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# What is the impact of clinically assisted hydration in the last days of life? A systematic literature review and narrative synthesis

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## ABSTRACT

**Background** Clinically assisted hydration (CAH) can be provided in the last days of life as drinking declines. The impact of this practice on quality of life or survival in the last days of life is unclear. Practice varies worldwide concerning this emotive issue.

**Method** Systematic literature review and narrative synthesis of studies evaluating the impact of, or attitudes toward, CAH in the last days of life. Databases were searched up to December 2019. Studies were included if the majority of participants were in the last 7 days of life, and were evaluated using Gough's 'Weight of Evidence' framework. Review protocol registered with PROSPERO, registration number CRD42019125837.

**Results** Fifteen studies were included in the synthesis. None were judged to be both of high quality and relevance. No evidence was found that the provision of CAH has an impact on symptoms or survival. Patient and family carer attitudes toward assisted hydration were diverse.

**Conclusion** There is currently insufficient evidence to draw firm conclusions on the impact of CAH in the last days of life. Future research needs to focus on patients specifically in the last days of life, include those with non-malignant diagnoses, and evaluate best ways to communicate effectively about this complex topic with patients and their families.

## INTRODUCTION

Expected deaths tend to be characterised by a preceding period of reduced consciousness alongside reduction or cessation of oral intake.<sup>1–3</sup> When drinking diminishes, clinically assisted hydration (CAH) can be commenced, involving medical administration of fluid via an intravenous or subcutaneous route.<sup>1</sup>

However, questions about the value of CAH in the last days of life are contentious, emotive and currently unanswered: practice varies considerably between individual clinicians, settings and countries.

Many patients, family carers, health-care professionals (HCPs) and members of the public have expressed the view that CAH should be given routinely near the end of life. A review of the Liverpool Care Pathway in the UK found that relatives were concerned that withholding CAH had led to dehydration that accelerated the dying process.<sup>4</sup> The belief that dehydration is distressing for dying patients is associated with high levels of emotional distress for bereaved relatives.<sup>5</sup> HCPs also report concern at the prospect of withholding CAH,<sup>6</sup> fearing the potential for dehydration to worsen symptoms including delirium, fatigue and thirst.<sup>7</sup>

Conversely, routine provision of CAH in the last days of life is often not supported by HCPs experienced in providing end-of-life care. CAH can be considered as hindering a 'natural' death, with hydration viewed as having the potential to increase nausea, dyspnoea, cough, respiratory secretions and the need to urinate.<sup>7</sup> No literature describes similar concerns from the public.

These opposing views frequently result in differences of opinion between HCPs and those in need of their services. Practice varies markedly between individuals, between healthcare organisations and across cultures, with a striking lack of consensus. One review noted a broad range of 10%–88% of patients with cancer receiving CAH in the last week of life<sup>8</sup>; in another, 22%–100% of HCPs preferred providing CAH at the end of

life, whereas 1%–75% preferred not to.<sup>7</sup> Demonstrating the impact of cultural norms on practice in this field, a Dutch study found 74% of dying hospitalised patients received intravenous hydration, compared with 2% of dying hospice patients.<sup>9</sup> A Delphi study defining optimal palliative care in older people with dementia found high or very high consensus for 51 out of 57 domains but only moderate consensus around the statement ‘Hydration... is inappropriate in the dying phase’.<sup>10</sup> Clinical guidance is also vague; UK guidelines state that hydration decisions should be ‘individualised’, but provide little specific information.<sup>11</sup>

Decisions about CAH can have broader implications, including impact on the place of the death. Although home is often the preferred place,<sup>12</sup> in many countries parenteral hydration is not available in the home setting. The UK’s comprehensive District Nursing Manual of Clinical Procedures does not mention home hydration.<sup>13</sup> A decision to provide CAH, therefore, has the potential to prevent a patient from dying at home.

Five systematic reviews have evaluated CAH near the end of life, the most recent published in 2014. Two reviews investigated attitudes,<sup>7 14</sup> one modes of CAH delivery,<sup>15</sup> and another CAH in palliative care patients.<sup>16</sup> These revealed a lack of research, with limited evidence of benefit. Only one focused on CAH at the very end of life; Raijmakers *et al*’s review of CAH in the last week of life of patients with cancer found little benefit from this practice.<sup>8</sup>

Evaluation of CAH in the last days of life is particularly important, as this is the point when drinking tends to diminish rapidly and clinical decision-making can be particularly challenging. A systematic review is, therefore, needed that focuses on the impact of CAH in the last days of life, while allowing broad eligibility in relation to study design and participants, in order to provide a comprehensive updated appraisal of this clinically relevant and emotive topic.

## Review aims

To undertake a systematic review of literature evaluating the impact of CAH in the last days of life on symptoms and survival, and the attitudes of patients and family carers with direct experience of this practice.

## METHODS

An information specialist (IK) developed a search strategy that was adapted for each database searched: Medline, CINAHL, PsycINFO all via EBSCO, Embase via OVID, Web of Science Core Collection, the Cochrane Library, ASSIA via Proquest and AMED via NHS HDAS. **Box 1** displays the search strategy used for Medline. Searches were conducted of the literature up to December 2019. Reference searches, citation searches and electronic searches of relevant journals (*Palliative Medicine*, *Journal of Clinical Oncology*, *Journal of Pain and Symptom Management*, *BMJ Supportive and Palliative Care*) were also undertaken.

## Box 1 . Medline search strategy

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((MH "Terminal Care+") OR (MH "Terminally III+") OR ("end of life" or "end-of—life" or terminal-stage* or terminal-phase* or (terminal* N3 (stage* or phase* or ill*)) OR ((last or final) N3 (day* or week* or month*)) OR ("end-stage disease*" or "end stage disease*" or "end-stage illness*" or "end stage illness") OR (("less than" N3 (week* or month*)) and (death or die or dying or life or live* or died))) AND ((fluid* N6 (balanc* or therap* or manag*)) OR (hydrat* or dehydrat* or rehydrat*) OR (MH "Fluid Therapy+") OR (MH "Dehydration"))
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Abstract screening was conducted independently by AK and GC after exclusion of duplicate or irrelevant titles, with any disagreements between reviewers being resolved by consensus. AK obtained the full text of potentially relevant articles. AK and RB assessed their eligibility (**box 2**), extracted data and independently graded the articles by Gough’s Weight of Evidence (WoE) framework (**box 3**).<sup>17</sup> This framework was considered well suited to this review given its emphasis on studies’ relevance to the review’s questions, as well their quality, along with its flexibility in allowing appraisal of studies with a wide range of methodology.<sup>18</sup> Disagreements were resolved by discussion to gain consensus.

AK conducted a narrative synthesis, given the utility of this approach when synthesising evidence from both qualitative and quantitative studies.<sup>19</sup> Meta-analysis was not possible due to heterogeneous methodology and outcome measures. The narrative synthesis involved three stages. Initially, a preliminary textual synthesis of each study was created, followed by inductive thematic analysis, using variable labels as themes. Second, to explore relationships within the data, AK compared data within and across studies, including a process of investigator triangulation that considered similarities and differences in methodological approaches between studies. Finally, the robustness of the synthesis was assessed. Articles of low Gough’s WoE rating were included to increase the breadth of the review and reveal areas without any research evidence, but were given less weight in the synthesis and discussion.

Database searches identified 4424 titles after deduplication. After screening 717 abstracts, 15 studies were judged to meet inclusion criteria and were included in the synthesis (**figure 1**). No additional eligible studies were found from the reference, citation and specific journal searches.

The review protocol was registered with PROSPERO (registration number CRD42019125837): [https://www.crd.york.ac.uk/PROSPERO/display\\_record.php?RecordID=125837](https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=125837).

## Box 2 . Eligibility criteria

### Inclusion criteria

- ▶ Published papers or abstracts presenting empirical research relating to clinically assisted hydration (CAH)
- ▶ Study population in the last days of life (mean/median survival <7 days; if average survival data not reported, evidence that the majority of participants were in the last 7 days of life)
- ▶ Any geographic location and any setting (hospital, hospice, nursing home or home)
- ▶ Research that assesses one or more of:
  - Symptoms of patients with or without CAH
  - Survival of patients with or without CAH
  - Attitudes towards CAH of patients in last days of life, and/or of their relatives (contemporaneous or when bereaved)

### Exclusion criteria

- ▶ Case series or case reports
- ▶ Papers not in English language
- ▶ Children (aged 17 years or under)
- ▶ Grey literature
- ▶ Research with no new empirical data (opinion papers, editorials, literature reviews)
- ▶ Research that assesses:
  - Attitudes towards CAH of healthcare professional, the general public or patients not in the last days of life
  - Withdrawal of CAH already being given, for example, for patients with prolonged disorders of consciousness
  - The enteral route, for example, fluids via nasogastric tube or percutaneous endoscopic gastrostomy
  - Artificial nutrition only

## Box 3 . Quality appraisal using Gough's Weight of Evidence (WoE)

For this review's assessment using WoE framework, papers were assigned scores of low, medium or high in the three domains A, B and C, as well as the composite fourth domain, D.

**WoE A:** Judged against the internal validity of included studies, that is, study rigour, transparency and repeatability of method, quality of description of results, accurate analysis, and whether conclusions were justified from methods and results.

**WoE B:** Judged on the appropriateness of the study design in relation to the review's questions. Regarding this review's primary question, study designs were rated more highly if they were better suited to demonstrating potential causal links between provision or withholding of clinically assisted hydration and the development of symptoms.

**WoE C:** Judged on the relevance of included studies regarding the review's questions. Studies were rated more highly if the included participants were in the last week of life and if relevant outcome measures were used.

**WoE D:** The above three judgements are combined to form an overall assessment of the extent to which a study lends evidence toward answering the review questions.

Review-specific criteria adapted from Gough.<sup>17</sup>

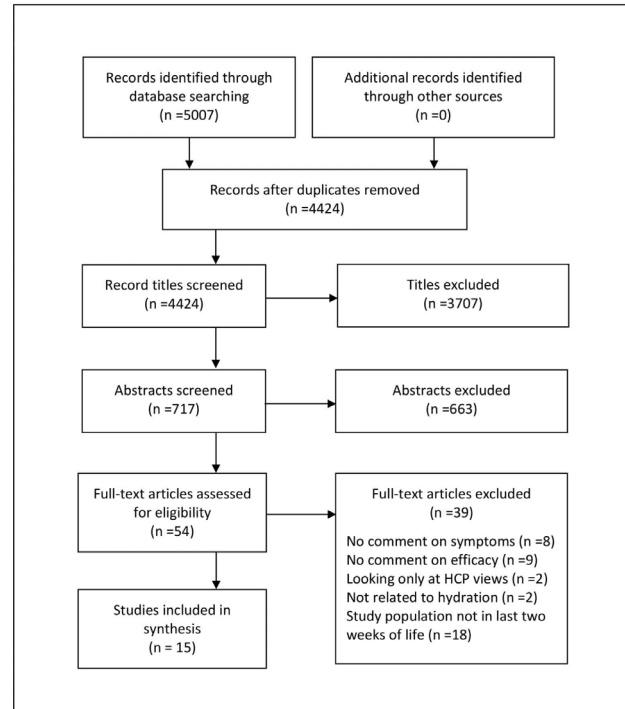


Figure 1 PRISMA flow diagram. HCP, healthcare professional.

## RESULTS

The fifteen included studies were described in twelve peer-reviewed journal papers, one MSc thesis and two published abstracts. Using Gough's framework, eight studies were judged to provide 'medium' and seven 'low' WoE. One trial was well designed and of high quality, but was rated 'medium', as it was a feasibility study without the design or power to provide definitive outcomes.<sup>20</sup>

The synthesis included data from 2327 patients and 131 family caregivers. Dates of publication ranged from 1995 to 2019, and studies were conducted in several continents: Asia (eight studies), Europe (three), North America (two), Oceania (one) and South America (one). Three studies reported data collected from inpatient participants in palliative care units or hospices; six hospital-based data, three from mixed locations and three were unclear. The majority of studies (13 of 15) recruited only patients with cancer. Online supplemental table 1 provides a summary of included studies.

### Symptoms

Excess respiratory secretions (n=8)

CAH was not associated with severity of respiratory secretions in six of eight studies.<sup>9 20–25</sup> Two, providing medium<sup>23</sup> and low<sup>25</sup> WoE, respectively, found secretions to be worse in the group that received more hydration.

Agitation (n=6)

The terms 'agitation', 'delirium' and 'restlessness' were frequently used interchangeably. A feasibility trial found an unchanged incidence of delirium, although its onset was delayed in the group receiving hydration.<sup>20</sup> Four small low WoE studies found no impact

from CAH.<sup>22 23 26 27</sup> An observational study showed no association between terminal restlessness and volume of fluid intake overall, but did see a significant association between higher fluid intake in the final 25–40 hours, and worse restlessness in the 24 hours preceding death.<sup>9</sup>

#### Nausea (n=5)

Four studies found no impact of CAH on nausea when compared with usual care.<sup>20 21 24 28</sup> One small prospective trial found better relief from nausea at 48 hours in the hydration group.<sup>26</sup>

#### Breathlessness (n=4)

CAH had no impact on the severity of breathlessness in three studies.<sup>20 25 28</sup> A retrospective observational study of medical records found an association between breathlessness severity and administration of higher fluid volumes near the end of life.<sup>21</sup>

#### Oedema/fluid overload (n=4)

Three of four studies found no impact of CAH on the incidence or severity of peripheral oedema.<sup>22 25 28</sup> One small observational study noted worse oedema in a group receiving higher volumes of hydration.<sup>23</sup> Pleural effusion severity was not influenced by the use of CAH,<sup>22 23</sup> but two of three studies found CAH to be associated with worsening ascites.<sup>22–24</sup>

#### Thirst or dry mouth (n=3)

None of the three studies, all published 20 or more years ago, demonstrated any impact of CAH on the experience of thirst.<sup>26 28 29</sup> These studies did not draw distinctions between reporting of thirst and dry mouth, or comment on use of measures to hydrate the oral cavity.

#### Other symptoms

No impact of CAH was found in relation to pain,<sup>20 28</sup> depression<sup>28</sup> or anxiety.<sup>21 28</sup>

#### Survival (n=5)

Four of five studies evaluating survival found no difference in survival between participants receiving or not receiving CAH.<sup>20 24 26 28 30</sup> The timing of death was slightly delayed in the CAH arm of a feasibility trial (4.3 vs 2.9 days,  $p=0.038$ ).<sup>20</sup>

#### Patient and carer attitudes (n=5)

Three studies evaluated patient and family caregiver attitudes<sup>30–32</sup> and two focused on bereaved relatives' views.<sup>33 34</sup> The 'meaning of oral intake' was recognised as important, and of a significance beyond nutritional value.<sup>33</sup> Although most bereaved relatives regarded reduced intake towards the end of life to be normal, concerns about both the giving and the withholding of assisted hydration were expressed, often simultaneously.<sup>33</sup> Torres-Vigil *et al* found that 76% of bereaved

family caregivers considered that CAH had been beneficial, and that this perception was associated with a better 'initial adjustment to death'.<sup>34</sup>

## DISCUSSION

Fifteen studies have evaluated the impact of, or attitudes towards, CAH on the last days of life. This review has found little evidence that CAH has an impact on symptoms or survival. Patients and informal carers demonstrated varied perspectives that reflect the many uncertainties inherent to the provision of CAH at the end of life.

Although a small number of studies did report changes to symptoms or survival, the heterogeneity and low WoE of research focusing specifically on the last days of life have precluded definitive conclusions. Davies *et al* made a noteworthy attempt to overcome the challenges of undertaking research in this patient group, undertaking a naturalistic cluster randomised trial involving patients in the last days of life.<sup>20</sup> The main study findings, of a slight delay in delirium onset and timing of death, are intriguing. However, this was a feasibility study, not designed to generate definitive clinical outcomes.

A number of otherwise highly relevant studies were excluded from this review because most participants were not in the last week of life, or because insufficient information had been provided to judge whether or not this was the case. In a rigorous trial, Bruera *et al* specifically excluded those in the last 7 days of life when randomising home hospice patients with advanced cancer to either 1000 or 100 mL of 0.9% saline daily; over 7 days there was no impact on symptoms or survival.<sup>35</sup> Matsuo *et al*'s naturalistic cohort study focused on CAH in patients with advanced cancer who had been prescribed steroids, revealing an association between lower received volume of CAH and the development of delirium ( $p=0.034$ ).<sup>36</sup> Yamaguchi *et al* found worse agitation ( $p=0.025$ ) and a higher prevalence of agitated delirium ( $p=0.009$ ) in patients with advanced abdominal malignancies receiving less CAH.<sup>37</sup> Although participants in the latter two studies were mostly in the last weeks, rather than last days, of life, (and thus excluded from this review), together with the findings from the feasibility study included in this review,<sup>20</sup> there is a suggestion that CAH may reduce the incidence or severity of delirium as oral intake declines.

Due to the challenges of undertaking research in dying patients, few studies have focused on the perspectives of patients and their family carers in the last week of life. The qualitative study of the views of bereaved relatives included in this review, demonstrated varied perspectives on CAH at the end of life, with individuals sometimes holding complex and conflicting views.<sup>33</sup> In contrast, a qualitative study of patients with advanced cancer in the last weeks, rather than last days, of life, found unambiguously positive views of CAH.<sup>38</sup> This



disparity may reflect the differences between views expressed in theory, and those resulting from lived experience.<sup>5</sup> Neither study provided information on whether participants had been involved in conversations with health professionals about potential risks and benefits of hydration; Morita *et al* found that patients and relatives tend to adopt the perspectives of their clinicians, whether these are for, or against, the provision of CAH.<sup>39</sup>

### Strengths and limitations

This study is the first to review literature evaluating the provision of CAH to patients with any diagnosis in the last week of life, a time when issues of hydration are particularly relevant and challenging. Its comprehensive approach, including a wide range of study designs, participant populations and outcome measures, supports accurate identification of gaps in the literature.

The generally low WoE of the included studies, reflecting the ethical and methodological difficulties of involving dying patients in research, limited the ability to reach firm conclusions that could influence clinical practice. Due to the proximity to unconsciousness and death, studies tended to incorporate clinician-based ratings rather than self-reported measures; several involved a retrospective design to overcome the difficulty in judging prognosis. Many studies were small and underpowered. Outcome measures were heterogeneous, and some tested parameters with little salience to CAH, such as depression. Most studies only included patients with cancer, reducing the generalisability of this review. The search strategy excluded grey literature and papers not available in English language, and publication bias was not assessed.

### Clinical implications

NICE guidance on 'Care of dying adults in the last week of life' suggests that clinicians should routinely raise and discuss the topic of hydration and CAH.<sup>11</sup> Given the lack of evidence to guide decision-making and the concerns about both giving and withholding CAH, this review reinforces the need for highly skilled communication, including explanation of the uncertainties involved. This needs to be carefully individualised, taking into account both patient and family perspectives, as well as the potential impact of CAH decisions on the place of care. Current evidence from the UK suggests these discussions are not routinely held with documented evidence of conversations relating to CAH with 9% of dying patients and 30% of their relatives.<sup>40</sup>

In the absence of evidence, pragmatic clinical guidance is likely to be helpful. A study of HCPs' views of guidelines for CAH in palliative care settings found that a majority (81%) would welcome guidelines that standardise care.<sup>41</sup> Current General Medical Council guidance avoids discussion of what the benefits and

burdens of CAH may be, citing a lack of clear evidence.<sup>1</sup> This guidance focuses on the process of best interests decision making, and emphasises the importance of frequent reassessment of clinical condition. Given that there is insufficient evidence to generate definitive criteria for the use of CAH, additional guidance could usefully take a case-based approach that encourages clinicians to think through ethical and clinical arguments, while avoiding being prescriptive. In 2007, the former National Council for Palliative Care published case-based guidance on artificial nutrition and hydration at the end-of-life care,<sup>42</sup> but this is now out of date and no longer easily accessible.

The importance of the symbolic significance and 'meaning' of CAH to patients and their families also has clinical implications. Guo and Jacelon argue that a major component of dignity at the end of life is 'feeling human'.<sup>43</sup> Some may feel that a drip detracts from feeling human by 'medicalising' death and keeping people in an inpatient setting; others may feel it contributes to a feeling of humanity and dignity, by symbolising 'nurturing' and 'health' in the way that drinking usually does.<sup>38</sup> Clinicians could helpfully explore patients' and relatives' interpretations of the meaning they attach to CAH in order to support the process of making decisions about its provision.

### Research implications

Definitive studies are urgently needed to determine whether CAH has any impact on patients' survival or symptoms. A number of findings from this review can helpfully influence the design of future research. This review included a feasibility study with an innovative methodological approach, involving advance consent and cluster randomisation,<sup>20</sup> that could be valuable in future trials involving dying patients. The high recruitment rate was particularly notable given the difficulties in recruiting and retaining vulnerable participants close to death. In addition, it is vital that future studies incorporate outcome measures of relevance to patients. Despite relatives' concerns about thirst as drinking diminishes towards the end of life,<sup>5 32 44</sup> no studies published in the last 20 years evaluated the impact of CAH on thirst.

Given the complexity of communication about an emotive topic, yet to be supported by definitive evidence, research is needed that evaluates strategies to support effective communication about CAH at the end of life. Although a recent literature review included five papers that touch on the potential for communication strategies to support families concerned about CAH-related issues,<sup>45</sup> there has been little research focused on CAH-related communication. Finally, future research needs to involve patients with other diagnoses, including dementia and organ failure, given the preponderance of studies in cancer populations to date.

## CONCLUSIONS

This review has found a limited amount of predominantly low-quality research evaluating the impact of CAH in the last days of life. There is a pressing need for well-designed studies that focus on patients specifically in the last days of life and incorporate outcome measures that take patients' concerns into account. In the meantime, clinicians will continue to have to answer dying patients' elemental questions about water and thirst, with little evidence on which to base the content or manner of their advice.

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## REFERENCES

- General Medical Council. Treatment and care towards the end of life: good practice in decision making, 2010. Available: <https://www.gmc-uk.org/ethical-guidance/ethical-guidance-for-doctors/treatment-and-care-towards-the-end-of-life/clinically-assisted-nutrition-and-hydration> [Accessed 21 Jul 2020].
- Hui D, dos Santos R, Chisholm G, *et al.* Clinical signs of impending death in cancer patients. *Oncologist* 2014;19:681–7.
- Morita T, Ichiki T, Tsunoda J, *et al.* A prospective study on the dying process in terminally ill cancer patients. *Am J Hosp Palliat Care* 1998;15:217–22.
- Neuberger J, Guthrie C, Aaronovich D. More care less pathway: a review of the Liverpool care pathway, 2013. Available: [https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment\\_data/file/212450/Liverpool\\_Care\\_Pathway.pdf](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/212450/Liverpool_Care_Pathway.pdf) [Accessed 21 Jul 2020].
- Yamagishi A, Morita T, Miyashita M, *et al.* The care strategy for families of terminally ill cancer patients who become unable to take nourishment orally: recommendations from a nationwide survey of bereaved family members' experiences. *J Pain Symptom Manage* 2010;40:671–83.
- Morita T, Shima Y, *et al.* Nurse views of the adequacy of decision making and nurse distress regarding artificial hydration for terminally ill cancer patients: a nationwide survey. *Am J Hosp Palliat Care* 2007;24:463–9.
- Raijmakers NJH, Fradsham S, van Zuylen L, *et al.* Variation in attitudes towards artificial hydration at the end of life: a systematic literature review. *Curr Opin Support Palliat Care* 2011;5:265–72.
- Raijmakers NJH, van Zuylen L, Costantini M, *et al.* Artificial nutrition and hydration in the last week of life in cancer patients. A systematic literature review of practices and effects. *Ann Oncol* 2011;22:1478–86.
- Lokker ME, van der Heide A, Oldenmenger WH, *et al.* Hydration and symptoms in the last days of life. *BMJ Support Palliat Care* 2019. doi:10.1136/bmjspcare-2018-001729. [Epub ahead of print: 31 Aug 2019].
- van der Steen JT, Radbruch L, Hertogh CMPM, *et al.* White paper defining optimal palliative care in older people with dementia: a Delphi study and recommendations from the European association for palliative care. *Palliat Med* 2014;28:197–209.
- National Institute for Health and Care Excellence (NICE). Care of dying adults in the last days of life, 2013. Available: <https://www.nice.org.uk/guidance/ng31> [Accessed 21 Jul 2020].
- Hoare S, Morris ZS, Kelly MP, *et al.* Do patients want to die at home? A systematic review of the UK literature, focused on missing preferences for place of death. *PLoS One* 2015;10:e0142723.
- O'Brien L. *District nursing manual of clinical procedures*. Chichester: John Wiley & Sons, 2012.
- Del Río MI, Shand B, Bonati P, *et al.* Hydration and nutrition at the end of life: a systematic review of emotional impact, perceptions, and decision-making among patients, family, and health care staff. *Psychooncology* 2012;21:913–21.
- Forbat L, Kunicki N, Chapman M, *et al.* How and why are subcutaneous fluids administered in an advanced illness population: a systematic review. *J Clin Nurs* 2017;26:1204–16.
- Good P, Richard R, Symmis W, *et al.* Medically assisted hydration for adult palliative care patients. *Cochrane Database Syst Rev* 2014;CD006273.
- Gough D. Weight of evidence: a framework for the appraisal of the quality and relevance of evidence. *Res Pap Educ* 2007;22:213–28.
- Barnett-Page E, Thomas J. Methods for the synthesis of qualitative research: a critical review. *BMC Med Res Methodol* 2009;9:59.
- Popay J. *Guidance on the conduct of narrative synthesis in systematic reviews: a product from the ESRC methods programme*. Lancaster: Lancaster University, 2006.
- Davies AN, Waghorn M, Webber K, *et al.* A cluster randomised feasibility trial of clinically assisted hydration in cancer patients in the last days of life. *Palliat Med* 2018;32:733–43.
- Fritzon A, Tavelin B, Axelsson B. Association between parenteral fluids and symptoms in hospital end-of-life care: an observational study of 280 patients. *BMJ Support Palliat Care* 2015;5:160–8.
- Morita T, Hyodo I, Yoshimi T, *et al.* Association between hydration volume and symptoms in terminally ill cancer patients with abdominal malignancies. *Ann Oncol* 2005;16:640–7.
- Nakajima N, Hata Y, Kusumoto K. A clinical study on the influence of hydration volume on the signs of terminally ill cancer patients with abdominal malignancies. *J Palliat Med* 2013;16:185–9.
- Krishna LK, Poulse J, Goh C. Artificial hydration at the end of life in an oncology ward in Singapore. *Indian J Palliat Care* 2010;16:165–73.
- Otani S, Yoshimoto M, Tokuyasu N, *et al.* PP088-MON the association between artificial hydration and symptoms in terminally ill cancer patients. *Clin Nutr* 2013;32:S155.

- 26 Cerchietti L, Navigante A, Sauri A, *et al.* Hypodermoclysis for control of dehydration in terminal-stage cancer. *Int J Palliat Nurs* 2000;6:370–4.
- 27 Morita T, Tei Y, Inoue S. Agitated terminal delirium and association with partial opioid substitution and hydration. *J Palliat Med* 2003;6:557–63.
- 28 Viola RA. *Studying fluid status and the dying - the challenge of clinical research in palliative care*, MSc thesis. Canada: University of Ottawa, 1997.
- 29 Musgrave CF, Bartal N, Opstad J. The sensation of thirst in dying patients receiving i.v. hydration. *J Palliat Care* 1995;11:17–21.
- 30 Chiu T-Y, Hu W-Y, Chuang R-B, *et al.* Nutrition and hydration for terminal cancer patients in Taiwan. *Support Care Cancer* 2002;10:630–6.
- 31 Musgrave CF, Bartal N, Opstad J. Intravenous hydration for terminal patients: what are the attitudes of Israeli terminal patients, their families, and their health professionals? *J Pain Symptom Manage* 1996;12:47–51.
- 32 Van der Riet P, Brooks D, Ashby M. Nutrition and hydration at the end of life: pilot study of a palliative care experience. *J Law Med* 2006;14:182–98.
- 33 Raijmakers NJH, Clark JB, van Zuylen L, *et al.* Bereaved relatives' perspectives of the patient's oral intake towards the end of life: a qualitative study. *Palliat Med* 2013;27:665–72.
- 34 Torres-Vigil I, Cohen MZ, De La Rosa A, *et al.* The association between past grief reactions and bereaved caregivers' perceptions of parenteral hydration during the last weeks of life. *Palliat Med* 2012;26:412.
- 35 Bruera E, Hui D, Dalal S, *et al.* Parenteral hydration in patients with advanced cancer: a multicenter, double-blind, placebo-controlled randomized trial. *J Clin Oncol* 2013;31:111–8.
- 36 Matsuo N, Morita T, Matsuda Y, *et al.* Predictors of delirium in corticosteroid-treated patients with advanced cancer: an exploratory, multicenter, prospective, observational study. *J Palliat Med* 2017;20:352–9.
- 37 Yamaguchi T, Morita T, Shinjo T, *et al.* Effect of parenteral hydration therapy based on the Japanese national clinical guideline on quality of life, discomfort, and symptom intensity in patients with advanced cancer. *J Pain Symptom Manage* 2012;43:1001–12.
- 38 Cohen MZ, Torres-Vigil I, Burbach BE, *et al.* The meaning of parenteral hydration to family caregivers and patients with advanced cancer receiving hospice care. *J Pain Symptom Manage* 2012;43:855–65.
- 39 Morita T, Tsunoda J, Inoue S, *et al.* Perceptions and decision-making on rehydration of terminally ill cancer patients and family members. *Am J Hosp Palliat Care* 1999;16:509–16.
- 40 NHS Benchmarking Network. National audit of care at the end of life: first round of audit report, 2019. Available: <https://s3.eu-west-2.amazonaws.com/nhsbn-static/NACEL/2019/NACEL%20-%20National%20Report%202018%20Final%20-%20Report.pdf> [Accessed 21 Jul 2020].
- 41 Cabañero-Martínez MJ, Ramos-Pichardo JD, Velasco-Álvarez ML, *et al.* Availability and perceived usefulness of guidelines and protocols for subcutaneous hydration in palliative care settings. *J Clin Nurs* 2019;28:4012–20.
- 42 Campbell C, Partridge R. *Artificial nutrition and hydration: guidance in end of life care for adults*. London: National Council for Palliative Care, 2007.
- 43 Guo Q, Jacelon CS. An integrative review of dignity in end-of-life care. *Palliat Med* 2014;28:931–40.
- 44 Bükki J, Unterpaul T, Nübling G, *et al.* Decision making at the end of life--cancer patients' and their caregivers' views on artificial nutrition and hydration. *Support Care Cancer* 2014;22:844.
- 45 Pettifer A, Froggatt K, Hughes S. The experiences of family members witnessing the diminishing drinking of a dying relative: an adapted meta-narrative literature review. *Palliat Med* 2019;33:1146–57.

Table 1. Summary of included studies							
First author, year, country	Design	Participants	Proximity to death	Aims / description	Research methods	Key findings	Gough's WoE (A B C - D)
<b>Weight of Evidence: Medium</b>							
Cerchiatti 2000 Argentina <sup>21</sup>	Prospective controlled trial	42 patients with "terminal advanced cancer" and inadequate hydration	Mean survival "close to 4 days in both groups" (exact figures not given)	Assess usefulness of SC hydration in relieving thirst and chronic nausea (measured by patient-rated VAS) or "delirium" (measured by MMSE)	Participants randomised to 1L fluid / day or usual care. Comparison of means between groups.	Both groups showed improvement in thirst/nausea at 24h. CAH group had better relief from chronic nausea at 48h (p=0.027).	L M H - M
Chiu 2002 Taiwan <sup>22</sup>	Cohort study	344 PCU inpatients with advanced cancer	Mean survival 23.9 days; retrospective review enabled analysis of data from 48 hours before death for most participants	Assess patients' views on acceptability of CAH as death approaches; also to perform survival analysis	Survey (piloted and assessed for content validity). Descriptive statistics (survey) and survival analysis (multiple Cox regression).	66-76% of patients perceived no effect of CAH; 19-32% felt it brought "more comfort", 2-6% felt it brought "less comfort". Hazard ratio for survival for using CAH 2 days before death of 1.03.	L M M - M
Davies 2018 UK <sup>20</sup>	Unblinded feasibility cluster randomised trial	200 PCU or cancer centre inpatients with advanced cancer, reduced oral intake and prognosis < 1 week	Median survival 2.9-4.2 days; inclusion criteria state last days of life	Determine if a definitively powered study of CAH at end of life can be done, with a hypothesis that adequate hydration will reduce incidence of delirium in cancer patients at end of life. Symptom measurements taken by HCPs	Sites randomised to receive usual care or usual care plus IV or SC hydration (volume determined by weight as per NICE guidance CG174). Intention-to-treat statistical analysis. Survival analysis with COX regression model.	38.5% in CAH group stopped hydration due to adverse effect. Frequency of hyperactive delirium was not reduced, but onset was delayed (p=0.098). No differences seen in other symptoms measured. Median survival 2.9 days (no hydration) vs 4.3 days (hydration group), p=0.038. HR 0.358 for survival at 3 days in CAH.	H M H - M
Fritzson 2015 Sweden <sup>23</sup>	Retrospective historical case-control study	280 inpatients who had an expected in-hospital death	Inclusion criteria: last week of life	Investigate whether dying patients with CAH have more or fewer symptoms than those without	Case note and chart review. Patients divided into 5 groups depending on received volume of hydration. Statistical comparisons included $\chi^2$ test, Mann-Whitney U test, and univariate logistic regression.	More dyspnoea recorded in patients who received CAH in the last 24h of life (p<0.0001) and in the last week (p=0.0005). No differences seen in anxiety and nausea.	M M H - M
Lokker 2019 The Netherlands <sup>9</sup>	Prospective observational study	371 inpatients judged to be dying by an MDT in hospital or hospice	Mean survival 25 hours from start of monitoring	Investigate whether the amount of fluid intake (oral or parenteral) preceding or during the dying phase is	Daily clinician / nurse assessment of restlessness (VICS scale) and "death rattle" (Back score). Mann-Whitney	No association seen between volume of fluid intake and occurrence of "death rattle" or restlessness. Higher fluid intake in	L M H - M



				related to occurrence of “death rattle” and terminal restlessness	U test used for significance testing.	the 25-48 hours before death associated with terminal restlessness in the final 24h of life (p=0.049)	
Morita 2005 Japan <sup>24</sup>	Prospective observational study	226 patients with abdominal malignancies, in community or on oncology ward	Inclusion criteria: last three weeks of life; study design allowed for review of data from 24 hours, 7 days and 3 weeks before death	Explore associations between hydration volume and symptoms in the last 3 weeks of life in patients with abdominal malignancies	Daily examination and physician rating of symptoms and potential covariates. Patients divided into groups receiving >1L/day or <1L/day, 1 and 3 weeks before death. Univariate analyses using $\chi^2$ and Mann-Whitney U tests.	Increase in dehydration score was higher in the non-hydration group (p=0.004). A significant increase in ascites was seen in the CAH group (p=0.035). No other significant differences were seen after controlling.	L H H - M
Nakajima 2013 Japan <sup>25</sup>	Prospective observational study	75 patients with abdominal malignancies and prognosis <3 months	Inclusion criteria: last three weeks of life; study design allowed for review of data from 24 hours, 7 days and 3 weeks before death	Explore influence of hydration volume on signs and symptoms in last 3 weeks of life in patients with abdominal malignancies	Patients divided into groups receiving >1L/day or <1L/day, 1 and 3 weeks before death. Signs and symptoms evaluated by clinicians prospectively. Fisher’s exact and Mann-Whitney U tests used.	The group receiving CAH >1L/day were found to have worse scores for peripheral oedema (p=0.04), ascites (p=0.037) and bronchial secretions (p=0.036). Dehydration score worse in the less-hydrated group (p=0.027).	M M H - M
Raijmakers 2013 The Netherlands <sup>26</sup>	Qualitative interview study	23 relatives of deceased patients under hospice care, bereaved in the last 2-4 months	N/A (study of bereaved relatives)	Contribute to better understanding of relatives’ concerns regarding reduced oral intake near end of life	Semi-structured interviews. Thematic analysis.	Themes identified as “meaning of oral intake”, “responding to decreased oral intake”, “part of the process”, “patient’s choice”, “the vicious circle”, and “communication and information”. Symbolic meaning seen to be more important than nutritional value to many.	M M L - M
<b>Weight of Evidence: Low</b>							
Krishna 2010 Singapore <sup>27</sup>	Record review study	238 inpatients with cancer on an oncology ward	Retrospective case note review examining data from last 48h of life	Determine occurrence of symptoms of hydration-related symptoms in last 48h of life; determine impact on survival	Retrospective case note review. Descriptive statistics and Kaplan-Meier survival analysis (time between palliative care referral and death).	No difference seen in survival. No differences seen in any symptoms except CCF (higher in non-CAH group, p=0.036) and peripheral oedema (higher in non-CAH group, p=0.05)	L L H - L
Morita 2003 Japan <sup>28</sup>	Uncontrolled before-after study	284 PCU inpatients with a cancer diagnosis	Inclusion criteria state participants had to die in order to be included;	Clarify effects of opioid rotation and CAH on prevalence of agitated delirium at end of life	Retrospective case note and chart review with multi-rater symptom measurements. Cohen’s $\kappa$ test for interrater	No differences in the prevalence of agitated delirium, communication or consciousness scores were seen in the two study periods.	L L M - L

			measurements taken from 1 week before death		reliability. Comparison of means in first and second study periods.		
Musgrave 1995 Israel <sup>29</sup>	Cross-sectional survey	19 terminally ill oncology ward inpatients with IV fluids	Inclusion criteria: prognosis < 10 days	Clarify the effects of IV hydration on the sensation of thirst in dying patients	Structured questionnaire developed and administered daily along with patient assessment of thirst, and nurse assessments of symptoms and IV intake. Descriptive statistics.	No relationship was seen between thirst and quantity of IV fluids used.	L L M - L
Musgrave 1996 Israel <sup>30</sup>	Cross sectional survey	33 inpatients with cancer in an oncology ward, and 32 family members	30 / 33 participants died within 10 days	Identify attitudes of patients and family to IV fluids in the terminal phase	Convenience sampling. Single administration of survey. Descriptive statistics.	7 out of 10 competent dying patients expressed a positive disposition towards IV fluids; 23 couldn't say. 81% of family members were positive.	L L M - L
Otani 2013 Japan <sup>31</sup>	Record review study	179 terminally ill cancer patients ( <i>no other information</i> )	Survival data not given explicitly, but the abstract suggests some measurements taken 1 week before death	Evaluate association between CAH and symptoms in the last week of life	Retrospective case note review. Patients classified into 3 groups (<0.5L, 0.5-1L, and >1L/day). Groups compared with $\chi^2$ test. Clinical factors and symptoms assessed with multiple regression analysis.	As hydration increased, incidence of dyspnoea (66% vs 25%) and bronchial secretions (49% vs 18%) "significantly" increased; no p-values quoted.	L L M - L
Torres-Vigil 2012 USA <sup>32</sup>	Cross sectional survey	76 relatives of deceased patients with cancer, bereaved in the last 3-23 months	N/A (study of bereaved relatives)	Identify factors associated with bereaved caregivers' perceptions regarding benefits patient derived from CAH in last weeks of life	16-item Likert scale survey (validation not mentioned). Descriptive statistics.	76% agreed that CAH had been beneficial. Views were mostly strongly positive towards CAH being helpful, not bothersome, and psychologically useful.	L M M - L
Viola 1997 Canada <sup>33</sup>	Prospective controlled trial	66 inpatients in two PCUs with advanced cancer who were dying and dehydrated	Inclusion criteria state last week of life; measurements taken through study period including last days of life	Identify symptoms in the dying that may be affected by CAH therapy	Patients at one site received AH therapy while those at the other site did not. Multiple clinician-rated symptoms and clinical outcomes recorded. Descriptive statistics.	Several major differences between cohorts at two sites noted at baseline, making results non-comparable. Several data are missing from the analysis. Author states that myoclonus is more common in the no-hydration group but does not quote figures.	L M M - L