# Carer administration of as-needed subcutaneous medication for breakthrough symptoms in people dying at home: the CARiAD feasibility RCT

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# Scientific summary

## CARiAD feasibility RCT

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# Scientific summary

## Background

Caring for the dying during their last few days of life in a place of their preference is an essential part of health and social care. The majority of people express a wish to die at home (79%), but only half of those achieve this. The likelihood of patients remaining at home often depends on the availability of able and willing informal carers, who take on numerous care tasks. Extending the role of carers to include administering subcutaneous injections has proven key in achieving better symptom control for those dying at home in other countries.

Pain, nausea/vomiting, restlessness/agitation and noisy breathing (rattle) are common symptoms in people who are dying. In addition to regular (background) medication, given via continuous subcutaneous infusion using a syringe pump, guidelines suggest using additional ('as-needed') medication for symptoms that 'break through'. As dying patients are commonly unable to take oral medication, as-needed medication is most often given as a subcutaneous injection by a health-care professional, in the UK usually a district nurse.

Medication for breakthrough symptoms is usually prescribed in advance (anticipatory prescribing) and kept in the patient's home. Medication administration can be severely delayed by health-care professionals' travel time to the patients' home and/or the non-availability of anticipatory medication in the home. Delays happen even with dedicated out-of-hours 'rapid response' nursing services for patients dying at home. Breakthrough pain is usually quick in onset and has a median duration of 30 minutes. Long waits mean that pain is often not adequately managed in the home setting, as shown in the National Survey of Bereaved People (VOICES).

This study focused on timely administration of as-needed medication for dying patients who were being cared for at home.

## Objectives

The research question was 'Is carer administration of as-needed subcutaneous medication for common breakthrough symptoms in people dying at home feasible and acceptable in the UK, and is it feasible to test this intervention in a future definitive randomised controlled trial?'.

- P (People) = people in their last days of life who are being cared for at home, and their carers.
- I (Intervention) = carer administration of as-needed subcutaneous medication for common breakthrough symptoms (pain, restlessness/agitation, nausea/vomiting and noisy breathing), supported by tailored education.
- C (Control) = usual care (health-care professional administration of as-needed subcutaneous medication).
- O (Outcome) = main outcomes of interest – feasibility and acceptability of the trial and intervention, recruitment, attrition and contamination.

To inform the design of a Phase III trial, we aimed to:

- Adapt a successful Australian intervention as a standardised, manualised intervention for UK carer administration of as-needed subcutaneous medication for breakthrough symptoms in patients dying at home.

- Establish the feasibility of the trial and the intervention by assessing acceptability, ability to recruit, attrition rates and suitability to a UK context. This was achieved by conducting an external randomised pilot trial with an embedded qualitative component.
- Identify attributes pertinent to carers' preferences for health-care professional versus own administration of as-needed subcutaneous medications for patients dying at home (as part of qualitative component) and to establish the feasibility of completion of the Carer Experience Scale (assessed in the pilot trial).

## Methods

Expert consensus workshops were conducted in the planned recruitment areas to map current processes and to gain a clearer understanding of how the intervention could be delivered in the local NHS context. These half-day, face-to-face workshops were attended by patients, carers, general practitioners, district nurses, pharmacists, specialist palliative care clinicians and research nurses, and informed the development of the trial processes and materials.

An existing well-established Australian manualised training package was reviewed and adapted for use in the trial through discussion with the Australian authors, input from the expert consensus workshops and consideration of the UK context. This formed the basis of the intervention for a multicentre randomised pilot trial carried out in North Wales, Vale of Glamorgan and Gloucestershire.

## Inclusion criteria

### *Dyads*

Dyads consisted of an adult (i.e. aged $\geq$ 18 years) patient in the last weeks of their life who was likely to lose the oral route of administration for medication and who had expressed a preference to die at home and their adult (unpaid) lay/family carer, who was willing to take on this extended role and receive subcutaneous injection training.

Prognostication was reliant on the professional judgement of, and agreement among, the attending health-care professional team (i.e. clinical estimate of survival). There was an assumption that the carer would spend a significant amount of time with the patient. When more than one carer was available, we asked the patient to identify which carer they would like to be included in the study.

A dyad was excluded if any one of the following criteria were met:

- safety concerns (e.g. drug allergies or the ability of the carer to carry out required tasks)
- relational concerns
- misuse of drugs concerns
- objections to the concept of lay carer administration
- lack of access to, or willingness to engage with, health-care support systems.

Recruitment of > 30% of eligible dyads and retention of > 40% of recruited dyads was assumed to indicate sufficient feasibility for progression to full trial.

Dyads were initially approached by their local district nurse or specialist palliative care team and were recruited by research nurses. Dynamic adaptive randomisation that stratified for recruitment centre and diagnosis (cancer/non-cancer) was carried out remotely by the recruiting research nurse using a secure online randomisation system.

Data were collected through an assessment from a research nurse at baseline and follow-up (with the carer at 6–8 weeks post bereavement) and via carer diaries. Baseline assessment included patient and carer demographic information, medical history, capacity assessment and current drug management. Carers were asked to complete the Carer Experience Scale at baseline and follow-up and the Quality of Life in Life-Threatening Illness – Family Carer Version (QOLLTI-F) at baseline and every 48 hours after the first subcutaneous medication was administered for breakthrough symptoms. Carers completed the Family Memorial Symptom Assessment Score – General Distress Index (MSAS-GDI) at follow-up. Carer diaries were used to record incidences of breakthrough symptoms, including the symptom score before and after subcutaneous medication was administered and the time to symptom relief. In the intervention arm, diaries were also used to record carer confidence and whether or not health-care professional support was sought. Carers were invited to a qualitative interview 2–4 months post bereavement, which included asking them to select attributes for a future discrete choice experiment. Health-care professionals were also invited to take part in separate qualitative interviews to share their experiences. Interviews were audio-recorded and transcribed verbatim. Carer interviews were analysed using interpretive phenomenological analysis and health-care professional interviews were analysed using the Framework approach.

## Results

There were 189 potential dyads identified across the three sites in which the patient was in the last weeks of their life and was likely to lose the oral route of medication administration. Of these, 169 were screened and 68 were ineligible. The main reasons for ineligibility were only paid or formal care being in place (18/68, 26.5%) and the patient not wishing to die at home (13/68, 19.1%). For 11 out of 169 dyads, eligibility was confirmed but no further information was provided ($n = 8$) or the patient died before approach ($n = 3$).

A total of 101 dyads were eligible: 90 dyads were approached to participate and 40 dyads completed the baseline visit and were randomised [39.6% (40/101) of the eligible population, 44.4% (40/90) of those approached]. This met the feasibility criterion of recruiting > 30% of eligible dyads. Twenty dyads were allocated to the intervention and 20 were allocated to usual care. The expected recruitment target (≈50) was not reached because fewer than expected participants were identified.

Twenty-two carers completed the follow-up visit (22/40, 55% of those randomised): 16 (16/20, 80%) from the intervention group and six (6/20, 30%) from the usual-care group. The feasibility criterion of > 40% retention was, therefore, considered not met. It was possible to obtain some information from medical notes for a further three patients; therefore, partial data are available for 25 patients at follow-up.

The majority of patients, 33 out of 40 (82.5%), had cancer. Their mean age was 68.3 years, 23 (57.5%) were male and 17 (42.5%) were female. In total, 18 out of 25 (72%) patients died at home, with others dying either in hospital ($n = 2$, 8%) or in a hospice ($n = 5$, 20%). The mean age of the carers in the study was 56.6 years and 35 out of 40 (87.5%) carers were female. Half of the carers were the patient's spouse/partner and the majority of the carers, 32 out of 40 (80%), lived with the patient.

At baseline, 33 out of 40 (82.5%) patients had anticipatory prescribing in place. All patients had anticipatory prescribing in place at death. Four patients did not have this in place at baseline. At baseline, 27 (67.5%) patients did not have a continuous subcutaneous infusion set up. There were 21 (84%) patients who had a continuous subcutaneous infusion at the time of their death.

At baseline, only one carer did not complete the QOLLTI-F (35 carers completed 100% and four carers completed 70–99%). It was intended that, after the baseline visit, to assess quality of life, the QUOLLTI-F would be completed every 48 hours after the first injection for breakthrough symptoms. However, the QOLLTI-F was completed for only six dyads: four in the intervention group and two in the usual-care

group. The high level of completion at baseline suggests that the measure is acceptable but that it is less feasible for carers to complete this independently and at regular intervals in this context (i.e. while caring for someone in the last days of their life).

All of the 22 carers who completed follow-up completed the Family MSAS-GDI. Of these, 19 (86.4%) carers completed all of the Family MSAS-GDI and three (13.6%) completed 75–99% of the measure. From these results, at least 80% of the measure is completed; therefore, from this perspective, the Family MSAS-GDI can be considered as a primary outcome in a definitive trial.

Three dyads from the usual-care group returned carer diaries, with 20 medication administration entries completed. Eleven dyads from the intervention group returned carer diaries, with 147 medication administration entries completed.

Calculation of time to symptom relief depended on how complete the medication administration entries were; this was possible in 91.3% of entries in the intervention group and 75% of entries in the control group. In the intervention group, 88.8% of these had resolved to an acceptable level within 30 minutes compared with 26.7% in the usual-care group.

The intervention group had a considerably shorter time to medication administration than the usual-care group: the median time to administer medication in the intervention group was 5 minutes and in the usual-care group was 105 minutes.

Carers in the intervention group were asked how confident they felt about administering the medication. This was on a scale from 1 to 7, with a higher score indicating higher confidence. Of the 11 carers in the intervention group who returned carer diaries, nine (81.8%) administered medications. Although there is fluctuation in the scores, the overall trend shows an increase in carer confidence over time, with the final score being 6 or 7 for all of the carers.

Health-care professional support was sought by carers in the intervention group in 24 out of 147 (16.3%) medication administration entries. These were not clustered at the beginning of the carer's time in the study.

In total, four (10%) dyads withdrew from the study. Three of these withdrew because they had been allocated to the usual-care group and one withdrew because of concerns around possibly giving the last injection to the patient.

Qualitative interviews with 12 carers (intervention group, $n = 10$; usual-care group, $n = 2$) show that the intervention is acceptable to patients and carers, who found it helpful and reassuring. Key findings from carer interviews show that carers have a strong desire to fulfil patient wishes to have a home death and are glad of the opportunity to be able to help them have a good death and keep them symptom free as much as possible. The intervention was shown to empower patients and carers by giving them greater control over the circumstances during end of life. The QOLLTI-F was a source of confusion for carers. Carer concerns regarding euthanasia or hastening death can be relieved with training and reassurance from health-care professionals.

Interviews with 20 health-care professionals revealed that, although they mostly found the intervention to be acceptable in terms of patient and carer benefit, they also had concerns regarding the screening and selection of dyads. Health-care professionals reported having to be very careful about who was approached, which may be a result of concerns regarding carer coping ability and the risk for patients, but also of a desire for self-protection and concern about culpability should mistakes occur. Health-care professionals reported time constraints owing to heavy workloads and were sometimes unable to prioritise recruitment and trial training over their other responsibilities. Health-care professionals had

a largely positive view of the intervention in terms of the dyads that they had supported and found that carers were also positive about the experience.

## Conclusions

The CARiAD study explored the feasibility of testing the clinical effectiveness of the intervention of carer administration of as-needed medication for breakthrough symptoms in people dying at home in the UK to inform the design of a future definitive trial. We concluded that the success of a future definitive trial is uncertain owing to equivocal results relating to trial feasibility, particularly that target recruitment was not reached and retention in the usual-care group was low. The context of the trial was not ideal; district nurses were seriously overstretched and unfamiliar with the research methods. However, the intervention was shown to be acceptable, feasible and safe in the study population, and the overall recruitment and retention rate was above what was stated to be necessary for a definitive trial.

Furthermore, noting that the intervention is already spreading across more areas in the UK, it should be considered whether or not there is still an unanswered clinical effectiveness question. The CARiAD study lends some weight to this notion by demonstrating considerably shorter time to medication administration and faster symptom control in the intervention group, and almost universal positivity from carers, albeit in a small sample size. For this reason, a 'common good' argument could increasingly be defended. Moreover, the disparity in readiness to consider the intervention between carers and health-care professionals was clearly demonstrated.

Future work is clearly needed. This should include understanding the context of the areas in the UK where the practice has already been adopted, ascertaining wider public views on the intervention and understanding health-care professionals motivations/views on burden and risk and interface with NHS context. Findings from both quantitative and qualitative data suggest that there is a need for consideration of the most appropriate outcome measures, including consideration of the expected impact of the intervention and where it can be best evidenced for effect. There should also be consideration of the need for national policy on the intervention. Owing to the small sample size and poor retention of the usual-care group, it may be that there are unanswered questions relating to the intervention that would be best studied in a trial in future; the work suggested above will help to ascertain if this is the case.

## Trial registration

This trial is registered as ISRCTN11211024.

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