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Multiple myeloma mortality in Latin America: Heterogeneous patterns and challenges in cross-country comparisons

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ABSTRACT

Introduction: Differences in death certification practices may affect cross-country comparisons of multiple myeloma (MM) mortality estimates. In Latin America, where access to transplantation and novel therapies remains limited, MM mortality patterns have not consistently aligned with expected differences. We describe MM mortality rates across Latin American countries and compare them to those of Hispanic individuals in the United States (US).

Methods: In this population-based study, we analyzed mortality data from 15 Latin American countries (World Health Organization Mortality Database) and the US (National Center for Health Statistics data). MM deaths among adults (≥20 years) during 2008–2019 were examined using US Hispanic individuals as reference.

Results: The highest mortality (per 100,000 persons) in Latin American countries was observed in Chile (4.12), Uruguay (4.11), and Costa Rica (3.57). Mortality for US Hispanic individuals was 3.8. Most countries exhibited lower or comparable mortality rate ratios (MMRs) relative to US Hispanic individuals. Stratified analyses by sex showed similar findings. However, this pattern was not consistent across age groups. Young adults (20–59 years) generally experienced higher mortality, particularly in Cuba (MRR=2.04, 95% CI=1.88–2.21; $P_{heterogeneity}<0.0001$). Countries with higher Human Development Index tended to exhibit mortality estimates more closely aligned with those of US Hispanic individuals.

Conclusion: MM mortality patterns across Latin America were heterogeneous and often lower than those observed among US Hispanic individuals, despite known differences in access to care. Strengthening MM surveillance systems is needed to improve the interpretation of mortality patterns across the region.

1. Introduction

Multiple myeloma (MM) is a plasma cell malignancy and a resource-intensive disease that often requires treatment with systemic therapies and autologous hematopoietic cell transplantation [1,2]. However, limited access to transplantation and novel therapies in Latin America may affect population-level mortality outcomes [3]. With the introduction of proteasome inhibitors (e.g., bortezomib) in 2008 and increasing access to autologous hematopoietic cell transplantation [1,4], survival outcomes improved significantly from approximately 30% in 1993–50% in 2012 [5]. More recently, novel immunotherapies such as immunomodulatory drugs have further shifted the treatment landscape of MM [1]. Access to these agents remains limited in Latin America [6]. Notably, a previous study reported similar or slightly lower rates across Latin American countries compared to high-income settings with greater access to these therapies [7]. These observations raise concerns regarding the impact of treatment access on MM mortality rates in the region.

Mortality rates in Latin American countries may differ from those observed in other populations with distinct healthcare systems and access to care. In the United States (US), one population-based study using death certification data reported similar MM mortality rates between

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non-Hispanic White and Hispanic individuals [8], and the Surveillance, Epidemiology, and End Results (SEER) program reports rates of 2.8 and 2.5 per 100,000 persons, respectively, in 2020 [9]. These findings suggest mortality rates among Hispanic individuals are relatively similar to those of non-Hispanic White patients. Cross-population comparisons between US Hispanic individuals and Latin American countries may provide insight into differences in MM mortality patterns, although such comparisons remain ecological in nature.

The lack of high-quality cancer registries in Latin America complicates the estimation of population-level survival rates [10], rendering mortality rates a common metric for evaluating MM mortality outcomes at the population level in the region. Differences in quality among mortality registries may affect comparisons of mortality estimates across countries. A previous study suggested that death certification-based estimates may underestimate lymphoma-specific mortality in Latin America [11], although the extent to which this applies to MM remains uncertain. To address these gaps, we describe MM mortality rates across Latin American countries and compare them to those observed among US Hispanic individuals between 2008 and 2019. We further estimate trends over time and explore the Human Development Index (HDI) as a proxy for the quality of death certification.

2. Methods

2.1. Design and data sources

Deaths from 15 Latin American countries (Argentina, Brazil, Chile, Colombia, Costa Rica, Cuba, Ecuador, Guatemala, Mexico, Nicaragua, Panama, Paraguay, Peru, Uruguay, and Venezuela) were abstracted from the World Health Organization (WHO) database [12]. The total population size for each Latin American country based on sex, 5-year age groups, and year was obtained from the United Nations World Population 2022 [13]. HDI for Latin American countries was extracted from the United Nations Development Programme [14]. MM deaths in the US were abstracted from the National Center for Health Statistics and the National Vital Statistics System for all states, which is accessed through the SEER*Stat software [15]. The population size for each race and ethnicity in the US was extracted from SEER*Stat.

Only mortality events occurring among adults aged ≥ 20 years were included in the analysis. For Latin America, we further restricted to countries with ≥ 60% mortality data usability (Table 1), corresponding to a medium quality according to the WHO [16]. Data usability is a metric that combines the completeness of mortality registries and the use of ill-defined causes of death (e.g., sepsis) in death certificates [17]. Individuals with unknown age at death, sex, and race and ethnicity were excluded from the analysis. The burden of MM within the period 2008–2019 was evaluated (Supplementary Figure 1). The initial observation year was set at 2008, as data quality indicators for Latin American countries have been available since then [16]. Due to the impact of the coronavirus pandemic on mortality and mortality reporting [3], 2019 was selected as the final observation year. The study period was extended to 2000–2019 for the assessment of mortality trends, although data quality indicators for years before 2008 were unavailable.

2.2. Variables

Individuals from the US were stratified as US non-Hispanic Asian and Pacific Islander (US Asian), US non-Hispanic Black (US Black), and US non-Hispanic White (US White). To provide comparison to the US, we use US Hispanic individuals as a reference group, given partially overlapping ancestry and prior reports of similar MM mortality to non-Hispanic White populations, although differences in demographic composition and healthcare access remain [8,9]. Age at death was grouped into young adults (20–59 years), adults (60–74 years), and older adults (≥75 years). We expanded the age range to include young adults up to age 59 years because of the age-at-onset distribution in MM. Sex on death certificates was defined as male and female. The average HDI during the 2008–2019 period for each Latin American country was obtained from the United Nations Development Programme [14].

2.3. Outcome

The primary outcome was MM mortality, defined as deaths due to MM or plasmacytoma. The 10th edition of the International

Table 1
Quality of data, multiple myeloma mortality rates, and Human Development Index among deceased individuals aged ≥ 20 years in Latin American countries and the United States race and ethnic groups, 2008–2019.

Country / US race and ethnicity	Data quality indicators				HDI	Multiple myeloma[a]		
	Mortality completeness (%)	Ill-defined causes of death (%)	Usability (%)	Available years		No. of deaths	Population	MR per 100,000
Argentina	100	28	72	2008–2019	0.85	7418	341,132,900	2.34
Brazil	100	16	84	2008–2019	0.76	32,426	1661,236,480	2.91
Chile	100	11	89	2008–2019	0.84	5520	152,802,614	4.12
Colombia	100	9	91	2008–2019	0.76	6423	367,864,362	2.65
Costa Rica	100	11	89	2008–2019	0.79	1020	39,458,570	3.57
Cuba	100	8	92	2008–2019	0.77	3782	103,827,099	3.51
Ecuador	86	15	73	2008–2019	0.75	1422	115,985,789	1.87
Guatemala	87	21	68	2008–2019	0.63	349	96,499,225	0.63
Mexico	100	8	92	2008–2019	0.77	12,511	883,422,110	1.97
Nicaragua	100	13	87	2008–2019	0.67	171	41,730,035	0.71
Panama	100	19	81	2008–2019	0.80	557	29,199,301	2.76
Paraguay	98	16	82	2008–2019	0.73	434	42,478,452	1.68
Peru	78	23	60	2008–2019	0.75	2710	227,382,482	1.62
US AI/An[b]	-	-	-	2008–2019	-	669	21,675,698	3.90
US Asian[b]	-	-	-	2008–2019	-	2957	164,204,433	2.30
US Black[b]	-	-	-	2008–2019	-	25,090	342,644,085	8.80
US Hispanic[b]	-	-	-	2008–2019	-	9667	418,955,935	3.80
US White[b]	-	-	-	2008–2019	-	102,429	1870,703,257	4.30
Uruguay	100	20	80	2008–2010, 2012–2019	0.81	1244	26,431,297	4.11
Venezuela	100	11	89	2008–2016	0.76	2595	162,254,426	2.50

a Includes the ICD-10 codes C90.0, C90.2, and C90.3
b Data for the United States was extracted from the SEER program, and data quality was not available
Abbreviations: AI/AN, American Indian/Alaska Native; HDI, Human Development Index; MR, mortality rate; US, United States

Classification of Diseases (ICD-10) was used to identify deaths attributed to MM in death certificates in the SEER and WHO data sources. The codes C90.0, C90.2, and C90.3 were queried to define MM mortality. We excluded C90.1 ("Plasma cell leukemia") from our analysis because the fixed mortality coding in SEER includes this ICD-10 code in another group labeled as 'Other leukemia,' and it was not possible to extract and re-group this code. Therefore, we used these specific ICD-10 codes in the WHO database to match the fixed MM mortality coding in the SEER*Stat program.

2.4. Data analysis

The age-standardized mortality rates per 100,000 were estimated through the direct method using the World standard population to account for differences in underlying population age structure [18]. Mortality rate ratios (MRRs) and 95% confidence intervals (CIs) were calculated using US Hispanic individuals as the reference group in Poisson regression models. The log of the population size was used as an offset to control for variations in population structure. The main model was adjusted for age groups and sex. Subgroup analyses involved estimating mortality rates and MRRs by sex and age group stratification. To evaluate if estimates from the stratified models differ statistically, models were fitted with an additional interaction term (e.g., country and sex) and compared to the overall adjusted model using the Likelihood ratio test. Each country and the US race and ethnic groups were compared individually to US Hispanic patients. The Bonferroni correction was applied to report the heterogeneity p-values. A linear regression model was fitted to assess if the country's development (i.e., a proxy for the quality of cause of death registration) was associated with the distribution of MRRs. A simple linear regression model was used for the overall and subgroup analyses, with HDI as the predictor of MRRs. Findings are reported with β coefficients and 95% CIs. Considering the limitations for providing high-quality care for patients with MM in Latin America, we assume that countries with higher MRRs have a better death certification registry and hypothesize that HDIs would predict MRRs. Analyses were conducted in the R Software (version 4.1.1); "ggplot2" and "ggsci" packages were used to generate plots.

To estimate changes in mortality rates over time, Joinpoint regression models for each country and race and ethnic groups were generated using the year-specific age-adjusted yearly mortality rates estimated in the 2000–2019 period. For countries with a low number of reported events defined as < 20 counts (Guatemala, Nicaragua, and Paraguay), mortality events were grouped in a two-year period (e.g., 2000–2001, 2002–2003, etc.). Analysis was conducted using the Joinpoint Regression Program to estimate the Annual Percent Change (APC) and its 95% CIs [19].

2.5. Ethical and data-sharing statements

Analysis was conducted using de-identified and publicly available data sources, which is deemed non-human subject research and does not require approval by an Institutional Review Board. De-identified data is available online at https://www.who.int/data/data-collection-tools/who-mortality-database and at https://seer.cancer.gov/.

3. Results

3.1. Mortality patterns in the entire cohort

The highest MM mortality rates (per 100,000 persons) among adults ≥ 20 years in Latin America were observed among Chile (4.12), Uruguay (4.11), Costa Rica (3.57), and Cuba (3.51). In contrast, the lowest rates were observed in Guatemala (0.50), Nicaragua (0.67), Peru (1.62), and Paraguay (1.68) (Fig. 1**A**). The mortality rate for US Hispanics was 3.8. Compared to the US Hispanic population, moderately higher mortality (MRR<1.5) was identified among Uruguay (MRR=1.18, 95% CI=1.11–1.25), and Chile (MRR=1.16, 95% CI=1.12–1.20), while only Cuba and Costa Rica had comparable mortality (Fig. 1**B** and Supplementary Table 1). The remaining Latin American countries had significantly lower mortality rates compared to US Hispanic patients.

3.2. Mortality patterns by sex

Stratified analyses by sex generally showed patterns similar to the overall analysis, with higher mortality among males than among females (Supplementary Table 1 and Supplementary Figure 2**A**). Only for Cuba, we observed an inverse association with higher mortality only among males (MRR=1.12, 95% CI=1.06–1.18) and marginally lower for females (MRR=0.95, 95% CI=0.90–1.00; $P_{heterogeneity}$=0.0005) compared to US Hispanic individuals (Supplementary Table 1 and Supplementary Figure 2B).

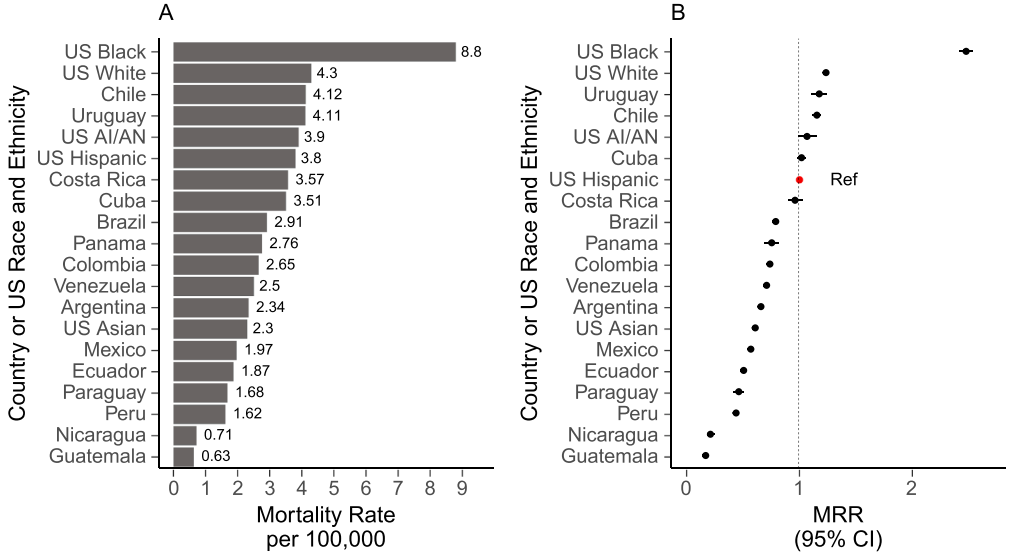


Fig. 1. Mortality rates per 100,000 (A) and mortality rate ratios (B) for multiple myeloma in Latin American countries and United States race and ethnic groups, 2008-2019. Abbreviations: AI/AN, American Indian/Alaska Native; CI, confidence interval; MMR, mortality rate ratio; Ref, reference category; US, United States.

3.3. Mortality patterns by age

For all Latin American countries, individuals aged ≥ 75 experienced the highest mortality rates compared to those aged 60–74 and 20–59 (Supplementary Table 2 and Supplementary Figure 2**C**), with the highest observed in Uruguay (23.09), Chile (22.3), and Costa Rica (20.37).

Stratified analysis by age groups suggests significantly different mortality patterns when compared to US Hispanic patients. The lower or comparable mortality identified in the overall analysis shifted toward significantly higher rates among young adults (20–59 years) in Cuba (MRR=2.04, 95% CI=1.88–2.21), Costa Rica (MRR=1.28, 95% CI=1.11–1.47), Venezuela (MRR=1.10, 95% CI=1.01–1.19), and Brazil (MRR=1.09, 95% CI=1.04–1.14), while mortality rates remained higher in Uruguay and Chile as in the overall analysis. Similarly, the initially lower mortality rates in Argentina, Colombia, Mexico, and Panama shifted toward comparable mortality outcomes to US Hispanic individuals among young adults (Fig. 2, Supplementary Table 2, and Supplementary Figure 2D).

Mortality patterns for adults (60−74) and older adults (≥75) were generally consistent with the overall analysis, with some isolated inverted observations. Older adults in Cuba (MRR=0.64, 95% CI=0.60–0.68), Costa Rica (MRR=0.80, 95% CI=0.72–0.89), and Chile (MRR=0.92, 95% CI=0.88–0.97) had lower mortality compared to US Hispanic individuals; while adults in Cuba (MRR=1.15, 95% CI=1.08–1.22) experienced a higher mortality. Although the age-stratified MRRs differed statistically across the remaining countries, the direction of the association was consistent with the overall analysis, with only differences in effect sizes.

3.4. Effect of HDI on mortality patterns

We fitted a linear regression model to evaluate if the higher mortality ratios identified in specific countries were associated with the HDI (Supplementary Table 3 and Supplementary Figure 3). Overall, HDI was significantly associated with MRRs (β=4.28, 95% CI=2.34–6.23). This finding remained significant across subgroups, with the largest estimate among individuals aged 20–39 (β=5.70, 95% CI=2.26–9.14).

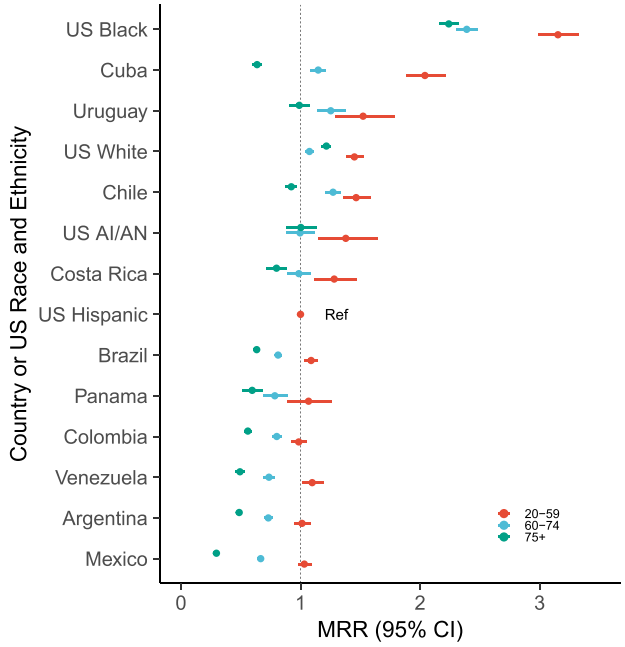


Fig. 2. Mortality rate ratios (95% CI) for multiple myeloma by age groups in selected Latin American countries and United States race and ethnic groups, 2008–2019. Abbreviations: AI/AN, American Indian/Alaska Native; CI, confidence interval; MMR, mortality rate ratio; Ref, reference category; US, United States.

3.5. Trends over time

During 2000–2019, significant downward trends were observed only in US White individuals, US Hispanic individuals, US Black individuals, and Argentina (Fig. 3 and Supplementary Table 4). Since 2000, Ecuador (APC=4.21, 95% CI=2.7, 6.38) and Mexico (APC=0.72, 95% CI=0.4, 1.11) experienced a constant upward trend, while the trend increased since 2010 in Peru (APC=5.39, 95% CI=1.57, 22.78) and Colombia (APC=3.38, 95% CI=1.65, 9.17). We observed an upward trend during 2000–2011 (APC=2.67, 95% CI=1.19, 16.17), followed by a stable trend (APC=-1.26, 95% CI=-10.52, 0.78) in Costa Rica, and Brazil had a constant upward trend since 2004 (APC=1.86, 95% CI=0.9, 3.1). The mortality rates over time were constant for the remaining eight Latin American countries.

4. Discussion

We conducted a large-scale study evaluating MM burden in Latin America and compared rates to those of US Hispanic individuals. Counterintuitively, despite lower access to the current standard of care and novel treatments, overall mortality was generally lower in Latin American countries. However, age-stratified models revealed reversed mortality ratios in some countries, particularly among young adults. Furthermore, Latin American countries exhibited stable or upward mortality trends. Notably, higher HDI predicted increased MRRs, possibly suggesting underascertainment of MM as the underlying cause of death. These heterogeneous patterns in our exploratory study suggest the need for improving MM mortality surveillance in Latin America.

The observed mortality patterns across Latin American countries, characterized by overall lower mortality but higher relative mortality among young adults compared to US Hispanic individuals, suggest multifactorial patterns. Given the limited access to complex therapies for MM management in Latin America [20,21], higher population-level mortality might be expected compared with the US Hispanic individuals, particularly as MM incidence appears broadly similar across these populations [22,23]. However, these patterns may reflect differences in death certification practices and challenges in attributing MM as the basic cause of death, especially among older adults with multiple comorbidities in whom competing causes may have been recorded instead [24]. In contrast, attribution of MM as the basic cause of death may have been more consistent among young adults, where the burden of comorbidities is lower. The observed association between higher MRRs and higher HDI may suggest challenges in MM attribution [25], although this proxy for data quality is imperfect and does not exclude alternative explanations. These include differences in the prevalence of risk factors (e.g., obesity), disease biology, access to diagnostic testing, or treatment availability across age groups and countries. Further studies comparing expert adjudication with death certificate-based assignment of the underlying cause of death using individual-level data are needed to better quantify potential misclassification. Our findings underscore the need to strengthen cancer registries in Latin America to improve MM surveillance and inform policy.

The stable mortality trends in most Latin American countries likely suggest that population-level MM mortality patterns have not substantially changed over time in most countries. Previous studies have described the limitations in Latin America accessing first-line therapies considered standard of care in high-income countries, such as quadruplet regimens or autologous hematopoietic cell transplantation [6]. Only a few Latin American countries showed upward mortality trends, suggesting improvements over time in cause-of-death reporting or worsening barriers in access to care. Additionally, as mortality rates are associated with disease incidence, improvement in MM diagnosis and death certification coding may partly explain this upward trend. In

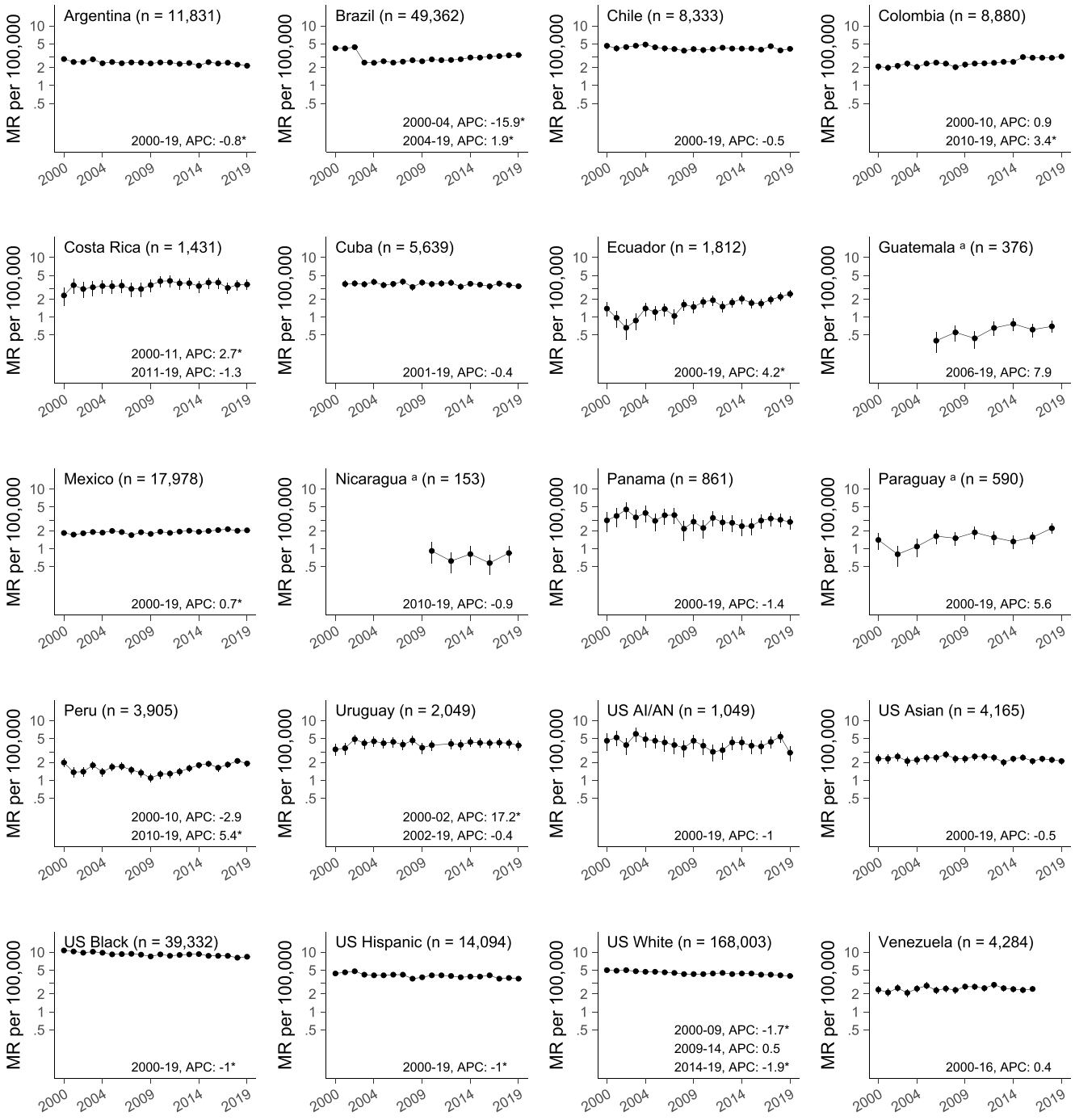


Fig. 3. Mortality rates and annual percentage change (95% CI) over time across Latin American countries and US race and ethnicity, 2000-2019. a Mortality rates were estimated in a 2-year period due to counts < 20 in single years. * Reflects P < .05.
Abbreviations: AI/AN, American Indian/Alaska Native; APC, Annual Percent Change; CI, confidence interval; MR, mortality rate; US, United States.

contrast, the downward mortality rates observed in the US align with the introduction of immunotherapies and increasing access to transplantation [1,4]. Survival analyses are required to better assess mortality outcomes of MM across Latin America over time.

This study has limitations to address. The ecological design, making it challenging to establish associations, is acknowledged. The trend analyses were conducted in the WHO data before 2008, where data quality indicators were lacking. Additionally, data quality varied across countries, with a usability percentage ranging from 60% to 92%. Mortality data do not distinguish between smoldering MM and symptomatic MM, limiting further analyses. Latin American countries do not make a distinction of race and ethnic demographic subgroups despite having several ethnicities in their territories. The US Hispanic population was used as a reference for the analysis, but may not be comparable to all populations in Latin America due to the unique population structures within and across countries. Population-based treatment data were not widely available or accessible across the included Latin American countries. Finally, HDI was used as a proxy for quality coding of cause of

death, which may not fully represent mortality coding practices. Similarly, HDI by US populations was unavailable, and thus, the US populations were excluded from the HDI analyses.

In conclusion, this population-based study identified heterogeneous patterns of MM mortality across Latin America. Mortality rates were generally lower than those observed among US Hispanic individuals but were higher among young adults, highlighting inconsistencies across age groups. These patterns are not fully aligned with expected differences given known disparities in access to care, raising concerns and calling for caution when interpreting mortality estimates derived from death certification. Higher MRRs observed in countries with higher HDI further support the possibility of differences in mortality ascertainment across settings, although confirmatory studies are needed. Strengthening population-based cancer registries across Latin America and international collaborations are needed to understand MM epidemiology and inform policy.

CRediT authorship contribution statement

Camila Peña: Writing – review & editing, Supervision, Project administration, Methodology, Investigation. **Eloísa Riva:** Writing – review & editing, Supervision, Project administration, Methodology, Investigation. **Bryan Valcarcel:** Writing – review & editing, Writing – original draft, Visualization, Software, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Michelle A.T. Hildebrandt:** Writing – review & editing, Supervision, Project administration, Methodology, Investigation. **Luis Malpica:** Writing – review & editing, Resources, Project administration, Methodology, Funding acquisition, Conceptualization. **Veronica Leautaud:** Writing – review & editing, Supervision, Project administration. **Alana von Glasenapp:** Writing – review & editing, Supervision, Project administration, Methodology, Investigation.

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Declaration of Competing Interest

none

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.canep.2026.103103.

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