

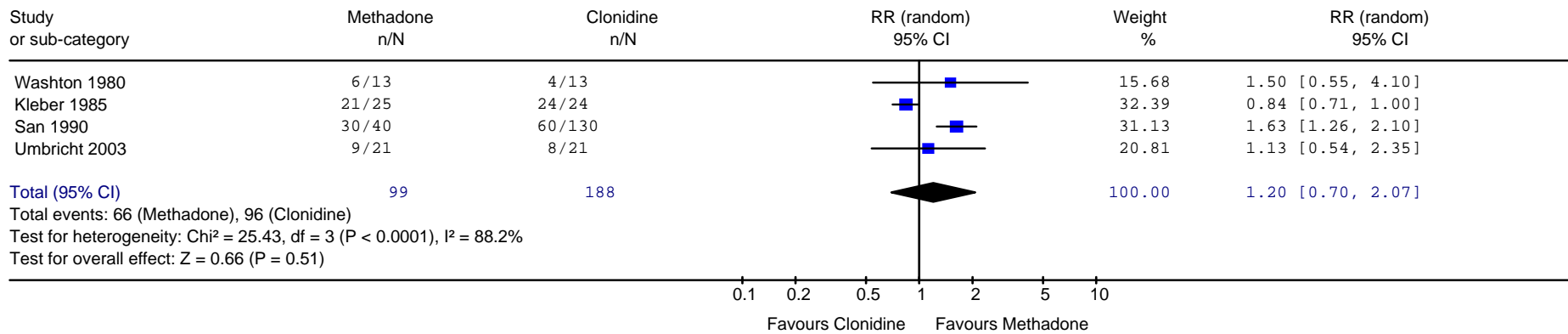
Appendix 16a: Clinical evidence forest plots (pharmacological interventions in opioid detoxification)

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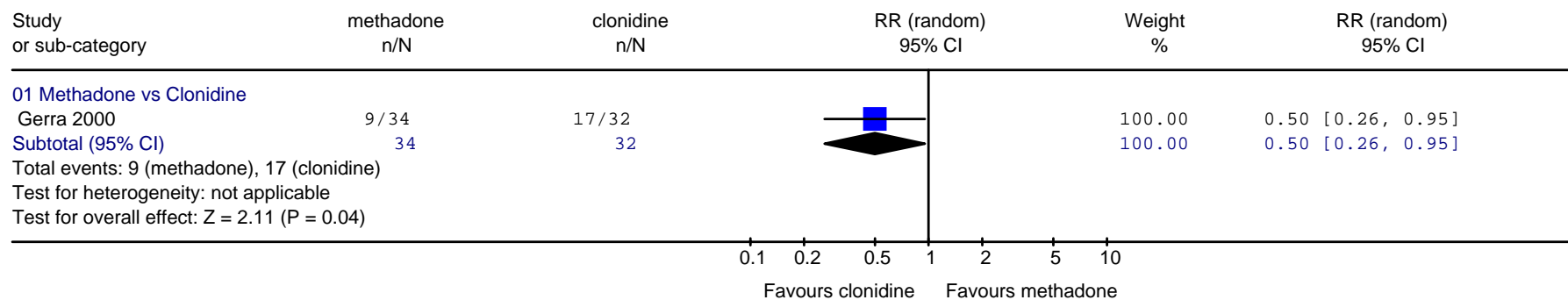
Pharmacology

Methadone

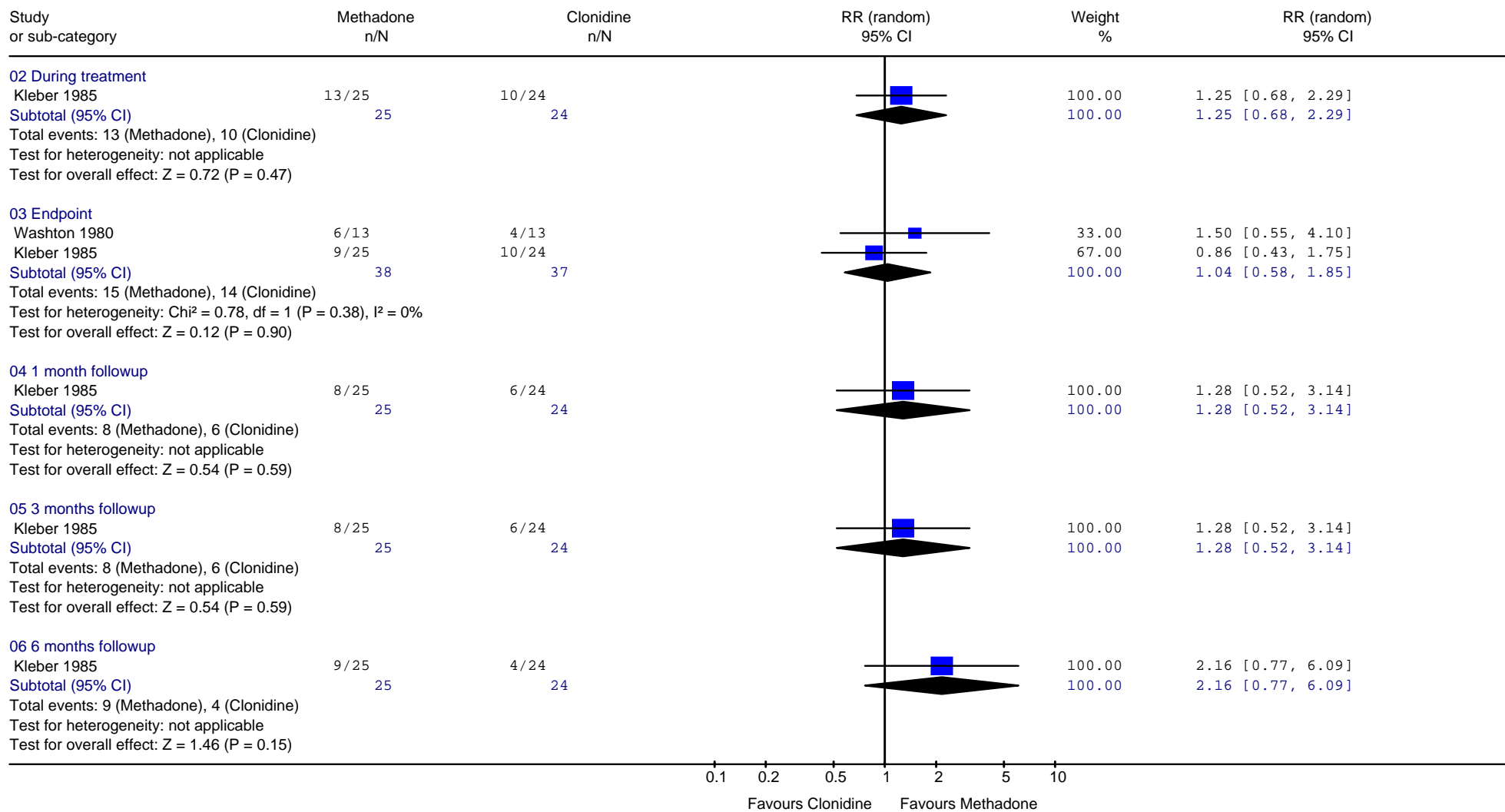
Review: DMD: Methadone
 Comparison: 04 Methadone vs Clonidine
 Outcome: 01 Completion of Treatment



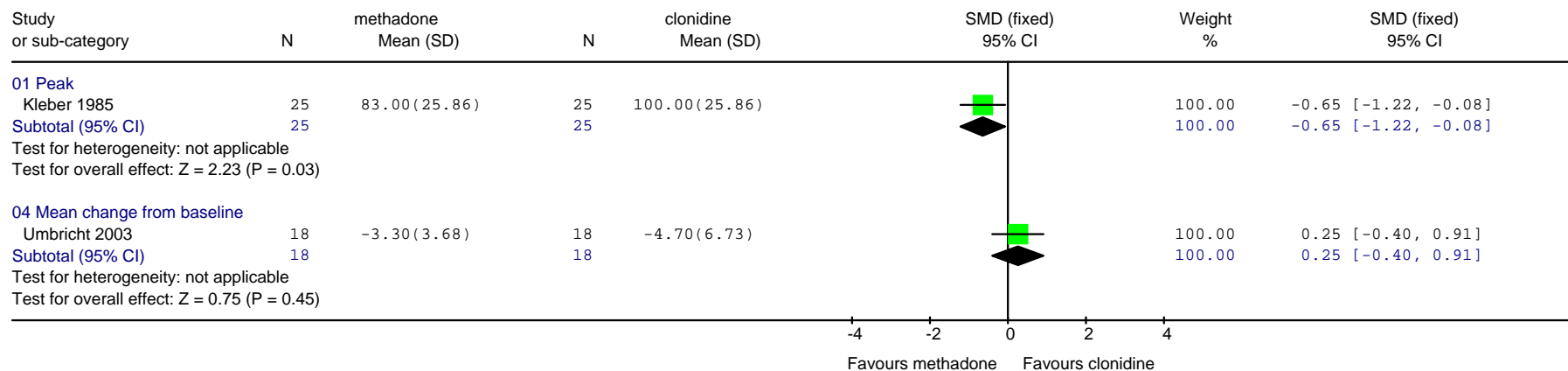
Review: DMD 1: Methadone
 Comparison: 04 Methadone versus clonidine
 Outcome: 02 Concordance with naltrexone maintenance (3-month follow-up)



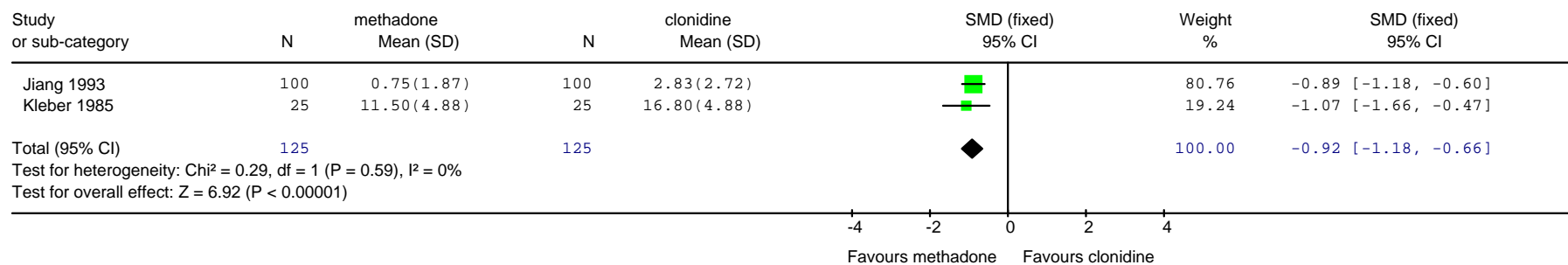
Review: DMD: Methadone
 Comparison: 04 Methadone vs Clonidine
 Outcome: 03 Abstinence



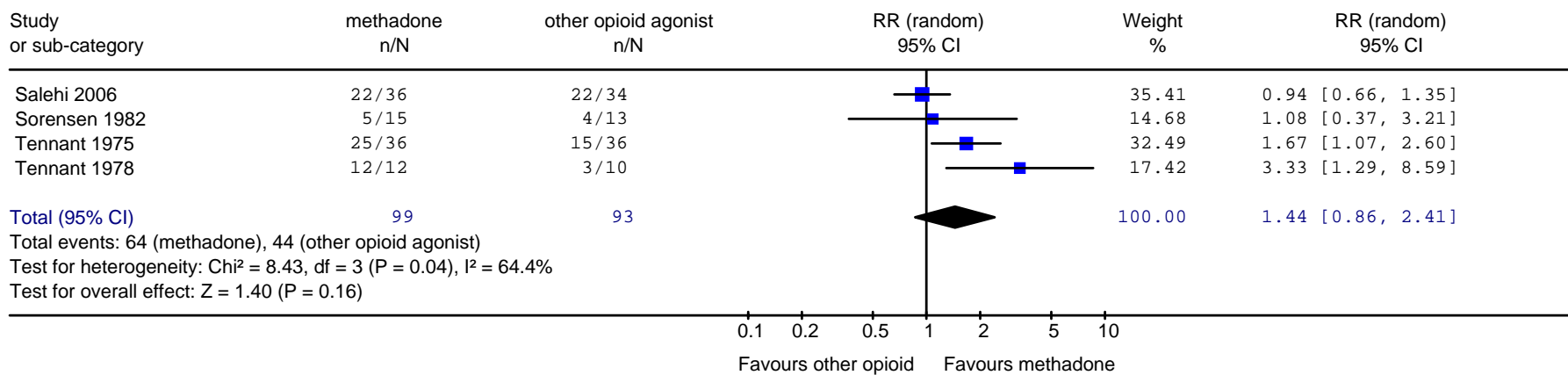
Review: DMD 1: Methadone
 Comparison: 04 Methadone versus clonidine
 Outcome: 05 Withdrawal: self-rated



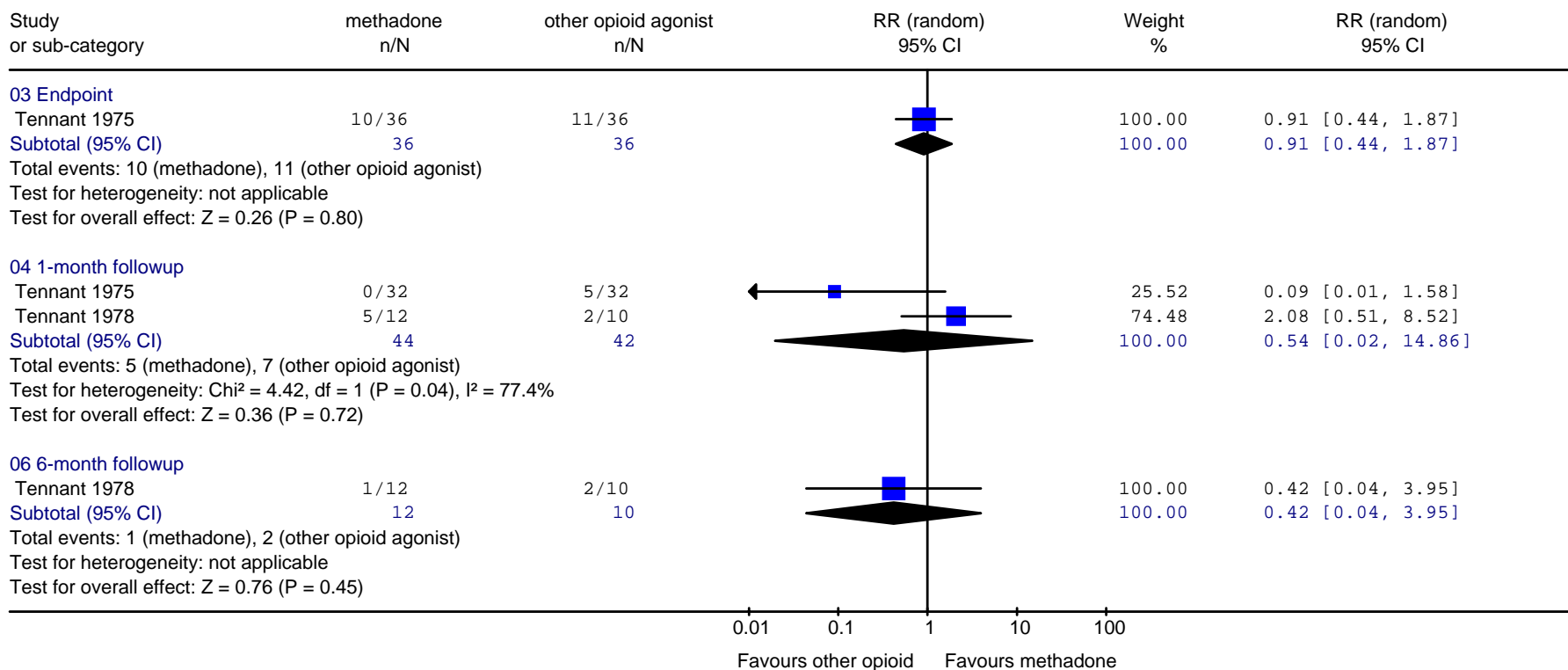
Review: DMD 1: Methadone
 Comparison: 04 Methadone versus clonidine
 Outcome: 06 Adverse events: side effects rating



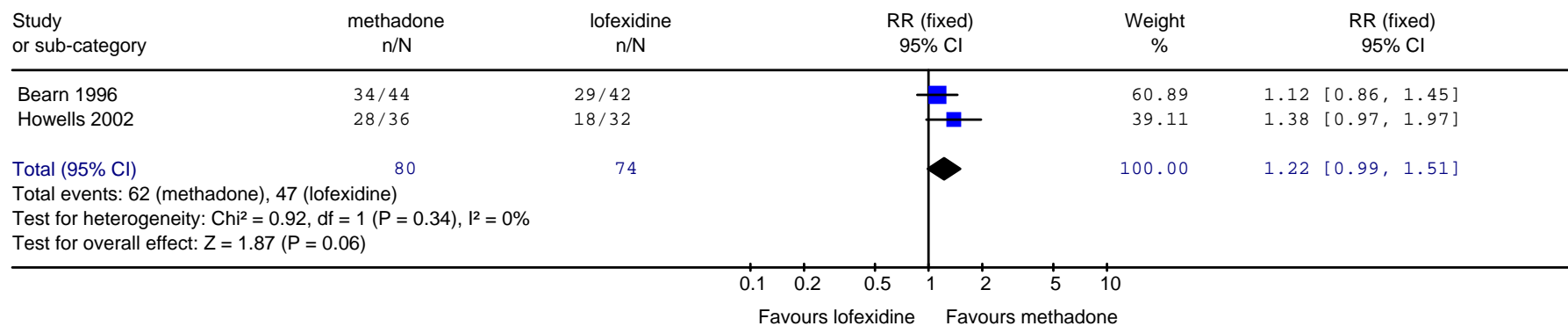
Review: DMD 1: Methadone
 Comparison: 07 Methadone versus other opioid agonist (not buprenorphine)
 Outcome: 01 Completion of treatment



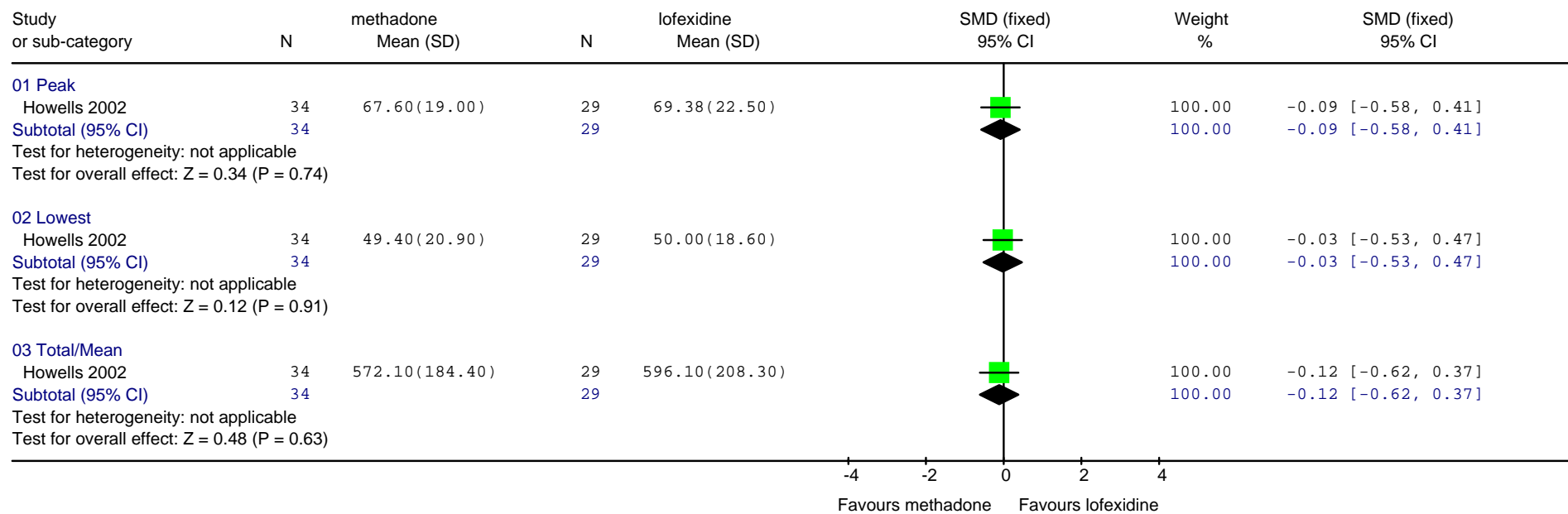
Review: DMD 1: Methadone
 Comparison: 07 Methadone versus other opioid agonist (not buprenorphine)
 Outcome: 05 Abstinence



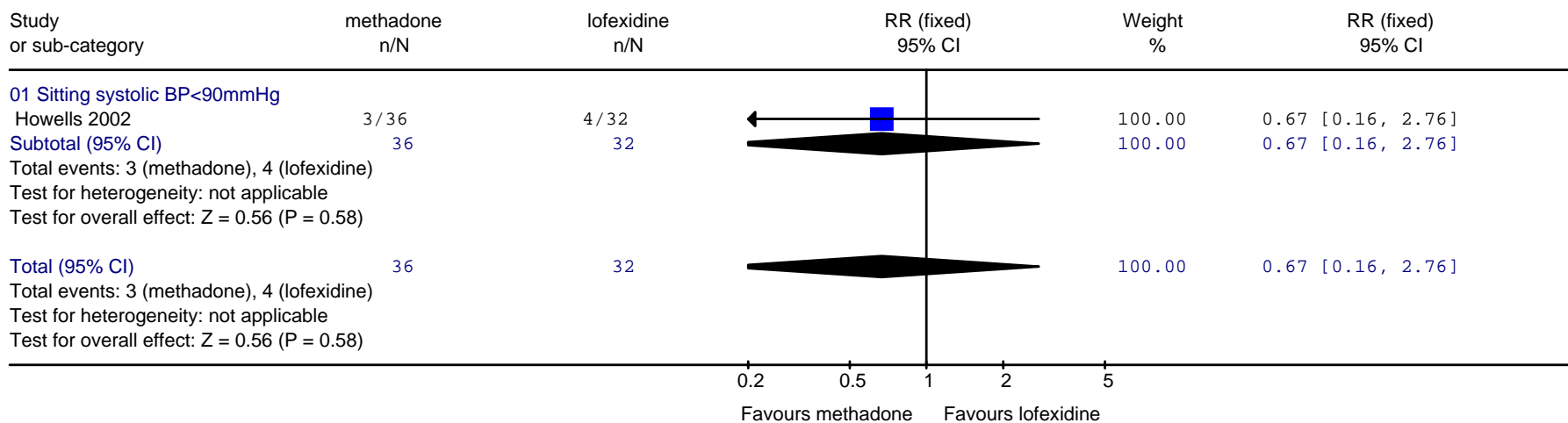
Review: DMD 1: Methadone
 Comparison: 08 Methadone versus lofexidine
 Outcome: 01 Completion of treatment



Review: DMD 1: Methadone
 Comparison: 08 Methadone versus lofexidine
 Outcome: 02 Withdrawal: self-rated (Short Opiate Withdrawal Scale)

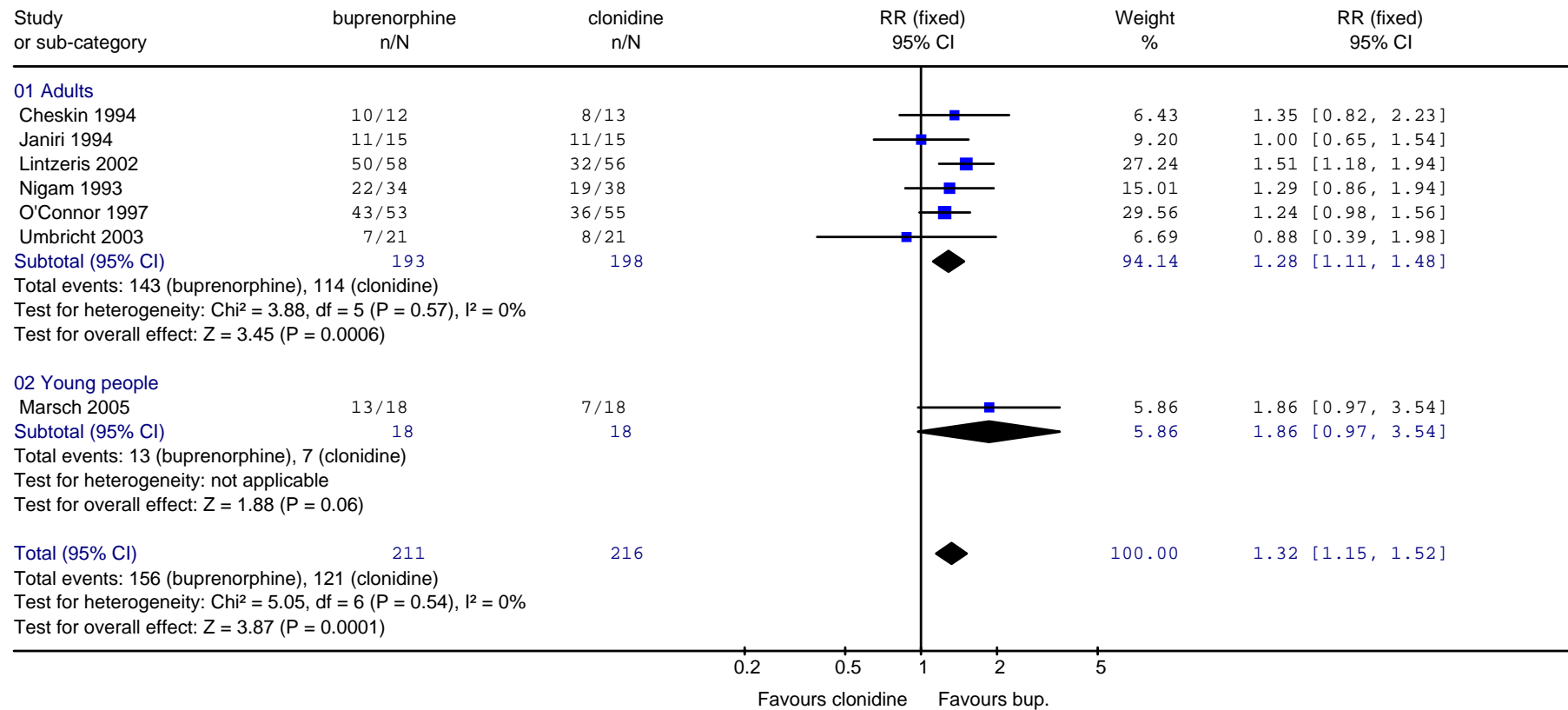


Review: DMD 1: Methadone
 Comparison: 08 Methadone versus lofexidine
 Outcome: 03 Hypotension

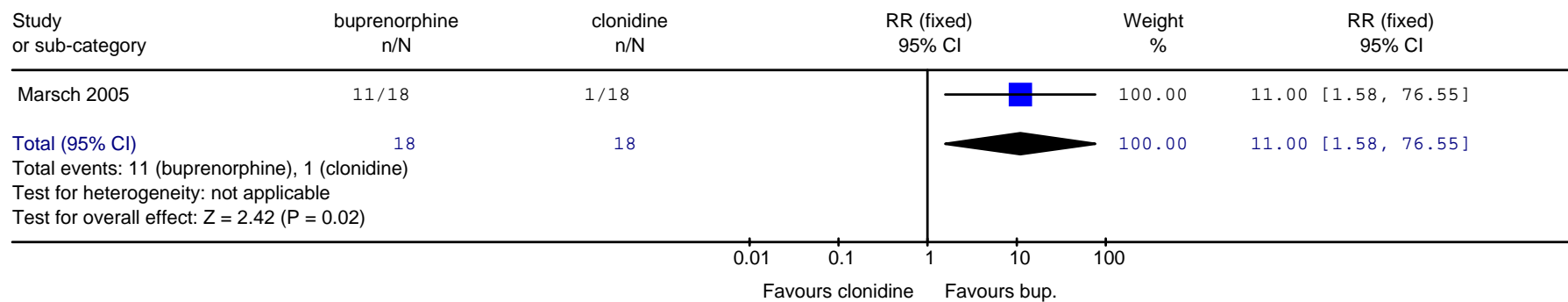


Buprenorphine

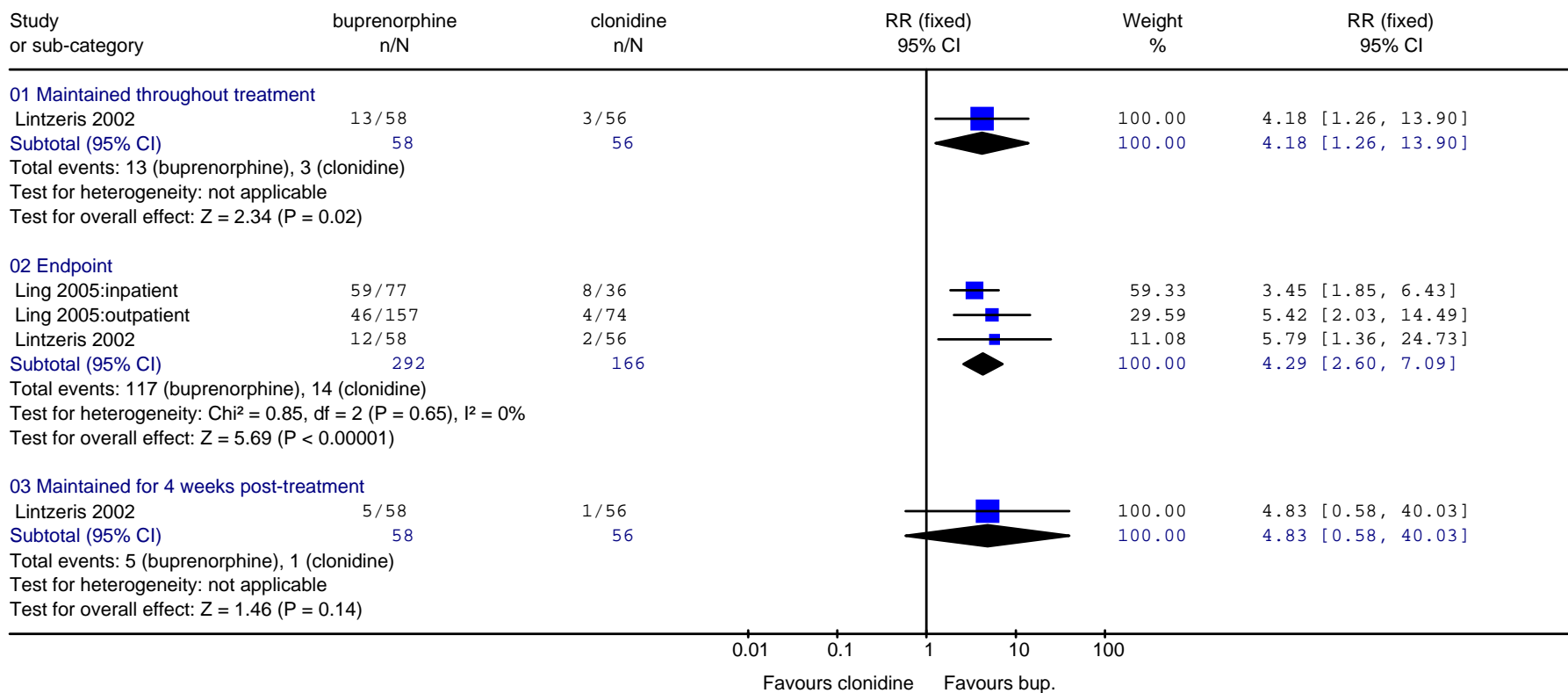
Review: DMD 2: Buprenorphine
 Comparison: 02 Buprenorphine versus clonidine
 Outcome: 01 Completion of treatment



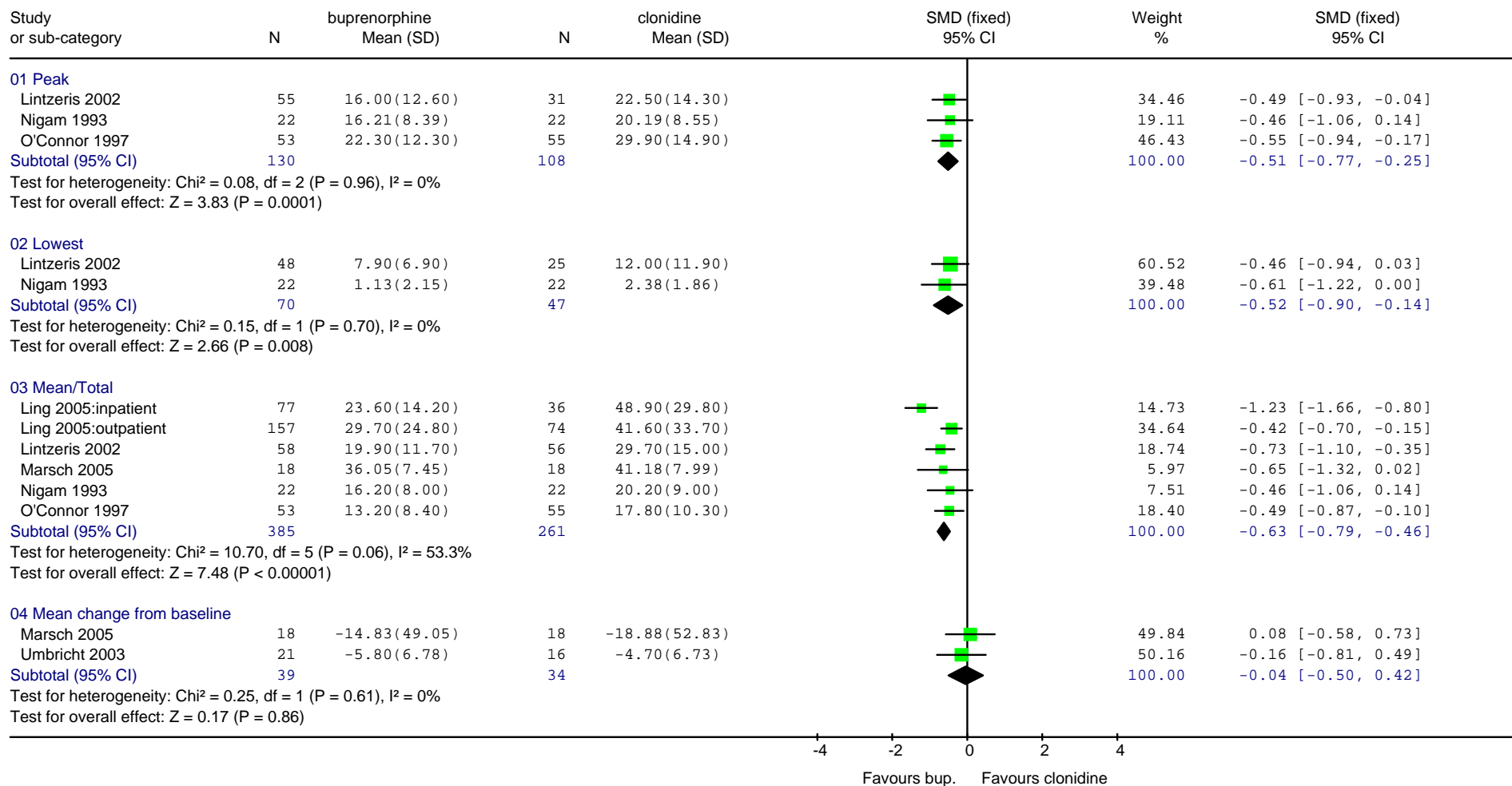
Review: DMD 2: Buprenorphine
 Comparison: 02 Buprenorphine versus clonidine
 Outcome: 02 Initiated naltrexone maintenance



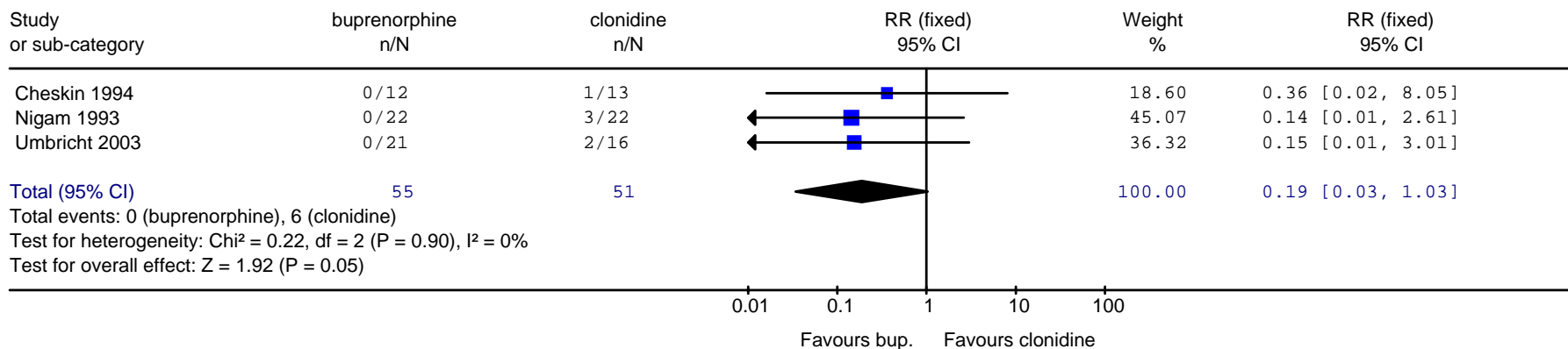
Review: DMD 2: Buprenorphine
 Comparison: 02 Buprenorphine versus clonidine
 Outcome: 04 Abstinence



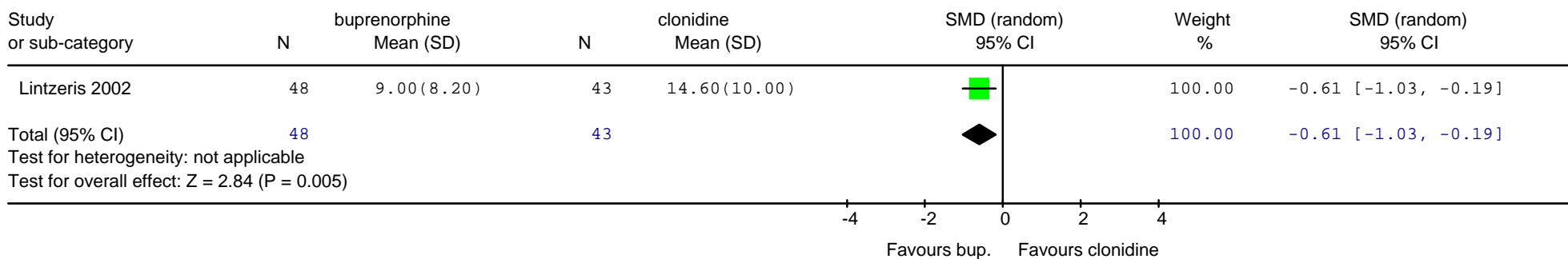
Review: DMD 2: Buprenorphine
 Comparison: 02 Buprenorphine versus clonidine
 Outcome: 06 Withdrawal: subjective



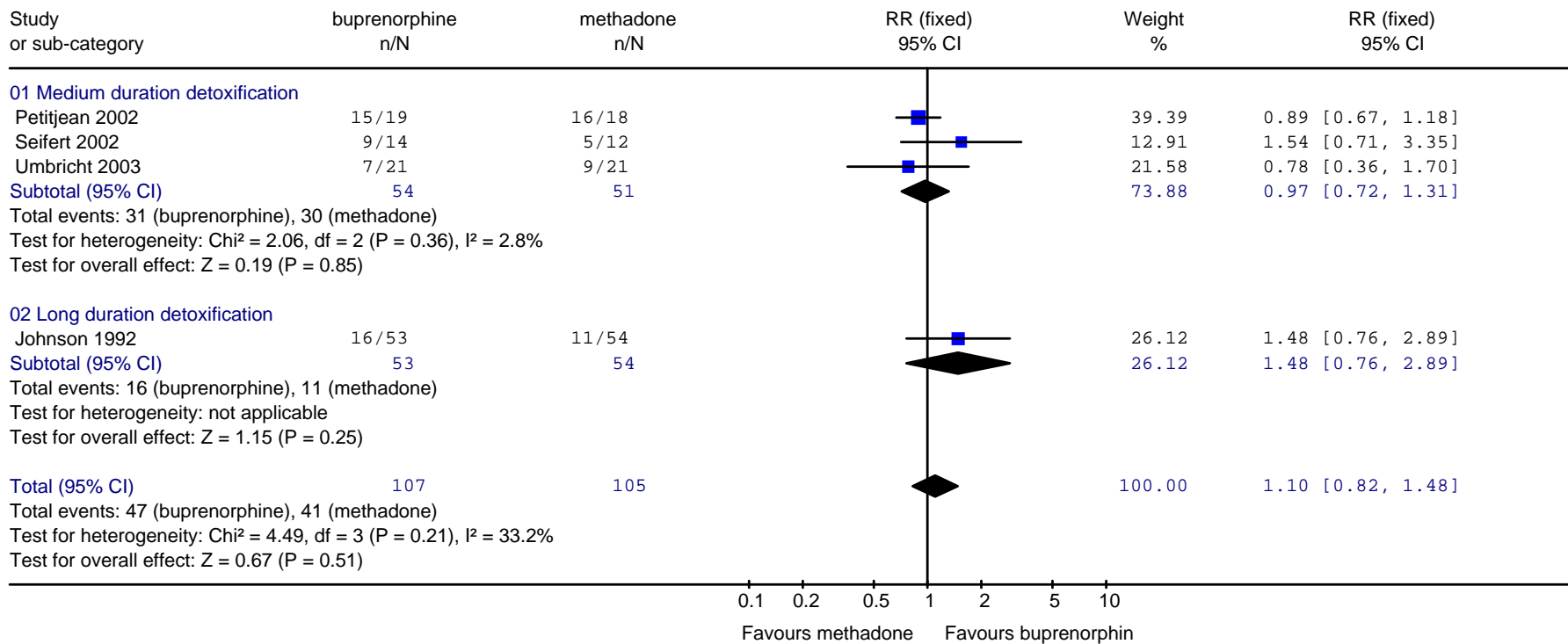
Review: DMD 2: Buprenorphine
 Comparison: 02 Buprenorphine versus clonidine
 Outcome: 08 Leaving study early due to adverse events



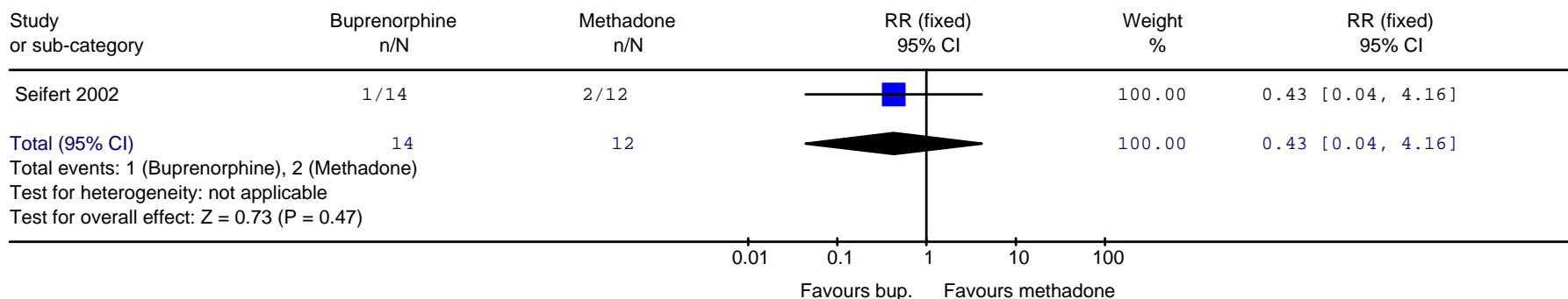
Review: DMD 2: Buprenorphine
 Comparison: 02 Buprenorphine versus clonidine
 Outcome: 09 Days of drug use (1-month follow up)



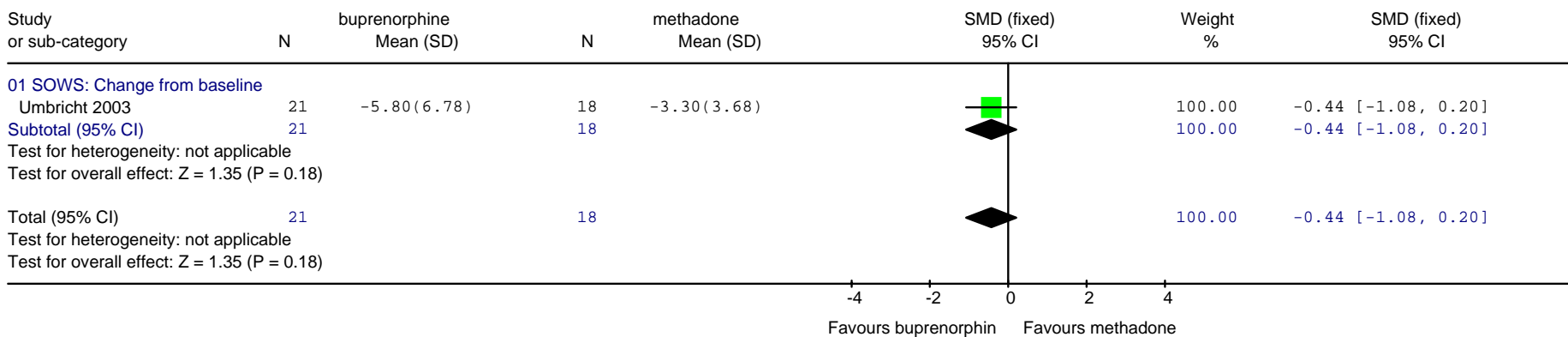
Review: DMD 2: Buprenorphine
 Comparison: 03 Buprenorphine versus methadone
 Outcome: 01 Completion of treatment



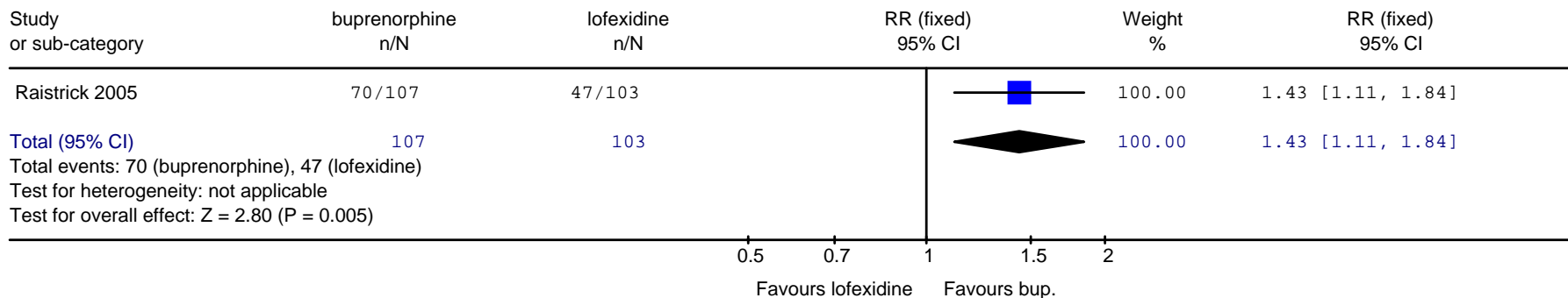
Review: DMD 2: Buprenorphine
 Comparison: 03 Buprenorphine versus methadone
 Outcome: 02 Relapse to opiate use (during treatment)



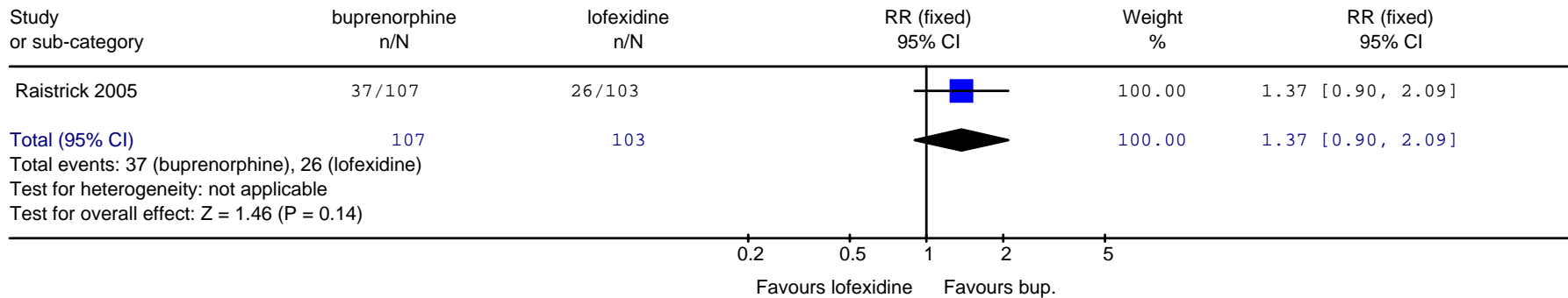
Review: DMD 2: Buprenorphine
 Comparison: 03 Buprenorphine versus methadone
 Outcome: 04 Withdrawal: self-rated



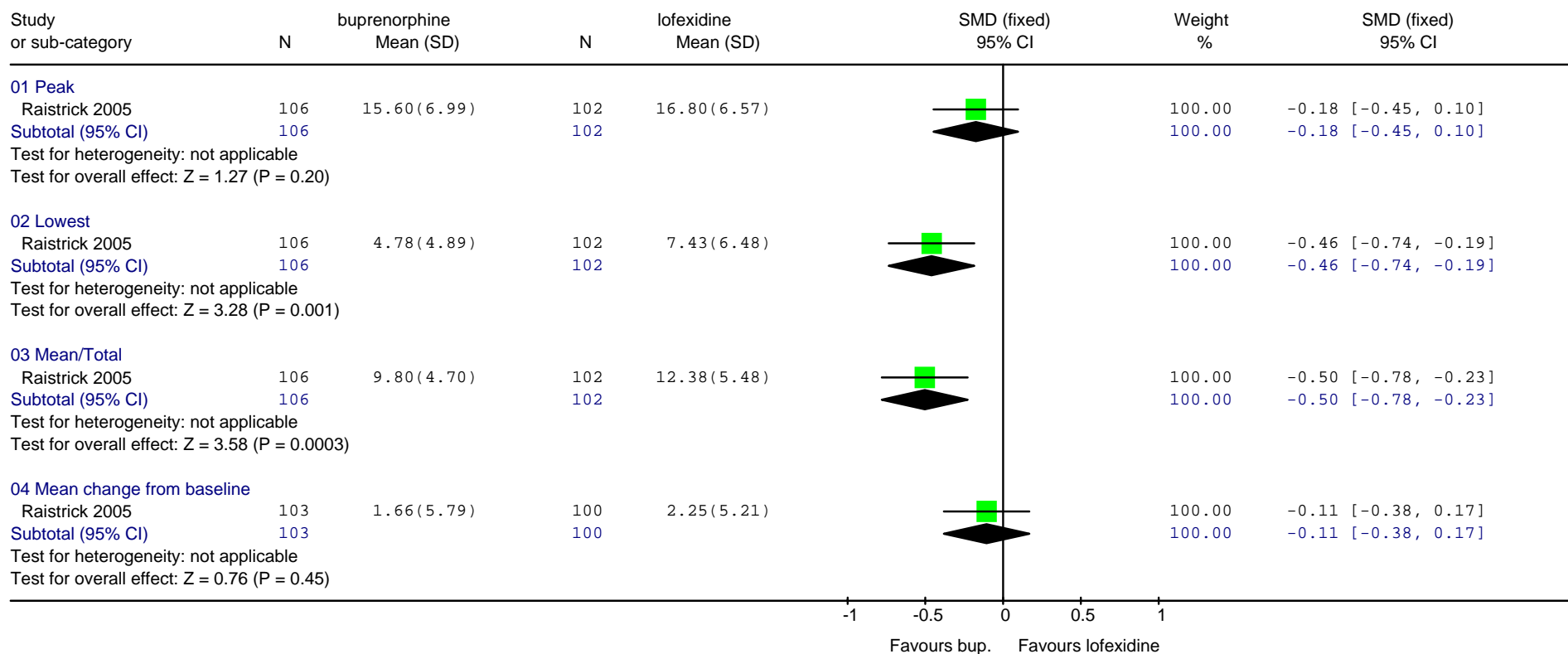
Review: DMD 2: Buprenorphine
 Comparison: 04 Buprenorphine versus lofexidine
 Outcome: 01 Completion of treatment



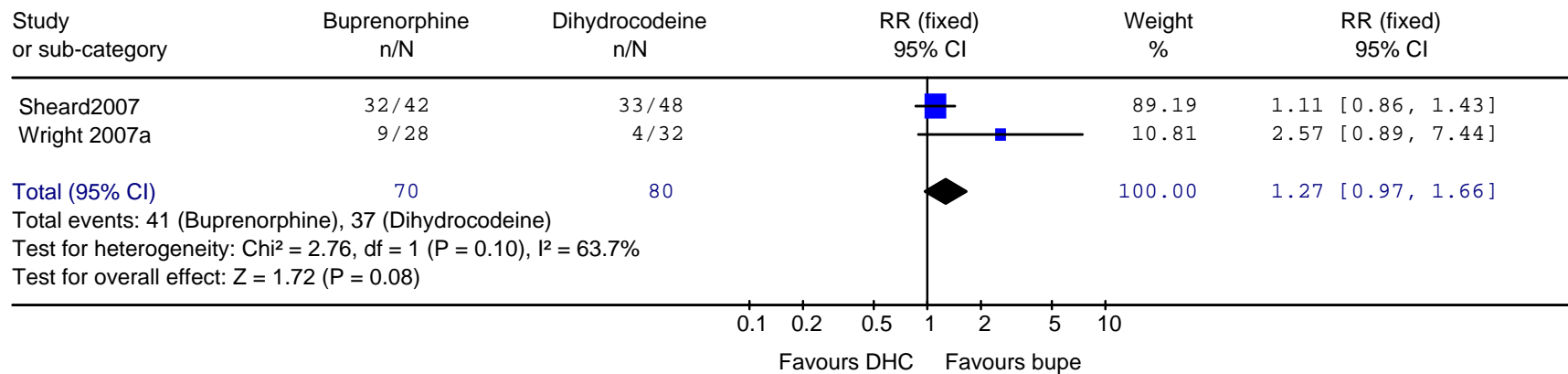
Review: DMD 2: Buprenorphine
 Comparison: 04 Buprenorphine versus lofexidine
 Outcome: 02 Abstinence (1-month follow-up)



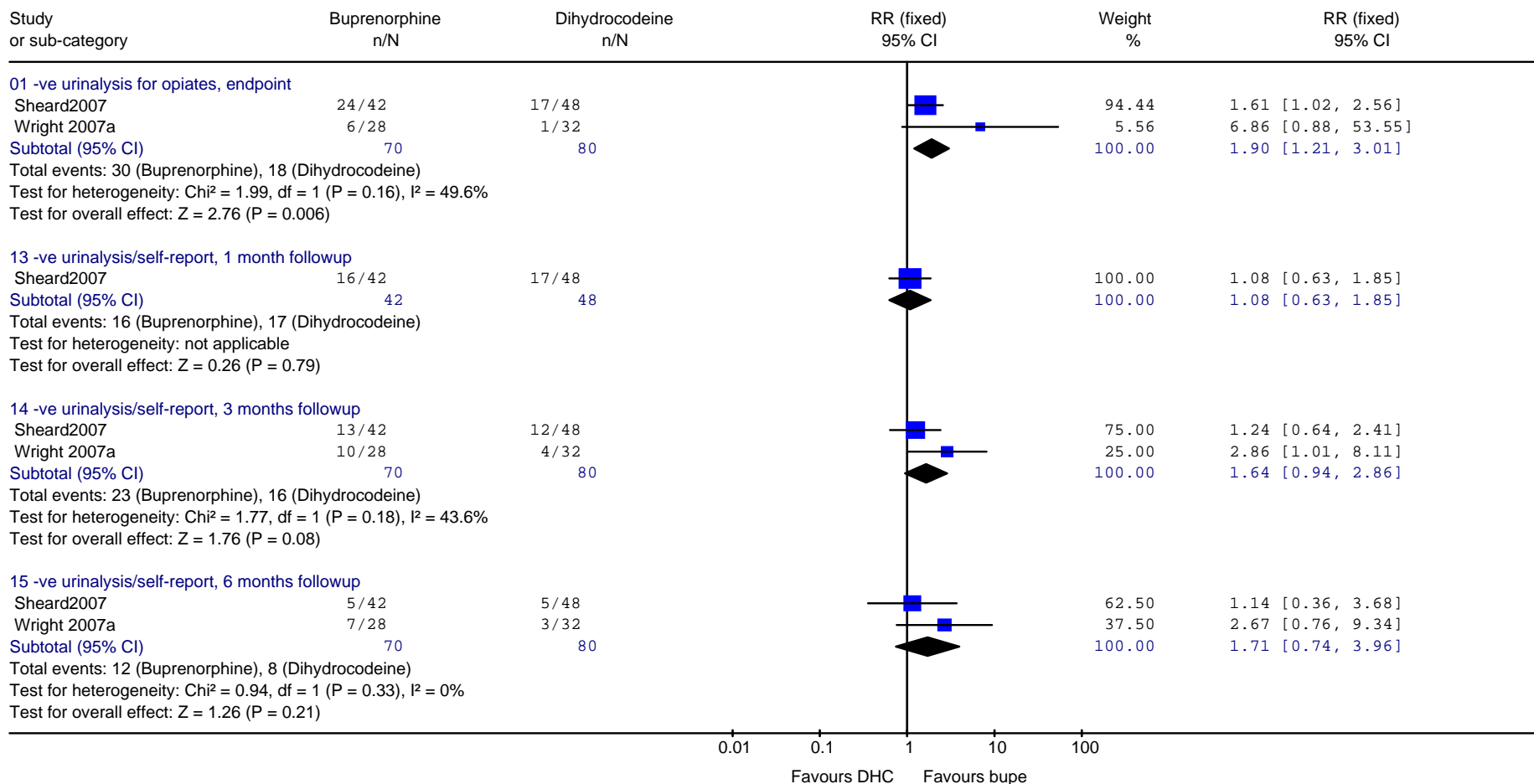
Review: DMD 2: Buprenorphine
 Comparison: 04 Buprenorphine versus lofexidine
 Outcome: 03 Withdrawal: self-rated



Review: DMD: Buprenorphine
 Comparison: 05 Buprenorphine vs Dihydrocodeine
 Outcome: 01 Completion of treatment

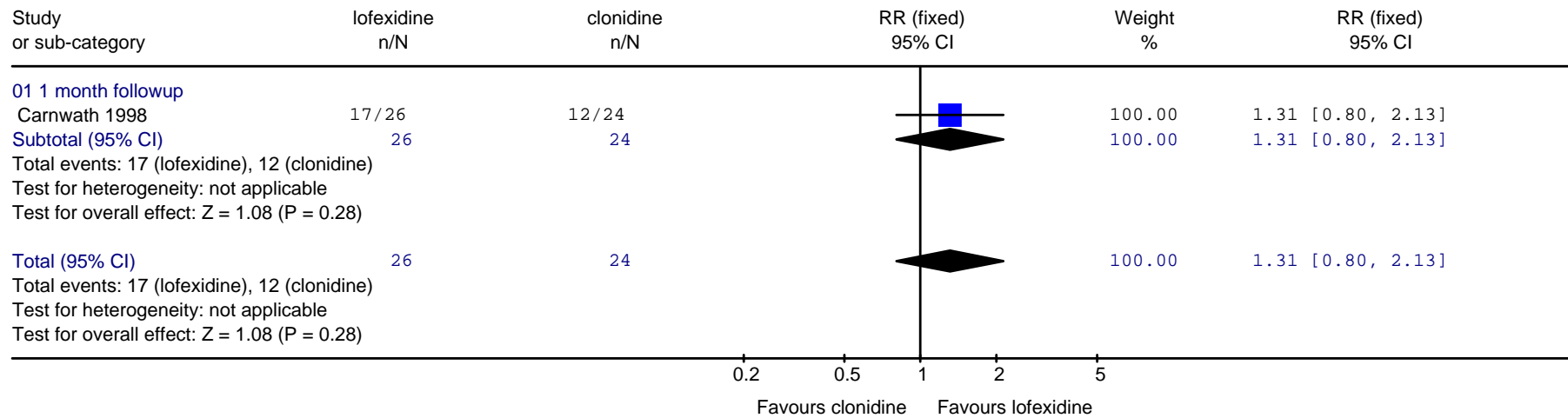


Review: DMD: Buprenorphine
 Comparison: 05 Buprenorphine vs Dihydrocodeine
 Outcome: 02 Abstinence (ITT)

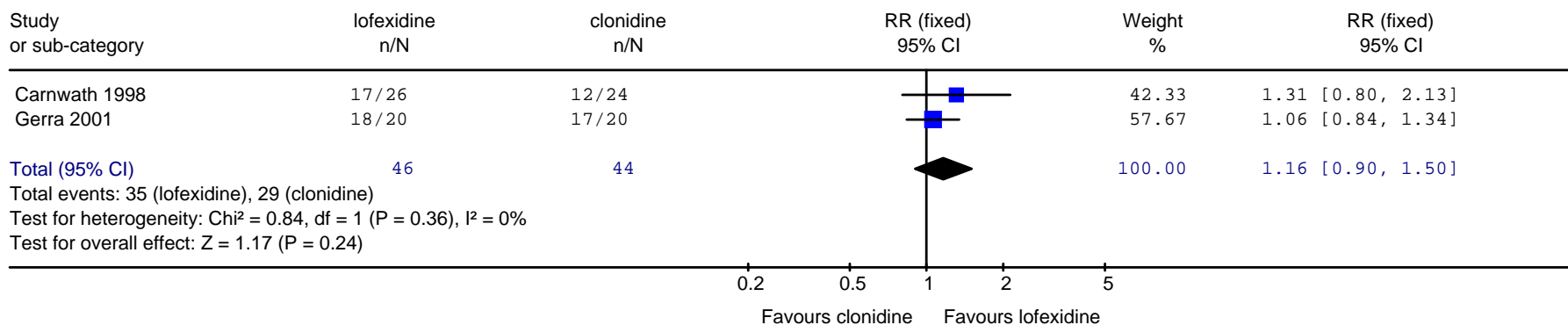


Alpha2 adrenergic agonists

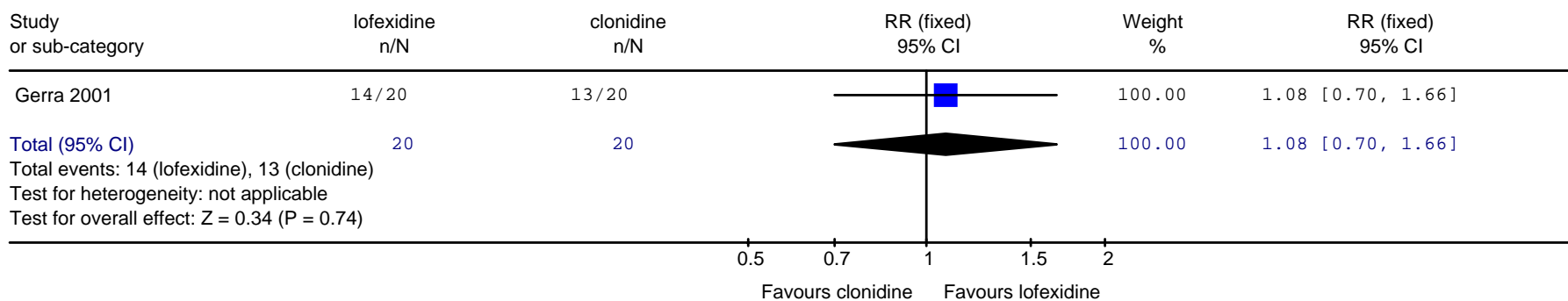
Review: DMD 3: Alpha2 adrenergic agonists
 Comparison: 03 Lofexidine versus clonidine
 Outcome: 01 Abstinence



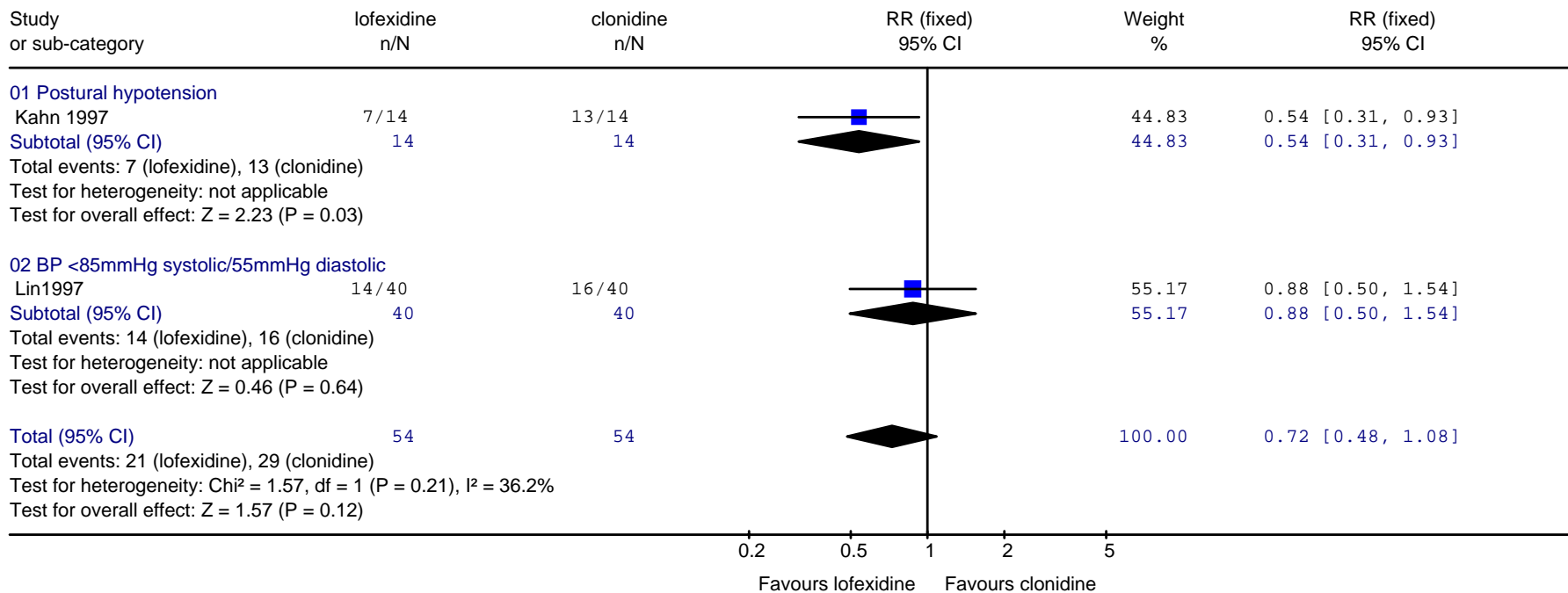
Review: DMD 3: Alpha2 adrenergic agonists
 Comparison: 03 Lofexidine versus clonidine
 Outcome: 02 Completion of treatment



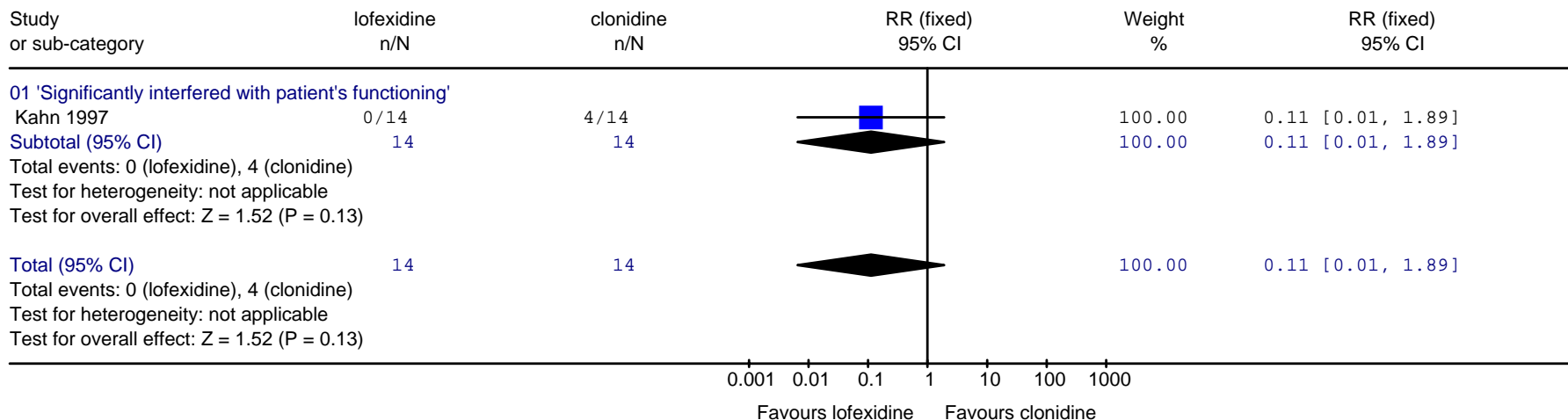
Review: DMD 3: Alpha2 adrenergic agonists
 Comparison: 03 Lofexidine versus clonidine
 Outcome: 03 Induction onto naltrexone maintenance



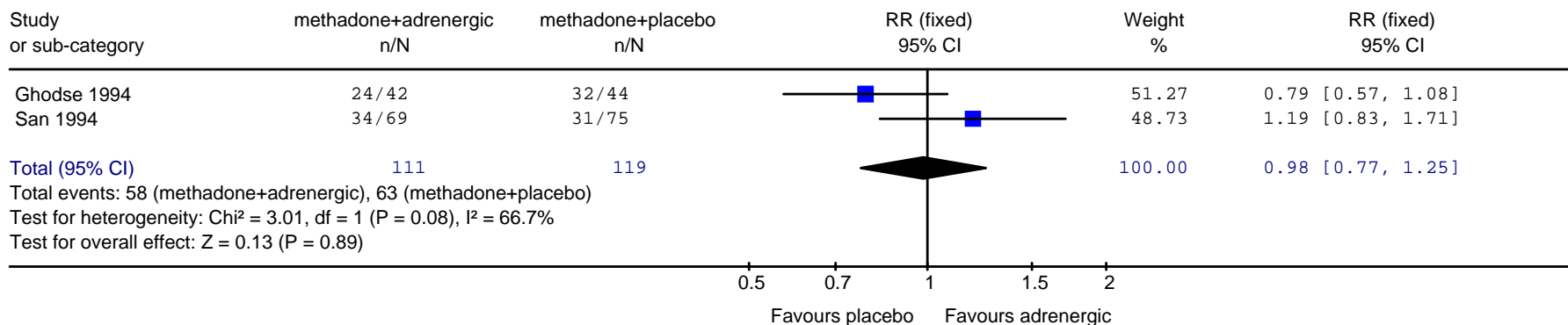
Review: DMD 3: Alpha2 adrenergic agonists
 Comparison: 03 Lofexidine versus clonidine
 Outcome: 04 Adverse events: hypotension



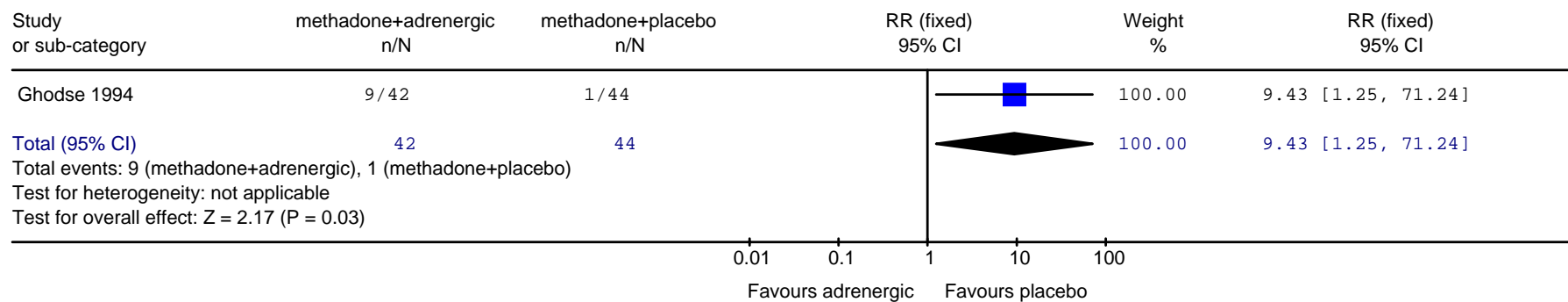
Review: DMD 3: Alpha2 adrenergic agonists
 Comparison: 03 Lofexidine versus clonidine
 Outcome: 05 Adverse events: serious



Review: DMD 3: Alpha2 adrenergic agonists
 Comparison: 07 Methadone + alpha2 adrenergic agonist versus methadone + placebo
 Outcome: 01 Completion of treatment

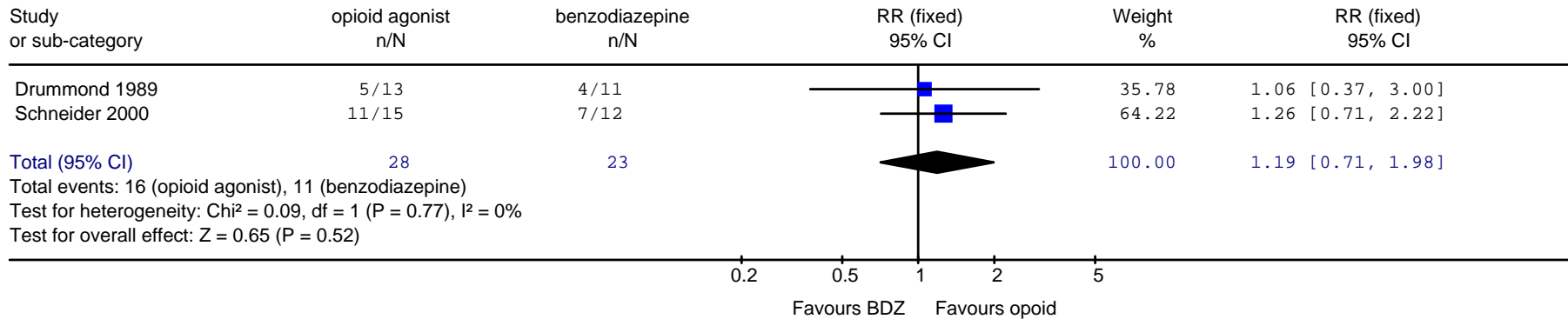


Review: DMD 3: Alpha2 adrenergic agonists
 Comparison: 07 Methadone + alpha2 adrenergic agonist versus methadone + placebo
 Outcome: 02 Left study early due to hypotension



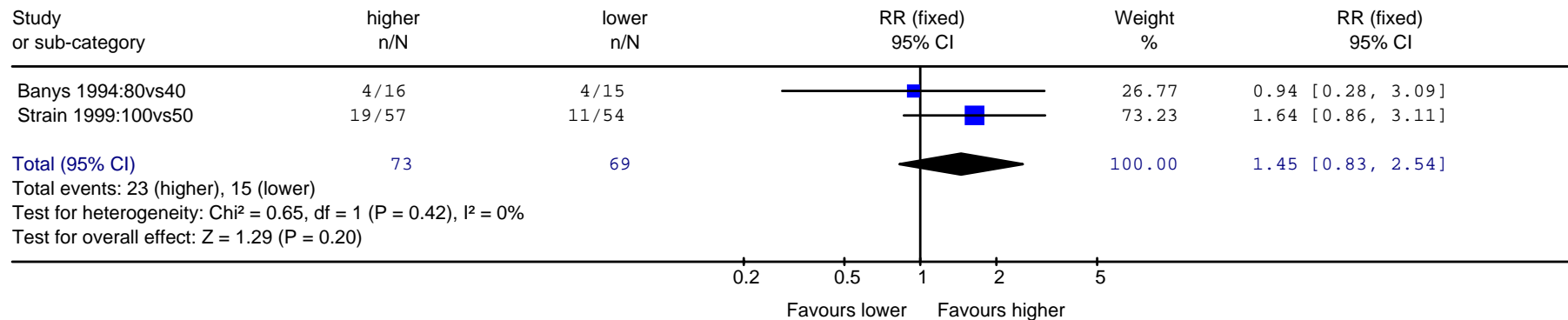
Benzodiazepines

Review: DMD 4: Benzodiazepines
 Comparison: 01 Methadone/buprenorphine vs Benzodiaepines
 Outcome: 01 Completion of treatment

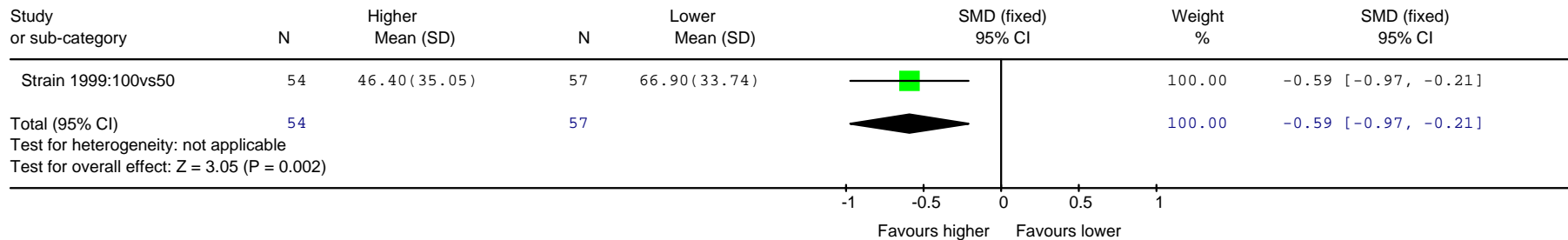


Detoxification dosage schedules

Review: DMD 5: Detoxification dosage schedules
 Comparison: 02 Higher versus lower methadone starting dose
 Outcome: 01 Completion of treatment

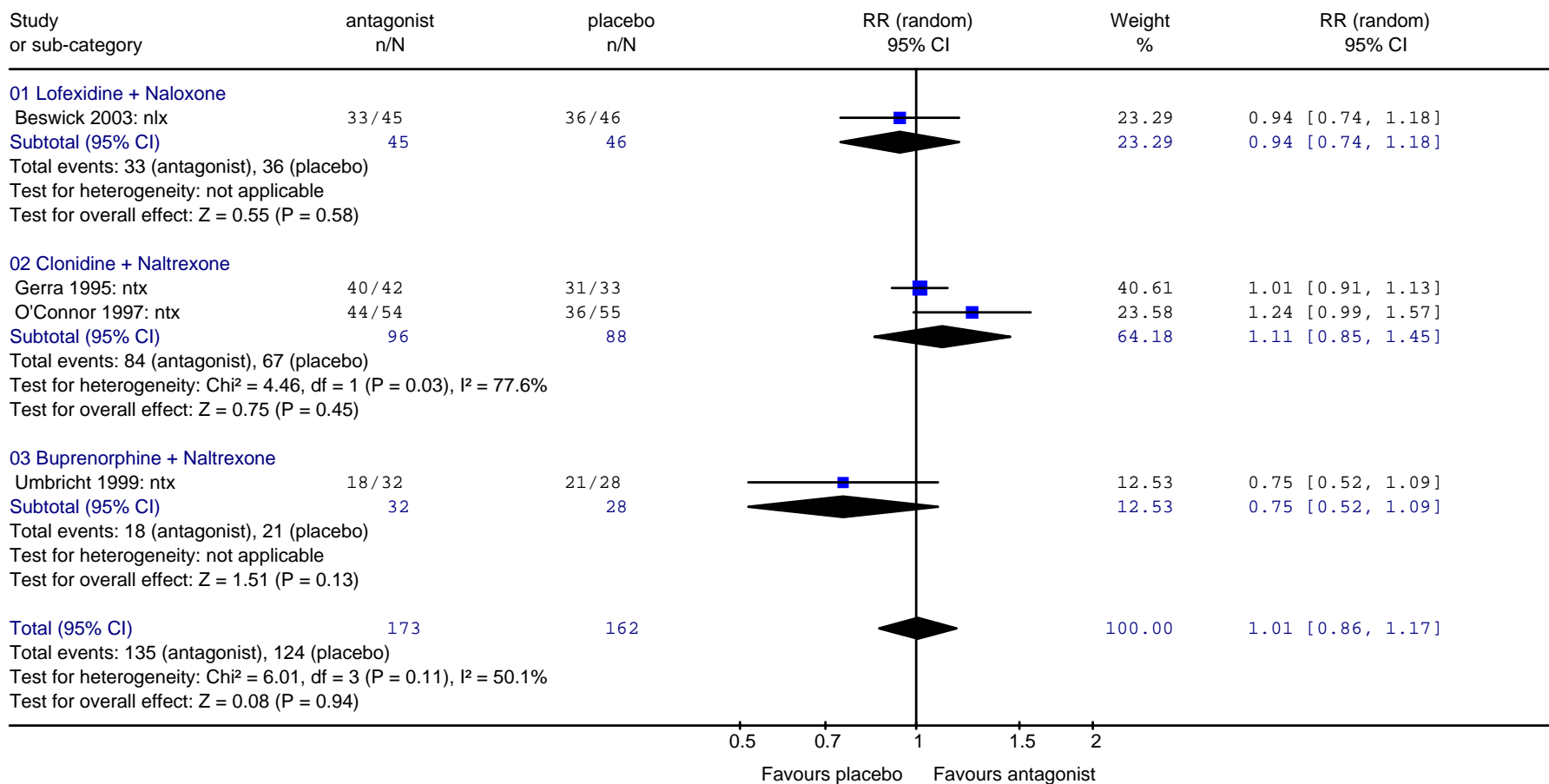


Review: DMD 5: Detoxification dosage schedules
 Comparison: 02 Higher versus lower methadone starting dose
 Outcome: 03 Proportion opiate-positive urines (completers analysis)

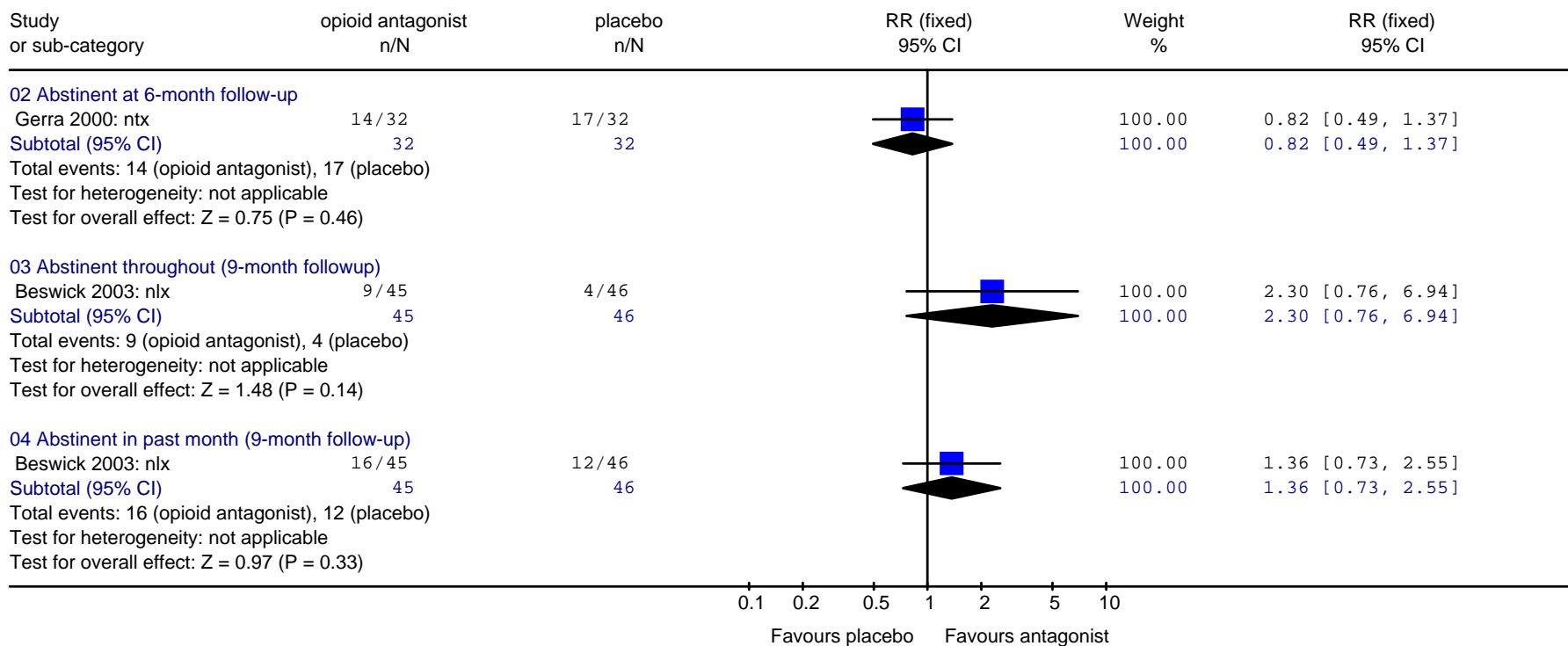


Opioid antagonist accelerated detoxification under minimal sedation

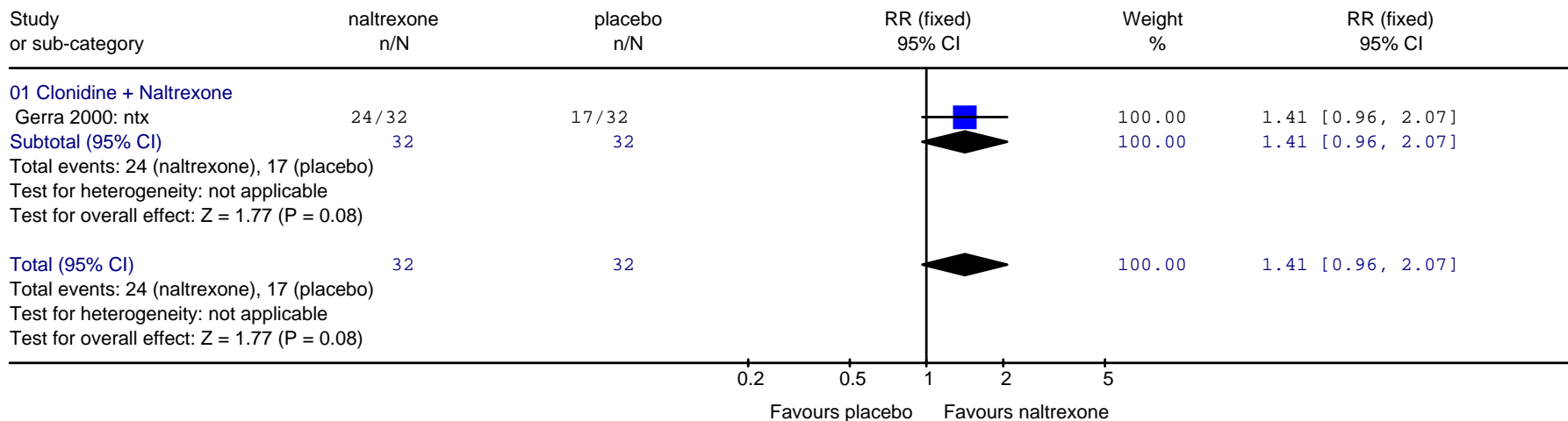
Review: DMD 6: Opioid antagonist accelerated detoxification under minimal sedation
 Comparison: 06 Any pharmacological + opioid antagonist versus no opioid antagonist
 Outcome: 01 Completion of treatment



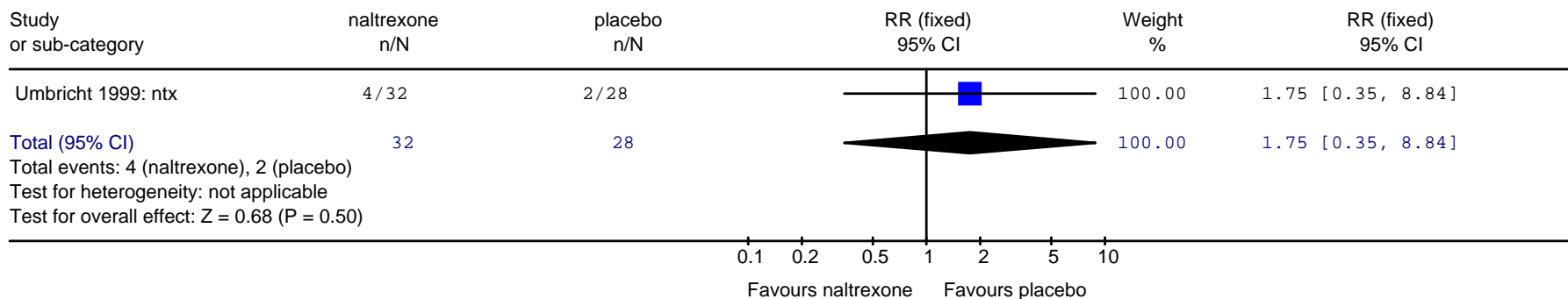
Review: DMD 6: Opioid antagonist accelerated detoxification under minimal sedation
 Comparison: 06 Any pharmacological + opioid antagonist versus no opioid antagonist
 Outcome: 02 Abstinence



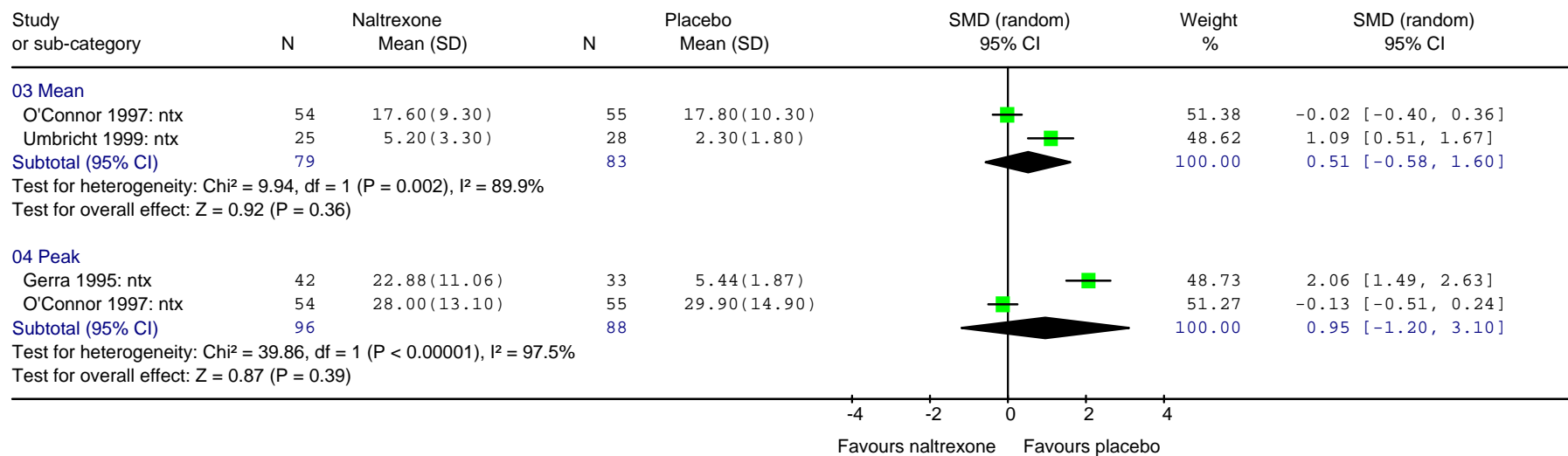
Review: DMD 6: Opioid antagonist accelerated detoxification under minimal sedation
 Comparison: 06 Any pharmacological + opioid antagonist versus no opioid antagonist
 Outcome: 07 Concordance with naltrexone maintenance (3-month follow-up)



Review: DMD 6: Opioid antagonist accelerated detoxification under minimal sedation
 Comparison: 06 Any pharmacological + opioid antagonist versus no opioid antagonist
 Outcome: 09 Left study early due to withdrawal

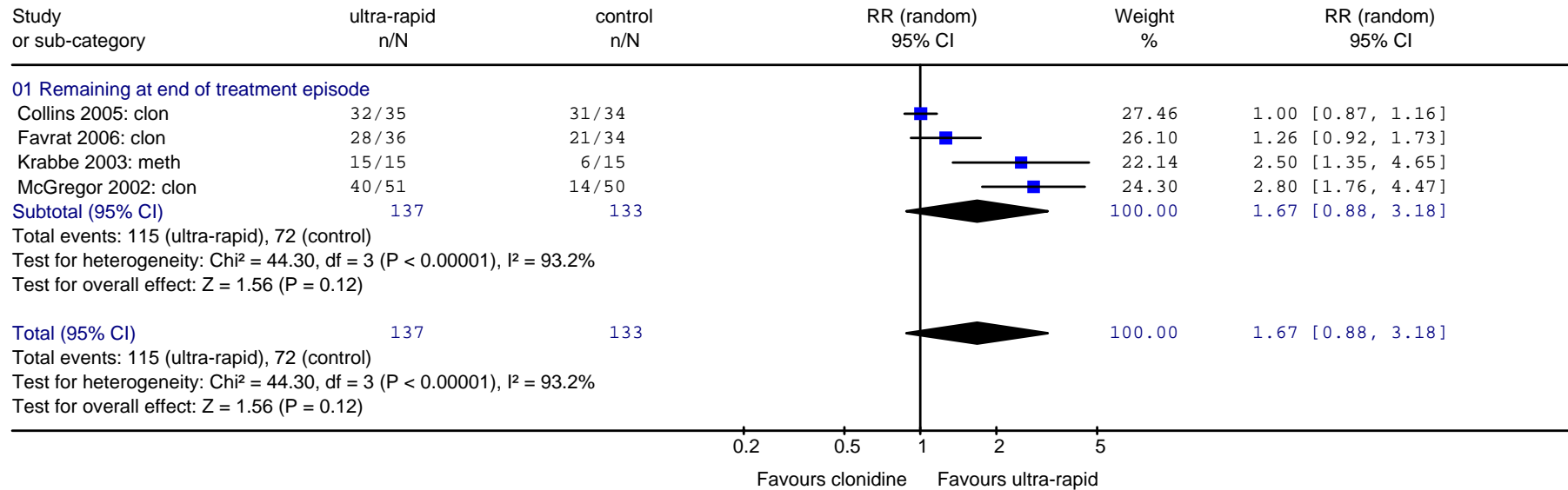


Review: DMD 6: Opioid antagonist accelerated detoxification under minimal sedation
 Comparison: 06 Any pharmacological + opioid antagonist versus no opioid antagonist
 Outcome: 10 Withdrawal

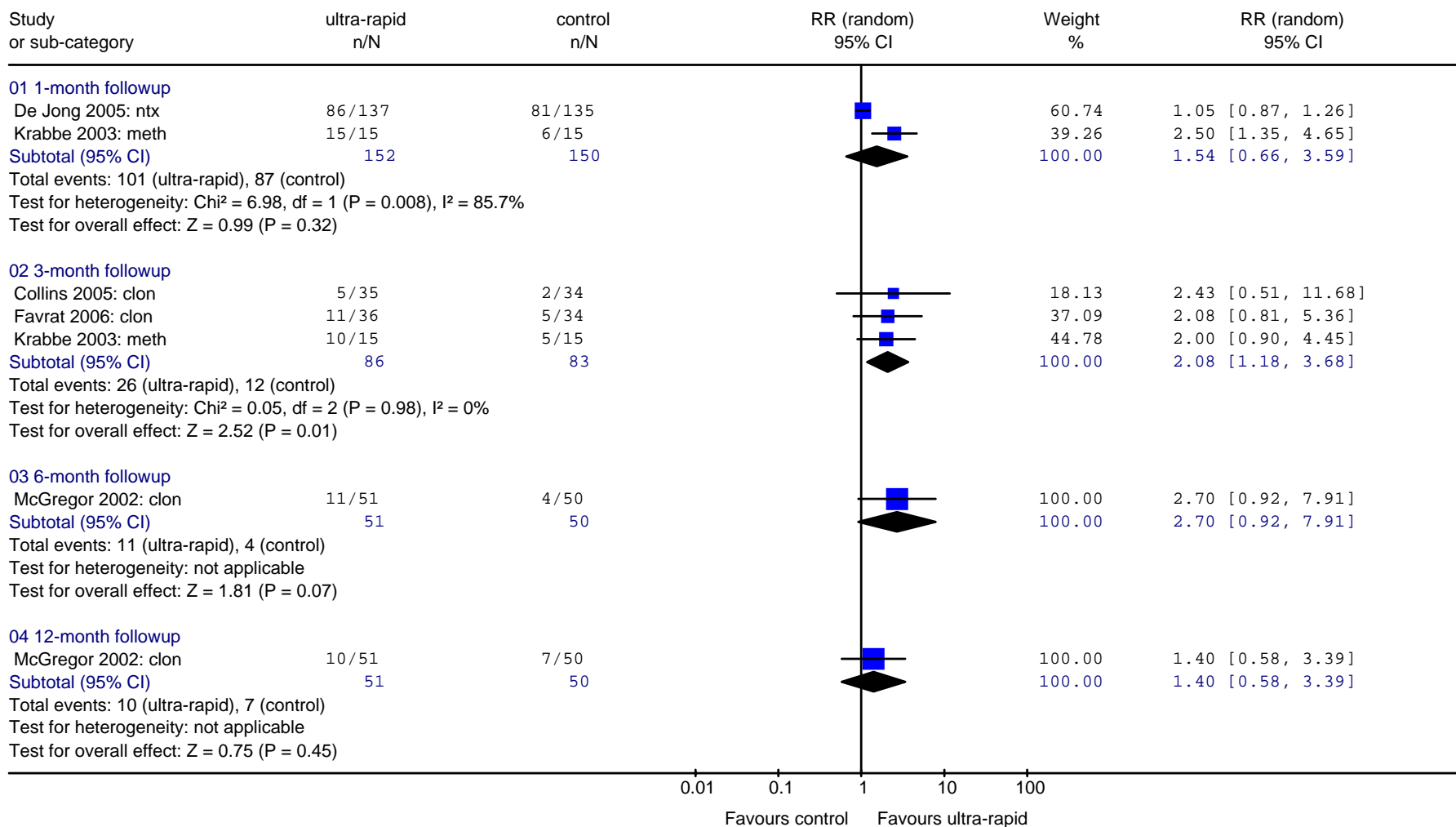


Rapid and ultra-rapid detoxification under anaesthesia or heavy sedation

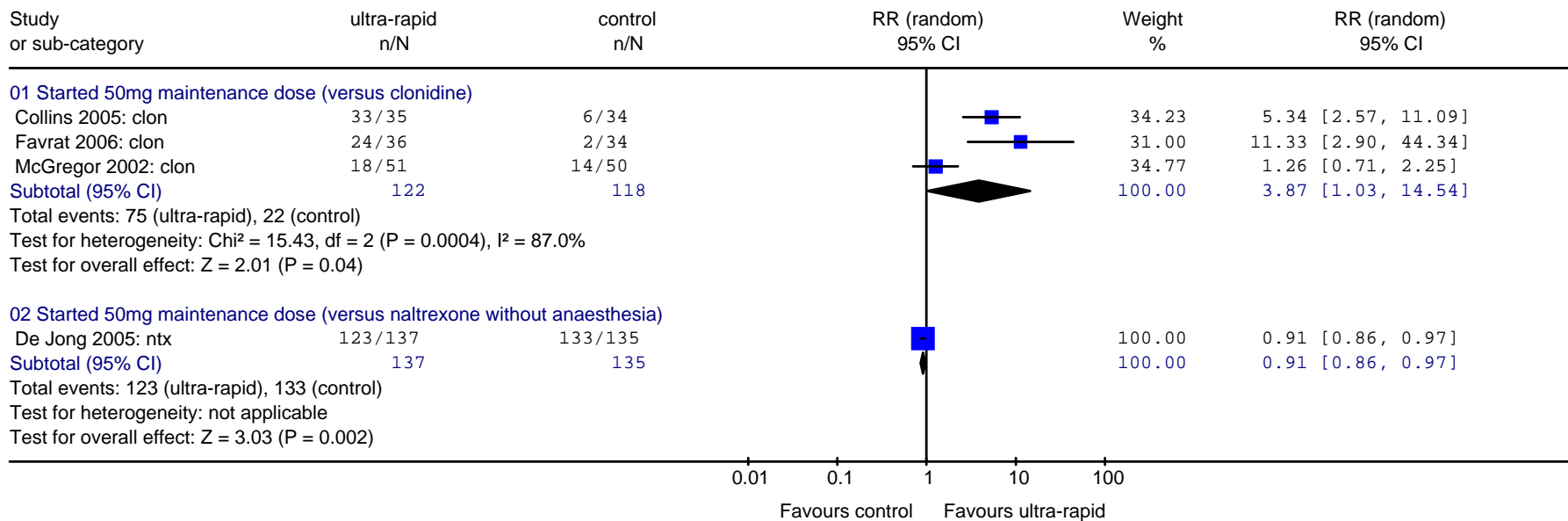
Review: DMD 7: Rapid and ultra-rapid detoxification under anaesthesia or heavy sedation
 Comparison: 01 Ultra-rapid detoxification under general anaesthesia versus any pharmacological with minimal sedation
 Outcome: 01 Completion of treatment



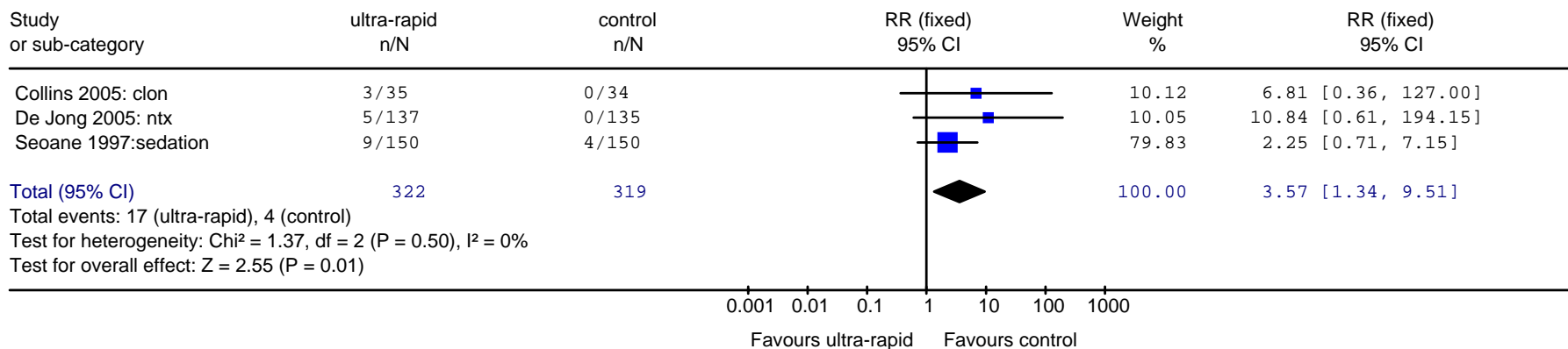
Review: DMD 7: Rapid and ultra-rapid detoxification under anaesthesia or heavy sedation
 Comparison: 01 Ultra-rapid detoxification under general anaesthesia versus any pharmacological with minimal sedation
 Outcome: 04 Abstinence: opiate-negative urinalysis, hair analysis or self-report



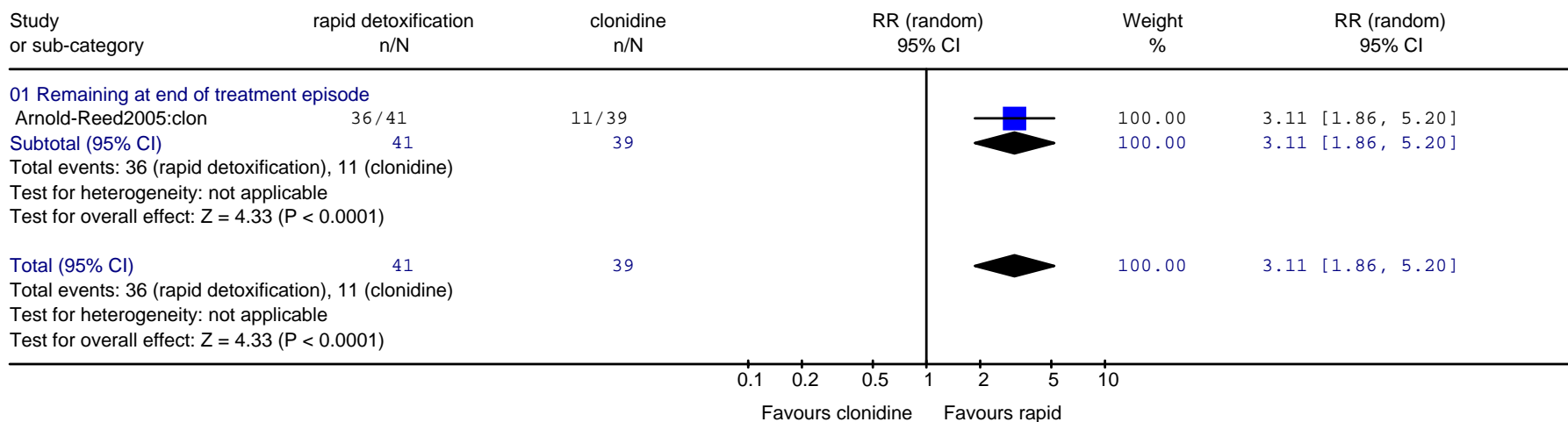
Review: DMD 7: Rapid and ultra-rapid detoxification under anaesthesia or heavy sedation
 Comparison: 01 Ultra-rapid detoxification under general anaesthesia versus any pharmacological with minimal sedation
 Outcome: 05 Concordance with naltrexone



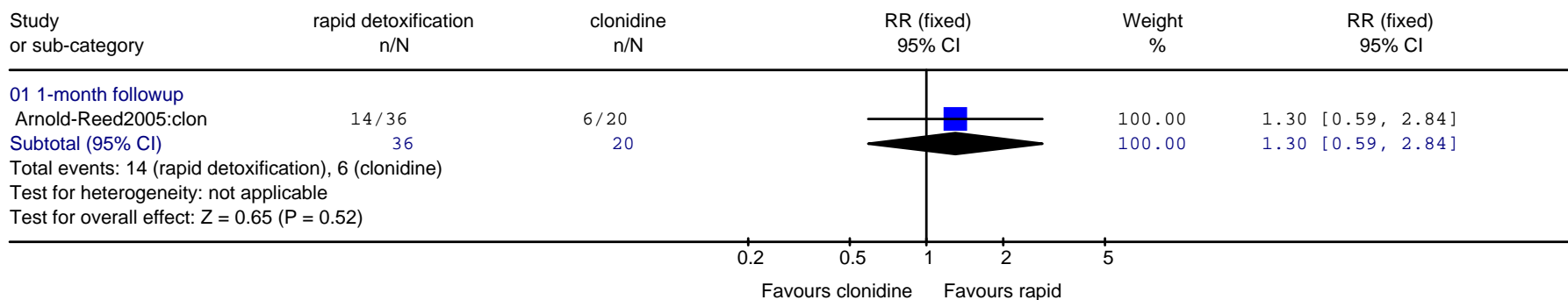
Review: DMD 7: Rapid and ultra-rapid detoxification under anaesthesia or heavy sedation
 Comparison: 01 Ultra-rapid detoxification under general anaesthesia versus any pharmacological with minimal sedation
 Outcome: 09 Adverse events: serious



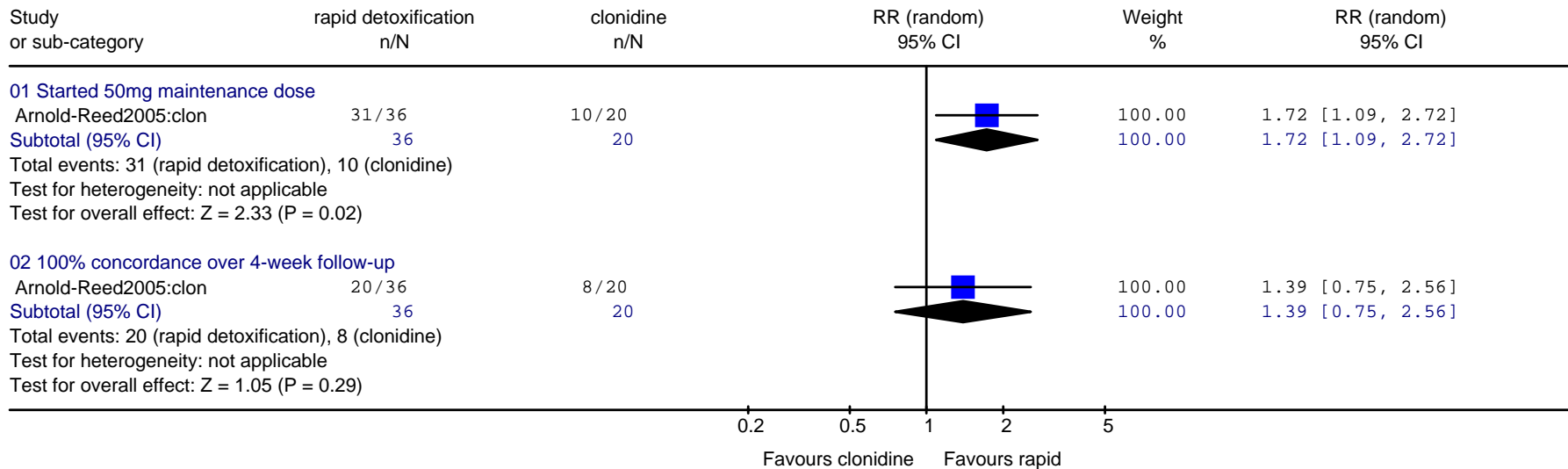
Review: DMD 7: Rapid and ultra-rapid detoxification under anaesthesia or heavy sedation
 Comparison: 02 Rapid detoxification under moderate sedation versus clonidine with minimal sedation
 Outcome: 01 Completion of treatment



Review: DMD 7: Rapid and ultra-rapid detoxification under anaesthesia or heavy sedation
 Comparison: 02 Rapid detoxification under moderate sedation versus clonidine with minimal sedation
 Outcome: 04 Abstinence: opiate-negative urinalysis, hair analysis or self-report



Review: DMD 7: Rapid and ultra-rapid detoxification under anaesthesia or heavy sedation
 Comparison: 02 Rapid detoxification under moderate sedation versus clonidine with minimal sedation
 Outcome: 05 Concordance with naltrexone



Review: DMD 7: Rapid and ultra-rapid detoxification under anaesthesia or heavy sedation
 Comparison: 02 Rapid detoxification under moderate sedation versus clonidine with minimal sedation
 Outcome: 10 Withdrawal

