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Asthma mortality based on death certificates: A demographic survey in Kagawa, Japan

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ABSTRACT

Background: We aimed to determine the reasons for the high rate of asthma mortality in Kagawa Prefecture, Japan, by analyzing death certificates.

Methods: We analyzed the death certificates between 2009 and 2011 in a demographic survey. Of 1187 patients with documented disease names suggesting bronchial asthma, analysis was performed on 103 patients in whom the cause of death was classified as asthma based on ICD-10 Codes. The patients were then classified into the following 4 groups: asthma death, asthma-related death, non-asthma death, and indistinguishable death. Based on this classification, consistency between ICD-10-based asthma death and asthma/asthma-related deaths was examined for each age group as well as for the site of death.

Abbreviations: ACO, asthma- chronic obstructive pulmonary disease overlap; COPD, chronic obstructive pulmonary disease; ICS, inhaled corticosteroid; MHLW, Ministry of Health, Labour and Welfare

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Ministry of Health
Labour and Welfare
Asthma mortality
Death certificate

Results: Of 103 asthma deaths based on the ICD-10 classification, 30 (29%) were classified as asthma death, 44 (43%) as asthma-related death, 16 (16%) as non-asthma death, and 13 (13%) as indistinguishable death. Asthma death based on our classification correlated with that of ICD-10-based classification as a cause of death in patients younger than the median age (87 years), but correlation was not observed in patients aged older than 87 years. Deaths occurred outside the hospital in 45% of patients, and many ICD-10-based deaths reported at nursing homes and geriatric health care facilities were classified as non-asthma deaths in this survey.
Conclusion: Re-examination of the death certificate revealed that asthma deaths were reported incorrectly on the death certificates of elderly patients who died outside the hospital.
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1. Introduction

Various guidelines in the treatment of bronchial asthma have been published based on the global consensus of using inhaled corticosteroid (ICS) as a basic therapy, and epidemiological analyses have confirmed a drastic reduction in asthma mortality with the widespread use of ICS. A telephone survey revealed that ICS was used in 34% of adults with asthma in Japan if combination therapy was prescribed (Asthma Insights and Reality in Japan 2011, published in Japanese). The National Health and Wellness Survey, conducted through the Internet, suggested the proportion of ICS use to be 40% among people with asthma in Japan, which is comparable to the reports from Europe and the USA. However, asthma mortality rate is still higher in Japan than in Europe and the USA. A demographic survey published by the Ministry of Health, Labour and Welfare (MHLW) showed that people older than 75 years accounted for most of the asthma deaths. However, details related to asthma deaths are unknown because the Personal Information Protection Law in Japan prevents obtaining personal information. Asthma mortality defined by the MHLW is based on the International Statistical Classification of Diseases and Related Health Problems (ICD)-10. Asthma is classified as J45 in the ICD-10 and is further subclassified as J45.0 (predominantly allergic asthma), J45.1 (non-allergic asthma), J45.8 (mixed asthma), and J45.9 (unspecified asthma). Status asthmaticus is classified as J46.

Kagawa Prefecture, where farming is prevalent, is considered to reflect the disease status for many pathologies across Japan. However, Kagawa Prefecture ranked the worst for asthma mortality in the Japanese demographic survey of 2010. Therefore, we aimed to determine the reasons for the high asthma mortality by analyzing the actual death certificates in a demographic survey. This study is the first asthma death survey in Japan based on death certificates.

2. Patients and methods

The Kagawa Asthma Study Group, primarily consisting of respiratory specialists, reviewed the death certificates in a demographic survey between 2009 and 2011 in Kagawa Prefecture with permission from the MHLW. We initially found 1187 patients with disease names suggesting bronchial asthma such as asthma, bronchial asthma, asthma attack, chronic asthma, and asthmatic bronchitis, or chronic obstructive pulmonary disease (COPD) such as pulmonary emphysema, chronic bronchitis, and chronic respiratory failure, in either section I (direct cause of death or status responsible for direct cause of death) or II (diseases having possibly affected the cause of death stated in section I) of the death certificates (Table 1). Of these patients, 103 were classified by the MHLW in the asthma death group based on the ICD classification and included in the study.

Table 1 – Format of the death certificate.

Classification		Diseases	Duration from diagnosis to death
I	(i) Direct cause of death		
	Indirect causes of death (ii) Cause of (i)		
	(iii) Cause of (ii)		
	(iv) Cause of (iii)		
II	Comorbidities (underlying diseases not directly related to death)		
Site of death		1. Hospital	
		2. Outside the hospital	
		Nursing home	
		Geriatric health care facility	
		Clinic	
		Home	
		Others	

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Table 2 – Classification criteria based on the death certificate.

Classification	I				II
	Direct cause of death	Indirect cause of death	Duration from diagnosis to death	Site of death	Underlying diseases
Asthma death	Asthma*				
Asthma-related death		Asthma*	≤1 month >1 month	Hospital	
Non-asthma death		Asthma*	>1 month	Outside the hospital	
					Asthma*
Indistinguishable death		Asthma*	Not recorded		
	Asthmatic bronchitis				

* Asthma includes asthma, bronchial asthma, chronic asthma, and asthma attack.

The causes of deaths were classified into asthma attack (asthma death), asthma attack related (asthma-related death), lacking validity to classify into asthma or asthma-related (non-asthma death), and indistinguishable deaths. The criteria for classification are shown in Table 2. The criteria also take into account information such as the duration from the diagnosis to death and site of death, which are also available in the death certificate (Table 1). First, the patients were classified based on the statement of asthma in section I. Of the patients with asthma mentioned in section I, those with asthma as the direct cause of death were classified in the asthma death group. If the direct cause of death was not asthma, patients were further subclassified depending on whether the underlying cause of death was asthma or whether the direct cause of death was a fatal disease. If the direct cause of death was a fatal disease other than asthma, the patients were classified in the non-asthma or asthma-related death group (not applicable case). If the direct cause of death was not asthma and the duration up to death was one month or longer, patients were not classified in the asthma-related death group. However, the patients who died at hospitals were considered to have an asthma-related death because the possible use of long-term artificial respiration could not be denied. If asthma was not mentioned in section I, but mentioned in section II and the disease duration of the direct cause of death in section I mostly agreed with the data in section II, the patient was considered to have an asthma-related death. Based on the above classification, consistency between ICD-10-based asthma death and asthma death/asthma-related death was examined for each age group. Chi-squared and Fisher's exact tests were used for comparison of the rate of concordance between our classification and ICD-10 based asthma deaths.

3. Results

3.1. *Details of asthma deaths determined by MHLW (ICD-10 classification)*

In total, 103 patients were classified by the MHLW in the asthma death group based on the ICD classification between 2009 and 2011. Among the 103 patients, 41 were men and 62 were women. The average and median ages were 88 (48–104) and 87 years, respectively. Patients older than 85 years accounted for 72% of patients. In this survey, 23 cases (22%) were classified as J46, and the remaining 80 cases (78%) were classified as J45.9. Many patients also had several comorbidities other than bronchial asthma, which were described in sections I or II, including respiratory diseases (31%), cardiovascular diseases (27%), cancer (7%), and psychoneurological diseases (5%) (data not shown).

3.2. *Reclassification of deaths*

In 84 of the 103 patients, asthma was mentioned in section I of the death certificate. Based on our classification (Table 2), 30 of these 84 patients were considered to have asthma death because the direct cause of death was due to an asthma attack. The indirect cause of death was asthma in the remaining 54 patients. Of these, the disease duration of the direct cause of death in 42 patients was less than 1 month (asthma-related death). In 11 patients whose disease duration of the direct cause of death exceeded 1 month, 2 died in the hospital (asthma-related death), while 9 died outside the hospital (non-asthma death). The disease duration of the direct cause of death was not recorded in 1 patient (indistinguishable death). Asthma was described in section II but not in section I in 8 patients (non-asthma death). Asthmatic bronchitis was mentioned as the direct or indirect causes of death in the remaining 11 patients (mean age, 90 years), in whom a definite diagnosis was not made (indistinguishable death). Thus, according to our classification, 30 cases (29%) were classified as asthma deaths, 44 (43%) as asthma-related deaths, 16 (16%) as non-asthma deaths, and 13 (13%) as indistinguishable deaths (Fig. 1A). Of 103 patients classified based on ICD-10 in the asthma death group, presumed asthma/asthma-related death occurred in 74 patients (72%) based on our classification; that is, the remaining 29 patients (28%) did not match the causes of death. Direct causes of death in cases classified as non-asthma death included senility (n=6),

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chronic respiratory failure (n=6), pneumonia (n=2), and heart failure. Direct causes of death in cases classified as indistinguishable death included asthmatic bronchitis (n=8), chronic respiratory failure, pneumonia, and hypoxia. The ICD-10 codes in the cases analyzed in this study were either J46 or J45.9. In all 23 cases coded as J46, the cause of death was also asthma/asthma-related death in our classification (i.e., the concordance was 100%). The concordance was significantly lower in cases coded as J45.9 at 65% (52 of 80 deaths, Fig. 1B, $p = 0.0002$).

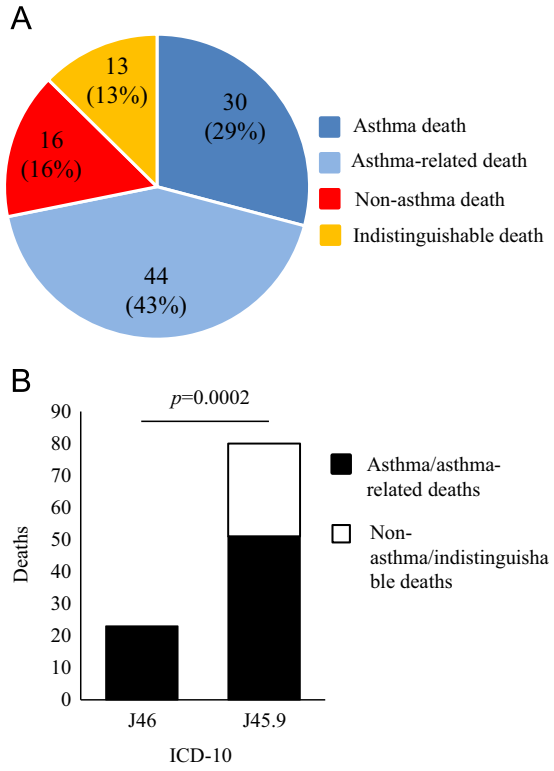

Fig. 1 – Classification of death according to the criteria using disease name, duration, and sites of death. (A) Rate of each group. (B) Asthma/asthma-related deaths in each ICD-10 code.

3.3. *Differences in classification of deaths by age or site of death*

Fig. 2A shows the classification of death for every age group. Interestingly, the rate of asthma/asthma-related deaths was lower for those above the median age (87 years) than for those below the median age (Fig. 2B, $p = 0.0087$). With respect to the site of death, 45% of patients died outside of the hospital (Fig. 3A). The rate of asthma/asthma-related deaths was lower in nursing homes or geriatric health care facilities than in the hospital or clinic (Fig. 3B).

4. Discussion

From the viewpoint of pulmonologists, we reviewed asthma deaths determined by the MHLW and classified the cases into four groups based on not only disease names but also duration from the diagnosis to death and the site of death. We noted a difference in estimated asthma and asthma-related deaths between the MHLW classification and our classification. Similar to the present study, inaccuracy of asthma diagnosis on death certificates has been also reported in the elderly population [1,2]. In the analysis of asthma mortality, the elderly population has also been often excluded in several reports [3,4].

Of 103 cases judged by the MHLW to be asthma deaths, we concluded that 30 cases (29%) were asthma deaths and 44 cases (43%) were asthma-related deaths according to our classification. Importantly, 16 cases (16%) were determined to be non-asthma deaths. These findings raise the possibility that the asthma mortality published by the Japanese government may be incorrect. Although our estimation of the causes of death could also be inaccurate, the real asthma mortality rate might be less than the published statistics.

Many misdiagnoses of bronchial asthma have been reported. For example, in the Netherlands and Canada, 33.1% to 52% of cases diagnosed as bronchial asthma were misdiagnosed [5,6]. This gap is mainly due to the difficulty of diagnosing bronchial asthma. There are several reasons for misdiagnosis or difficulty in diagnosing bronchial asthma.

First, physicians often diagnose bronchial asthma clinically, based on the symptoms. It has been reported that

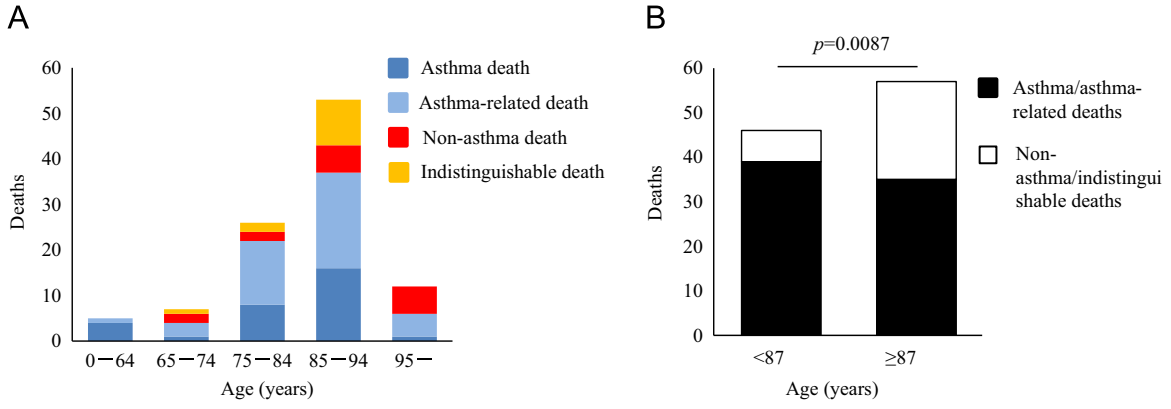

Fig. 2 – Classification of deaths in each age group. (A) Rate in each age group. (B) Difference in rate of asthma/asthma-related deaths between younger and older groups.

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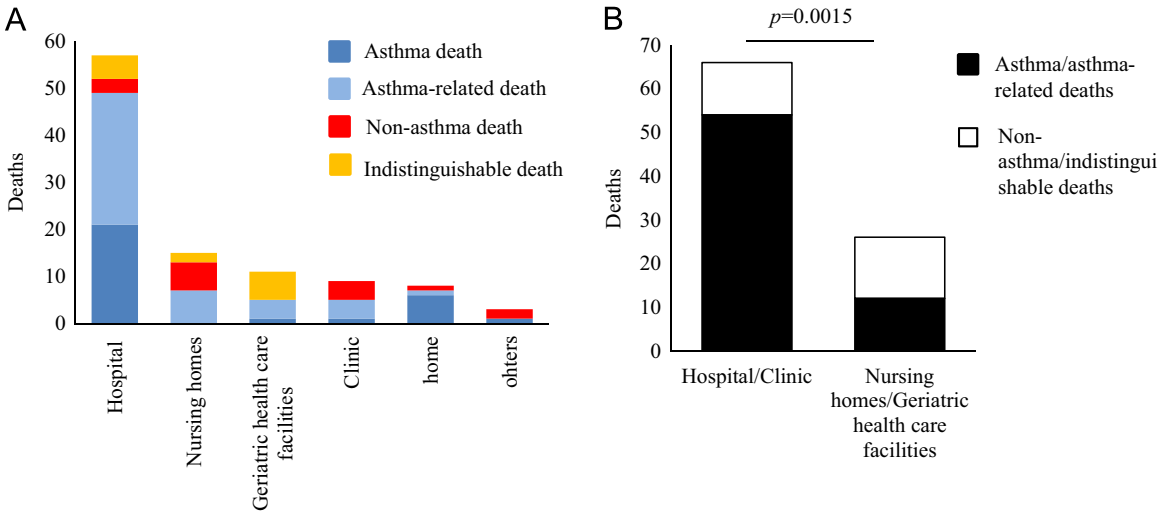

Fig. 3 – Classification based on the sites of death. (A) Rate in each site. (B) Difference in rate between hospital/clinic and nursing home/geriatric health care facilities.

bronchial asthma should not be diagnosed without spirometry [7]. However, in clinics, there are few doctors who use spirometry for a diagnosis of bronchial asthma in Japan.

Second, many underlying complications make the diagnosis of bronchial asthma difficult, particularly in the elderly population. There are many diseases associated with wheezing on auscultation, such as heart failure, bronchitis, pulmonary embolism, and exacerbation of COPD. Without sufficient time for the symptoms and signs to evolve, it is difficult to distinguish these diseases accurately. In support of this notion, the autopsy results suggest the risk of misdiagnosis when the diagnosis of bronchial asthma has been made clinically without spirometry investigation [8]. In Japan, "asthmatic bronchitis" has often been used for convenience as a provisional diagnosis for patients presenting with wheezing. However, use of asthmatic bronchitis should be avoided because there is no definition of this word. In the present study, asthmatic bronchitis was described in 11 patients, and the average age in these patients was 90 years. It is possible that these people may have died from diseases other than bronchial asthma.

Recently, there has been a proposal of a treatment strategy for the disease entity of asthma-COPD overlap (ACO) [9]. In the USA and UK, half of the elderly patients with asthma aged over 80 years were reported to have ACO [10]. In Japan, nearly half of elderly patients with asthma show coexisting COPD components when assessed by diffusing capacity for carbon monoxide %predicted and low attenuation area in HRCT [11]. In the present study, there were no patients who could be clearly described to have died from "COPD" on the death certificate. However, 19 patients (18.4%) were considered to have COPD concomitantly, given the description of "emphysema" or "chronic respiratory failure." This suggests that the understanding of the disease concept of not only ACO but also COPD was poor for general physicians at least until 2011 in Kagawa Prefecture. In contrast, in 73.8% of asthma deaths, COPD-related disease names have been described in a Canadian report [12]. We are convinced that dissemination of the concept and diagnosis of COPD is important.

The rate of asthma/asthma-related deaths was also different based on the site of death. The concordance of ICD-10-based decision and our classification was lower in nursing homes and geriatric health care facilities. One reason may be that people living in these facilities are mostly elderly people. The education for diagnosis and therapy of bronchial asthma in these facilities would be desired.

Regarding our classification criteria, deaths occurring beyond 1 month after an asthma attack was diagnosed were not considered as asthma-related deaths. This decision was made based on the following reasons: Hospitalization period of patients admitted to the Intensive Care Unit was 5.4 days on average, even in patients who required artificial respiration [13]. Autopsy findings of slow-onset patients, which account for 80% of asthma mortality, suggested that airway changes leading to death would occur in the course of 1–3 weeks [14–16].

To reduce asthma/asthma-related deaths, appropriate treatment is definitely important. In the current study, 64% of patients according to MHLW and 49% according to our classification had less than 1 month duration from diagnosis of bronchial asthma to death. Although no information regarding treatment was available, there is a possibility that, in some cases, the presence of bronchial asthma was misdiagnosed, and appropriate treatment was not performed. A detailed survey of asthma mortality recently published in the UK concluded that 29% of mortality was not attributable to asthma and death was avoidable in approximately two-thirds of patients if they had received appropriate treatment [17].

There are several limitations in the current study. The biggest limitation of this study is that the classification of causes of death was an estimation based only on information from the death certificates. We could not examine any actual patient or medical record because the Personal Information Protection Law and the Statics Law prohibit access to the medical records and interviews to the doctors or family members. The accurate cause of death for each patient remains unclear. Second, the influence of treatment such as ICS could not be assessed in this study. Lastly, this study was

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held only in Kagawa Prefecture, which may not necessarily reflect the situation across Japan.

An analysis of the statistics of the MHLW was previously reported [18]. However, the current study is the first report based on actual death certificates and can serve as a guide in addressing asthma mortality in the future.

5. Conclusion

This survey showed that the ICD-10-based death statistics of the MHLW did not match the asthma/asthma-related deaths based on our classification, and inconsistency was notable particularly in elderly patients. An accurate understanding of the patients with avoidable death is the priority in reducing asthma mortality, and all patients with asthma/asthma-related death should be individually surveyed rather than rely on the current ICD-10-based analysis. The impact of an aging society on mortality analysis of various diseases is enormous, and establishment of appropriate death classification is desired in analyzing deaths in the elderly population.

Acknowledgement

This survey would not have materialized under the restrictions of the statistical law in Japan without the total cooperation of the government of Kagawa Prefecture. The authors are deeply grateful to the governor of Kagawa Prefecture for permitting this survey based on his wish for improving asthma treatment, to the staff of the Health and Welfare Department for providing insightful and important information, and to the public health nurses for collecting the data.

Conflicts of interest

The authors have no conflicts of interest.

REFERENCES

[1] Reid DW, Hendrick VJ, Aitken TC, Berrill WT, Stenton SC, Hendrick DJ. Age-dependent inaccuracy of asthma death certification in Northern England, 1991–1992. Eur Respir J 1998;12:1079–83.

[2] Macy E, Yao JF, Chen W. Fatal asthma: an audit of 30 million patient-years of health plan membership from 2007 to 2015. J Allergy Clin Immunol Pract 2018 [pii:S2213-2198(18)[30555-5].

[3] Goeman DP, Abramson MJ, McCarthy EA, Zubrinich CM, Douglass JA. Asthma mortality in Australia in the 21st century: a case series analysis. BMJ Open 2013;3 [pii:e002539].

[4] Lotufo PA, Bensenor IM. Temporal trends of asthma mortality rates in Brazil from 1980 to 2010. 2012;49:779–84.

[5] Gillis RME, van Litsenburg W, van Balkom RH, Muris JW, Smeenk FW. The contribution of an asthma diagnostic consultation service in obtaining an accurate asthma diagnosis for primary care patients: results of a real-life study. NPJ Prim Care Respir Med 2017;27:35.

[6] Aaron SD, Vandemheen KL, FitzGerald JM, Ainslie M, Gupta S, Lemière C, et al. Canadian Respiratory Research Network. Reevaluation of diagnosis in adults with physician-diagnosed asthma. JAMA 2017;317:269–79.

[7] American Academy of Allergy, Asthma & Immunology. Ten things physicians and patients should question, ⟨http://www.choosingwisely.org/doctor-patient-lists/american-academy-of-allergy-asthma-immunology/⟩ [Accessed 19 September 2018].

[8] Byard RW. All that wheezes is not asthma—alternative findings at autopsy. J Forensic Sci 2011;56:252–5.

[9] Papaiwannou A, Zarogoulidis P, Porpodis K, Spyratos D, Kioumis I, Pitsiou G, et al. Asthma-chronic obstructive pulmonary disease overlap syndrome (ACOS): current literature review. J Thorac Dis 2014;6(Suppl 1):S146–51.

[10] Soriano JB, Davis KJ, Coleman B, Visick G, Mannino D, Pride NB. The proportional Venn diagram of obstructive lung disease: two approximations from the United States and the United Kingdom. Chest 2003;124:474–81.

[11] Tamada T, Sugiura H, Takahashi T, Matsunaga K, Kimura K, Katsumata U, et al. Coexisting COPD in elderly asthma with fixed airflow limitation: assessment by DLco %predicted and HRCT. J Asthma 2017;54:606–15.

[12] To T, Simatovic J, Zhu J, Feldman L, Dell SD, Lougheed MD, et al. Asthma deaths in a large provincial health system. A 10-year population-based study. Ann Am Thorac Soc 2014;11:1210–7.

[13] Krishnan V, Diette GB, Rand CS, Bilderback AL, Merriman B, Hansel NN, et al. Mortality in patients hospitalized for asthma exacerbations in the United States. Am J Respir Crit Care Med 2006;174:633–8.

[14] de Magalhães Simões S, dos Santos MA, da Silva Oliveira M, Fontes ES, Fernezlian S, Garippo AL, et al. Inflammatory cell mapping of the respiratory tract in fatal asthma. Clin Exp Allergy 2005;35:602–11.

[15] Dunnill MS. The pathology of asthma, with special reference to changes in the bronchial mucosa. J Clin Pathol 1960;13:27–33.

[16] James AL, Elliot JG, Abramson MJ, Walters EH. Time to death, airway wall inflammation and remodelling in fatal asthma. Eur Respir J 2005;26:429–34.

[17] Royal College of Physicians. Why asthma still kills report and key recommendations. National review of asthma deaths (NRAD) 2014; Chapter 6:39–51.

[18] Ito Y, Tamakoshi A, Wakai K, Takagi K, Yamaki K, Ohno Y. Trends in asthma mortality in Japan. J Asthma 2002;39:633–9.

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