CASE STUDY

Mini-Cat Presentation

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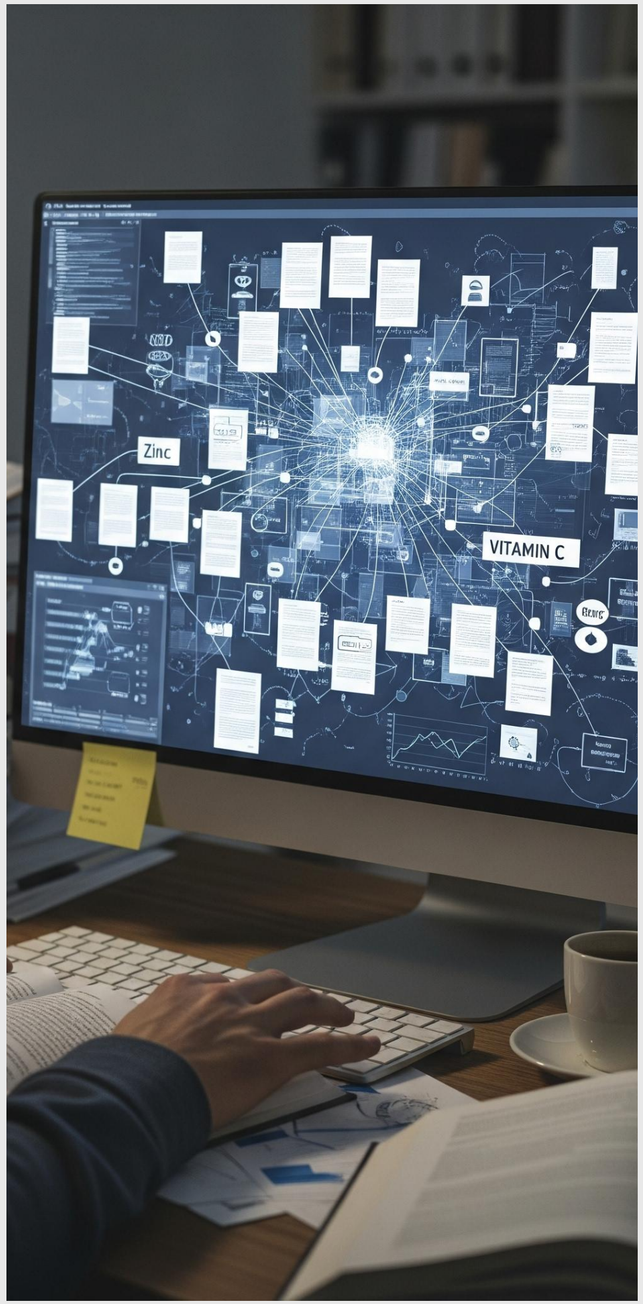
Introduction

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

Can zinc or vitamin C pill supplementation prevent the common cold in healthy adults compared to no intervention?

Patient	Intervention	Comparison	Outcome
Adult Women	Vitamin C	No intervention	Incidence of common cold symptom
Adults	Zinc	Placebo	Prevent cold
			common cold



Search Strategy Summary

Terms Used:

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

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 e
outcomes measured by the studies.

- PubMed - 4 articles
- Cochrane - 1 articles

Zinc for prevention and treatment of the common cold

Daryl Nault et.al

A systematic review included 34 studies involving 8526 participants (adults and children) to assess the effectiveness and safety of zinc for the prevention and treatment of the common cold or upper respiratory tract infection (URTI).

The methodology involved summarizing data from RCTs that compared any form of zinc against placebo.

The primary outcomes measured included:

- Duration of cold (measured in days from start to resolution).
- Proportion of participants developing colds (in prevention trials only).
- Adverse events (including non-serious events potentially due to zinc supplements and serious events potentially due to complications of the common cold

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Zinc for prevention and treatment of the common cold

Daryl Nault et.al

Impact on Cold Treatment:

- Cold Duration (8 studies, 972 participants): Zinc may shorten colds compared to placebo, reducing mean duration by 2.37 days (95% CI -4.21 to -0.53).
- Symptom Duration: Zinc reduced the duration of cough (MD -1.67), nasal drainage (MD -1.75), and muscle aches (MD -0.66).
- Global Severity (2 studies, 261 participants): No clear difference in global symptom severity (SMD -0.03).

Impact on Cold Prevention:

- Risk of Developing a Cold/URTI (9 studies, 1449 participants): Zinc supplementation resulted in little to no reduction in cold risk (RR 0.93).
- Days Missed from Work/School (2 studies, 394 participants): Mean days missed were reduced (MD -0.65).

Safety and Adverse Events:

- Non-Serious Adverse Events (16 studies, 2084 participants): An increased risk of non-serious adverse events is probable with zinc (RR 1.34), especially with lozenges (RR 1.44). (Moderate-certainty evidence).
- Serious Adverse Events: No data on serious adverse events was reported.

Zinc for prevention and treatment of the common cold

Daryl Nault et.al

Limitations:

- Low Evidence Certainty: Confidence in the evidence is generally low to very low.
- Large Heterogeneity: Results showed very high statistical heterogeneity (e.g., $I^2 = 97\%$ for cold duration).
- Risk of Bias: Almost all studies (33/34) had an unclear or high risk of bias (e.g., inadequate randomization or selective outcome reporting).
- Inconsistent Interventions: Studies varied widely in zinc formulations, dosages (0.044 mg/d to 300 mg/d), and delivery methods.
- Small Sample Sizes: Only 12 of 34 studies had ≥ 200 participants, contributing to imprecision.

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

Systematic Review of 20 randomized controlled trials which included all participants over the age of 18 years old. this study was conducted in multiple countries such as USA, india Iran turkey. which the zinc formulations primarily was provided in tablets with an approximate range of dosage of 30 - 160 mg per day as a single tablet. which was primarily used for prevention or treatment for patients symptoms.

primary outcomes includes

- Determine Whether zinc supplementation reduces the risk of developing a cold in healthy adults.
- Number of symptomatic days; effect of zinc when started at onset or continuously.
- Overall symptom scores and individual symptoms (nasal congestion, cough, sore throat, muscle aches).
- adverse effects : metallic taste, nausea, gastrointestinal discomfort

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

clinical outcome

Prevention: Zinc does not reduce the risk of developing a cold in healthy adults Routine daily prophylactic zinc is not recommended.

Treatment (Duration of illness): Zinc shortens cold duration by 2 days on average. Most effective when started within 24 hours of symptom onset. Zinc acetate is more effective than gluconate; doses greater than 75 mg/day show better outcomes. Early oral zinc is recommended for treatment at symptom onset, not for long-term prevention.

Symptom Severity: Zinc does not consistently reduce symptom severity.-Minor improvements in some symptoms (nasal congestion, cough, sore throat, muscle aches) are inconsistent. Patients may have shorter colds but should not expect significant symptom relief.

Safety / Adverse Effects: commonly occurs with lozenges where patients primarily complain of a metallic taste, nausea and GI discomfort. Short-term oral zinc is generally safe where counseling of adverse effects is recommended.

Clinical Implication: Do not use zinc for routine prevention. Use oral zinc early at first cold symptoms to moderately reduce duration; avoid intranasal forms.

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

Key Findings

Zinc supplementation does not reduce the risk of developing a cold but can shorten the duration by approximately 2.25 days on average, with the greatest benefit observed when started within 24 hours of symptom onset. Zinc acetate appears more effective than zinc gluconate, and doses of 75 mg/day or higher provide the strongest reduction in duration. Symptom severity does not show consistent improvement. Adverse effects are common but generally mild, including metallic taste, nausea, and gastrointestinal upset. Intranasal zinc is not recommended due to the risk of anosmia.

Limitations and Biases

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- High heterogeneity across trials (dose, formulation, symptom scoring).
- Many studies had small sample sizes.
- Inconsistent methods for tracking symptom severity.
- Blinding difficult due to zinc metallic taste.
- Preventive studies underpowered and inconsistent.
- Results downgraded to low-certainty for prevention outcomes.

Does Vitamin C Prevent the Common Cold?

Evelyn Gomez et al.

Study Design

- Systematic Review & Meta-Analysis of 31 randomized control trials

Population

- Generally healthy adults and children, consisting of 8,472 participants

Intervention

- Oral Vitamin C supplement of 0.08-3 g/day vs. placebo

Outcomes measured

- Incidence of common cold, duration and severity of cold symptoms

Does Vitamin C Prevent the Common Cold?

Evelyn Gomez et al.

- **Impact on Common Cold Prevention**
  - *Vitamin C did not significantly reduce incidence of common cold* in the general population
  - Control group had a common cold incidence of 487 per 1,000; with vitamin C, the incidence was 473 per 1,000 (**RR approx. 0.97** (95% CI 0.94—1.00))
  - May slightly shorten duration or lessen symptom sevērity once infected
    - [] Results revealed reductions of approximately **8% in adults** and **14% in children** for cold duration with regular vitamin C supplementation

- **Safety / Adverse Events**
  - Generally well tolerated at doses ≤ 2 g/day
  - Occasional mild gastrointestinal discomfort reported at high doses

Does Vitamin C Prevent the Common Cold?

Evelyn Gomez et al.

Limitations

- Variation in vitamin C dosages and duration of supplementation amongst studies

- Inconsistent definitions of ‘common cold' used

- Clinician-diagnosed vs. participant reported

[] Some studies required clinical confirmation, while others relied solely on patient questionnaires, symptom checklists, etc.

Vitamin C for Preventing and Treating the Common Cold

Harri Hemila & Elizabeth Chalker, 2013 - Systemic Review & Meta-Analysis

Meta-analysis & Systematic review included 63 trial comparisons from 44 publications, totaling over 11,000 participants (adults and children).

- **Populations:**
  - General community
  - Specific subgroups under heavy short-term physical stress (marathon runners, skiers)
- **Interventions: Oral vitamin C ≥ 0.2 g/day, either:**
  - Regular daily supplementation
  - Therapeutic treatment (after cold onset)

Primary outcomes measured:

- Incidence of colds (≥1 cold per participant)
- Duration of colds (number of days)
- Severity of colds (days confined indoors or symptom severity scores)
- Adverse events (side effects related to vitamin C)

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Vitamin C for Preventing and Treating the Common Cold

Harri Hemila & Elizabeth Chalker, 2013 - Systemic Review & Meta-Analysis

<u>Vitamin C – Prevention (Regular Supplementation)</u>

Effect on Incidence of Colds:

- General community: No reduction (**RR 0.97;** 95% CI 0.94–1.00)
- Under heavy physical stress: Risk halved (**RR 0.48**; 95% CI 0.35–0.64)

Effect on Duration:

- Adults: 8% reduction → Ex: 8-day cold shortened by ~0.64 days
- Children: 14% reduction → Ex: 7-day cold shortened by ~0.98 days

Effect on Severity:

- 5% reduction in severity (p=0.023)
- Quicker recovery and milder symptoms

Vitamin C for Preventing and Treating the Common Cold

Harri Hemila & Elizabeth Chalker, 2013 - Systemic Review & Meta-Analysis

<u>Vitamin C – Therapeutic Treatment (After Cold Onset)</u>

Effect on Incidence of Colds:

- Generally no reduction when started after symptoms begin
- Exception: Tyrrell 1977 – 40% reduction in recurrent colds in adults

Effect on Duration:

- Short supplementation (<3 days): no effect
- Longer supplementation (>5 days): reduced colds by 0.73 days
- Early use (within 24h): reduced duration from 6.9 → 3.6 days
- Extended supplementation (up to 2 weeks): no effect

Effect on Severity:

- Overall: no significant reduction
- 5-day supplementation: 25% reduction in days confined indoors in one study

Vitamin C for Preventing and Treating the Common Cold

Harri Hemila & Elizabeth Chalker, 2013 - Systemic Review & Meta-Analysis

Safety and Adverse Events

- No significant difference between vitamin C and placebo
  - Vitamin C: 5.8% reported mild adverse events
  - Placebo: 6.0% reported mild adverse events
- No serious adverse events reported

Limitations

- Heterogeneity of effects: Benefits vary widely by population (general community vs. athletes)
- Cannot generalize for all populations
- Effect size is modest (especially in duration and severity reduction)
- Difficult to create broad public health guidelines (variable results)

Final Remarks

- Routine supplementation: Not justified to prevent cold for the general public
- Athletes under extreme physical stress: May benefit from prophylactic supplementation
- Therapeutic use (after symptom onset): Generally not effective, except if started very early (within 24 hours)
- Safety: Well-tolerated, minimal side effects

Zinc for the Treatment of the Common Cold— Systematic Review & Meta-Analysis

Science et al., 2012

Study Design

- **Level I** systematic review and meta-analysis of randomized controlled trials
- **7 RCTs** included with a **total of 575 adult participants**
- All trials tested **zinc lozenges (dissolvable tablets) only** (not syrup or intranasal forms)
- Participants were **otherwise healthy adults with naturally acquired colds**
- Purpose: determine whether **zinc lozenges shorten cold duration and/or improve symptoms once sick**

Zinc for the Treatment of the Common Cold— Systematic Review & Meta-Analysis

Science et al., 2012

Outcomes Studied

Researchers examined whether zinc lozenges provided **clinical benefit after cold symptom onset**.

- **Duration of cold symptoms** (primary outcome)
- Differences in benefit between **zinc acetate vs zinc gluconate** lozenges
- Whether **zinc dose influenced effectiveness** (dose–response)
- Secondary safety monitoring (side effects), though reporting varied across trials

Zinc for the Treatment of the Common Cold— Systematic Review & Meta-Analysis

Science et al., 2012

- Across all trials, zinc lozenges **shortened the duration of colds by about one-third (~33%)**

→ Example: a 7-day cold might shorten to ~4–5 days with zinc

- **Zinc acetate** produced the strongest effect

→ ~40% reduction in symptoms (95% CI 31%–50%)

- **Zinc gluconate** also reduced duration

→ ~28% reduction (95% CI 6%–50%)

- **Higher doses (>100 mg/day) did not improve results further**, indicating **more zinc is not better**
- Benefits appeared to depend heavily on **lozenge formulation and zinc ion availability**

BOTTOM LINE: When taken after symptoms begin, **zinc lozenges can meaningfully shorten cold duration**, but effectiveness depends on the **specific formulation** — not all zinc products work the same.

Zinc for the Treatment of the Common Cold— Systematic Review & Meta-Analysis

Science et al., 2012

Limitations & Clinical Conclusion

Limitations

• **High variability** between trials (formulation, dose, additives) — affects reliability

• Some lozenges contained ingredients that **bind zinc and block absorption** (e.g., citric acid, sorbitol), possibly weakening the effect

• **Symptoms were self-reported**, not clinically validated

• **Only adults studied** — cannot generalize to children

• **Adverse effects and long-term safety were not consistently reported**

Clinical Conclusion

Zinc lozenges **may shorten the duration of colds when treatment begins early**, especially **zinc acetate formulations with adequate elemental zinc doses (~75 mg/day or more)**.

However, **results vary widely between products**, and **not all zinc lozenges are effective**. Safety reporting was incomplete, so counseling should be **cautious and formulation-specific**.

Summary of mini- cat Grid

Article	Level of Evidence	Key findings	Limitations
Zinc for prevention and treatment of the common cold by Daryl Nault Et.al	Level 1: Systemic review	**Prevention:** Zinc doesn't really prevent colds or make them shorter/milder if taken before getting sick; it only slightly reduces missed days of work/school. T**reatment & Safety:** When taken after symptoms start, zinc may shorten colds by ~2 days but can cause more non-serious side effects (metallic taste, GI issues), especially with lozenges.	Evidence is low to very low certainty due to high risk of bias, inconsistent findings, small trials, and wide variation in zinc doses, forms, and outcome measurements. Generalizability is limited because studies were small, mostly in healthy adults, with inconsistent adverse-event reporting and no long-term safety data.
Zinc Supplementation Reduces Common Cold Duration among Healthy Adults: A Systematic Review of Randomized Controlled Trials with Micronutrients Supplementation	level 1: systematic review	Prevention: Zinc does not reduce the risk of developing a cold in healthy adults Routine daily prophylactic zinc is not recommended. Treatment (Duration of illness): Zinc shortens cold duration by 2 days on average. Most effective when started within 24 hours of symptom onset. Zinc acetate is more effective than gluconate; doses greater than 75 mg/day show better outcomes. Early oral zinc is recommended for treatment at symptom onset, not for long-term prevention.	High heterogeneity across trials (dose, formulation, symptom scoring).Many studies had small sample sizes.Inconsistent methods for tracking symptom severity.Blinding difficult due to zinc metallic taste.Preventive studies underpowered and inconsistent.Results downgraded to low-certainty for prevention outcomes.
Hemilä & Chalker, 2013 – Vitamin C for preventing and treating the common cold	Systematic Review & Meta-Analysis (Level 1)	**Prevention**: Routine Vitamin C does not prevent colds in the general population but slightly shortens the duration and reduces the severity. It is effective for preventing cold in athletes under extreme physical stress **Treatment**: Taking vitamin C after cold symptoms begin generally has little effect on duration and severity, unless very early. Some benefit may occur with early or longer supplementation	Effects vary by population (general vs athlete), modest benefits (small effects), results are not generalizable for all.

Summary of mini- cat Grid

Article	Level of Evidence	Key findings	Limitations
Does Vitamin C Prevent the Common Cold?	Systematic Review & Meta-Analysis (Level 1)	Regular consumption of vitamin C does not prevent the incidence of the common cold in the general population	Variation in vitamin C doses and duration of supplementation Inconsistent definitions of ‘common cold' used Confounding variables: baseline vitamin C status & nutritional status not fully controlled
Science et al., 2012. Zinc for the treatment of the common cold	Systematic Review & Meta-Analysis (Level 1)	**Prevention:** (Not applicable — this review did not evaluate zinc for routine prevention. All included trials examined zinc **only after cold symptoms began**. This review focuses on **treatment**, not prevention.) **Treatment:** When zinc lozenges were taken **after the onset of symptoms**, they **shortened the duration of colds by about one-third (~33%) overall**. Benefits were stronger with **zinc acetate lozenges** (≈40% reduction) and more modest with **zinc gluconate** (≈28% reduction). Higher doses **did not lead to greater benefit**, indicating that more zinc is not necessarily better. Symptom relief depended heavily on the **specific lozenge formulation and the bioavailability of zinc ions**, meaning not all zinc products work the same.	**Limitations:** The certainty of evidence was affected by **high variability between trials**, especially in **lozenge ingredients, zinc dose, and formulation** — some lozenges contained compounds (e.g., citric acid, sorbitol) that **bind zinc and reduce absorption**, potentially weakening effect. **Symptoms were self-reported**, not clinically verified, increasing risk of measurement bias. Trials included **only adults**, so results cannot be confidently applied to children. **Adverse effects and long-term safety were not reported consistently**, limiting confidence in safety conclusions and generalizability.

Clinical Bottom Line:
Can zinc or vitamin C pill supplementation prevent the common cold in healthy adults compared to no intervention?

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; Hemilä & Chalker, 2013;

- Level I evidence: Highest-quality systematic reviews/meta-analyses.
- Largest number of trials/participants: Most comprehensive data.
- Rigorous methods: Strong bias assessment and clear analysis.
- Most clinically applicable: Best separation of prevention vs treatment effects.

Clinical Bottom Line:
Can zinc or vitamin C pill supplementation prevent the common cold in healthy adults compared to no intervention?

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.

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.

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.

Clinical Bottom Line:
Can zinc or vitamin C pill supplementation prevent the common cold in healthy adults compared to no intervention?

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, skiers) — incidence was cut by ~50%.

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% reduction
Children: ~14% reduction
Symptom severity is only slightly reduced, and results are inconsistent.

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).

Clinical Bottom Line:
Can zinc or vitamin C pill supplementation prevent the common cold in healthy adults compared to no intervention?

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.

Clinical Bottom Line:
Can zinc or vitamin C pill supplementation prevent the common cold in healthy adults compared to no intervention?

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 may offer a small reduction in duration.

Evidence certainty is limited and findings should be interpreted cautiously.

References

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