Appendix 2 (as supplied by the authors): Supplementary Information

Table A. Risk of bias assessment for observational studies

		SELECTION BIAS	PERFORMANC	CE BIAS	DETECTION BIA	S	INFORMATION BIA	۱S	
Author, Last name	Year	Is the source population representative?	Is the sample size adequate and is there sufficient power?	Did the study adjust for confounders ?	Did the study use appropriate statistics for outcome of interest?	Is there little missing data and was it handled appropriately?	Are the methods or outcome measurements explicitly stated and is it appropriate?	Is there an objective assessment of outcomes?	Total (out of 21)
Anglin	1987	2	1	1	2	1	1	1	9
Brown	1993	1	1	1	2	2	2	1	10
Camacho	1996	2	2	1	2	2	3	1	13
Chatham	1999	2	2	1	2	2	3	3	15
Grella	2012	1	2	1	1	1	2	1	9
Haug	2005	1	1	1	2	2	3	3	13
Hser	1990	2	2	1	2	2	1	0	10
Jimenez- Trevino	2011	1	1	1	2	0	2	1	8
Marsh	1986	1	1	1	1	2	1	0	7
Mulvaney	1999	2	2	1	2	2	2	2	13
Peles	2006	2	1	1	2	1	3	2	12
Rutherford	1997	1	1	1	2	1	2	0	8
Savage	1980	2	2	1	1	2	1	0	9
Schiff	2007	2	2	1	2	1	1	3	12
Schilling	1991	1	1	1	2	2	2	0	9
Steer	1980	2	1	2	3	2	2	0	12
Stenbacka	2003	2	2	1	2	1	3	3	14
Webber	1999	1	2	2	2	2	2	2	13

0 = Definitely no; 1 = Mostly no; 2 = Mostly yes; 3 = Definitely yes

Appendix to: Bawor M, Dennis BB, Bhalerao A, et al. Sex differences in outcomes of methadone maintenance treatment for opioid use disorder: a systematic review and meta-analysis. CMAJ Open 2015. DOI:10.9778/cmajo.20140089.Copyright © 2015 The Author(s) or their employer(s). To receive this resource in an accessible format, please contact us at cmajgroup@cmaj.ca.

Table B. Risk of bias assessment for RCTs

Author, Last	Year	1. Was the	2. Was	3. Was	4. Were	5. Are reports of the	6. Was the study
name		allocation	allocation	knowledge of	incomplete data	study free of	free of other
		sequence	concealed	intervention	adequately	selective outcome	problems that
		generated	adequately?	adequately	addressed?	reporting?	could put it at high
		adequately?		prevented?			risk of bias?
Jones	2005	1	1	1	1	1	1
Schottenfeld	1998	1	1	1	1	1	1

1 = Low risk of bias

	Wome	en	Men	l		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% CI
1.1.2 Cohort studies							
Anglin 1987	96	264	96	282	27.0%	1.11 [0.78, 1.57]	
Hser 1990	223	328	269	392	28.2%	0.97 [0.71, 1.33]	
Webber 1999	127	222	221	302	26.5%	0.49 [0.34, 0.71]	
Subtotal (95% CI)		814		976	81.7%	0.81 [0.50, 1.31]	
Total events	446		586				
Heterogeneity: Tau ² = 0.15;	Chi ² = 11.	41, df =	= 2 (P = 0	.003); l	² = 82%		
Test for overall effect: Z = 0	.86 (P = 0.	39)					
1.1.3 Randomized control	led trials						
Jones 2005	6	19	10	36	8.1%	1.20 [0.36, 4.03]	
Schottenfeld 1998 - 20mg	3	7	10	23	4.6%	0.97 [0.18, 5.39]	· · · · · · · · · · · · · · · · · · ·
Schottenfeld 1998 - 65mg	7	12	6	16	5.6%	2.33 [0.51, 10.78]	
Subtotal (95% CI)		38		75	18.3%	1.39 [0.61, 3.19]	
Total events	16		26				
Heterogeneity: Tau ² = 0.00;	Chi ² = 0.6	6, df = 1	2 (P = 0.7	′2); l² =	0%		
Test for overall effect: Z = 0	.78 (P = 0.	44)					
Total (95% CI)		852		1051	100.0%	0.90 [0.60, 1.33]	-
Total events	462		612				
Heterogeneity: Tau ² = 0.12;	Chi ² = 13.	47, df =	= 5 (P = 0	.02); l²	= 63%		
Test for overall effect: Z = 0							0.5 0.7 1 1.5 2 Favors [Men] Favors [Women]
Test for subgroup difference	es: Chi² = ′	1.21, df	= 1 (P =	0.27), l ^a	² = 17.6%		

Figure A. Cohort and randomized controlled studies measuring illicit opioid use during treatment

Figure B. Number of subjects with 12-20 months of treatment retention

	Wome	en	Mer	n		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
Chatham 1999	45	126	81	279	31.7%	1.36 [0.87, 2.12]	
Hser 1990	100	131	246	339	30.9%	1.22 [0.76, 1.95]	
Peles 2006	129	328	193	392	37.4%	0.67 [0.50, 0.90]	
Total (95% CI)		585		1010	100.0%	1.01 [0.62, 1.63]	
Total events	274		520				
Heterogeneity: Tau ² = Test for overall effect:				P = 0.01); l² = 77%	, D	0.5 0.7 1 1.5 2 Favors [Men] Favors [Women]

	Wome	en	Men	1		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% Cl
Peles 2006	68	131	198	339	35.6%	0.77 [0.51, 1.15] 🔶	
Schiff 2007	158	331	1091	2352	64.4%	1.06 [0.84, 1.33]	
Total (95% CI)		462		2691	100.0%	0.94 [0.70, 1.27]	
Total events	226		1289				
Heterogeneity: Tau ² =	0.02; Chi ²	= 1.78	df = 1 (P	= 0.18); l² = 44%		
Test for overall effect:	Z = 0.39 (I	P = 0.7	D)				0.7 0.85 1 1.2 1.5 Favours [Men] Favours [Women]

Figure C. Benzodiazepine use over the last six months measured using urine toxicology

Figure D. Cannabis use over the last six months measured using urine toxicology

	Wome	en	Mer	n		Odds Ratio		Odds	s Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl		M-H, Rano	dom, 95% Cl	
Peles 2006	15	131	40	339	13.7%	0.97 [0.51, 1.82]				
Schiff 2007	97	331	781	2352	86.3%	0.83 [0.65, 1.07]			-	
Total (95% CI)		462		2691	100.0%	0.85 [0.67, 1.08]			-	
Total events	112		821							
Heterogeneity: Tau ² =	0.00; Chi ²	= 0.18	, df = 1 (F	P = 0.67	'); l² = 0%		+	0.7		<u> </u>
Test for overall effect:	Z = 1.35 (l	P = 0.1	8)				0.5	0.7 Favors [Men]	1 1.5 Favors [Wome	2 en]

Figure E. Cocaine use over the last six months measured using urine toxicology

	Wome	en	Mer	n		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% Cl
Peles 2006	26	131	38	339	29.4%	1.96 [1.14, 3.39]	-
Schiff 2007	107	331	760	2352	40.2%	1.00 [0.78, 1.28]	— —
Schilling 1991	38	109	61	135	30.4%	0.65 [0.39, 1.09]	
Total (95% CI)		571		2826	100.0%	1.07 [0.64, 1.78]	
Total events	171		859				
Heterogeneity: Tau ² =	0.15; Chi ²	= 8.43	, df = 2 (F	9 = 0.01); l² = 76%		
Test for overall effect:							0.5 0.7 1 1.5 2 Favors [Men] Favors [Women]

Figure F. Mean methadone dose after 6-12 months in treatment (mg/day)

	W	omen			Men			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Camacho 1996	38.4	15.3	103	40.9	13.6	223	90.7%	-2.50 [-5.95, 0.95]	
Peles 2006	131.1	54.8	131	132.3	49.5	339	9.3%	-1.20 [-11.96, 9.56]	
Total (95% CI)			234			562	100.0%	-2.38 [-5.67, 0.91]	
Heterogeneity: Tau ² = Test for overall effect:				= 1 (P =	0.82);	l ² = 0%)	-	-10 -5 0 5 10 Favors [Men] Favors [Women]

Figure G. Number of subjects currently married or living with spouse

	Wome	n	Men	1		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
Anglin 1987	237	264	252	282	18.8%	1.04 [0.60, 1.81]	
Brown 1993	25	177	33	291	18.2%	1.29 [0.74, 2.24]	
Hser 1990	228	328	282	392	54.5%	0.89 [0.64, 1.23]	
Schilling 1991	10	109	18	135	8.5%	0.66 [0.29, 1.49]	
Total (95% CI)		878		1100	100.0%	0.96 [0.75, 1.21]	•
Total events	500		585				
Heterogeneity: Tau ² =	0.00; Chi ²	= 2.19,	df = 3 (P	= 0.53	s); l ² = 0%		
Test for overall effect:							0.5 0.7 1 1.5 2 Favors [Men] Favors [Women]

Figure H. Number of deaths reported at one year after treatment completion

	Wome	en	Men	1		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
Chatham 1999	17	131	14	279	44.6%	2.82 [1.35, 5.92]	· · · · · · · · · · · · · · · · · · ·
Webber 1999	96	222	129	302	55.4%	1.02 [0.72, 1.45]	-
Total (95% CI)		353		581	100.0%	1.61 [0.60, 4.33]	
Total events	113		143				
Heterogeneity: Tau ² = Test for overall effect:				9 = 0.02); l² = 83%	, D	0.2 0.5 1 2 5 Favors [Men] Favors [Women]