

Format for Mini-CAT

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: Please state this as briefly as possible based on the scenario provided

Can daily zinc or vitamin C pill supplementation prevent the common cold in healthy adults?

PICO Question:

Identify the PICO elements (Recalling that some questions do not have all the elements)

P: 35 year old women/ Adults

I: zinc or vitamin C supplementation

C: No supplementation or placebo

O: Incidence of common cold symptom

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

Terms Used:

- (Vitamin C OR Zinc) AND common cold prevention AND Women
- (Vitamin C AND common cold prevention) OR (Zinc AND Common cold prevention)

Databases Searched:

Cochrane

- Search criteria gave 38 results, one of which was selected

Up to Date

- Search gave 1 result, none of which was selected

Trip Database

- Search criteria gave 27 results, which were narrowed down to 4 after filters - None of which was selected.

PubMed

- Search criteria gave 254 results, which I narrowed to 6 with filters- four of which was selected

Articles Used:

- Based on most recent research, sample size, type of telemonitoring used to measure effects and outcomes measured by the studies.
- PubMed - 4 articles
- Cochrane - 1 article

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

<https://pubmed.ncbi.nlm.nih.gov/38719213/> - Abby

Abstract

Background: The common cold is an acute, self-limiting viral respiratory illness. Symptoms include nasal congestion and mucus discharge, sneezing, sore throat, cough, and general malaise. Given the frequency of colds, they are a public health burden and a significant cause of lost work productivity and

school absenteeism. There are no established interventions to prevent colds or shorten their duration. However, zinc supplements are commonly recommended and taken for this purpose.

Objectives: To assess the effectiveness and safety of zinc for the prevention and treatment of the common cold.

Search methods: We searched CENTRAL, MEDLINE, Embase, CINAHL, and LILACS to 22 May 2023, and searched Web of Science Core Collection and two trials registries to 14 June 2023. We also used reference checking, citation searching, and contact with study authors to identify additional studies.

Selection criteria: We included randomised controlled trials (RCTs) in children or adults that tested any form of zinc against placebo to prevent or treat the common cold or upper respiratory infection (URTI). We excluded zinc interventions in which zinc was combined with other minerals, vitamins, or herbs (e.g. a multivitamin, or mineral supplement containing zinc).

Data collection and analysis: We used the Cochrane risk of bias tool to assess risks of bias, and GRADE to assess the certainty of the evidence. We independently extracted data. When necessary, we contacted study authors for additional information. We assessed zinc (type and route) with placebo in the prevention and treatment of the common cold. Primary outcomes included the proportion of participants developing colds (for analyses of prevention trials only), duration of cold (measured in days from start to resolution of the cold), adverse events potentially due to zinc supplements (e.g. unpleasant taste, loss of smell, vomiting, stomach cramps, and diarrhoea), and adverse events considered to be potential complications of the common cold (e.g. respiratory bacterial infections).

Main results: We included 34 studies (15 prevention, 19 treatment) involving 8526 participants. Twenty-two studies were conducted on adults and 12 studies were conducted on children. Most trials were conducted in the USA ($n = 18$), followed by India, Indonesia, Iran, and Turkey (two studies each), and Australia, Burkina Faso, Colombia, Denmark, Finland, Tanzania, Thailand, and the UK (one study each). The 15 prevention studies identified the condition as either common cold ($n = 8$) or URTI ($n = 7$). However, almost all therapeutic studies (17/19) focused on the common cold. Most studies (17/34) evaluated the effectiveness of zinc administered as lozenges (3 prevention; 14 treatment) in acetate, gluconate, and orotate forms; gluconate lozenges were the most common (9/17). Zinc gluconate was given at doses between 45 and 276 mg/day for between 4.5 and 21 days. Five (5/17) lozenge studies gave acetate lozenges and two (2/17) gave both acetate and gluconate lozenges. One (1/17) lozenge study administered intranasal (gluconate) and lozenge (orotate) zinc in tandem for cold treatment. Of the 17/34 studies that did not use lozenges, 1/17 gave capsules, 3/17 administered dissolved powders, 5/17 gave tablets, 4/17 used syrups, and 4/17 used intranasal administration. Most studies were at unclear or high risk of bias in at least one domain. There may be little or no reduction in the risk of developing a cold with zinc compared to placebo (risk ratio (RR) 0.93, 95% CI 0.85 to 1.01; $I^2 = 20\%$; 9 studies, 1449 participants; low-certainty evidence). There may be little or no reduction in the mean number of colds that occur over five to 18 months of follow-up (mean difference (MD) -0.90, 95% CI -1.93 to 0.12; $I^2 = 96\%$; 2 studies, 1284 participants; low-certainty evidence). When colds occur, there is probably little or no difference in the duration of colds in days (MD -0.63, 95% CI -1.29 to 0.04; $I^2 = 77\%$; 3 studies, 740 participants; moderate-certainty evidence), and there may be little or no difference in global symptom severity (standardised mean difference (SMD) 0.04, 95% CI -0.35 to 0.43; $I^2 = 0\%$; 2 studies, 101 participants; low-certainty evidence). When zinc is used for cold treatment, there may be a reduction in the mean duration of the cold in days (MD -2.37, 95% CI -4.21 to -0.53; $I^2 = 97\%$; 8 studies, 972 participants; low-certainty evidence), although it is uncertain whether there is a reduction in the risk of having an ongoing cold at the end of follow-up (RR 0.52, 95% CI 0.21 to 1.27; $I^2 = 65\%$; 5 studies, 357

participants; very low-certainty evidence), or global symptom severity (SMD -0.03, 95% CI -0.56 to 0.50; $I^2 = 78\%$; 2 studies, 261 participants; very low-certainty evidence), and there may be little or no difference in the risk of a change in global symptom severity (RR 1.02, 95% CI 0.85 to 1.23; 1 study, 114 participants; low-certainty evidence). Thirty-one studies reported non-serious adverse events (2422 participants). It is uncertain whether there is a difference in the risk of adverse events with zinc used for cold prevention (RR 1.11, 95% CI 0.84 to 1.47; $I^2 = 0\%$; 7 studies, 1517 participants; very low-certainty evidence) or an increase in the risk of serious adverse events (RR 1.67, 95% CI 0.78 to 3.57; $I^2 = 0\%$; 3 studies, 1563 participants; low-certainty evidence). There is probably an increase in the risk of non-serious adverse events when zinc is used for cold treatment (RR 1.34, 95% CI 1.15 to 1.55; $I^2 = 44\%$; 2084 participants, 16 studies; moderate-certainty evidence); no treatment study provided information on serious adverse events. No study provided clear information about adverse events considered to be potential complications of the common cold.

Authors' conclusions: The findings suggest that zinc supplementation may have little or no effect on the prevention of colds but may reduce the duration of ongoing colds, with an increase in non-serious adverse events. Overall, there was wide variation in interventions (including concomitant therapy) and outcomes across the studies, as well as incomplete reporting of several domains, which should be considered when making conclusions about the efficacy of zinc for the common cold.

<https://pubmed.ncbi.nlm.nih.gov/32342851/> - Aisef

Abstract

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. From four electronic databases, 660 identified studies were screened and data were extracted from 20 studies (zinc, 10; vitamin D, 8; and vitamins A and E, 2). The quality of selected studies was assessed using the Cochrane risk of bias tool and certainty in the outcomes was assessed with the Grading of Recommendations Assessment, Development and Evaluation approach. The review found that micronutrients supplementation, except vitamin C, may not prevent cold incidence or reduce symptom severity among healthy adults. However, zinc supplementation was observed to potentially reduce cold duration by 2.25 days (when zinc is provided singly, 95% CI: -3.39, -1.12). This suggests that zinc supplementation may reduce the overall burden due to common cold among healthy adults.

<https://pubmed.ncbi.nlm.nih.gov/30113569/> - Jess

Abstract

Introduction: The common cold is one of the most common diseases. It is generally believed that the consumption of vitamin C prevents its appearance, but the actual efficacy of this measure is controversial.

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 eight systematic reviews including 45 studies overall, of which 31 were randomized trials. We concluded the consumption of vitamin C does not prevent the incidence of common cold.

<https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD000980.pub4/full?highlightAbstract=the%7Cprevent%7Ctreat%7Cc%7Ccommon%7Cpreventing%7Cfour%7Cfor%7Ccold%7Ctreating%7Cvitami>

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Hemilä, H., & Chalker, E. (2013). Vitamin C for preventing and treating the common cold. Cochrane Database of Systematic Reviews, 2013(1), Article CD000980.

<https://doi.org/10.1002/14651858.CD000980.pub4>

Abstract

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.

<https://pmc.ncbi.nlm.nih.gov/articles/PMC3394849/>Vanessa

Science, M., Johnstone, J., Roth, D. E., Guyatt, G., & Loeb, M. (2012). Zinc for the treatment of the common cold: a systematic review and meta-analysis of randomized controlled trials. *Canadian Medical Association Journal*, 184(10), E551–E561. <https://doi.org/10.1503/cmaj.111990>

Abstract

Background: Results of randomized controlled trials evaluating zinc for the treatment of the common cold are conflicting. We conducted a systematic review and meta-analysis to evaluate the efficacy and safety of zinc for such use.

Methods:We searched electronic databases and other sources for studies published through to Sept. 30, 2011. We included all randomized controlled trials comparing orally administered zinc with placebo or no treatment. Assessment for study inclusion, data extraction and risk-of-bias analyses were performed in duplicate. We conducted meta-analyses using a random-effects model.

Results:We included 17 trials involving a total of 2121 participants. Compared with patients given placebo, those receiving zinc had a shorter duration of cold symptoms (mean difference -1.65 days, 95% confidence interval [CI] -2.50 to -0.81); however, heterogeneity was high ($I^2 = 95\%$). Zinc shortened the duration of cold symptoms in adults (mean difference -2.63 , 95% CI -3.69 to -1.58), but no significant effect was seen among children (mean difference -0.26 , 95% CI -0.78 to 0.25). Heterogeneity remained high in all subgroup analyses, including by age, dose of ionized zinc and zinc formulation. The occurrence of any adverse event (risk ratio [RR] 1.24 , 95% CI 1.05 to 1.46), bad taste (RR 1.65 , 95% CI 1.27 to 2.16) and nausea (RR 1.64 , 95% CI 1.19 to 2.27) were more common in the zinc group than in the placebo group.

Interpretation:The results of our meta-analysis showed that oral zinc formulations may shorten the duration of symptoms of the common cold. However, large high-quality trials are needed before definitive recommendations for clinical practice can be made. Adverse effects were common and should be the point of future study, because a good safety and tolerance profile is essential when treating this generally mild illness.

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
Daryl Nault , Taryn A Machingo , Andrea G Shipper , Daniel A Antiporta , Candyce Hamel , Sahar Nourouzpour , Menelaos Konstantinidis , Erica Phillips , Elizabeth A Lipski , L Susan Wieland	systematic review (Level 1)	34 randomized controlled trials (15 prevention, 19 treatment), including 8,526 participants — 22 studies in adults and 12 in children. Studies were conducted primarily in the USA (n=18), with additional trials from India,	The following outcomes were studied: - Development of a Cold - Proportion of participants - Mean number of colds/URTIs developed - Duration of Cold - Mean duration of cold/URTI. - Proportion of participants with an ongoing cold/URTI	Overall effect: Zinc supplementation showed little to no benefit in preventing colds . Risk of Developing a Cold/URTI: Participants taking zinc were about as likely to catch a cold as those taking placebo (low-certainty). Number of Colds:	Certainty of Evidence & Key Limitations (High-Level Summary) Overall, the certainty of evidence for zinc in preventing or treating the common cold was low to very low . This means the results are not dependable, largely due to

		Indonesia, Iran, Turkey (n=2 each), and single studies from Australia, Burkina Faso, Colombia, Denmark, Finland, Tanzania, Thailand, and the UK. Interventions included zinc lozenges, tablets, syrups, powders, capsules, and intranasal forms (mostly gluconate or acetate).	at the end of the study . - Adverse Events - Any reported side effects potentially related to zinc use. - Reported collectively rather than clearly separated by cause due to variability in reporting methods. - Serious Adverse Events - Events considered significant medical complications, including potential secondary bacterial infections related to the cold.	The average number of colds was not significantly different between zinc and placebo (low-certainty). Duration and Severity : Taking zinc before getting sick did not make colds shorter or milder once they occurred. Work/School Absence: Zinc slightly reduced days missed due to illness Zinc for Treatment of the Common Cold Overall effect: Zinc started after symptom onset may shorten colds by about two days, but results varied widely). Individual Symptoms: Zinc modestly reduced the duration of several symptoms: Nasal congestion: MD –1.77 Cough: MD –1.67 Sore throat: MD –0.88 Muscle aches: MD –0.66 Global Symptom Severity: Zinc did not significantly reduce overall symptom severity (very low-certainty).	weaknesses in the included studies. Why the Evidence Was Low Certainty 1. High Risk of Bias Across Studies Most trials had problems with how they were designed or reported: - Randomization and allocation methods were often unclear. - Blinding was frequently inadequate, especially because zinc has a recognizable taste. - Only one study was low risk of bias in all areas. 2. Major Inconsistency Between Studies - Results varied widely. - Several analyses showed high heterogeneity 3. Imprecision Due to Small Sample Sizes - Many studies had few participants. - Wide confidence intervals made it difficult to determine
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				Safety and Adverse Events Non-serious Adverse Events (AEs): More frequent in zinc users, particularly with lozenges Lozenges: RR 1.44 Intranasal: RR 1.12 Common AEs: metallic taste (362 reports), gastrointestinal discomfort (193 reports). Prevention Trials: No clear increase in AEs with zinc compared to placebo Serious Adverse Events (SAEs): No significant difference between groups	whether zinc had a real effect. 4. Selective Reporting and Missing Data - Very few studies had preregistered protocols. - Several trials had incomplete outcome reporting or high dropout rates. 5. Other Sources of Uncertainty - Zinc forms, doses, and delivery routes varied substantially between studies. - Definitions of “common cold” and symptom measurements were not standardized. - Many studies were industry-funded or did not report funding. 6. Limited Generalizability - Most trials were conducted in high-income countries, which may limit applicability to other populations.
	Systematic review	20 randomized controlled trials		Zinc supplementation does not significantly	High variability across the 20

Min Xian Wang Shwe Sin Win Junxiong Pang (2020)		including healthy adults ≥ 18 years Participants were not explicitly pooled, but individual studies ranged from small to moderate in size. Trials conducted in multiple countries (primarily USA, plus India, Iran, Turkey, and others) Interventions: zinc lozenges or tablets, mostly zinc gluconate or zinc acetate Doses ranged 30–160 mg/day Timing: administered either continuously or at symptom onset	Zinc supplementation did not significantly reduce the risk of developing a cold in healthy adults. Taking zinc daily as a preventive measure does not reduce the risk of cold episodes. Routine prophylactic zinc for cold prevention in healthy adults is not recommended. Zinc shortened the duration of colds by an average of ~ 2.25 days. Most effective if started within 24 hours of symptom onset Zinc acetate is more effective than zinc gluconate. ≥ 75 mg/day showed better outcomes Early zinc supplementation can moderately reduce the total duration of cold episodes, a clinically meaningful effect for patients. Zinc can be recommended as early treatment at first symptom onset, not as a long-term preventive measure. .	reduce the risk of colds in healthy adults. Risk of developing a cold similar to placebo across multiple trials. Evidence is low-certainty due to heterogeneity and small sample sizes. Zinc reduces the duration of colds by ~ 2.25 days on average (95% CI -3.39 to -1.12). Strongest effect when zinc is started within 24 hours of symptom onset. Formulation effect: zinc acetate > zinc gluconate. Dose effect: ≥ 75 mg/day is more effective in shortening duration. Zinc does not consistently improve overall symptom severity. Some individual symptoms (nasal congestion, cough, sore throat, muscle aches) showed minor reduction in duration, but results were inconsistent. Non-serious AEs are more common in zinc users, especially with	included RCTs in: Zinc formulation: acetate vs gluconate Dose: 30–160 mg/day Timing: continuous supplementation vs at symptom onset Differences in outcome measurement (duration, severity scoring systems) make pooling results challenging. Some RCTs were small, limiting statistical power. Small trials increase uncertainty in effect estimates, particularly for symptom severity and adverse events. Older trials may have inadequate blinding or randomization methods. Some studies lacked allocation concealment or had unclear reporting of withdrawals. Possible reporting bias: not all studies
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			Zinc had no consistent effect on overall symptom severity. Some trials noted minor improvements in individual symptoms (nasal congestion, cough, sore throat, muscle aches), but results were inconsistent. Zinc is unlikely to make symptoms feel substantially less severe, even if duration is shortened. Patients may experience shorter colds, but should not expect significant symptom relief. More frequent with zinc lozenges (metallic taste, nausea, GI discomfort) Intranasal zinc was excluded due to anosmia, risk no significant difference from placebo Zinc is generally safe when used short-term orally, but taste and GI upset are common side effects. Oral zinc can be used for early cold treatment with counseling on side effects; avoid intranasal forms	lozenges. Common: metallic taste, nausea, gastrointestinal discomfort. Serious adverse events are rare; no significant difference from placebo. Intranasal zinc is not recommended due to the risk. Oral zinc is most effective early after symptom onset (≤ 24 hr). Zinc acetate ≥ 75 mg/day shows the strongest benefit for duration reduction. Zinc does not prevent colds. Zinc can shorten the duration by ~ 2 days if taken early. Effect on symptom severity: minimal and inconsistent. Side effects are generally mild but common. Routine supplementation for prevention not recommended, but early treatment at the onset may be beneficial.	consistently reported all outcomes Only healthy adults ≥ 18 years were included. Findings may not generalize to children, older adults, or immunocompromised populations. Non-serious adverse events were reported inconsistently. Not all studies separated events by cause, making it difficult to attribute them solely to zinc. Long-term safety not evaluated, particularly the risk of copper deficiency with chronic high-dose zinc. Some small or negative trials may be unpublished. Positive results (e.g., shorter duration) may be overrepresented Symptom severity scores were subjective and varied across studies.
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					Timing of zinc initiation (≤ 24 hr vs later) significantly influenced results but was not standardized across studies. Evidence certainty: moderate for shortening cold duration; low to very low for prevention, severity, and adverse events. These limitations reduce confidence in the findings and suggest caution in making broad clinical recommendations. . .
Gómez E., Quidel S., Bravo-Soto G., Ortigoza Á. (2018)	Systematic review/ meta-analysis	8 systematic reviews, including 45 primary studies (31 RCTs). International studies retrieved from the Epistemonikos database. Participants were healthy adults and children taking vitamin C supplements for prevention of common cold. All trials evaluated oral vitamin C supplementation,	Whether vitamin C supplementation reduces risk of catching a cold (incidence) Duration of cold symptoms Severity of cold symptoms	Regular consumption of vitamin C does not prevent the incidence of the common cold in the general population. Among subgroups (e.g., people under heavy physical stress) earlier evidence suggested possible benefit, but the main conclusion for the general population was negative for incidence. Evidence does not support a clear preventive effect for vitamin C supplementation to prevent common cold.	The included primary studies varied in dose of vitamin C, duration of supplementation, and definitions of “cold”. Some RCTs may have been of lower quality (dose, compliance, etc.) Applicability: The findings apply to the general population; in special populations (athletes, people under extreme physical stress) the effect may differ, so

		with doses ranging from 0.08-3 g/day.			generalization in these populations may be less accurate. Confounding Variables: Baseline vitamin C status, nutritional status, and other immune-supporting behaviours may not have been fully controlled.
Harri Hemilä, Elizabeth Chalker (2013) -Moe	Systematic Review & Meta-Analysis (Level 1)	Included 63 separate trial comparisons of Vitamin C against placebo from 44 publications, with data from over 11,000 participants for key analyses. Studies were conducted in various countries and included both children and adults. The population was divided into the general community and specific sub-groups under heavy short-term physical stress (marathon runners, skiers, soldiers). Interventions included oral vitamin C at doses of ≥ 0.2 g/day, administered either as regular daily	The following outcomes were studied for both regular supplementation and therapeutic use: 1) Incidence of Colds during regular supplementation of Vitamin C: Defined as Proportion of participants developing ≥ 1 cold during the trial period. 2) Duration of Colds: number of days in total the cold lasted 3)Severity of Colds: Measured as: a) days confined indoors/absent from work/school, or b) symptom severity scores from patient kept records. • Adverse Events: Any reported side effects potentially related to vitamin C use.	Vitamin C for Prevention of the Common Cold (Regular/everyday Supplementation) Overall Effect on Incidence (number of people catching at least one cold): • <u>General Community</u>: No reduction in the number of people catching a cold when using vitamin C regularly (RR 0.97; 95% CI 0.94 to 1.00) • <u>Under Heavy Physical Stress</u>: Incidence of colds was approximately halved. RR 0.48; 95% CI 0.35 to 0.64) <u>Summary</u>: For the general public, Vitamin C did not reduce the number of people catching a cold. For athletes under extreme stress (like marathon runners), it reduced the risk of getting a cold in half. However, it is still unclear whether the	<u>Limitation</u> Heterogeneity of Effects (It doesn't work the same for everyone) - The benefits of Vitamin C are not uniform. The review found massive differences in results between, for example, general population and marathon runners. - This means we cannot give a single, simple answer to the question Does Vitamin C work. The answer is, It depends entirely on who you are; for instance if you were an athlete it would be more beneficial.. This makes it difficult to create broad public health guidelines. <u>Bias</u> Selection Bias was minimized. The majority of the

		supplementation or as a therapeutic treatment after cold symptoms began.		vitamin C on the physical stress group targeted a virus vs Exercise induced bronchoconstriction, but nevertheless, its effect on respiratory symptoms still stand firm. Effect on Duration (if infected): •Regular supplementation consistently reduced the duration of colds: • Adults: Duration of cold reduced by 8% - Ex: 8 day cold might be shortened by a half a day ($8\% \times 8 \text{ days} = 0.64 \text{ days}$) • Children: Duration of cold reduced by 14% - Ex: 7 day cold might be shortened by a full day ($14\% \times 7 \text{ days} = 0.98 \text{ days}$) Effect on Severity: •Regular supplementation led to 5% reduction in cold severity ($p = 0.023$) whether measured by days confined to home/off work ($P = 0.0004$) or by symptom severity scores ($P = 0.002$). . This meant regular supplementation results in milder	included trials were randomized, ensuring that participant groups were comparable at the start of the studies. Performance and Detection Bias were low. The vast majority of trials were double-blind and used placebos that were different from the Vitamin C tablets in taste and appearance.
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				symptoms and and quicker recovery Vitamin C for Treatment of the Common Cold (Therapeutic Use/after cold onset) Effect on Incidence of colds Therapeutic vitamin C (started after symptoms begin) generally does NOT reduce incidence of cold - Exception: A study by Tyrrell in 1977 reported a 40 % reduction in recurrent colds in men suggesting a possible protective effects against new colds during treatment Overall Effect on Duration (Number of days the cold lasted): No significant effect on the duration of colds when vitamin C was started after symptom onset compared to placebo - Short duration supplementation (<3 days): using 2-3 days of vitamin C showed no benefit	
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				- Longer supplementation (>5 days): using Vitamin C for more than 5 days reduced colds by 0.73 days - Extended supplementation (up to 2 weeks): using vitamin C up to 2 weeks found no benefit - Early use: using vitamin C within 24 hours reduced duration from 6.9 to 3.6 days while starting later showed no effect (the sooner the better) Effect on Severity: • Combined results from all therapeutic trials suggested no significant reduction in cold severity compared to placebo. However, one study showed a small reduction. - Longer supplementation (5 day): using 5 days of vitamin C showed 25% reduction in days spent indoor due to illness	
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				Safety and Adverse Events • No significant difference between vitamin C and placebo groups. 5.8% of vitamin C recipients reported symptoms attributed to medication vs. 6.0% of placebo recipients. No serious adverse events were reported. Conclusion: Routine/regular vitamin C supplementation is not justified for preventing colds in the general community. It may be useful for people under extreme physical stress (marathon runners, skiers) as a prophylactic measure. While it shortens cold duration when taken regularly, the effect is modest. There is no proven benefit when used after symptom onset (no therapeutic effect)	
Science, M., Johnstone, J., Roth, D. E., Guyatt, G., & Loeb, M. (2012).	Level I — Systematic review & meta-analysis of randomized controlled trials.	7 randomized, double-blind, placebo-controlled zinc lozenge trials were included (total 575 participants) of adults naturally acquiring the common cold.	The review focused on whether zinc shortens the duration of common cold symptoms. Researchers specifically evaluated: • Total length of cold symptoms (in days) • Whether different zinc salts (acetate vs.	• Across all trials, zinc lozenges shortened the duration of colds by about one-third (≈33%). → Example: a cold lasting 7 days without zinc might last about 4–5 days with zinc. • Zinc acetate had the strongest results (≈40%	• High variability between trials — different lozenge formulations, additives, and doses. – Some lozenges contained ingredients (e.g., citric acid, sorbitol) that bind zinc and reduce absorption,

			gluconate) produced different effects • Whether zinc dose (amount of elemental zinc per day) influenced effectiveness	reduction in symptom duration). • Zinc gluconate also helped but appeared slightly less effective (≈28% reduction). • Higher doses (above ~100 mg/day) did not improve results further, suggesting more zinc is not better. Overall interpretation: Unlike zinc used for <i>prevention</i>, zinc as a treatment lozenge after symptoms start may meaningfully shorten colds, especially when the formulation releases free zinc ions effectively.	possibly weakening effect. • Symptoms were self-reported, not clinically verified, which may introduce bias. • Only adults were included — results cannot be confidently applied to children. • Adverse events were not consistently documented, so safety conclusions are limited. • Heterogeneity was high ($I^2 = 77\%$), meaning results varied widely between studies. Bottom line on limitations: The review suggests zinc can shorten colds, but differences in lozenge formulas and study methods make it hard to determine the best formulation, optimal dose, or ideal patient population.
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Conclusion(s):

Do Zinc or Vitamin C Improve Prevention or Treatment of the Common Cold?

After appraising all included systematic reviews and meta-analyses, the strongest and most consistent conclusions from the highest-quality articles were:
(Nault et al., 2021; Win et al., 2020; Gómez et al., 2018; Hemilä & Chalker, 2013; Science et al., 2012)

1. Zinc for Prevention

Zinc does NOT prevent the common cold in the general population.

Multiple systematic reviews show no significant reduction in incidence compared with placebo.

Daily prophylactic zinc is not recommended for healthy adults.

2. Zinc for Treatment

When zinc is started within 24 hours of symptom onset, it can reduce duration by ~2 days or by ~30–40% (depending on formulation).

Zinc acetate lozenges appear more effective than zinc gluconate.

Doses ≥ 75 mg/day show the best effect; higher doses do not improve outcomes further.

Overall symptom severity is not consistently reduced even when duration is shortened.

3. Safety of Zinc

Non-serious side effects are common, especially with lozenges (metallic taste, nausea, GI upset).

Serious adverse events are rare.

Intranasal zinc is not recommended due to the risk of anosmia.

4. Vitamin C for Prevention

Routine daily vitamin C does NOT reduce the incidence of colds in the general population.

The only subgroup with benefit:

Those under heavy physical stress (marathon runners, soldiers) — incidence was cut by ~50%.

5. Vitamin C for Treatment

Vitamin C does not reliably shorten colds once symptoms begin.

Regular vitamin C (taken before illness) modestly shortens duration:

Adults: ~8% shorter

Children: ~14% shorter

Symptom severity is only slightly reduced, and results are inconsistent.

6. Safety of Vitamin C

Vitamin C is generally safe, with no major difference in side effects compared to placebo.

Long-term high doses may risk GI upset or potential nutrient imbalance (e.g., copper).

However...

Limitations Across the Evidence:

Low to very low certainty for many outcomes due to poor randomization, blinding issues, and inconsistent reporting.

High heterogeneity across studies—different doses, formulations, definitions of cold, and symptom scoring systems.

Small sample sizes in many RCTs reduce precision and confidence.

Selective reporting and lack of preregistered protocols introduce bias.

Limited generalizability: most data come from healthy adults in high-income countries.

Formulation variability (especially in zinc lozenges) makes it difficult to determine the “optimal” product.

Further Studies Should:

- a) Standardize zinc and vitamin C formulations, doses, and symptom scoring systems.
- b) Evaluate long-term safety, including nutrient interactions with high-dose zinc or vitamin C.
- c) Compare outcomes in different populations (children, older adults, immunocompromised).
- d) Investigate whether timing (e.g., within 12 hours vs 24 hours) significantly affects zinc's effectiveness.
- e) Assess whether vitamin C benefits are truly due to cold prevention or related to exercise-induced respiratory stress in athletes.

Overall Summary:

Zinc does not prevent colds, but can meaningfully shorten duration if taken early, with mild but common side effects.

Vitamin C does not prevent colds for the general population and has minimal impact as a treatment, though regular supplementation offers small reductions in duration.

Evidence certainty is limited, and findings should be interpreted cautiously.

Clinical Bottom Line:(what we say to patients)

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