Table 61: Clemens 2009[106]

Study	Clemens 2009[106]
Study type	Non-randomised comparative study.
Number of studies (number of participants)	1 (n=46)
Countries and setting	Conducted in Germany; Setting: Palliative care unit inpatients.
Line of therapy	Not applicable.
Duration of study	Intervention time.
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Mean survival.
Stratum	Breathlessness management.
Subgroup analysis within study	Not stratified but pre-specified: Hypoxic (SaO2 <90%)/non-hypoxic and opioid naive/pre-treated.

Inclusion criteria	Advanced terminal cancer or other terminal incurable disease and dyspnoea at rest; normal cognitive status; Hb at least 10 g/dl measured within 2 weeks.
Exclusion criteria	Evidence of non-compensated congestive heart failure, severe renal or haptic failure, other uncontrolled symptoms that could require opioids.
Recruitment/selection of patients	Not stated.
Age, gender and ethnicity	Age - Median (range): Hypoxic: 66.5 (40-90); non-hypoxic: 70.5 (40-86). Gender (M:F): 50/50. Ethnicity: Not stated.
Further population details	
Indirectness of population	Serious indirectness: Mean (SD) survival 16.2 (11.9) days and 28.4 (22.4) days, hypoxic and non-hypoxic groups.
Interventions	(n=46) Intervention 1: Breathing gas - Oxygen. Oxygen 4 l/min via nasal cannula. Duration 60 minutes. Concurrent medication/care: Unclear Further details: 1. Delivery system: Delivery system: nasal tube 2. Drug class: Breathing gas 3. Route of administration: Route of administration: transmucosal Comments: Unclear washout period. (n=46) Intervention 2: Breathing gas - Room air. Baseline conditions. Duration Initial assessment. Concurrent medication/care: Unclear Further details: 1. Delivery system : Not applicable / Not stated / Unclear 2. Drug class: Breathing gas 3. Route of administration: Not applicable / Not stated / Unclear Comments: Unclear washout period. (n=46) Intervention 3: Opioids - Morphine. Initially immediate-release opioids every 4 hours and rescue doses if required (1/6 of daily dose) for breakthrough dyspnoea, followed by sustained release preparations q8-12h once dyspnoea and pain had reached tolerable levels. Initial dose defined according to dyspnoea intensity and performance status, and was increased in the titration phase. The choice of opioid (morphine or hydromorphone) was also based on dyspnoea intensity and performance status (patients pre-treated with high dose opioids or with low performance status, severe dyspnoea and/or mild renal dysfunction were given hydromorphone). Duration Ongoing. Concurrent medication/care: Rescue doses permitted. Further details: 1. Delivery system: Delivery system: oral tablet or liquid 2. Drug class: Opioid 3. Route of administration: Route of administration: enteral Comments: Unclear washout period.

Funding	Academic or government funding.

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: OXYGEN versus ROOM AIR.

Protocol outcome 1: Control of breathlessness at Any
- Actual outcome for Breathlessness management: Dyspnoea intensity at rest (patient-rated 0-10 scale) in opioid-naive hypoxic patients at During 60 minutes oxygen vs. baseline; Group 1: mean 5.8 (SD 2); n=11, Risk of bias: Very high; Indirectness of outcome: Serious indirectness.
- Actual outcome for Breathlessness management: Dyspnoea intensity at rest (patient-rated 0-10 scale) in opioid-pretreated hypoxic patients at During 60 minutes oxygen vs. baseline; Group 1: mean 5.5 (SD 2.3); n=7, Risk of bias: Very high; Indirectness of outcome: Serious indirectness.
- Actual outcome for Breathlessness management: Dyspnoea intensity at rest (patient-rated 0-10 scale) in opioid-pretreated non-hypoxic patients at During 60 minutes oxygen vs. baseline; Group 1: mean 5.5 (SD 2.3); n=11, Risk of bias: Very high; Indirectness of outcome: Serious indirectness.
- Actual outcome for Breathlessness management: Dyspnoea intensity at rest (patient-rated 0-10 scale) in opioid-naïve non-hypoxic patients at During 60 minutes oxygen vs. baseline; Group 1: mean 6 (SD 2); n=17, Risk of bias: Very high; Indirectness of outcome: Serious indirectness.

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: OXYGEN versus MORPHINE

Protocol outcome 1: Control of breathlessness at Any
- Actual outcome for Breathlessness management: Dyspnoea intensity at rest (patient-rated 0-10 scale) in opioid-naive non-hypoxic patients at During 60 minutes oxygen vs. 120 min after opioid; Group 1: mean 6 (SD 2); n=17, Risk of bias: Very high; Indirectness of outcome: Serious indirectness.
- Actual outcome for Breathlessness management: Dyspnoea intensity at rest (patient-rated 0-10 scale) in opioid-pretreated non-hypoxic patients at During 60 minutes oxygen vs. 120 min after opioid; Group 1: mean 5.5 (SD 2.3); n=11, Risk of bias: Very high; Indirectness of outcome: Serious indirectness.
- Actual outcome for Breathlessness management: Dyspnoea intensity at rest (patient-rated 0-10 scale) in opioid-pretreated hypoxic patients at During 60 minutes oxygen vs. 120 min after opioid; Group 1: mean 5.5 (SD 2.3); n=7, Risk of bias: Very high; Indirectness of outcome: Serious indirectness.
- Actual outcome for Breathlessness management: Dyspnoea intensity at rest (patient-rated 0-10 scale) in opioid-naive hypoxic patients at During 60 minutes oxygen vs. 120 min after opioid; Group 1: mean 5.8 (SD 2); n=11, Risk of bias: Very high; Indirectness of outcome: Serious indirectness.

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: MORPHINE versus ROOM AIR

Protocol outcome 1: Control of breathlessness at Any
- Actual outcome for Breathlessness management: Dyspnoea intensity at rest (patient-rated 0-10 scale) in opioid-naive non-hypoxic patients at 120 min after opioid vs. baseline; Group 1: mean 1 (SD 1.07); n=17, Risk of bias: Very high; Indirectness of outcome: Serious indirectness.
- Actual outcome for Breathlessness management: Dyspnoea intensity at rest (patient-rated 0-10 scale) in opioid-pretreated non-hypoxic patients at 120 min after opioid vs. baseline; Group 1: mean 1.3 (SD 1); n=11, Risk of bias: Very high; Indirectness of outcome: Serious indirectness.
- Actual outcome for Breathlessness management: Dyspnoea intensity at rest (patient-rated 0-10 scale) in opioid-pretreated hypoxic patients at 120 min after opioid vs. baseline; Group 1: mean 2 (SD 0.5); n=7, Risk of bias: Very high; Indirectness of outcome: Serious indirectness.

- Actual outcome for Breathlessness management: Dyspnoea intensity at rest (patient-rated 0-10 scale) in opioid-naive hypoxic patients at 120 min after opioid vs. baseline; Group 1: mean 2 (SD 1.07); n=11, Risk of bias: Very high; Indirectness of outcome: Serious indirectness.	
Protocol outcomes not reported by the study	Quality of life at Any; Sedation (GCS/AVPU) at Any; Adverse events/withdrawal of the medication due to adverse events 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; Pain control at Any