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Australian mortality statistics for rheumatoid arthritis 1950–81: analysis of death certificate data

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SUMMARY An analysis of mortality related to rheumatoid arthritis (RA) in Australia for the period 1950 to 1981 was undertaken based on information recorded in death certificates. These data include every death over a 32 year period where RA was considered to be the underlying cause. Death from RA was commonly reported (0·17% of all deaths). The mean age at death from RA in both sexes exceeded that of the general population for most of the period. There was little difference between patients dying of RA and the general population for age at death in the over 50 years' age group. There was a significant decrease in mortality for women dying of RA over the age of 75. RA accounted for more deaths in women than in men (in a ratio of 2·2:1). Men tended to die at a younger age from RA than did women. The impact of RA remained relatively constant in relation both to the total causes of death and to deaths due to other musculoskeletal diseases. There was a significant decline, however, in female RA deaths as a percentage of deaths due to all musculoskeletal diseases. Cohort analysis does not indicate any marked effect from extrinsic factors on mortality due to RA.

There have been no previous reports of national mortality studies of RA over an extended period, though this is one of the most common chronic inflammatory diseases. There are no Australian data on the mortality of this disease. Although other publications have given conflicting results, there appears to be general acceptance that RA does decrease survival.[1] It is suggested this decreased expectancy may be related to a subgroup with onset at an early age[2–4] (particularly in men[2 3 5]) or to a subgroup with more severe disease.[2 6 7] Most studies showing decreased life expectancy appear to be biased towards more severe disease, with patients recruited from hospital inpatient or outpatient services.[3 4 6 8–12] In contrast, studies which include non-hospitalised patients show lower mortality,[7 13] though this wider sampling is also open to criticism because of possibly inadequate diagnostic criteria or a bias towards milder disease.

Death certificate analysis has been used in previous smaller studies of RA mortality.[4 7 14] The reliability of information obtained in this way has been questioned,[4 7 14 15] though the death certificate has been widely used in cause of death analysis.[3 5 7–10 12 16] An Australian study outlining some of the epidemiological problems of death certification has recently been reported.[17]

Despite recorded limitations the information derived from death certificate analysis for an entire population over a 32 year period provides an important opportunity to examine aspects of disease process and impact. Our study examines the mortality of RA, its relationship to other causes of death, and the possible effects of environmental factors in the entire Australian population for the years 1950 to 1981 inclusive, as recorded on death certificates.

Methods

Part one of the death certificate lists a sequence of conditions leading to death, with the underlying cause stated last. This sequence is compiled by the attending doctor[18] and is then analysed according to a series of rules devised by the World Health Organisation (WHO).[19] In Australia this function is performed by the Australian Bureau of Statistics and the results published annually in *Deaths Australia* (1963 to 1981).[20] Before 1963 the information was published annually in *Demography*.[21] Our data for RA cover a 32 year period and were tabulated under the International Classification of Diseases (ICD)

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codes 722 from 1950 to 1967 ('RA and allied conditions'); 712 from 1968 to 1978 ('RA and allied conditions'); and 714 from 1979 to 1981 ('RA and other inflammatory polyarthropathies'). Although RA represents most cases in these categories, other disorders may be included if not covered by another ICD code within class 13 ('Diseases of the bones and organs of movement' 1950 to 1967; 'Diseases of the musculoskeletal system and connective tissue' 1968 to 1981). The arrangement of the data for computer analysis has been previously described.[22]

The average age of death is the arithmetic mean. Owing to the relatively small number of deaths involved, fluctuations about the arithmetic mean are to be expected. Trend lines were fitted to the data in Figs 1, 2, 3, 4, and 6 using ordinary least square regression. To compare recorded mortality more specifically with those of the population more likely to have developed RA, mean age of death for the population over 50 years of age was calculated. Age specific mortality is the mortality per 100 000 for each of the five age groups 65–69, 70–74, 75–79, 80–84, 85+. This rate is multiplied by 100 000. The population chosen to calculate age standardised mortality was that of Australia in 1950.

Z is the standard normal variate used to test the null hypothesis for each of the 32 years and can be expressed as follows:

$$Z=(\bar{x}_1-\bar{x}_2) \Big/ \sqrt{\frac{S_1^2}{n_1}+\frac{S_2^2}{n_2}}$$

where $\bar{x}_1$=mean age of death from all causes (or

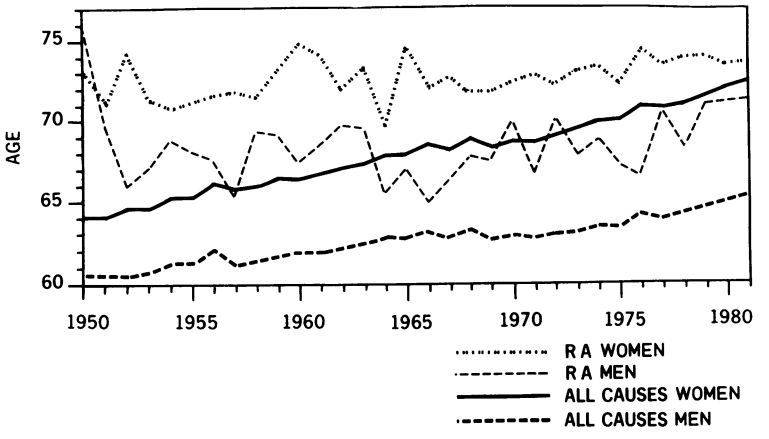

Fig. 1 *Mean age of death from RA and from all causes in Australia, by year of death for both sexes.*

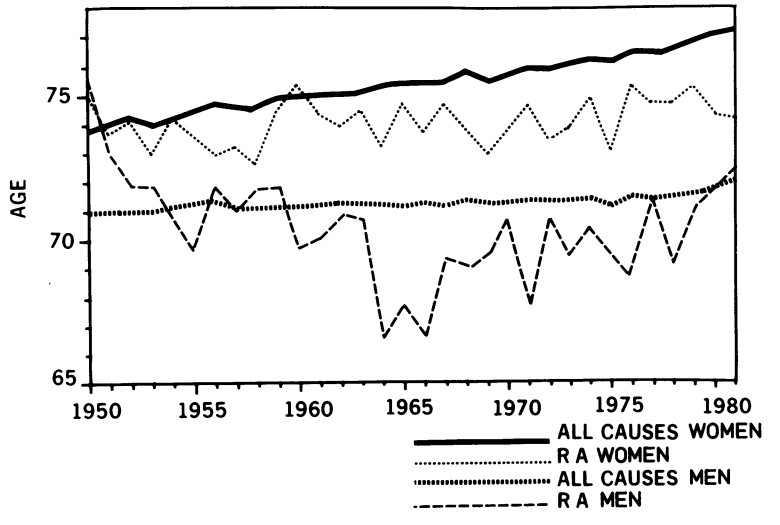

Fig. 2 *Mean age of death in Australia of those dying over the age of 50 from RA and all causes, by year of death for both sexes.*

from all causes, over the age of 50 years); $\bar{x}_2$=mean age of death from RA (or from RA, over the age of 50 years); S_1=variance of deaths from all causes (or from all causes, over the age of 50 years); S_2= variance of deaths from RA (or from RA, over the age of 50 years); n_1=number of deaths from all causes (or from all causes, over the age of 50 years); and n_2=number of deaths from RA (or from RA, over the age of 50 years).

For absolute values of Z greater than 1·96, the null hypothesis is rejected with $p<0·05$. In Table 3 the null hypothesis was that there would be no sex difference and hence the sex ratio of deaths due to RA would be 1. To calculate Z the actual ratio was subtracted from 1.

An age, period, and cohort analysis starting with the age groups 50–54 for women and 55–59 for men was performed using the algorithm of Barrett.[23] Younger age groups did not contain sufficient deaths for valid analysis. As linear trends are not estimable by this technique tests of statistical significance were not applied. The cohort effect reflects that part of the mortality which may be attributed to the five year span in which birth occurred. If an environmental factor operated in a differential way, this might subsequently be reflected in the mortality of a particular cohort(s). The period effect reflects that part of the mortality which may be attributed to the five year span in which death occurred. The period effect is virtually synonymous with the effect of a treatment regimen which influences mortality.

Results

Mean age of death in RA was significantly greater for both sexes than mean age of death from all causes for most of the period (Fig. 1 and Table 1). For deaths in women over 50 there was a significant difference between RA and the general population in eight of the 32 years, with no significant trend evident (Fig. 2 and Table 2). For deaths in men over 50 there was a significant difference between RA

Table 1 *Mean age of death from RA for both sexes compared with mean age of death from all causes*

Year	*Z value*	
	Women	*Men*
1950	−5·71**	−7·17**
1951	−4·73**	−4·02**
1952	−8·99**	−1·85 NS
1953	−4·62**	−2·58**
1954	−3·04**	−3·90**
1955	−4·09**	−3·93**
1956	−4·35**	−2·13*
1957	−4·07**	−1·39 NS
1958	−5·01**	−3·99**
1959	−5·55**	−3·87**
1960	−7·11**	−3·02**
1961	−7·08**	−3·75**
1962	−3·80**	−4·35**
1963	−5·27**	−4·14**
1964	−1·07 NS	−1·91 NS
1965	−6·58**	−3·02**
1966	−2·92**	−0·98 NS
1967	−3·31**	−2·01*
1968	−2·09**	−3·12**
1969	−3·19**	−2·74**
1970	−3·39**	−5·40**
1971	−4·11**	−2·88**
1972	−3·01**	−4·51**
1973	−3·37**	−3·54**
1974	−2·87**	−3·54**
1975	−2·08*	−2·38**
1976	−3·23**	−1·34 NS
1977	−2·20*	−4·24**
1978	−2·66**	−3·56**
1979	−2·35*	−5·68**
1980	−1·50 NS	−4·02**
1981	−1·31 NS	−4·35**

*p<0·05; **p<0·01; NS=not significant.

Table 2 *Deaths over 50—mean age of death from RA for both sexes compared with mean age of death from all causes*

Year	*Z value*	
	Women	*Men*
1950	1·04	2·16*
1951	−0·18	1·20
1952	0·20	0·38
1953	−0·91	0·52
1954	0·00	−0·40
1955	−0·68	−1·11
1956	−1·64	0·29
1957	−1·11	−0·04
1958	−2·13*	0·48
1959	−0·48	0·44
1960	0·45	−1·05
1961	−0·70	−0·85
1962	−1·15	−0·25
1963	−0·59	−0·32
1964	−1·91	−3·60**
1965	−0·59	−2·51*
1966	−1·63	−2·86**
1967	−0·59	−1·35
1968	−1·70	−1·74
1969	−2·72**	−1·50
1970	−2·11*	−0·40
1971	−1·46	−2·81**
1972	−2·86**	−0·41
1973	−2·21*	−1·60
1974	−1·27	−0·87
1975	−3·11**	−1·30
1976	−1·08	−1·87
1977	−1·72	0·07
1978	−1·89	−2·18*
1979	−1·64	−0·53
1980	−3·07**	0·00
1981	−3·35**	0·48

*p<0·05; **p<0·01.

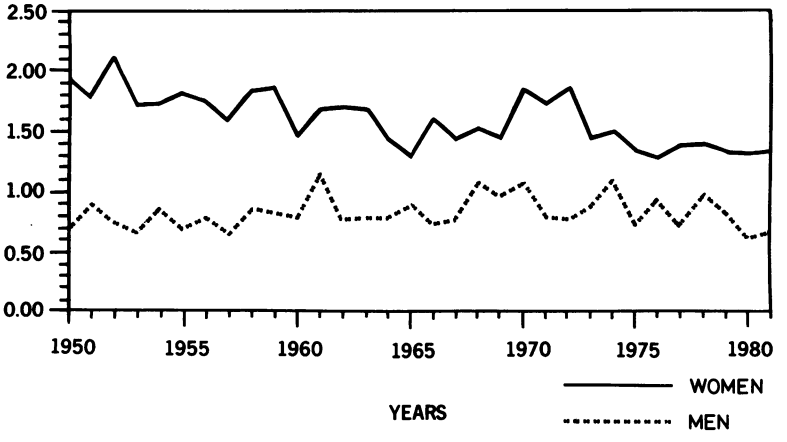

Fig. 3 *Age standardised mortality for deaths due to RA in Australia, by year of death for both sexes.*

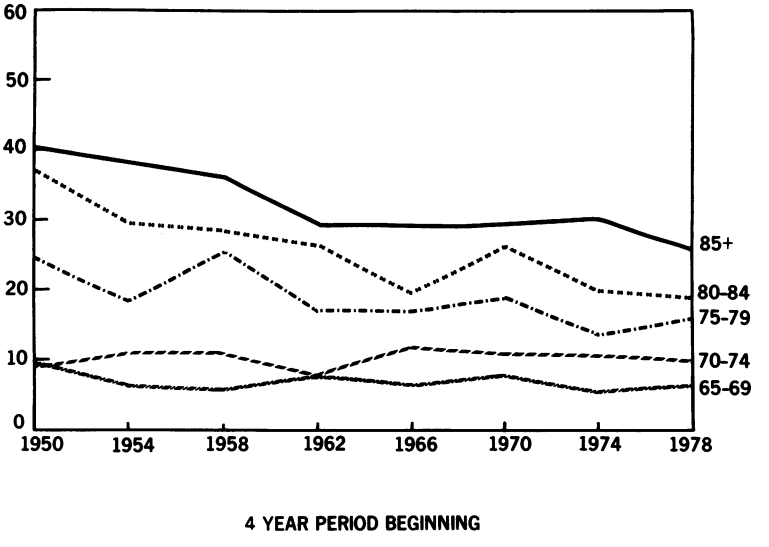

Fig. 4 *Age specific mortality for women dying of RA in Australia, by four year periods for each of five age groups older than 65 years.*

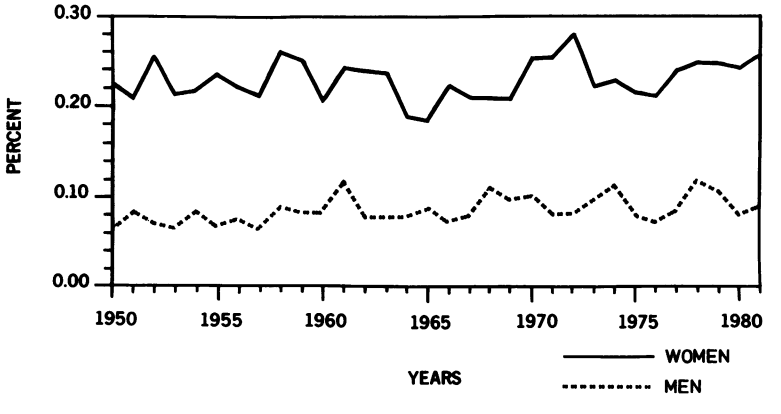

Fig. 5 *Percentage of all deaths in Australia due to RA, by year of death for both sexes.*

and the general population in six of the 32 years, with no significant trend evident (Fig. 2 and Table 2).

Women dying of RA live longer than men dying of RA ($p<0{\cdot}01$) (Fig. 1). Age standardised mortality for men dying of RA has not changed significantly, but there has been a significant fall ($p<0{\cdot}01$) for women dying of RA (Fig. 3). Analysis of age specific mortality shows this improvement for women occurred in the over 75 years' age groups (75–79, $p<0{\cdot}05$; 80–84, $p<0{\cdot}01$; 85+, $p<0{\cdot}01$) (Fig. 4).

RA is a common cause of death (approximately 0·2% of all female deaths and 0·1% of all male deaths), with no significant change in these percentages over the 32 year period for either sex (Fig. 5). More women died of RA than men (with an average ratio of 2·2:1), and this ratio has remained relatively constant (Table 3). Deaths due to RA as a percentage of deaths from all musculoskeletal diseases have been relatively constant for men, but have shown a significant decline ($p<0{\cdot}01$) over the 32 year period for women (Fig. 6).

A cohort and period analysis shows that for neither sex are there any birth cohorts or death periods which differ markedly from others (Fig. 7).

Discussion

The arguments outlining the limitations inherent in

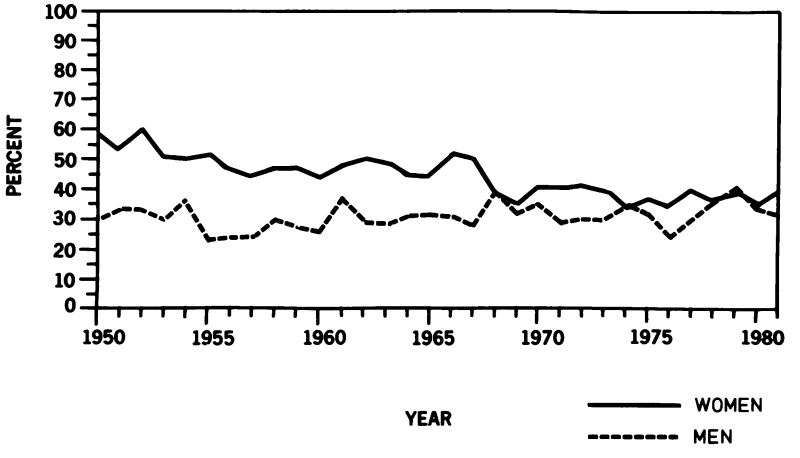

Fig. 6 *Deaths due to RA in Australia as a percentage of deaths due to all musculoskeletal diseases (class XIII) by year of death for both sexes.*

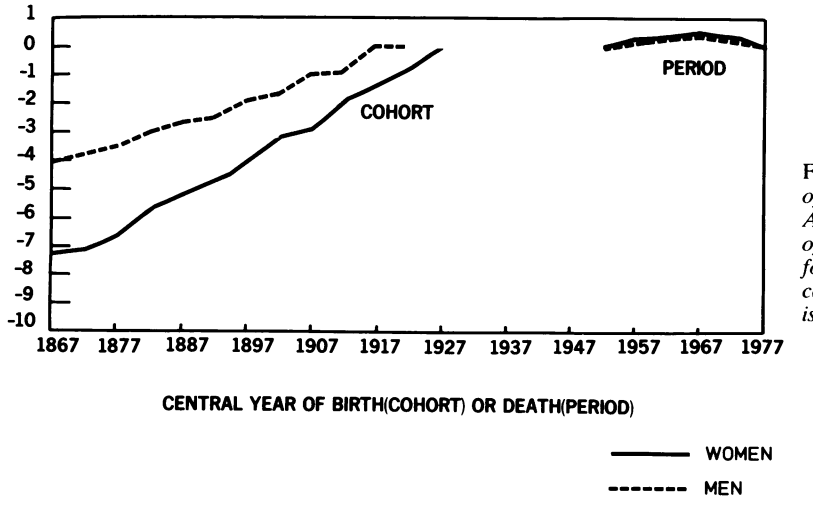

Fig. 7 *Cohort of birth and period of death for deaths due to RA in Australia, by central years of birth of cohorts above the ages of 50–54 for women and 55–59 for men, and central year of death. The ordinate is divided into arbitrary units.*

Table 3 *Sex ratio of deaths due to RA*

Year	*Sex ratio (F:M)*	*Z value*
1950	2·79	−1·01
1951	2·00	−0·61
1952	2·81	−2·58
1953	2·59	−1·51
1954	2·05	−0·81
1955	2·71	−1·45
1956	2·31	−1·33
1957	2·60	−2·03
1958	2·32	−1·00
1959	2·37	−1·68
1960	1·98	−3·40
1961	1·60	−2·76
1962	2·42	−1·04
1963	2·39	−1·84
1964	1·95	−1·90
1965	1·67	−4·53
1966	2·49	−3·29
1967	2·14	−3·08
1968	1·53	−2·27
1969	1·70	−2·09
1970	2·00	−1·42
1971	2·55	−3·64
1972	2·76	−1·33
1973	1·89	−3·09
1974	1·62	−2·40
1975	2·15	−2·59
1976	2·39	−3·90
1977	2·30	−1·47
1978	1·70	−3·48
1979	1·89	−1·91
1980	2·47	−1·26
1981	2·30	−1·41

the use of death certificate data have been well rehearsed.[14 24–27] These may include lack of experience of the doctor completing the certificate; brief contact between the patient and doctor attending the final illness; lack of appreciation of the possible life threatening complications of a disease; lack of postmortem validation; problems of causal sequencing in a complicated illness; inadequate death certificate narrative; changes in the medical concepts of a disease over time; changes in coding practices or classification systems of the WHO. A series of rules has been devised by the WHO in order to interpret the death certificate accurately and improve its epidemiological value.[18 19] Despite these limitations death certificates remain the most comprehensive method of gathering mortality statistics for the whole community. Furthermore, periodic review of the data obtained from death certificates is a prerequisite to improving the quality of these data.[28]

It is difficult to devise a practical system to study mortality in a chronic relapsing multisystem disorder with a wide range of severity, such as RA, without incurring methodological problems. Most previous reports have included patients drawn primarily from hospital based rheumatology services. This method contains a case acquisition bias with a possible tendency for such patients to have a more severe disease and worse outcome. Treatment of such patients may also be more aggressive, and the well recognised toxicity of antirheumatic drugs could itself influence mortality.[29] Our study is a national profile of patients, drawn from both hospital and community, who were considered to have died from RA. It is not a study of mortality in all patients previously diagnosed as having RA, nor is it known from our data how often RA appears on the death certificate other than as the underlying cause of death. Our study minimises factors which can complicate the analysis of death certificates. We have taken only deaths due to RA, rather than examining causes of death in patients known to have RA. In addition, we have analysed the annual national total of deaths due to RA over a prolonged period of time.

Survival in RA has been a controversial issue. In general, studies indicate some reduction in life expectancy, more marked for men with early disease onset. Our findings based on death certificate data in the Australian population over a 32 year period do not confirm this, and overall the mean age of death from RA has exceeded that of the general population. The onset of RA appears to be relatively age specific, however. We therefore analysed deaths over the age of 50 to examine more closely the population at risk and to minimise the bias inherent in earlier deaths in the general population (e.g., from trauma). In this group age at death from RA did not differ significantly from that of the general population. It is of interest that the study of Linos *et al*,[13] which came to a similar conclusion, was also a more broadly based community study. In addition, Allebeck *et al* found the death rate in the 25% of patients who had never been hospitalised for RA was below that of the whole RA group and less than that of the general population.[7] A recent report from Tasmania suggests that RA in the community is a less aggressive disease than that seen in a hospital setting.[30] In contrast, it now seems clear that mortality is increased among patients with RA treated in the rheumatology clinic or hospital setting.[31 32]

RA is a very common disease, with definite RA having a prevalence of approximately 1% in Caucasians, increasing with age to approach 2% in men and 5% in women over 55 years of age.[33] Nonetheless, the frequency with which RA was reported as a cause of death in our study (approximately 0·17%) was high. It may be that the frequent occurrence of a disorder which compromises physical capacity and

independence in an aging population predisposes to its regular inclusion on death certificates.

Our data show that although RA accounts for more deaths in women, in a ratio which accords with the sex prevalence of RA during life, men with RA die younger. This may reflect the well documented sex difference in overall life expectancy of men and women.[34] This difference, however, occurs because men die at a younger age of other common diseases, especially ischaemic heart disease.[34] The lack of any significant improvement in survival of men with RA over a period when life expectancy increased for men in general, plus the failure of the RA male age standardised mortality to fall over this period (as it did for women with RA), may also suggest that RA is a more aggressive disease in men. It has been stated that over 50 years of age the prognosis is worse for women with RA than for men.[35] Our data do not support this, with a significant fall in the age specific mortality of Australian women with RA greater than 75 years of age occurring over the 32 year period.

The aetiopathogenesis of RA is unclear. It is possible that major environmental effects could be important causes. Similarly, other influences, including the introduction of potent treatment regimens, could subsequently affect mortality. Our analysis, however, shows that for neither sex are there any five year birth cohorts or five year death periods differing markedly from others. This implies a lack of any variable environmental influences on disease process as measured by mortality.

Figures were produced by the Department of Medical Illustration, University of NSW and teaching hospitals.

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