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

# Is the exercise effective for the prevention of upper respiratory tract infections?

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**Citation** Rocco M, Bravo-Soto GA, Ortigoza A. Is the exercise effective for the prevention of upper respiratory tract infections?. *Medwave* 2018 Jul-Ago;18(4):e7225

Doi 10.5867/medwave.2018.04.7225

Submission date 2/3/2018 Acceptance date 24/4/2018 Publication date 20/7/2018

**Origin** This article is a product of the Evidence Synthesis Project of Epistemonikos Fundation, in collaboration with Medwave for its publication

**Type of review** Non-blinded peer review by members of the methodological team of Epistemonikos Evidence Synthesis Project

**Potential conflicts of interest** The authors do not have relevant interests to declare.

#### Abstract

#### Introduction

Upper respiratory tract infections are one of the main causes of medical consultation in the world. Considering the lack of specific treatment, prevention becomes essential. It has been postulated that exercise could have a preventive role, but its clinical effectiveness remains a topic of discussion.

#### 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 four systematic reviews including fourteen studies overall, of which six were randomized trials. We concluded it is not clear whether exercise of moderate intensity prevents or not upper respiratory infections, because the certainty of the evidence is very low.

## Problem

Upper respiratory infections have a high prevalence, and impose important financial burden to the systems through costs derived from frequent consultations and absenteeism. It is estimated that each year a child suffers about five upper respiratory infections, and an adult between two and three<sup>1</sup>.

It has been suggested that the relationship between exercise and upper respiratory infections follows a "type j" curve, where moderate and regular exercise would improve the ability to resist infections and reduce the number of symptomatic days of those who suffer them<sup>2</sup>. This effect would be mediated by varying concentration of different cells or cell products that affect immune system, especially immunoglobulin A and natural killer cells<sup>3</sup>. On the other hand, high intensity or chronic exercise would decrease the ability to resist infections, which could constitute a potential risk.



The role of regular physical activity in preventing diseases, such as colds or other upper respiratory diseases, is not well defined. The objective of this summary is to evaluate the existing evidence, in order to improve our understanding of this problem.

#### Key messages

• Is not clear whether moderate intensity exercise decreases the risk of developing upper respiratory infections because the certainty of the evidence is very low.

## About the body of evidence for this question

| What is the evidence.<br>See evidence matrix in<br>Epistemonikos later | We found four systematic reviews <sup>4-7</sup> including 14 pri-<br>mary studies (reported in 18 references) <sup>8-25</sup> , of which<br>six corresponded to randomized trials (included in 10<br>references) <sup>8-15,21,25</sup> . This table and the summary in<br>general are based on the latter, since the observational<br>studies did not increase the certainty of the existing<br>evidence, or provide relevant additional information. |  |
|--|---|--|
| What types of patients<br>were included*                               | Four trials included only women, between 25 and 75 years, sedentary (less than 60 minutes per week of moderate or vigorous physical activity), without allergies, without using medications and with no previous illnesses <sup>9,10,11,14</sup> .  |  |
|  | Two trials included adults of either sex <sup>8,25</sup> , between 67 to 85 years <sup>25</sup> and 56 years on average <sup>8</sup> , sedentary, non-smokers, not using medications that affect the immune system.   |  |
|  | All trials excluded people vaccinated against influ-<br>enza, or with chronic diseases, history of cardiovascu-<br>lar disease or tobacco consumption in the last two<br>years.   |  |
|  | No trial reported the period of the year in which the intervention was carried out.   |  |
| What types of interven-<br>tions were included*                        | Five trials evaluated the effect of moderate intensity<br>physical activity, from 30 to 45 minutes, during five<br>days per week, with an increase of 60% to 75% of<br>their maximum heart rate.  |  |
|  | Among the exercises performed, all of the trials in-<br>cluded rapid treadmill walking and one trial used a<br>stationary bicycle <sup>10</sup> . In all the trials heart rate and dis-<br>tance traveled were monitored, and supervised by an<br>instructor.   |  |
|  | In two trials, the control group performed stretching sessions during the period of the intervention [25,10] and in three trials heart rate was recorded during their daily activities <sup>9,14,11</sup> . All trials compared against placebo or standard treatment.  |  |

## 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 decisionmaking.

| What types of outcomes<br>were measured | The trials measured several outcomes, which were grouped by the systematic reviews in the following way:   |  |
|---|--|--|
|   | <ul> <li>Incidence of upper respiratory infections, registered as<br/>the number of recorded episodes during the period of<br/>follow-up.</li> <li>Severity and duration of episodes of acute respiratory<br/>infections.</li> </ul> |  |
| were measured                           | <ul> <li>Adverse effects, measured as injuries caused by exercise.</li> </ul>  |  |
|   | In two trials the average follow-up was 12 weeks <sup>25,11</sup> , in two trials the follow-up was 15 weeks <sup>9,14</sup> , one trial   |  |
|   | had a follow-up of 12 months <sup>10</sup> and one trial had a follow-up of only 8 weeks <sup>8</sup> .  |  |

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

## Summary of Findings

Information about the effects of exercise for the prevention of upper respiratory tract infections is based on five randomized trials involving 311 participants in total<sup>8-10,14,25</sup>. It was not possible to incorporate the information of one trial<sup>11</sup>, because it did not have data that could be incorporated into the meta-analysis. Five trials reported the effect of exercise on the incidence of upper respiratory tract infections (311 participants) and only one trial<sup>25</sup> measured adverse effects of exercise (injuries associated with the practice) (30 participants).

The summary of findings is as follows:

- It is not clear whether moderate intensity physical exercise decreases the risk of developing upper respiratory infections because the certainty of the evidence is very low.
- It is not clear whether there are adverse effects associated with moderate intensity physical exercise in the prevention of upper respiratory infections because the certainty of the evidence is very low.

| Exercise for the prevention of upper respiratory tract infections           |   |                        |                             |              |  |  |  |
|---|---|------------------------|-----------------------------|--------------|--|--|--|
| Patients<br>Intervention<br>Comparison                                      | Healthy adults<br>Moderate intensity physical exercise<br>Placebo or stretching   |                        |                             |              |  |  |  |
| Outcome   | Absolute effect*  |                        |                             | Certainty of |  |  |  |
|   | WITHOUT moderate exercise   | WITH moderate exercise | Relative effect<br>(IC 95%) | evidence     |  |  |  |
|   | Difference: people per 1000   |                        |                             | (GRADE)      |  |  |  |
| Incidence of Up-<br>per respiratory<br>tract infections                     | 448 per 1000  | 376 per 1000           | RR 0.84                     |              |  |  |  |
|   | Difference: 72 people less<br>(margin of error: 157 less to 45 more).   |                        | (0.65 to 1.10)              | very low     |  |  |  |
| Adverse effects   | Only one trial [25] reported injuries secondary to exercise, in which there was no significant differences between the two intervention groups (RR 5.67; 0.29 to 108.91). $\bigcirc \bigcirc \bigcirc 3$ very low |                        |                             |              |  |  |  |
| Margin of error: Confidence interval of 95% (IC 95%).<br>RR: Relative risk. |   |                        |                             |              |  |  |  |

**GRADE**: Evidence grades of the GRADE Working Group (see later).

\*Risks **WITHOUT moderate exercise** are based on the risks of the control group in the trials. The Risk **WITH moderate exercise** (and its margin of error) is calculated from the relative effect (and its margin of error).

<sup>1</sup> The certainty of the evidence was downgraded in two levels due to very serious limitations in the design of the trials (randomization, allocation concealment and blinding of participants and personnel)

<sup>2</sup> The certainty of evidence was downgraded in one level due to imprecision, since at the extremes of the confidence interval the effects were opposite.

<sup>3</sup> The certainty of the evidence was downgraded in one level because of risk of bias

<sup>4</sup> The certainty of the evidence was downgraded in two levels due to imprecision, since the confidence interval is broad, because there is only one trial with a very small population.

## About the certainty of the evidence

## (GRADE)\*

#### $\oplus \oplus \oplus \oplus$

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

#### $\oplus \oplus \oplus \bigcirc \bigcirc$

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

#### $\oplus \oplus \bigcirc \bigcirc$

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

#### $\oplus OOO$

Very low: This research does not provide a reliable indication of the likely effect. The likelihood that the effect will be substantially different<sup>†</sup> 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

To whom this evidence does and does not applyThe evidence presented in this summary is broadly applicable to an adult population, for both women and men, without chronic diseases.

An important limitation of the evidence is the lack of mention of the period of the year during which the intervention was conducted, which is fundamental considering the seasonality of upper respiratory tract infections.

None of the trials included high-intensity exercise, which has been suggested could increase the incidence of upper respiratory tract infections<sup>6</sup>.

#### About the outcomes included in this summary

The outcomes presented in the summary of findings table are those critical for the decision-making, according to the opinion of the authors of this summary. In general, they coincide with the outcomes selected by the systematic reviews identified.

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

It is an intervention with an uncertain benefit and poorly reported adverse effects, which although may not be serious, could have relevance in the decision-making process. It is not possible to make an adequate balance between benefits and risks due to the existing uncertainty.

#### Resource considerations

The practice of exercise is a low-cost intervention, with benefits in other health related areas and quality of life. However, its effect on respiratory infections is not clear, so for this particular purpose it is not possible to make an adequate cost-benefit balance.

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

Considering the high levels of sedentary lifestyle in developed countries, most patients and their physicians should lean in favor of performing physical exercise. However, the evidence provided in this summary does not allow to ascertain if there is an effect in the prevention of upper respiratory tract infections, so other behaviours with proved preventive effects should be reinforced.

#### Differences between this summary and other sources

The conclusions of this summary agree with those presented by the identified systematic reviews.

Neither the NICE guideline (National Institute for Health and Clinical Excellence)<sup>26</sup> nor the IDSA guideline (Infectious Diseases Society of America)<sup>27</sup> analyze physical exercise as a measure for prevention of upper respiratory tract infections.

#### Could this evidence change in the future?

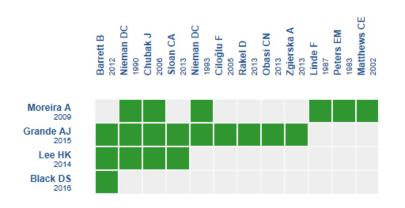
The probability of future evidence changing the conclusions of this summary is high, due to the uncertainty about the benefits. We did not identify a high quality systematic review including all of the trials identified in this summary, so a future review could summarize all the relevant information.

We did not identified relevant ongoing trials in the International Clinical Trials Registry Platform of the World Health Organization.



## 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**: <u>Exercise for prevention of</u> <u>upper respiratory tract infections</u>

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#### 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.

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