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Spatial clusters with high mortality rates for chronic obstructive pulmonary disease among municipalities in Japan between 2017 and 2021: a flexible spatial scan statistics approach

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ABSTRACT

Chronic obstructive pulmonary disease is one of the leading causes of death worldwide and in Japan. This study aimed to detect the location and area of spatial clusters with high chronic obstructive pulmonary disease mortality rates in Japan during 2017–2021. Age-standardized numbers of expected chronic obstructive pulmonary disease deaths by sex and municipality were estimated from publicly available data from 1,895 municipalities in Japan. We performed flexible spatial scan statistics to detect the clusters with significantly high risk of chronic obstructive pulmonary disease death using the expected and observed cumulative mortality. During 2017–2021, the cumulative expected number of chronic obstructive pulmonary disease deaths was 87,450 (72,551 males and 14,899 females). There were 23 significant spatial clusters for males and 14 for females. The 23 clusters were scattered in 251 municipalities of 27 prefectures for males, while the 14 clusters for females were localized in 105 municipalities of 12 prefectures. The primary cluster for both sexes was detected in the Osaka Prefecture (males: log-likelihood ratio [LLR] = 188.23, relative risk [RR] = 1.46, p = 0.001; females: LLR = 106.42, RR = 1.95, p = 0.001). We found 23 significant spatial clusters for males and 14 for females. There were obvious sex differences in the distribution of the clusters. Our findings provide supporting evidence to discuss the prioritized areas in the allocation of health care resources to prevent and control the deaths associated with chronic obstructive pulmonary disease.

Keywords: chronic obstructive pulmonary disease, disease spatial clusters, ecological research, flexible scan statistics, mortality

Abbreviations:
COPD: chronic obstructive pulmonary disease
RR: relative risk

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a global public health problem. It is the third leading cause of death worldwide, with 3.23 million deaths in 2019[1] as well as one of the leading causes of death in Japan, particularly for males.[2] When COPD deaths are excluded, life expectancy at birth in Japan is expected to extend by 0.13 years for males and 0.03 years for females in 2022.[3] Thus, to extend healthy life expectancy, handling COPD is a priority issue in Japan.[4] In addition, compared with non-COPD patients, patients with COPD have a significantly higher risk of developing complications after lung resection surgery.[5]

COPD burden is not uniformly distributed across Japan. Recent prefectural-level data showed the highest age-standardized mortality for both sexes in the Okinawa Prefecture and the lowest in the Aichi Prefecture for males and the Niigata Prefecture for females.[6] Yet, it is unclear whether these differences are significant when compared to other regions. Rigorous statistical and epidemiological research of spatial patterns and identification of high-risk clusters are indispensable to combat the spread of the disease.

It is necessary to identify areas with an elevated risk of COPD mortality and initiate further discussion to renew strategies for the control and prevention of COPD in these areas. Performing spatial cluster analysis provides the location and size of statistically significant clusters with high COPD mortality rates. Such evidence would provide public health policy makers with exact data on areas that are at highest risk and with highest need for intervention. Therefore, this study aimed to specifically detect spatial clusters of high mortality rates for COPD among municipalities in Japan during 2017–2021 using rigorous epidemiological approaches to improve control and prevention efforts.

METHODS

Data sources

The number of COPD deaths by sex, age, and residential municipality from 2017 to 2021 was acquired on September 25, 2023 from the Japanese Vital Statistics,[7] where COPD death was coded as J41, J42, J43, or J44 in the 10th revision of the International Classification of Diseases. The Vital Statistics of Japan includes all deaths in Japan reported to the municipality of residence under the Family Register Act. Each municipality reports the statistics to the Ministry of Health, Labour and Welfare via the public health office and prefecture. The demographic data corresponding to COPD mortality, derived from a Japanese basic resident registration system, was obtained on September 25, 2023 from the portal site of Official Statistics of Japan (e-Stat).[8] For building a neighbor municipality connection list and visualization, the boundary map data of municipalities was downloaded from the Japanese Ministry of Land, Infrastructure, Transport and Tourism on October 1, 2023.[9] The final dataset of this study included 1,895 municipalities (198 wards in metropolitan cities, 777 cities, 743 towns, and 177 villages).

This study used publicly available, municipality-level data that does not contain personally identifiable information. As this study does not fall under the "Scope of Application" of the Ethical Guidelines for Medical and Biological Research Involving Human Subjects by the Japanese Ministries,[10] ethics approval was waived by the institutional review board.

Data processing

The cumulative expected number of COPD deaths during 2017–2021 by sex and municipality was estimated using an indirect age-standardized method, ie, the total of all age-stratified expected deaths, each calculated as the product of the 5-year sum of the age-stratified population of the municipality and the national age-stratified COPD mortality rate. The national morality rate was computed by dividing the 5-year cumulative age-stratified number of COPD deaths in Japan by the 5-year total of the age-stratified national population.

Detection of spatial clusters

To identify spatial clusters over municipalities with excessive COPD deaths, Tango's restricted flexible spatial scan statistics method[11,12] with R smerc package was used in this study.[13] During detection, an area of single or neighbor-merged municipalities (maximally 20 municipalities) was set as exploring window, and the ratio of COPD death likelihood inside and outside the window was estimated for all windows. As a result, windows with the highest or higher restricted log-likelihood ratio (LLR) were considered candidates for clusters; then, each was statistically tested using Monte Carlo simulation with a Poisson model and 999 repetitions to calculate p-values to three decimal places. Significant clusters with the highest LLR were defined as primary clusters, and the other clusters were considered secondary clusters. All data processing and analyses were performed independently by sex using R version 4.3.1.[14]

RESULTS

The cumulative observed number of COPD deaths during 2017–2021 was 87,450 (72,551 males and 14,899 females). There were 23 significant spatial clusters for males (Tables 1 and 2, Figure 1A) and 14 for females (Tables 1 and 2, Figure 1B). The significant clusters for males were scattered in 251 municipalities of 28 prefectures (Figure 1A), while those for females were localized in 105 municipalities of 12 prefectures (Figure 1B). For both sexes, the primary cluster was detected in the Osaka Prefecture (males: LLR = 188.23, relative risk [RR] = 1.46, p = 0.001; females: LLR = 106.42, RR = 1.95, p = 0.001). For males, the highest RR was observed in the 23rd cluster, including municipalities in the Hokkaido Prefecture (RR = 2.37, p = 0.033). For females, the highest RR was observed in the 13th cluster, including only one municipality (ie, Nagata Ward, Kobe City) of the Hyogo Prefecture (RR = 3.42, p = 0.011).

Table 1 Spatial clusters of high mortality rates for COPD among municipalities in Japan during 2017–2021

Cluster	Population	Observed number of cases	Expected number of cases	RR[a]	LLR[b]	p[c]
Male						
1	5728632	1980	1243.71	1.46	188.23	0.001
2	2514349	981	628.85	1.65	84.95	0.001
3	10345895	2383	1894.29	0.97	59.92	0.001
4	1655311	626	403.80	1.59	52.60	0.001
5	3550321	1041	759.60	1.23	47.22	0.001
6	1811053	762	525.76	1.77	46.93	0.001
7	2413273	842	597.50	1.47	44.75	0.001
8	2267332	767	538.75	1.42	43.04	0.001
9	1239047	442	304.82	1.50	27.19	0.001
10	976466	356	237.48	1.53	25.71	0.001
11	2793749	880	688.98	1.33	24.58	0.001
12	2274428	663	500.39	1.23	24.13	0.001
13	856598	305	199.73	1.50	23.93	0.001
14	1707700	542	398.94	1.33	23.18	0.001
15	2553486	705	553.58	1.16	19.20	0.001
16	539480	213	134.98	1.66	19.18	0.001
17	956003	245	161.47	1.08	18.67	0.002
18	1209227	329	231.47	1.14	18.21	0.002
19	936145	309	218.18	1.39	16.77	0.005
20	268937	133	79.93	2.08	14.67	0.018
21	635317	272	193.15	1.80	14.31	0.025
22	1771452	537	424.22	1.27	13.90	0.028
23	277999	157	100.46	2.37	13.58	0.033
24	779925	269	194.22	1.45	12.88	0.056
25	1632397	525	418.70	1.35	12.56	0.068
Female						
1	5299433	474	224.90	1.95	106.42	0.001
2	596091	93	26.61	3.36	50.13	0.001
3	1719047	179	77.84	2.25	48.25	0.001
4	934436	95	32.23	2.19	40.06	0.001
5	6835972	416	261.43	1.31	39.49	0.001
6	6303419	377	242.83	1.29	32.28	0.001
7	6460071	357	228.63	1.19	31.28	0.001
8	4113856	243	150.19	1.27	24.40	0.001
9	1473968	139	76.58	2.03	20.57	0.001
10	2776555	194	124.51	1.50	16.71	0.003
11	229734	28	7.70	2.62	15.85	0.005
12	3486421	224	150.56	1.38	15.73	0.005
13	238335	38	13.65	3.42	14.58	0.011
14	1110489	96	54.73	1.86	12.74	0.049
15	290011	43	17.85	3.19	12.68	0.051
16	693328	89	49.62	2.76	12.67	0.051

COPD: chronic obstructive pulmonary disease
[a] Relative risk (RR) in the cluster window
[b] Log-likelihood ratio (LLR) for the cluster window
[c] Tango's flexible spatial scan statistics

Table 2 Municipalities in spatial clusters of high mortality rates for COPD

	Name of municipality
Male	
1	**Osaka Prefecture**: Osaka City (Miyakojima Ward, Konohana Ward, Minato Ward, Taisho Ward, Naniwa Ward, Nishiyodogawa Ward, Higashiyodogawa Ward, Higashinari Ward, Ikuno Ward, Asahi Ward, Sumiyoshi Ward, Higashisumiyoshi Ward, Nishinari Ward, Yodogawa Ward, Suminoe Ward, Hirano Ward), Sakai City (Sakai Ward). **Hyogo Prefecture**: Amagasaki City
2	**Kyoto Prefecture**: Fukuchiyama City, Miyazu City. **Hyogo Prefecture**: Himeji City, Toyooka City, Nishiwaki City, Tambasasayama City, Yabu City, Tamba City, Asago City, Shiso City, Kato City, Ichikawa Town, Fukusaki Town, Kamikawa Town, Kami Town
3	**Tokyo Prefecture**: Sumida Ward, Koto Ward, Ota Ward, Kita Ward, Arakawa Ward, Adachi Ward, Katsushika Ward, Edogawa Ward. **Kanagawa Prefecture**: Kawasaki City (Kawasaki Ward, Saiwai Ward)
4	**Fukuoka Prefecture**: Kurume City, Yame City, Buzen City, Ukiha City, Asakura City, Chikuzen Town, Tachiarai Town, Hirokawa Town. **Kumamoto Prefecture**: Nagomi Town. **Oita Prefecture**: Nakatsu City, Hita City
5	**Osaka Prefecture**: Osaka City (Tsurumi Ward), Moriguchi City, Yao City, Neyagawa City, Kashiwara City, Kadoma City, Fujiidera City, Higashiosaka City
6	**Miyazaki Prefecture**: Miyakonojo City, Nichinan City, Kobayashi City, Kushima City, Ebino City, Mimata Town. **Kagoshima Prefecture**: Kanoya City, Soo City, Kirishima City, Shibushi City, Isa City, Aira City, Yusui Town, Higashikushira Town, Kinko Town, Kimotsuki Town
7	**Tokushima Prefecture**: Tokushima City, Awa City, Mima City, Sanagouchi Village, Ishii Town, Kamiyama Town, Kitajima Town, Aizumi Town, Kamiita Town, Tsurugi Town, Higashimiyoshi Town. **Kagawa Prefecture**: Takamatsu City, Zentsuji City, Sanuki City, Miki Town, Kotohira Town, Manno Town
8	**Tochigi Prefecture**: Nikko City. **Gunma Prefecture**: Maebashi City, Kiryu City, Ota City, Numata City, Midori City, Shinto Village, Yoshioka Town, Takayama Village, Kawaba Village, Showa Village, Oizumi Town
9	**Osaka Prefecture**: Izumisano City, Sennan City, Kumatori Town, Tajiri Town. **Wakayama Prefecture:** Kainan City, Tanabe City, Kinokawa City, Iwade City, Katsuragi Town, Yuasa Town, Aridagawa Town, Hidakagawa Town
10	**Saga Prefecture**: Saga City, Taku City, Takeo City, Kashima City, Ogi City, Omachi Town, Kohoku Town, Shiroishi Town
11	**Kanagawa Prefecture**: Hakone Town, Manazuru Town, Yugawara Town. **Shizuoka Prefecture**: Shizuoka City (Shimizu Ward), Numazu City, Atami City, Fujinomiya City, Fuji City, Gotemba City, Susono City, Izu City, Izunokuni City, Higashiizu Town, Kawazu Town, Matsuzaki Town, Nishiizu Town
12	**Mie Prefecture**: Tsu City, Kuwana City, Suzuka City, Kameyama City, Inabe City, Toin Town, Komono Town. **Shiga Prefecture**: Ritto City, Koka City, Taga Town
13	**Ibaraki Prefecture**: Ishioka City, Naka City, Chikusei City, Kasumigaura City, Kawachi Town, Goka Town, Kaminokawa Town, Motegi Town, Ichikai Town
14	**Yamagata Prefecture**: Yonezawa City, Kawanishi Town, Iide Town. **Fukushima Prefecture**: Koriyama City, Sukagawa City, Kitakata City, Nihonmatsu City, Motomiya City, Kawamata Town, Kagamiishi Town, Tenei Village, Inawashiro Town, Miharu Town
15	**Osaka Prefecture**: Sakai City (Naka Ward, Kita Ward, Mihara Ward), Tondabayashi City, Kawachinagano City, Matsubara City, Izumi City, Habikino City, Takaishi City. **Wakayama Prefecture**: Hashimoto City
16	**Fukushima Prefecture**: Shirakawa City, Nishigo Village, Yabuki Town, Samegawa Village, Ishikawa Town, Tamakawa Village, Hirata Village, Furudono Town, Ono Town. **Ibaraki Prefecture**: Takahagi City, Kitaibaraki City

17 **Okinawa Prefecture**: Nago City, Okinawa City, Uruma City, Ginoza Village, Kin Town, Chatan Town, Kitanakagusuku Village

18 **Tokyo Prefecture**: Hinohara Village. **Kanagawa Prefecture**: Sagamihara City (Midori Ward, ChuoWard), Aikawa Town, Kiyokawa Village

19 **Ibaraki Prefecture**: Inashiki City, Kasumigaura City, Kamisu City, Hokota City, Omitama City, Miho Village, Kawachi Town. **Chiba Prefecture**: Katori City

20 **Miyagi Prefecture**: Shikama Town, Kami Town. **Yamagata Prefecture**: Higashine City, Obanazawa City, Oishida Town, Mogami Town

21 **Tottori Prefecture**: Kurayoshi City, Chizu Town), Yurihama Town. **Okayama Prefecture**: Tsuyama City, Maniwa City, Shinjo Village, Shoo Town, Nagi Town, Kumenan Town, Misaki Town, Kibichuo Town

22 **Chiba Prefecture**: Chiba City (Midori Ward), Tateyama City, Mobara City, Ichihara City, Kamogawa City, Kimitsu City, Minamiboso City, Otaki Town, Kyonan Town

23 **Hokkaido Prefecture**: Yubari City, Ashibetsu City, Akabira City, Takikawa City, Fukagawa City, Naie Town, Kuriyama Town, Shintotsukawa Town, Chippubetsu Town

24 **Fukuoka Prefecture**: Kitakyushu City (Moji Ward, Tobata Ward, Kokurakita Ward)

25 **Okayama Prefecture**: Ibara City. **Hiroshima Prefecture**: Onomichi City, Fukuyama City, Fuchu City

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Female

1 **Osaka Prefecture**: Osaka City (Tennoji Ward, Naniwa Ward, Ikuno Ward, Abeno Ward, Sumiyoshi Ward, Higashisumiyoshi Ward, Nishinari Ward, Suminoe Ward, Hirano Ward, Chuo Ward), Sakai City (Sakai Ward, Mihara Ward), Matsubara City, Kashiwara City, Habikino City, Higashiosaka City

2 **Aomori Prefecture**: Hachinohe City

3 **Hyogo Prefecture**: Kobe City (Hyogo Ward, Kita Ward, Chuo Ward), Sanda City, Tambasasayama City, Tamba City

4 **Okinawa Prefecture**: Okinawa City, Uruma City, Ginoza Village, Kin Town, Yomitan Village, Chatan Town, Kitanakagusuku Village

5 **Kanagawa Prefecture**: Yokohama City (Tsurumi Ward, Kanagawa Ward, Naka Ward, Minami Ward, Hodogaya Ward, Isogo Ward, Totsuka Ward, Asahi Ward), Kawasaki City (Kawasaki Ward, Saiwai Ward), Fujisawa City, Yamato City

6 **Osaka Prefecture**: Osaka City (Fukushima Ward, Nishiyodogawa Ward, Higashiyodogawa Ward, Asahi Ward, Tsurumi Ward), Toyonaka City, Suita City, Moriguchi City, Neyagawa City, Kadoma City. **Hyogo Prefecture**: Amagasaki City, Itami City

7 **Saitama Prefecture**: Kawaguchi City, Yashio City. **Tokyo Prefecture**: Taito Ward, Sumida Ward, Arakawa Ward, Adachi Ward, Edogawa Ward

8 **Tokyo Prefecture**: Hachioji City, Hinohara Village. **Kanagawa Prefecture**: Sagamihara City (Midori Ward, ChuoWard, Minami Ward), Atsugi City, Zama City, Matsuda Town, Yamakita Town, Aikawa Town

9 **Tokushima Prefecture**: Awa City, Mima City, Miyoshi City, Itano Town, Kamiita Town, Tsurugi Town. **Kagawa Prefecture**: Takamatsu City, Manno Town

10 **Osaka Prefecture**: Kishiwada City, Kaizuka City, Izumisano City, Kawachinagano City, Sennan City, Kumatori Town. **Nara Prefecture**: Gojo City. **Wakayama Prefecture**: Wakayama City, Kinokawa City, Katsuragi Town

11 **Okinawa Prefecture**: Itoman City, Yaese Town

12 **Kyoto Prefecture**: Kyoto City (Kita Ward, Higashiyama Ward, Minami Ward, Ukyo Ward, Fushimi Ward, Yamashina Ward, Nishikyo Ward), Uji City, Kameoka City, Yawata City, Nantan City

13 **Hyogo Prefecture**: Kobe City (Nagata Ward)

14	**Kanagawa Prefecture**: Yokosuka City, Miura City
15	**Saga Prefecture**: Kashima City, Ureshino City, Kohoku Town, Shiroishi Town. **Nagasaki Prefecture**: Higashisonogi Town, Kawatana Town
16	**Kumamoto Prefecture**: Hitoyoshi City, Kuma Village. **Miyazaki Prefecture**: Kobayashi City, Ebino City. **Kagoshima Prefecture**: Akune City, Satsumasendai City, Isa City, Satsuma Town

COPD: chronic obstructive pulmonary disease

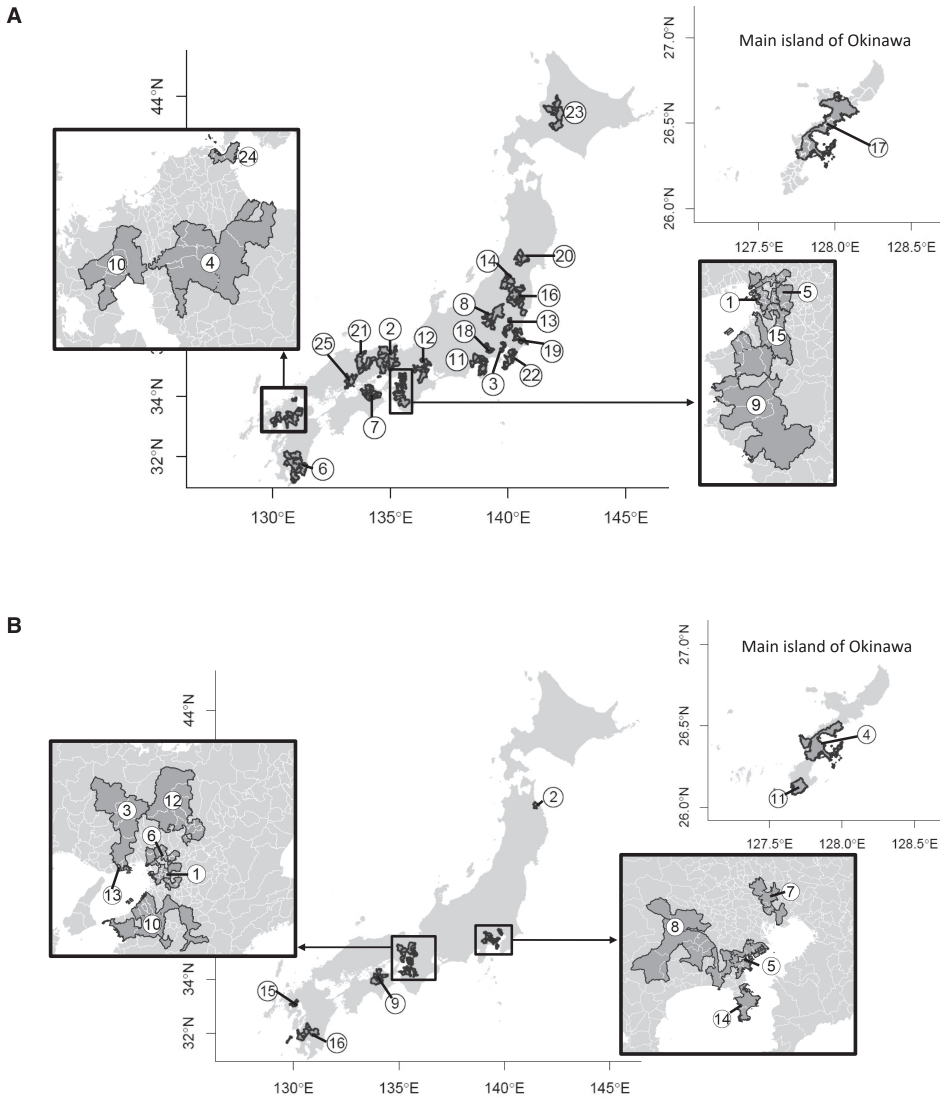

Fig. 1 Spatial clusters of high mortality rates for COPD detected using flexible spatial scan statistics, 2017–2021

Fig. 1A: Male
Fig. 1B: Female
COPD: chronic obstructive pulmonary disease

DISCUSSION

The strength of this study was its statistical investigation of spatial patterns of high mortality rates for COPD among 1,895 municipalities across all of Japan during 2017–2021. This study identified spatial clusters with high mortality rates due to COPD in both sexes: 23 clusters for males and 14 for females. There was an obvious difference in cluster distribution by sex. The clusters were scattered all over Japan for males, but were localized for females.

Possible reasons for the geographical variation in COPD mortality include the prevalence of tobacco smoke,[15] occupational exposure,[16] air pollution,[17] socioeconomic status,[18,19] or other unknown regional factors. However, further research is warranted to assess the geographical variation in these factors and explore their correlation with COPD mortality.

There are some possible reasons to explain the difference in cluster distribution by sex. First, tobacco smoking is the most important individual risk factor,[20-22] which accounts for to the disability-adjusted life years (DALYs) rates for COPD.[23] Although the smoking prevalence (ie, adults aged ≥20 years who smoke every day or sometimes) of males in Japan has decreased from 83.7% in 1966[24] to 27.1% in 2019, it is still much higher than that of females (7.6%) in 2019.[25] In addition, the distribution of smoking prevalence at the municipality level in Japan[26] differs by sex. The smoking prevalence in males is considerably high in a wider range of municipalities in Japan, while the highest prevalence for females is concentrated in urban municipalities. As a result, the distribution of clusters of high mortality rates for COPD was more localized for females.

Second, past occupational exposure is an important environmental risk factor,[20,21,27] accounting for 15.6% of the DALYs rates for COPD.[23] Since the employment rate for males has been higher than that for females in the past five decades (male: 80.9%, female: 47.1% in 1972; male: 69.4%, female: 53.0% in 2022),[28] long-term occupational exposure may have reflected the scattered distribution of clusters for males. Further research is necessary to explore the association between the spatial distribution of COPD mortality with the prevalence of smoking and occupational exposure in Japan.

Third, as socioeconomic status (SES) is an important risk factor for the prevalence, exacerbation, and mortality of COPD,[29-31] regional differences in SES may have influenced the distributions of clusters. Household income was more strongly associated with COPD for men than for women.[32] This gender difference may have contributed to the scattered distribution of clusters for males.

Our findings may have the potential to contribute to the updating of public health resource allocation for the control and prevention of COPD deaths. It has been reported that increasing COPD severity is negatively associated with higher health care resource utilization.[33,34] For example, if resources are allocated to select areas for additional training regarding self-management support skills for health professionals, including staff in clinics, visiting nurses, and nurses in long-term care facilities, it may mitigate COPD deaths. This is because self-management promotes healthier behaviors in patients (eg, receiving effective drug therapy) to prevent exacerbations.[35] Moreover, the allocation of resources for public awareness campaign may improve outcomes. Therefore, 23 spatial clusters for males and 14 for females with high COPD mortality rates, which were identified in this study, could be candidates for high priority areas of resource allocation.

This study has five limitations. First, due to our secondary data analysis, the accuracy of our results entirely depends on the data source; however, the quality of Japanese Vital Statistics is considered sufficient.[36] Second, since the place of deaths and risk exposure for COPD do not always coincide, our results provide limited insights into the etiology of COPD, yet our findings are quite important for health policy makers as they can help prevent COPD death. Third, although risk factors such as tobacco smoke, occupational exposure, and air pollution have been previously reported, they were not included in this study because of limited data. Fourth, we did not assess the cause of death from lung cancer in patients with COPD having comorbid lung cancer. To clarify this situation, it will be necessary find a method to estimate excess mortality from lung cancer due to COPD. Tobacco smoking is the primary cause of COPD and lung cancer mortality[37]; therefore, the cluster pattern may not alter significantly after integrating lung cancer mortality. Fifth, this was an ecological study using municipality-level data. The municipality-level scan window used in our analysis may have overlooked small clusters at a smaller scale.

CONCLUSIONS

This study detected spatial clusters with high mortality rates for COPD among municipalities in Japan between 2017 and 2021. We found 23 significant spatial clusters for males and 14 for females. In addition, we detected an obvious sex difference in the cluster distribution. Clusters were scattered all over Japan for males but localized for females.

AUTHOR CONTRIBUTIONS

All authors contributed to the conceptualization, design, interpretation of the results, as well as critically revising and approving the final manuscript. KI performed data collection and cleaning. KI, MM, and ST conducted data analyses and drafted the manuscript.

CONFLICT OF INTEREST

The authors declare no conflicts of interest for this article.

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