

A1.5 What maintenance doses of methadone should be used?

GRADE evidence profile

Author(s):	Amato L, Minozzi S
Date:	24 March 2006
Question:	Should methadone maintenance (40–59 mg/day) versus methadone maintenance (1–39 mg/day) be used for opioid dependence?
Patient or population:	Opioid dependents
Settings:	Outpatient
Systematic review:	Faggiano F et al. <i>Methadone maintenance at different dosages for heroin dependence</i> (CLIB 3, 2003) ^{140j} .

Quality assessment						Summary of findings				Quality	Importance
No. studies	Design	Limitations	Consistency	Directness	Other considerations	No of patients		Effect			
						Methadone maintenance medium doses (40–59 mg/day)	Methadone maintenance low doses (1–39 mg/day)	Relative risk (RR) (95% CI)	Absolute risk (AR) (95% CI)		
Retention in treatment ¹⁰⁸ⁱ (objective follow-up: 20 weeks)											
1 ^a	Randomized trial	No limitations ^b	No important inconsistency	No uncertainty	Imprecise or sparse data (–1) ^c	44/84 (52.4%)	34/82 (41.5%)	RR 1.26 ^d (0.91 to 1.75)	110/1000 more (40 less to 260 more)	⊕⊕⊕○ Moderate	7
Mortality ^{196j} (objective follow-up: 6 years)											
1 ^a	Observational studies ^h	No limitations ^b	No important inconsistency	No uncertainty	Imprecise or sparse data (–1) ^a	1/362 (0.3%)	4/822 (0.5%)	RR 0.57 ^d (0.06 to 5.06)	2/1000 less (20 less to 5 more)	⊕○○○ Very low	9

- ^a Outpatient, conducted in the United States.
^b Double blind, allocation concealment unclear.
^c Only one study.
^d Fixed effect model.
^e One CPS, outpatient, conducted in Dutch; for CPS medium doses = 55–70 mg/day, low doses = 5–55 mg/day.
^f One CPS of moderate quality.
^g Large confidence interval.
^h CPS.

GRADE evidence profile

Author(s):	Amato L, Minozzi S
Date:	24 March 2006
Question:	Should methadone maintenance (60–120 mg/day) versus methadone maintenance (1–39 mg/day) be used for opioid dependence?
Patient or population:	Opioid dependents
Settings:	Outpatient
Systematic review:	Faggiano F et al. <i>Methadone maintenance at different dosages for heroin dependence</i> (CLIB 3, 2003) ^{140j} .

Quality assessment						Summary of findings				Quality	Importance
No. studies	Design	Limitations	Consistency	Directness	Other considerations	No of patients		Effect			
						Methadone maintenance (60–120 mg/day)	Methadone maintenance (1–39 mg/day)	Relative risk (RR) (95% CI)	Absolute risk (AR) (95% CI)		
Retention in treatment at 7–26 weeks (objective follow-up: 7–26 weeks)											
5	Randomized trials	No limitations	No important inconsistency	No uncertainty	None	138/247 (55.9%)	102/249 (41.0%)	RR 1.36 (1.13 to 1.63)	150/1000 more (50 to 260)	⊕⊕⊕⊕ High	7
Opioid abstinence (proportion of negative urine samples over 12 weeks)											
1	Randomized trials	No limitations	No important inconsistency	No uncertainty	Very imprecise or sparse data (–2)	55	55	—	WMD –2.0 (–4.8 to –0.8)	⊕⊕○○ Low	7
Opioid abstinence at 3–4 weeks (urinalysis)											
3	Randomized trials	No limitations	Inconsistent findings (–1) ^a	No uncertainty	Imprecise or sparse data (–1)	55/118	34/119	—	RR 1.59 (1.16 to 2.18)	⊕⊕○○ Low	7
Cocaine abstinence at 3–4 weeks (urinalysis)											
2	Randomized trials	No limitations	No important inconsistency	No uncertainty	Imprecise or sparse data (–1)	35/83	20/85	—	RR 1.81 (1.15 to 2.85)	⊕⊕⊕○ Moderate	6

^a Significant heterogeneity.

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Author(s): Amato L, Minozzi S
Date: 24 March 2006
Question: Should methadone maintenance (60–120 mg/day) versus methadone maintenance (40–59 mg/day) be used for opioid dependence?
Patient or population: Opioid dependents
Settings: Outpatient
Systematic review: Faggiano F et al. *Methadone maintenance at different dosages for heroin dependence* (CLIB 3, 2003)^{140j}.

Quality assessment						Summary of findings				Quality	Importance
No. studies	Design	Limitations	Consistency	Directness	Other considerations	No of patients		Effect			
						Methadone maintenance (60–120 mg/day)	Methadone maintenance (40–59 mg/day)	Relative risk (RR) (95% CI)	Absolute risk (AR) (95% CI)		
Retention in treatment at 7–13 weeks ^[211, 212] (Objective follow-up: 7–13 weeks)											
2 ^a	Randomized trials	No limitations ^b	No important inconsistency	No uncertainty	Imprecise or sparse data (-1)	138/173 (79,8%)	137/174 (78,7%)	RR 1.01 ^c (0.91 to 1.12)	10 more/1 000 (80 less to 90 more)	⊕⊕⊕○	7 Moderate
Retention in treatment at 27–40 weeks ^[213, 211, 214] (Objective follow-up: 27–40 weeks)											
3 ^d	Randomized trials	No limitations ^e	No important inconsistency	No uncertainty	None	157/277 (56,7%)	130/283 (45,9%)	RR 1.23 ^e (1.05 to 1.45)	100/1 000 more (30 more to 190 more)	⊕⊕⊕⊕	7 High
Opioid abstinence ^[212] (Objective ^f follow-up: 3–4 weeks)											
1 ^f	Randomized trials	No limitations ^b	No important inconsistency	No uncertainty	Very imprecise or sparse data (-2) ^g	10/31 (32,3%)	6/28 (21,4%)	RR 1.51 ^c (0.63 to 3.61)	110/1 000 more (120 less to 330 more)	⊕⊕○○	7 Low
Criminal activity ^[212] (Objective and subjective ^h Range: to . Better indicated by: lower scores)											
1 ^f	Randomized trials	No limitations ^b	No important inconsistency	No uncertainty	Very imprecise or sparse data (-2) ^g	31	28	-	WMD 0.05 (-0.03 to 0.13)	⊕⊕○○	6 Low
Mortality ^[196] (Objective follow-up: 6 years)											
1 ^m	Observational studies ⁿ	No limitations ^b	No important inconsistency	No uncertainty	Very imprecise or sparse data (-2) ^g	0/316 (0%)	1/362 (0,3%)	RR 0.38 ^e (0.02 to 9.34)	0/1 000 (10 less to 10 more)	⊕○○○	9 Very low

- ^a Both outpatient and both conducted in USA
^b Both double blind, allocation concealment unclear
^c Fixed effect model
^d All outpatient and all conducted in USA
^e adequate allocation concealment, 2 unclear; 2 double blind, 1 single blind
^f Outpatient, conducted in USA
^g Based on urinalysis
^h Double blind, allocation concealment unclear
ⁱ only 1 study, few participants
^j During the treatment
^k Outpatient, conducted in USA
^l Medium number/week of criminal activities
^m 1 CPS, outpatient, conducted in Dutch. For CPS high doses = >75 mg/day, medium dose = 55–70 mg/day
ⁿ 1 CPS of moderate quality
^o Few events

GRADE evidence profile

Author(s): Amato, Minozzi
Date: 24/03/2006
Question: Should Methadone maintenance very high doses (>120 mg/day) versus Methadone maintenance high doses (60–120 mg/day) be used for Opioid dependence?
Patient or population: Opioid-dependent patients Settings: Outpatient
Systematic review: Faggiano F et al. *Methadone maintenance at different dosages for heroin dependence* (CLIB 3, 2003)^{140j}.

Quality assessment						Summary of findings				Quality	Importance
No. studies	Design	Limitations	Consistency	Directness	Other considerations	No of patients		Effect			
						Methadone maintenance very high doses (>109 mg/day)	Methadone maintenance high doses (60–109 mg/day)	Relative risk (RR) (95% CI)	Absolute risk (AR) (95% CI)		
Retention in treatment ^[213] (Objective follow-up: 27 weeks)											
1 ^a	Randomized trials	No limitations ^b	No important inconsistency	No uncertainty	Imprecise or sparse data (-2) ^c	25/40 (62,5%)	26/40 (65%)	RR 0.96 ^d (0.69 to 1.34)	30/1 000 less (240 less to 190 more)	⊕⊕○○	1 Low

- ^a Outpatient, conducted in USA
^b Single blind, adequate allocation concealment
^c 1 study, few participants
^d Fixed effect model