

**Frisbee**

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## Does antibiotic lock therapy prevent catheter-associated bacteremia in hemodialysis?

**Authors:** Macarena Jiménez[1], Trinidad Madrid[1]

**Affiliation:**

[1] Departamento de Medicina Interna, Facultad de Medicina, Pontificia Universidad Católica de Chile, Santiago, Chile

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**E-mail:** [mtmadrid@uc.cl](mailto:mtmadrid@uc.cl)

### Abstract

Central venous catheter-related blood stream infection is a major cause of morbidity and mortality in patients with renal disease treated with hemodialysis. Antibiotic lock solutions can be effective in preventing this complication in patients with hemodialysis. Searching in Epistemonikos database, which is maintained by screening more than twenty databases, we identified eight systematic reviews including seventeen randomized trials. We combined the evidence using meta-analysis and generated a summary of findings table following the GRADE approach. We concluded that antibiotic lock solutions probably decrease catheter-related blood stream infection in hemodialysis patients.

### Resumen

Las infecciones del torrente sanguíneo asociadas a catéteres venosos centrales son una de las principales complicaciones de su uso, lo cual conlleva a un aumento de morbimortalidad en pacientes con insuficiencia renal en hemodiálisis. El uso de soluciones de sellado con antibióticos podría ser efectivo para prevenir esta complicación. Utilizando la base de datos Epistemonikos, la cual es mantenida mediante búsquedas en más de veinte bases de datos, identificamos ocho revisiones sistemáticas que en conjunto incluyen diecisiete estudios aleatorizados. Realizamos un metanálisis y tablas de resumen de los resultados utilizando el método GRADE. Concluimos que el uso de soluciones de sellado con antibióticos probablemente disminuye el número de infecciones del torrente sanguíneo asociadas a catéteres venosos centrales en pacientes en hemodiálisis.

## Problem

Central venous catheter-related blood stream infections can lead to serious infectious complications in patients with renal disease treated with hemodialysis, such as infective endocarditis, septic pulmonary emboli, osteomyelitis and abscesses as a result of hematogenous seeding.

Despite the risks associated to this type of vascular access, many times it is the only option because of temporary loss of permanent hemodialysis access, peripheral vascular disease or as transitory alternative while waiting for the maturation of arteriovenous fistula. Intraluminal antibiotic lock solutions that are maintained for a specified time before being removed can be useful for decreasing the risk of central venous catheter-related blood stream infections.

## Methods

We used Epistemonikos database, which is maintained by screening more than 20 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

- Antibiotic lock solutions probably decrease catheter-related blood stream infections in hemodialysis patients.
- The benefit/risk and benefit/cost balance probably favor the intervention

## About the body of evidence for this question

What is the evidence See evidence matrix in Epistemonikos later.	We found 8 systematic reviews [1],[2],[3],[4],[5],[6],[7],[8] that include 17 randomized trials [9],[10],[11],[12],[13],[14],[15],[16],[17],[18],[19],[20],[21],[22],[23],[24],[25].
What types of patients were included	The trials included patients with no distinction by sex or age.  All of the trials included hemodialysis patients, using tunneled (11 trials), non-tunneled (4 trials) or both types of catheters (2 trials).  The randomized trials included 1921 adult patients.
What types of interventions were included	The studies employed different kind of antibiotics as lock therapy (vancomycin, gentamicin, minocycline, cefotaxime, cefazoline and linezolid; associated to heparin, tricitasol, citrate or etildiaminotetraacetic acid). All trials compared against heparin in the control group.
What types of outcomes were measured	Bacteremia/ central venous catheter-related blood stream infection, time until infection, exit-site infection, catheter-associated mortality, total mortality.

### Summary of findings

This information is based on 17 randomized trials. All of them reported central venous catheter-related blood stream infection.

- Antibiotic lock solutions probably decrease catheter-related blood stream infection in hemodialysis patients.

Antibiotic lock in hemodialysis catheter				
<b>Patients</b>		Patients with hemodialysis catheter		
<b>Intervention</b>		Antibiotic lock (with or without citrate)		
<b>Comparison</b>		Heparin lock		
Outcomes	Absolute effect*		Relative effect (CI 95%)	Certainty of the evidence (GRADE)
	WITHOUT Antibiotic lock	WITH Antibiotic lock		
	Diferencia: pacientes por 1000			
Central venous catheter- related blood stream infection	335 per 1000	114 per 1000	RR 0,35 (0,25 a 0,47)	⊕⊕⊕○ <sup>1,2</sup> Moderate
	Difference: 221 patients less per 1000 (Margin of error: 181 to 251 less)			
<p>Margin of error= Confidence interval of 95%. RR: Relative risk.            GRADE: evidence grades of the GRADE Working Group (see last page)            * The risk in the group WITHOUT antibiotic lock is based on the risk in the control group of the trials. The risk with antibiotic lock ( and it margin of error) is calculated from relative effect (and its margin of error)  <sup>1</sup>Even though there is heterogeneity, this is determined more by the magnitude of the benefit (how much benefit) than the direction of it (if there is benefit or not). We did not reduce the quality of the evidence for this reason.  <sup>2</sup>Most of the trials have limitations; the most important is the lack of blinding.</p>				

### Antibiotic lock therapy for prevention of central venous catheter-related blood stream infection in hemodialysis

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## Other considerations for decision-making

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

- Trials included patients treated with hemodialysis, with tunneled or non tunneled catheter, so this evidence applies to all these groups.
- This evidence does not apply directly to other kind of users of central venous catheter, such as hematologic patients or children.

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### About the outcomes included in this summary

- Most guidelines consider central venous catheter –related blood stream infection as the critical outcome for decision making.
- There is no description of adverse effects in the included trials, being this an important outcome.

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

- There is certainty about the benefits. However, the uncertainty about the adverse effects, such as toxicity or antibiotic resistance, limit the ability to estimate the risk/benefit.
- However, it seems likely that the balance is favorable, especially in patients at increased risk of infection

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### What do patients and their doctors think about

- Due to the high incidence of central venous catheter-related blood stream infections in patients treated with hemodialysis, with consequent morbidity and mortality, longer hospital stay and associated costs, patients and their physicians will be probably inclined to use this option.

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### Resource considerations

- It is difficult to estimate costs given the heterogeneity in type and dose of drugs in use.
- However, it is likely that this balance will be favorable to the intervention.

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### Feasibility and implementation

- Given the variety of antibiotics and preparations used it is difficult to implement a uniform prevention strategy for different health centers. Availability and local microbiological data are key to implement the most appropriate option.

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### Differences between this summary and other sources

- The key messages of our summary are consistent with the findings of the individual systematic reviews identified.
- The key messages of our summary are discordant with the main clinical practice guideline identified [26] which recommends its use only in patients with multiple central venous catheter-related blood stream infections. The guideline states that current evidence supports its use, but more trials are lacking with more patients and more homogeneity in the therapy implemented.

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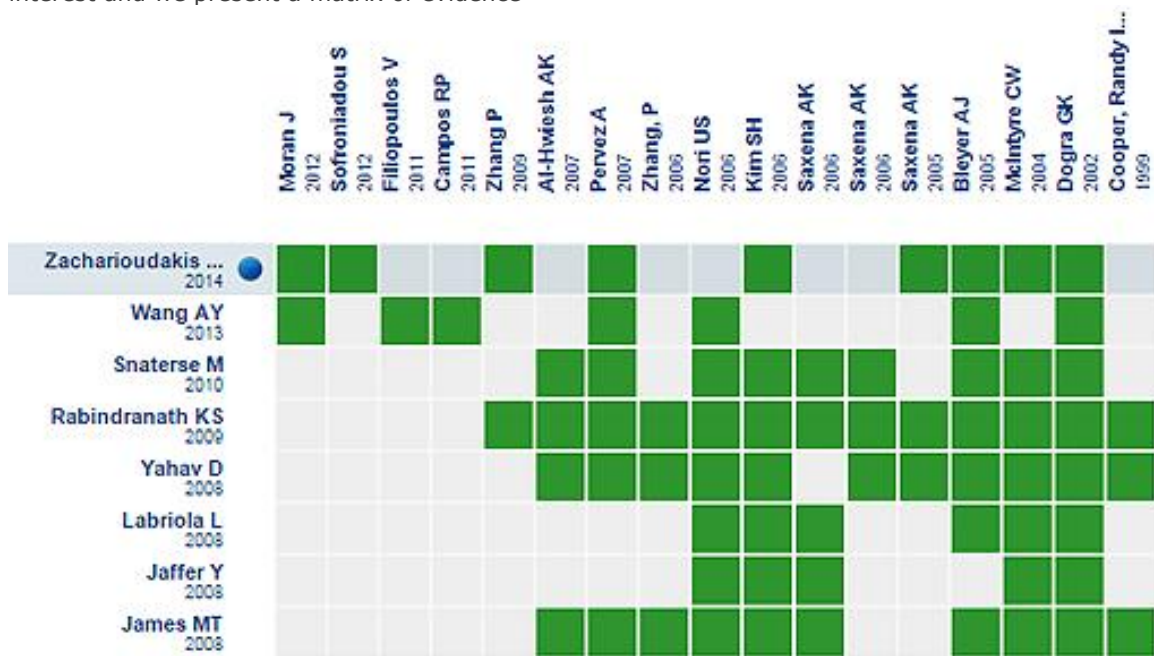
### Could this evidence change in the future?

- The probability that new trials change the conclusions of this summary is very low, because the certainty of the evidence is high.
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- New trials comparing different antibiotics could give relevant information for the implementation in specific setting, but the availability and local microbiology might be sufficient to make a decision.
- As trials with longer follow up are conducted, we will know if there are adverse effects related to this intervention.

**How we conducted this summary**

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



Starting from any systematic review, Epistemikos builds a matrix based on existing connections in the database (the review from which the matrix is built, appears highlighted).

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.

**Matrix of evidence**

Follow the link to access the interactive version: [Antibiotic lock therapy for prevention of central venous catheter-related blood stream infection in hemodialysis](#)

## 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.

## 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 the website of *Medwave* or to contact the authors through email if they realize there is 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 this summaries are described here

<http://dx.doi.org/10.5867/medwave.2014.06.5997>.

Epistemonikos foundation is a non-for-profit organisation aiming to bring information closer to those making health decisions, through the use of technology. Its main development is Epistemonikos database ([www.epistemonikos.org](http://www.epistemonikos.org)).

These summaries follow a rigorous process of internal peer review.

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**Author Address:**

Facultad de Medicina  
Pontificia Universidad Católica de Chile  
Lira 63,  
Santiago Centro  
Chile



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