

## Living Friendly Summaries of the Body of Evidence using Epistemonikos (FRISBEE)

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# Is parenteral hydration beneficial in terminally ill cancer patients?

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## Abstract

### INTRODUCTION

It is common for terminally ill patients to have a reduced fluid intake, which often results in a need for more medical support. However, it is not clear if this measure has a real clinical impact.

### METHODS

To answer this question we used Epistemonikos, the largest database of systematic reviews in health, which is maintained by screening multiple information sources, including MEDLINE, EMBASE, Cochrane, among others. We extracted data from the systematic reviews, reanalyzed data from primary studies and generated a summary of findings table using the GRADE approach.

### RESULTS AND CONCLUSIONS

We identified four systematic reviews including 51 studies overall, from which three were randomized trials. We concluded the administration of parenteral hydration might make little or no difference in terms of survival and quality of life in terminally ill cancer patients, and that it is not clear whether it has any other benefit because the certainty of the evidence is very low.

### Problem

Reduced fluid intake in patients with end-stage cancer is a frequent event. It can be caused by different factors, such as complication of the disease (i.e obstruction due to neoplasia), or other symptoms like nausea or generalized weakness. Therefore, it is common for these patients to develop clinical signs of dehydration.

It is unknown whether parenteral hydration helps prolong life or reduce symptoms in these situation, or if it carries more risks than benefits such as local complications at the

puncture site (e.g. erythema, edema, pain), or at systemic level (e.g. edema, congestive heart failure)..

### Methods

To answer the question, we used Epistemonikos, the largest database of systematic reviews in health, which is maintained by screening multiple information sources, including MEDLINE, EMBASE, Cochrane, among others, to identify systematic reviews and their included primary

studies. We extracted data from the identified reviews and reanalyzed data from primary studies included in those reviews. With this information, we generated a structured summary denominated FRISBEE (Friendly Summary of Body of Evidence using Epistemonikos) using a pre-established format, which includes key messages, a

summary of the body of evidence (presented as an evidence matrix in Epistemonikos), meta-analysis of the total of studies when it is possible, a summary of findings table following the GRADE approach and a table of other considerations for decision-making.

**Key messages**

- The administration of parenteral hydration might make little or no difference in survival and quality of life in terminally ill cancer patients.
- It is not clear whether parenteral hydration has any clinical impact on dehydration, thirst and delirium, or if it increases local adverse effects, because the certainty of the evidence is very low.

## About the body of evidence for this question

What is the evidence. See evidence matrix in Epistemonikos later	We found four systematic reviews [1],[2],[3],[4] that included 51 primary studies [5],[6],[7],[8],[9],[10],[11],[12],[13],[14],[15],[16],[17],[18],[19],[20],[21],[22],[23],[24],[25],[26],[27],[28],[29],[30],[31],[32],[33],[34],[35],[36],[37],[38],[39],[40],[41],[42],[43],[44],[45],[46],[47],[48],[49],[50],[51],[52],[53],[54],[55], from which, three are randomized controlled trials [5],[6],[7]. This table and the summary are based on the latter, since the observational studies did not increase the certainty of the existing evidence or provide relevant additional information.
What types of patients were included*	All trials included patients with terminal cancer, clinical dehydration and reduced fluid intake. Two trials [5],[6] included patients older than 18 years and one trial [7] did not specify it.
What types of interventions were included*	Two trials [5],[6] evaluated parenteral hydration with saline (1 liter) SC versus placebo (defined as saline 100 cc SC). One trial [7] evaluated parenteral hydration with 5% dextrose + 140 mEq/L NaCl SC versus no intervention.
What types of outcomes were measured	The trials measured multiple outcomes, but the identified systematic reviews grouped them as follows: clinical signs of dehydration, thirst, delirium, survival, quality of life and complications.

\* The information about primary studies is extracted from the systematic reviews identified, unless otherwise specified.

## Summary of Findings

The information on the effects of parenteral hydration is based on three randomized trials [5],[6],[7] that included 230 patients.

Two trials [5],[6] reported the outcome clinical dehydration (defined as the following symptoms: fatigue, myoclonus, sedation, hallucinations) (180 patients). One trial [7] reported thirst (50 patients). Two trials [5],[7] (179 patients) evaluated incidence of delirium (according to Memorial Delirium Assessment Scale or MDAS), one trial [5] (129 patients) reported survival (at 17 days) and quality of life (FACIT-F and FACIT-G scores). Two trials [6],[7] (101 patients) measured local adverse effects of the puncture site (pain, edema).

The summary of findings is the following:

- It is not clear if parenteral hydration improves clinical dehydration in terminally ill cancer patients because the certainty of the evidence is very low.
- It is not clear if parenteral hydration improves thirst in terminally ill cancer patients because the certainty of the evidence is very low.
- Parenteral hydration might have little or no effect on survival of terminally ill cancer patients, but the certainty of the evidence is low.
- It is not clear if parenteral hydration prevents delirium in terminally ill cancer patients because the certainty of the evidence is very low
- It is not clear if parenteral hydration leads to greater local adverse effects in terminally ill cancer patients because the certainty of the evidence is very low
- Parenteral hydration may make little or no difference in the quality of life of terminally ill cancer patients, but the certainty of the evidence is low.

Parenteral hydration in terminally ill cancer patients		
Patients	Terminally ill patients	
Intervention	Parenteral hydration	
Comparison	Placebo or no intervention	
Outcome	Effect	Certainty of evidence (GRADE)
Clinical dehydration*	One trial [5] showed no changes in any symptom, whereas in the other [6] only an improvement in myoclonus and sedation was observed in the intervention group	⊗○○○ <sup>1,2,3</sup> Very low
Thirst	No changes on thirst were observed [7].	⊕○○○ <sup>2,4</sup> Very Low
Survival	No changes on survival were observed [5].	⊕⊕○○ <sup>4</sup> Low
Delirium	Only one trial [5] showed delirium improvement, whereas the other [7] showed no changes.	⊗○○○ <sup>1,2,3</sup> Very Low
Local adverse effects	No differences on local adverse effects were observed [6],[7].	⊕○○○ <sup>2,4</sup> Very Low
Quality of life**	No changes were observed on quality of life [5].	⊕⊕○○ <sup>4</sup> Low
GRADE: Evidence grades of the GRADE Working Group (see later). * Defined as the presence of symptoms: fatigue, myoclonus, sedation and hallucinations ** According to scores FACIT-F and FACIT-G <sup>1</sup> The certainty of the evidence was downgraded one level for inconsistency on the results. <sup>2</sup> The certainty of the evidence was downgraded two levels for high risk of bias. <sup>3</sup> The certainty of the evidence was downgraded one level for imprecision, due to low number of patients <sup>4</sup> The certainty of the evidence was downgraded two levels for imprecision, due to low number of patients		

About the certainty of the evidence (GRADE)*
⊕⊕⊕⊕ <b>High:</b> This research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different† is low.
⊕⊕⊕○ <b>Moderate:</b> This research provides a good indication of the likely effect. The likelihood that the effect will be substantially different† is moderate
⊕⊕○○ <b>Low:</b> This research provides some indication of the likely effect. However, the likelihood that it will be substantially different† is high.
⊕○○○ <b>Very low:</b> This research does not provide a reliable indication of the likely effect. The likelihood that the effect will be substantially different† is very high.
*This concept is also called 'quality of the evidence' or 'confidence in effect estimates'. † Substantially different = a large enough difference that it might affect a decision.

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## Other considerations for decision-making

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### To whom this evidence does and does not apply

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- This evidence applies to adult patients, of both sexes, diagnosed with terminal stage cancer.
  - Even though the trials only included adult population, in the absence of direct evidence it would be reasonable to extrapolate this evidence to pediatric population with terminal stage cancer.
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### About the outcomes included in this summary

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- The outcomes presented in the summary of findings are those considered critical for decision-making by the authors of this article. They generally agree with those presented by the main systematic reviews included.
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### Balance between benefits and risks, and certainty of the evidence

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- Parenteral hydration might lead to little or no difference in survival and quality of life in terminal cancer patients, and it is not clear whether it has benefit on other outcomes.
  - However, it is not possible to make an adequate risk/benefit balance because of the poor certainty of the evidence.
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### Resource considerations

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- Costs reports were not included in the trials. However, it is generally recognized that parenteral hydration is a low-cost intervention.
  - In spite of this and given parenteral hydration could lead to little or no benefit, the cost/benefit balance would not be favorable. But it is not possible to make an appropriate assessment because of the associated uncertainty.
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### What would patients and their doctors think about this intervention

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- Based on the evidence presented in this summary, the decision to use or not parenteral hydration should be individualized.
  - The opinions of the families of terminally ill patients regarding parenteral hydration are divided: although some would consider it would be better not to disturb them unless is strictly necessary, others could perceive not providing this intervention as a sign of abandonment by the physicians.
  - It is unlikely that the limited evidence available modifies decision-making, so by now other factors should drive the decision to hydrate or not an individual patient.
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### Differences between this summary and other sources

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- Just as this article, the included systematic reviews conclude the observed effects with parenteral hydration in terminally ill cancer patients are limited. However, good quality evidence is lacking to inform definitive recommendations.
  - The National Comprehensive Cancer Network (NCCN) [56] does not provide clear recommendations for the use of parenteral hydration, but states its use involves a shared decision between the patient, his family and the healthcare team.
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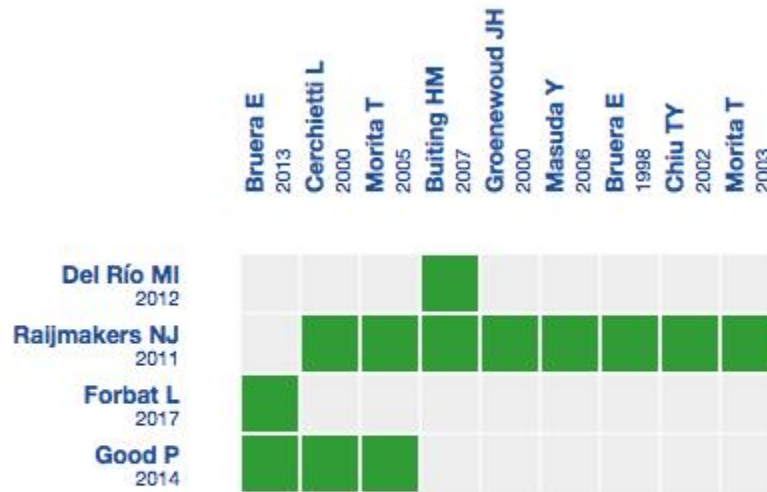
### Could this evidence change in the future?

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- The probability of future evidence changing the conclusions of this summary is high, due to the low certainty of the existing evidence.
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## How we conducted this summary

Using automated and collaborative means, we compiled all the relevant evidence for the question of interest and we present it as a matrix of evidence.



An evidence matrix is a table that compares systematic reviews that answer the same question.

Rows represent systematic reviews, and columns show primary studies.

The boxes in green correspond to studies included in the respective revisions.

The system automatically detects new systematic reviews including any of the primary studies in the matrix, which will be added if they actually answer the same question.

Follow the link to access the **interactive version**: [Parenteral hydration in terminally ill patients](#)

## Notes

The upper portion of the matrix of evidence will display a warning of “new evidence” if new systematic reviews are published after the publication of this summary. Even though the project considers the periodical update of these summaries, users are invited to comment in Medwave or to contact the authors through email if they find new evidence and the summary should be updated earlier.

After creating an account in Epistemonikos, users will be able to save the matrixes and to receive automated notifications any time new evidence potentially relevant for the question appears.

This article is part of the Epistemonikos Evidence Synthesis project. It is elaborated with a pre-established methodology, following rigorous methodological standards and internal peer review process. Each of these articles

corresponds to a summary, denominated FRISBEE (Friendly Summary of Body of Evidence using Epistemonikos), whose main objective is to synthesize the body of evidence for a specific question, with a friendly format to clinical professionals. Its main resources are based on the evidence matrix of Epistemonikos and analysis of results using GRADE methodology. Further details of the methods for developing this FRISBEE are described here (<http://dx.doi.org/10.5867/medwave.2014.06.5997>)

Epistemonikos foundation is a non-for-profit organization aiming to bring information closer to health decision-makers with technology. Its main development is Epistemonikos database ([www.epistemonikos.org](http://www.epistemonikos.org))

### Potencial conflicts of interest

The authors do not have relevant interests to declare.

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