Brit. J.prev. soc. Med. (1976), 30, 193-196

A randomized controlled trial of vitamin C in the prevention and amelioration of the common cold

P. C. ELWOOD, H. P. LEE, A. S. ST. LEGER,[1] I. McLEAN BAIRD,[2] AND A. N. HOWARD[3]

MRC Epidemiology Unit, Cardiff,[1] West Middlesex Hospital,[2] and Department of Investigative Medicine, University of Cambridge[3]

Elwood, P. C., Lee, H. P., St. Leger, A. S., McLean Baird, I., and Howard, A. N. (1976). *British Journal of Preventive and Social Medicine,* **30,**193-196. **A randomized controlled trial of vitamin C in the prevention and amelioration of the common cold.** A randomized controlled trial of the effect of 1 g ascorbic acid per day in the prevention of the common cold was conducted on 688 adult women. There is evidence of a small reduction by vitamin C in the mean number of chest colds, but no evidence of any effect on simple colds. The existence of a subgroup of vulnerable women in the community who benefit from vitamin C was considered but further examination of the data gives no support to this conclusion.

Besides being antiscorbutic, many other protective functions have been claimed for vitamin C, including an effect on the common cold, although the suggestion by Pauling (1970) that high doses of ascorbic acid could reduce the frequency and duration of colds has yet to be verified. The fact that colds are a most frequent source of morbidity and a most important source of absence from work makes clarification of the situation an urgent task.

This paper reports a randomized controlled trial of a daily dose of 1 g ascorbic acid in the prevention of respiratory infections conducted among young women in South Wales. The trial was held in the winter of 1973-74.

METHOD

Women living in two towns in South Wales who had had a confinement within the previous two years, and were not again pregnant were visited and asked to co-operate. They were already helping in a long-term study on the growth and nutrition of their babies. Those who agreed were given sufficient tablets to last 100 days. These contained either 1 g ascorbic acid in an effervescent base or a matching placebo, and one was to be taken each day. A record card was given, on which was to be recorded any respiratory symptom which was sufficiently severe to 'bother her'. At approximate monthly intervals each woman was visited, her record card inspected, and a new card issued.

For the purposes of analysis the respiratory symptoms were grouped as follows:

A simple cold: a running nose, and/or sneezing, and/or sore throat, with or without other symptoms such as fever, headache or malaise.

A chest cold: a cough, or any other chest symptom either on its own or with any other symptom.

In discriminating between episodes, the following criteria (based on Anderson, Reid, and Beaton, 1972) were used:

If two episodes of symptoms were separated only by one or two symptom-free days, a single cold was counted.

If the separation between episodes was three to six days then one episode was counted unless the symptom pattern had changed, in which case two episodes were counted.

If the separation was seven or more days then two episodes were counted however similar the symptoms.

Subjects who had cold symptoms on the day they were first seen were not considered to have entered the trial until the first symptom-free day.

Comparisons of means have been performed using one-sided *t* tests, the appropriate null hypothesis being that ascorbic acid is no more effective than the placebo.

RESULTS

Altogether 946 women were asked to participate in the trial. All but 23 agreed to do so but a further 235 had subsequently to be omitted. The most frequent reason for these omissions was poor co-operation, and women, who at the end of the 100 days had 25 or more tablets left unused, were omitted (Table I).

TABLE I

STUDY POPULATION AND REASONS FOR OMISSION

Total contacted	**946 (100%)**
Refused to co-operate	**23**
Total admitted to trial	**923 (98%)**
Subsequently omitted:	
Moved away	**5**
Records lost	**2**
Inadequate co-operation	**228***
Total completed trial	**688 (75%)**

*Of these, 107 had been in the vitamin C group and 121 in the placebo group.

Table II shows the distribution of women by type of cold; it also gives a breakdown of the total number of colds recorded in the trial. These colds are further subdivided in order to test two specific hypotheses. First, that ascorbic acid, in the dosage given, has a protective effect against the common cold, and secondly, that once a cold is caught ascorbic acid reduces its severity, as measured by duration.

TABLE II

DISTRIBUTION OF WOMEN BY NUMBER AND TYPE OF COLD AND BY TREATMENT

	Treatment Group	
	Ascorbic Acid	Placebo
Number of women		
No colds of any kind	**43**	**51**
Simple only	**139**	**121**
Chest only	**57**	**69**
Both simple and chest	**100**	**108**
Total in trial	**339**	**349**
Number of colds		
Simple	**416**	**424**
Chest	**211**	**266**
Total colds	**627**	**690**

Table III displays the frequency distribution of the number of colds per individual. The mean number of chest colds in the treatment group is significantly less than in the placebo group but a comparison of simple colds and of all colds does not reveal a difference. The distributions of colds, defined by treatment and by type, were then examined (Table III). All but one of these, that for simple colds in the placebo group, appear to approximate to a Poisson distribution. This suggests that catching cold is a random process, that is, it is unlikely that there was a 'cold prone' subgroup among the women. Had the distributions fitted better negative binomial distributions then one could not infer random susceptibility, but an analogy would exist with models for accident proneness such as that of Greenwood and Yule (1920).

The figures in Table III had been abstracted from the subjects' record-cards regardless of the other colds recorded. For instance, the colds in the first column come both from women who had had only simple colds and from women who had had episodes of both simple and chest colds. It may be that

TABLE III

NUMBER OF COLDS IN THE WOMEN

Number of Colds	Simple Colds		Chest Colds		All Colds	
	Ascorbic Acid	Placebo	Ascorbic Acid	Placebo	Ascorbic Acid	Placebo
0	**100**	**120**	**182**	**172**	**43**	**51**
1	**122**	**115**	**114**	**111**	**100**	**97**
2	**79**	**65**	**34**	**46**	**109**	**87**
3	**24**	**30**	**7**	**17**	**55**	**69**
4	**9**	**11**	**2**	**3**	**22**	**27**
5+	**5**	**8**	**0**	**0**	**10**	**18**
Total women	**339**	**349**	**339**	**349**	**339**	**349**
Mean number of colds	**1·23**	**1·22**	**0·62**	**0·76**	**1·85**	**1·98**
Variance	**1·32**	**1·63**	**0·63**	**0·84**	**1·60**	**2·18**

Differences between means for treatment groups only significant ($P < 0.02$) for chest colds

χ^2 goodness of fit test of Poisson distribution only significant ($P < 0.05$) for simple colds in women on placebo

women who have only chest colds differ fundamentally from women who have only simple colds. Table IV therefore sets out the distributions of the number of colds among those women who had had only simple colds and those who had had only chest colds. The numbers are now very small and the difference between the treatments for chest colds suggested by Table III is no longer statistically significant.

TABLE IV

NUMBER OF COLDS IN WOMEN AFTER DIVIDING THEM INTO 'SIMPLE' AND 'CHEST' SUFFERERS

Number of Colds	Simple Colds		Chest Colds	
	Ascorbic Acid	Placebo	Ascorbic Acid	Placebo
1*	60	54	40	43
2	52	34	13	19
3	16	21	4	7
4	7	8	0	0
5+	4	4	0	0
Total women	139	121	57	69
Mean number of colds	1·89	1·99	1·37	1·48
Variance	1·16	1·48	0·38	0·46

Differences between means for treatment groups not significant for either type of cold

*The distributions are truncated at zero because it is not possible to decide which of the women who had no colds would have had simple or chest colds had they had a cold

Table V displays the distributions of duration of colds divided by treatment groups. There is no evidence of significant differences in mean durations of colds between the subjects on ascorbic acid and the control group. These data were further broken down into subjects who had had only one or the other type of cold, in a manner analogous to Table IV, and no significant differences became evident.

DISCUSSION

In general, the evidence makes it seem unlikely that small doses of ascorbic acid, of a size which might be regarded as physiological, have any effect on the common cold. However the Food Education Society of Great Britain (1969) after an uncontrolled study, found suggestive evidence that a supplement of fresh orange juice containing about 50 mg ascorbic acid reduced absenteeism in schoolchildren by two-thirds as well as decreasing the incidence of colds and coughs.

The evidence relating to large doses, while not consistent, is more promising. Ritzel (1961) reported a decline of 45 % in the total incidence of colds in 279 skiers given 1 g of ascorbic acid per day for one week. A similar reduction was claimed by Charleston and Clegg (1972) but their trial was not double-blind. On the other hand Walker, Bynoe, and Tyrrell (1967) found no evidence of a protective effect of 3 g ascorbic acid given for three days before the inoculation of subjects with a virus culture. Wilson and Loh (1973) reported a significant reduction in the incidence and severity of colds in schoolgirls but Kinlen and Peto (1973) claimed that the significance of the differences observed by Wilson and Loh most probably arose as a consequence of multiple significance testing and the correct interpretation of these data is that vitamin C had no effect. Anderson *et al.* (1972) found that during a period of about two months 26 % of subjects who were given 1 g ascorbic acid per day remained free of symptoms compared with 18% of those given a placebo. Although this is statistically significant two further studies, both of which were based on large numbers of subjects, gave no conclusive evidence of any protective effect (Anderson, Suranyi, and Beaton, 1974; Anderson *et al.*, 1975). Nor did a trial by Karlowski *et al.* (1975) demonstrate any significant reduction in incidence by 1 g vitamin C per day.

TABLE V

DURATION OF COLDS

Duration (days)	Simple Colds		Chest Colds		All Colds	
	Ascorbic Acid	Placebo	Ascorbic Acid	Placebo	Ascorbic Acid	Placebo
1-3	236	235	38	46	274	281
4-6	97	101	55	67	152	168
7-9	43	44	39	61	82	105
10-12	19	22	30	33	49	55
13-15	12	12	19	22	31	34
16+	9	10	30	37	39	47
Total	416	424	211	266	627	690
Mean number of days	4·44	4·43	8·99	9·50	5·97	6·38
Variance	20·19	15·78	44·05	63·19	32·80	40·09

Differences between means for treatment groups not statistically significant for any type of cold

It is difficult to draw general conclusions from these and other trials. Some of the studies have been poorly designed and the 'double-blind' intentions of others may not have been adequately achieved (Karlowski *et al.,* 1975). Furthermore, although the trial of Anderson *et al.* (1972) was admirably designed and conducted, it was based on carefully selected volunteers who may have been especially vulnerable to respiratory infections and who represented only about 10% of the available population (Anderson *et al.,* 1974). This selection may have led to an eventual overestimate of the average effect of vitamin C, but on the other hand these subjects had an above average interest in nutrition and a high proportion were probably already receiving a generous intake of vitamin C (Anderson *et al,* 1974).

The present trial was based on a group of women who had been involved in a nutrition study on their children. While they cannot be assumed to represent the community adequately they were selected neither by factors directly relevant to respiratory infections, nor by their interest in either vitamin C or the common cold. Bias in their recording of colds is therefore unlikely and furthermore, there was no reason to believe that their dietary intake of vitamin C was high.

The present data are consistent with a small preventive effect of vitamin C on chest colds. This interpretation raises the concept of a vulnerable subgroup, but an examination of the distribution of colds in our subjects gives no support to the existence of such a subgroup. It might be argued that this examination is too crude to detect a small subgroup within the total population but it is equally likely that the apparent beneficial effect of vitamin C has arisen by chance simply as a consequence of the numerous comparisons in our analyses.

At the same time, the concept of a small vulnerable group in the community is attractive and would go a long way to reconciling inconsistencies in the results of published trials as many of these have been based on volunteers chosen in a way which is likely to have selected those with increased susceptibility to the common cold. At present there is no evidence of a vulnerable subgroup within the community, and further trials designed specifically to test this hypothesis would be necessary. In the meantime it must be recognized that reference to such a subgroup in the population can all too easily be used to give meaning to what are no more than random fluctuations in data.

We are grateful to Roche Products Ltd for supplying the tablets of ascorbic acid and matching placebo for this study.

Requests for reprints: P. C. Elwood, MRC Epidemiology Unit (South Wales), 4 Richmond Road, Cardiff CF2 3AS.

REFERENCES

ANDERSON, T. W., BEATON, G. H., COREY, P. N., and SPERO, L. (1975). Winter illness and vitamin C: the effect of relatively low doses. *Canad. med. Ass. J.,* **112,** 823.

----- , REID, D. W., and BEATON, G. H. (1972). Vitamin C and the common cold: a double blind trial. *Canad. med. Ass. J.,* **107,** 503.

----- , SURANYI, G., and BEATON, G. H. (1974). The effect on winter illness of large doses of vitamin C. *Canad. med. Ass. J.,* **111,** 31.

CHARLESTON, S. S. and CLEGG, K. M. (1972). Ascorbic acid and the common cold. (Letter). *Lancet,* **1,** 1401.

FOOD EDUCATION SOCIETY OF GREAT BRITAIN (1969). *The Orange Juice Experiment.* London.

GREENWOOD, M. and YULE,G. U. (1920). An inquiry into the nature of frequency distributions of multiple happenings. *J. roy. statist. Soc.,* **83,** 255.

KARLOWSKI, T. R., CHALMERS, T. C., FRENKEL, L. D., ZAPIKIAN, A. Z., LEWIS, T. L., and LYNCH, J. M. (1975). Ascorbic acid for the common cold: a prophylactic and therapeutic trial. *J. Amer. med. Ass.,* **231,** 1038.

KINLEN, L. and PETO, R. (1973). Vitamin C and colds. (Letter). *Lancet,* **1,** 944.

PAULING, L. (1970). *Vitamin C and the Common Cold.* Freeman, San Francisco.

RITZEL, G. (1961). Critical evaluation of vitamin C as a prophylactic and therapeutic agent in colds. *Helv. med. Acta,* **28,** 63.

WALKER, G. H., BYNOE, M. L., and TYRRELL, D. A. J. (1967). Trial of ascorbic acid in the prevention of colds. *Brit. med. J.,* **1,** 603.

WILSON, C. W. M. and LOH, H. S. (1973). Common cold and vitamin C. *Lancet,* **1,** 638.