

Appendix 2: Supplementary tables [posted as supplied by author]

Table A Cohort studies reporting all cause and overdose mortality rate ratios comparing first and subsequent episodes of methadone treatment*

First author, year	Treatment episode	No of person years	All cause mortality			Overdose mortality		
			No of deaths	Rate†	Rate ratio (95% CI)	No of deaths	Rate†	Rate ratio (95% CI)
Caplehorn et al, 1994, 1996	First	1200	9	7.5	3.00 (0.65 to 13.89)	3	2.7	1.84 (0.19 to 17.68)
	Subsequent	800	2	2.5		1	1.5	
Cornish et al, 2010‡	First	7926	80	10.1	1.01 (0.75 to 1.36)			
	Subsequent	9806	98	10.0				
Nosyk et al, 2015	First	1892	81	42.8	0.76 (0.58 to 0.98)			
	Subsequent	3418	193	56.5				
Cousins et al, 2016	First	6313	37	5.9	0.75 (0.53 to 1.07)	17	2.7	1.00 (0.58 to 1.71)
	Subsequent	22583	176	7.8		61	2.7	

*Episodes included periods in and out of treatment, except for Caplehorn et al in which only periods in treatment were considered.

†Rates per 1000 person years.

‡Mortality during first and subsequent treatment episodes was reported combining methadone with buprenorphine (13.7% of person years).

Table B Cohort studies comparing all cause and overdose mortality rates after incomplete and complete methadone treatment*

First author, year	Treatment completeness	No of person years	All cause mortality			Overdose mortality		
			No of deaths	Rate [†]	Rate ratio (95% CI)	No of deaths	Rate [†]	Rate ratio (95% CI)
Grönbladh et al, 1990	Incomplete	376	26	69.1	4.19 (1.72 to 10.18)	22	58.5	4.25 (1.61 to 11.23)
	Complete	364	6	16.5		5	13.7	
Cornish et al, 2010‡	Incomplete				0.95 (0.24 to 3.73)			
	Complete							
Peles et al, 2010	Incomplete	563	47	83.5	3.26 (1.30 to 8.21)			
	Complete	196	5	25.6				

*Entire periods out of treatment were included in all cohort studies except Cornish et al, which only considered the first four weeks after leaving treatment.

[†]Rates per 1000 person years.

[‡]Mortality after incomplete and complete treatment was reported combining methadone with buprenorphine (14.9% of person years out of treatment).