





Clinical science

Mortality estimates and excess mortality in rheumatoid arthritis

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Abstract

Objectives: To determine long-term (20 year) survival in RA patients enrolled in the Australian Rheumatology Association Database (ARAD).

Methods: ARAD patients with RA and data linkage consent who were diagnosed from 1995 onwards were included. Death data were obtained through linkage to the Australian National Death Index. Results were compared with age-, gender- and calendar year-matched Australian population mortality rates. Analysis included both the standardized mortality ratio (SMR) and relative survival models. Restricted mean survival time (RMST) at 20 years was calculated as a measure of life lost. Cause-specific SMRs (CS-SMRs) were estimated for International Classification of Diseases, Tenth Revision cause of death classifications.

Results: A total of 1895 RA patients were included; 74% were female, baseline median age 50 years (interquartile range 41–58), with 204 deaths. There was no increase in mortality over the first 10 years of follow up, but at 20 years the SMR was 1.49 (95% CI 1.30, 1.71) and the relative survival was 94% (95% CI 91, 97). The difference between observed (18.41 years) and expected (18.68 years) RMST was 4 months. Respiratory conditions were an important underlying cause of death in RA, primarily attributable to pneumonia [CS-SMR 5.2 (95% CI 2.3, 10.3)] and interstitial lung disease [CS-SMR 7.6 (95% CI 3.0, 14.7)], however, coronary heart disease [CS-SMR 0.82 (95% CI 0.42, 1.4)] and neoplasms [CS-SMR 1.2 (95% CI 0.89, 1.5)] were not.

Conclusion: Mortality risk in this RA cohort accrues over time and is moderately increased at 20 years of follow-up. Respiratory diseases may have supplanted cardiovascular diseases as a major contributor to this mortality gap.

Keywords: RA, mortality, epidemiology, registry data

Rheumatology key messages

- Mortality risk in rheumatoid arthritis is time variable and accrues with time since diagnosis.
- Excess mortality is delayed until the second decade post-diagnosis, equating to a minimal reduction in life expectancy.
- Respiratory diseases are an important underlying cause of death in rheumatoid arthritis patients, surpassing cardiovascular diseases.

Introduction

RA is a chronic autoimmune inflammatory disease with an Australian prevalence of 1.7% [1]. Historically, RA has been associated with increased mortality [2–4], with some [5–8]

but not all [9, 10] studies suggesting that the excess mortality associated with RA has decreased over time. This reduction has been attributed to better therapeutic strategies such as

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early intervention within the ‘window of opportunity’, adoption of a treat-to-target approach and the widespread availability of biologic and targeted synthetic DMARDs (bDMARDs, tsDMARDs) [11–15]. bDMARDs have been available in Australia for RA since 2003. Australians have access to universal healthcare, which includes subsidized medicines. This means that RA patients with ongoing disease activity despite the combination of methotrexate and another conventional synthetic DMARD (csDMARD) can access, with a minimal co-pay, b/tsDMARDs if they are under the care of a rheumatologist. The last Australian estimate of mortality in RA reported deaths through 2004, with the cohort recruited between January 1990 and December 1994, thus predating contemporary management strategies [16].

RA is a chronic disease, with most patients requiring life-long therapy. Rheumatologists and other members of the treating team provide education and advice about the disease and treatment options to engage patients in a shared decision-making treatment journey [17–19]. This process requires up-to-date data on prognosis and disease outcomes, including mortality. While many studies assume the mortality associated with RA is constant over time, it is likely that in fact it varies with time since diagnosis and may be impacted by other factors such as age, sex and date of diagnosis.

The aims of this study were to provide updated estimates of the mortality associated with RA in Australian patients exposed to contemporary treatment strategies, including b/tsDMARDs, compared with the general Australian population; explore different survival models to establish a model that best fits the mortality associated with RA over time; explore the impact of patient factors (age, sex and diagnosis date) on mortality and examine the frequency of differing causes of death among RA patients and compare this with the general Australian population.

Methods

Australian Rheumatology Association Database

The Australian Rheumatology Association Database (ARAD) is a voluntary registry established in 2001 to collect patient-reported long-term safety and other outcome data from patients with inflammatory arthritis, including RA, PsA, AS and JIA who are taking biologic therapies [20]. Participants include patients prescribed b/tsDMARDs as well as patients on csDMARDs alone (controls since 2007). There are no restrictions on participants commencing or switching b/tsDMARDs during ARAD follow-up. Patients are referred by their treating rheumatologist from public hospital and private practice settings across Australia. Following written informed consent, participants complete a baseline ARAD questionnaire, with a follow-up questionnaire completed every 6 months for 2 years, then at 12-month intervals.

The ARAD collects a wide range of patient-reported information, including demographics (education, employment, health insurance, smoking and alcohol consumption), medical history, infections, malignancy and medications. The questionnaire also includes patient outcome measures including the HAQ Disability Index (HAQ-DI) [21], quality of life measures such as the 36-item short form health survey (SF-36) [22] and pain experienced in the last week, scored on a 0–100 visual analogue scale (VAS; 0 indicates no pain and 100 indicates pain as bad as it could be). SF-36 results were

reported as the physical and mental component scores standardized [mean 50 (s.d. 12)] relative to Australian population data from the 1995 National Health Survey and estimated using the Stata ado file ‘sf36’ (StataCorp, College Station, TX, USA).

Data linkage

In 2006, consent for data linkage to the ARAD was introduced to enable additional health information to be obtained from other Australian health registries including the Medicare Benefits Schedule (MBS), Pharmaceutical Benefit Scheme (PBS) and Australian National Death Index (NDI). The NDI is a database maintained by the Australian Institute of Health and Welfare (AIHW), containing records of registered deaths in Australia that have occurred since 1980. It has previously been shown to have 93.7% sensitivity and 100% specificity for the identification of deaths [23]. Cause of death information was also obtained through data linkage with the Australian NDI.

Participants and analysis time

Adult ARAD participants with RA were included in the study if they had prospective data linkage consent, were diagnosed on or after 1995 and were ≤ 80 years of age at their time of diagnosis. Patients who joined ARAD prior to 2006 were excluded because linkage consent was only obtained prospectively from this time forward. Analysis time was years from diagnosis, restricted to a maximum of 20 years. There was often a time lag between diagnosis and recruitment into the ARAD, therefore a delayed entry model was used to avoid survivor bias. Participants entered the study at their first ARAD date and only contributed data to the survival analysis for the follow-up years in which they were under observation in the ARAD.

Survival analysis

Death data were obtained through data linkage to the Australian NDI on 29 February 2020, which became the designated study end date. Mortality in RA patients was compared with age-, sex- and calendar year-matched Australian population mortality rates [24], and all analyses were performed in Stata version 16 (StataCorp) with user-written ado files.

Initial analysis was performed using a life-table approach implemented in the Stata ado program ‘strs’ [25], where follow-up times were divided into 1-year intervals. Output included observed and expected deaths, observed and expected cumulative survival and relative survival (the ratio of observed to expected cumulative survival), where expected values were calculated from matched population mortality rates by the Ederer II method. The Standardized Mortality Ratio (SMR; the ratio of observed to expected deaths) was calculated at 10- and 20-years follow-up.

Relative survival models offer an alternative analytic approach comparable to a conventional survival model framework. They specifically analyse excess mortality, which is the difference between observed and expected mortality rates, and therefore mortality that may be specifically attributable to disease. Relative survival models were implemented in the Stata ado program ‘stpm2’ [26, 27]. The ‘bhazard’ option in these models incorporates the expected mortality hazard at the time of death, which was derived from Australian population mortality rates. The stpm2 program uses restricted cubic

splines to model the excess hazard rate, and in this data the best fitting model (as determined by the Akaike information criterion) used a spline with 1 degree of freedom, indicating a linear increase in the RA-specific excess mortality rate with increasing follow-up time. Covariates included in this analysis were sex, age group (three levels: 20–40, 41–60, 61–80 years) and diagnosis year (pre-2005 and ≥ 2005), with regression coefficients expressed as excess mortality rate ratios (EMRR). The Stata ado 'standsurv' [28] was then used to obtain population-averaged predictions of the relative survival for levels of each covariate from this model, with predictions for diagnosis year ≥ 2005 up to 20 years involving some out-of-sample prediction.

Premature loss of life was estimated from these relative survival models by both the restricted mean survival time (RMST) at 20 years (as implemented in standsurv) and overall years of life lost (as implemented in stpm2 [29]).

Cause of death information for RA patients who died during the study was also obtained through data linkage with the Australian NDI. Cause of death information from the NDI was provided as International Classification of Diseases, Tenth Revision (ICD-10) codes for underlying (primary) and contributing cause of death. However, for comparison purposes, Australian population cause-specific mortality rates were only available for the underlying cause of death. Causes of death were grouped according to Australian General Record of Incidence of Mortality (GRIM) classifications [24], and cause-specific SMRs were calculated.

This study complies with the Declaration of Helsinki and written informed consent was obtained from the subjects (or their legally authorized representative). Ethics approval for the ARAD was obtained from the Cabrini Institute (12-23-04-01) and Central Adelaide Local Health Network (HREC/17/TQEH/139). Additional ethics approval was obtained for ARAD data linkage via the Australian Institute of Health and Welfare (AIHW 430). This ARAD substudy protocol was also scientifically reviewed and endorsed by the ARAD Steering Committee prior to commencement.

Results

Participant demographics

Participant demographics ($n = 1895$) are reported in Table 1. The majority were female [1397 (74%)], with a median age at diagnosis of 50 years and mild-moderate disability and pain at ARAD entry. Most [1534 (81%)] had a history of b/tsDMARD use during their ARAD follow-up, indicative of severe, active RA on csDMARDs.

Standardized Mortality Rates (using a life-table approach)

The life-table cumulative survival curve for RA patients compared with expected survival calculated from matched Australian population mortality data is reported in Fig. 1, with relevant tabulations in Table 2. Numbers at risk at the start of each 1-year time interval are shown in Supplementary Fig. S1, available at Rheumatology online. When assessed over 20 years, mortality was increased in ARAD RA participants compared with Australian population controls (Fig. 1, Table 2). There were 204 deaths in RA participants over 20 years of follow-up (total person-years 15 641.3), compared with an expected value of 137 [SMR 1.49 (95% CI 1.30,

Table 1. Study participant characteristics

Characteristics	Values
Participants, <i>N</i>	1895
Females, <i>n</i> (%)	1397 (74)
Age at diagnosis, years, mean (s.d.)	49 (13)
20–40, <i>n</i> (%)	470 (25)
41–60, <i>n</i> (%)	1067 (56)
61–80, <i>n</i> (%)	358 (19)
HAQ-DI, mean (s.d.)	1.0 (0.7)
Pain VAS, mean (s.d.)	46 (26)
SF-36, mean (s.d.)	
Physical component score	33 (11)
Mental component score	46 (12)
Diagnosis year, <i>n</i> (%)	
<2005	993 (52)
≥ 2005	902 (48)
Disease duration at ARAD entry, years, median (IQR)	5.0 (2.2–9.2)
b/tsDMARD use ^a , <i>n</i> (%)	1534 (81)

^a During ARAD follow-up.

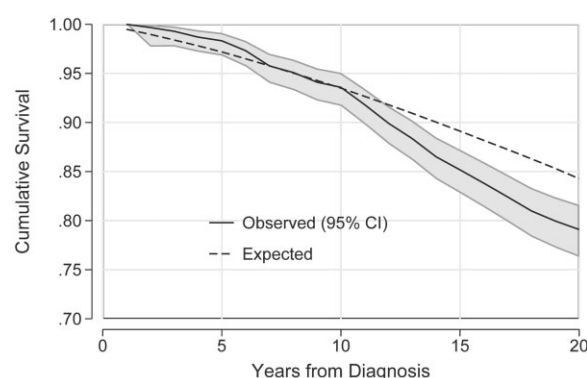


Figure 1. Observed survival in RA patients compared with expected survival calculated from Australian population mortality rates (life-table analysis approach)

Table 2. Mortality in RA patients compared with Australian population controls from a life-table analysis

Characteristics	Disease duration	
	≤ 10 years	≤ 20 years
Observed deaths, <i>n</i>	58	204
Expected deaths, <i>n</i>	52.52	136.72
Follow-up duration (person-years)	7303.474	15641.28
SMR (95% CI)	1.10 (0.85, 1.42)	1.49 (1.30, 1.71)
SMR <i>P</i> -value	0.44	<0.001
Observed survival (95% CI)	0.936 (0.917, 0.951)	0.791 (0.763, 0.816)
Expected survival	0.935	0.843
Relative survival (95% CI)	1.000 (0.981, 1.017)	0.935 (0.905, 0.968)

1.71), $P < 0.001$]. Survival in RA patients at 20 years was 79.1%, compared with an expected value of 81.6%, with a relative survival estimate (i.e. the ratio of observed to expected cumulative survival) of 93.5% (95% CI 90.5, 96.8). However, it was also clear that increased mortality in RA was dependent on the disease duration/follow-up time, with the

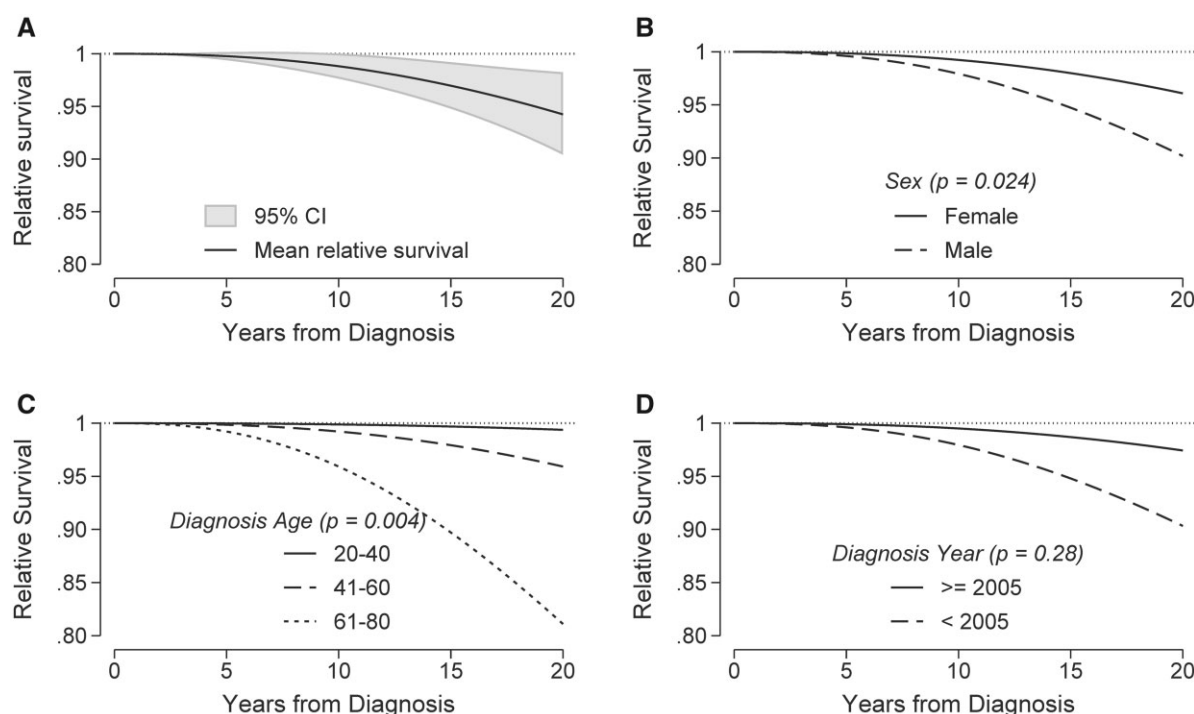


Figure 2. Population-averaged relative survival curves for RA patients compared with Australian population controls predicted from a multivariable relative survival model: (A) overall relative survival, (B) sex, (C) diagnosis age and (D) diagnosis year

observed and expected survival curves only starting to diverge after a disease duration of 10 years (Fig. 1). The SMR estimated at 10 years of follow-up was not significantly increased [SMR 1.10 (95% CI 0.85, 1.42), $P = 0.44$; Table 2] and the proportional hazards assumption, which implies a constant SMR during follow-up, did not hold for these data (Supplementary Fig. S2, available at *Rheumatology* online).

Excess mortality

In the relative survival model analysis, the excess mortality due to RA was shown to increase with disease duration (Supplementary Fig. S3, available at *Rheumatology* online). A second relative survival model, estimated with covariates sex, age group and diagnosis year, predicted the population-averaged relative survival at 20 years (Fig. 2A) to be 94.2% (95% CI 90.4, 98.3), which was very similar to estimates from the life-table approach (Table 2). Regression coefficients from this model are interpreted as EMRR (Table 3). Population-averaged relative survival curves were predicted for sex (Fig. 2B), diagnosis age (Fig. 2C) and diagnosis year (Fig. 2D).

Excess mortality rates for RA were lower in females than males [EMRR 0.36 (95% CI 0.15, 0.87); Table 3, Fig. 2B], and patients who were older at diagnosis (61–80 years) were at substantially greater risk compared with patients who were 41–60 years at diagnosis [EMRR 5.34 (95% CI 1.26, 13.33), Table 3, Fig. 2C]. While not reaching statistical significance, RA-associated mortality risk was essentially normalized in patients who were younger at diagnosis (20–40 years) and patients who were diagnosed on or after 2005 (Table 3, Fig. 2C, D).

Life lost (average life loss and years of life lost)

The RMST is the area under the survival curve for a given follow-up time and was 18.41 years (95% CI 18.21, 18.62)

Table 3. EMRR for sex, age at diagnosis and year of diagnosis^a

Covariate	EMRR (95% CI)	P-value
Sex		
Male (reference)	1	
Female	0.36 (0.15, 0.87)	0.024
Age at diagnosis, years		
20–40	0.15 (0.01, 2.78)	0.20
41–60 (reference)	1	
61–80	5.34 (1.26, 13.33)	<0.001
Year of diagnosis		
<2005 (reference)	1	
≥ 2005	0.24 (0.02, 3.24)	0.28

^a EMRRs for covariates from a multivariable relative survival model for RA patients compared with Australian population controls. Excess mortality rates are the difference between observed and expected mortality rates and may be interpreted as mortality rates specifically attributable to disease.

for RA patients compared with an expected value of 18.68 years for Australian population controls. This represents an average life loss in RA patients of ≈ 4 months over 20 years of follow-up. Overall years of life lost due to RA was estimated to be 2.0 years over the entire expected future lifespan.

Cause of death

Cause of death information was available for 183/204 (89.7%) RA patients who died during the study. Causes of death, grouped according to GRIM classifications, and cause-specific SMRs are summarized in Table 4, with full tabulations, including ICD-10 codes, reported in Supplementary Table S1, available at *Rheumatology* online.

RA was a frequent underlying cause of death [cause-specific SMR 87.5 (95% CI 53.44, 135.1)], but 'diseases of the circulatory system', which included coronary heart disease

Table 4. Cause-specific mortality in RA

GRIM chapter-level causes of death	Underlying COD			Any COD ^a	
	<i>n</i>	Expected	SMR (95% CI) ^b	<i>n</i>	%
Certain infectious and parasitic diseases	4	2.09	1.91 (0.52, 4.89)	27	14.8
Neoplasms	61	52.35	1.17 (0.89, 1.50)	70	38.3
Colorectal cancer	8	5.77	1.39 (0.60, 2.73)	10	5.5
Pancreatic cancer	3	3.32		3	1.6
Lung cancer	12	10.62	1.13 (0.58, 1.97)	15	8.2
Skin cancer (including melanoma)	6	2.00	3.00 (1.10, 6.53)	8	4.4
Breast cancer (females only)	4	5.00	0.80 (0.22, 2.05)	4	2.2
Prostate cancer (males only)	2	2.22		3	1.6
Diseases of the circulatory system	32	32.29	0.99 (0.68, 1.40)	87	47.5
Coronary heart disease	12	14.71	0.82 (0.42, 1.42)	36	19.7
Cerebrovascular disease	9	7.71	1.17 (0.53, 2.22)	22	12.0
Diseases of the respiratory system	27	11.67	2.31 (1.53, 3.37)	72	39.3
Pneumonia	8	1.53	5.22 (2.26, 10.29)	29	15.8
Other acute lower respiratory infections	1			7	3.8
Chronic obstructive pulmonary disease	5	6.58	0.76 (0.250, 1.77)	19	10.4
Other respiratory diseases principally affecting the interstitium	9	1.18	7.64 (3.98, 14.69)	21	11.5
Diseases of the musculoskeletal system and connective tissue	22	1.14	19.32 (12.11, 29.26)	66	36.1
RA	20	0.23	87.50 (53.44, 135.14)	61	33.3

Causes of death (COD) were reported for 183 patients. These were classified according to the Australian GRIM book ICD-10 codes [24].

^a Any COD refers to either an underlying or contributing cause of death. Full COD tabulations and ICD-10 codes are reported in [Supplementary Table S1](#), available at *Rheumatology* online.

^b Cause-specific SMRs were estimated for the underlying (primary) COD for which Australian mortality rates were available.

and cerebrovascular disease, were not [cause-specific SMR 0.99 (95% CI 0.68, 1.40)]. Respiratory diseases were an important underlying cause of death in RA, primarily attributable to pneumonia [cause-specific SMR 5.22 (95% CI 2.26, 10.29)] and interstitial lung disease [ILD; cause-specific SMR 7.64 (95% CI 2.98, 14.69)], but not chronic obstructive pulmonary disease [cause-specific SMR 0.76 (95% CI 0.25, 1.77)]. There was no overall increased risk with cancer, apart from skin cancer/melanoma [cause-specific SMR 3.00 (95% CI 1.10, 6.53)] and no clear evidence of increased infections other than pneumonia [cause-specific SMR 1.91 (95% CI 0.52, 4.89)].

Contributing causes of death are also tabulated in [Table 4](#), although formal analysis was not possible because this information was not available for the Australian population. Of note, of the 20 participants with an essentially non-specific primary or underlying cause of death reported as RA, respiratory disease was a contributing cause in 15 (75%) and circulatory disease a contributing cause in 8 (40%), which is

consistent with respiratory diseases being an important contributor to mortality in this RA cohort.

Discussion

This study estimates the 20-year long-term all-cause mortality risk associated with RA in Australian patients diagnosed since 1995, and therefore exposed to contemporary treatment strategies. Reassuringly, it found no increase in mortality in the first decade post-diagnosis, with an increase in mortality not seen until the second decade. The SMR at 20 years was 1.49 when compared with Australian population mortality rates, and the relative survival was 94%. The RMST difference was 0.27 years, which equates to an overall reduction in life expectancy of only 4 months over 20 years. Therefore, while mortality was increased in RA patients, this risk was relatively modest. These findings are comparable to an earlier Australian study that reported an SMR of 1.31 (95% CI 0.93, 1.80) in a cohort of 113 early RA patients diagnosed between 1990–1994 and followed up for 14 years [16].

Australia is a high-income country with a universal healthcare system that allows all patients access to rheumatology services and subsidized therapies, including csDMARDs and b/tsDMARDs through the pharmaceutical benefits scheme (PBS). While this study's results are generalizable to the broader Australian experience and can likely be extrapolated to other high-income countries with similar healthcare access, the mortality gap is likely to differ in lower-income countries and those with more variable access to services and treatments as has been shown in global reports of mortality in RA [30].

An important finding in our study was that mortality risk in RA accrues during follow-up, similar to our understanding of disease damage. In this respect, our study is comparable to a recent matched case-control mortality study of incident patients from the Oslo RA Register, which also noted no increase in the hazard ratio (HR) at 10 years of follow-up, but increasing estimates at 15 and 20 years [8]. If the underlying mortality risk in RA accrues over time, then summary estimates such as the SMR and HR will increase with increasing follow-up time from diagnosis. Follow-up duration will therefore be an important confounder when comparing studies or, in particular, interpreting results for improvements in mortality risk over calendar time, as more recent inception cohorts will, by design, have shorter follow-up times.

Whether there has been an improvement in RA-associated mortality risk in recent years is a relevant question given the increasing availability and diversity of b/tsDMARDs combined with improvements in disease management strategies, but one which has proved difficult to answer definitively. A large UK-based study using primary healthcare records [Clinical Practice Research Datalink (CPRD)] for incident RA, identified an inflexion point in incident RA mortality risk in 2004, with decreasing mortality risk thereafter [6]. In our study, the difference in mortality risk in RA patients diagnosed before and after 2005 did not reach statistical significance. However, estimation uncertainty would have been increased with the excess mortality rate close to zero. Therefore, while not conclusive, there is some evidence that improvements in RA management from ≈2005 onwards may have resulted in better mortality outcomes, but longer-term follow-up is required. With ongoing improvements in RA

management, future studies may require long follow-up times to determine whether the mortality gap in RA has closed.

Contrary to expectations, we found that cardiovascular disease did not contribute to increased mortality risk in ARAD RA patients. It is possible that misclassification bias may have led to some cardiovascular deaths being missed in those who had RA listed as their primary cause of death, as we were unable to compare contributing causes. However, supporting evidence that cardiovascular deaths may be decreasing in RA patients in more recent years also comes from the UK CPRD study [6]. Similarly, a decrease in cardiovascular deaths over time has also been seen in the general population [31, 32]. Cardiovascular disease risk in RA may arise from both inflammatory disease activity and comorbidities associated with increased cardiovascular disease risk, which accrue at a greater rate in RA compared with matched controls [33]. It is likely that better management of both disease activity and comorbidities in RA patients may have contributed to this decrease in cardiovascular disease mortality. For example, earlier studies in ARAD participants demonstrated that cardiovascular events were less frequent in those currently on bDMARDs [34] and that pharmacological treatment was reported by 93% of participants with hypertension and 70% with hyperlipidaemia [35]. The importance of managing comorbidities in RA patients is demonstrated by a recent meta-analysis that reported the initiation of statins was associated with a 28% decreased risk of all-cause mortality in RA [36].

Respiratory disease was an important contributor to increased mortality in ARAD RA patients, largely attributable to an increased cause-specific mortality risk of ILD and pneumonia. ILD is a recognized extra-articular manifestation of RA that has previously been linked to higher mortality in RA [37]. Interestingly, male gender and older age at diagnosis, which we observed to be associated with increased all-cause mortality risk, are both risk factors for ILD [37] and increased ILD-related mortality [38] in RA patients. While markers of RA disease activity and severity are also risk factors for the development of ILD [37], our results from a b/tsDMARD-treated cohort suggest that control of disease activity alone may not be sufficient to minimize ILD-related mortality in RA. This observation is supported by the UK CPRD study in which respiratory disease-related mortality did not change over time even though there was a concurrent marked decrease in cardiovascular disease-related mortality [6].

There are some limitations to this study. First, these results are drawn from RA patients with a high prevalence of b/tsDMARD use who were under the routine care of a rheumatologist. As such, the results may represent a 'best-case' scenario rather than being broadly generalizable. Second, it was not possible to evaluate the effect of disease activity on mortality risk because this information is not available in the ARAD, which only collects patient-reported data. Finally, the analysis of cause-specific mortality was incomplete because many primary causes of death were simply listed, uninformatively, as RA. Further, it was not possible to analyse contributing causes of death because no Australian population comparison data were available. Although this RA cohort was quite large, the number of cause-specific deaths was generally low because the overall death rate was low and cause of death was not available for a number of participants. This may have biased some association towards the null.

There are also several strengths to this study. This is a relatively large study with broad recruitment of ARAD participants from across Australia in both public and private rheumatology settings. Additionally, data linkage to the Australian NDI assured death and cause of death data were reliable and provided the most recent estimate of long-term (20 year) mortality risk in RA. Robust contemporary statistical methodology was also a strength of this study. While the SMR, widely used in rheumatology mortality research, is a useful mortality summary measure, it may be dependent on follow-up time, is confounded by differences in the underlying population risk (the denominator) and there is no corresponding statistical survival model to analyse the influence of covariates or changes in mortality risk over time. Relative survival models used in this study analyse the excess hazards and therefore the additional mortality risk that can be directly attributable to disease. These models are widely used in cancer-related mortality research and, more recently, during the coronavirus disease 2019 pandemic [39].

In conclusion, Australian RA patients exposed to contemporary treatment strategies are not at increased risk of mortality in the first decade following diagnosis. The increase in mortality in the second decade equates to a small reduction in life expectancy of only 4 months over 20 years. Respiratory conditions may have surpassed cardiovascular disease as the most important contributor to the mortality gap in RA. This information will be useful to Australian RA patients and clinicians when making treatment decisions. Further Australian studies are warranted to identify whether potentially modifiable factors such as treatment and disease activity influence mortality rates or cause of death.

Supplementary material

Supplementary material is available at *Rheumatology* online.

Data availability

Data may be made available upon valid request to the ARAD steering committee (<https://arad.org.au>).

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