

Bilaga 4 Kompletterande sökning för vitamin C

Den inkluderade översikten av Abioye och medförfattare har brister i litteratursökning och relevansgranskning [36]. SBU har därför gjort sökningar efter randomiserade kontrollerade studier om behandling med vitamin C för förkylning i databaserna Medline, Embase, Scopus, samt i INAHTA¹:s databas för HTA²-rapporter.

Två projektledare på SBU läste, oberoende av varandra, alla artikelsammanfattningar, och de som bedömdes som relevanta för frågan av minst en person granskades sedan i fulltext. Dessa fulltextartiklar lästes också av två projektledare oberoende av varandra och de artiklar som inte var relevanta för frågan exkluderades. Vid oenighet tillfrågades projektets sakkunnige. Det gjordes ingen bedömning av risk för bias.

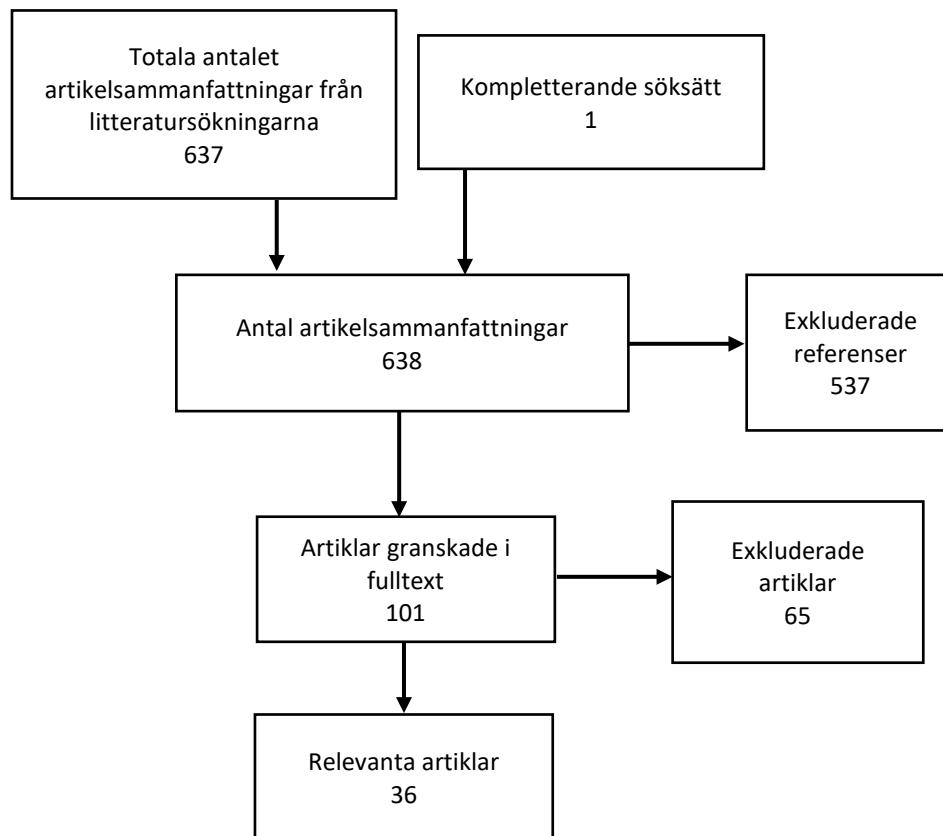
Efter genomgång av de 36 relevanta artiklarna, som den kompletterande litteratursökningen resulterade i, identifierades tio relevanta studier som inte ingick i översikten av Abioye och medförfattare. Av dessa var två studier publicerade efter sista sökdatum för översikten vilket förklarar varför de inte inkluderats och ytterligare två kan anses vara kvasirandomiserade varför de eventuellt inte inkluderats i översikten av Abioye och medförfattare. Merparten av studierna är publicerade på 1970-talet under en tid då studiernas metoddel generellt var mer knapphändig beskriven jämfört med vad som är vedertaget idag. Detta skulle också kunna vara en orsak till att studierna inte har inkluderats. Eftersom översiktsförfattarna inte har publicerat någon lista över exkluderade studier vet man inte om de i sitt arbete med översikten identifierat och sedan exkluderat några av dessa studier.

Efter att ha analyserat de studier som SBU identifierat, och som inte ingick i översikten av Abioye och medförfattare, bedömer vi sammanfattningsvis att de inte skulle haft någon betydande påverkan på översiktens resultat.

¹ International Network of Agencies for Health Technology Assessment (INAHTA)

² Utvärdering av hälso- och sjukvårdens (och i SBU:s fall socialtjänstens) metoder (engelska: *Health Technology Assessment*)

Figur 1 Flödesschema för randomiserade kontrollerade studier om vitamin C.



Relevanta RCT inte inkluderade i Abioye et al [36]
Baird IM, Hughes RE, Wilson HK, Davies JE, Howard AN. The effects of ascorbic acid and flavonoids on the occurrence of symptoms normally associated with the common cold. <i>Am J Clin Nutr.</i> 1979;32(8):1686-90. Available from: https://dx.doi.org/10.1093/ajcn/32.8.1686 .
Constantini NW, Dubnov-Raz G, Eyal B-B, Berry EM, Cohen AH, Hemila H. The effect of vitamin C on upper respiratory infections in adolescent swimmers: a randomized trial. <i>Eur J Pediatr.</i> 2011;170(1):59-63. Available from: https://dx.doi.org/10.1007/s00431-010-1270-z .
Coulehan JL, Reisinger KS, Rogers KD, Bradley DW. Vitamin C prophylaxis in a boarding school. <i>N Engl J Med.</i> 1974;290(1):6-10. Available from: https://dx.doi.org/10.1056/NEJM197401032900102 .
Ferrara P, Ianniello F, Bianchi V, Quintarelli F, Cammerata M, Quattrocchi E, et al. Beneficial therapeutic effects of vitamin C on recurrent respiratory tract infections in children: preliminary data. <i>Minerva Pediatr (Torino).</i> 2021;73(1):22-7. Available from: https://dx.doi.org/10.23736/S2724-5276.16.04621-1 .
Kim TK, Lim HR, Byun JS. Vitamin C supplementation reduces the odds of developing a common cold in Republic of Korea Army recruits: randomised controlled trial. <i>BMJ Mil Health.</i> 2022;168(2):117-23. Available from: https://dx.doi.org/10.1136/bmjmilitary-2019-001384 .
Ludvigsson J, Hansson LO, Tibbling G. Vitamin C as a preventive medicine against common colds in children. <i>Scand J Infect Dis.</i> 1977;9(2):91-8. Available from: https://dx.doi.org/10.3109/inf.1977.9.issue-2.07 .
Miller JZ, Nance WE, Kang K. A co-twin control study of the effects of vitamin C. <i>Prog Clin Biol Res.</i> 1978;24:151-6.
Miller JZ, Nance WE, Norton JA, Wolen RL, Griffith RS, Rose RJ. Therapeutic effect of vitamin C. A co-twin control study. <i>JAMA.</i> 1977;237(3):248-51.
Wilson CW, Loh HS, Foster FG. The beneficial effect of vitamin C on the common cold. <i>Eur J Clin Pharmacol.</i> 1973;6(1):26-32. Available from: https://dx.doi.org/10.1007/BF00561798 .
Wilson CW, Loh HS, Foster FG. Common cold symptomatology and vitamin C. <i>Eur J Clin Pharmacol.</i> 1973;6(3):196-202. Available from: https://dx.doi.org/10.1007/BF00558286 .

Medline via OvidSP 27 May 2024**Title:** Vitamin C for the common cold

Search terms		Items found
Population:		
1.	exp Respiratory Tract Infections/ or exp Common Cold/ or Rhinovirus/ or Paramyxoviridae Infections/ or parainfluenza virus 1, human/ or parainfluenza virus 3, human/ or parainfluenza virus 2, human/ or parainfluenza virus 4, human/ or Adenovirus Infections, Human/ or respiratory syncytial viruses/ or respiratory syncytial virus, human/ or Respiratory Syncytial Virus Infections/	671 495
2.	(common cold* or coryza or (acute adj5 (respiratory infection* or respiratory tract infection* or urti or uri)) or rhinovir* or hrv or parainfluenza* or adenovir* or picornavir* or respiratory syncytial virus* or rsv*).ab,bt,kf,ti.	123 215
3.	1 or 2	760 043
Intervention:		
4.	Ascorbic Acid.mp. or exp Ascorbic Acid/	65 161
5.	(vitamin\$ adj5 C).mp.	35 081
6.	4 or 5	81 236
Study types: randomised controlled trials		
7.	(randomized controlled trial.pt. OR controlled clinical trial.pt. OR clinical trial, phase iii.pt. OR ((randomized or randomised).ab.) OR placebo.ab. OR clinical trials as topic.sh. OR randomly.ab. OR trial.ti. OR (("Phase 3" or "phase3" or "phase III" or P3 or "PIII").ti,ab,kw.)) NOT (exp animals/ not humans.sh.)	1 565 751
8.	3 AND 6 AND 7	387

The search result, usually found at the end of the documentation, forms the list of abstracts.

/ = Term from the MeSH controlled vocabulary

.sh = Term from the MeSH controlled vocabulary

exp= Term from MeSH including terms found below this term in the MeSH hierarchy

.ti,ab = Title or abstract

.kf = Keywords

.bt = Book title. NLM Bookshelf.

.pt = Publication type

adjn = Adjacent. Proximity operator retrieving adjacent words, adj3 retrieves records with search terms within two terms from each other.

* = Truncation

“ ” = Citation Marks; searches for an exact phrase

.mp=text, heading word, subject area node, title

Scopus via scopus.com 27 May 2024**Title: Vitamin C for the common cold**

Search terms		Items found
Population:		
1.	TITLE-ABS-KEY("common cold*" OR coryza OR (acute W/5 ("respiratory infection*" OR "respiratory tract infection*" OR urti OR uri)) OR rhinovir* OR hrv OR parainfluenza* OR adenovir* OR "picornavir*" OR respiratory syncytial virus*" OR rsv*)	173 321
Intervention:		
2.	TITLE-ABS-KEY("Vitamin C" OR C-vitamin* OR "ascorbic acid*")	186 773
Study types: randomised controlled trials		
3.	INDEXTERMS ("clinical trials as a topic" OR "Randomized Controlled Trials as Topic" OR "multicenter study" OR "double blind procedure" OR "single blind procedure" OR "crossover procedure" OR "clinical trial" OR "controlled study" OR "randomization" OR "placebo") OR TITLE-ABS-KEY ("clinical trials" OR "randomized controlled trial" OR "randomized controlled trials" OR "controlled clinical trial" OR "controlled clinical trials" OR "random allocation" OR "randomly allocated" OR "allocated randomly" OR "Double-Blind Method" OR "single-blind method" OR "cross-over studies" OR placebo* OR "cross-over trial" OR "single blind" OR "double blind" OR "factorial design" OR "factorial trial") OR TITLE (trial* OR rct OR randomised* OR randomized*)	9 764 112
4.	1 AND 2 AND 3	470

The search result, usually found at the end of the documentation, forms the list of abstracts.

TITLE-ABS-KEY = Title, abstract or keywords (including indexed keywords and author keywords)

W/n = Within. Proximity operator retrieving terms within *n* words from each other.

INDEXTERMS = Controlled vocabulary terms assigned to the document

* = Truncation

“ ” = Citation Marks; searches for an exact phrase

Embase via Elsevier 27 May 2024

Title: Vitamin C for the common cold

Search terms	Items found
Population:	
1. 'common cold'/exp	11 633
2. 'rhinovirus infection'/exp	14 287
3. 'paramyxovirus infection'/de	578
4. 'parainfluenza virus infection'/exp	2006
5. 'respiratory tract infection'/de	77 638
6. 'upper respiratory tract infection'/de	38 516
7. 'viral respiratory tract infection'/de	6069
8. 'respiratory syncytial virus infection'/exp	9003
9. 'viral upper respiratory tract infection'/exp	1755
10. 'human parainfluenza virus 1'/exp	3816
11. 'human parainfluenza virus 3'/exp	2625
12. 'human adenovirus infection'/exp	836
13. 'human respiratory syncytial virus'/exp	22 989
14. 'common cold*':ab,kw,ti	6658
15. coryza:ab,kw,ti	894
16. acute:ab,kw,ti AND ('respiratory infection*':ab,kw,ti OR 'respiratory tract infection*':ab,kw,ti OR urti:ab,kw,ti OR uri:ab,kw,ti)	25 908
17. rhinovir*:ab,kw,ti OR hrv:ab,kw,ti OR parainfluenza*:ab,kw,ti OR adenovir*:ab,kw,ti OR picornavir*:ab,kw,ti OR 'respiratory syncytial virus*':ab,kw,ti OR rsv*:ab,kw,ti	143 667
18. #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17	28 386
Intervention:	
19. 'ascorbic acid'/exp	122 249
20. (vitamin* NEAR/5 c):ab,ti	41 667
21. ascorb*:ab,ti	64 305
22. #19 OR #20 OR #21	148 328
Study types: randomised controlled trials	
23. ('randomized controlled trial'/exp OR 'controlled clinical trial'/de OR random*:ti,ab,tt OR 'randomization'/de OR 'intermethod comparison'/de OR placebo:ti,ab,tt OR compare:ti,tt OR compared:ti,tt OR comparison:ti,tt OR ((evaluated:ab OR evaluate:ab OR evaluating:ab OR assessed:ab OR assess:ab) AND (compare:ab OR compared:ab OR comparing:ab OR comparison:ab)) OR ((open NEXT/1 label):ti,ab,tt) OR (((double OR single OR doubly OR singly) NEXT/1 (blind OR blinded OR blindly)):ti,ab,tt) OR 'double blind procedure'/de OR ((parallel NEXT/1 group*):ti,ab,tt) OR crossover:ti,ab,tt OR 'cross over':ti,ab,tt OR (((assign* OR match OR matched OR allocation) NEAR/6 (alternate OR group OR groups OR intervention OR interventions OR patient OR patients OR subject OR subjects OR participant OR participants)):ti,ab,tt) OR assigned:ti,ab,tt OR allocated:ti,ab,tt OR ((controlled NEAR/8 (study OR design OR trial)):ti,ab,tt) OR volunteer:ti,ab,tt OR volunteers:ti,ab,tt OR 'human experiment'/de OR trial:ti,tt) NOT (((random* NEXT/1 sampl* NEAR/8 ('cross section*' OR questionnaire* OR survey OR surveys OR database OR databases)):ti,ab,tt) NOT ('comparative study'/de OR 'controlled study'/de OR 'randomised controlled':ti,ab,tt OR 'randomized controlled':ti,ab,tt OR 'randomly assigned':ti,ab,tt) OR ('cross-sectional study' NOT ('randomized controlled trial'/exp OR 'controlled clinical trial'/de OR 'controlled study'/de OR 'randomised controlled':ti,ab,tt OR 'randomized controlled':ti,ab,tt OR 'control group':ti,ab,tt OR 'control groups':ti,ab,tt)) OR ('case control*':ti,ab,tt AND random*:ti,ab,tt) NOT ('randomised controlled':ti,ab,tt OR 'randomized controlled':ti,ab,tt) OR ('systematic review':ti,tt NOT (trial:ti,tt OR study:ti,tt)) OR (nonrandom*:ti,ab,tt NOT random*:ti,ab,tt) OR 'random field*':ti,ab,tt OR (('random cluster' NEAR/4 sampl*):ti,ab,tt) OR (review:ab AND review:it NOT trial:ti,tt) OR ('we searched':ab AND (review:ti,tt OR review:it)) OR 'update review':ab OR ((databases NEAR/5 searched):ab) OR ((rat:ti,tt OR rats:ti,tt OR	5 858 237

mouse:ti,tt OR mice:ti,tt OR swine:ti,tt OR porcine:ti,tt OR murine:ti,tt OR sheep:ti,tt OR
 lambs:ti,tt OR pigs:ti,tt OR piglets:ti,tt OR rabbit:ti,tt OR rabbits:ti,tt OR cat:ti,tt OR cats:ti,tt
 OR dog:ti,tt OR dogs:ti,tt OR cattle:ti,tt OR bovine:ti,tt OR monkey:ti,tt OR monkeys:ti,tt OR
 trout:ti,tt OR marmoset*:ti,tt) AND 'animal experiment'/de) OR ('animal experiment'/de
 NOT ('human experiment'/de OR 'human'/de)))

24. #18 AND #22 AND #23

256

The search result, usually found at the end of the documentation, forms the list of abstracts.

/de = Term from the EMTREE controlled vocabulary

/exp = Term from the EMTREE controlled vocabulary, including all narrower terms in the hierarchy

ti = Title

ab = Abstract

kw = Author keywords

it = Publication type

NEAR/*n* = Near. Proximity operator retrieving terms within *n* words from each other.

* = Truncation

' ' = Citation Marks; searches for an exact phrase

/de= Term from the EMTREE controlled vocabulary

/exp= Includes terms found below this term in the EMTREE hierarchy

/mj = Major Topic

:ab = Abstract

:au = Author

:ti = Article Title

:ti:ab = Title or abstract

* = Truncation

" " = Citation Marks; searches for an exact phrase