



Supporting Information

Supplementary results

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

Appendix to: Yiallourou S, Magliano D, Haregu TN, et al. Long term all-cause and cardiovascular disease mortality among women who undergo fertility treatment. *Med J Aust* 2022; doi: 10.5694/mja2.51734.

Figure 1. Linkage of Monash IVF data records with National Death Index (NDI) records by the Australian Institute of Health and Welfare (AIHW)

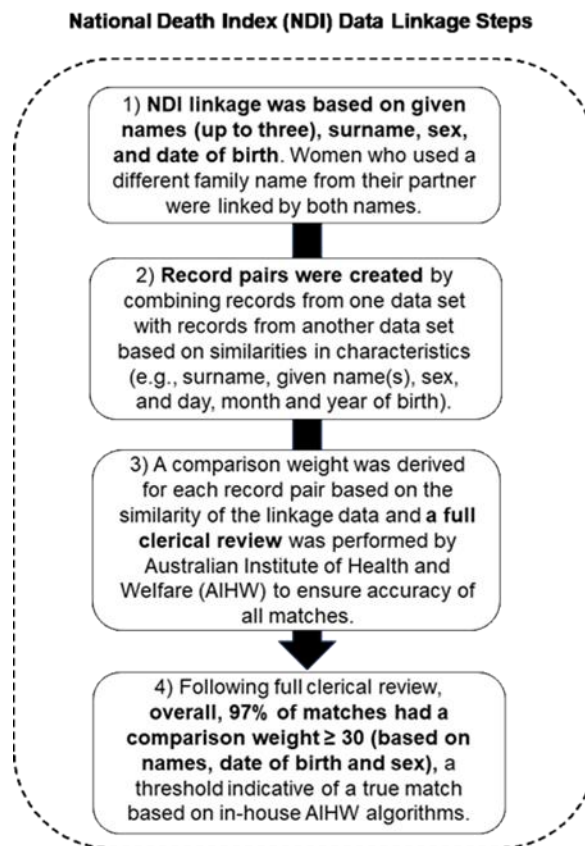


Table 1. Standardised mortality ratio (SMR) calculation

1. Data were split by single year and by 10-year age group (0-85+ years) for women registered for fertility treatment.
2. 10-year age-specific mortality rates by single year for the time period 1978–2018 were derived for the general Australian population, obtained from the Australian Institute of Health and Welfare GRIM books (<https://www.aihw.gov.au/reports/life-expectancy-deaths/grim-books/contents/general-record-of-incidence-of-mortality-grim-data>).
3. The single year-specific mortality rates (10-year age groups) for the general population were then applied to the number of women in each 10-year age group registered for fertility treatment to obtain the expected number of deaths, and then summed to obtain the total expected number of deaths.
4. SMRs were calculated as the ratio of the observed and expected deaths.

Table 2. Index of relative Socioeconomic disadvantage (IRSD)

Measure of Social Disadvantage	Variables in the Index of Socioeconomic Disadvantage*
Index of relative Socioeconomic disadvantage (IRSD): a validated index created by the Australian Bureau of Statistics to assess socio-economic status	INC_LOW: % of people with stated household equivalised income between \$1 and \$25,999 per year CHILDJOBLESS: % of families with children under 15 years of age who live with jobless parents NONET: % of occupied private dwellings with no internet connection NOYEAR12ORHIGHER: % of people aged 15 years and over whose highest level of education is Year 11 or lower UNEMPLOYED: % of people (in the labour force) who are unemployed OCC_LABOUR: % of employed people classified as Labourers LOWRENT: % of occupied private dwellings paying rent less than \$215 per week (excluding \$0 per week) ONEPARENT: % of one parent families with dependent offspring only DISABILITYU70: % of people under the age of 70 who have a long-term health condition or disability and need assistance with core activities SEPDIVORCED: % of people aged 15 years and over who are separated or divorced OCC_DRIVERS: % of employed people classified as Machinery Operators and Drivers OCC_SERVICE_L: % of employed people classified as low skill Community and Personal Service workers NOCAR: % of occupied private dwellings with no cars OVERCROWD: % of occupied private dwellings requiring one or more extra bedrooms NOEDU: % of people aged 15 years and over who have no educational attainment ENGLISHPOOR: % of people who do not speak English well

Information source: Census of Population and Housing: Socio-Economic Indexes for Areas (SEIFA), Australia, 2016
<https://www.abs.gov.au/ausstats/abs@.nsf/Lookup/by%20Subject/2033.0.55.001~2016~Main%20Features~IRSD~19>.

Table 3. All-cause mortality in untreated and treated women who registered for fertility therapy at Monash IVF

	Untreated	Treated	P
Combined Cohort			
Number of women	10,628	33,519	
Number of observed deaths	326	427	
Number of expected deaths	518	780	
SMR (95% CI)	0.63 (0.56 - 0.70)	0.55 (0.50 - 0.60)	0.06
IVF Cancer Database			
Number of women	4,267	3,085	
Number of observed deaths	216	176	
Number of expected deaths	337	263	
SMR (95% CI)	0.64 (0.56 - 0.73)	0.67 (0.58 - 0.77)	0.68
Monash IVF Registry			
Number of women	6,361	30,434	
Number of observed deaths	110	251	
Number of expected deaths	184	517	
SMR (95% CI)	0.61 (0.50 - 0.73)	0.49 (0.43 - 0.55)	0.07

Standardised mortality ratio (SMR), 95% confidence interval (95% CI).

Table 4. All-cause mortality stratified for number of stimulate cycles and number of oocytes produced in treated women who registered for fertility therapy at Monash IVF

	Number of Stimulated Cycles			Number of Oocytes per cycle ^a		
	<3	≥ 3	P	<6	≥ 6	P
Combined Cohort						
Number of women	17,448	16,071				
Number of observed deaths	253	174		-	-	
Number of expected deaths	420	359		-	-	
SMR (95% CI)	0.60 (0.53 - 0.68)	0.48 (0.42 - 0.56)	0.026	-	-	
IVF Cancer Database						
Number of women	1,988	1,097				
Number of observed deaths	116	60		-	-	
Number of expected deaths	166	98		-	-	
SMR (95% CI)	0.70 (0.58 - 0.84)	0.62 (0.48 - 0.79)	0.42	-	-	
Monash IVF Registry						
Number of women	15,460	14,974		12,913	17,470	
Number of observed deaths	137	114		134	117	
Number of expected deaths	254	262		248	268	
SMR (95% CI)	0.54 (0.46 - 0.64)	0.44 (0.36 - 0.52)	0.10	0.54 (0.46 - 0.64)	0.44 (0.36 - 0.52)	0.10

Standardised mortality ratio (SMR), 95% confidence interval (95% CI)

^aData were only available for the 36,796 women registered in the Monash IVF clinical registry and SMR was calculated only for women who had complete dataset on oocyte collection.

Table 5. Cardiovascular disease mortality in untreated and treated women who registered for fertility therapy at Monash IVF

	Untreated	Treated	P
Combined Cohort			
Number of women	10,628	33,519	
Number of observed deaths	35	24	
Number of expected deaths	60	84	
SMR (95% CI)	0.58 (0.42 - 0.81)	0.29 (0.19-0.43)	0.011
IVF Cancer Database			
Number of women	4,267	3,085	
Number of observed deaths	21	9	
Number of expected deaths	41	33	
SMR (95% CI)	0.52 (0.34 – 0.80)	0.28 (0.14 – 0.53)	0.11
Monash IVF Registry			
Number of women	6,361	30,434	
Number of observed deaths	14	15	
Number of expected deaths	19	51	
SMR (95% CI)	0.72 (0.43 – 1.2)	0.29 (0.18 – 0.49)	0.048

Standardised mortality ratio (SMR), 95% confidence interval (95% CI)

Table 6: Data for Box 4 representing all-cause standardised mortality ratios (SMRs) and 95% CIs for 44 147 women registered for fertility treatment at Monash IVF, 1 January 1975 – 1 January 2014, by area-based Index of Relative Socioeconomic Disadvantage (IRSD) quintile

Treatment	IRSD level	SMR	95% CI Lower	95% CI Upper
Untreated	1	0.913	0.706	1.181
Untreated	2	0.634	0.446	0.902
Untreated	3	0.720	0.551	0.940
Untreated	4	0.626	0.493	0.796
Untreated	5	0.530	0.442	0.635
Treated	1	0.589	0.445	0.780
Treated	2	0.636	0.476	0.849
Treated	3	0.632	0.503	0.794
Treated	4	0.627	0.516	0.762
Treated	5	0.467	0.398	0.548