

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

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# At which stage of end-stage kidney disease should chronic dialysis be started?

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## Abstract

The number of patients requiring renal replacement therapy has increased exponentially in recent years. However, there is still controversy regarding the best moment to initiate chronic dialysis. Searching in Epistemonikos database, which is maintained by screening 30 databases, we identified five systematic reviews comprising 21 trials addressing the question of this article. We combined the evidence using meta-analysis and generated a summary of findings following the GRADE approach. We concluded delaying the initiation of dialysis probably does not increase mortality risk in chronic kidney disease and makes little or no difference in the risk of requiring a temporary catheter or having to check the vascular access.

### Problem

Since the onset of renal replacement therapy, both peritoneal dialysis and hemodialysis have experienced an exponential growth.

Traditionally, early initiation of dialysis has been proposed in order to avoid patient's general condition deterioration, especially nutritional status. However, dialysis carries a high-cost, and leads to complications and risks, so there are also arguments for delaying its initiation.

### Methods

We used Epistemonikos database, which is maintained by screening more than 30 databases, to identify systematic reviews and their included primary studies. With this information, we generated a structured summary 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, a summary of findings table following the GRADE approach and a table of other considerations for decision-making.

### Key messages

- Delaying initiation of dialysis probably does not increase mortality in chronic kidney disease.
- The timing of initiation of dialysis makes little or no difference in the risk of requiring a temporary catheter or having to check the vascular access.
- Costs that could be reduced by delaying the moment of initiation of dialysis are large, but the feasibility of this measure may vary in different health systems.

## About the body of evidence for this question

What is the evidence. See evidence matrix in Epistemonikos later	<p>We found five systematic reviews [1],[2],[3],[4],[5] including 21 studies reported in 23 references [6],[7],[8],[9],[10],[11],[12],[13],[14],[15],[16],[17],[18],[19],[20],[21],[22],[23],[24],[25],[26],[27],[28].</p> <p>Of these, only one study corresponds to a randomized controlled trial, reported in three references [10],[11],[14]. This table and the summary in general are based on the latter because observational studies did not increase the certainty of the evidence, or provide additional relevant information.</p>
What types of patients were included	<p>The characteristics of participants enrolled in the randomized trial [10] are:</p> <ul style="list-style-type: none"> <li>• The average age was 60 years, and 66% were men.</li> <li>• The percentage of diabetics was 43%.</li> <li>• The trial did not make differences based on initial dialysis mode (hemodialysis or peritoneal dialysis).</li> </ul>
What types of interventions were included	<p>The randomized trial [10] defined early dialysis as GFR 10-14 ml/min and late dialysis as GFR 5-7 ml/min.</p>
What types of outcomes were measured	<p>The outcomes were pooled by the different systematic reviews as follows:</p> <ul style="list-style-type: none"> <li>• Total mortality.</li> <li>• Mortality per 1 mL/min decrease in GFR (not reported in the randomized trial).</li> <li>• Hospitalizations (not reported in the trial).</li> <li>• Temporary catheterization.</li> <li>• Need to check access.</li> </ul>

## Summary of findings

The information about the timing of initiation of dialysis is based on one randomized trial [10] including 828 patients. The inclusion of observational studies did not increase the certainty of the evidence.

The summary of findings is the following:

- Delaying initiation of dialysis probably does not increase mortality in chronic kidney disease. The certainty of the evidence is moderate.
- The timing of initiation of dialysis makes little or no difference in the risk of requiring a temporary catheter. The certainty of the evidence is high.
- Early initiation of dialysis makes little or no difference in the risk of having to check the vascular access. The certainty of the evidence is high.

Early versus late dialysis in chronic kidney disease				
Patients	Chronic kidney disease			
Intervention	Early dialysis (10-14 ml/min)			
Comparison	Late dialysis (5-7 ml/min)			
Outcomes	Absolute effect*		Relative effect (95% CI)	Certainty of the evidence (GRADE)
	WITH late dialysis	WITH early dialysis		
	Difference: patients per 1000			
Mortality	366 per 1000	377 per 1000	RR 1.03 (0.86 to 1.23)	⊕⊕⊕○ <sup>1</sup> Moderate
	Difference: 11 patients more per 1000 (Margin of error: 51 less to 84 more)			
Temporary catheter	292 per 1000	292 per 1000	RR 1.00 (0.81 to 1.23)	⊕⊕⊕⊕ High
	Difference: 0 patients (Margin of error: 56 less to 67 more)			
Need to check access	347 por 1000	361 por 1000	RR 1.04 (0.86 to 1.25)	⊕⊕⊕⊕ High
	Difference: 14 patients more per 1000 (Margin of error: 49 less to 87 more)			
RR= Risk ratio. Margin of error = 95% confidence interval (CI). GRADE: evidence grades of the GRADE Working Group (see later in this article)  * The risk <b>WITH early dialysis</b> is based on the risk in the control group of the trials. The risk <b>WITH late dialysis</b> (and its margin of error) is calculated from relative effect (and its margin of error)  1 The certainty of the evidence was downgraded in one level for imprecision because the confidence interval includes the possibility of a difference in favor of any of the alternatives.				

## About the certainty of the evidence (GRADE)\*

⊕⊕⊕⊕

**High:** This research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different† is low.

⊕⊕⊕○

**Moderate:** This research provides a good indication of the likely effect. The likelihood that the effect will be substantially different† is moderate

⊕⊕○○

**Low:** This research provides some indication of the likely effect. However, the likelihood that it will be substantially different† is high.

⊕○○○

**Very low:** 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.

## Other considerations for decision-making

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

- The evidence presented in this summary applies to all patients with chronic kidney disease who are contemplating the initiation of dialysis as chronic renal replacement therapy. This evidence does not apply to patients with acute dialysis requirement or symptomatic disease.
- This summary does not make a comparison between hemodialysis and peritoneal dialysis.

### About the outcomes included in this summary

- We selected mortality, need for temporary catheterization and need for revision of access for the summary of findings table because they are critical outcomes for decision-making about time of initiation of dialysis. This selection is based on the opinion of the authors of the summary, but coincides with the outcomes mentioned by most systematic reviews.

### Balance between benefits and risks, and certainty of the evidence

- Delaying initiation of dialysis probably does not carry an important risk for patients. Considering dialysis involves a substantial burden for patients, and often deterioration in their quality of life, the benefit/risk is probably favorable to late initiation of dialysis.

### What would patients and their doctors think about this intervention

- Most patients and their doctors should prefer late dialysis initiation considering the evidence presented in this summary.
- However, some clinicians may still prefer early dialysis because it is the predominant dialysis mode, and it is still recommended in most guidelines. Feasibility considerations may also influence the decision.

### Resource considerations

- Costs associated to dialysis as renal replacement therapy worldwide are high. Late initiation could potentially lead to large savings to the health system

### Feasibility and implementation

- Delaying the initiation of dialysis requires a health system able to monitor patients closely and respond quickly to any emergency. This might be the main limitation in many health systems, and in its absence, it is possible that risks of late dialysis are higher than those observed in the trial.

### Differences between this summary and other sources

- The findings of this summary are consistent with the systematic reviews identified, although some give more weight to the observational studies. Some of them show differences in mortality, but when adjusted for confounding factors, the effect on mortality is similar to what was observed in the trial.
- The findings of this summary partially agree with the main guidelines, as KDIGO guideline [29], the guideline of the National Kidney Foundation (KDOQI) [30] and the guideline of the Canadian Society of Nephrology [31]. They mention three circumstances for the initiation of dialysis: symptoms attributable to chronic kidney disease, failure to regulate blood pressure or volume overload, and clinical malnutrition. It is mentioned this occurs close to a glomerular filtration rate of 15 ml/min, but they do not recommend initiation of dialysis at a given numerical value.
- Additionally, the three guidelines recognize the general tendency to favor early dialysis without a clear evidence base, but rather based on historical reasons related to starting dialysis in better general conditions. Only KDIGO [29] guideline cites the trial [10] included in this summary.

### Could this evidence change in the future?

- The probability that future evidence changes the conclusions of this summary is low due to the certainty of the evidence.
- We did not identify ongoing studies in the International Clinical Trials Registry Platform of the World Health Organization or published studies not included in the systematic reviews identified.

## 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.

		Cooper BA 2010	Kazmi WH 2005	Beddhu S 2003	Wright S 2010	Korevaar JC 2001	Traynor JP 2002	Wilson B 2007	Hwang SJ 2010	Clark WF 2011	Lassalle M 2010	Tang SC 2007
		x	x	x	x	x	x	x	x	x	x	x
Susantitaphong .. 2012	x											
Pan Y 2012												
Nacak H 2018	x											
Cantero-Muñoz P 2010	x											
Slinin Y 2015	x											

Starting from any systematic review, Epistemonikos builds a matrix based on existing connections in the database.

The author of the matrix can select relevant information for a specific health question (typically in PICO format) in order to display the information set for the question.

The rows represent systematic reviews that share at least one primary study, and columns display the studies.

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

Follow the link to access the **interactive version**: [Early versus late initiation of dialysis in end-stage renal failure](#)

## 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.

The details about the methods used to produce these summaries 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)).

These summaries follow a rigorous process of internal peer review.

### Conflicts of interest

The authors do not have relevant interests to declare.



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