

# Mortality associated with polymyalgia rheumatica in the United States in the 1999-2020 period: a multiple-cause-of-death study

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**Abstract.** – **OBJECTIVE:** Multicause-of-death methods were used to analyze mortality and leading causes of death associated with polymyalgia rheumatica (PMR) in the United States from 1999 to 2020.

**MATERIALS AND METHODS:** We analyzed mortality data from the Centers for Disease Control and Prevention (CDC) Data analysis system and selected death certificates that listed PMR as the cause of death based on the International Statistical Classification of Diseases and Related Health Problems (ICD-10) category code. Relevant mortality rates, number of deaths and historical trends were analyzed. The number of PMR-related deaths and age-standardized mortality rate (ASMR) trend charts were made using Excel 2010 version and trend lines were added.

**RESULTS:** Over the last 22 years, the total number of PMR-related deaths in the United States was 15,421 women (89.8%), a ratio of about 1:9 men to women. When PMR is listed as the underlying cause of death, the ASMR for women and men (per 100,000 people) is approximately 1.8-5.1:1, and when it is listed as the non-underlying cause of death, it is 1.8-3.3:1. PMR deaths are more frequent in individuals aged 70 years and above, with patients aged 80 years and above being most affected. Among different ethnicities, the highest number of deaths was found in Caucasians, followed by Black or African American. When it comes to causes of death, heart disease still ranks first, followed by cancer. In addition, we also found that when PMR combined with malignant tumors as a multiple cause of death, the number of female deaths was higher than that of male deaths, the overall number of deaths of both showed an upward trend, and the overall ASMR of both showed a downward trend.

**CONCLUSIONS:** In the past 22 years, we have observed a low mortality rate of PMR in the United States.

However, for patients with PMR, especially elderly women, medical workers should be vigilant and pay attention to whether they are combined with other complications, such as malignant neoplasms, and make timely diagnosis and treatment to further reduce the mortality rate of patients with PMR.

*Key Words:*

Polymyalgia rheumatica, Age-standardized mortality, Malignant neoplasms.

## Introduction

Polymyalgia rheumatica PMR is a rheumatic disease associated with moderate to severe musculoskeletal pain and stiffness in the neck, shoulders, and hips. It affects people over the age of 50, with an average age of onset of about 70. Women are more affected than men<sup>1</sup>. The incidence increases with age. Previous studies<sup>2,3</sup> have found that between 1970 and 1999, the incidence of PMR in Olmsted County was 59 per 100,000, and the survival rate was similar to that of the general population. In different populations, the prevalence of PMR is 12-60/100,000, and the age-standardized mortality rate (ASMR) is about 0.70<sup>4,5</sup>.

Other complications may occur with PMR, and there is a lack of conclusive evidence as to which comorbidities are co-existing with or possibly related to PMR. Some evidence<sup>6</sup> shows that PMR significantly increases the risk of cardiovascular disease (CVD) and malignant tumors and may become one of the main causes of death. It remains unclear if the cause of death mentioned in PMR and its ranking have changed in the last 22 years.

Among diseases that mimic PMR, tumors deserve further study. The possibility that PMR may be a paraneoplastic syndrome has been unanimously accepted, but how often this occurs is still under discussion<sup>7,8</sup>. Patients with PMR have a 69% increased risk of developing cancer within the first 6 months after a PMR diagnosis<sup>9</sup>. In similar studies<sup>10</sup>, an increased risk of cancer was observed after one year of hospitalization, with malignancy observed in about 5.5% of patients. At present, there is a lack of relevant studies on the death of PMR complicated with malignant tumors.

Therefore, this study aimed to describe PMR-related deaths and the leading causes of death using multiple cause-of-death methods based on nearly 22 years of death certificate data from the the Centers for Disease Control and Prevention (CDC).

## Materials and Methods

We used the U.S. CDC database to derive deaths per 100,000 people and age-standardized mortality rates from 1999 to 2020. According to the 10<sup>th</sup> Revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10)<sup>11</sup>, category code: polymyalgia rheumatica (M35.3), malignancy (C00-D97). By analyzing data on fatalities, mortality rates, and past patterns, we examined various factors, including gender, age at death (categorized as < 60 years, 60-69 years, 70-79 years, ≥ 80 years), alterations in the hierarchy of causes of death when PMR was cited as the primary cause, and the comparison of fatalities and ASMR when PMR was associated with malignant tumors over the past 22 years. The ratio of female to male deaths was calculated when PMR was listed as the underlying cause of death and when PMR was listed as the non-underlying cause of death. The number of PMR-related deaths and ASMR (per 100,000 people) were trended in Excel 2010 and trendlines were added. This research was not conducted on either humans or animals. Therefore, no ethics approval was required.

## Results

During the period 1999-2020, the total number of PMR-related deaths in the United States was 21,136, of whom 5,715 (10.2%) were men and

15,421 (89.8%) were women (Table I), for a ratio of approximately 1:9 men to women. When PMR is listed as the underlying cause of death, there are 2,000 deaths (9.5%) in the period 1999-2020, and there is a decreasing trend, with a separate decreasing trend in the number of female deaths and no significant change in the number of male deaths. ASMR (per 100,000 people) is approximately 1.8-5.1:1 in women and men, with a decreasing trend, and PMR deaths are more common in patients aged 70 years and older, mainly concentrated in patients in the 80 + age group (Table I and Table II). When PMR is classified as a non-underlying cause of death, there are 19,136 deaths (90.5%) in the period 1999-2020. The annual number of deaths has a downward trend and then an upward trend; the number of female deaths shows a downward trend, the number of male deaths shows a fluctuating trend, and the ASMR of women and men (per 100,000 population) is about 1.8-3.3:1. PMR deaths are more common in patients over the age of 80 years (Table I).

In addition, when PMR was used as a multiple cause of death, we found that there were 798 deaths under 70 years old, 3,458 deaths between 70 and 79 years old, and 16,880 deaths over 80 years old when we analyzed the number and proportion of deaths in different age groups. The proportion of deaths by age group is shown in Figure 1. The number of deaths is mainly concentrated in people over 70 years of age, especially those 80 years of age and above.

At the same time, we analyzed the number of sex-specific deaths in PMR as a multiple cause of death and the number of ASMR and ethnic deaths. We found that between 1999 and 2020, women had a higher death rate and age-standardized mortality rate (ASMR) than men. The number of female deaths and ASMR showed a decreasing trend. The number of deaths among males and the popularity of ASMR have been decreasing in general, but both have shown an increase during the years 2018-2022 (Figures 2 and 3). For different ethnic groups (including Asian or Pacific Islander and American Indian or Alaska Native, Black or African American, and White), we found that the highest number of deaths between 1999-2020 were White, with 20,296 deaths, followed by Black or African American with 604 deaths, Asian or Pacific Islander and American Indian or Alaska Native had the fewest deaths, with 236 deaths. The number of deaths by ethnicity is shown in Figure 4.

**Table I.** Number of PMR-related deaths in the US from 1999 to 2020 stratified by year.

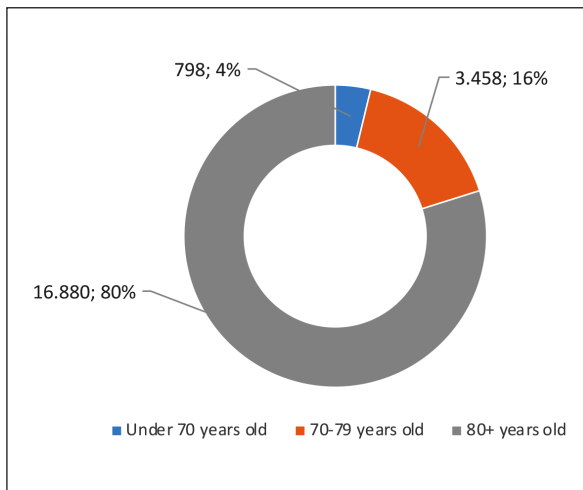
	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010
All PMR-related deaths No.	1,016	994	1,064	1,053	1,039	963	920	986	896	954	937	1,012
PMR listed as the UCD	84	96	111	124	92	92	93	99	77	100	87	101
Men, No.	25	20	27	28	15	22	32	21	21	25	19	24
Women, No.	59	76	84	96	77	70	61	78	56	75	68	77
Ratio of women to men	2.4	3.8	3.1	3.4	5.1	3.2	1.9	3.7	2.7	3.0	3.6	3.2
Age, No.												
< 60 years	-	-	-	-	-	-	-	-	-	-	-	-
60-69 years	-	-	-	-	-	-	-	-	-	-	-	-
70-79 years	13	13	14	14	13	17	16	16	10	19	15	15
> 80 years	68	78	93	101	71	67	71	82	66	78	67	81
PMR listed as the NUCD	932	898	953	929	947	871	827	887	792	854	850	911
Men, No.	218	217	232	244	232	213	212	244	204	212	242	243
Women, No.	714	681	721	685	715	658	615	643	588	642	608	668
Ratio of women to men	3.3	3.1	3.1	2.8	3.1	3.1	2.9	2.6	2.9	3.0	2.5	2.7
Age, No.												
< 60 years	-	-	-	-	-	-	-	-	-	-	-	-
60-69 years	30	25	32	25	44	40	23	28	26	30	29	21
70-79 years	203	185	204	189	187	163	177	149	140	159	157	149
> 80 years	782	776	819	832	804	754	713	802	727	758	747	832

Polymyalgia rheumatica (PMR); underlying cause of death (UCD); non-underlying cause of death (NUCD).

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**Table II.** Number of PMR-related deaths in the US from 2011 to 2020 stratified by year.

	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	All
All PMR-related deaths No.	963	944	911	865	882	900	919	861	908	1,149	21,136
PMR listed as the UCD	102	110	84	83	95	79	63	70	78	80	2,000
Men, No.	28	31	20	20	27	23	13	20	28	22	511
Women, No.	74	79	64	63	68	56	50	50	50	68	1,489
Ratio of women to men	2.6	2.5	3.2	3.2	2.5	2.5	3.8	2.5	1.8	3.1	2.9
Age, No.											
< 60 years	-	-	-	-	-	-	-	-	-	-	12
60-69 years	-	-	-	-	-	-	-	-	-	-	70
70-79 years	14	15	0	0	14	13	14	11	10	12	294
> 80 years	85	93	73	72	79	61	49	56	67	66	1,624
PMR listed as the NUCD	861	834	827	782	787	821	856	791	830	1,069	19,136
Men, No.	240	223	248	198	217	251	263	218	283	360	5,204
Women, No.	621	611	579	584	570	570	593	573	547	709	13,932
Ratio of women to men	2.6	2.7	2.3	2.9	2.6	2.3	2.3	2.6	1.9	2.0	2.7
Age, No.											
< 60 years	-	-	-	-	-	-	-	-	-	-	132
60-69 years	26	28	31	30	24	40	38	26	29	41	666
70-79 years	131	142	117	128	127	135	135	123	157	201	3,458
> 80 years	797	773	760	701	725	717	741	707	714	889	16,880

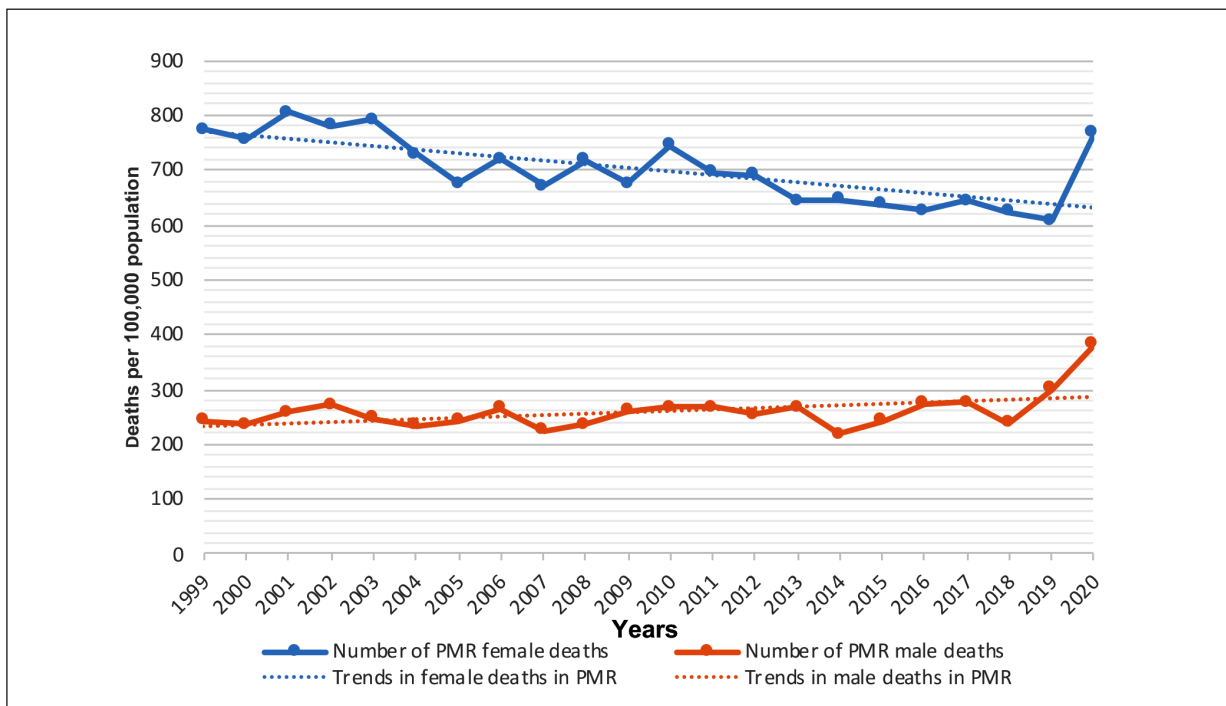


**Figure 1.** The number and proportion of deaths in different age groups.

We also looked for the ranking of the top 10 causes of death in the last 22 years (1999-2008) and the next 10 years (2011-2020) that mentioned PMR as the underlying cause of death (Tables III and IV) and found that the last 10 years compared with the first 10 years, diseases of heart and malignant neoplasms ranked first and sec-

ond, respectively. Some new diseases were added or changed in the rankings, including accidents (unintentional injuries) (ninth) and COVID-19 (tenth). Alzheimer’s disease and chronic lower respiratory diseases have swapped their positions on the list of leading causes of death. Alzheimer’s disease now ranks third, while chronic lower respiratory diseases rank fourth. Cerebrovascular diseases dropped from third to fifth. Diabetes mellitus dropped from fourth to sixth place. Influenza and pneumonia fell from seventh to eighth.

In our study, we also found that during 1999-2020, the total number of PMR patients combined with malignant tumors as multiple causes of death was 2,982, accounting for 14.1% of the total number, including 1,788 (60.0%) women and 1,194 (40.0%) men. The number of deaths caused by PMR was higher in women compared to men. In the recent period (2018-2020), the number of PMR deaths in women gradually increased, with the overall trend being slow and fluctuating. On the other hand, the number of PMR deaths in men also increased recently (2017-2020), with the overall trend being more obvious than that in women (Figure 5). Women’s ASMR was lower than men’s in 2000, 2004, 2007-2008, 2012, 2015,



**Figure 2.** PMR deaths by gender in the US from 1999 to 2020.

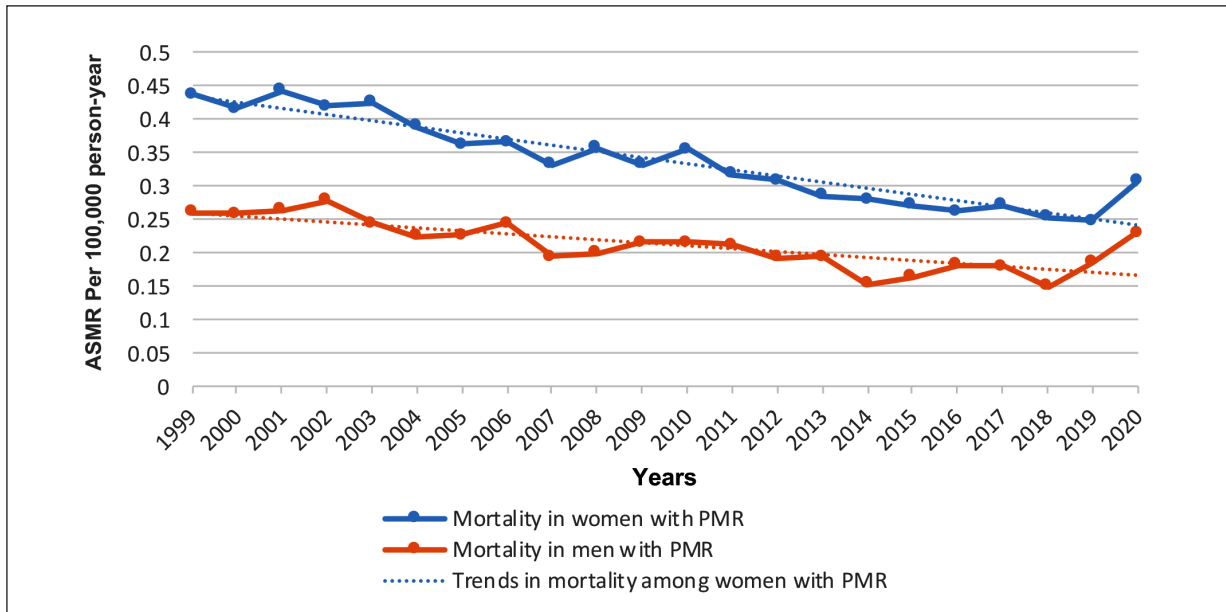


Figure 3. ASMR by gender PMR in the US from 1999 to 2020.

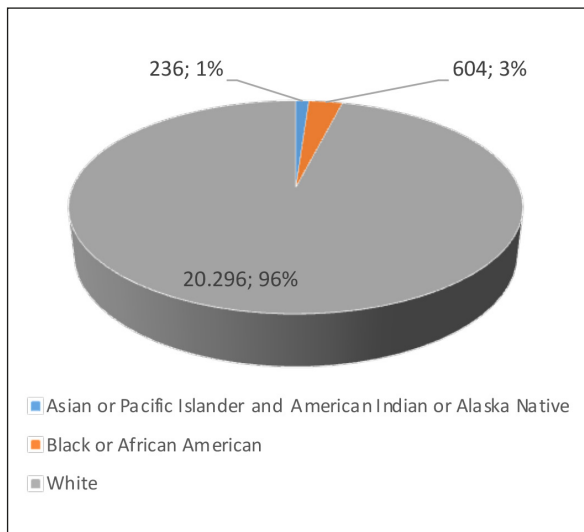


Figure 4. The number and proportion of PMR deaths by race in the US from 1999 to 2020.

and 2017, and higher than men’s in the remaining years. After 2018, ASMR increased year by year, while the overall ASMR of both showed a downward trend (Figure 6).

### Discussion

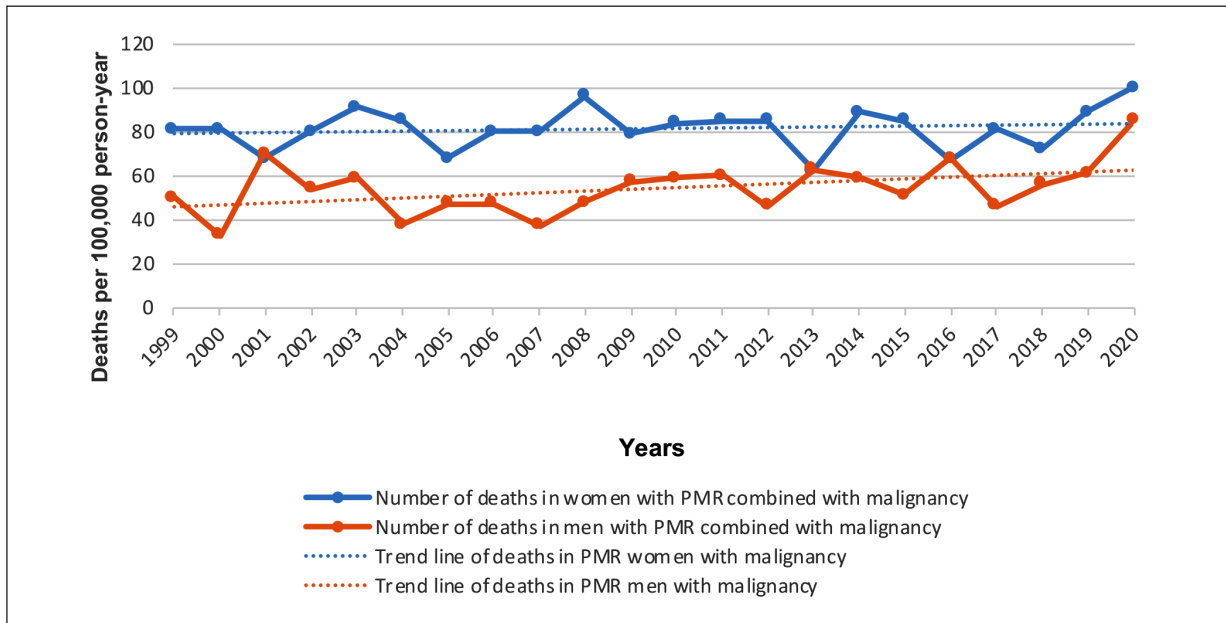
The results of this study show that from 1999 to 2020, ASMR in women with PMR was higher

Table III. Ranking of underlying causes of death in PMR mentioned from 1999 to 2008.

UCD - ICD-10 113 cause list	Deaths
#Diseases of heart (I00-I09,I11,I13,I20-I51)	2,896
#Malignant neoplasms (C00-C97)	916
#Cerebrovascular diseases (I60-I69)	664
#Diabetes mellitus (E10-E14)	432
#Chronic lower respiratory diseases (J40-J47)	409
#Alzheimer disease (G30)	356
#Influenza and pneumonia (J09-J18)	278
#Essential hypertension and hypertensive renal disease (I10,I12,I15)	229
#Septicemia (A40-A41)	121
#Nephritis, nephrotic syndrome and nephrosis (N00-N07,N17-N19,N25-N27)	104

Table IV. Ranking of underlying causes of death in PMR mentioned from 2011-2020.

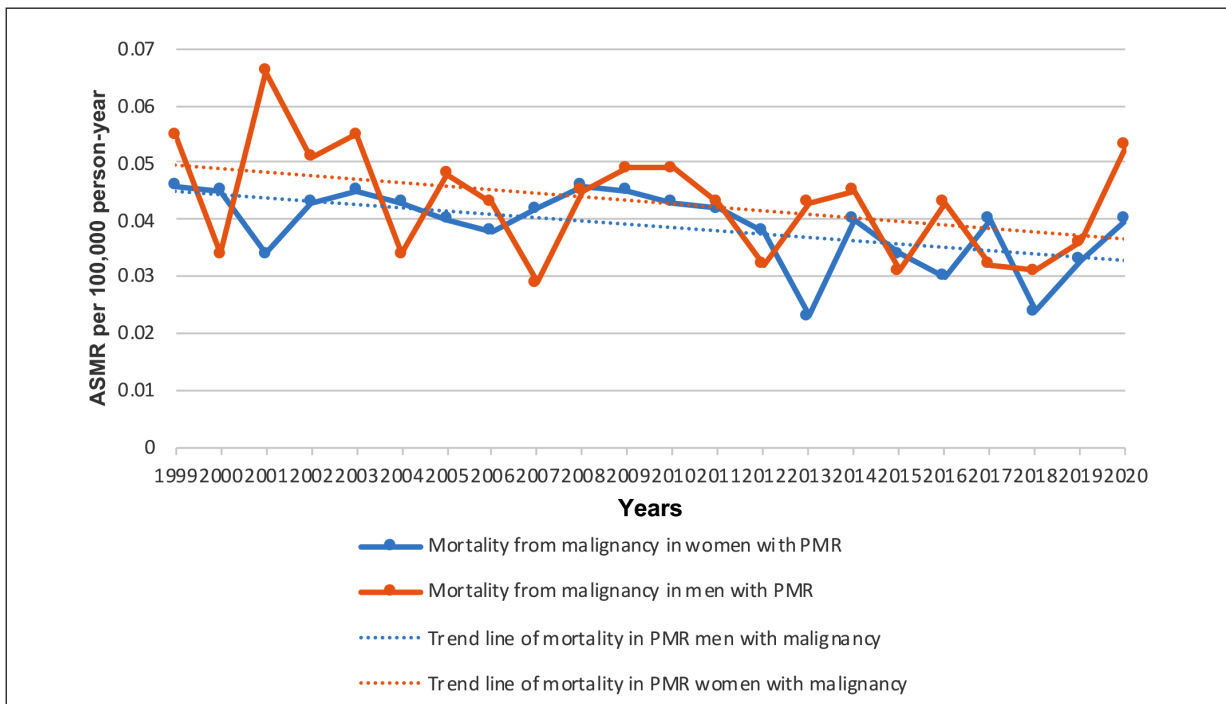
UCD - ICD-10 113 cause list	Deaths
#Diseases of heart (I00-I09,I11,I13,I20-I51)	2,083
#Malignant neoplasms (C00-C97)	935
#Alzheimer disease (G30)	516
#Chronic lower respiratory diseases (J40-J47)	454
#Cerebrovascular diseases (I60-I69)	432
#Diabetes mellitus (E10-E14)	355
#Essential hypertension and hypertensive renal disease (I10,I12,I15)	259
#Influenza and pneumonia (J09-J18)	198
#Accidents (unintentional injuries) (V01-X59,Y85-Y86)	174
#COVID-19 (U07.1)	122



**Figure 5.** The number of deaths from PMR combined with malignant tumors by gender between 1999 and 2020.

than in men, with a mortality ratio of about 9:1. A higher PMR-related mortality in women is associated with a higher prevalence in women<sup>2</sup>. When PMR was listed as the underlying cause of death and the non-underlying cause of death,

the number of deaths showed an increasing trend, and the number of deaths of men showed an increasing trend, while the number of deaths of women showed a decreasing trend, which may be related to the more obvious symptoms



**Figure 6.** The ASMS from PMR combined with malignant tumors by gender between 1999 and 2020.

of women's timely medical treatment. In addition, we also found that when PMR was listed as the underlying cause of death or non-underlying cause of death, the number of deaths mainly occurred in patients over 70 years old, especially in patients over 80 years old, which may be related to the age at diagnosis. Some studies<sup>12</sup> found that the peak was between 70 and 75 years old, and the average age at the first diagnosis of PMR was 70 years old. 25% were aged between 70 and 79 at the time of diagnosis. The highest proportion of deaths at age 80 and older may be associated with aging of the immune system and also with increased susceptibility to autoimmune processes and infections<sup>13,14</sup>. In our study, it was also found that both the number of deaths and ASMR in female patients with PMR were higher than those in male patients, which may be related to the ratio of male to female patients. Some research<sup>15</sup> results showed that women may be 2-3 times more affected by PMR than men. Overall, female ASMR exhibited a downward trend, whereas male ASMR showed an upward trend. This may be related to the emergence of new drugs and the more apparent symptoms in female patients. Regarding different ethnic groups, the study found that between 1999 and 2020, the highest number of deaths occurred among Caucasians, with the lowest number of deaths occurring among Asian or Pacific Islanders and American Indians or Alaska Natives. Previous studies<sup>16</sup> have found that PMR is more prevalent in people of Northern European descent than in other populations. In Southern Europe and other parts of the world, the estimated incidence and prevalence of PMR are much lower, and a low incidence of PMR has been reported in South Korea<sup>17</sup>, thus indicating that PMR is significantly less common in the Asian or Pacific Islander and American Indian or Alaska Native. In addition, while all racial and ethnic groups can be affected, PMR is rarely reported among African American and Hispanic populations<sup>16</sup>.

In this study, Tables II and III present the ranking of PMR as the underlying cause of death from 1999 to 2008 and from 2011 to 2020. Heart diseases and malignant neoplasms still rank in the front, which may be closely related to age. Previous studies<sup>18</sup> believed that cardiovascular diseases and malignant tumors were the main causes of death caused by rheumatic diseases, which was basically consistent with our findings. The new cause of death is COVID-19, which is

related to the occurrence of the epidemic in recent years and the use of immunosuppressants in PMR patients, which can increase the severity of the disease in patients<sup>19</sup>. Accidents (unintentional injuries) are related to the improvement of people's living standards and the widespread use of cars as a means of transportation. The ranking of Alzheimer's disease increased in the last 10 years, which is closely related to the older age of onset of the disease and the aging population. The rise in chronic lower respiratory disease ranking may be related to lower resistance and greater susceptibility to respiratory infections in the elderly. Cerebrovascular diseases, diabetes mellitus, influenza, and pneumonia fell from the previous decade; it is related to the application of upgraded drugs such as antiplatelet drugs, hypoglycemic drugs, insulin, antibiotics, and antiviral drugs in recent years<sup>20-23</sup>.

With the progression of the disease, PMR is closely related to the increased risk of malignant tumors. Our study found that PMR accounted for 14.1% of the total number of malignant tumors combined with PMR. The death toll of women and men showed an upward trend, and ASMR showed an overall upward trend, and the trend was more obvious than that of women. Studies have shown that PMR patients have a 69% increased risk of developing cancer in the first 6 months after a PMR diagnosis<sup>9</sup>, and in a similar study, it was observed that the cancer risk in PMR patients was highest in the first year after hospitalization<sup>10</sup>. In the first year after a PMR diagnosis, some researchers<sup>24</sup> have observed that a high risk of cancer may lead to misdiagnosis. Finally, it has been emphasized that PMR and metastatic symmetry serosynovitis with pitting edema may be neoplastic warnings.

This study revisited the question of PMR-related mortality over the last 22 years. The use of multiple cause-of-death analysis is one of the main characteristics and strengths of this study. Multiple cause-of-death analysis methods were used to determine the maximum number of likely deaths associated with autoimmune diseases, which are often referred to as related causes of death<sup>25</sup>. In this study, PMR was classified as a related cause of 90.5% of deaths. The underestimation of rheumatic diseases in mortality statistics is attributed to the identification of one of its complications, such as infection or cardiovascular disease<sup>26,27</sup>, which often become the underlying cause of death. It is important to note that this study has some limitations. For instance,



even though mortality data in the United States is processed automatically, recording the cause of death still relies on trained disease logists. These experts may unintentionally introduce incorrect ICD-10 codes, which could affect the accuracy of the data.

## Conclusions

In this study, we used multiple cause-of-death analyses to characterize PMR-related mortality in the United States over a nearly 22-year period. We observed a predominance of deaths in women aged 80 years and older with PMR. Caucasians accounted for the largest number of deaths. The number of PMR deaths and ASMR deaths has declined, but only 9.5% of deaths were identified as the underlying cause of PMR. This suggests that PMR mortality statistics may be underestimated. When referring to PMR as the underlying cause of death, diseases of heart were still the primary cause, followed by malignant neoplasms. Although the results of this study show that PMR mortality is generally low, clinicians should actively regulate and rationally treat PMR, and closely monitor patients with risk factors (such as screening for malignant tumors) to improve patient prognosis and further reduce mortality.

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## Authors' Contributions

RXH, YTY, and JYL performed and wrote the manuscript; YY, XCH, DLM, RJH, YJH, and XZ collected the references, designed the table, and drew the figures; CCW and XXH reviewed and proofread the manuscripts. All authors read and approved the final manuscript.

## Conflict of Interest

The authors declare that they have no conflict of interest.

## Data Availability

The data supporting this article are available from the corresponding author upon reasonable request.

## Ethics Approval and Informed Consent

Not applicable.

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## References

- 1) Mahmood SB, Nelson E, Padniewski J, Nasr R. Polymyalgia rheumatica: An updated review. *Cleve Clin J Med* 2020; 87: 549-556.
- 2) Salvarani C, Gabriel SE, O'Fallon WM, Hunder GG. Epidemiology of polymyalgia rheumatica in Olmsted County, Minnesota, 1970-1991. *Arthritis Rheum* 1995; 38: 369-373.
- 3) Doran MF, Crowson CS, O'Fallon WM, Hunder GG, Gabriel SE. Trends in the incidence of polymyalgia rheumatica over a 30 year period in Olmsted County, Minnesota, USA. *J Rheumatol* 2002; 29: 1694-1697.
- 4) Raheel S, Shbeeb I, Crowson CS, Matteson EL. Epidemiology of Polymyalgia Rheumatica 2000-2014 and Examination of Incidence and Survival Trends Over 45 Years: A Population-Based Study. *Arthritis Care Res (Hoboken)* 2017; 69: 1282-1285.
- 5) Salvarani C, Macchioni P, Zizzi F, Mantovani W, Rossi F, Castri C, Capozzoli N, Baricchi R, Boiardi L, Chiaravalotti F. Epidemiologic and immunogenetic aspects of polymyalgia rheumatica and giant cell arteritis in northern Italy. *Arthritis Rheum* 1991; 34: 351-356.
- 6) Partington R, Helliwell T, Muller S, Abdul Sultan A, Mallen C. Comorbidities in polymyalgia rheumatica: a systematic review. *Arthritis Res Ther* 2018; 20: 258.
- 7) Manzo C. Paraneoplastic syndromes and inflammatory rheumatic diseases: Not everything that glitters is gold. The case of polymyalgia rheumatica. *J Med Oncol Ther* 2018; 3: 21-22.
- 8) Muller S, Hider S, Helliwell T, Partington R, Mallen C. The real evidence for polymyalgia rheumatica as a paraneoplastic syndrome. *Reumatismo* 2018; 70: 23-34.
- 9) Muller S, Hider SL, Belcher J, Helliwell T, Mallen CD. Is cancer associated with polymyalgia rheumatica? A cohort study in the General Practice Research Database. *Ann Rheum Dis* 2014; 73: 1769-1773.
- 10) Ji J, Liu X, Sundquist K, Sundquist J, Hemminki K. Cancer risk in patients hospitalized with polymyalgia rheumatica and giant cell arteritis: a follow-up study in Sweden. *Rheumatology (Oxford)* 2010; 49: 1158-1163.
- 11) World Health Organization. *Manual of the International Statistical Classification of Diseases, Injuries and Causes of Death. Vol. 1. World Health Organization Geneva; 1997. Ninth Revision.*
- 12) Manzo C. Incidence and Prevalence of Polymyalgia Rheumatica (PMR): The Importance of the Epidemiological Context. The Italian Case. *Med Sci (Basel)* 2019; 7: 92.

- 13) Gazitt T, Zisman D, Gardner G. Polymyalgia Rheumatica: a Common Disease in Seniors. *Curr Rheumatol Rep* 2020; 22: 40.
- 14) Carvajal Alegria G, Boukhlal S, Cornec D, Devauchelle-Pensec V. The pathophysiology of polymyalgia rheumatica, small pieces of a big puzzle. *Autoimmun Rev* 2020; 19: 102670.
- 15) Michet CJ, Matteson EL. Polymyalgia rheumatica. *BMJ* 2008; 336: 765-769.
- 16) Lundberg IE, Sharma A, Turesson C, Mohammad AJ. An update on polymyalgia rheumatica. *J Intern Med* 2022; 292: 717-732.
- 17) Lee KA, Kim HS, Lee SH, Kim HR. Diagnostic performance of the 2012 EULAR/ACR classification criteria for polymyalgia rheumatica in Korean patients. *Int J Rheum Dis* 2020; 23: 1311-1317.
- 18) Nannini C, Jebakumar AJ, Crowson CS, Ryu JH, Matteson EL. Primary Sjogren's syndrome 1976-2005 and associated interstitial lung disease: a population-based study of incidence and mortality. *BMJ Open* 2013; 3: e003569.
- 19) Martínez-López D, Ferraz-Amaro I, Prieto-Peña D, Sánchez-Bilbao L, Herrero-Morant A, Álvarez-Reguera C, Benavides-Villanueva F, Corrales-Selaya C, Trigueros-Vázquez M, González-Gay MÁ, Blanco R. Coronavirus disease 2019 in patients with rheumatic immune-mediated diseases in a single University Hospital, matched case-control study and literature review. *Front Med (Lausanne)* 2022; 9: 1056374.
- 20) Kamarova M, Baig S, Patel H, Monks K, Wasay M, Ali A, Redgrave J, Majid A, Bell SM. Antiplatelet Use in Ischemic Stroke. *Ann Pharmacother* 2022; 56: 1159-1173.
- 21) Lv W, Wang X, Xu Q, Lu W. Mechanisms and Characteristics of Sulfonylureas and Glinides. *Curr Top Med Chem* 2020; 20: 37-56.
- 22) Home P. The evolution of insulin therapy. *Diabetes Res Clin Pract* 2021; 175: 108816.
- 23) Hutchings MI, Truman AW, Wilkinson B. Antibiotics: past, present and future. *Curr Opin Microbiol* 2019; 51: 72-80.
- 24) Manzo C, Natale M. Polymyalgia Rheumatica in Association with Remitting Seronegative Sinovitis with Pitting Edema: a Neoplastic Warning. *Can Geriatr J* 2017; 20: 94-96.
- 25) Walsh SJ, DeChello LM. Excess autoimmune disease mortality among school teachers. *J Rheumatol* 2001; 28: 1537-1545.
- 26) Gargiulo G, Serino F, Esposito G. Cardiovascular mortality in patients with acute and chronic coronary syndrome: insights from the clinical evidence on ticagrelor. *Eur Rev Med Pharmacol Sci* 2022; 26: 2524-2542.
- 27) Oboza P, Ogarek N, Olszanecka-Glinianowicz M, Kocelak P. The main causes of death in patients with COVID-19. *Eur Rev Med Pharmacol Sci* 2023; 27: 2165-2172.