Mini-CAT

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Clinical Scenario

Its winter and you're working in a family practice office. Many pts are coming in with runny noses and general malaise. Brenda, a 35 yr old working mom comes in for a checkup and says, "I'm so busy between work and home that I definitely don't have time to get sick! Can those Zinc or Vitamin C pills I hear about prevent colds?"

PICO Question

Does the use of zinc or vitamin c pills help prevent the common cold in adults, during the winter?

P	I	C	O
Adults	Zinc	No supplements	Viral illness prevention
	Vitamin C	Placebo	Viral Prophylaxis
	Zinc micronutrient		Rhinorrhea Prophylaxis
			Common cold prevention

Search Strategy

PubMed

- ***246 articles retrieved*** using (vitamin c) OR (zinc) AND (common cold prevention)
- ***38 articles*** after 10 year publication date filter
- ***4 articles*** were Meta Analysis and/or Systematic Review
- ***3 articles*** were Randomized Control Studies

Google Scholar

- ***83,300 articles retrieved*** using (cold prevention) AND (zinc) AND (vitamin c)
- ***17,300 articles*** after 10 year publication date filter

CUNY OneSearch

- ***464,745 articles retrieved*** using (common cold prevention) AND (zinc) OR (vitamin c)
- ***201,761 articles*** after 10 year publication date filter

Articles chosen

Articles chosen based on the date of publication, level of evidence, route of administration, and primary outcomes.

- PubMed → 3
- Google Scholar → 1

Appraised Articles

1. **Zinc Supplementation Reduces Common Cold Duration among Healthy Adults: A Systematic Review of Randomized Controlled Trials with Micronutrients Supplementation.** *Min Xian Wang, Shwe Sin Win, and Junxiong Pang (2020, July)*
2. **Zinc for the prevention or treatment of acute viral respiratory tract infections in adults: a rapid systematic review and meta-analysis of randomised controlled trials.** *Jennifer Hunter, Susan Arentz, Joshua Goldenberg, Guoyan Yang, Jennifer Beardsley, Stephen P Myers, Dominik Mertz and Stephen Leeder. (2021, Nov 2).*
3. **Vitamin C supplementation slightly improves physical activity levels and reduces cold incidence in men with marginal vitamin C status.** *Johnston, C. S., Barkyoumb, G. M., & Schumacher, S. S. (2014, July 9).*
4. **¿Previene la vitamina C el resfrío común? (Does vitamin C prevent the common cold?)** *Evelyn Gómez, Sebastián Quidel, Gonzalo Bravo-Soto, Ángela Ortigoza (August, 2018)*

Zinc Supplementation Reduces Common Cold Duration among Healthy Adults: A Systematic Review of Randomized Controlled Trials with Micronutrients Supplementation

- Systematic review including 20 studies:
  - 10 studies on zinc
  - 2 studies on vitamins A and E
  - 8 studies on vitamin D

  All assessed for their effects on cold prevention and/or management

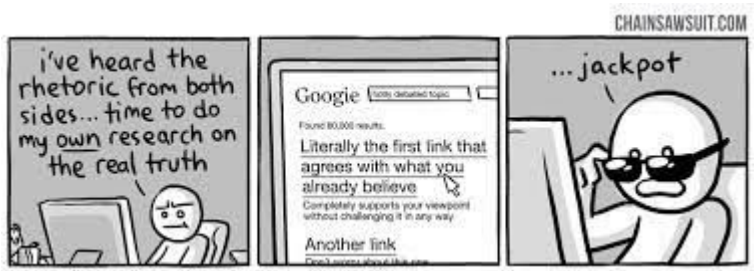
- Inclusion criteria:
  - Published on PubMed, Cochrane Library, Embase, and Scopus in August 2018
  - Published in English
  - Healthy subjects **aged 18-65** (with no comorbidity or chronic disease)
  - Trials that compared single micronutrient orally and placebo or no treatment
  - Trials that reported **primary outcome** (incidence, duration, or severity of colds) or **secondary outcome** (incidence of CAP)
- Exclusion criteria:
  - Not an RCT
  - Measuring more than one micronutrient
  - Micronutrient not administered orally
  - Duplicate record

Results:

- Zinc helps boost the immune system- in children, with a weaker immune system, it has proven to be helpful in preventing colds. However, in adults with a more robust immune system it is not as helpful. **No matter how high the dose is.**
- Zinc deficiency has been associated with immunodeficiency: **if someone is low in zinc, giving them zinc may help prevent a common cold.** This is NOT TRUE for an individual with adequate zinc levels.
- The balance of how much zinc to take is very fine- too much may cause immunodeficiency, too little may not be helpful.
- Give zinc **within 24 hrs of symptoms** for max benefit.
- Efficacy varies with the different forms of zinc. Zinc gluconate is best at replicating zinc ions and preventing colds.
- Use of zinc seems to decrease severity and length **(by 2.25 days)** of colds in adults.

Limitations/Bias:

- Low external validity
- Only studied in Western population and we don't know how it will be applied to other populations
- Cold severity was self reported which lends itself towards a bias
- Publication bias due to the small number of RCTs included



Zinc for the prevention or treatment of acute viral respiratory tract infections in adults: a rapid systematic review and meta-analysis of randomised controlled trials

Criteria: Adult at risk at risk of contracting viral URI taking ZInc supplement

Methods: The study included 28 RCTs with a total of 5,446 participants. These trials were conducted in various settings and populations, including adults at risk of viral respiratory tract infections. In order to answer this question, seventeen databases were searched in April/May 2020 for randomised controlled trials (RCTs), and from April/May 2020 to August 2020 for SARS-CoV-2 RCTs. Cochrane rapid review methods were applied. Quality appraisals used the Risk of Bias 2.0 and Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach.

Procedure:

- The study included systematic reviews and meta analysis from studies that research zinc in relation to URIs.
- Adults at risk of contracting a viral RTI, clinically confirmed viral RTI, or non-specific respiratory tract illness predominantly caused by a viral infection were included, while bacterial infections and other respiratory illnesses were excluded.
- The study included interventions of zinc conjugates, dose, duration, and administration route, with co-interventions excluded unless both groups received the co-intervention.

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Zinc for the prevention or treatment of acute viral respiratory tract infections in adults: a rapid systematic review and meta-analysis of randomised controlled trials

Results and Conclusion:

- Oral or intranasal zinc compared to placebo prevented 5 Respiratory Tract Infections (RTIs) per 100 person-months.
- Sublingual zinc did not prevent clinical colds following human rhinovirus inoculations.
- On average, symptoms resolved 2 days earlier with sublingual or intranasal zinc compared with placebo.
- 19 more adults per 100 likely to remain symptomatic on day 7 without zinc.
- Non-serious adverse events (e.g., nausea, mouth/nasal irritation) were higher with zinc compared to placebo.
- No serious adverse events reported in the 25 RCTs that monitored them.

Limitations: The study failed to provide answers on the comparative efficacy, effectiveness, and acceptability of various zinc formulations and doses as well as mechanism of action.. The study primarily examined adults who are unlikely to be zinc deficient, and the findings may not be applicable to zinc-deficient populations.

Bias: The study suggests that the rapid review methods used in the review may introduce biases, such as selective reporting bias.

¿Previene la vitamina C el resfrío común? (Does vitamin C prevent the common cold?)

Level of Evidence: Meta-Analysis

Sample Method: After exclusion criteria, 8472 patients, including **adults and children**, from 18 RCTs from MEDLINE, EMBASE, Cochrane, and others unspecified.

Outcome studied: All trials evaluated supplementation with oral doses higher than 0.08 g/day of **vitamin C** and the **incidence**, duration, and severity of the cold, among others.

Key Findings: The consumption of vitamin C does not prevent the incidence of common cold with high certainty of evidence based on GRADE.

Vitamin C to prevent the common cold

Patients	Healthy patients, adults and children
Intervention	Vitamin C in doses greater than 0.08 g/day
Comparison	Placebo

Outcome	Absolute effect*		Relative effect (95% CI)	Certainty of evidence (GRADE)
	WITHOUT vitamin C	**WITH vitamin C**		
	Difference: patients per 1000			
Incidence of common cold	487 per 1000	473 per 1000	RR 0.97 (0.92 to 1.01)	⊕⊕⊕⊕ High
	Difference: 15 patients less (Margin of error: 5 less to 39 more)			

Margin of error: 95% confidence interval (CI).
RR: Risk ratio.
GRADE: Evidence grades of the GRADE Working Group (see later).

*The risk **WITHOUT vitamin C** is based on the risk in the control group of the trials. The risk **WITH vitamin C** (and its margin of error) is calculated from relative effect (and its margin of error).

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.

Limitations

- Trials did not evaluate patients with specific comorbidities.
- Does not apply to high performance athletes or other people subjected to major physical stress.
- Trials did not report the season in which they were conducted and did not provide a clear definition of common cold (based on sxs).

Biases

- Did not declare relevant interests for potential conflicts of interest.

Vitamin C Supplementation Slightly Improves Physical Activity Levels and Reduces Cold Incidence in Men with Marginal Vitamin C Status: A Randomized Controlled Trial

Criteria:Healthy, non smoking adult men aged 18–35 years with a body mass index (BMI) less than 34 and plasma vitamin C levels below 45.

Methods:

- 28 individuals were randomly assigned into two groups =vitamin C (*n* = 15) or placebo (*n* = 13) groups.
- The WURRS-21 scale was employed to assess symptoms and the impact of upper respiratory tract infections, specifically symptoms related to the common cold, addressing the severity and the impact of these symptoms on daily living.

Procedures:

- Vitamin C Supplementation: The vitamin C group received 1000 mg of vitamin C daily, while the placebo group received a placebo in the form of capsules. The participants were instructed to take two capsules daily in a divided dose (morning and evening).
- Blood Sample Collection: Fasting venous blood samples were collected at intervals of weeks 4 and 8 for the analysis of plasma vitamin C concentrations. The samples were processed for vitamin C analysis using the 2,4-dinitrophenylhydrazine(Brady's reagent) colorimetric method.

Results:

- Less participants reported cold episodes in the vitamin c group compared to the placebo group. Specifically, 7 participants in the vitamin C group reported colds, while 11 participants in the placebo group reported colds during the eight-week trial.
- The rate ratio for participants with colds in the vitamin C group compared to the placebo group was 0.55, indicating a lower likelihood of developing a cold in the vitamin C group.
- Cold duration was reduced in the vitamin C group compared to the placebo group. The reduction in cold duration was 59%, although the difference did not reach statistical significance.
- Cold severity scores and the impact of cold on daily living scores did not show significant differences between the vitamin C and placebo groups.

Overall, the results suggest a measurable benefit of vitamin C supplementation in reducing the incidence of colds and potentially decreasing the duration of colds in young men with low to average vitamin C status during the study period.

Limitations: Small sample size, only consisting of male participants

Summary of Mini-CAT Grid

Zinc

Wang et. al, 2020:

- Zinc supplementation is not proven to prevent colds in healthy adults with already sufficient amounts of zinc.
- Zinc does help decrease duration and severity of symptoms of the common cold in healthy adults.

Hunter et al., 2021

- In adult populations, there was some evidence suggesting zinc might prevent common cold symptoms and shorten duration.

Vitamin C

Johnston, C. S., Barkyoumb, G. M., & Schumacher, S. S. (2014, July 9).

- The randomized control trial suggest that vitamin C supplementation may provide health advantages by reducing the likelihood of catching a cold and potentially shortening its duration, particularly in individuals with low to average vitamin C status.

Evelyn Gómez, Sebastián Quidel, Gonzalo Bravo-Soto, Ángela Ortigoza (August, 2018)

- The consumption of vitamin C does not prevent the incidence of common cold with high certainty of evidence based on GRADE.

Clinical Bottom Line

- We conclude that common cold prophylaxis using Zinc is not strongly supported by literature.
  - However, it may help in reducing the duration of symptoms by about 2 days.
- We conclude that routine use of Vitamin C supplements does not have any effect at preventing the common cold.
  - However, at higher doses (2 G or more) it may provide some benefit at preventing and decreasing the duration of the common cold.

Future Considerations

- We propose the need for further trials investigating the impact of higher doses of Vitamin C (2mg daily) supplementation, and its efficacy of preventing the common cold.
- Additionally, in future studies regarding micronutrients and their effects on the common cold, a universal system for grading symptom severity should be implemented. This will help in reducing bias in the study.

Sources

1. Hunter, J., Arentz, S., Goldenberg, J., Yang, G., Beardsley, J., Myers, S. P., Mertz, D., & Leeder, S. (2021). Zinc for the prevention or treatment of acute viral respiratory tract infections in adults: a rapid systematic review and meta-analysis of randomised controlled trials. BMJ open, 11(11), e047474. https://doi.org/10.1136/bmjopen-2020-047474
2. Johnston, C. S., Barkyoumb, G. M., & Schumacher, S. S. (2014c, July 9). *Vitamin C supplementation slightly improves physical activity levels and reduces cold incidence in men with marginal vitamin C status: A randomized controlled trial*. Nutrients. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4113757/
3. ¿Previene la vitamina C el resfrío común? (Does vitamin C prevent the common cold?) Evelyn Gómez, Sebastián Quidel, Gonzalo Bravo-Soto, Ángela Ortigoza (August, 2018) https://www.medwave.cl/puestadia/resepis/7235.html?lang=en
4. Wang, M. X., Win, S. S., & Pang, J. (2020). Zinc Supplementation Reduces Common Cold Duration among Healthy Adults: A Systematic Review of Randomized Controlled Trials with Micronutrients Supplementation. *The American journal of tropical medicine and hygiene*, *103*(1), 86–99. https://doi.org/10.4269/ajtmh.19-0718

Questions?