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Supporting Information

Supplementary methods and results

This appendix was part of the submitted manuscript and has been peer reviewed. It is posted as supplied by the authors.

Appendix to: Luo Q, Jenkin D, Weber MF, et al. Multiple myeloma incidence, mortality, and prevalence estimates and projections, Australia, 1982–2043: a statistical modelling study. *Med J Aust* 2024; doi: 10.5694/mja2.52366.

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1. Methods

1.1. Projections of incidence and mortality rates

Age−period−cohort (APC) model effects for incidence or mortality rates for multiple myeloma

Age-period-cohort models can implicitly incorporate many of the factors that contribute to cancer incidence and mortality, as age, period and cohort effects can capture the effects of changes in exposure to a range of risk factors, and cancer diagnostic and treatment factors. The basic APC model with the log−link function can be expressed as:

$$lnD_{ij} = lnN_{ij} + \alpha_i Age_i + \beta_j Period_j + \gamma_k Cohort_k$$

where

D_{ij} denotes the number of new cases or deaths for multiple myeloma for the i^{th} age group during the j^{th} calendar year;

N_{ij} denotes the number at risk in the population for the i^{th} age group during the j^{th} calendar year;

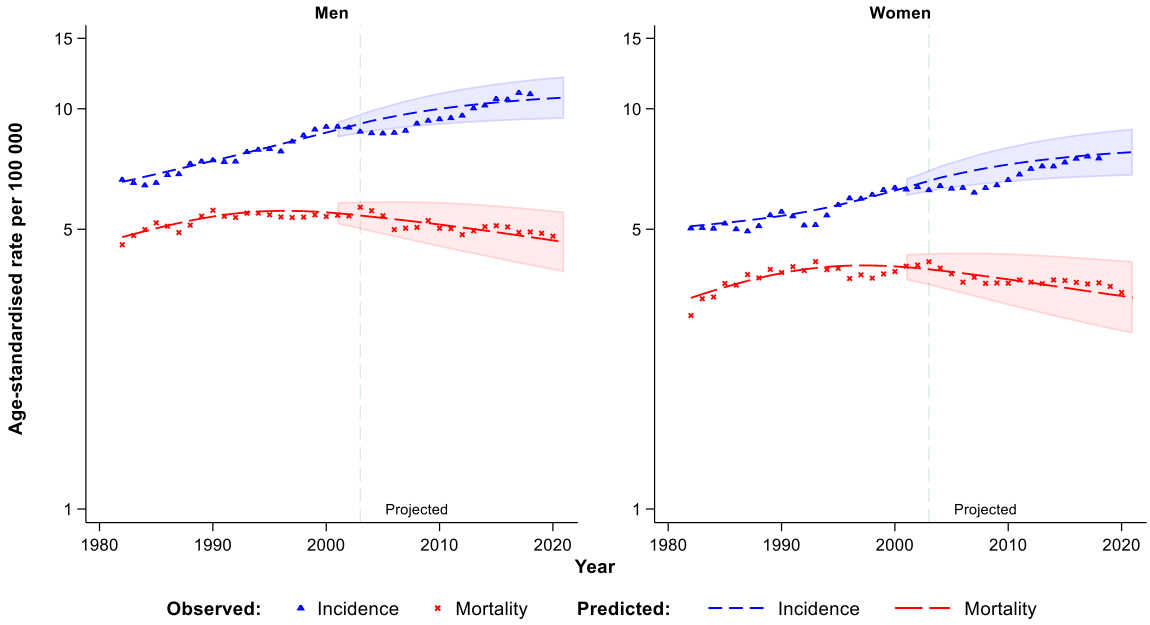
α_i is the coefficient of the age component for age group i;

β_j is the non−linear coefficient of the period component for calendar year j, and

γ_k is the non−linear coefficient of the cohort component for birth cohort k. APC models were fitted by the *apcspline* command in Stata 17 with natural cubic splines for smoothing for multiple myeloma.[1] The most appropriate statistical projection model with the lowest Bayesian information criterion (BIC) was selected. To project incidence and mortality rates beyond the observed period, future periods and cohorts were assumed to have the same effect as those for the most recent observed period and cohort. As these historical trends will not continue indefinitely, the default setting for the damping factor (equal to 0.92) was used, so that the drift was reduced by 8% for each year following the last observation.[1]

Model validation provides important information on the performance and reliability of the projection model. A validation analysis was performed by withholding the observed data for 2004−2018 from the model fitting using the same modelling approach, and then comparing the projected rates for those years with the actual observed values.[2] In the validation, the 15-year projected incidence and mortality rates for both males and females were found to be close to the observed values and the prediction intervals of the projected rates generally captured the observed rates, suggesting that the final models provide valid projections of incidence and mortality for multiple myeloma in Australia (Figure 1).

Figure 1. Validation of 15-year projections for incidence and mortality rates for multiple myeloma in Australia: projections for 2004−2018 based on historical data for 1982−2003, compared with historical data for 1982−2018



All rates are age-standardised to the 2021 Australian population.

1.2. Projections of prevalence

Modified counting method to estimate prevalence for multiple myeloma

Cancer prevalence is a count of the number of people in the population who were previously diagnosed with a cancer at a given time point. A direct counting method for estimating the prevalence of a cancer was described in detail elsewhere,[3] which uses individual incidence and vital status at follow up to count people who were living with a cancer in a calendar year. In this study, we developed a modified counting method to estimate prevalence based on tabulated incidence and survival data and adjusted prevalence estimates as the running average number of patients over two intervals. This method assumes a group of people within a given age and year of diagnosis contributed to cancer prevalence equally within 1-year intervals. For estimating the attained age after initial diagnosis, number of new cases observed in 1982−2018 and projected in 2019−2043 by sex and 5−year age group were interpolated into single year age. To account for the impact of the recent advance in treatment,[4-6] the observed sex−age−specific survival rates for 1989 to 2018 were extrapolated forward to 2028 and assumed to remain constant to 2043 and we also conducted sensitivity analyses by estimating the prevalence under the assumption that (1) the increase in survival levelled off after 2023 and (2) there had been no changes in observed survival after 2018 (Figures 2 and 3). For each year, numbers of patients expected to be alive at k years after initial diagnosis in calendar year j, were estimated for new multiple myeloma cases of sex i and age a, using the following notation:

$$Survivors_{ibp} = \left(New\ cases_{iaj} \times Observed\ survival_{ia(k-1)} + New\ cases_{iaj} \times Observed\ survival_{iak}\right)/2$$

where

Let p denote attained year $p=j+k$.

Let b attained age $b=a+k$,

Let j denote year of diagnosis.

Let a denote age at diagnosis.

Let k denote the years after diagnosis (1 to 30 years).

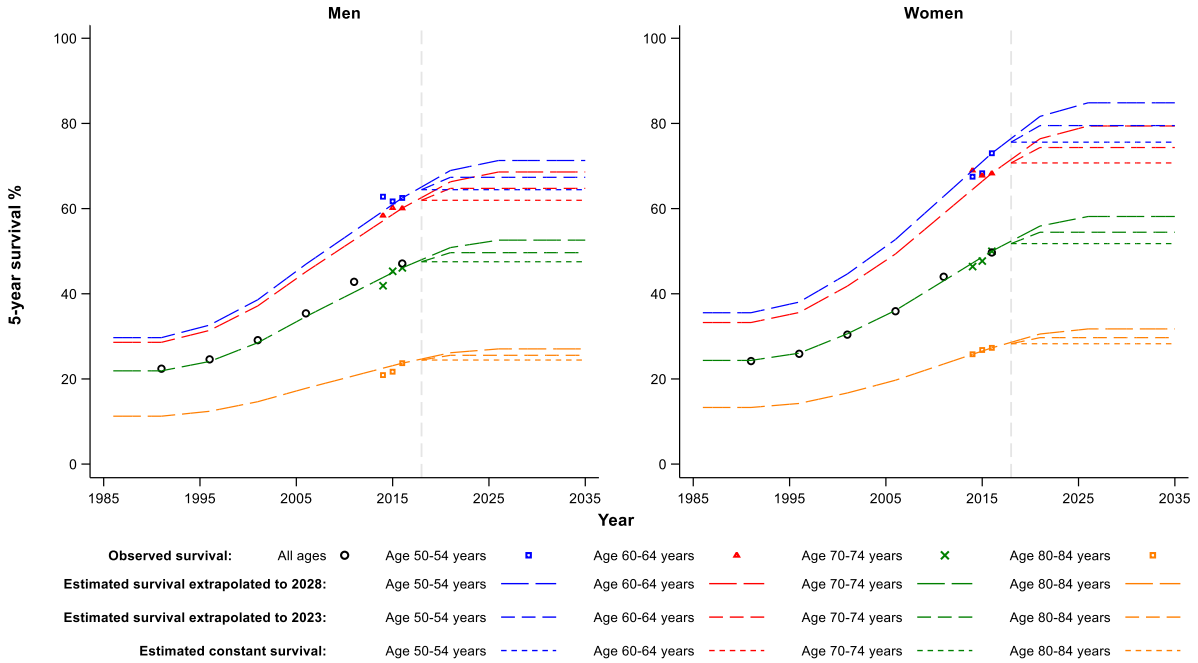
Let i denote sex, i.e. $i=1$ for men and $i=2$ for women.

The total prevalence of multiple myeloma at year p is

$$Prevalence_p = \sum_{i=1}^{2}\sum_{b=0}^{99} Survivors_{ibp}$$

The prediction interval for the estimated prevalence were estimated based on the confidence intervals of the number of new cases and survival rates.

Figure 2. Historical and estimated sex−age−specific survival for multiple myeloma in Australia



2. Supplementary results

Table 1. Projected age-standardised incidence rates and numbers of new cases for multiple myeloma for selected years in Australia

	Projected age-standardised incidence rate (95% prediction interval)*				
	2023	**2028**	**2033**	**2038**	**2043**
Overall	**9.2 (8.8–9.6)**	**9.5 (9.0–10.1)**	**9.7 (9.2–10.4)**	**9.9 (9.3–10.5)**	**10.0 (9.4–10.7)**
Under 70 years	4.5 (4.3–4.7)	4.6 (4.4–4.9)	4.7 (4.5–5.1)	4.8 (4.5–5.1)	4.9 (4.6–5.2)
70-79 years	41.2 (39.4–43.1)	42.6 (40.4–44.8)	43.5 (41.1–46.1)	44.1 (41.5–46.9)	44.5 (41.8–47.5)
80 years or older	56.5 (53.9–59.3)	58.9 (55.8–62.2)	60.4 (56.9–64.1)	61.2 (57.4–65.2)	61.7 (57.8–65.9)
Men	**11.4 (10.9–11.9)**	**11.8 (11.2–12.4)**	**12.1 (11.4–12.8)**	**12.3 (11.6–13.0)**	**12.4 (11.7–13.2)**
Under 70 years	5.4 (5.1–5.6)	5.6 (5.3–5.9)	5.7 (5.4–6.0)	5.8 (5.5–6.2)	5.9 (5.5–6.2)
70-79 years	50.4 (48.3–52.5)	52.2 (49.7–54.8)	53.4 (50.6–56.4)	54.3 (51.2–57.5)	54.8 (51.6–58.2)
80 years or older	75.8 (72.5–79.4)	78.6 (74.6–82.8)	80.4 (76.0–85.2)	81.7 (76.9–86.8)	82.5 (77.5–87.8)
Women	**8.0 (7.6–8.5)**	**8.3 (7.8–8.8)**	**8.5 (8.0–9.1)**	**8.6 (8.1–9.2)**	**8.7 (8.1–9.3)**
Under 70 years	3.8 (3.6–4.0)	4.0 (3.7–4.2)	4.0 (3.8–4.3)	4.1 (3.8–4.4)	4.1 (3.9–4.5)
70-79 years	32.8 (31.2–34.4)	33.9 (32.0–35.9)	34.7 (32.6–36.9)	35.2 (32.9–37.6)	35.5 (33.2–38.0)
80 years or older	42.3 (40.2–44.5)	43.8 (41.3–46.5)	44.8 (42.0–47.8)	45.4 (42.4–48.6)	45.9 (42.7–49.2)
	Projected number of new multiple myeloma cases (95% prediction interval)				
	2023	**2028**	**2033**	**2038**	**2043**
Overall	**2550 (2432–2674)**	**2973 (2814–3143)**	**3367 (3173–3576)**	**3711 (3483–3954)**	**4012 (3756–4285)**
Under 70 years	1045 (994–1098)	1143 (1080–1211)	1210 (1138–1288)	1304 (1222–1392)	1384 (1293–1481)
70-79 years	858 (821–897)	986 (935–1039)	1111 (1050–1177)	1185 (1115–1260)	1240 (1164–1322)
80 years or older	647 (617–679)	844 (799–893)	1046 (985–1111)	1222 (1146–1302)	1388 (1299–1482)
Men	**1485 (1421–1554)**	**1735 (1647–1828)**	**1964 (1857–2079)**	**2161 (2036–2294)**	**2335 (2194–2484)**
Under 70 years	609 (581–638)	666 (631–703)	704 (665–747)	760 (715–808)	809 (759–862)
70-79 years	505 (485–527)	574 (546–603)	644 (611–680)	686 (648–727)	716 (674–760)
80 years or older	371 (355–389)	495 (470–522)	616 (581–652)	715 (673–759)	810 (761–862)
Women	**1065 (1011–1120)**	**1238 (1167–1315)**	**1403 (1316–1497)**	**1550 (1447–1660)**	**1677 (1562–1801)**
Under 70 years	436 (413–460)	477 (449–508)	506 (473–541)	544 (507–584)	575 (534–619)
70-79 years	353 (336–370)	412 (389–436)	467 (439–497)	499 (467–533)	524 (490–562)
80 years or older	276 (262–290)	349 (329–371)	430 (404–459)	507 (473–543)	578 (538–620)

*All rates are age-standardised to the 2021 Australian population.

Table 2. Projected age-standardised mortality rates and numbers of deaths from multiple myeloma for selected years in Australia

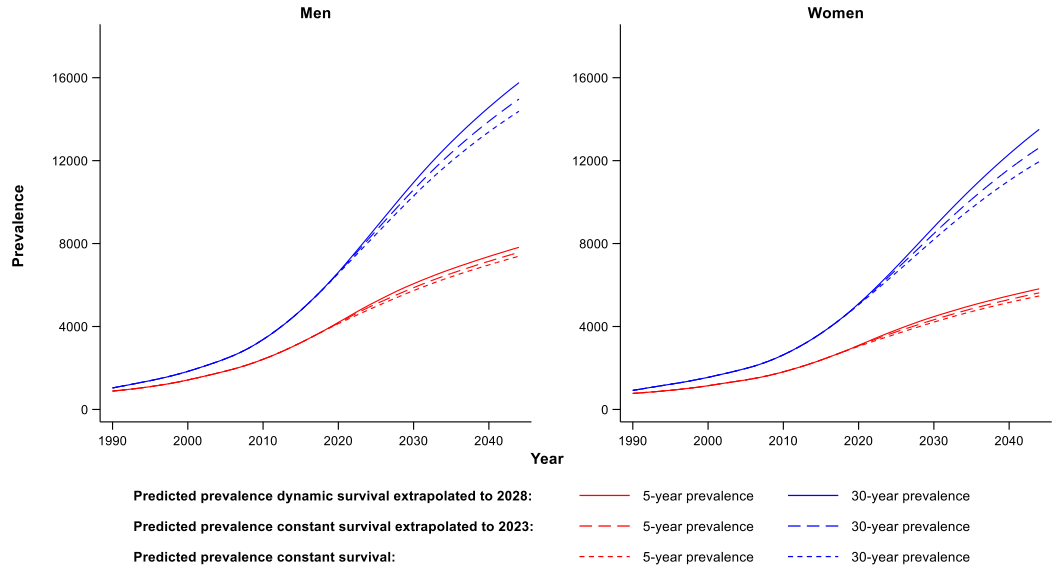
	Projected age-standardised mortality rate (95% prediction interval)*				
	2023	**2028**	**2033**	**2038**	**2043**
Overall	**3.6 (3.4–3.9)**	**3.4 (3.1–3.7)**	**3.2 (2.9–3.5)**	**3.0 (2.7–3.4)**	**2.9 (2.6–3.3)**
Under 70 years	1.1 (1.0–1.2)	1.0 (0.9–1.1)	1.0 (0.9–1.1)	1.0 (0.9–1.1)	1.0 (0.9–1.1)
70-79 years	17.0 (15.9–18.1)	15.6 (14.4–16.9)	14.4 (13.0–15.9)	13.5 (12.1–15.1)	13.1 (11.7–14.8)
80 years or older	36.9 (34.5–39.4)	35.1 (32.5–37.8)	32.9 (30.3–35.7)	30.6 (27.9–33.4)	28.4 (25.6–31.4)
Men	**4.5 (4.2–4.8)**	**4.2 (3.9–4.6)**	**4.0 (3.7–4.4)**	**3.8 (3.5–4.2)**	**3.6 (3.3–4.0)**
Under 70 years	1.3 (1.2–1.4)	1.2 (1.1–1.4)	1.2 (1.1–1.3)	1.2 (1.1–1.3)	1.2 (1.1–1.3)
70-79 years	20.6 (19.3–21.8)	19.0 (17.6–20.5)	17.6 (16.2–19.2)	16.5 (15.0–18.2)	16.0 (14.5–17.7)
80 years or older	48.3 (45.3–51.5)	45.9 (42.7–49.3)	43.1 (39.9–46.6)	40.3 (37.1–43.8)	37.6 (34.4–41.1)
Women	**3.3 (3.0–3.6)**	**3.1 (2.8–3.4)**	**2.9 (2.6–3.2)**	**2.7 (2.4–3.1)**	**2.6 (2.3–3.0)**
Under 70 years	0.9 (0.8–1.0)	0.9 (0.8–1.0)	0.8 (0.7–1.0)	0.8 (0.7–1.0)	0.8 (0.7–1.0)
70-79 years	13.6 (12.7–14.7)	12.5 (11.4–13.8)	11.5 (10.2–12.9)	10.9 (9.5–12.4)	10.6 (9.2–12.3)
80 years or older	29.0 (27.0–31.2)	27.3 (25.2–29.6)	25.4 (23.3–27.8)	23.5 (21.3–26.0)	21.7 (19.3–24.5)
	Projected number of deaths from multiple myeloma (95% prediction interval)				
	2023	**2028**	**2033**	**2038**	**2043**
Overall	**1034 (961–1111)**	**1121 (1030–1221)**	**1199 (1090–1317)**	**1251 (1128–1387)**	**1289 (1154–1443)**
Under 70 years	252 (230–277)	252 (227–282)	252 (224–284)	264 (233–298)	273 (241–310)
70-79 years	356 (333–380)	365 (336–396)	371 (336–409)	368 (329–412)	368 (327–416)
80 years or older	426 (398–454)	504 (467–543)	576 (530–624)	619 (566–677)	648 (586–717)
Men	**594 (555–635)**	**648 (600–700)**	**694 (638–755)**	**723 (660–792)**	**744 (676–820)**
Under 70 years	149 (138–162)	149 (136–164)	148 (134–164)	155 (139–172)	161 (144–179)
70-79 years	208 (195–221)	211 (196–227)	214 (197–233)	212 (193–233)	210 (190–233)
80 years or older	237 (222–252)	288 (268–309)	332 (307–358)	356 (328–387)	373 (342–408)
Women	**440 (406–476)**	**473 (430–521)**	**505 (452–562)**	**528 (468–595)**	**545 (478–623)**
Under 70 years	103 (92–115)	103 (91–118)	104 (90–120)	109 (94–126)	112 (97–131)
70-79 years	148 (138–159)	154 (140–169)	157 (139–176)	156 (136–179)	158 (137–183)
80 years or older	189 (176–202)	216 (199–234)	244 (223–266)	263 (238–290)	275 (244–309)

*All rates are age−standardised to the 2021 Australian population.

Table 3. Estimates of prevalence with 95% prediction interval of multiple myeloma for selected years in Australia

	Number of patients living with multiple myeloma (95% prediction interval)				
Age group	**2023**	**2028**	**2033**	**2038**	**2043**
30-year prevalence					
Overall	**13 868 (12 310 – 15 521)**	**17 604 (15 641 – 19 704)**	**21 186 (18 765 – 23 795)**	**24 348 (21 459 – 27 473)**	**27 093 (23 749 – 30 746)**
Under 70 years	5322 (4902 – 5774)	6210 (5696 – 6766)	6836 (6238 – 7492)	7478 (6790 – 8229)	8064 (7295 – 8913)
70-79 years	4974 (4585 – 5383)	6247 (5748 – 6779)	7376 (6760 – 8036)	8176 (7460 – 8944)	8704 (7913 – 9559)
80 years or older	3572 (2823 – 4364)	5147 (4197 – 6159)	6974 (5767 – 8267)	8694 (7209 – 10 300)	10 325 (8541 – 12 274)
Men	**7804 (6975 – 8682)**	**9819 (8769 – 10 937)**	**11 698 (10 403 – 13 086)**	**13 316 (11 776 – 14 973)**	**14 717 (12 939 – 16 649)**
Under 70 years	2987 (2761 – 3230)	3456 (3180 – 3752)	3778 (3458 – 4125)	4122 (3757 – 4518)	4450 (4042 – 4897)
70-79 years	2848 (2635 – 3072)	3506 (3237 – 3792)	4085 (3756 – 4436)	4494 (4114 – 4899)	4753 (4336 – 5201)
80 years or older	1969 (1579 – 2380)	2857 (2352 – 3393)	3835 (3189 – 4525)	4700 (3905 – 5556)	5514 (4561 – 6551)
Women	**6064 (5335 – 6839)**	**7785 (6872 – 8767)**	**9488 (8362 – 10 709)**	**11 032 (9683 – 12 500)**	**12 376 (10 810 – 14 097)**
Under 70 years	2335 (2141 – 2544)	2754 (2516 – 3014)	3058 (2780 – 3367)	3356 (3033 – 3711)	3614 (3253 – 4016)
70-79 years	2126 (1950 – 2311)	2741 (2511 – 2987)	3291 (3004 – 3600)	3682 (3346 – 4045)	3951 (3577 – 4358)
80 years or older	1603 (1244 – 1984)	2290 (1845 – 2766)	3139 (2578 – 3742)	3994 (3304 – 4744)	4811 (3980 – 5723)
5-year prevalence					
Overall	**8236 (7708 – 8796)**	**9668 (8967 – 10 418)**	**10 949 (10 088 – 11 884)**	**12 044 (11 036 – 13 138)**	**13 019 (11 884 – 14 250)**
Under 70 years	3414 (3202 – 3641)	3775 (3510 – 4058)	4031 (3731 – 4361)	4334 (3990 – 4705)	4637 (4256 – 5051)
70-79 years	2906 (2747 – 3072)	3395 (3182 – 3623)	3818 (3553 – 4103)	4100 (3799 – 4426)	4294 (3965 – 4646)
80 years or older	1916 (1759 – 2083)	2498 (2275 – 2737)	3100 (2804 – 3420)	3610 (3247 – 4007)	4088 (3663 – 4553)
Men	**4743 (4456 – 5048)**	**5569 (5187 – 5977)**	**6298 (5828 – 6808)**	**6918 (6368 – 7510)**	**7471 (6854 – 8141)**
Under 70 years	1960 (1844 – 2084)	2165 (2021 – 2319)	2310 (2146 – 2491)	2487 (2299 – 2687)	2666 (2458 – 2894)
70-79 years	1692 (1605 – 1783)	1955 (1840 – 2078)	2187 (2045 – 2340)	2345 (2183 – 2519)	2449 (2273 – 2637)
80 years or older	1091 (1007 – 1181)	1449 (1326 – 1580)	1801 (1637 – 1977)	2086 (1886 – 2304)	2356 (2123 – 2610)
Women	**3493 (3252 – 3748)**	**4099 (3780 – 4441)**	**4651 (4260 – 5076)**	**5126 (4668 – 5628)**	**5548 (5030 – 6109)**
Under 70 years	1454 (1358 – 1557)	1610 (1489 – 1739)	1721 (1585 – 1870)	1847 (1691 – 2018)	1971 (1798 – 2157)
70-79 years	1214 (1142 – 1289)	1440 (1342 – 1545)	1631 (1508 – 1763)	1755 (1616 – 1907)	1845 (1692 – 2009)
80 years or older	825 (752 – 902)	1049 (949 – 1157)	1299 (1167 – 1443)	1524 (1361 – 1703)	1732 (1540 – 1943)

Figure 3. Sensitivity analyses: prevalence estimates and projections for multiple myeloma in Australia*

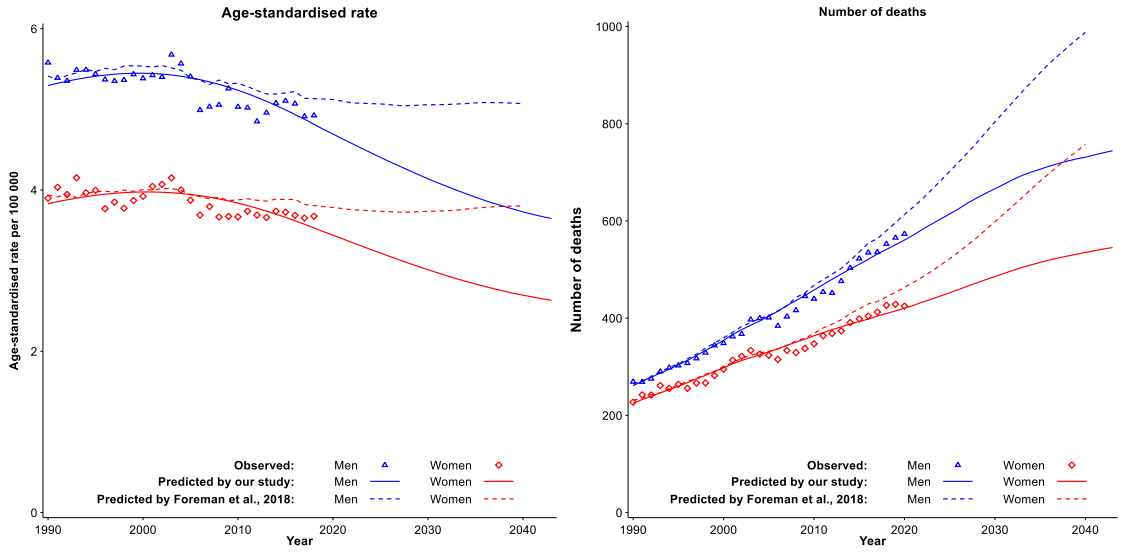


* Predicted prevalence dynamic survival extrapolated to 2028: prevalence was estimated assuming that the increase in survival plateaued from 2028.

Predicted prevalence dynamic survival extrapolated to 2023: prevalence was estimated assuming that the increase in survival plateaued from 2023.

Predicted prevalence constant survival: prevalence was estimated assuming that survival did not increase after 2018.

Figure 4. Comparison of projected multiple myeloma mortality rates and number of deaths in our study with those of Foreman et al. 2018



Numbers of deaths from multiple myeloma by sex, 5-year age group, and calendar year for the Foreman et al. 2018[7] study were extracted from the open source online https://vizhub.healthdata.org/gbd-foresight (viewed 2 Nov 2022). The ICD-10 codes for multiple myeloma used by Foreman et al. 2018 included C88−C90.9. All rates are age-standardised to the 2021 Australian population.

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EPIFORGE 2020 checklist

Title: Multiple myeloma incidence, mortality, and prevalence estimates and projections for Australia, 1982 to 2043: a statistical modelling study

Section of manuscript	#	Checklist item	Reported on page*
Title/Abstract	1	Describe the study as forecast or prediction research in at least the title or abstract	1 – "projections" used
Introduction	2	Define the purpose of study and forecasting targets	4
Methods	3	Fully document the methods	4-6, Appendix pp 3-5
Methods	4	Identify whether the forecast was performed prospectively, in real time, and/or retrospectively	5-6
Methods	5	Explicitly describe the origin of input source data, with references	4
Methods	6	Provide source data with publication, or document reasons as to why this was not possible	9
Methods	7	Describe input data processing procedures in detail	4-5, Appendix pp 3-4
Methods	8	State and describe the model type, and document model assumptions, including references	5-6, Appendix pp 3-4
Methods	9	Make the model code available, or document the reasons why this was not possible	5, Appendix p 3
Methods	10	Describe the model validation, and justify the approach	5, Appendix pp 3-4
Methods	11	Describe the forecast accuracy evaluation method used, with justification	Appendix pp 3-4
Methods	12	Where possible, compare model results to a benchmark or other comparator model, with justification of comparator choice	7, Appendix p 9
Methods	13	Describe the forecast horizon, with justification of its length	4
Results	14	Present and explain uncertainty of forecasting results	5-6, Figures, Tables
Results[b]	15	Briefly summarize the results in nontechnical terms, including a nontechnical interpretation of forecast uncertainty	6-7
Results	16	If results are published as a data object, encourage a time-stamped version number	NA
Discussion	17	Describe the weaknesses of the forecast, including weaknesses specific to data quality and methods	9
Discussion	18	If the research is applicable to a specific epidemic, comment on its potential implications and impact for public health action and decision-making	7-9
Discussion	19	If the research is applicable to a specific epidemic, comment on how generalizable it may be across populations	8

* Page numbers do not apply to the published version of the article or its Supporting Information.