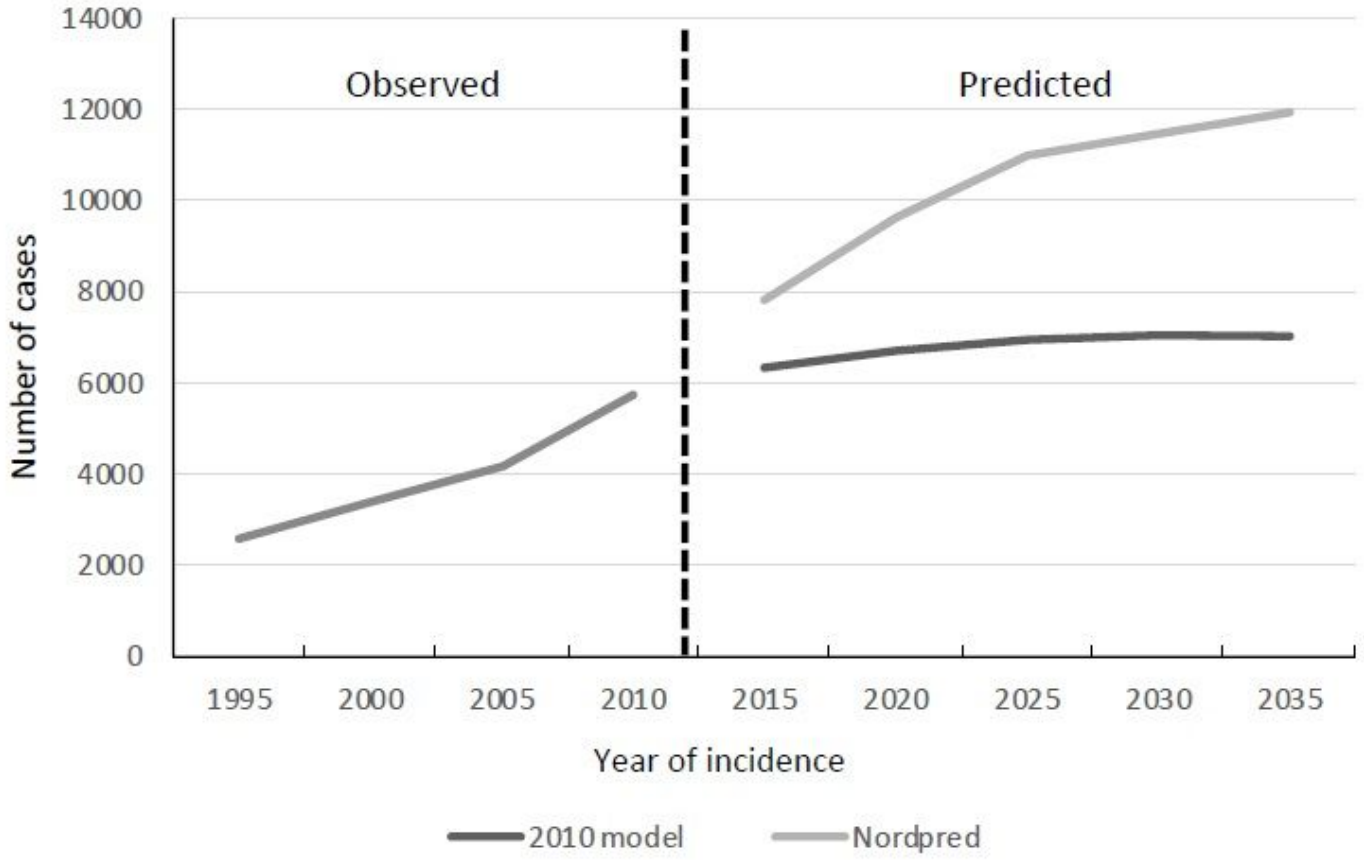

Figure 1

Predicted incidence of hematological malignancies in the Kanagawa Prefecture.

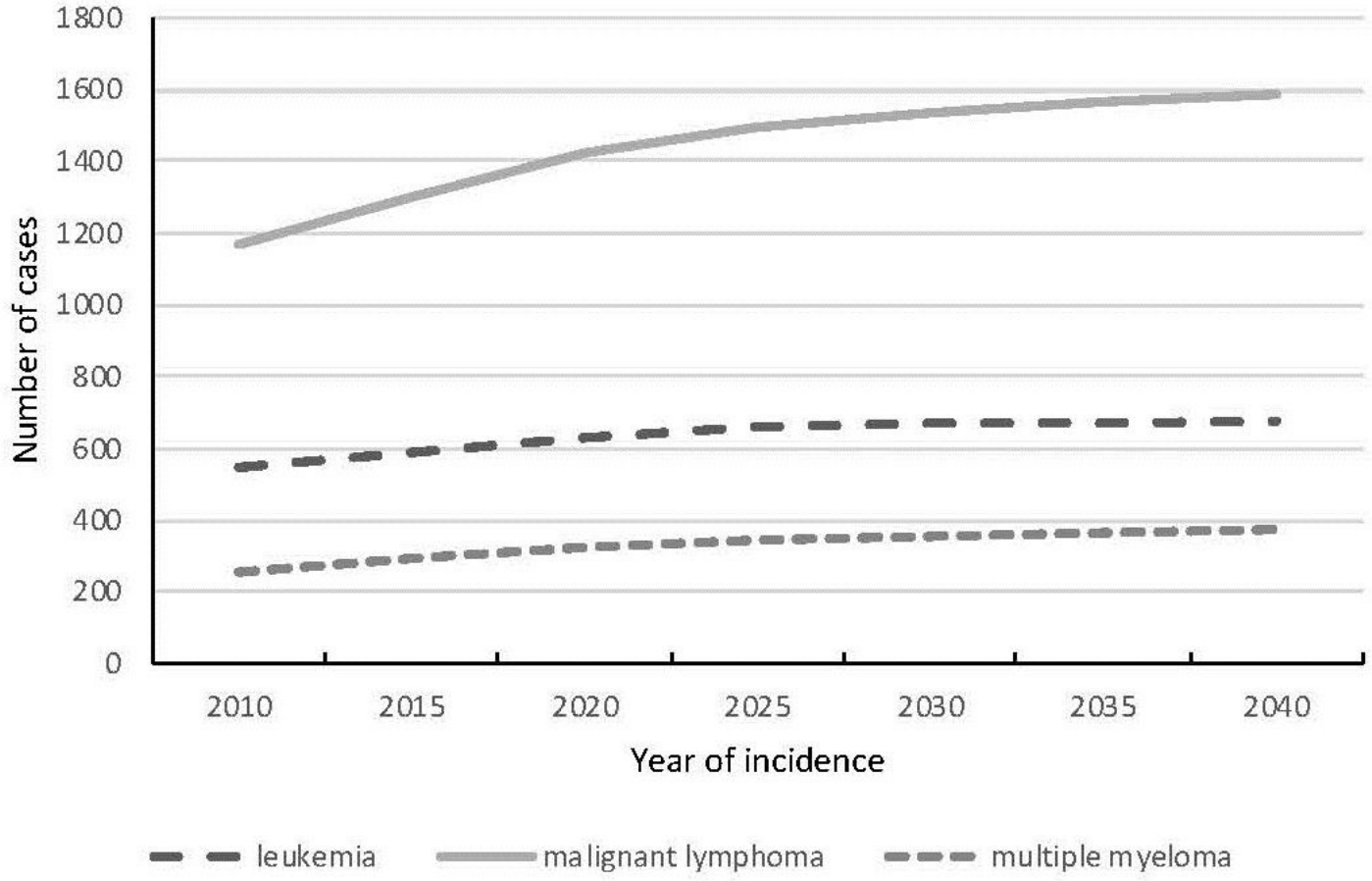

Figure 2

Predicted incidence rates of the three hematological malignancies in the 2010 model. Those for leukemia (a), malignant lymphoma (b), and multiple myeloma (c) are shown.

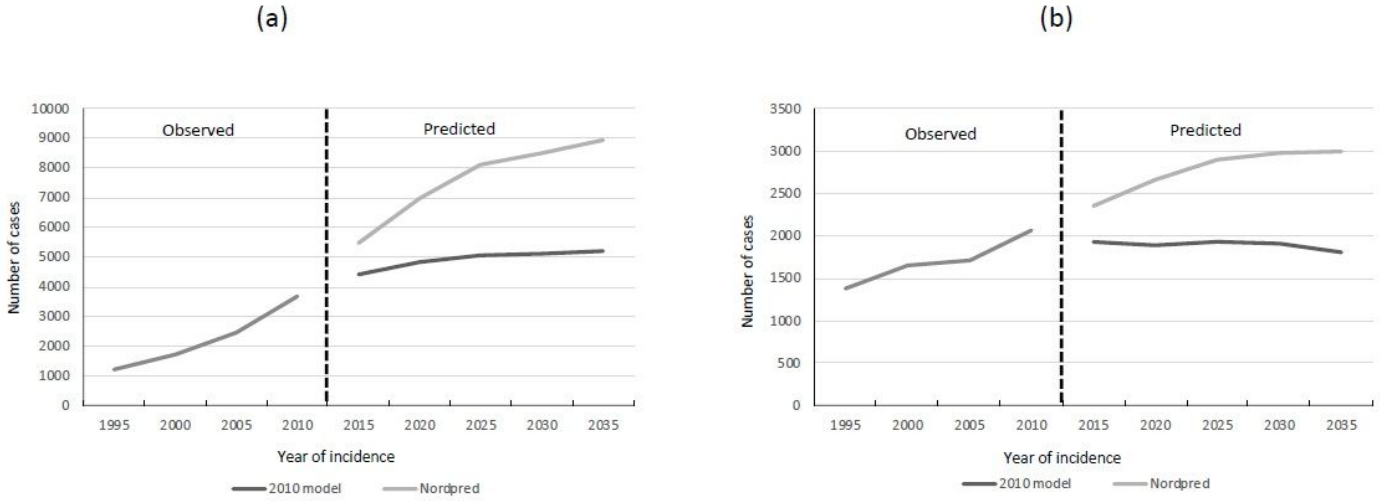

Figure 3

Predicted incidence rates of hematological malignancies in those aged 65 years and older in the 2010 model and according to NORDPRED. Those of the exponential and Power 5 as link functions are shown.

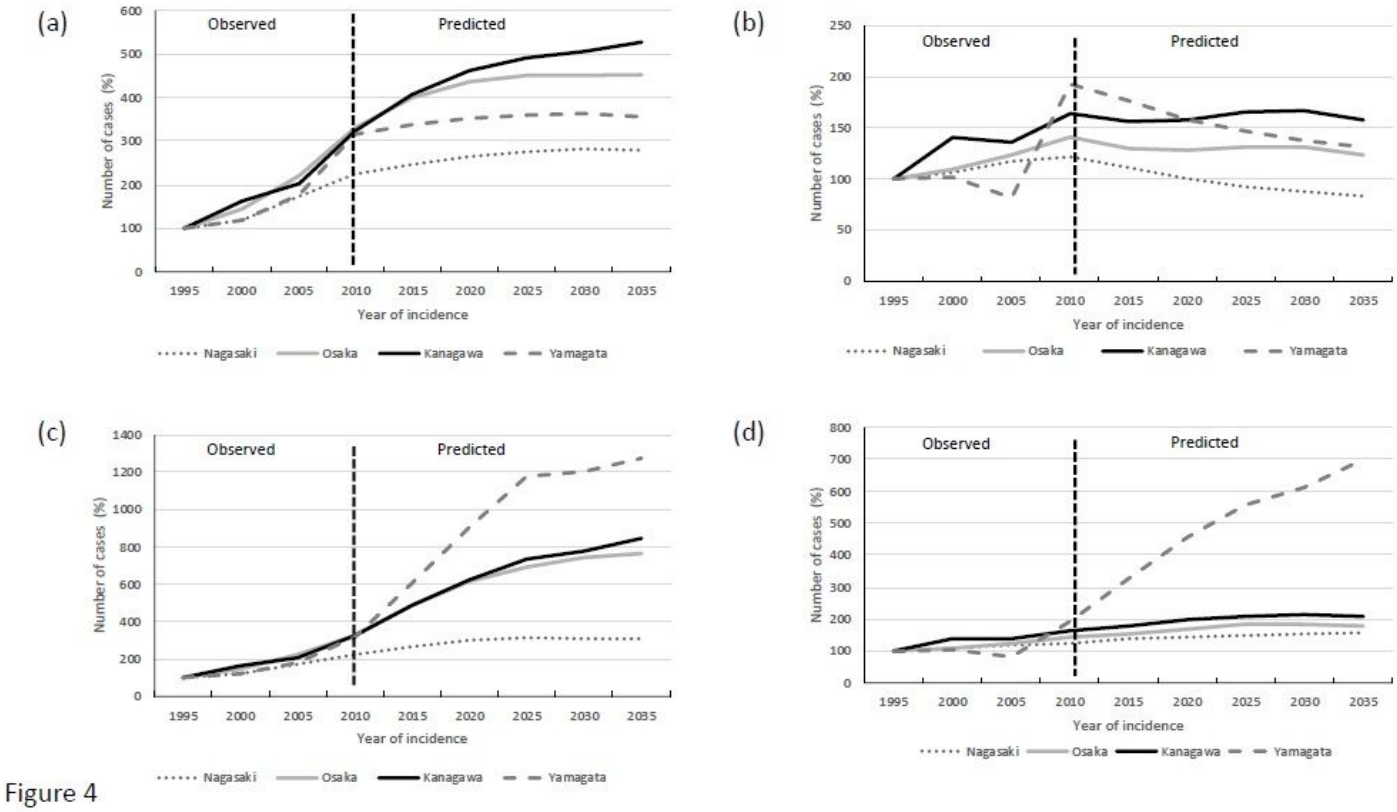

Figure 4

Figure 4

Predicted incidence rates of hematological malignancies in those aged 64 years and younger in the 2010 model and according to NORDPRED. Those of the exponential and Power 5 as link functions are shown.