

Scenario: It's winter and you're working in a family practice office. Many patients are coming in with runny noses and general malaise. Brenda, a 35 year old working mother 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?"

Clinical Question:

In the adult population, does ascorbic acid and zinc supplementation provide prophylaxis against common colds, shorten duration, or severity of the symptoms?

PICO Question:

P: Adults

I: Ascorbic acid & zinc supplement

C: Placebo, no intervention

O: Common cold prevention, prophylaxis, symptom relief, shorten duration of symptoms

Search Strategy:

Outline the terms used, databases or other tools used, how many articles returned, and how you selected the final articles to base your CAT on

Articles Chosen for Inclusion (please copy and paste the abstract with link):

1. Vitamin C for preventing and treating the common cold, Harri Hemilä, Elizabeth Chalker expand
PMID: 23440782 PMCID: PMC8078152 DOI: 10.1002/14651858.CD000980.pub4

Background: Vitamin C (ascorbic acid) for preventing and treating the common cold has been a subject of controversy for 70 years.

Objectives: To find out whether vitamin C reduces the incidence, the duration or severity of the common cold when used either as a continuous regular supplementation every day or as a therapy at the onset of cold symptoms.

Search methods: We searched CENTRAL 2012, Issue 11, MEDLINE (1966 to November week 3, 2012), EMBASE (1990 to November 2012), CINAHL (January 2010 to November 2012), LILACS (January 2010 to November 2012) and Web of Science (January 2010 to November 2012). We also searched the U.S. National Institutes of Health trials register and WHO ICTRP on 29 November 2012.

Selection criteria: We excluded trials which used less than 0.2 g per day of vitamin C and trials without a placebo comparison. We restricted our review to placebo-controlled trials.

Data collection and analysis: Two review authors independently extracted data. We assessed 'incidence' of colds during regular supplementation as the proportion of participants experiencing one or more colds during the study period. 'Duration' was the mean number of days of illness of cold episodes.

Main results: Twenty-nine trial comparisons involving 11,306 participants contributed to the meta-analysis on the risk ratio (RR) of developing a cold whilst taking vitamin C regularly over the study period. In the general community trials involving 10,708 participants, the pooled RR was 0.97 (95% confidence interval (CI) 0.94 to 1.00). Five trials involving a total of 598 marathon runners, skiers and soldiers on subarctic exercises yielded a pooled RR of 0.48 (95% CI 0.35 to 0.64). Thirty-one comparisons examined the effect of regular vitamin C on common cold duration (9745 episodes). In adults the duration of colds was reduced by 8% (3% to 12%) and in children by 14% (7% to 21%). In children, 1 to 2

g/day vitamin C shortened colds by 18%. The severity of colds was also reduced by regular vitamin C administration. Seven comparisons examined the effect of therapeutic vitamin C (3249 episodes). No consistent effect of vitamin C was seen on the duration or severity of colds in the therapeutic trials. The majority of included trials were randomised, double-blind trials. The exclusion of trials that were either not randomised or not double-blind had no effect on the conclusions.

Authors' conclusions: The failure of vitamin C supplementation to reduce the incidence of colds in the general population indicates that routine vitamin C supplementation is not justified, yet vitamin C may be useful for people exposed to brief periods of severe physical exercise. Regular supplementation trials have shown that vitamin C reduces the duration of colds, but this was not replicated in the few therapeutic trials that have been carried out. Nevertheless, given the consistent effect of vitamin C on the duration and severity of colds in the regular supplementation studies, and the low cost and safety, it may be worthwhile for common cold patients to test on an individual basis whether therapeutic vitamin C is beneficial for them. Further therapeutic RCTs are warranted.

Link: <https://pubmed.ncbi.nlm.nih.gov/23440782/>

2. Zinc for the common cold, [Meenu Singh](#) and [Rashmi R Das](#), PMID: [25924708](#), PMCID: PMC6457799

Background: The common cold is one of the most widespread illnesses and is a leading cause of visits to the doctor and absence from school and work. Trials conducted in high-income countries since 1984 investigating the role of zinc for the common cold symptoms have had mixed results. Inadequate treatment masking and reduced bioavailability of zinc from some formulations have been cited as influencing results.

Objectives: To assess whether zinc (irrespective of the zinc salt or formulation used) is efficacious in reducing the incidence, severity and duration of common cold symptoms. In addition, we aimed to identify potential sources of heterogeneity in results obtained and to assess their clinical significance.

Search methods: In this updated review, we searched CENTRAL (2012, Issue 12), MEDLINE (1966 to January week 2, 2013), EMBASE (1974 to January 2013), CINAHL (1981 to January 2013), Web of Science (1985 to January 2013), LILACS (1982 to January 2013), WHO ICTRP and [clinicaltrials.gov](#). Randomised, double-blind, placebo-controlled trials using zinc for at least five consecutive days to treat, or for at least five months to prevent the common cold.

Results: Five trials were identified in the updated searches in January 2013 and two of them did not meet inclusion criteria. Included 16 therapeutic trials (1387 participants) and two preventive trials (394 participants). Intake of zinc was associated with a significant reduction in the duration (days) (mean difference (MD) -1.03, 95% confidence interval (CI) -1.72 to -0.34) ($P = 0.003$) (I² statistic = 89%) but not the severity of common cold symptoms (MD -1.06, 95% CI -2.36 to 0.23) ($P = 0.11$) (I² statistic = 84%). The proportion of participants who were symptomatic after seven days of treatment

was significantly smaller (odds ratio (OR) 0.45, 95% CI 0.20 to 1.00) ($P = 0.05$) than those in the control, (I2 statistic = 75%). The incidence rate ratio (IRR) of developing a cold (IRR 0.64, 95% CI 0.47 to 0.88) ($P = 0.006$) (I2 statistic = 88%), school absence ($P = 0.0003$) and prescription of antibiotics ($P < 0.00001$) was lower in the zinc group. Overall adverse events (OR 1.58, 95% CI 1.19 to 2.09) ($P = 0.002$), bad taste (OR 2.31, 95% CI 1.71 to 3.11) ($P < 0.00001$) and nausea (OR 2.15, 95% CI 1.44 to 3.23) ($P = 0.002$) were higher in the zinc group. The very high heterogeneity means that the averaged estimates must be viewed with caution.

Conclusion: Regarding prophylactic zinc supplementation, currently no firm recommendation can be made. Zinc administered within 24 hours of onset of symptoms reduces the duration of common cold symptoms in healthy people but some caution is needed due to the heterogeneity of the data.

Keywords: Humans, Common Cold, Common Cold/drug therapy, Common Cold/prevention & control, Dosage Forms, Gluconates, Gluconates/adverse effects, Gluconates/therapeutic use, Randomized Controlled Trials as Topic, Severity of Illness Index, Zinc, Zinc/adverse effects, Zinc/therapeutic use, Zinc Acetate, Zinc Acetate/adverse effects, Zinc Acetate/therapeutic use, Zinc Compounds, Zinc Compounds/adverse effects, Zinc Compounds/therapeutic use, Zinc Sulfate, Zinc Sulfate/adverse effects, Zinc Sulfate/therapeutic use

Link: <https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD001364.pub4/full>

3. Extra Dose of Vitamin C Based on a Daily Supplementation Shortens the Common Cold: A Meta-Analysis of 9 Randomized Controlled Trials

Li Ran, Wenli Zhao, Jingxia Wang, Hongwu Wang, Ye Zhao, Yiider Tseng, and Huaïen Bu

Aim: Determine if vitamin C is effective in treating the common cold

Methods: Cochrane, Elsevier, National Library of Medicine (PubMed), and China National Knowledge Infrastructure (CNKI), VIP databases, and WANFANG databases were searched with a result of 9 chosen randomized placebo control trials in a meta-analysis

Results: Those taking an extra-therapeutic dose of vitamin C were found to have a cold of shorter duration, relieve symptoms such as chest pain, and return to the outdoors sooner than control.

Conclusions: Even patients who are currently taking daily vitamin C supplements may benefit from extra doses of vitamin C in early stages of the common cold

KEYWORDS: URI, Common Cold, Vitamin C, Ascorbic Acid

Link: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6057395/>

4. Citation

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

BACKGROUND: The common cold had resulted in significant economic and social burden worldwide. The effect of vitamin C on preventing common cold in healthy adults has been investigated extensively, but not that of other micronutrients. Thus, we aim to assess the effects of providing micronutrients singly through oral means, on cold incidence, and/or management (in terms of cold duration and symptom severity) in healthy adults from systematically searched randomized controlled trials.

MATERIALS AND METHODS: The systematic search methods were carried out in accordance with the relevant guidelines and regulations in the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines in this systematic review. For each micronutrient of interest, a literature search identifying relevant studies published in PubMed, Cochrane Library, Embase, and Scopus was carried out within the month of August 2018 using specific search terms defined with the population, intervention, comparator, outcome, study design criteria. Studies using a combination of > 1 micronutrient as an intervention or administered a micronutrient via non-oral methods were excluded because it does not address the research question in this review. Self-reported colds are defined by the presence of at least two of the symptoms in a day, which are not attributable to allergy.

RESULTS: The pooled summary estimate of 11 studies showed a significant reduction in cold duration by 1.36 days (95% CI: -2.43, -0.29) when micronutrients, specifically vitamin D or zinc, was administered on cold infection. Based on pooled results from the 6 studies, cold duration was estimated to be reduced by 2.25 days (95% CI: -3.39, -1.12) when zinc lozenges used to manage cold, compared with a placebo. In addition to serious inconsistency observed ($I^2 = 83\%$, $P < 0.00001$), there was a serious risk of bias due to design limitations of pooled studies. Thus, the GRADE certainty of evidence for zinc on this outcome is low.

CONCLUSION: Overall, the results suggest that micronutrients other than vitamin C may have limited effects on cold prevention among healthy adults, but zinc shows potential reduction of cold duration.

KEYWORDS: Cold duration; vitamin C; micronutrient; cold severity; cold prevention; zinc

Link: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7356429/pdf/tpmd190718.pdf>

Summary of the Evidence:

Author (Date)	Level of Evidence	Sample/Setting (# of subjects/studies, cohort definition etc.)	Outcome(s) studied	Key Findings	Limitations and Biases
Harri Hemilä, Elizabeth Chalker (2013)	Meta Analysis	63 studies including double blind randomized	<u>Primary:</u> Studied incidence and duration of the common	Benefit of vitamin C supplementation in the general population is limited but may be	Few trials' results showed a mild to moderate level of heterogeneity - possibly

		trials & separate comparisons of vitamin C against placebo	colds with vitamin C supplementation <u>Secondary:</u> Severity of the episodes & evidence of Vitamin C side effect for treatment	helpful to people exposed to brief periods of severe physical exercise.	due to the differences in clinical settings and parameters of each study Some studies included did not report statistical methods suitable for meta analysis and study result finding was inconsistent. Unreported biases in few studies may have skewed the results.
Meenu Singh, Rashmi R. Das (2015)	Systematic Review of Randomized Control Trials	18 Trials: 1,781 participants	<u>Primary outcomes</u> Incidence of the common cold. Duration of symptoms. Severity of symptoms. <u>Secondary outcomes</u> Proportion of participants symptomatic after three, five or seven days of treatment. Time to resolution of individual symptoms: cough, nasal congestion, nasal drainage and sore throat. Change in individual severity symptom scores: cough, nasal score. Work absence (days). Antibiotic use. Adverse events	Zinc used to prevent common cold for at least 5 months reduces incidence, work absences and prescription of antibiotics (although not required for cold). No firm recommendation can be made because of insufficient evidence. Proportion of participants symptomatic after 3 days of treatment: no significant difference between intervention and control group. Proportion of participants symptomatic after 5 days of treatment: no significant difference between intervention and control group had a significant difference between intervention and control group. Proportion of	No serious study limitations: double blinded study to decrease risk of bias. High heterogeneity: zinc was distributed differently: zinc gluconate, acetate lozenges, and zinc syrup with wide range doses.

				participants symptomatic after 7 days of treatment: there was a significant difference between intervention and control group	
Li Ran, Wenli Zhao, Jingxia Wang, Hongwu Wang, Ye Zhao, Yiider Tseng, and Huaïen Bu (2018)	Meta-Analysis	9 Studies, 3,497 subjects	Impact of vitamin C supplementation on duration and severity of symptoms of the common cold	Fever, chills, and other symptoms relieved by combination of supplemental and therapeutic doses of vitamin C. The time of indoor confinement and the mean duration of illness were both shortened	Incorporates studies that have a very wide time span, 1950 to present.
Min Xian Wang, Shwe Sin Win, and Junxiong Pang (2021)	Systematic Review	10 studies, 938 subjects	Zinc gluconate or zinc acetate in lozenges or capsules with 5 mg to 42.9 mg of zinc effect on cold prevention (followed for 7 months) and time til resolution of symptoms	Self-reported and clinically diagnosed cold incidence Subjective symptom severity daily	Most zinc studies provided inadequate details on random sequence generation and allocation concealment methods. Across all studies, there was a high risk of other bias mainly due to underpowered studies or the lack of clinical or laboratory confirmation for cold resolution.

Conclusion(s):

-Zinc used to prevent common cold for at least 5 months reduced incidence, work absences and prescription of antibiotics (although not required for cold). However, no firm recommendation can be

made due to insufficient evidence. In regards to cold duration, 7 days of zinc supplementation significantly reduced symptoms. (Meenu Singh, Rashmi R. Das 2015)

-Zinc supplementation was observed to potentially reduce cold duration by 2.25 days (Wang, Win & Pang, 2021)

- Cold duration and symptom severity was significantly reduced when patients with common cold were provided with a combination of 1,000 mg vitamin C and 10 mg zinc together for 5 days

- Supplemental vitamin C combined with therapeutic doses are effective in decreasing duration of illness by a half day, with a degree of relief from symptoms including chest pain, fever, and chills.

Clinical Bottom Line:

There is inconsistent data on whether vitamin C and/or zinc supplementation should be recommended in the general population. However, current literature does show the possibility of reduction in symptoms, duration and prevention of cold. This data along with the low risk profile of supplementing appropriate amounts of vitamin C and zinc is why vitamin C and zinc can be recommended for cold duration, symptoms and prevention.

It is important to discuss possible interactions, dosage, and lack of consistent statistical significance with these supplementations.