SUPPLEMENTARY MATERIAL 2

Zinc Lozenges May Shorten the Duration of Colds: A Systematic Review

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The Tables in this Document Describe:

- Characteristics of the included trials

- Calculation of the the daily Zn dose from the lozenges (marked by bold)

- The P-value for Table **1** of the paper (marked by bold)

- The mean and SD of the common cold duration for Fig. (**1**) of the paper (marked by bold)

The Last Page of this Document Describes:

The normalization of common cold duration to the scale with 100% as the mean duration in the placebo group

Douglas (1987) [26]	http://aac.asm.org/cgi/reprint/31/8/1263
Methods	Randomized, placebo-controlled, double-blind trial
Participants	Included in the analysis: 30 Zn and 28 placebo participants (33 Zn and 30 placebo treatment courses: a few participants had more than one course) 27 M 31 F, mean age 33 yr Participants in the trial were healthy adults who had in the previous year participated in a study of interferon prophylaxis against rhinovirus infection, which is described in ref. 3 of [26]: "recruitment of families was carried out in collaboration with family practitioners in three Adelaide suburban areas... Families had to comprise at least four members sharing a common residence" The duration of the common cold was ≤2 days before starting treatment for 56 of the 58 participants
Intervention	Zn acetate: one lozenge contained 10 mg Zn (see note) Placebo lozenges contained Na acetate Each participant used 6 to 8 lozenges at about 2-hr intervals each day The mean number of lozenges used per day in the Zn group was 6.4
Losses to follow-up and late exclusions	2 Zn and 5 placebo treatment courses were excluded because lozenges had not been used for ≥3 days and at the rate of ≥4 per day
Common cold definition	When a participant developed 2 respiratory symptoms for 1 day or 1 respiratory symptom for 2 days, the medication was commenced. Ref. 3 of [26] describes the symptoms: "runny nose; stopped-up nose; sore, scratchy throat; cough; hoarseness; chills; fever; or muscle ache".
Calculation of the daily Zn dose from lozenges	**64 mg/d** = 6.4/d × 10 mg
Mean and SD of the common cold duration	Douglas (1987) reported (table 2: respiratory symptoms [26]): Zn group: mean common cold duration: **12.1 d** Placebo group: mean common cold duration: **7.7 d** P(2-tail) = 0.08 The SD values were not reported **P(1-tail) = 0.96 for Table 1** Given the reported mean-values, the P(2-tail) = 0.08 corresponds to **SD = 9.8 for both groups**
Notes	The composition of the zinc lozenge was not described in the original study report. Eby (1997) asked for the composition and found that "several hundreds milligrams of tartaric acid and sodium bicarbonate were included to produce effervescence. Tartaric acid was present in considerable excess relative to zinc, and it has high log K_1 of 5.00. Zinc dissociates from acetate and binds instantly to tartrate" p. 486 in [11]. See also p. 31 in [13] and p. 484 in [14].

Eby (1984) [7]	http://aac.asm.org/cgi/reprint/25/1/20
Methods	Randomized, placebo-controlled, double-blind trial
Participants	Included in the analysis: 37 Zn and 28 placebo participants 35 M 30 F, mean age 37 yr (range 11 to 63 yr) Local media were used to invite persons with colds to volunteer for the trial. All were accepted who were diagnosed by a physician to have the common cold. The mean duration of the common colds of the 65 analyzed participants was 1.6 days (range 0.2 to 3 days) at entry
Intervention	Zn gluconate: one lozenge contained 23 mg Zn Placebo lozenges contained Ca lactate Initial dose for all participants was 2 lozenges, one followed by the other, dissolved in the mouth for 10 to 20 min each. Thereafter, adults and youths dissolved 1 tablet every 2 hr awake, not exceeding 12 and 9 lozenges daily, respectively. Children under 27 kg received ½ tablet every 2 hr awake, not exceeding 6 lozenges daily.
Losses to follow-up and late exclusions	Of the 146 original volunteers, 120 returned reports. The analysis was restricted to 65 participants, who reported being ill for ≤3 days before starting the treatment. 11 Zn and 5 placebo treated participants were excluded from analysis because they prematurely stopped recording symptoms
Common cold definition	Presence of any of 10 common cold symptoms: headache, fever, muscle pain, sneezing, nasal drainage, nasal obstruction, sore throat, scratchy throat, cough, hoarseness
Calculation of the daily Zn dose from lozenges	**207 mg/d** = 9/d × 23 mg 9/day is based on the instruction to use "1 tablet every 2 wakeful hr"
Mean and SD of the common cold duration	Eby (1984) modeled the duration of common cold episodes by an exponential model and calculated estimates for average duration of colds [7]: Zn group: average common cold duration: 3.9 d Placebo group: average common cold duration: 10.8 d The SD values were not reported At the end of the 7-d follow-up, 86% (32/37) of the Zn-treated participants reported no symptoms, compared with 46% (13/28) of the placebo-treated subjects, which gives Fisher test P(2-tail) = 0.0009. This gives **P(1-tail) = 0.0005 for Table 1** In this meta-analysis, the mean and SD were estimated from Eby's fig. 1 which shows the fraction of participants who still had symptoms as a function of time (last follow-up time point 7 d). 5 Zn and 15 placebo participants had colds longer than 7 d; the rate of recovery for them was imputed as 3 participants per day (based on the trends of the graphs). Based on this analysis (Table S3): Zn group: mean common cold duration **3.92 d (SD 2.61)** Placebo group: mean common cold duration **7.54 d (SD 3.18)**
Notes	Post-randomization exclusion of participants who had had colds lasting over 3 days before treatment was started is a weakness of the study. Nevertheless, this restriction is consistent with later trials which have largely been limited to participants who had had colds lasting only for 1 to 2 days before treatment.

Godfrey (1992) [20]	http://www.ltdk.helsinki.fi/users/hemila/Zn/Godfrey_1992.pdf
Methods	Randomized, placebo-controlled, double-blind trial
Participants	Included in the analysis: 35 Zn and 38 placebo participants
	44 M 29 F, median age 21 yr (range 18 to 40 yr)
	Participants were recruited from among Darthmouth College students and staff who spontaneously presented to the cold clinic at the College Health Service
	Exclusions: a positive bacteriological throat culture, pregnancy, symptoms consistent with influenza or any other illness
	Inclusion required that the cold had lasted for ≤2 days
	The mean duration of the common cold was 1.3 days at entry
Intervention	Zn gluconate glycine: one lozenge contained 23.7 mg Zn (see note)
	Placebo lozenges contained tannic acid, glycine and Ca saccharinate
	Participants were instructed to suck, not chew, the lozenges at not less than 2-hr intervals taking up to a maximum of 8 lozenges per day
	The mean number of lozenges used per day in the Zn group was 8.1
Losses to follow-up and late exclusions	8 Zn and 6 placebo participants withdrew from the trial: other diseases (5), failure to appear at follow-up (4), efficacy doubted by the participant (2), nausea (1 Zn, 1 placebo), sports injury (1)
Common cold definition	Presence of ≥2 of the following symptoms: cough, fever, headache, hoarseness, muscle ache, nasal drainage, nasal congestion, scratchy throat, sore throat, sneezing
Calculation of the daily Zn dose from lozenges	**192 mg/d** = 8.1/d × 23.7 mg
Mean and SD of the common cold duration	Godfrey (1992) reported (p. 237 [20]):
	Zn group: mean common cold duration: **4.86 d**
	Placebo group: mean common cold duration: **6.13 d**
	For the difference between the groups, the t(71 df) = 2.01
	The SD values were not reported
	The t-value gives **P(1-tail) = 0.024 for Table 1**
	Given the reported mean duration values, the t = 2.01 corresponds to **SD = 2.70 for both groups.**
Notes	The zinc lozenge contained glycine, which binds zinc tightly and therefore the free Zn ion level probably was much lower than suggested by the total Zn dose (see figs. 2 and 3 and p. 29-30 in [13] and table 2 in [12])

Macknin (1998) [27]	http://dx.doi.org/10.1001/jama.279.24.1962
Methods	Randomized, placebo-controlled, double-blind trial
Participants	Included in the analysis: 123 Zn and 124 placebo participants 117 M 130 F, median age 13 yr (range 6 to 16 yr) Students were recruited from two school districts in Cleveland, Ohio Exclusions: fever (>37.7°C), had previously taken the zinc preparation, pregnancy, a known adverse reaction to zinc, a known immune deficiency, acute illnesses other than the common cold Inclusion required that the cold had lasted for ≤24 hr
Intervention	Zn gluconate glycine: one lozenge contained 10 mg Zn (see note) Placebo lozenges contained Ca lactate Participants were instructed to take 3 lozenges per day in the school study personnel offices: before school, at lunchtime, and before school was dismissed. Students in grades 1 to 6 were instructed to take 2 lozenges at home on school nights and 5 lozenges per day at home on weekends. Students in grades 7 to 12 were instructed to take 3 lozenges at home on school nights and 6 lozenges per day at home on weekends. The median percentage of prescribed lozenges taken was 82.5% in the Zn group
Losses to follow-up and late exclusions	2 students (1 Zn, 1 placebo) provided false information at entry and were excluded from analysis
Common cold definition	Presence of ≥1 of the following symptoms: cough, hoarseness, nasal drainage, nasal congestion, throat redness and exudate, enlarged tonsils, sneezing
Calculation of the daily Zn dose from lozenges	**45 mg/d** = 5.5/d × 10 mg × 0.825 The average for grades 1 to 6 and for grades 7 to 12 was taken as 5.5 lozenges per day. Correction for the median percentage of lozenges taken (82.5%)
Mean and SD of the common cold duration	Macknin (1998) reported (p. 1965 [27]): Zn group: median time to resolution of cold symptoms: 9.0 d Placebo group: median time to resolution of cold symptoms: 9.0 d Cox regression model for the difference between the groups: P(2-tail) = 0.7 Mean and SD were not reported The lack of difference corresponds to **P(1-tail) = 0.5 for Table 1** In this meta-analysis, the mean and SD were estimated from Macknin's fig. 2 which shows the percentage of participants whose cold symptoms had resolved as a function of time (last follow-up time point 18 d). 7 Zn and 3 placebo participants' colds did not resolve during the period of observation. They are assumed to have colds longer than 18 d: the rate of recovery for them was imputed as 2 per day (based on the trends of the graphs). Based on this analysis (Table S3): Zn group: mean common cold duration: **9.37 d (SD 4.81)** Placebo group: mean common cold duration: **9.50 d (SD 4.53)**
Notes	The zinc lozenge contained glycine, which binds zinc tightly and therefore the free Zn ion level probably was lower than suggested by the total Zn dose (see figs. 2 and 3 and p. 29-30 in [13] and table 2 in [12])

Mossad (1996) [24]	http://www.annals.org/content/125/2/81
Methods	Randomized, placebo-controlled, double-blind trial
Participants	Included in the analysis: 49 Zn and 50 placebo participants 19 M 80 F, mean age 37 yr (range 21 to 69 yr) Participants were recruited from among the Cleveland Clinic staff through announcements in internal clinic publications and by word of mouth Exclusions: pregnancy, a known immune deficiency Inclusion required that the cold had lasted for ≤24 hr
Intervention	Zn gluconate glycine: one lozenge contained 13.3 mg Zn (see note) Placebo lozenges contained Ca lactate Participants were instructed to dissolve 1 lozenge in their mouth every 2 hr while awake The mean number of lozenges used per day in the Zn group was 6
Losses to follow-up and late exclusions	1 in the Zn group withdrew from the study on the first day because she could not tolerate the lozenges
Common cold definition	Presence of ≥2 of the following symptoms: cough, headache, hoarseness, muscle ache, nasal drainage, nasal congestion, scratchy throat, sore throat, sneezing, oral temperature >37.7°C
Calculation of the daily Zn dose from lozenges	**80 mg/d** = 6/d × 13.3 mg
Mean and SD of the common cold duration	Mossad (1996) reported (p. 84 [24]): Zn group: median time to resolution of cold symptoms: 4.4 d Placebo group: median time to resolution of cold symptoms: 7.6 d Log-rank test for the difference between the groups: P(2-tail) < 0.001 Mean and SD were not reported **P(1-tail) = 0.0005 for Table 1** In this meta-analysis, the mean and SD for both groups were estimated from Mossad's fig. 1 which shows the percentage of participants who still had symptoms as a function of time (last follow-up time point 18 d). 2 Zn and 4 placebo participants dropped out after 7 to 16 d (these are censored observations in the survival curves and explain minor divergence between the calculated and reported numbers). In addition, 1 placebo participant recorded that his cold resolved on day 19, and the duration of 1 other placebo participant was over 18 d. Based on this analysis (Table S3): Zn group: mean cold duration **5.20 d (SD 2.83)** Placebo group: mean cold duration **9.38 d (SD 5.47)**
Notes	The zinc lozenge contained glycine, which binds zinc tightly and therefore the free Zn ion level probably was lower than suggested by the total Zn dose (see figs. 2 and 3 and p. 29-30 in [13] and table 2 in [12])

Petrus (1998) [22]	http://dx.doi.org/10.1016/S0011-393X(98)85058-3
Methods	Randomized, placebo-controlled, double-blind trial
Participants	Included in the analysis: 52 Zn and 49 placebo participants 47 M 54 F, mean age 26 yr (range 18 to 54 yr) Participants were recruited from the campus of the University of Texas through posted announcements Exclusions: serious illnesses, organ transplants, disability
Intervention	Zn acetate: one lozenge contained 9 mg Zn Placebo lozenges contained sucrose octaacetate Participants were instructed to use 1 lozenge every 1½ hr while awake during day 0, then 1 lozenge every 2 hr while awake on following days The mean number of lozenges used per day in all participants was 9.9
Losses to follow-up and late exclusions	1 was lost to follow-up
Common cold definition	Presence of ≥2 of the following symptoms: nasal drainage, nasal congestion, cough, fever, myalgia, headache, sore throat, scratchy throat, hoarseness, sneezing, malaise
Calculation of the daily Zn dose from lozenges	**89 mg/d** = 9.9/d × 9 mg
Mean and SD of the common cold duration	Petrus (1998) reported (table II [22]): Zn group: mean common cold duration: 3.8 d (SE 0.2) Placebo group: mean common cold duration: 5.1 d (SE 0.4) To an inquiry for more accurate trial results, Kenneth Lawson (statistician of the study) replied (email 4 March, 2009): Zn group: mean common cold duration: **3.797 d (SD 1.630)** Placebo group: mean common cold duration: **5.106 d (SD 2.955)** These latter figures were used in the current meta-analysis The figures give **P(1-tail) = 0.0033 for Table 1**
Notes	

Prasad (2000) [25]	http://www.annals.org/content/133/4/245.1
Methods	Randomized, placebo-controlled, double-blind trial
Participants	Included in the analysis: 25 Zn and 23 placebo participants 18 M 30 F, mean age 37 yr (SD 11 yr) Participants were students, staff, and employees at Wayne State University, Michigan, who were ≥18 yr Exclusions: pregnancy, a known immunodeficiency disorder, chronic illnesses, previous use of zinc lozenges Inclusion required that the cold had lasted for ≤24 hr
Intervention	Zn acetate: one lozenge contained 12.8 mg Zn Placebo lozenges contained sucrose octaacetate Participants were asked to dissolve 1 lozenge in their mouth every 2 to 3 hr while awake The mean number of lozenges used per day in the Zn group was 6.2
Losses to follow-up and late exclusions	2 in the placebo group dropped out on day 2
Common cold definition	Presence of ≥2 of the following symptoms: cough, headache, hoarseness, muscle ache, nasal drainage, nasal congestion, scratchy throat, sore throat, sneezing, fever
Calculation of the daily Zn dose from lozenges	**80 mg/d** = 6.2/d × 12.8 mg
Mean and SD of the common cold duration	Prasad (2000) reported (table 2: overall symptoms [25]): Zn group: mean common cold duration: **4.5 d (SD 1.6)** Placebo group: mean common cold duration: **8.1 d (SD 1.8)** These give **P(1-tail) = 2×10^{-9} for Table 1**
Notes	

Prasad (2008) [21]	http://dx.doi.org/10.1086/528803
Methods	Randomized, placebo-controlled, double-blind trial
Participants	Included in the analysis: 25 Zn and 25 placebo participants 16 M 34 F, mean age 35 yr (SD 14 yr) Participants were students, staff, and employees at Wayne State University, Michigan, who were ≥18 yr Exclusions: pregnancy, any known immune deficiency disorder or chronic illness, previous use of zinc lozenges Inclusion required that the cold had lasted for ≤24 hr
Intervention	Zn acetate: one lozenge contained 13.3 mg Zn Placebo lozenges contained sucrose octaacetate Participants were asked to dissolve 1 lozenge in their mouth every 2 to 3 hr while awake The mean number of lozenges used per day in the Zn group was 6.9
Losses to follow-up and late exclusions	None
Common cold definition	Presence of ≥2 of the following symptoms: cough, headache, hoarseness, muscle ache, nasal drainage, nasal congestion, scratchy throat, sore throat, sneezing, fever
Calculation of the daily Zn dose from lozenges	**92 mg/d** = 6.9/d × 13.3 mg
Mean and SD of the common cold duration	Prasad (2008) reported (table 2: overall symptoms, all subjects [21]): Zn group: mean common cold duration: **4.00 d (SD 1.04)** Placebo group: mean common cold duration: **7.12 d (SD 1.26)** These give **P(1-tail) = 6 × 10^{-13} for Table 1**
Notes	

Smith (1998) [19]	http://aac.asm.org/cgi/content/abstract/33/5/646
Methods	Randomized, placebo-controlled, double-blind trial
Participants	Included in the analysis: 57 Zn and 53 placebo participants M/F ratio not described. All were students ≥18 yr Participants were recruited from among the students of three colleges and from one family practice. Exclusions: serious acute or chronic medical conditions, seasonal allergies, productive cough, indication for antibiotic therapy, had taken treatment for symptoms within 8 hr of the baseline evaluation
Intervention	Zn gluconate: one lozenge contained 11.5 mg Zn Placebo lozenges contained sucrose octaacetate An initial dose of 4 lozenges was used, followed by 2 lozenges dissolved in the mouth every 2 hr while awake
Losses to follow-up and late exclusions	64 were excluded because of insufficient dose (<10 lozenges on any day) or insufficient duration of therapy 2 were lost to follow-up
Common cold definition	Upon enrollment and at the end of each study day, subjects rated the severity of 11 symptoms and the overall severity of their URI on a scale of 0 to 3 (absent to severe). The individual symptoms assessed were sneezing, runny nose, stopped-up nose, sore or scratchy throat, hoarseness, postnasal drip, cough, watery eyes, headache, chilliness, muscle aches
Calculation of the daily Zn dose from lozenges	**207 mg/d** = 9/d × 2 × 11.5 mg 9/day × 2 is based on the instruction to dissolve 2 lozenges in the mouth "every 2 hr while awake"
Mean and SD of the common cold duration	Smith (1989) reported the proportion of participants who were symptomatic as a function of time (fig. 1 [19]). Median duration cannot be measured, because half of the placebo participants did not become asymptomatic by the end of the follow-up Smith did not report mean and SD values The lack of overall difference in the curves (fig. 1 [19]) corresponds to **P(1-tail) = 0.5 for Table 1** In this meta-analysis, the mean and SD were estimated from Smith's fig. 1 which shows the proportion of participants who were symptomatic as a function of time (latest follow-up time point 7 d). 24 Zn and 28 placebo participants had colds longer than 7 d; the rate of recovery for them was imputed as 6 participants per day (based on the trends of the graphs). Based on this analysis (Table S3): Zn group: mean common cold duration: **7.23 d (SD 2.29)** Placebo group: mean common cold duration: **7.57 d (SD 3.01)**
Notes	

Turner A (2000) [23]	http://dx.doi.org/10.1086/317437
Methods	Randomized, placebo-controlled, double-blind trial
Participants	Included in the analysis: 68 Zn gluconate and 71 placebo participants M/F ratio not described; age range 18 to 65 yr Participants were recruited at 4 different study sites: IMTCI (Lenexa, KS), GFI Pharmaceutical Services (Evansville, IN), TKL Research (Paramus, NJ), and Research Across America (RAA; Dallas) Exclusions: not described Inclusion required that the cold had lasted for ≤1 calendar days ("effectively <36 hr")
Intervention	Zn gluconate glycine: one lozenge contained 13.3 mg Zn (see note) Placebo lozenges contained tannic acid, sucrose octaacetate, quinine The study medications were dissolved in the mouth and taken every 2 to 3 hr while awake (total of 6 lozenges per day)
Losses to follow-up and late exclusions	None described
Common cold definition	Presence of ≥2 of the following symptoms: sneezing, rhinorrhea, nasal obstruction, sore throat, cough, headache, hoarseness
Calculation of the daily Zn dose from lozenges	**80 mg/d** = 6/d × 13.3 mg
Mean and SD of the common cold duration	Turner (2000) reported (p. 1204 [23]): Zn gluconate group: median duration of the common cold: 6.0 d Placebo group: median duration of the common cold: 5.5 d The lack of difference corresponds to **P(1-tail) = 0.5 for Table 1** Turner did not report the mean and SD In this meta-analysis, the mean and SD were estimated from Turner's fig. 1B (naturally acquired colds) which shows the percentage of participants who still had common cold symptoms as a function of time (latest follow-up time point 13.5 d). For the participants who had colds longer than 13.5 days, the rate of recovery was imputed as 3 participants per day (based on the trends of the graphs). Based on this analysis (Table S3): Zn gluconate group: mean common cold duration: **7.41 d (SD 3.88)** Placebo group: mean common cold duration: **7.55 d (SD 3.96)**
Notes	The zinc gluconate lozenge contained glycine, which effectively binds to zinc and therefore the free Zn ion level probably was lower than suggested by the total Zn dose (see figs. 2 and 3 and p. 29-30 in [13] and table 2 in [12])

Turner B (2000) [23]	
Methods	See Turner A (2000)
Participants	Included in the analysis: 68 Zn acetate (11.5 mg Zn) and 71 placebo participants See Turner A (2000)
Intervention	Zn acetate: one lozenge contained 11.5 mg Zn (see note) Placebo lozenges contained tannic acid, sucrose octaacetate, quinine
Losses to follow-up and late exclusions	None described
Common cold definition	See Turner A (2000)
Calculation of the daily Zn dose from lozenges	**69 mg/d** = 6/d × 11.5 mg
Mean and SD of the common cold duration	Turner (2000) reported (p. 1204 [23]): Zn acetate (11.5 mg) group: median duration of the common cold: 5.5 d Placebo group: median duration of the common cold: 5.5 d The lack of difference corresponds to **P(1-tail) = 0.5 for Table 1** Turner did not report the mean and SD For the measurement and imputation of common cold duration, see Turner A. Based on this analysis (Table S3): Zn acetate (11.5 mg) group: mean common cold duration: **6.89 d (SD 3.35)** Placebo group: mean common cold duration: **7.55 d (SD 3.96)**
Notes	Eby (2001) pointed out that "hydrogenated palm kernel and cotton seed oils were also constituents of the lozenges, according to the list of ingredients provided with the commercial product (Halls Zinc Defense) marketed by Warner Lambert, which is also the supplier of the zinc acetate lozenge clinical prototypes studied by Turner et al. At the high temperatures (157ºC) used in the manufacture of hard candy, these ingredients react with positively charged zinc ions derived from zinc acetate to yield zinc oleate, stearate, and palmitate waxes, which are incapable of releasing Zn ions" [40] http://dx.doi.org/10.1086/320177 The authors did not publish a reply to this comment

Turner C (2000) [23]	
Methods	See Turner A (2000)
Participants	Included in the analysis: 72 Zn acetate (5 mg Zn) and 71 placebo participants See Turner A (2000)
Intervention	Zn acetate: one lozenge contained 5 mg Zn (see note in Turner B) Placebo lozenges contained tannic acid, sucrose octaacetate, quinine
Losses to follow-up and late exclusions	None described
Common cold definition	See Turner A (2000)
Calculation of the daily Zn dose from lozenges	**30 mg/d** = 6/d × 5 mg
Mean and SD of the common cold duration	Turner (2000) reported (p. 1204 [23]): Zn acetate (5 mg) group: median duration of the common cold: 6.0 d Placebo group: median duration of the common cold: 5.5 d The lack of difference corresponds to **P(1-tail) = 0.5 for Table 1** Turner did not report the mean and SD For the measurement and imputation of common cold duration, see Turner A. Based on this analysis (Table S3): Zn acetate (5 mg) group: mean common cold duration: **7.90 d (SD 4.25)** Placebo group: mean common cold duration: **7.55 d (SD 3.96)**
Notes	See Turner B (2000)

Weismann (1990) [28]	http://www.ltdk.helsinki.fi/users/hemila/Zn/Weismann_1990.pdf
Methods	Consecutive allocation (see note), placebo-controlled, double-blind trial
Participants	Included in the analysis: 61 Zn and 69 placebo participants M/F ratio not described; age range 18 to 65 yr Six general practitioners residing in the suburban area of Copenhagen conducted the study Exclusions: pregnant and lactating women, diabetes
Intervention	Zn gluconate: one lozenge contained 4.5 mg Zn Placebo lozenges were not described Participants were instructed to start therapy immediately after the first symptoms of common cold appeared. The lozenges were to be taken every 1 to 1½ waking hours, in all 10 lozenges daily
Losses to follow-up and late exclusions	14 were excluded because of lacking records and 1 because of too low age
Common cold definition	At the start of the study, the patients registered the following symptoms: indisposition, headache, fever, muscle pain, running nose, nasal congestion, sore throat, coughing, hoarseness
Calculation of the daily Zn dose from lozenges	**45 mg/d** = 10/d × 4.5 mg
Mean and SD of the common cold duration	Weismann (1990) reported the probability of still having common cold symptoms as a function of time (fig. 1 [28]): Zn group: median duration of the common cold: 7 d Placebo group: median duration of the common cold: 6 d The lack of difference corresponds to **P(1-tail) = 0.5 for Table 1** Weismann did not report the mean and SD In this meta-analysis, the mean and SD were estimated from Weismann's fig. 1 which shows the probability of still having common cold symptoms as a function of time (latest follow-up time point 10 d). 4 Zn and 4 placebo participants had colds longer than 10 d; all were imputed as being cured on day 11 (based on the trends of the graphs). Based on this analysis (Table S3): Zn group: mean common cold duration: **7.16 d (SD 2.62)** Placebo group: mean common cold duration: **6.72 d (SD 2.29)**
Notes	The 1990 study report did not describe the method of allocation. Dr. Kaare Weismann described that they had used consecutive allocation (personal communication by email 2 July 2010). Initially Zn and placebo tablets were administered to 239+239 participants using consecutive allocation. The participants were instructed to start therapy immediately after the first symptoms of common cold appeared. 318 participants did not start treatment. It does not seem reasonable to assume that consecutive allocation in this double-blind trial could have led to systematic bias between the study groups. In this respect the study is a good-quality pseudo-randomized trial.

Normalization of the Common Cold Duration to Placebo Mean Duration = 100%

The values on the right side are used in Fig. (**1**).

These values are calculated by dividing the figures on the left side with the duration in the placebo group on the left side.

This leads to percentage scale so that all differences between Zn and placebo groups are percentages.

Trial	Duration is Based on:	Duration of Colds (Days)				Duration of Colds (% of Placebo)			
		Zn		Placebo		Zn		Placebo	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD
Eby 1984 [7]	Fig	3.92	2.61	7.54	3.18	52	35	100	42
Smith 1989 [19]	Fig	7.23	2.29	7.57	3.01	96	30	100	40
Godfrey 1992 [20]	from t	4.86	2.70	6.13	2.70	79	44	100	44
Prasad 2008 [21]	Report	4.00	1.04	7.12	1.26	56	15	100	18
Petrus 1998 [22]	Report	3.80	1.63	5.10	2.96	75	32	100	58
Turner A 2000 [23]	Fig	7.41	3.88	7.55	3.96	98	51	100	52
Mossad 1996 [24]	Fig	5.20	2.83	9.38	5.47	55	30	100	58
Prasad 2000 [25]	Report+Fig	4.50	1.60	8.10	1.80	56	20	100	22
Turner B 2000 [23]	Fig	6.89	3.35	7.55	3.96	91	44	100	52
Douglas 1987 [26]	from P	12.10	9.80	7.70	9.80	157	127	100	127
Macknin 1998 [27]	Fig	9.37	4.81	9.50	4.53	99	51	100	48
Weismann 1990 [28]	Fig	7.16	2.62	6.72	2.29	107	39	100	34
Turner C 2000 [23]	Fig	7.90	4.25	7.55	3.96	105	56	100	52

[a] "Report" indicates that the mean and SD were reported in the study report.

"from t/P" indicates that the t or P was reported and the corresponding SD was calculated from it.

"Fig" indicates that the results were reported as a survival curve: see Table S3 for the calculation of the mean and SD.