# VITAMIN C FOR PREVENTING AND TREATING THE COMMON COLD

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## ABSTRACT

### Background

The role of oral vitamin C (ascorbic acid) in the prevention and treatment of the common cold has been a subject of controversy for at least sixty years. Public interest in the topic continues to be high and vitamin C continues to be widely sold and used as a preventive and therapeutic agent for this common ailment.

### Objectives

To discover whether oral vitamin C in doses of 200 mg or more daily, reduces the incidence, duration or severity of the common cold when used either as continuous prophylaxis or after the onset of cold symptoms.

### Search Strategy

This updated review added to earlier searches, a full search of the following electronic databases: the Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* Issue 2, 2004); MEDLINE (January 1966 to June 2004); and EMBASE (1990 to June 2004).

### Selection Criteria

Papers were excluded if a dose less than 200 mg daily of vitamin C was used; if there was no placebo comparison; if methods of outcome assessment were inadequately described; and if the report did not record any of the three study outcomes (incidence, duration or severity) in sufficient detail to enter into the meta-analysis. Three criteria of study quality were assessed: Jadad scores, placebo distinguish-ability, and allocation concealment.

### Data collection and analysis

Two reviewers independently extracted data and assessed trial quality. 'Incidence' of colds during prophylaxis was assessed as the proportion of participants experiencing one or more colds during the study period. 'Duration' was the mean days of illness of cold episodes and 'severity' of these episodes was assessed by days confined indoors, off work or school. or by symptom severity scores.

### Main Results

Twenty-nine trial comparisons involving 11,077 study participants contributed to the meta-analysis on the relative risk (RR) of developing a cold while taking prophylaxis. The pooled RR was 0.96 (95% CI 0.92 to 1.00). A subgroup of six trials that involved a total of 642 marathon runners, skiers, and soldiers on sub-arctic exercises reported a pooled RR of 0.50 (95%CI 0.38 to 0.66).

Thirty comparisons that involved 9,676 respiratory episodes contributed to the meta-analysis on common cold duration during prophylaxis . A consistent benefit was observed, representing a reduction in cold duration of 8% (95% CI 3% to 13%) for adult participants and 13.5% (95% CI 5% to 21%) for child participants.

Fifteen trial comparisons that involved 7,045 respiratory episodes contributed to the meta-analysis of severity of episodes experienced while on prophylaxis. The pooled results revealed a difference favouring those on vitamin C when days confined to home and off work or school were taken as a measure of severity ($p = 0.02$), and when restricting to studies which used symptom severity scores ($p = 0.16$), and for the both measures of severity combined ($p = 0.004$).

Seven trial comparisons that involved 3,294 respiratory episodes contributed to the meta-analysis of cold duration during therapy with vitamin C that was initiated after the onset of cold symptoms, and no significant difference from placebo was seen.

Four trial comparisons that involved 2,753 respiratory episodes, contributed to the meta-analysis of cold severity during therapy and no significant difference from placebo was seen.

In laboratory studies, differing methods of artificial transmission of virus to vitamin C or placebo treated volunteers in residential experiments gave different results. Volunteers infected by nasal installation showed small or no benefit from vitamin C, whereas a group who were infected more naturally, reported less severe symptom severity scores ($p = 0.04$).

**Reviewers' conclusions**

The failure of vitamin C supplementation to reduce the incidence of colds in the normal population indicates that routine mega-dose prophylaxis is not rationally justified for community use. But evidence shows that it could be justified in persons exposed to brief periods of severe physical exercise and/or cold environments. Also, the consistent and statistically significant small benefits on duration and severity for those using regular vitamin C prophylaxis indicates that vitamin C plays some role in respiratory defence mechanisms. The trials in which vitamin C was introduced at the onset of colds as therapy did not show any benefit in doses up to 4 grams daily, but one large trial reported equivocal benefit from an 8 gram therapeutic dose at onset of symptoms.

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## BACKGROUND

Numerous animal studies with different species have shown that vitamin C affects resistance to diverse infections by viruses and bacteria (Hemilä 1997c) . It might therefore be expected that this vitamin would also play such a role in human beings, but its importance in this regard is unresolved. Since the early 1940s, a large number of controlled trials have been carried out to examine the possible effects of vitamin C on the common cold, a ubiquitous problem caused by a wide range of viral agents. The common cold causes enormous morbidity worldwide and the search for simple and effective preventive and/or therapeutic agents has been elusive.

In 1970, the publication of Pauling 1970a, a book for the general public entitled "Vitamin C and the Common Cold" generated huge public interest which persists today. Linus Pauling was a double Nobel Laureate in chemistry and peace. In Pauling 1971a he carried out a meta-analysis in which he combined the p-values derived from four placebo-controlled trials

by Fisher's method and found that there was strong evidence that vitamin C decreases the 'incidence of colds' (p = 0.003). In a second meta-analysis, Pauling 1971b focused on 'days of illness per person' in the best of these four trials Cowan 1942, Ritzel 1961 and combining the p-values by Fisher's method led him to conclude that "the null hypothesis of equal effectiveness of ascorbic acid and placebo is rejected at the level p less than 0.001."

Ritzel 1961 had reported a brief randomised controlled trial of children at a ski school in the Swiss Alps in which he administered 1 g daily and found reduced incidence and duration of colds in the recipients of vitamin C. Pauling put much weight on the Ritzel trial and based his expectations of vitamin C benefits on it. Pauling 1970b and Pauling 1976 also presented other data suggesting that human diets might not provide sufficient intake of vitamin C for optimal health, and proposed that mega-dose supplementation might profoundly influence both the incidence and severity of the common cold.

Pauling's advocacy of vitamin C led to numerous careful trials in a number of countries in the following decade, the largest of which were performed on healthy adult volunteers in Canada (Anderson 1972; Anderson 1974a; Anderson 1975a).

The evidence emerging from these trials was often confusing (Anderson 1977), but generally failed to support Pauling's hope that vitamin C would be a panacea. Chalmers 1975 calculated an unweighted average of the treatment effect in seven placebo-controlled trials and found that colds in vitamin C groups were 0.11 ± 0.24 standard error (SE) days shorter, and the incidence of colds in vitamin C groups was 0.09 ± 0.06 (SE) episodes less per year, neither of which is a statistically or clinically significant difference. In a qualitative review on vitamin C and the common cold published in the same year, Dykes 1975 also concluded that vitamin C had no effects on colds.

The reviews by Chalmers 1975 and Dykes 1975 were, however, subsequently claimed to contain errors ( Hemilä 1995; Hemilä 1996a). Furthermore, both Chalmers 1975 and Dykes 1975 placed considerable weight on the double-blind placebo-controlled trial carried out by Karlowski 1975a at the National Instiute of Health (NIH) , which concluded that a statistically significant benefit of vitamin C supplementation was caused by the placebo effect. It was subsequently argued that the placebo-explanation in the Karlowski 1975 paper was not consistent with their own data (Chalmers 1996; Hemilä 1996b; Hemilä 1996d).

Hemilä 1997b claimed that the highly cited reviews of Chalmers 1975 and Dykes 1975, and the Karlowski 1975a trial, quelled interest in the real, but modest effects of vitamin C on the common cold after the mid-seventies. Hemilä 1997c pooled the results of the six largest trials and found no effect on common cold incidence using 1 g/day or more of vitamin C (RR = 0.99; 95% CI 0.93 to 1.04). However, four trials with UK males found moderate reduction in common cold incidence by vitamin C (RR = 0.70; 95% CI 0.60 to 0.81) which was suggested to be caused by the particularly low dietary vitamin C intake in the UK rather than high supplement doses. Also, three trials with subjects under heavy acute physical stress had reported reduced incidence of colds with vitamin C (RR = 0.50; 95% CI 0.35 to 0.69) (Hemilä 1996b).

Although regular vitamin C supplementation at doses of 1 g/day or more has consistently decreased the duration or alleviated the symptoms of the common cold, there was substantial heterogeneity in the results (Hemilä 1994). In a further meta-analysis there was a trend for trials in children to show greater benefit than trials with adults, and another trend for trials where a dose was used of 2 g/day to show greater benefit than trials with 1 g/day of vitamin C (Hemilä 1999a).

In the first edition of this Cochrane review in 1998, an analysis was made of the 30 published trial comparisons that had been selected for attention by two previous systematic reviewers, Hemilä 1992 and Kleijnen 1989. That selection of trials was one of convenience and was justified by the fact that all had been carried out post-Pauling in an era of relatively sophisticated trial methodology, and mainly using doses of vitamin C at the level recommended by Pauling.

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| **Study** | **Bancalari 1984** |
| Methods | Double-blind, randomized prophylaxis trial. Duration 84 days |
| Participants | Healthy Chilean school children, male and female, aged 10 to 12 years. 32 active and 30 placebo |
| Interventions | 2 g of vit C compared with placebo |
| Outcomes | Incidence Fig 1, Duration Fig 2 |
| Notes | Jadad 3<br>PD=I |
| Allocation concealment | B |
| **Study** | **Briggs 1984** |
| Methods | Double blind randomised prophylaxis trial which ran over eight winters for one winter period of three or six months of commitment by each volunteer, |
| Participants | Australian healthy adults, male and female. 265 high dose recipients versus 263 low dose "placebo" |
| Interventions | 1g of ascorbic acid plus 4g daily when respiratory symptoms occurred versus 50 mgs daily plus 200 mgs daily while symptoms lasted. |
| Outcomes | Incidence Fig 1, Duration Fig 2. |
| Notes | Jadad 3<br>PD=I<br>SD for duration was not published and it was estimated in the current review as SD=mean. |
| Allocation concealment | A |
| **Study** | **Carr 1981a** |
| Methods | Double blind identical twin prophylaxis study involving two groups of twins one group of which were living together and the other living apart. Carr 1981a deals with those living together. Duration 100 days |
| Participants | Australian males and females age range 14-64 years (mean 25 years) 51 pairs living together |
| Interventions | 1G daily plus a multi vitamin tablet that contained 70 mgs vit C daily in each group, versus placebo. |
| Outcomes | Duration Fig 2 and Severity, Fig 3. |
| Notes | Jadad 4<br>PD=I<br>SD for duration was not published and the SD for the current review was calculated from the p value. |
| Allocation concealment | A |
| **Study** | **Carr 1981b** |
| Methods | As for Carr 1981, this report refers to the identical twins who lived apart, |
| Participants | Australian males and females age range 14-64 years (mean 25 years) 44 identical twin pairs living apart. |
| Interventions | As for Carr 1981 |
| Outcomes | Duration Fig 2 and Severity, Fig 3. |
| Notes | Jadad 4 . |

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| | PD=I<br>SD for duration was not published and the SD for the current review was calculated from the p value. |
| Allocation concealment | A |
| **Study** | **Carson 1975** |
| Methods | Double blind controlled prophylaxis trial Forty days duration. |
| Participants | UK healthy adults 121 vit C and 123 placebo |
| Interventions | 1g vit C daily vs placebo |
| Outcomes | Incidence Fig 1 |
| Notes | Jadad 3<br>PD=? |
| Allocation concealment | C |
| **Study** | **Charleston 1972** |
| Methods | Controlled prophylaxis trial. Single blind not randomised. Duration 15 weeks |
| Participants | Staff and students of The University of Strathclyde. UK. 47 active arm and 43 placebo arm participants. |
| Interventions | 1g of vit C versus placebo. 1g vit C daily versus placebo |
| Outcomes | Incidence Fig 1, Duration Fig 2 |
| Notes | Jadad 0<br>PD=? |
| Allocation concealment | C |
| **Study** | **Clegg 1975** |
| Methods | Apparently double blind randomised prophylaxis trial. 15 weeks duration |
| Participants | Healthy Scottish students 67 active and 70 placebo . |
| Interventions | 1g vit C daily versus indistinguishable placebo. |
| Outcomes | Incidence Fig 1, Duration Fig 2 |
| Notes | Jadad 2.<br>PD=I |
| Allocation concealment | B |
| **Study** | **Coulehan 1974a** |
| Methods | Double blind prophylaxis trial. Alternate allocation. Duration 14 weeks |
| Participants | USA. Residential students at a Navaho Indian school 131 active and 128 placebo . |
| Interventions | 2g of vit C or placebo daily or placebo. |
| Outcomes | Incidence Fig 1, Duration Fig 2 |
| Notes | Jadad 4.<br>PD=I<br>SD for duration was not published and it was estimated in the current review as SD=mean. |
| Allocation | C |

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| **Study** | **Coulehan 1974b** |
| Methods | See Coulehan 1974 |
| Participants | Younger residential children. 190 active and 192 placebo |
| Interventions | 1g vit C or placebo daily |
| Outcomes | Incidence Fig 1, Duration Fig 2 |
| Notes | Jadad 4.<br>PD=I<br>SD for duration was not published and it was estimated in the current review as SD=mean. |
| Allocation concealment | C |
| **Study** | **Coulehan 1976** |
| Methods | Randomised double blind prophylaxis trial Duration 18 weeks in one school and 15 weeks in the other. |
| Participants | USA Children at two Navaho Indian residential schools aged 6-15 years. Both sexes. 428 active and 428 placebo |
| Interventions | 1g vit C or placebo daily |
| Outcomes | Incidence Fig 1, Duration Fig 2 |
| Notes | Jadad 4.<br>PD=I<br>SD for duration was not published and it was estimated in the current review as SD=mean. |
| Allocation concealment | A |
| **Study** | **Cowan 1942** |
| Methods | Controlled prophylaxis trial |
| Participants | US College students 208 active 155 placebo |
| Interventions | 200 mg of vitamin C or placebo |
| Outcomes | Incidence Fig 1 |
| Notes | Jadad 2<br>PD=?<br>SD for duration was not published and it was estimated in the current review as SD=mean. |
| Allocation concealment | B |
| **Study** | **Cowan 1950** |
| Methods | Randomised probably double blind therapeutic trial |
| Participants | US College students. 76 vit C and 77 placebo treated colds |
| Interventions | 6g vitamin C versus placebo during the first 48 hours of symptoms |
| Outcomes | Duration Fig 4 |
| Notes | Jadad 3<br>PD=? |
| Allocation concealment | B |

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| Reviewer(s) | **Douglas RM, Hemila H, D'Souza R, Chalker EB, Treacy B** |
| Contribution of reviewer(s) | **Bob Douglas (BD) conceived the review, screened retrieved papers against inclusion criteria, appraised the quality of papers, abstracted data, entered data into RevMan, analysed and interpreted the data, and wrote the review. He is the guarantor of the review.**<br><br>**Harri Hemila (HH) carefully reviewed drafts of the second edition of the review (2004), assisted in paper retrieval, proposed alterations to data presentation, checked data entries and contributed significant input to the text. He will take over responsibility for maintaining future editions of the review.**<br><br>**Ron D'Souza (RS) helped to assemble the update review database and shared with BD in the re-screening of all papers and their assessment of quality.**<br><br>**Elizabeth Chalker (EC) wrote the protocol of the first edition of the review developed the initial search strategy, undertook the searches, organised retrieval of papers, screened papers against inclusion criteria and appraised the quality of papers for that edtion**<br><br>**Barbara Treacy (BT) prepared overviews and summaries of published studies in preparation for the first version of the review (1998).** |
| Issue protocol first published | Information not available |
| Issue review first published | 1998/1 |
| Date of most recent amendment | 06 July 2004 |
| Date of most recent SUBSTANTIVE amendment | 10 August 2004 |
| Most recent changes | This is the second edition of this review. The first edition covered the period from 1970 to 1997 and overviewed, using Cochrane methods, trials which had been previously studied by two other meta-analysts Kleijnen and Hemilä. For this edition, Hemilä who has been extensively involved in over-viewing this literature in the past fifteen years has joined the Cochrane review team and the review has been completely rewritten and includes studies from 1942 up to the present. 25 new trials have been added to the review. Of particular interest in this edition is the evidence presented of the effect of vitamin C on the common colds of marathon runners and others exposed to |

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| | severe physical and cold stress. The review argues that vitamin C plays some biological role in defence against the common cold but that prophylaxis with high doses of vitamin C has no evidence based justification for members of the general population. It also points to the fact that most of the trials in which Vitamin C was used as therapy at onset of cold symptoms have revealed no benefit. It proposes further work on this aspect of the issue as there have been no therapeutic trials in children. |
| Date new studies sought but none found | Information not supplied by reviewer |
| Date new studies found but not yet included/excluded | Information not supplied by reviewer |
| Date new studies found and included/excluded | 13 January 2004 |
| Date reviewers' conclusions section amended | 13 June 2004 |
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## SOURCES OF SUPPORT

**External sources of support**

- Commonwealth Department of Health and Ageing AUSTRALIA

**Internal sources of support**

Australian National University AUSTRALIA

## SYNOPSIS

Vitamin C in daily doses as high as 2g daily is not a panacea for either the prevention or treatment of the common cold

Evidence from trials of vitamin C tablets in the prevention and treatment of the common cold shows that with the exception of trials in people exposed to short periods of extreme physical and/or cold stress (including marathon runners and skiers), regular supplementation does not lower the probability of getting a cold. Regular supplementation is fairly consistently associated with minor reduction in duration, and sometimes in the severity of cold symptoms but this is of doubtful clinical usefulness. When high doses of vitamin C are taken at the onset of cold symptoms in an effort to treat colds, they have not been shown to reduce either the duration or severity of symptoms.

## Index Terms

**Medical Subject Headings (MeSH)**
Administration, Oral; Ascorbic Acid [administration & dosage] [therapeutic use]; Common Cold [drug therapy] [prevention & control]; Respiratory Tract Infections [drug therapy] [prevention & control]
Mesh check words: Human