

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

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### Are diuretics effective for Ménière`s disease?

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### Abstract

**INTRODUCTION**

Ménière`s disease is an inner ear disorder characterized by episodes of spontaneous vertigo, fluctuating hearing loss and tinnitus. Diuretics have been widely used for the treatment of attacks, but there is controversy about their effectiveness.

**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 of primary studies, conducted a meta-analysis and generated a summary of findings table using the GRADE approach.

**RESULTS AND CONCLUSIONS**

We identified three systematic reviews including nineteen studies overall, of which four were randomized trials. We concluded it is not clear whether diuretics lead to a symptomatic improvement of vertigo or an objective decrease in hearing loss in patients with Ménière`s disease, because the certainty of the evidence is very low.

**Problem**

Ménière`s disease is an inner ear disorder characterized by episodes of spontaneous vertigo, fluctuating hearing loss and *tinnitus*. The American Academy of Otolaryngology and Head and Neck Surgery (AAO-HNS) has created guidelines to define the diagnosis, including two episodes of vertigo greater than 20 minutes, sensorineural hearing loss confirmed by audiometry, added to *tinnitus* or aural fullness [1]. However, these guidelines are not universally accepted. Pathophysiologically, Ménière`s disease is secondary to an increase in endolymphatic pressure in the inner ear, whose cause is idiopathic. The attacks of this

disorder occur on average between 6 to 11 months per year [2].

The ideal treatment aims to reduce the number and severity of vertigo attacks, to reduce hearing loss and *tinnitus* associated with the attacks, to alleviate chronic symptoms and to prevent the progression of the disease in terms of hearing and balance. While no treatment has met all of these goals, diuretics are frequently used. Different diuretics act by different mechanisms, but all of them would reduce volume and pressure of endolymph, either by increasing clearance or decreasing production. Despite the

above, there is controversy regarding the efficacy of this treatment in Ménière's disease.

## 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

- It is not clear whether the use of diuretics leads to a symptomatic improvement of vertigo or to an objective decrease in hearing loss in Ménière's disease, because the certainty of the evidence is very low.
- The use of diuretics in Ménière's disease is probably associated with minimal adverse effects.

### About the body of evidence for this question

<p>What is the evidence. See evidence matrix in Epistemonikos later</p>	<p>We identified three systematic reviews [3],[4],[5] including nineteen studies overall [6],[7],[8],[9],[10],[11],[12],[13],[14],[15],[16],[17],[18],[19],[20],[21],[22],[23],[24], of which four were randomized trials [8],[15],[17],[20]. One trial [20] used isosorbide as an intervention, which is not considered as a diuretic. Another trial [8] did not compare the intervention against placebo, but against betahistine. Both trials were excluded from the analysis.</p> <p>This table and the summary in general are based on the two relevant trials [15],[17], since the observational studies did not increase the certainty of the existing evidence or provide additional relevant information.</p>
<p>What types of patients were included*</p>	<p>Both trials used criteria different to AAO-HNS [1] to define Ménière's disease [15],[17].</p>
<p>What types of interventions were included*</p>	<p>The trials used hydrochlorothiazide at a dose of 25 mg every 8 hours [15] and hydrochlorothiazide plus triamterene (50 mg/ 25 mg) 2 capsules every 48 hours [17]. Both trials compared the intervention against placebo [15],[17].</p>
<p>What types of outcomes were measured</p>	<p>The outcomes, according to how they were grouped in the identified systematic reviews, were:</p> <ul style="list-style-type: none"> <li>• Number and severity of vertigo attacks</li> <li>• Changes in hearing loss</li> <li>• Intensity of tinnitus</li> <li>• Changes in the perception of aural fullness</li> <li>• Functional disability</li> <li>• Global changes in wellbeing and quality of life</li> <li>• Adverse effects of the treatment</li> <li>• The average follow-up was between 4 and 31.7 months.</li> </ul>

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

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## Summary of Findings

The information on the effects of diuretics for Ménière`s disease is based on two randomized trials involving 63 patients overall [15],[17].

Both trials reported symptomatic improvement in vertigo, changes in hearing loss and adverse effects. None of the identified reviews could conduct a meta-analysis of the identified trials. The summary of findings is the following:

- It is not clear whether the use of diuretics leads to a symptomatic improvement of vertigo in Ménière's disease, because the certainty of the evidence is very low.
- It is not clear whether the use of diuretics leads to an objective improvement of hearing loss in Ménière's disease, because the certainty of the evidence is very low.
- The use of diuretics in Ménière's disease is probably associated with minimal adverse effects. The certainty of the evidence is moderate.

Diuretics for Ménière's disease		
<b>Patients</b>	Ménière's disease	
<b>Intervention</b>	Diuretics (hydrochlorothiazide and hydrochlorothiazide plus triamterene)	
<b>Comparison</b>	placebo	
Outcome	Impact	Certainty of evidence (GRADE)
Symptomatic improvement of vertigo	Both included trials reported significant symptomatic improvement of vertigo [15], [17].	⊕○○○ <sup>1,2</sup> Very low
Objective improvement of hearing loss	One [15] trial reported a slight improvement in hearing loss (18 of 26 patients)	⊕○○○ <sup>1,2</sup> Very low
Adverse effects*	One [15] trial reported fatigue as adverse effect.	⊕⊕⊕○ <sup>3</sup> Moderate
<p><b>GRADE:</b> Evidence grades of the GRADE Working Group (see later).            * The only adverse effect reported in the included trials was fatigue.</p> <p><sup>1</sup> The certainty of the evidence was downgraded in two levels due to risk of bias, due to the important limitations of the trials.  <sup>2</sup> The certainty of the evidence was downgraded by one level for imprecision, due to the small sample size of the trials.  <sup>3</sup> The certainty of the evidence was downgraded due to inconsistency between the results of the trials.</p>		

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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- The conclusions of this summary apply to patients with Ménière`s disease who present with symptoms of vertigo and hearing loss.
  - All of the trials included in this summary used inclusion criteria different from the AAO-NHS definition [1], so they may not correspond the clinical definition of Ménière`s disease consistent with international guidelines.
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### About the outcomes included in this summary

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- The outcomes included in the table are those considered critical for decision-making, according to the opinion of the authors of this summary.
  - There could be effects on other outcomes such as *tinnitus* and aural fullness, but they were not reported in the systematic reviews identified.
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### Balance between benefits and risks, and certainty of the evidence

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- It is not possible to make an adequate balance between the risks and benefits of diuretics in Ménière's disease due to the uncertainty about the benefits.
  - On the other hand, diuretics probably have few or no adverse effects in the dose used in Ménière's disease.
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### Resource considerations

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- Diuretics are generally low cost drugs.
  - However, it is not possible to make a balance between costs and benefits due to the uncertainty about the latter.
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### What would patients and their doctors think about this intervention

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- Variability in decision-making regarding this intervention can be expected. Patients who put more value on the uncertain benefit could lean in favor of its use. Those who put more value on the certainty of the evidence, the costs or the adverse effects, are likely to lean against it.
  - One factor to consider is diuretics have been used frequently by clinicians, especially in the early stages of the disease. In addition, there is heterogeneity in existing recommendations in clinical guidelines. This would probably lead to even greater variability in decision-making.
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### Differences between this summary and other sources

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- This summary presents information concordant with two of the three systematic reviews evaluated. The Cochrane review [3] did not identify studies of sufficient quality that could be included. The second review [4] concluded the use of diuretics could be beneficial in Ménière's disease, more to reduce the frequency of vertigo attacks than to improve hearing loss. The third review concluded diuretics reduce the symptoms of vertigo, without evidence in the reduction of hearing loss and *tinnitus* [5].
  - We did not identify international guidelines widely recognized in this topic. However, Mexican otorhinolaryngology society guidelines [25] are consistent with these results, referring to the systematic reviews previously discussed. The American AAO-NHS guidelines on Ménière are currently being developed.
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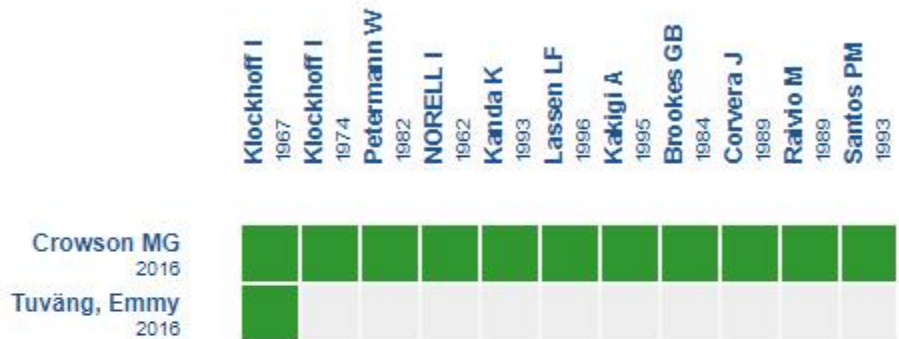
### Could this evidence change in the future?

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- The likelihood of future research changing the conclusions of this summary is high because of the uncertainty of the existing evidence.
  - We did not identify clinical trials on this topic that have not been included in systematic reviews.
  - We performed a search in the World Health Organization's clinical trials platform and did not identify ongoing trials.
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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**: [Diuretics for Ménière's disease](#)

### 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)).

#### Potential conflicts of interest

The authors do not have relevant interests to declare.

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