

# Evidence Synthesis Ireland Fellowship Scheme 2019

**Review Centre/Group Mentor (RCM)**

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| Shelley O’Neill  |

**Review title** *– please provide the review title*

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| For people in the last days of life, which pharmacological agents are most effective in relieving pain, breathlessness, anxiety, agitation and delirium and what degree of sedation do they cause? |

**Review type** *– please identify the type of review in question e.g. qualitative synthesis, Cochrane review of effectiveness, rapid review*

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| Review of effectiveness |

**Review details***– please identify the topic of the review and a very brief background, objectives and PICO (or other question format details) of the review. Please also include current status of review (e.g. protocol on PROSPERO, searches started etc.)*

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| The National Clinical Programme for Palliative Care, proposed developing a National Clinical Guideline (NCG), *Care of dying adults in the last days of life,* for the Irish healthcare system. This was prioritised by the National Clinical Effectiveness Committee (NCEC) and a guideline development group (GDG) has been set up to develop this NCG. This NCG will focus on care for adults deemed to be within a few days of death, as opposed to those in the last year or so of a chronic condition, in all healthcare settings. The GDG identified a recent high-quality clinical guideline that was considered applicable to the Irish healthcare setting: the *Clinical guideline NG31 Care of dying adults in the last days of life*, which was informed by a systematic literature review up to 2014 or 2015 (depending on the specific question), and published by the National Institute for Health and Care Excellence (NICE) in the UK in 2015. The GDG received permission from the Royal College of Physicians to use and update the evidence base for *NICE Clinical guideline NG31* in the development of a NCG. The purpose of this systematic literature review is to:Update the review of clinical effectiveness and cost-effectiveness literature conducted to support the development of *NICE Clinical guideline NG31* so that changes in the evidence base can inform the development of this Irish NCG. This review will form part the update. The specific question is:* For people in the last days of life, which pharmacological agents are most effective in relieving pain, breathlessness, anxiety, agitation and delirium and what degree of sedation do they cause?

The specific objectives are to identify: * the most effective pharmacological treatment for pain, breathlessness, anxiety, agitation and delirium in the last days of life
* relevant economic evaluations.

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| **Population** | Adults (aged ≥ 18 years) in the last days of life  |
| **Intervention**  | **Benzodiazepines** * lorazepam
* midazolam
* diazepam
* clonazepam

**Opioids** * morphine
* oxycodone
* fentanyl
* alfentanil
* buprenorphine
* Hydromorphone

  | **Antipsychotics** * haloperidol
* levomepromazine
* olanzapine
* chlorpromazine

**Corticosteroids** * Dexamethasone
* Prednisolone

**Diuretics** * Furosemide

**Non-steroidal anti-inflammatories** * ketorolac
* diclofenac

**Oxygen** * Heliox
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| Note: the use of these interventions for palliative sedation is not being considered in this review |
| **Comparator**  | * Any of the above
* Placebo
* Usual care
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| **Outcomes** | Primary: * Quality of life (either patient-rated, clinician-rated, carer-rated)
* Control of specific symptoms (for pain, breathlessness, nausea, vomiting, anxiety, agitation and delirium)

Secondary: * Carer satisfaction
* Duration of symptom control
* Length of survival
* Level of sedation
* Adverse effects of treatment, including:
	+ For antihistamines this may include urinary retention or dizziness.
	+ For antipsychotics it may include extrapyramidal side effects, akathisia (restlessness) neuroleptic malignant syndrome, urinary retention and constipation.
	+ For benzodiazepines this may include hypotension respiratory depression or increased restlessness, confusion, ataxia and falls.
	+ For opiates it may include respiratory depression, nausea and vomiting, drowsiness, itching dry mouth and constipation.
	+ For steroids it may include a change in mental state or gastritis.

Any relevant measures of costs and benefits. |
| **Subgroup analysis**  | **Drug class -** Routes of administration * Enteral (includes oral and enteral tubes)
* Intramuscular
* Intravenous
* Subcutaneous
* Transdermal
* Transmucosal (includes sublingual, buccal, nasal)
 | **Delivery system** * ‘Melt’ tablet
* Bolus SC injection or continuous SC delivery by syringe driver
* Continuous IV delivery by pump or Intermittent IV delivery by PCA
* IM injection
* Nasogastric tube
* PEG tube
* Skin patch
* Sublingual, buccal, dissolving tablet
* Tablet, liquid for enteral access
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| **Study design** | * Systematic reviews of RCTs
* RCTs
* Non randomised comparative studies (i.e. studies where the investigator controls allocation)
* Economic evaluations
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| **Search period** | 09.01.15 – current  |

For further details see protocol on PROSPERO <https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=122062>  |