Table 63: Twycross 1977[439]

Study	Twycross 1977[439]
Study type	RCT (Patient randomised; Crossover: 1 day).
Number of studies (number of participants)	1 (n=699)

Countries and setting	Conducted in United Kingdom; Setting: Hospice.
Line of therapy	Not applicable.
Duration of study	Intervention time: 5 days.
Method of assessment of guideline condition	Method of assessment /diagnosis not stated.
Stratum	Pain management.
Subgroup analysis within study	Post-hoc subgroup analysis: Male/female.
Inclusion criteria	People with terminal cancer prescribed diamorphine for pain relief.
Exclusion criteria	Not stated.
Recruitment/selection of patients	Not stated.
Age, gender and ethnicity	Age - Median (range): 67 years. Gender (M:F): 43/57%. Ethnicity: Not stated.
Further population details	
Extra comments	Very high rate of attrition.
Indirectness of population	Serious indirectness: Only states that median survival of people admitted to the unit is <2 weeks.
Interventions	(n=350) Intervention 1: Opioids - Diamorphine. Standard diamorphine hydrochloride elixir as prescribed; supplied in a series of doses from 2.5 to 60 mg and increased until pain free throughout 4-h between drug rounds. Elixir also contained cocaine hydrochloride 10 mg/dose. Duration 2 days. Concurrent medication/care: Prochlorperazine or chlorpromazine as antiemetic. Other drugs prescribed as required. Further details: 1. Delivery system : Delivery system: oral tablet or liquid 2. Drug class: Opioid 3. Route of administration: Route of administration: enteral. Comments: After 2 days participants were crossed over to the other intervention. (n=349) Intervention 2: Opioids - Morphine. Morphine sulphate supplied in a series of doses from 3.75 to 90 mg and increased until pain free throughout 4-h between drug rounds. Elixir also contained cocaine hydrochloride 10 mg/dose. Duration 2 days. Concurrent medication/care: Prochlorperazine or chlorpromazine as antiemetic. Other drugs prescribed as required. Further details: 1. Delivery system: Delivery system: oral tablet or liquid 2. Drug class: Opioid 3. Route of administration: Route of administration: enteral. Comments: After 2 days participants were crossed over to the other intervention.

Funding	Academic or government funding.
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DIAMORPHINE FIRST versus MORPHINE FIRST Protocol outcome 1: Pain control at Any - Actual outcome for Pain management: Difference on pain VAS (0-100) before and after crossover (pre- minus post- crossover scores) at 5 days; Risk of bias: Very high; Indirectness of outcome: No indirectness. Protocol outcome 2: Adverse events/withdrawal of the medication due to adverse events at Any - Actual outcome for Pain management: Difference on nausea VAS (0-100) before and after crossover (pre- minus post- crossover scores) at 5 days; Risk of bias: Very high; Indirectness of outcome: No indirectness. - Actual outcome for Pain management: Difference on sleep VAS (0-100) before and after crossover (pre- minus post- crossover scores) at 5 days; Mean Male subgroup D to M: -3.8 (SE 3.5); M to D 6.0 (SE 5.5); difference -9.8 favouring morphine Female subgroup D to M: -5.8 (SE 4.3); M to D: 0.6 (SE 3.2); difference -6.2 favouring morphine; Risk of bias: Indirectness of outcome: No indirectness.	
Protocol outcomes not reported by the study	Quality of life at Any; Control of breathlessness at Any; Control of anxiety at Any; Control of agitation at Any; Control of delirium at Any; Duration of symptom control at Any; Time to symptom control at Any; Duration of institutional care at Any; Carer satisfaction at Any; Time to death at Any; Sedation (GCS/AVPU) at Any.