Twenty-year incidence trend of hematologic malignancies in the Republic of Korea: 1999–2018

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Background
In this study, we presented the national cancer statistics on the incidence of hematologic malignancies in the Republic of Korea (ROK) over a period of 20 years, from 1999 to 2018.

Methods
We obtained data on the incidence of hematologic malignancies using the Korean Statistical Information Service (KOSIS). For each hematologic malignancy, the number of cases, crude incidence rate, and age-standardized incidence rate were calculated, and the statistical trends were confirmed by Poisson regression and Joinpoint regression analysis.

Results
All the investigated hematologic malignancies showed a statistically significant increase in incidence over 20 years. The 20-year trend of the age-standardized incidence rate was as follows: non-Hodgkin lymphoma [average annual percent change (AAPC)=2.26%, P-trend < 0.05], leukemia (AAPC=0.94%, P-trend < 0.05), myeloid leukemia (AAPC=1.44%, P-trend < 0.05), multiple myeloma (AAPC=3.05%, P-trend < 0.05), myeloproliferative disorders (AAPC=9.87%, P-trend < 0.05), myelodysplastic syndrome (AAPC=7.59%, P-trend < 0.05), malignant immunoproliferative diseases (AAPC=11.82%, P-trend < 0.05), lymphoid leukemia (AAPC=2.21%, P-trend < 0.05), and Hodgkin lymphoma (AAPC=4.04%, P < 0.05).

Conclusion
It was confirmed that the incidence of hematologic malignancies has increased significantly in the ROK over the past 20 years. This study can be used as foundational data source for future studies. In addition, it can aid in the necessary actions of predicting future incidences and establishing future healthcare policies.

Key Words Epidemiology, Hematologic neoplasms, Neoplasms, Registries, Statistics

INTRODUCTION

Since the national causes of death statistics were officially established in 1983, cancer has been the number one cause of death in the Republic of Korea (ROK) to date [1]. With the aging of the population, the incidence of cancer has also been increasing rapidly [2]. The Korea Central Cancer Registry (KCCR) registers cancer-related data and publishes books on cancer statistics every year. However, since the cancer statistics book mainly describes only the most common types of cancers, it is up to each researcher to analyze the statistical data of detailed cancers. This study intends to provide statistics on the incidence of hematologic malignancies over the past 20 years based on open national statistical data. The results of this study will be used as foundational data for future research and policy establishment on hematologic malignancies.
### MATERIALS AND METHODS

**Data collection**

We obtained data on hematologic malignancies from 1999 to 2018 through the Korean Statistical Information Service (KOSIS). KOSIS is a national statistical database operated by Statistics Korea. As a gateway for Korea’s official statistics, KOSIS offers a convenient one-stop service to a full range of major domestic statistics. Currently, official statistics produced by over 120 statistical agencies covering more than 500 subject matter are available on the KOSIS. Data are provided in an open form and can be easily accessed by anyone [3]. The data we obtained were as follows: the number of incidences of hematologic malignancies by 5-year age groups and sex, and the population structure for each year. The cancer data registered in the KOSIS were created by the KCCR, Ministry of Health and Welfare.

**Malignancy classification**

Hematologic malignancies were categorized according to the International Classification of Diseases for Oncology 3rd edition (ICD-O-3) [4]. For consistent comparison and convenience, these malignancies were converted to the International Classification of Diseases, 10th edition (ICD-10) [5]. Diseases not classified as malignant according to ICD-10 (myeloproliferative disorders and myelodysplastic syndromes) were referred to using ICD-O-3 codes without

### Table 1. The classification of hematologic malignancies according to the Republic of Korea’s Cancer Control Act and Statistics Act.

| Abbreviation                  | ICD-10 code (or ICD-O-3 code)                                                                 |
|-------------------------------|-----------------------------------------------------------------------------------------------|
| Non-Hodgkin lymphoma          | ICD-10 C82–C86, C96 Follicular lymphoma. Follicle center lymphoma. Other types of follicular lymphoma. Follicular lymphoma, unspecified. Small cell B-cell lymphoma. Mantle cell lymphoma. Diffuse large B-cell lymphoma. Lymphoblastic (diffuse) lymphoma. Burkitt lymphoma. Other non-follicular lymphoma. Non-follicular (diffuse) lymphoma, unspecified. Mature T/NK-cell lymphomas. Mycosis fungoides. Sézary disease. Peripheral T-cell lymphoma, not classified. Anaplastic large cell lymphoma. Cutaneous T-cell lymphoma, unspecified. Other mature T/NK-cell lymphomas. Mature T/NK-cell lymphomas, unspecified. Unspecified B-cell lymphoma. Mediastinal (thymic) large B-cell lymphoma. Other specified types of non-Hodgkin lymphoma. Non-Hodgkin lymphoma, unspecified. Other specified types of T/NK-cell lymphoma. Multifocal and unisystemic Langerhans-cell histiocytosis. Malignant mast cell neoplasm. Sarcoma of dendritic cells (accessory cells). Multifocal and unisystemic Langerhans-cell histiocytosis. Unifocal Langerhans-cell histiocytosis. Histiocytic sarcoma. Other specified. |
| Leukemia                      | ICD-10 C91-95 See myeloid leukemia, lymphoid leukemia, and leukemia unspecified.              |
| Myeloid leukemia              | ICD-10 C92–C94 Acute myeloblastic leukemia. Chronic myeloid leukemia. Myeloid sarcoma. Acute promyelocytic leukemia. Acute myelomonocytic leukemia. Acute myeloid leukemia. Other myeloid leukemia. Myeloid leukemia, unspecified. Acute monocytic leukemia. Chronic myelomonocytic leukemia. Myeloid leukemia, unspecified. Monocytic leukemia, unspecified. Acute erythroid leukemia. Acute megakaryoblastic leukemia. Mast cell leukemia. Acute pancytopenia with myelofibrosis. |
| Multiple myeloma              | ICD-10 C90 Multiple myeloma. Plasma cell leukemia. Extramedullary plasmacytoma. Solitary plasmacytoma. |
| Myeloproliferative disorders  | ICD-0-3 M995 /3, M996 /3, M997 /3 Pancytopenia vera. Chronic myeloproliferative disease. Essential thrombocytopenia. Osteomyelofibrosis. Chronic eosinophilic leukemia. |
| Myelodysplastic syndrome       | ICD-0-3 M9980/3, M9985/3, M9989/3 Myelodysplastic syndromes.                                   |
| Malignant immunoproliferative diseases | ICD-10 C88 Waldenström macroglobulinemia. Heavy chain disease. Immunoproliferative small intestinal disease. Extramedullary zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT-lymphoma). Other malignant immunoproliferative diseases. Malignant immunoproliferative disease, unspecified. |
| Lymphoid leukemia              | ICD-10 C91 Acute lymphoblastic leukemia. Chronic lymphocytic leukemia of B-cell type. Prolymphocytic leukemia of B-cell type. Hairy cell leukemia. Adult T-cell lymphoma/leukemia. Prolymphocytic leukemia of T-cell type. Mature B-cell leukemia Burkitt-type. Other lymphoid leukemia. Lymphoid leukemia, unspecified. |
| Hodgkin lymphoma               | ICD-10 C81 Hodgkin lymphoma. Other Hodgkin lymphoma. Hodgkin lymphoma, unspecified.           |
| Leukemia unspecified           | ICD-10 C95 Acute leukemia of unspecified cell type. Chronic leukemia of unspecified cell type. Leukemia, unspecified. |
conversion. The classification of hematologic malignancies according to the ICD-10 was as follows: non-Hodgkin lymphoma (C82-86, C96), leukemia (C91-95), myeloid leukemia (C92-94), multiple myeloma (C90), myeloproliferative disorders (ICD-O-3 M995_/3, M996_/3, M997_/3), myelodysplastic syndrome (ICD-O-3 M9980/3, M9981/3, M9982/3, M9983/3, M9985/3, M9986/3, M9987/3, M9988/3, M9989/3), malignant immunoproliferative diseases (C88), lymphoid leukemia (C91), Hodgkin lymphoma (C81), and leukemia of unspecified cell type (C95) (Table 1).

Table 2. The incidence case number of non-Hodgkin lymphoma and trend in crude incidence rates and age-standardized incidence rates per million population in the Republic of Korea from 1999 to 2018.

| Years | Men | Women | Total | AAPC (%) | CIR  | ASRb | AAPC (%) | ASRb |
|-------|-----|-------|-------|----------|------|-------|----------|-------|
| 1999  | 1,252 | 851 | 2,103 | 5.16b | 44.58964 | 45.47851 | 2.26b | 1.023b |
| 2000  | 1,222 | 816 | 2,038 | 42.87447 | 42.87447 | 42.87447 | 42.87447 |
| 2001  | 1,332 | 905 | 2,237 | 46.72385 | 46.72385 | 46.72385 | 46.72385 |
| 2002  | 1,322 | 919 | 2,241 | 46.56351 | 46.56351 | 46.56351 | 46.56351 |
| 2003  | 1,375 | 981 | 2,356 | 48.77000 | 48.77000 | 48.77000 | 48.77000 |
| 2004  | 1,511 | 1,057 | 2,568 | 52.96449 | 52.96449 | 52.96449 | 52.96449 |
| 2005  | 1,505 | 1,091 | 2,596 | 53.32453 | 53.32453 | 53.32453 | 53.32453 |
| 2006  | 1,651 | 1,121 | 2,772 | 56.70216 | 56.70216 | 56.70216 | 56.70216 |
| 2007  | 1,741 | 1,194 | 2,935 | 59.73904 | 59.73904 | 59.73904 | 59.73904 |
| 2008  | 1,745 | 1,256 | 3,001 | 60.74327 | 60.74327 | 60.74327 | 60.74327 |
| 2009  | 1,876 | 1,362 | 3,238 | 65.20764 | 65.20764 | 65.20764 | 65.20764 |
| 2010  | 1,954 | 1,429 | 3,383 | 67.82302 | 67.82302 | 67.82302 | 67.82302 |
| 2011  | 2,110 | 1,551 | 3,661 | 70.05712 | 70.05712 | 70.05712 | 70.05712 |
| 2012  | 2,194 | 1,580 | 3,774 | 74.96227 | 74.96227 | 74.96227 | 74.96227 |
| 2013  | 2,314 | 1,691 | 4,005 | 79.21446 | 79.21446 | 79.21446 | 79.21446 |
| 2014  | 2,400 | 1,713 | 4,113 | 81.02333 | 81.02333 | 81.02333 | 81.02333 |
| 2015  | 2,560 | 1,884 | 4,444 | 87.21982 | 87.21982 | 87.21982 | 87.21982 |
| 2016  | 2,805 | 2,019 | 4,824 | 94.37917 | 94.37917 | 94.37917 | 94.37917 |
| 2017  | 2,736 | 2,080 | 4,816 | 94.00613 | 94.00613 | 94.00613 | 94.00613 |
| 2018  | 3,001 | 2,215 | 5,216 | 101.67467 | 101.67467 | 101.67467 | 101.67467 |

a) Calculated by defining the 2000 mid-year Korean population (July 1, 2000) as the standard population. b) Statistically significant trend (P<0.05).

Abbreviations: AAPC, average annual percent change; ASR, age-standardized incidence rate; CIR, crude incidence rate; IRR, incidence rate ratio.

Fig. 1. Annual incidence of non-Hodgkin lymphoma in the Republic of Korea. Number of non-Hodgkin lymphoma cases (A). Crude and age-standardized incidence rate of non-Hodgkin lymphoma per million using the 2000 Korean standard population (B). b) Comparing 1999 and 2018. b) Average annual percent change by Joinpoint regression analysis. b) Incidence rate ratio per year from 1999 to 2018 as calculated by Poisson regression.

Abbreviations: AAPC, average annual percent change; ASR, age-standardized incidence rate; CI, confidence interval; CIR, crude incidence rate; IRR, incidence rate ratio.
Statistical analysis

From the collected data, the number of incidence cases of each hematologic malignancy by year was determined. The average annual percent change (AAPC) was analyzed using the Joinpoint regression model which is a trend analysis software developed by the US National Cancer Institute [6]. This method describes changes in data trends by connecting several different line segments on a logarithmic scale at Joinpoints. Tests of significance were performed using the Monte Carlo permutation method. An AAPC for each line segment and the corresponding 95% confidence interval (CI) were estimated. The AAPC is tested to determine whether a difference exists from the null hypothesis of no change. In the final model, each Joinpoint informs a statistically significant change in trends, and each of these trends is described by an AAPC [7]. The crude incidence rate (CIR) for each year and the age-standardized incidence rate (ASR) was calculated by defining the 2000 mid-year population (the population count as of July 1, 2000) as the standard population. From 1998 to 2018, each incidence ratio (IRR) was calculated according to the one-year increase through Poisson regression, and the 95% CI and P-value were calculated. The CIRs and ASRs were rounded to six decimal places. Poisson regression was performed by converting the number of cases per 10 million people into an integer. Poisson regression analyses were performed using SPSS (version 27.0, IBM Corp., Armonk, NY, USA), and the significance level was set at $P<0.05$.

RESULTS

Non-Hodgkin lymphoma

The number of newly diagnosed NHL cases increased by 148.0%, from 2,103 in 1999 to 5,216 in 2018. The AAPC in incidence cases during this period was 5.16%, and the trend was statistically significant. Within a one-year increase, the IRR increased significantly to 1.052 (95% CI, 1.051–1.054; $P<0.001$). The CIR per million population increased by 128.0% from 44.59 in 1999 to 101.67 in 2018. Within a one-year increase, the IRR increased significantly to 1.047 (95% CI, 1.044–1.051; $P<0.001$). The ASR per million population increased by 47.1% from 45.48 in 1999 to 66.88 in 2018. Within a one-year increase, the IRR increased significantly to 1.023 (95% CI, 1.019–1.026; $P<0.001$). The AAPC in the ASR during this period was 2.26%, and the trend was statistically significant ($P<0.05$) (Table 2, Fig. 1).

Leukemia

The number of newly diagnosed leukemia cases increased by 64.5%, from 2,124 in 1999 to 3,494 in 2018. The AAPC in incidence cases during this period was 2.89%, and the trend was statistically significant. Within a one-year increase,

### Table 3. The incidence case number of leukemia and trend in crude incidence rates and age-standardized incidence rates per million population in the Republic of Korea from 1999 to 2018.

| Years | N of cases | CIR | ASR$^{a}$ | ASR$^{b}$ |
|-------|------------|-----|-----------|-----------|
|       | Men | Women | Total | AAPC (%) | AAPC (%) | CIR | ASR$^{a}$ | ASR$^{b}$ |
|       |     |       |       |         |         |     |       |         |          |
| 1999  | 1,188 | 936 | 2,124 | 2.89$^{b}$ | 45.03490 | 45.45859 | 0.94$^{b}$ | 1.009$^{b}$ |
| 2000  | 1,105 | 901 | 2,006 |          | 42.20127 | 42.20127 | | |
| 2001  | 1,210 | 998 | 2,208 |          | 46.11813 | 45.74454 | | |
| 2002  | 1,333 | 987 | 2,320 |          | 48.20705 | 47.29788 | | |
| 2003  | 1,247 | 1,034 | 2,281 |          | 47.21748 | 45.74993 | | |
| 2004  | 1,321 | 1,051 | 2,372 |          | 48.92203 | 46.79217 | | |
| 2005  | 1,332 | 1,015 | 2,347 |          | 48.20981 | 45.83396 | | |
| 2006  | 1,342 | 1,102 | 2,444 |          | 49.99281 | 47.05533 | | |
| 2007  | 1,388 | 1,090 | 2,478 |          | 50.43725 | 46.91184 | | |
| 2008  | 1,455 | 1,145 | 2,600 |          | 52.62663 | 48.27268 | | |
| 2009  | 1,504 | 1,212 | 2,716 |          | 54.69548 | 48.90856 | | |
| 2010  | 1,572 | 1,186 | 2,758 |          | 55.29291 | 48.55470 | | |
| 2011  | 1,618 | 1,283 | 2,901 |          | 57.89093 | 50.27748 | | |
| 2012  | 1,621 | 1,246 | 2,867 |          | 56.94670 | 48.31113 | | |
| 2013  | 1,754 | 1,317 | 3,071 |          | 60.74097 | 50.21212 | | |
| 2014  | 1,785 | 1,324 | 3,109 |          | 61.24520 | 50.30621 | | |
| 2015  | 1,855 | 1,433 | 3,288 |          | 64.53168 | 52.86386 | | |
| 2016  | 1,995 | 1,438 | 3,433 |          | 67.16495 | 54.19071 | | |
| 2017  | 1,934 | 1,454 | 3,388 |          | 66.13222 | 51.23865 | | |
| 2018  | 2,037 | 1,457 | 3,494 |          | 68.10799 | 52.44745 | | |

$^{a}$Calculated by defining the 2000 mid-year Korean population (July 1, 2000) as the standard population. $^{b}$Statistically significant trend ($P<0.05$).

Abbreviations: AAPC, average annual percent change; ASR, age-standardized incidence rate; CIR, crude incidence rate; IRR, incidence rate ratio.
the IRR increased significantly to 1.029 (95% CI, 1.028–1.031; \(P<0.001\)). The CIR per million population increased by 51.3% from 45.03 in 1999 to 68.11 in 2018. Within a one-year increase, the IRR increased significantly to 1.025 (95% CI, 1.021–1.028; \(P<0.001\)). The ASR per million population increased by 15.4% from 45.46 in 1999 to 52.45 in 2018. Within a one-year increase, the IRR increased significantly to 1.009 (95% CI, 1.006–1.013; \(P<0.001\)). The AAPC in the ASR during this period was 0.94%, and the trend was statistically significant (\(P<0.05\)) (Table 3, Fig. 2).

**Fig. 2.** Annual incidence of leukemia in the Republic of Korea. Number of leukemia cases (A). Crude and age-standardized incidence rate of leukemia per million using the 2000 Korean standard population (B). a)Comparing to 1999 and 2018. b)Average annual percent change by Joinpoint regression analysis. c)Incidence rate ratio per year from 1999 to 2018 as calculated by Poisson regression.

**Table 4.** The incidence case number of myeloid leukemia and trend in crude incidence rates and age-standardized incidence rates per million population in the Republic of Korea from 1999 to 2018.

| Years | N of cases | CIR | ASR\(^{a}\) | ASR\(^{b}\) |
|-------|------------|-----|-------------|-------------|
|       | Men | Women | Total | AAPC (%) | 25.09991 | 26.21218 | 1.44\(^{b}\) | 1.014\(^{b}\) |
| 1999  | 696 | 526   | 1,222 | 3.81\(^{b}\) | 24.65597 | 24.65597 |
| 2000  | 630 | 542   | 1,172 | 4.16\(^{b}\) | 27.71683 | 27.39936 |
| 2001  | 720 | 607   | 1,327 | 3.90\(^{b}\) | 28.96579 | 28.20531 |
| 2002  | 806 | 588   | 1,394 | 3.94\(^{b}\) | 31.16408 | 29.40229 |
| 2003  | 768 | 641   | 1,409 | 4.00\(^{b}\) | 30.17478 | 28.04162 |
| 2004  | 853 | 658   | 1,511 | 4.20\(^{b}\) | 31.01027 | 28.33077 |
| 2005  | 812 | 657   | 1,469 | 4.48\(^{b}\) | 31.52837 | 28.48103 |
| 2006  | 839 | 677   | 1,516 | 4.52\(^{b}\) | 34.20731 | 30.20098 |
| 2007  | 873 | 676   | 1,549 | 4.64\(^{b}\) | 34.93986 | 30.13031 |
| 2008  | 947 | 743   | 1,690 | 4.90\(^{b}\) | 36.04665 | 30.26675 |
| 2009  | 980 | 755   | 1,735 | 5.30\(^{b}\) | 38.41435 | 32.02027 |
| 2010  | 1,050|748 | 1,798 | 5.57\(^{b}\) | 36.86662 | 29.73230 |
| 2011  | 1,084|841 | 1,925 | 6.00\(^{b}\) | 41.87191 | 32.97980 |
| 2012  | 1,060|787 | 1,847 | 6.24\(^{b}\) | 41.23069 | 32.13509 |
| 2013  | 1,238|879 | 2,117 | 7.00\(^{b}\) | 44.13983 | 34.03683 |
| 2014  | 1,231|862 | 2,093 | 7.10\(^{b}\) | 44.95923 | 33.80285 |
| 2015  | 1,285|964 | 2,249 | 7.60\(^{b}\) | 45.22678 | 32.37206 |
| 2016  | 1,384|914 | 2,298 | 8.10\(^{b}\) | 47.27014 | 34.03950 |
| 2017  | 1,345|972 | 2,317 | 8.20\(^{b}\) | 45.03 |
| 2018  | 1,435|990 | 2,425 | 8.30\(^{b}\) | 52.45 |

*Calculated by defining the 2000 mid-year Korean population (July 1, 2000) as the standard population. \(^b\)Statistically significant trend (\(P<0.05\)).

Abbreviations: AAPC, average annual percent change; ASR, age-standardized incidence rate; CIR, crude incidence rate; IRR, incidence rate ratio.
Myeloid leukemia

The number of newly diagnosed myeloid leukemia cases increased by 98.4%, from 1,222 in 1999 to 2,425 in 2018. The AAPC in incidence cases during this period was 3.81%, and the trend was statistically significant. Within a one-year increase, the IRR increased significantly to 1.038 (95% CI, 1.036–1.040; P < 0.001). The CIR per million population increased by 82.4% from 25.91 in 1999 to 47.27 in 2018. Within a one-year increase, the IRR increased significantly to 1.034 (95% CI, 1.029–1.038; P < 0.001). The ASR per million pop-

![Fig. 3. Annual incidence of myeloid leukemia in the Republic of Korea. Number of myeloid leukemia cases (A). Crude and age-standardized incidence rate of myeloid leukemia per million using the 2000 Korean standard population (B). a)Comparing 1999 and 2018. b)Average annual percent change by Joinpoint regression analysis. c)Incidence rate ratio per year from 1999 to 2018 as calculated by Poisson regression. AAbbreviations: AAPC, average annual percent change; ASR, age-standardized incidence rate; CI, confidence interval; CIR, crude incidence rate; IRR, incidence rate ratio.]

| Years | Men | Women | Total | AAPC (%) | CIR | ASR<sup>a</sup> | ASR<sup>b</sup> |
|-------|-----|-------|-------|----------|-----|----------------|----------------|
|       |     |       |       |          |     | AAPC (%) | IRR (per yr) |
| 1999  | 257 | 212   | 469   | 7.33<sup>b</sup> | 9.94415 | 10.22460 | 3.05<sup>b</sup> |
| 2000  | 275 | 217   | 492   | 10.35046 | 10.35046 |
| 2001  | 313 | 251   | 564   | 11.78017 | 11.46171 |
| 2002  | 328 | 239   | 567   | 11.78164 | 11.07893 |
| 2003  | 331 | 285   | 616   | 12.75141 | 11.55148 |
| 2004  | 362 | 315   | 677   | 13.96299 | 12.21290 |
| 2005  | 407 | 387   | 794   | 16.30958 | 13.71200 |
| 2006  | 386 | 384   | 770   | 15.75060 | 12.94935 |
| 2007  | 459 | 430   | 889   | 18.09472 | 14.16175 |
| 2008  | 492 | 425   | 917   | 18.56101 | 14.26485 |
| 2009  | 575 | 462   | 1,037 | 20.88336 | 15.34012 |
| 2010  | 569 | 510   | 1,079 | 21.63200 | 15.12175 |
| 2011  | 610 | 469   | 1,079 | 21.53199 | 14.62146 |
| 2012  | 706 | 589   | 1,295 | 25.72235 | 17.05821 |
| 2013  | 704 | 646   | 1,350 | 26.70150 | 16.71056 |
| 2014  | 711 | 649   | 1,350 | 27.97304 | 16.87157 |
| 2015  | 772 | 704   | 1,476 | 28.96860 | 16.91477 |
| 2016  | 845 | 708   | 1,553 | 30.38368 | 17.22267 |
| 2017  | 864 | 779   | 1,643 | 32.07601 | 17.32490 |
| 2018  | 927 | 792   | 1,719 | 33.50820 | 17.51734 |

<sup>a</sup>Calculated by defining the 2000 mid-year Korean population (July 1, 2000) as the standard population. <sup>b</sup>Statistically significant trend (P < 0.05). Abbreviations: AAPC, average annual percent change; ASR, age-standardized incidence rate; CIR, crude incidence rate; IRR, incidence rate ratio.
Incidence of hematologic malignancies increased by 29.9% from 26.21 in 1999 to 34.04 in 2018. Within a one-year increase, the IRR increased significantly to 1.014 (95% CI, 1.010–1.019; P < 0.001). The AAPC in the ASR during this period was 1.44%, and the trend was statistically significant (P < 0.05) (Table 4, Fig. 3).

**Multiple myeloma**

The number of newly diagnosed MM cases increased by 266.5% from 469 in 1999 to 1,719 in 2018. The AAPC in incidence cases during this period was 7.33%, and the trend was statistically significant. Within a one-year increase, the IRR increased significantly to 1.071 (95% CI, 1.069–1.074; Fig. 4).

### Table 6. The incidence case number of myeloproliferative disorders and trend in crude incidence rates and age-standardized incidence rates per million population in the Republic of Korea from 1999 to 2018.

| Years | Men | Women | Total | CIR | ASR\(^a\) | ASR\(^b\) |
|-------|-----|-------|-------|-----|----------|----------|
|       |     |       |       |     |          |          |
| 1999  | 55  | 55    | 110   | 13.28\(^d\) | 2.33232  | 2.38291  |
| 2000  | 65  | 75    | 140   | 2.94525 | 2.94525  | 2.94525  |
| 2001  | 86  | 92    | 178   | 3.71766 | 3.64427  | 3.64427  |
| 2002  | 135 | 116   | 251   | 5.21550 | 4.96014  | 4.96014  |
| 2003  | 200 | 154   | 354   | 7.32792 | 6.76541  | 6.76541  |
| 2004  | 194 | 169   | 363   | 7.48680 | 6.68212  | 6.68212  |
| 2005  | 283 | 242   | 525   | 10.78404| 9.50474  | 9.50474  |
| 2006  | 282 | 245   | 527   | 10.7796 | 9.23111  | 9.23111  |
| 2007  | 365 | 287   | 652   | 13.27082| 11.12117 | 11.12117 |
| 2008  | 370 | 327   | 697   | 14.10798| 11.45405 | 11.45405 |
| 2009  | 409 | 402   | 811   | 16.33212| 12.78754 | 12.78754 |
| 2010  | 431 | 401   | 832   | 16.68010| 12.76728 | 12.76728 |
| 2011  | 506 | 418   | 924   | 18.43892| 13.80286 | 13.80286 |
| 2012  | 477 | 444   | 921   | 18.29366| 13.27581 | 13.27581 |
| 2013  | 509 | 456   | 965   | 19.08663| 13.55994 | 13.55994 |
| 2014  | 595 | 481   | 1,076 | 21.19647| 14.81846 | 14.81846 |
| 2015  | 621 | 511   | 1,132 | 22.21711| 15.05132 | 15.05132 |
| 2016  | 640 | 620   | 1,260 | 24.65128| 16.13719 | 16.13719 |
| 2017  | 723 | 584   | 1,307 | 25.51204| 16.36598 | 16.36598 |
| 2018  | 809 | 739   | 1,548 | 30.17492| 19.00324 | 19.00324 |

\(^a\)Calculated by defining the 2000 mid-year Korean population (July 1, 2000) as the standard population. \(^b\)Statistically significant trend (P < 0.05). Abbreviations: AAPC, average annual percent change; ASR, age-standardized incidence rate; CIR, crude incidence rate; IRR, incidence rate ratio.
The CIR per million population increased by 237.1% from 9.94 in 1999 to 33.51 in 2018. Within a one-year increase, the IRR increased significantly to 1.067 (95% CI, 1.023–1.036; \( P < 0.001 \)). The ASR per million population increased by 71.4% from 10.22 in 1999 to 17.52 in 2018. Within a one-year increase, the IRR increased significantly to 1.030 (95% CI, 1.023–1.036; \( P < 0.001 \)). The AAPC in the ASR during this period was 3.05%, and the trend was statistically significant (\( P < 0.05 \)) (Table 5, Fig. 4).

### Myeloproliferative disorders

The number of newly diagnosed myeloproliferative dis-

### Table 7

The incidence case number of myelodysplastic syndrome and trend in crude incidence rates and age-standardized incidence rates per million population in the Republic of Korea from 1999 to 2018.

| Years | N of cases | CIR | ASR$^a$ | ASR$^b$ |
|-------|------------|-----|---------|---------|
|       | Men | Women | Total | AAPC (%) |       | AAPC (%) | IRR (per yr) |
|-------|-----|-------|-------|---------|-------|---------|--------------|
| 1999  | 88  | 51    | 139   | 11.49   | 2.94720 | 2.99630 | 7.59          |
| 2000  | 90  | 77    | 167   | 3.51    | 3.51327 | 3.51327 | 7.59          |
| 2001  | 129 | 91    | 220   | 4.59    | 4.59510 | 4.48965 | 7.59          |
| 2002  | 165 | 97    | 262   | 5.44    | 5.44407 | 5.22327 | 7.59          |
| 2003  | 234 | 160   | 394   | 8.16    | 8.15593 | 7.54460 | 7.59          |
| 2004  | 253 | 165   | 418   | 8.62    | 8.62117 | 7.76107 | 7.59          |
| 2005  | 280 | 190   | 470   | 9.65    | 9.65429 | 8.59289 | 7.59          |
| 2006  | 299 | 190   | 489   | 10.00   | 10.00265| 8.63391 | 7.59          |
| 2007  | 314 | 250   | 564   | 11.48   | 11.47967| 9.47229 | 7.59          |
| 2008  | 377 | 268   | 645   | 13.06   | 13.05545| 10.52395| 7.59          |
| 2009  | 446 | 280   | 726   | 14.62   | 14.62037| 11.37083| 7.59          |
| 2010  | 479 | 305   | 784   | 15.72   | 15.71778| 11.62239| 7.59          |
| 2011  | 486 | 390   | 876   | 17.48   | 17.48103| 12.72050| 7.59          |
| 2012  | 521 | 318   | 839   | 16.67   | 16.66490| 11.46736| 7.59          |
| 2013  | 543 | 396   | 939   | 18.57   | 18.57238| 12.55258| 7.59          |
| 2014  | 600 | 386   | 986   | 19.42   | 19.42354| 12.77860| 7.59          |
| 2015  | 626 | 407   | 1,033 | 20.27   | 20.27410| 13.04959| 7.59          |
| 2016  | 742 | 428   | 1,170 | 22.90   | 22.89047| 13.84107| 7.59          |
| 2017  | 707 | 451   | 1,158 | 22.60   | 22.60363| 13.39313| 7.59          |
| 2018  | 828 | 537   | 1,365 | 26.61   | 26.60773| 15.30694| 7.59          |

$^a$Calculated by defining the 2000 mid-year Korean population (July 1, 2000) as the standard population. $^b$Statistically significant trend (\( P < 0.05 \)).

Abbreviations: AAPC, average annual percent change; ASR, age-standardized incidence rate; CIR, crude incidence rate; IRR, incidence rate ratio.
Incidence of hematologic malignancies

Fig. 6. Annual incidence of myelodysplastic syndrome in the Republic of Korea. Number of myelodysplastic syndrome cases (A). Crude and age-standardized incidence rate of myelodysplastic syndrome per million using the 2000 Korean standard population (B). a)Comparing 1999 and 2018. b)Average annual percent change by Joinpoint regression analysis. c)Incidence rate ratio per year from 1999 to 2018 as calculated by Poisson regression.

Abbreviations: AAPC, average annual percent change; ASR, age-standardized incidence rate; CIR, crude incidence rate; IRR, incidence rate ratio.

Table 8. The incidence case number of malignant immunoproliferative diseases and trend in crude incidence rates and age-standardized incidence rates per million population in the Republic of Korea from 1999 to 2018.

| Years | N of cases | CIR       | ASR<sup>a</sup> | ASR<sup>b</sup> |
|-------|------------|-----------|-----------------|-----------------|
|       | Men | Women | Total | AAPC (%) | 20.1427 | 2.04994 | AAPC (%) | IRR (per yr) |
| 1999  | 45  | 50   | 95   | 14.76<sup>b</sup> | 2.01427 | 2.04994 | 11.82<sup>b</sup> | 1.090<sup>b</sup> |
| 2000  | 39  | 39   | 78   | 1.64093  | 1.64093 | 1.60931 | 1.09031 | 1.09031 |
| 2001  | 49  | 30   | 79   | 2.06780  | 2.06780 | 2.06780 | 2.06780 | 2.06780 |
| 2002  | 98  | 96   | 194  | 4.03111  | 3.87658 | 3.87658 | 3.87658 | 3.87658 |
| 2003  | 165 | 171  | 336  | 6.95531  | 6.50034 | 6.50034 | 6.50034 | 6.50034 |
| 2004  | 175 | 174  | 349  | 7.19806  | 6.56316 | 6.56316 | 6.56316 | 6.56316 |
| 2005  | 198 | 252  | 450  | 9.24347  | 8.26204 | 8.26204 | 8.26204 | 8.26204 |
| 2006  | 212 | 272  | 484  | 9.90038  | 8.66932 | 8.66932 | 8.66932 | 8.66932 |
| 2007  | 227 | 250  | 477  | 9.70887  | 8.37596 | 8.37596 | 8.37596 | 8.37596 |
| 2008  | 251 | 327  | 578  | 11.69930 | 9.91273 | 9.91273 | 9.91273 | 9.91273 |
| 2009  | 348 | 386  | 734  | 14.78147 | 12.09930 | 12.09930 | 12.09930 | 12.09930 |
| 2010  | 315 | 416  | 731  | 14.65523 | 11.92735 | 11.92735 | 11.92735 | 11.92735 |
| 2011  | 348 | 480  | 828  | 16.52316 | 12.85307 | 12.85307 | 12.85307 | 12.85307 |
| 2012  | 413 | 471  | 884  | 17.55573 | 13.52600 | 13.52600 | 13.52600 | 13.52600 |
| 2013  | 412 | 509  | 921  | 18.21636 | 13.44186 | 13.44186 | 13.44186 | 13.44186 |
| 2014  | 437 | 507  | 944  | 18.59616 | 13.78266 | 13.78266 | 13.78266 | 13.78266 |
| 2015  | 459 | 492  | 951  | 18.66473 | 13.50497 | 13.50497 | 13.50497 | 13.50497 |
| 2016  | 592 | 603  | 1,195| 23.37958 | 16.40845 | 16.40845 | 16.40845 | 16.40845 |
| 2017  | 574 | 609  | 1,183| 23.09162 | 15.98123 | 15.98123 | 15.98123 | 15.98123 |
| 2018  | 601 | 710  | 1,311| 25.55512 | 17.46422 | 17.46422 | 17.46422 | 17.46422 |

<sup>a</sup>Calculated by defining the 2000 mid-year Korean population (July 1, 2000) as the standard population. <sup>b</sup>Statistically significant trend ($P<0.05$).

Abbreviations: AAPC, average annual percent change; ASR, age-standardized incidence rate; CIR, crude incidence rate; IRR, incidence rate ratio.
period was 9.87%, and the trend was statistically significant ($P<0.05$) (Table 6, Fig. 5).

**Myelodysplastic syndrome**

The number of newly diagnosed myelodysplastic syndromes increased by 882.0% from 139 in 1999 to 1,365 in 2018. The AAPC in incidence cases during this period was 11.49%, and the trend was statistically significant. Within a one-year increase, the IRR increased significantly to 1.099 (95% CI, 1.095–1.102; $P<0.001$). The CIR per million population increased by 802.0% from 2.95 in 1999 to 26.61 in 2018. Within a one-year increase, the IRR increased sig-

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**Table 9.** The incidence case number of lymphoid leukemia and trend in crude incidence rates and age-standardized incidence rates per million population in the Republic of Korea from 1999 to 2018.

| Years | N of cases | CIR | ASR<sup>a</sup> | ASR<sup>b</sup> |
|-------|------------|-----|-----------------|-----------------|
|       | Men | Women | Total | AAPC (%) |       | AAPC (%) | IRR (per yr) |
| 1999  | 316 | 234  | 550   | 2.77<sup>b</sup> | 11.66158 | 11.61904 | 2.21<sup>b</sup> |
| 2000  | 280 | 216  | 496   | 10.43461 | 10.43461 |
| 2001  | 316 | 228  | 544   | 11.36244 | 11.42331 |
| 2002  | 335 | 222  | 557   | 11.57385 | 11.76349 |
| 2003  | 303 | 248  | 551   | 11.40589 | 11.63373 |
| 2004  | 301 | 232  | 533   | 10.99302 | 11.23614 |
| 2005  | 328 | 226  | 554   | 11.37973 | 11.87085 |
| 2006  | 331 | 272  | 603   | 12.33456 | 12.82142 |
| 2007  | 344 | 260  | 604   | 12.29383 | 12.87728 |
| 2008  | 349 | 260  | 609   | 12.32678 | 12.97963 |
| 2009  | 373 | 289  | 662   | 13.33152 | 13.75206 |
| 2010  | 361 | 281  | 642   | 12.87094 | 13.44971 |
| 2011  | 363 | 305  | 668   | 13.30028 | 13.76827 |
| 2012  | 388 | 312  | 700   | 13.90397 | 14.16193 |
| 2013  | 371 | 314  | 685   | 13.54854 | 13.57623 |
| 2014  | 434 | 326  | 760   | 14.97149 | 15.01366 |
| 2015  | 456 | 359  | 815   | 15.99553 | 16.01589 |
| 2016  | 481 | 383  | 864   | 16.90373 | 16.92706 |
| 2017  | 463 | 365  | 828   | 16.16218 | 16.11329 |
| 2018  | 465 | 352  | 817   | 15.92565 | 15.53953 |

<sup>a</sup>Calculated by defining the 2000 mid-year Korean population (July 1, 2000) as the standard population. <sup>b</sup>Statistically significant trend ($P<0.05$).

Abbreviations: AAPC, average annual percent change; ASR, age-standardized incidence rate; CIR, crude incidence rate; IRR, incidence rate ratio.
Incidence of hematologic malignancies

Fig. 8. Annual incidence of lymphoid leukemia in the Republic of Korea. Number of lymphoid leukemia cases (A). Crude and age-standardized incidence rate of lymphoid leukemia per million using the 2000 Korean standard population (B). a) Comparing 1999 and 2018. b) Average annual percent change by Joinpoint regression analysis. c) Incidence rate ratio per year from 1999 to 2018 as calculated by Poisson regression. Abbreviations: AAPC, average annual percent change; ASR, age-standardized incidence rate; CI, confidence interval; CIR, crude incidence rate; IRR, incidence rate ratio.

In the ROK, hematologic malignancies have a relatively low proportion of all cancers. None of the hematologic malignancies were among the top 10 types of cancers with the highest incidence in the ROK in 2018. Non-Hodgkin’s lymphoma (5,216 cases), leukemia (3,494 cases), and multiple myeloma (1,719 cases) were ranked 11th, 14th, and 20th in the ROK in 2018, respectively [5]. The number of deaths in the ROK from non-Hodgkin lymphoma, leukemia, and multiple myeloma was 2,015, 1,911, and 961, respectively, in 2019, ranking 9th, 10th, and 16th in total cancer deaths, all in respective order [1]. Since the Annual Report of Cancer
Table 10. The incidence case number of Hodgkin lymphoma, trend in crude incidence rates, and age-standardized incidence rates per million population in the Republic of Korea from 1999 to 2018.

| Years | N of cases | CIR | ASR\(^a\) | ASR\(^b\) |
|-------|------------|-----|-----------|-----------|
|       | Men        | Women | Total     | AAPC (%)  | AAPC (%) | IRR (per yr) |
| 1999  | 86         | 37   | 123       | 4.96\(^b\) | 2.60795  | 2.63335      |
| 2000  | 90         | 44   | 134       | 5.10903   | 2.81903  | 2.81903      |
| 2001  | 100        | 48   | 148       | 3.09125   | 3.07055  | 3.07055      |
| 2002  | 83         | 62   | 145       | 3.01294   | 2.98565  | 2.98565      |
| 2003  | 112        | 46   | 158       | 3.27065   | 3.22256  | 3.22256      |
| 2004  | 145        | 59   | 204       | 4.20746   | 4.14143  | 4.14143      |
| 2005  | 105        | 53   | 158       | 3.24548   | 3.09513  | 3.09513      |
| 2006  | 109        | 68   | 177       | 3.62059   | 3.47111  | 3.47111      |
| 2007  | 131        | 74   | 205       | 4.17257   | 3.92396  | 3.92396      |
| 2008  | 131        | 88   | 219       | 4.43278   | 4.23004  | 4.23004      |
| 2009  | 146        | 74   | 220       | 4.43041   | 4.16283  | 4.16283      |
| 2010  | 171        | 77   | 248       | 4.97195   | 4.57967  | 4.57967      |
| 2011  | 168        | 98   | 266       | 5.30817   | 5.12413  | 5.12413      |
| 2012  | 179        | 90   | 269       | 5.34310   | 5.02603  | 5.02603      |
| 2013  | 171        | 93   | 264       | 5.22163   | 4.82687  | 4.82687      |
| 2014  | 170        | 111  | 281       | 5.53551   | 5.16737  | 5.16737      |
| 2015  | 174        | 98   | 272       | 5.33839   | 4.95872  | 4.95872      |
| 2016  | 205        | 110  | 315       | 6.16282   | 5.66606  | 5.66606      |
| 2017  | 172        | 117  | 289       | 5.64115   | 5.47652  | 5.47652      |
| 2018  | 181        | 118  | 299       | 5.82836   | 5.27499  | 5.27499      |

\(^a\)Calculated by defining the 2000 mid-year Korean population (July 1, 2000) as the standard population. \(^b\)Statistically significant trend (\(P<0.05\)).

Abbreviations: AAPC, average annual percent change; ASR, age-standardized incidence rate; CIR, crude incidence rate; IRR, incidence rate ratio.

Fig. 9. Annual incidence of Hodgkin lymphoma in the Republic of Korea. Number of Hodgkin lymphoma cases (A). Crude and age-standardized incidence rate of Hodgkin lymphoma per million using the 2000 Korean standard population (B). \(^a\)Comparing 1999 and 2018. \(^b\)Average annual percent change by Joinpoint regression analysis. \(^c\)Incidence rate ratio per year from 1999 to 2018 as calculated by Poisson regression.

Abbreviations: AAPC, average annual percent change; ASR, age-standardized incidence rate; CI, confidence interval; CIR, crude incidence rate; IRR, incidence rate ratio.

Statistics mainly describes the most common types of cancer, it is up to each researcher to analyze the statistical data of specific cancers. However, the incidence of hematologic malignancies has been increasing in the ROK. Thus, a more precise and periodic statistical analysis is needed [8]. All hematologic malignancies that were analyzed in this study showed a significant increase in the incidence. The order of increase in ASR over 20 years was as follows: malignant immunoproliferative diseases (AAPC=11.82%, IRR=1.090, \(P<0.05\)), myeloproliferative disorders (AAPC=9.87%, IRR=1.080,
Several previous studies on hematologic malignancies in the ROK have shown similar results as obtained in this study. In the analysis from 1999 to 2008, the incidence and the ASR of all hematologic malignancies showed an increasing trend. The latter increased from 10.2% to 13.7%, and the ASR was 3.9% [9]. Other studies from 1999 to 2012 on myeloid and lymphoid malignancies showed an increasing trend in CIR and overall ASR. The ASR for all myeloid malignancies increased from 3.31 in 1999 to 5.70 in 2012, with an AAPC of 5.4% [10]. In 2012, the ASR per 100,000 persons with Hodgkin’s lymphoma, mature B-cell neoplasm, mature T/natural killer (NK)-cell neoplasm, and precursor cell neoplasm were 0.46, 6.60, 0.95, and 1.50, respectively, and increased yearly from 1999 [11]. In a recent study from 2005 to 2015, the incidence and prevalence rates of hematological malignancies increased steadily. From 2005 to 2015, the number of new patients with hematologic malignancies showed an overall gradual increase, with an increase rate of up to 56.7% over 10 years [8]. A similar trend has been observed worldwide. In an analysis of the global burden of disease data from 1990 to 2017, the number of new cases increased [12]. The ASR for all hematologic malignancies increased, except for acute lymphocytic leukemia and chronic myeloid leukemia [13]. Han et al. also demonstrated decreased ASR of acute lymphocytic leukemia and chronic myeloid leukemia, but this was not statistically significant, which is similar to the results from previous global research [8, 12, 13]. In this study, the incidence of leukemia was relatively low compared to that of other hematologic malignancies. In addition, in most hematological malignancies, the incidence was higher in males, which is also similar to the results of previous studies [8-15].

There are several possible factors contributing to the increasing trend in the incidence of hematologic malignancies. Age is the most important risk factor for cancer, and the overall incidence of cancer increases with an aging population [16]. Previous studies have also shown that the incidence of hematologic malignancies increases with age [9, 17]. However, it is difficult to explain how the incidence of hematologic malignancies increases because of the aging population alone. In addition to the increase in CIR, ASR also tends to increase significantly. In addition to the aging population, the following possibilities can be considered as possible causes for the increase in hematologic malignancies. First, there is a possibility of a detection bias. Improved access to healthcare facilities and the use of new screening and diagnostic technologies may be another cause [18, 19]. Exposure to diagnostic or therapeutic ionizing radiation, such as X-rays, computed tomography (CT), gamma rays, radio-pharmaceuticals, and charged particles can also increase the risk of hematologic malignancies [20, 21]. One study found that the risk of radiation-induced malignancies from CT radiation may increase as CT-based screening becomes more widely used at the population level [22]. The increased exposure to extremely low-frequency electric and magnetic fields (ELF-EMFs) may be another cause [23, 24]. Over the last half century, the use of chemicals has continuously increased, and new chemicals have been developed. The possibility that such exposure to diverse chemical pollution in the workplace or residence may have been a cause of hematologic malignancies cannot be ruled out [25, 26]. Efforts are needed to determine new environmental cancer risk factors in the future.

This study had the following limitations. First, this study used the 61 sets of cancer incidence data provided by the KOSIS. Therefore, hematologic malignancies cannot be analyzed in greater detail. In the future, it will be necessary to analyze hematologic malignancies in a more subdivided manner. Clinically important diseases such as acute myeloid leukemia, acute lymphoid leukemia, chronic myeloid leukemia, chronic lymphoid leukemia, T-cell lymphoma, and B-cell lymphoma require additional detailed analysis. Second, the analysis results of this study may be slightly different from the annual report of cancer statistics. This is due to differences in statistical analysis methods, statistics package programs, and/or standard population settings (Segi’s world standard population or Korean standard population) used, along with differences in the handling of decimal places. It would be better to interpret the current state of occurrence based on trends rather than detailed numbers.

An aging society is when the proportion of the population aged ≥65 years comprises 7% of the total population, an ‘aged society’ when it is over 14%, and a ‘post-aged society’ when it is over 20%. The ROK entered an aging society in 2000, an aged society in 2018, and is expected to enter a post-aged society by 2025. In 2050, the proportion of the population aged ≥65 years is expected to be 39.8% [27]. It is highly likely that the incidence of hematologic malignancies will continue to increase with the aging population. In addition to social and medical preparations for the possibility of this increase, more research should be conducted in the future. More well-designed studies are needed to elucidate the causes of this increase.

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Authors’ Disclosures of Potential Conflicts of Interest

No potential conflicts of interest relevant to this article were reported.

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