Table 71: Wildiers 2009[468]

Study	Wildiers 2009[468]
Study type	RCT (Patient randomised; Parallel).
Number of studies (number of participants)	Multicentre (n=333)
Countries and setting	Conducted in Belgium; Setting: Hospital.
Line of therapy	Not applicable.
Duration of study	Intervention time: Until death - data were reported up to 120 hours.
Method of assessment of guideline condition	Unclear method of assessment/diagnosis.
Stratum	Overall.
Subgroup analysis within study	Not applicable.
Inclusion criteria	People at the end of life with noticeable death rattle.
Exclusion criteria	People with clear clinical indications of a secondary cause of rattle, including respiratory infection, food/fluid aspiration or cardiac failure with pulmonary oedema.
Age, gender and ethnicity	Age - Mean (SD): Mean 72.5. Gender (M:F): 158/175. Ethnicity:
Extra comments	N = 316 cancer, N = 17 non-cancer
Indirectness of population	No indirectness.
Interventions	(n=112) Intervention 1: Anti-muscarinic - Hyoscine hydrobromide. Scopolamine (hyoscine hydrobromide) 0.25 mg subcutaneous bolus, followed by 1.5 mg/24 hours. Duration Until death or until no longer clinically indicated. Concurrent medication/care: Not described. (n=106) Intervention 2: Anti-muscarinic - Hyoscine butylbromide. Hyoscine butylbromide 20 mg subcutaneous bolus, followed by 60 mg/24 hours). Duration Up to death or no longer clinically indicated. Concurrent medication/care: Not stated. (n=115) Intervention 3: Muscarinic acetylcholine receptor antagonist - Atropine. Atropine 0.5 mg subcutaneous bolus, followed by 3 mg/24 hours. Duration Until death or no longer clinically indicated. Concurrent medication/care: Not stated.

Funding	Academic or government funding

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HYOSCINE BUTYLBROMIDE versus HYOSCINE HYDROBROMIDE

Protocol outcome 1: Subjective or objective improvement in respiratory secretions at hours/days
- Actual outcome: Subjective rating of noisy breathing on a 4 point scale. at 4 hours; Group 1: 46/85, Group 2: 44/94; Risk of bias: High; Indirectness of outcome: No indirectness.
- Actual outcome: Subjective rating of noisy breathing on a 4 point scale. at 12 hours; Group 1: 35/68, Group 2: 40/70; Risk of bias: High; Indirectness of outcome: No indirectness.
- Actual outcome: Subjective rating of noisy breathing on a 4 point scale. at 24 hours; Group 1: 28/47, Group 2: 36/53; Risk of bias: High; Indirectness of outcome: No indirectness.

Protocol outcome 2: Sedation (patient-rated, clinician-rated, carer-rated) at hours/days
- Actual outcome: Worsening levels of consciousness - rated by attending nurse at 24 hours; Group 1: 11/45, Group 2: 25/52; Risk of bias: High; Indirectness of outcome: No indirectness.
- Actual outcome: Worsening levels of consciousness - rated by attending nurse at 12 hours; Group 1: 14/66, Group 2: 31/68; Risk of bias: High; Indirectness of outcome: No indirectness.

Protocol outcome 3: Adverse events (particularly paradoxical agitation, failure to expectorate, dry mouth at hours/days
- Actual outcome: Improvement in confusion (for those with sufficient level of consciousness to assess) - rated by attending nurse at 12 hours; Group 1: 4/12, Group 2: 0/2; Risk of bias: High; Indirectness of outcome: No indirectness.
- Actual outcome: Improvement in confusion (for those with sufficient level of consciousness to assess) - rated by attending nurse at 24 hours; Group 1: 1/9, Group 2: 0/4; Risk of bias: High; Indirectness of outcome: No indirectness.

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ATROPINE versus HYOSCINE HYDROBROMIDE

Protocol outcome 1: Subjective or objective improvement in respiratory secretions at hours/days
- Actual outcome: Subjective rating of noisy breathing on a 4 point scale. at 4 hours; Group 1: 46/92, Group 2: 44/94; Risk of bias: High; Indirectness of outcome: No indirectness.
- Actual outcome: Subjective rating of noisy breathing on a 4 point scale. at 12 hours; Group 1: 46/65, Group 2: 40/70; Risk of bias: High; Indirectness of outcome: No indirectness.
- Actual outcome: Subjective rating of noisy breathing on a 4 point scale. at 24 hours; Group 1: 41/54, Group 2: 36/53; Risk of bias: High; Indirectness of outcome: No indirectness.

Protocol outcome 2: Sedation (patient-rated, clinician-rated, carer-rated) at hours/days
- Actual outcome: Worsening levels of consciousness - rated by attending nurse at 12 hours; Group 1: 18/62, Group 2: 31/68; Risk of bias: High; Indirectness of outcome: No indirectness.
- Actual outcome: Worsening levels of consciousness - rated by attending nurse at 24 hours; Group 1: 19/51, Group 2: 25/52; Risk of bias: High; Indirectness of outcome: No indirectness.

Protocol outcome 3: Adverse events (particularly paradoxical agitation, failure to expectorate, dry mouth at hours/days
- Actual outcome: Improvement in confusion (for those with sufficient level of consciousness to assess) - rated by attending nurse at 12 hours; Group 1: 1/5, Group 2: 0/2; Risk of bias: High; Indirectness of outcome: No indirectness.
- Actual outcome: Improvement in confusion (for those with sufficient level of consciousness to assess) - rated by attending nurse at 24 hours; Group 1: 0/6, Group 2: 0/4; Risk of bias: High; Indirectness of outcome: No indirectness.

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ATROPINE versus HYOSCINE BUTYLBROMIDE

Protocol outcome 1: Subjective or objective improvement in respiratory secretions at hours/days
- Actual outcome: Subjective rating of noisy breathing on a 4 point scale. At 4 hours; Group 1: 46/92, Group 2: 46/85; Risk of bias: High; Indirectness of outcome: No indirectness.
- Actual outcome: Subjective rating of noisy breathing on a 4 point scale. At 12 hours; Group 1: 46/65, Group 2: 35/68; Risk of bias: High; Indirectness of outcome: No indirectness.
- Actual outcome: Subjective rating of noisy breathing on a 4 point scale. At 24 hours; Group 1: 41/54, Group 2: 28/47; Risk of bias: High; Indirectness of outcome: No indirectness.

Protocol outcome 2: Sedation (patient-rated, clinician-rated, carer-rated) at hours/days
- Actual outcome: Worsening levels of consciousness - rated by attending nurse at 12 hours; Group 1: 18/62, Group 2: 31/68; Risk of bias: High; Indirectness of outcome: No indirectness.
- Actual outcome: Worsening levels of consciousness - rated by attending nurse at 24 hours; Group 1: 19/51, Group 2: 25/52; Risk of bias: High; Indirectness of outcome: No indirectness.

Protocol outcome 3: Adverse events (particularly paradoxical agitation, failure to expectorate, dry mouth at hours/days
- Actual outcome: Improvement in confusion (for those with sufficient level of consciousness to assess) - rated by attending nurse at 12 hours; Group 1: 1/5, Group 2: 0/2; Risk of bias: High; Indirectness of outcome: No indirectness.
- Actual outcome: Improvement in confusion (for those with sufficient level of consciousness to assess) - rated by attending nurse at 24 hours; Group 1: 0/6, Group 2: 0/4; Risk of bias: High; Indirectness of outcome: No indirectness.

Protocol outcomes not reported by the study	Quality of life at hours/days; Hospitalisation at hours/days; Subjective ratings from people on distress related to noisy breathing /respiratory secretions at hours/days; Subjective ratings from informal carers' on distress relating to noisy breathing/respiratory secretions at hours/days; Hydration status at hours/days; Length of survival at hours/days; Length of stay at hours/days.